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Children with Hypoglycaemia and their Later Development

Outcomes of Neonatal Hypoglycaemia

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, The University of Auckland, 2014.

Abstract

Neonatal hypoglycaemia is common and potentially impairs neurodevelopment. Uncertainty exists over the blood glucose concentration that defines neonatal hypoglycaemia, neurodevelopmental outcomes of at-risk children, and neurodevelopmental differences between at-risk children who do and do not experience hypoglycaemia. We aimed to describe the neurodevelopmental outcomes of 2-year-olds born at risk of neonatal hypoglycaemia, to test whether hypoglycaemia was associated with poorer outcomes, and to examine relationships between neurodevelopmental outcome and other health and sociodemographic variables.

Children born at risk of hypoglycaemia (infant of a diabetic mother, small (<10th centile or < 2500g), large (>90th centile or > 4500g), late preterm (35 or 36 weeks' gestation) or other) were assessed at 24 ±1 months' corrected age. Assessments included Bayley III, executive function tasks, BRIEF-P and health and sociodemographic information by parental questionnaire.

We assessed 404 (77%) children from the neonatal cohort. Children who had and had not experienced neonatal hypoglycaemia had similar neurodevelopmental outcomes. However, children born small and to diabetic mothers achieved worse Bayley-III, executive function and BRIEF-P scores than large or preterm children. Girls and breastfed babies were more likely to experience hypoglycaemia but had better outcomes. Socioeconomic status was strongly associated with 2-year neurodevelopmental outcome. We found interactions between gender and risk factor, socioeconomic status and preschool attendance, with boys, but not girls, of diabetic mothers and low socioeconomic groups achieving worse, and those who attended preschool better, results than other groups, suggesting a greater vulnerability to environmental factors for boys. Assessed executive functions were related but separable and only weakly associated with parent-report but strongly related to language development.

Children born at risk of neonatal hypoglycaemia are at risk of adverse neurodevelopmental outcome independent of whether or not they actually experience hypoglycaemia. This risk is higher in those born small, to diabetic mothers, not breast fed, and to low socioeconomic status families, with boys more vulnerable to poor outcome than girls. Executive function can be assessed at 2 years and appears to comprise separate but related constructs, most strongly related to language development. This cohort may benefit from continued monitoring, with early intervention service referrals where needed.

Dedication

Dedicated to my parents, who made it all possible

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“Somewhere in the heart of experience there is an order and a coherence which we might surprise if we were attentive enough, loving enough, or patient enough.”

- Lawrence Durrell

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Glossary

ADHD: Attention Deficit Hyperactivity Disorder

AGA: Appropriate for gestational age, usually weight and length between 10^{th} and 90^{th} centiles for gestational age.

Bayley III: The Bayley Scales of Infant and Toddler Development -3^{rd} edition; Bayley (2006).

BRIEF-P: Behavior Rating Inventory of Executive Function – Preschool version; Gioia, G. A., Espy, K. A., & Isquith, P. K. (2000).

CBF: Cerebral blood flow

CGMS: Continuous glucose monitoring system - provides a measurement of interstitial glucose concentration every 5 minutes.

CHYLD study: Children with Hypoglycaemia and their Later Development study

EEG: Electroencephalogram, a measure of electrical activity in the brain

EF: Executive function, higher order cognitive function important for control of thought and action, problem solving and learning

EMI: Emergent Metacognition Index of the BRIEF-P, derived by adding Working Memory and Plan/Organise scales

FI: Flexibility Index of the BRIEF-P, derived from adding Shift and Emotional Control scales

GEC: Global Executive Composite score of the BRIEF-P, derived by adding the 5 separate scales: Inhibition, Shift, Emotional Control, Working Memory and Plan/Organise.

GLUT: Glucose transporter molecule, of which there are several, e.g GLUT1

Home and Family: Home and Family questionnaire created for the CHYLD study to gather data on family health, education, SES and parental smoking, alcohol and drug use.

HPA: Hypothalamic pituitary adrenal axis

IDM: Infant of a diabetic mother

IGF: Insulin-like growth factors. There are two similar proteins (IGF-1, IGF-2) structurally similar to insulin and important to growth.

IQ: Intelligence quotient. A standardised score indicative of intelligence or cognitive ability.

ISCI: Inhibitory Self-control Index of the BRIEF-P, derived from adding Inhibit and Emotional Control scales.

IUGR: Intra-uterine growth restriction, fetal growth failing to meet genetic potential.

LGA: Large for gestational age, usually weight and length above 90th centile for gestational age.

mg/dL: milligrams per decilitre

mmol/L: millimole per litre

MSML: Multisearch multilocation, a preschool measure of working memory

NICU: Neonatal intensive care unit

NZDep: New Zealand deprivation index, a national index of relative socioeconomic deprivation based on small geographic areas (meshblocks), using data derived from the NZ census. Version is usually reported with year of release e.g. NZDep2006.

OKR: Optokinetic reflex, used to indicate perception of motion coherence of random dot kinetogram and hence an indication of dorsal stream functioning.

PET: Positron emission tomography. An imaging technique that produces three-dimensional, functional images of metabolically active areas

SD: Standard deviation

SES: Socioeconomic status

SGA: Small for gestational age, usually weight and length below 10th centile for gestational age.

STROBE: Strengthening the Reporting of Observational studies in Epidemiology (Vandenbroucke et al., 2007; von Elm et al., 2007)

Tikanga: Traditional Māori practice and process, including the appropriate manner to approach and interact with families, and requiring cultural sensitivity and understanding on the part of practitioners.

WDHB: Waikato District Health Board; provides hospital, health and disability services to the population of the Waikato District (373,000 people).

Chapter 1. Literature review

1.1. Introduction

Neonatal hypoglycaemia is recognised as a significant metabolic disorder for newborn babies (Cornblath & Ichord, 2000). It has been described as the most common metabolic disorder of the newborn (Cornblath, 1997) and the only known common preventable cause of brain damage in newborn babies (Volpe, 2008). However, there is uncertainty over the blood glucose concentration that defines neonatal hypoglycaemia and the outcomes of asymptomatic neonatal hypoglycaemia (W. W. Hay, Jr. et al., 2009). Furthermore, child development is influenced by many other factors including maternal and child antenatal, perinatal and postnatal health factors (Annaz, Karmiloff-Smith, & Thomas, 2008; Gao, Paterson, Carter & Percival, 2006; McGowan, Alderdice, Holmes, & Johnston, 2011) and the sociodemographic environment in which the child is raised (Bradley & Corwyn, 2002; Tucker-Drob, Rhemtulla, Harden, Turkheimer, & Fask, 2011).

In order to understand the factors associated with the developmental outcome of children born at risk of neonatal hypoglycaemia, we examined relationships between developmental domains, executive function, child health, family sociodemographic factors and neonatal hypoglycaemic status. Therefore, while the focus of this thesis is the developmental outcome of neonatal hypoglycaemia, this chapter also examines additional factors including early childhood development, executive function and socioeconomic influences such as family income, parental education and neighbourhood effects.

1.2. History of neonatal hypoglycaemia research

The history leading to the current understanding of neonatal hypoglycaemia is comparatively short. In little over 70 years the understanding of neonatal hypoglycaemia has progressed from descriptive studies of symptomatic babies with extremely low blood glucose concentrations (Hartmann & Jaudon, 1937) to a complex array of data on neonatal hypoglycaemia with, as yet, no agreement on definition (Cornblath & Ichord, 2000). Neonatal hypoglycaemia continues to be an area of debate and uncertainty (W. W. Hay, Jr., Raju, Higgins, Kalhan, & Devaskar, 2009) and one which may even have legal implications for practitioners (Cornblath et al., 2000; Williams, 2005).

In 1937 Hartmann and Jaudon described hypoglycaemia as a common occurrence in normal newborn babies and argued for retention of the term hypoglycaemia rather than hyperinsulinism as had been advocated by Harris 3 years earlier (Hartmann & Jaudon, 1937). Hartmann and Jaudon reported on 286 newborn babies diagnosed with hypoglycaemia at a single hospital over a fifteen year period. Their report concluded that “Hypoglycemia (sic) during the first 4 or 5 days of life occurs quite regularly in normal newborn infants...” (p35). They proposed an etiologically based classification of hypoglycaemia which included a definition of hypoglycaemia as mild (2.2 to 2.8 mmol/L); moderate

(1.1 to 2.2 mmol/L) and extreme (less than 1.1 mmol/L) (Hartmann & Jaudon, 1937). Their extensive documentation of cases included treatment protocols for different types of hypoglycaemia and allowed them to argue against early caesarean delivery and sterilisation of diabetic mothers as had been previously proposed (Randall & Rynearson, 1936). Twelve years later a study of fifty one "normal newborns" confirmed that asymptomatic hypoglycaemia was not uncommon and that following a period of instability blood glucose concentrations rose steadily during the first 6 days after birth (Norval, Kennedy, & Berkson, 1949).

Early studies identified individual cases of hypoglycaemia from the observation of clinical symptoms such as seizures, tremors and apnoea (Cornblath, Odell, & Levin, 1959). The presence of hypoglycaemia was then confirmed by blood test. Many of the babies studied at that time were likely to have had very low blood glucose concentrations as evidenced by the severity of symptoms reported. The described developmental consequences were correspondingly severe: mental retardation, spasticity, death. Norval's (1950) study of 42 preterm babies reported that four of the nine who died had blood glucose levels as low as 4 to 20 mg/dL (0.2 – 1.1 mmol/L).

This increasing understanding of hypoglycaemia included the knowledge that blood glucose concentrations in fasting normal newborns were lower than in older children (Cornblath & Ichord, 2000) and adults (Gregory & Aynsley-Green, 1993), with some reports suggesting a possible difference between men and women (Gregory & Aynsley-Green, 1993). Because of this acceptance and arguably, normalisation, of hypoglycaemia in newborns, the link between adverse outcomes and moderate, asymptomatic hypoglycaemia was slow to be established. Although it was known that some newborns with hypoglycaemia were asymptomatic (Cornblath et al., 1959), there were no studies reported at the time which followed the development of these children.

Cornblath, Levin and Odell (1959) reported on eight babies born to mothers with toxaemia. All babies began to display hypoglycaemic symptoms at between 44 and 57 hours after birth and had convulsions along with other symptoms which included cyanosis, limpness, tremor and apnoea. These babies showed an immediate response to intravenous glucose, thus confirming hypoglycaemia as the cause of the symptoms. Of these eight babies, five were well at follow-up, at 44 days to 11 months of age; 1 baby was described as "spastic and jittery" at 4 months; another was "severely retarded, spastic with myoclonic seizures. Institutionalized at 3 years" (p552). The remaining baby died at 17 days of Pseudomonas sepsis.

The significance of this study was that it identified several risk factors associated with neonatal hypoglycaemia. The babies were all born to mothers who were diagnosed with toxaemia; they all weighed less than 2580 grams and were described by the authors as "premature by weight". Furthermore, this study highlighted the lack of direct correlation between the number of symptoms recorded and outcome, with the one baby who displayed symptoms in all 5 categories being described as "Well at 11 months" (p552), while the baby who died had been recorded as displaying symptoms in 4 categories. The authors commented that while newborns with hypoglycaemia rarely show discernible signs, some do manifest clinical symptoms.

At this time a controversy developed over the significance of asymptomatic hypoglycaemia (Haworth, 1974). Koivisto and colleagues (1972) reported that asymptomatic hypoglycaemia had no effect on the central nervous system (CNS), yet elsewhere the same report advised that asymptomatic hypoglycaemia "should be detected by a screening system and ..... should be treated to avoid possible permanent CNS damage..." (p. 610). Others argued that in some instances of symptomatic hypoglycaemia both the symptoms and hypoglycaemia may have been the result of "primary neurological abnormalities" (Haworth & McCrae, 1965, p. 865).

Further confounding attempts to bring clarity to the issue was the fact that hypoglycaemia did not have a generally accepted definition. Koivisto's study (Koivisto et al., 1972) divided 151 newborn babies into three groups with the low group being those with two or more blood glucose concentrations below 1.11 mmol/L. The middle group had one concentration at this level and others below 1.67 mmol/L, with the third group being those whose blood glucose concentrations fell below 1.67 mmol/L on only one occasion. Other researchers argued for different acceptable blood glucose concentrations for low birth weight and full-sized infants, namely 1.39 mmol/L and 1.94 mmol/L, respectively (Pildes et al., 1974). Srinivasan and colleagues' (Srinivasan, Pildes, Cattamanchi, Voora, & Lilien, 1986) study of full-term newborn babies of appropriate weight for gestational age (AGA) showed that the mean plasma glucose concentration in normal newborn babies dropped in the first hour after birth from a mean (SD) of 5.9 (1.9) to 3.1 (1.1), with none of the 60 babies in their study having a plasma glucose concentration <2.2 mmol/L after 3 hours. These babies were formula-fed at 3 hours and then 4 hourly, with mothers having received intravenous dextrose during labour and delivery. The authors concluded that plasma glucose concentration <2.5 mmol/L after 3 hours should be considered low. However, research published in the following year (Heck & Erenberg, 1987) defined hypoglycaemia in full-term newborn babies as serum glucose concentrations of <1.7 mmol/L in the first 24hrs and < 2.2 mmol/L beyond that. This confusion of definition was further highlighted in a short report (Koh, Eyre, & Aynsley-Green, 1988) which studied 36 paediatric textbooks and questioned 242 neonatologists in the United Kingdom. In this survey definitions of hypoglycaemia ranged from <1mmol/L to <4mmol/L.

In an attempt to objectively measure neural function in relation to blood glucose concentrations and to further elucidate any link between neural function and symptomatic and asymptomatic hypoglycaemia, Koh and colleagues measured sensory evoked potentials in 17 children (Koh, Aynsley-Green, Tarbit, & Eyre, 1988). Abnormal evoked potentials were recorded in 10 of the 17 children during induced hypoglycaemia. Half of these 10 children were asymptomatic, with four of these five being newborn babies. The authors reported that 6 of the 7 babies who displayed only normal evoked potentials maintained their blood glucose concentrations above 2.6 mmol/L, with the seventh showing no abnormal symptoms with a blood glucose concentration of 1.9 mmol/L. They concluded that no signs of neural dysfunction were seen in children whose blood glucose

concentrations did not fall below 2.6 mmol/L; hence they recommended maintaining blood glucose concentrations above 2.6 mmol/L in children and babies.

A second study published in the same year was a multicentre study of feeding which recruited 661 preterm infants (Lucas, Morley, & Cole, 1988). These infants were all less than 1850g birth weight, with the mean (SD) birth weight being 1337 (315) g and mean gestational age being 30.5 (2.7) weeks. This study found that moderate hypoglycaemia was common, with 433 infants having blood glucose concentrations < 2.6 mmol/L and in 104 infants this occurred on between 3 and 30 days. The authors concluded that the number of days of moderate hypoglycaemia was strongly related to neurodevelopmental outcomes at 18 months corrected age. They reported that within this cohort, hypoglycaemia on five or more separate days was significantly related to reduced mental and motor scores and an increased incidence of neurodevelopmental impairment such as cerebral palsy and developmental delay. The authors of this paper described identifying a "prevailing view" that blood glucose concentrations in the 1.5 – 2.5 mmol/L range were of little significance. They concluded with a recommendation for urgent re-appraisal of the management of neonatal hypoglycaemia and reiterated the view of Koh and colleagues (1988) that blood glucose concentrations in newborns should be maintained above 2.6 mmol/L.

That two independent studies, in the same year, reached identical conclusions as to the 'safe' blood glucose level in newborns was perceived as strong evidence for adopting this as a clinical standard. However, subjects in neither of the studies were representative of a normal newborn cohort. The Koh study included only 17 subjects, of whom only 4 were newborns and the Lucas study included only very preterm babies, who represent approximately 2% of births. Despite this, the 'safe' blood glucose concentration of 2.6 mmol/L is still commonly referred to in clinical practice. A recent survey of Australasian neonatologists showed general agreement that 2.6 mmol/L defines the blood glucose concentration below which treatment for hypoglycaemia is needed, although responses ranged from 1.0 to 3.5 mmol/L and decision to treat was inconsistent in response to example scenarios where blood glucose concentrations were said to fall below 2.6 mmol/L (D. L. Harris, Weston, Battin, & Harding, 2009).

The primary reason for maintaining the recommendation from the 1988 studies is a lack of consistent evidence for a change. A large number of studies have investigated aspects of neurodevelopment after neonatal hypoglycaemia, yet many of them have been identified as having methodological flaws (Boluyt, van Kempen, & Offringa, 2006). A 2006 meta-analysis considered 45 potential cohort studies of neurodevelopment after hypoglycaemia in the first week after birth (Boluyt et al., 2006). Of this number, 17 were included in the meta-analysis and of these, just two were considered to be 'High-Quality' studies. This definition was on the basis that they met pre-determined criteria of having a well-defined study group; had a follow-up rate of >80% or loss to follow-up was well-described; outcome measures were objective or the outcome assessment was blinded; and all important risk factors were considered (Boluyt et al., 2006). This low inclusion rate for the meta-analysis is indicative of the logistical problems encountered in establishing sound research with large groups of

vulnerable newborns. The authors of this meta-analysis concluded that the neurodevelopmental outcome of neonatal hypoglycaemia in the first week after birth was unclear, reported results were conflicting, methodological problems were common and "Recommendations for clinical practice cannot be based on valid scientific evidence in this field".

There has been a range of approaches in the attempt to define neonatal hypoglycaemia (Cornblath et al., 2000) (Cowett & Farrag, 2004). The statistical approach attempted to develop a normal distribution curve of blood glucose concentrations with values beyond two standard deviations being seen as 'abnormal' (Srinivasan et al., 1986). A clinical approach attempted to establish a 'safe' limit above which no hypoglycaemic symptoms were observable (Cornblath et al., 1959). A third approach has been the neurophysiological definition which sets out to establish the glucose concentration above which no neurophysiological functions appear altered (Koh, Aynsley-Green, et al., 1988) and fourthly, an attempt has been made to establish a definition of hypoglycaemia based on neurodevelopmental outcome (Lucas et al., 1988). Each of these approaches has its limitations and these include the need to consider gestational age, size for gestational age, feeding schedules, feeding type (breast or bottle-fed), other health issues or diagnoses, method of glucose concentration assessment and the possible presence of asymptomatic hypoglycaemia.

In 2009, a workshop on neonatal hypoglycemia was held by the Eunice Kennedy Shriver National Institute of Child Health and Human Development in the United States with the key objective being to identify major knowledge gaps (W. W. Hay, Jr. et al., 2009). The workshop produced 18 research agenda items and 5 general knowledge gaps. The key general knowledge gap in clinical issues was the fact that there was no evidence-based study which established the glucose concentration that defined pathologic hypoglycaemia. The authors reiterated the need for studies that would identify relationships between neonatal glucose concentrations and later neurologic outcomes.

1.3. Neonatal and perinatal carbohydrate metabolism

Prior to birth the fetus is dependent on the diffusion of oxygen and nutrients across the placenta from the maternal blood supply. However, at this stage the energy requirements of the fetus are restricted to tissue accretion, maintenance of existing tissues and limited movement, whereas after birth energy requirements also include thermoregulation, breathing and increased movement. Fetal growth and development during the approximately 40 weeks of gestation depends on an appropriate supply of carbon, nitrogen, ions and water. Glucose is the most important source of energy for the human fetus, supplying approximately 80% of energy requirements (Fowden, 1994). During fetal life new structural tissue is created, fuel reserves such as glycogen and fat are laid down and energy is provided to the growing tissues (Fowden, 2001). Fetal growth rate varies with gestational age. The typical growth pattern for a human fetus follows a sigmoid trajectory with an average weight increase of 15g/kg/day during the 24^{th} to the 37^{th}-39^{th} week. After this, the weight gain slows as tissue growth decreases and vital tissues such as lungs, liver and gut begin to differentiate in preparation for life *ex utero* (Fowden, 2001). Extensive changes begin at birth that allow the transition from fetus to neonate with an external source of oxygen and nutrients.

In utero the blood glucose concentration of the fetus is maintained solely by the placental glucose supply and the metabolic processes of the mother (Beardsall, Acerini, & Dunger, 2010; Cowett & Farrag, 2004). There is no evidence that a lowered maternal blood glucose concentration stimulates glucose production in the human fetus (Kalhan, D'Angelo, Savin, & Adam, 1979; Marconi et al., 1996). However, there is some evidence that extended periods of abnormally low blood glucose concentrations stimulate gluconeogenesis in fetal sheep (DiGiacomo & Hay Jr, 1990). Although fetal and maternal blood glucose concentrations are closely linked (Kalhan et al., 1979), fetal concentrations are only 60 – 70% that of maternal concentrations (Bloomfield & Harding, 2006). This difference assists in maintaining the necessary concentration gradient and is, in part, due to placental energy requirement which is responsible for utilisation of approximately 60 - 75% of the glucose that diffuses from the maternal circulation in sheep (Bloomfield & Harding, 2006). The placenta, therefore, significantly reduces the amount of glucose available to the fetus from maternal circulation (Fowden, 1994). Furthermore, it has been shown in sheep that when the maternal blood glucose concentration is low the placenta may utilise glucose that diffuses back from the fetus (Bloomfield & Harding, 2006).

Transport of nutrients across the placenta may occur via one of several processes: simple diffusion, paracellular diffusion, active and facilitated transfer, and by endocytosis-exocytosis across the cell layers. Molecules such as oxygen cross via simple diffusion down a concentration gradient, with the placenta accounting for approximately 50% of oxygen usage en route. However, glucose crosses the placenta via a process of facilitated diffusion which requires both concentration gradient and glucose transporter molecules (GLUTs). In the human placenta, and within the fetus, the most commonly occurring of these is GLUT1, which has a high affinity for glucose and hence is an efficient transport molecule (Cowett & Farrag, 2004). GLUT1 molecules are found within the syncytium layer of the placenta, GLUT3 in the arterial vascular endothelium and small amounts of GLUT4 have been identified in intravillous cells (Illsley, 2000).

The efficiency of transplacental glucose transport is increased by several important features. Firstly, in humans, as in other animals, there is an uneven distribution of GLUT1 in the syncytium with a higher concentration of GLUT1 on the maternal microvillous membrane (MVM) than on the fetal-facing basal membrane (Bloomfield & Harding, 2006). Secondly, the microvilli of the maternal facing syncytium create a surface area six times that of the fetal facing basal membrane. These features ensure that the glucose concentration in the placenta is close to maternal blood concentration of glucose, hence there is a ready supply of glucose for transport to the fetus, despite the high rate of utilisation of glucose by the placenta itself (Simmons, 2006) and the movement of glucose back to the fetus is restricted (Schneider, Reiber, Sager, & Malek, 2003).

Maintenance of blood glucose concentration in the normal range after birth is dependent on two glucose production pathways which are interlinked via a regulatory feedback process. In addition, glucose may also be absorbed directly from the intestinal tract after feeding (Cowett & Farrag, 2004). Glycogen is a long-chain carbohydrate stored in the liver, skeletal and cardiac muscles, intestine, brain and placenta. It is converted to simple glucose via glycogenolysis and released into the blood. During early fetal life glycogen is present in small quantities, although there is a rapid increase in

quantity in the last 4 weeks of gestation (Simmons, 2006). The timing of this increase in glycogen is one of the reasons that pre-term babies are at increased risk of hypoglycaemia. Gluconeogenesis also produces glucose via the metabolism of non-carbohydrate carbon molecules such as lactate, glycerol, and glucogenic amino acids. The enzyme glucose-6-phosphatase has an important role in both glycogenolysis and gluconeogenesis. Liver glucose-6-phosphatase is developmentally regulated, with amounts remaining low in the fetal period and a dramatic increase at birth resulting in most newborn babies attaining an adult level within approximately 2 days after birth (Burchell, Gibb, Waddell, Giles, & Hume, 1990). Hence low levels of glucose-6-phosphatase as the result of genetic deficiencies or prematurity can be another cause of hypoglycaemia.

The glycogenolysis-gluconeogenesis pathway is regulated, in normal circumstances, by the hormones insulin and glucagon. Glucagon and insulin are pancreatic peptides detectable from 6 and 10 weeks gestation, respectively (Shulkes, 1994). During fetal life glucagon is found in higher concentrations than insulin, although there appear to be fewer glucagon receptors (Shulkes, 1994). Its role is unclear, but glucagon has a role in fetal metabolism during times of fetal stress (Fowden, 1994). Insulin receptors are numerous and widespread throughout fetal tissue and insulin has an important role in fetal glucose regulation (Shulkes, 1994). Insulin regulates the uptake of glucose into cells when it binds to insulin receptor sites on the cell membrane which results in the activation of glucose transporter molecules. The resulting intracellular metabolic reactions include glycogenolysis, glycolysis and fatty acid synthesis. In fetal life insulin production is primarily responsible for glycogen and fat production and hence it is closely associated with fetal growth. Insulin may be directly responsible for growth through these processes but also regulates growth indirectly via the insulin-like growth factor (IGF – 1) pathway (Beardsall et al., 2010).

The fetus develops with a constant supply of glucose delivered via the placenta. However, after birth the newborn baby must adapt to intermittent feeding and an interrupted supply of glucose and other nutrients (Cowett & Farrag, 2004). Because of the numerous rapid metabolic changes required the newborn is particularly vulnerable to disrupted glucose homeostasis (Cowett & Farrag, 2004). Maintenance of a stable blood glucose concentration depends on a rapid upregulation of a number of enzymes and pancreatic hormone production, in particular glucagon, which controls the release of glucose into the blood and rises at birth (Simmons, 2006) with a 3- to 5- fold increase over fetal levels, while insulin levels fall (Shulkes, 1994). In the normally transitioning newborn blood glucose concentration declines rapidly in the first 1 to 2 hours after birth and on average takes approximately 72 hours to reach a stable concentration (Srinivasan et al., 1986).

Although other organic substrates can be utilised during periods of starvation or hypoglycaemia (Fung & Devaskar, 2006), under normal circumstances glucose is the primary source of energy for the brain (Maher, Davies-Hill, Lysko, Henneberry, & Simpson, 1991) with as much as 90% of neonatal glucose consumption being for cerebral function (McGowan, 2006). Glucose transporter molecules, therefore, have an important role in the transport of glucose to the brain. Glucose uptake by the brain is not solely dependent on cerebral blood flow and can be increased in specific areas as a response to normal increased requirements as well as hypoxia or hypoglycaemia (Maher et al., 1991). There are

two principle areas of glucose uptake in the brain: the endothelial cells of the blood-brain barrier and the plasma membranes of the glial and neuronal cells (Maher et al., 1991). GLUT1 is responsible for transport of glucose across the blood-brain barrier (Mantych, Sotelo-Avila, & Devaskar, 1993) and GLUT3 is found predominantly in neurons (Mantych, James, Chung, & Devaskar, 1992). Neonatal GLUT1 concentrations are the same as adult levels (Mantych et al., 1993), and GLUT3 concentrations are similar to adult levels in the cerebellum but not in the cerebral cortex. It has been proposed that these differences reflect differing energy requirements within anatomically distinct areas of the brain (Mantych et al., 1992). Glucose uptake in the brain does not require insulin and hence is somewhat independent of the insulin-glucagon regulation process.

Other organic substrates which may contribute to fetal and neonatal energy supply are ketones and lactate (Hawdon, 1999). Ketone bodies from the β-oxidation of fatty acids may be an important source of energy for healthy, appropriate weight for gestational age (AGA), breastfed babies who are often found to have low blood glucose concentrations (Hawdon, 1999). Improved mental health of breastfed children at adolescence (Oddy et al., 2010) and protection from neural damage resulting from hypoglycaemia have each been attributed to the neonatal ability to use ketones (Hawdon, 1999).

1.4. Measurement of blood glucose concentration

There is a long-standing lack of consensus on the definition of neonatal hypoglycaemia and uncertainty about its significance (W. W. Hay, Jr. et al., 2009; Volpe, 1995). This lack of clarity is compounded by the fact that glucose concentration of any given sample can vary as a result of the measurement processes employed and the type of sample used. There are three primary considerations when interpreting glucose concentration results either individually or in terms of study results. Firstly, there is likely to be variation in glucose concentration depending on whether the sample analysed was whole blood, serum or interstitial fluid, with plasma glucose concentrations approximately 10 – 18 % higher than whole blood concentrations. Measurements of blood glucose concentrations are likely to be less accurate than plasma or serum measurements because variation in haematocrit may affect the accuracy of results (Aynsley-Green, 1991; Deshpande & Ward Platt, 2005) and because erythrocytes are metabolically active and hence will consume glucose unless the blood sample is immediately 'fixed' (Aynsley-Green, 1991). Erythrocyte membranes are less permeable to glucose than capillary membranes hence the site at which the sample was taken may contribute to variation in glucose concentration. In addition, the process of facilitated diffusion by which glucose enters the erythrocyte is related to the concentration of glucose in the surrounding blood (Brahm, 1983).

A second confounding issue in assessing glucose concentration is the fact that there are variations in glucose concentrations between capillary, arterial and venous blood (Burrin & Alberti, 1990). These differences are primarily due to different haematocrit levels along with the obvious differences resulting from the arterial supply of nutrients and venous removal of metabolites (Aynsley-Green, 1991, 1996).

Thirdly, the process employed to assess glucose concentration has important implications for the accuracy of results. Clinical management of neonatal hypoglycaemia requires a process that is quick and accurate (Deshpande & Ward Platt, 2005), hence initial cot-side screening of infants is often by capillary blood obtained via heel prick and assessed using portable reflectance meters (PRMs) which require a single drop of blood on a reagent test strip (Deshpande & Ward Platt, 2005; D. L. Harris, Battin, Weston, & Harding, 2010). Results obtained via PRM have the advantage of convenience and speed although accuracy is not as good as those obtained via the glucose oxidase method (Bonacruz, Arnold, Leslie, Wyndham, & Koumantakis, 1996). Inaccuracies in PRM results are attributed to haematocrit variations between samples and technical issues related to the low glucose concentrations being assessed (Balion, Grey, Ismaila, Blatz, & Seidlitz, 2006). PRMs were designed for diabetic use and are considered accurate for normal and high blood glucose concentrations, but their accuracy declines with low blood glucose concentrations (Bonacruz et al., 1996). Because of the inherent inaccuracies (Aynsley-Green, 1991) their use is said to be contraindicated in neonatal medicine (Deshpande & Ward Platt, 2005), although it is still widespread (Bonacruz et al., 1996; D. L. Harris et al., 2009).

Greater accuracy in assessing glucose concentration is achieved using the so-called 'gold standard' glucose oxidase method (Aynsley-Green, 1991) which is the process used in both continuous glucose monitoring systems (CGMS) and glucose oxidase analysers. Approximately half of the newborn nurseries in Australasia use glucose oxidase analysers (D. L. Harris et al., 2009). However, the expense and technical expertise required prohibits the use of this process in many hospitals (Aynsley-Green, 1991). In most centres this is a laboratory procedure with inevitable delays, therefore blood samples are required to be transferred in vials treated with fluoride to prevent on-going glucose metabolism by the erythrocytes (Committee on Fetus & Newborn, 2011). A further disadvantage in this method is the larger sample of blood required for analysis.

One problem inherent in all of the above mentioned methods is that they rely on intermittent sampling and thus it is possible that periods of low blood glucose concentration may be missed and no information is made available about the profile of the blood glucose concentration in between assessments (D. L. Harris et al., 2010). Recently it has been shown that continuous glucose monitoring systems (CGMS), which were initially designed for use by diabetics, are accurate for neonatal use even when glucose concentration is low (D. L. Harris et al., 2010) and in very low birth weight (VLBW) babies requiring intensive care (Beardsall, Ogilvy-Stuart, Ahluwalia, Thompson, & Dunger, 2005). CGMS detect interstitial glucose concentrations at five minute intervals via a small electrode attached subcutaneously. Their use has detected a greater number of episodes of hypoglycaemia in at-risk newborns than did intermittent sampling methods (D. L. Harris et al., 2010).

1.5. Known developmental sequelae of neonatal hypoglycaemia

Rapid increase in neural cell numbers means that between 10 to 18 weeks of gestation the adult number of brain cells has been reached. However, the transient period of rapid brain growth known as the growth spurt occurs around the time of birth and is characterised by further rapid growth in glial

cells followed by a period of myelination. At this stage neuronal migration is largely complete (ten Donkelaar, 2008). There is then a period of rapid synaptogenesis and an increase in dendritic complexity (Dobbing & Sands, 1973), followed by a period of pruning and decrease in dendrite numbers. During this period of rapid growth and development of dendritic complexity around the time of birth the developing brain is particularly vulnerable to disturbed nutrition (Dobbing & Sands, 1973). Some areas of the brain show differential vulnerability to hypoglycaemia with the duration of hypoglycaemic episodes one factor determining which cerebral areas are most affected (Auer, Wieloch, Olsson, & Siesjo, 1984).

It has been estimated that 90% of neonatal glucose utilization is accounted for by metabolism in the relatively large neonatal brain, which requires glucose as both a metabolic fuel and as a precursor to the macromolecules required for structural growth (Glazer & Weber, 1971). Therefore, restriction of glucose supply is likely to be deleterious to both immediate cerebral function and cerebral development as evidenced by subsequent developmental sequelae. The extent and severity of these effects appears to be, in part, related to the severity of neonatal hypoglycaemia. However, the relationship between degree of hypoglycaemia and the extent of neural damage is not linear, as duration and frequency of hypoglycaemia also appear to be important factors (Lucas et al., 1988).

Both neuronal and glial cells can be adversely affected by neonatal hypoglycaemia, with disrupted development or even death the result (Lucas et al., 1988). The pathway via which neuronal damage occurs in hypoglycaemic infants is not fully understood, although animal studies suggest that neuronal necrosis occurs at low blood glucose concentration via an excitotoxic process which creates a distinctive pattern of cell death in the brain (Auer et al., 1984; Cornblath & Ichord, 2000). This excitotoxic process is a possible explanation for the seizure activity which occurs at very low blood glucose concentrations. However, neuronal necrosis has been shown to occur in both humans and animals only after EEG recordings have become isoelectric (Auer, 1986).

Early studies of symptomatic hypoglycaemia listed apnoea, cyanosis, coma, convulsions and death as results (Cornblath et al., 1959). Subsequently symptomatic hypoglycaemia has also been associated with epilepsy (Montassir, Maegaki, Ohno, & Ogura, 2010; Udani, Munot, Ursekar, & Gupta, 2009), learning disabilities, cerebral palsy, mental retardation and death (Armentrout & Caple, 1999; Wintergerst et al., 2006), reduced IQ scores (Pildes et al., 1974)and lowered McCarthy Scale developmental scores after twelve months (Duvanel, Fawer, Cotting, Hohlfeld, & Matthieu, 1999). Hypoglycaemic infants have also been shown to have reduced scores on McCarthy scales perceptive performance and motricity indices at three and half years of age (Duvanel et al., 1999) and these results indicated that frequency of hypoglycaemic events was a more significant predictor of neurodevelopmental outcome than the severity of a single event of hypoglycaemia (Duvanel et al., 1999). Small for gestational age preterm infants who had repeated episodes of hypoglycaemia have been shown to have significantly reduced head circumferences compared with euglycaemic controls, with this difference persisting through to five years of age (Duvanel et al., 1999; Pildes et al., 1974). Head circumference has been shown to correlate with neurological outcome (Cresto, Abdenur, Bergada, & Martino, 1998).

One MRI investigation of full-term newborns with symptomatic hypoglycaemia showed abnormalities at four times the rate of the control group, although the lesions identified were not present at follow-up 2 months later (Kinnala et al., 1999). However, other MRI studies have identified cortical thinning, particularly in the occipital region, as permanent sequelae of neonatal hypoglycaemia (Kinnala, Korvenranta, & Parkkola, 2000) with haemorrhage, middle cerebral artery infarction, and basal ganglia/thalamic abnormalities also identified (Burns, Rutherford, Boardman, & Cowan, 2008). Positron emission tomography (PET) studies show that the pattern of glucose metabolism in the newborn brain mirrors the areas of highest activity. Thus, the highest glucose metabolism is seen in the primary sensory and motor cortex, thalamus, brain stem and cerebellar vermis, with the cingulate gyrus, hippocampus and basal ganglia sometimes also showing high rates of glucose metabolism in comparison to the cerebral cortex (Chugani, 1998). This pattern of glucose metabolism has implications for the pattern of neural damage and hence brain functions that could be expected as a result of hypoglycaemia.

Abnormal sensory evoked potentials (Koh, Aynsley-Green, et al., 1988) and reduced Bayley motor and mental development scores (Lucas et al., 1988) were found in both symptomatic and asymptomatic newborns and children after hypoglycaemia, with learning disabilities and seizure disorders associated in approximately 6% of children who experienced asymptomatic neonatal hypoglycaemia (Armentrout & Caple, 1999). Neonatal hypoglycaemia in asymptomatic infants born to diabetic mothers (IDM) has been shown to be associated with lower total development score and decreased attention, motor control and perception scores at eight years of age (Stenninger, Flink, Eriksson, & Sahlen, 1998).

As previously outlined, synaptogenesis and the development of dendritic complexity continues after birth. The visual pathway, which has had little stimulation prior to birth, undergoes a period of intense axonal migration and synaptogenesis after birth, which makes it particularly vulnerable to neonatal hypoglycaemia (Filan, Inder, Cameron, Kean, & Hunt, 2006; Kinnala et al., 2000). This vulnerability appears to be greater in full-term babies than in pre-term babies, suggesting that vulnerability is greater at different stages of maturation (Tam et al., 2008). Occipital lobe epilepsy (Montassir et al.), cataract, optic atrophy, squint and nystagmus have all been reported as results of neonatal hypoglycaemia (Koivisto et al., 1972). The dorsal visual stream is also particularly vulnerable to disruption in developmental syndromes such as Williams, Downs and Fragile X and MRI imaging has shown decreased dorsal stream function to be associated with white matter injury in children born very preterm (Janette Atkinson & Braddick, 2011; Braddick, Atkinson, & Wattam-Bell, 2011; MacKay et al., 2005). The dorsal visual stream connects to the occipital lobe and is important to cortical visuo-spatial processing, including motion detection, and overlaps with neural subsystems important to the development of attention and executive function (EF) (Braddick & Atkinson, 2011). No assessment of the effect of neonatal hypoglycaemia on dorsal visual stream function has been reported.

1.6. At-risk groups of newborn babies

Glucose is the only energy source for the brain that does not necessarily require oxygen for metabolism. However, anaerobic glycolysis requires significantly more glucose molecules to release the same amount of energy than does aerobic glucose metabolism, meaning that newborn babies suffering from hypoxia (DiGiacomo & Hay Jr, 1990; Lubchenco & Bard, 1971; Shelley, 1969; Vannucci & Vannucci, 2001) or septic shock (Cornblath & Ichord, 2000) are at heightened risk of developing hypoglycaemia. Excessive energy requirement as a result of thermoregulation or brain injury will also result in rapid depletion of glucose and glycogen and hence hypoglycaemia may result (Cornblath & Ichord, 2000). Hypoglycaemia is more common in male than female babies at a ratio of 1.6:1, although the reason for this difference is unknown (Cornblath, Wybregt, Baens, & Klein, 1964; A. M. Moore & Perlman, 1999). The smaller twin is also at increased risk of hypoglycaemia (Cornblath et al., 1964).

Prematurity is a common risk factor for hypoglycaemia as many of the metabolic processes which begin in preparation for birth occur within the final 4 weeks of gestation. For example, glycogen storage and production of glucose-6-phosphatase occur from 36 weeks gestation, hence depending on length of gestation, prematurity may result in delivery of a newborn with low glycogen reserves and immature metabolic processes to utilise any reserves available (Garg & Devaskar, 2006; Hawdon, Ward Platt, & Aynsley-Green, 1992). Small for gestational age (SGA) preterm babies are at particular risk of hypoglycaemia with an incident rate up to 73% (Duvanel et al., 1999). However, late preterm birth (Garg & Devaskar, 2006) and even earlier gestational age in term babies have been shown to be risk factors. (DePuy, Coassolo, Som, & Smulian, 2009).

Under- and over-nutrition have both been suggested as risk factors for hypoglycaemia, with babies who suffered intrauterine growth restriction (IUGR) being particularly at risk (Lubchenco & Bard, 1971). Size alone is not the risk factor and standardised fetal growth curves have been shown not to accurately predict hypoglycaemia in newborns (T. S. Johnson, Hillery, & Engstrom, 2006) with mid-arm circumference/head circumference ratio mooted as a better clinical predictor of hypoglycaemia than birth weight for gestational age (T. S. Johnson, 2002).

Babies of diabetic mothers are at particular risk of hypoglycaemia as high maternal blood glucose concentration results in high fetal blood glucose concentration and hence fetal hyperinsulinism. Following delivery and once placental glucose supply has ceased, neonatal hyperinsulinism often results in neonatal hypoglycaemia. Insulin production may take up to 7 days to down-regulate, resulting in an extended period of risk of hypoglycaemia for these babies (Nold & Georgieff, 2004). Babies of diabetic mothers may be macrosomic or large for gestational age (LGA) as a result of the high levels of insulin they have been exposed to in the fetal period, and are thus at risk of difficult delivery and more likely than AGA babies to be delivered preterm (Lubchenco & Bard, 1971). Transient hypoglycaemia in healthy LGA infants born to non-diabetic mothers does not appear to be associated with negative neuropsychological development (Brand, Molenaar, Kaaijk, & Wierenga, 2005).

Maternal health contributes significantly to the glycaemic status of the newborn with intrapartum fever (DePuy et al., 2009), maternal weight gain (Hedderson et al., 2006), caesarean delivery (DePuy et al., 2009), maternal selective serotonin reuptake inhibitor (SSRI) use for depression (Lund, Pedersen, & Henriksen, 2009) and neonatal drug withdrawal as a result of maternal drug use (Cornblath & Ichord, 2000), all contributing to the risk of neonatal hypoglycaemia. In the United States maternal public insurance, in contrast to private health insurance, is viewed as a collective indicator of socio-economic status, health care, and diet, and has been shown to be a risk factor for neonatal hypoglycaemia (DePuy et al., 2009).

Delayed or inadequate feeding can result in neonatal hypoglycaemia and hence, has implications for choice of post-delivery feeding. Breast-fed babies appear to be able to better produce and utilise ketones which provides a buffer against hypoglycaemia which is not uncommon while breast feeding is being established (Hawdon, 1999). Animal studies have shown that lactate (Hawdon, 1999) and ketones (Vannucci & Vannucci, 2001) supplied via parental feeds, may be utilised in lieu of glucose.

Animal studies have shown that newborns have a greater ability to survive low blood glucose concentrations than do adults (Mujsce, Christensen, & Vannucci, 1989; Vannucci & Vannucci, 2001). A range of mechanisms have been proposed to account for this including, in newborn dogs, lower metabolic needs (Hernandez, Brennan, Vannucci, & Bowman, 1978) and hence a lower glucose demand along with higher endogenous carbohydrate stores (Mujsce et al., 1989). Newborn dogs were shown to have a cerebral metabolic rate for oxygen 40% less than the adult level, indicating a comparably reduced glucose requirement (Mujsce et al., 1989). The rate of movement of glucose across the blood-brain barrier in newborn rats is half that of adult rats (Cremer, Cunningham, Pardridge, Braun, & Oldendorf, 1979). However, it has also been demonstrated in newborn dogs (Anwar & Vannucci, 1988) and preterm infants (Pryds, Christensen, & Friis-Hansen, 1990) that low blood glucose concentrations causes an increase in cerebral blood flow (CBF) through vasodilation, and hence a greater supply of glucose may be available at lower concentration.

The lower metabolic demand of newborns is thought to confer some resistance to anoxia and has been demonstrated in newborn rats (Duffy, Kohle, & Vannucci, 1975). In addition, the use of alternate cerebral energy fuels at blood glucose concentration less than 1.0 mmol/l has been demonstrated in newborn dogs (Mujsce et al., 1989). Lactate is one such alternate fuel which has been shown to be actively consumed during insulin-induced hypoglycaemia in newborn dogs, and is proposed as a more significant alternate fuel source than ketones (Hellmann, Vannucci, & Nardis, 1982). The ability of newborn animals to use alternate organic substrates instead of glucose has complicated attempts to define an animal model of hypoglycaemic brain damage (Vannucci & Vannucci, 2001).

1.7. Late preterm babies

Preterm birth, defined as birth prior to 37 weeks gestation, represents a significant risk in terms of neonatal morbidity and mortality (Volpe, 1998) with the degree of risk related to degree of prematurity (McGowan et al., 2011). Approximately 75% of preterm births are late preterm infants born between

34 weeks and 36 weeks (Baron et al., 2009) with infants in this group at greater risk for morbidity and mortality than infants born after 37 weeks (Morse, Zheng, Tang, & Roth, 2009; Woythaler, McCormick, & Smith, 2011). Approximately 70% of the increased number of preterm births in the US in the last 20 years has been late preterm deliveries and hence there are economic and planning concerns as a result of this increased medical burden (Inder & Liao, 2009).

Prior to 2005 this group of newborn babies were referred to as 'near term'. However, the National Institutes of Child Health and Human Development in the United States recommended that the description be changed to emphasise the fact that, despite many late preterm babies being a similar size and weight to full term babies, they face increased challenges in comparison to term babies (Engle, Tomashek, & Wallman, 2007; Garg & Devaskar, 2006; Mohl, 2010). Although there is still a paucity of systematic prospective research of the developmental sequelae and educational outcomes of late preterm infants (Engle et al., 2007; Garg & Devaskar, 2006), there is a growing recognition of their poorer outcomes (McGowan et al., 2011), especially amongst those babies who required Neonatal Intensive Care Unit (NICU) admission (Baron, Erickson, Ahronovich, Baker, & Litman, 2011).

Large studies in the United States have shown that late preterm infants are three times more likely to suffer from cerebral palsy than full term infants (Petrini et al., 2009), that they have a 36% higher risk of developmental delay or disability and a 19% higher risk of suspension from kindergarten than full term infants (Morse et al., 2009). In addition, they are more likely to require special education services for reading and maths support through to grade 5 than full term infants (Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008). A Danish study has shown that at age 10 late preterm children are more likely to have spelling and reading difficulties (Kirkegaard, Obel, Hedegaard, & Henriksen, 2006). Prevalence of schooling difficulties has been assessed as approximately one third of children born between 32 and 35 weeks gestation as compared to 10 – 20 per cent in studies of normal controls (Huddy, Johnson, & Hope, 2001). At young adulthood, those born late preterm are at significantly increased risk of disability, and failure to complete a tertiary education with a resultant increased likelihood of lower net salary (Lindström, Winbladh, Haglund, & Hjern, 2007).

One reason late preterm babies are at greater risk of adverse developmental outcomes than term babies is because of the degree of immaturity of their nervous system (Adams-Chapman, 2006). At 34 weeks the weight of a fetal brain is approximately 65% that of a term baby's (Billiards, Pierson, Haynes, Folkerth, & Kinney, 2006) with the subsequent period of gestation characterised by rapid growth in cortical volume and an exponential increase in cortical surface area (Adams-Chapman, 2006).

Late preterm infants have an increased risk of developing hypoglycaemia when compared with full-term babies, as a result of reduced body fuel stores, inadequate dietary intake and greater vulnerability to sepsis and temperature regulation issues which may result in hypoglycaemia (Wang, Dorer, Fleming, & Catlin, 2004). Contributing further to their risk is the fact that late preterm infants have poor postnatal metabolic adaptation resulting in a greater postnatal decrease in plasma glucose

concentrations than in full term infants (Garg & Devaskar, 2006). Moreover, blood ketone concentrations are likely to be lower in late preterm infants, even in the presence of low glucose concentrations, suggesting that they have a more restricted access to alternative fuels and a reduced ability to compensate for low glucose concentrations than do full term infants (Hawdon et al., 1992). Although the mechanism of cerebral injury in late preterm infants is not fully understood, factors which contribute to vulnerability include misperception as to the degree of risk faced, respiratory system dysfunction, glycaemic instability, inadequate oral intake, susceptibility to infection and neurologic immaturity (Mohl, 2010).

The distinction between term and late preterm is somewhat arbitrary and problematic, and has the potential to mask the perinatal risk to which newborns are exposed, as this continues to decrease in proportion to gestational age through to term (Inder & Liao, 2009; Kirkegaard et al., 2006). Different methods of calculating gestational age based on ultrasound, last menstrual period (LMP) or midwife determination confounds the problem of determining risk based on gestational age categories (Kirkegaard et al., 2006). Apparently healthy, breastfed babies at 38 weeks gestation are known to have suffered long term developmental sequelae after developing hypoglycaemia, highlighting the potential impact of a combination of subtle risk factors such as 'borderline' gestational age of 36 -38 weeks, maternal primiparity, poorly established breastfeeding, and lack of social support (A. M. Moore & Perlman, 1999).

1.8. Socio-economic status and development

Family socioeconomic status (SES) has a significant impact on a child's development both pre- and post-natally through a complex set of factors operating in a synergistic manner (Bradley & Corwyn, 2002). However, the concept of SES continues to change and where it was once an indicator of social position and prestige, heavily reliant on employment and the associated social status, it has become an even less tangible concept as the older notions of social hierarchy change (Oakes, 2012). Although the definition of SES is still debated, it is generally agreed to include income, education and employment and more recently has been conceptualised as including access to social resources (American Psychological Association task force on socioeconomic status, 2007). The difficulty then becomes one of appropriate and adequate measure, because although income appears to define SES as effectively as composite measures (Oakes, 2012), parents are frequently willing to share education and employment but not income data with researchers (Noble, McCandliss, & Farah, 2007).

The robust relationship between SES and development means that SES is commonly included as a covariate in studies of cognitive ability (Petrill, Pike, Price, & Plomin, 2004). Children from low SES families are more likely to grow up in an impoverished environment (American Psychological Association task force on socioeconomic status, 2007) with less access to a wide range of educational toys and recreational and educational events out of the home (Bradley & Corwyn, 2002) and harsher parenting practices (American Psychological Association task force on socioeconomic status, 2007). Children from lower SES families have lower cognitive and academic scores, fewer

years of formal schooling and lower income earning potential (Bradley & Corwyn, 2002; Brooks-Gunn & Duncan, 1997). In New Zealand, low SES children are less likely to be enrolled at preschool (Early Childhood Education Taskforce, 2012), more likely to move school frequently (Dale, O'Brien, & St John, 2011) and less likely to complete secondary school (Fergusson & Woodward, 2000). Neurocognitive development in children is influenced by family SES (Hackman & Farah, 2009) with working memory and cognitive control (Farah et al., 2006), language development (Hackman & Farah, 2009; Wild, Betancourt, Brodsky, & Hurt, 2013), and executive function (Ardila, Rosselli, Matute, & Guajardo, 2005) being strongly affected. All of these differences result in educational gaps between children from low and high SES families starting from an early age (Dale et al., 2011).

Low socioeconomic status is a strong predictor of poorer cognitive (Johnston, Low, de Baessa, & MacVean, 1987; Tucker-Drob et al., 2011), language (Wild et al., 2013), educational (Gibb, Fergusson, & Horwood, 2012) and physical health status (Adler & Ostrove, 1999; Sherry, Adelman, Farwell, & Linton, 2013; Weinfield, Sroufe, & Egeland, 2000) outcomes. These differences are associated with differences in functional brain development in children from low SES families (Tomalski et al., 2013), including reduced cortical development (Lawson, Duda, Avants, Wu, & Farah, 2013). The relationship between low SES and health status has been shown to be independent of access to health-care services (Cohen, Doyle, & Baum, 2006) and to be persistent throughout the lifespan (Poulton et al., 2002). In New Zealand, children from low SES families are more likely to be admitted to hospital as a result of acute infection, with those in the most deprived neighbourhoods 2.8 times more likely to be hospitalised than those living in the least deprived neighbourhoods (Baker et al., 2012). Children from low SES families are more likely to suffer from intra-uterine growth restriction (IUGR) (Kramer, 1987), preventable diseases, to die before the age of five, and to have reduced childhood growth (Bradley & Corwyn, 2002). Lower SES families are less likely to seek early medical assistance when children are unwell and these children are less likely to be seen for follow-up of chronic illness (Bradley & Corwyn, 2002).

Children growing up in low SES families are likely to experience more family turmoil, family separation, more crowded living conditions, higher levels of violence (Evans & English, 2002) and higher levels of pre- and post-natal cigarette smoke exposure (van den Berg, van Eijsden, Vrijkotte, & Gemke, 2012). Measures of family chaos are likely to be higher in families with lower SES scores and these environmental conditions are negatively correlated with cognitive functioning (S. A. Hart, Petrill, Deater Deckard, & Thompson, 2007), mother infant attachment (Sherry et al., 2013) and toddler temperament (Matheny Jr, Wachs, Ludwig, & Phillips, 1995). SES mediates gene expression in toddlers with little genetic influence on cognitive development at 10 months and this remains unchanged at 2 years of age for children of low SES families. However, for high SES families genetic difference accounts for approximately 50% of variability in mental ability at 2 years of age (Tucker-Drob et al., 2011). The difference is thought to be a result of the ceiling effect imposed by the less favourable developmental environment of low SES households and as yet there is no clear agreement as to whether this early disadvantage can be overcome (Heckman, 2006; Tucker-Drob et al., 2011).

Low SES is associated with increased weight and poorer diet in adults, with the difference more pronounced amongst women than amongst men (C. J. Moore & Cunningham, 2012). Under-nutrition (Dale et al., 2011), obesity (University of Otago & Ministry of Health, 2011) and gestational diabetes, which are all risk factors for neonatal hypoglycaemia and are more likely to affect low SES mothers (Everson, Maty, Lynch, & Kaplan, 2002; Robbins, Vaccarino, Zhang, & Kasl, 2005). Low SES is also significantly related to an increased risk of very preterm birth (Smith, Draper, Manktelow, Dorling, & Field, 2007).

Psychophysiological stress, as indicated by cortisol and adrenaline concentrations, have been shown to be significantly higher for children as young as 6-years-old (Evans & English, 2002; Lupien, King, Meaney, & McEwen, 2000) and adults (Cohen et al., 2006) from low SES families, with these effects showing lifetime persistence (Gustafsson, Janlert, Theorell, & Hammarström, 2010). Chronic heightened hypothalamic pituitary adrenal axis and sympathetic nervous system activity, as evidenced by increased cortisol and adrenaline concentrations, are associated with suppressed immune function, increased blood pressure and heart rate, psychiatric disorders and increased central adiposity, which is a risk factor for coronary heart disease and diabetes (Cohen et al., 2006). Increased cortisol concentrations are also associated with increased blood concentrations of glucose, free fatty acids and insulin, and insulin resistance (McEwen, 1998; Roy, 2004). Leukocyte telomere length in 7 and 8 year old children from low SES families is reduced by an amount which is approximately equivalent to 6 years of increased cell aging (Needham, Fernandez, Lin, Epel, & Blackburn, 2012).

The relationship between SES and individual health status is complex, with indicators of social inequality within a country, rather than income or SES per se, negatively associated with child well-being for children from low SES families (Dale et al., 2011; Pickett & Wilkinson, 2007). Self-perception appears to be an important aspect of stress arousal and this subjective response has been posited as an explanation for the poorer outcome associated with relative SES (Brunner, 1997; Roy, 2004). In New Zealand there are now an estimated 200,000 children living in poverty where poverty is defined as a family income below 60% of the median household income (Dale et al., 2011), with Māori children disproportionately represented in these figures (Dale et al., 2011), which are strongly associated with the increased rate of disability amongst Māori children (15%) compared with New Zealand European children (10%) (Crampton, Salmond, & Kirkpatrick, 2000; Ministry of Health, 2004b). The presence of a disability predicts a greater than 2.5 times increase in likelihood of unemployment (American Psychological Association task force on socioeconomic status, 2007) thereby compounding lower family SES.

Health research and public health policy planning may employ measures of deprivation rather than socio-economic status (Salmond & Crampton, 2001; Waikato District Health Board, 2010a). Deprivation has been defined as “a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which an individual, family or group belong” (Townsend, 1987). The New Zealand Deprivation Index (NZDep) (Salmond, Crampton, & Sutton, 1998) is an area-based measure of deprivation which uses census data made available by Statistics

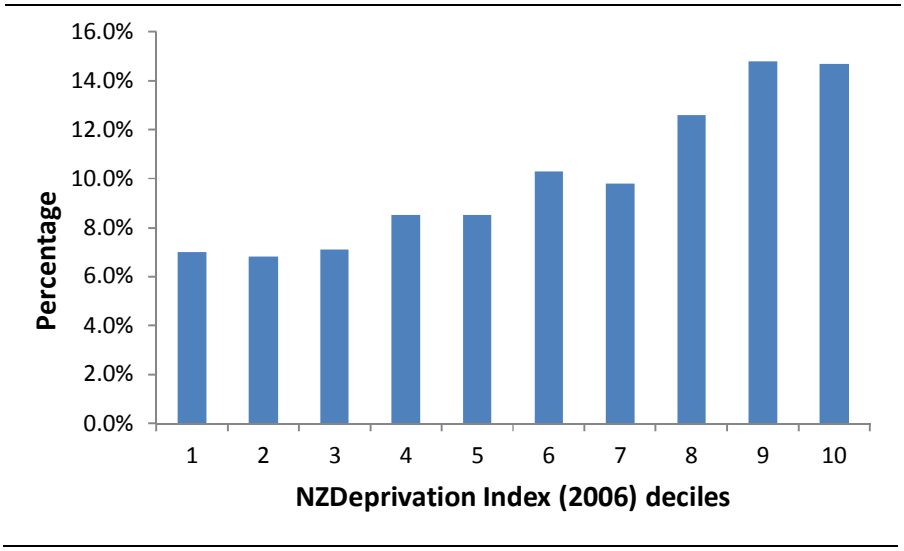
New Zealand and is currently available in its fifth iteration (June Atkinson, Salmond, & Crampton, 2013). Statistics New Zealand meshblocks, small geographic regions which represent population groups of approximately 90 people, are used as the primary geographic units, although in areas of low population density meshblocks may be aggregated to achieve a more standard population size (Salmond et al., 1998). The NZ Deprivation Index (NZDep) includes measures of household income, transport, living space, home ownership, employment, qualifications and support. Aspects of income and support are reflected in more than one measure, bringing the total number of components on the scale to 9 with the components then weighted to reflect their degree of contribution to deprivation as a whole (Table 1.1) (White, Gunston, Salmond, Atkinson, & Crampton, 2008). NZDep scores are used to divide New Zealand's population into ten equal decile groups with an index score of 1 representing the least and 10 the most deprived groups (Salmond & Crampton, 2001; Waikato District Health Board, 2010a). New Zealand birth records include nationwide NZDep2006 data for 2008 which showed that there was a skewed distribution of births with a higher proportion of babies born in areas of higher deprivation (Fig 1.1) (Ministry of Health, 2008a).

Table 1.1: A description of the dimensions of the New Zealand Deprivation Index (2006) with weightings used for each dimension.

Dimension of Deprivation	**Variable Description** (in order of decreasing weight)	**Weighting**
Income	People aged 18-64 receiving a means tested benefit	.371
Income	People living in equivalised* households with income below an income threshold	.356
Owned Home	People not living in own home	.334
Support	People aged <65 living in a single parent family	.333
Employment	People aged 18-64 unemployed	.332
Qualifications	People aged 18-64 without any qualifications	.326
Living Space	People living in equivalised* households below a bedroom occupancy threshold	.318
Communication	People with no access to a telephone	.314
Transport	People with no access to a car	.311

*equivalisation: methods used to control for household composition. Based on (Salmond, Crampton, & Atkinson, 2007)

Figure 1.1: The distribution of New Zealand births in 2008 across New Zealand Deprivation Index (2006) deciles.



From New Zealand Maternity Data Collection (Ministry of Health, 2008a).

Analysis of the components of the NZDep Index suggests that they are not independent and that the index measures "a single underlying construct of deprivation" (p836) (Salmond et al., 1998). In addition, some individual health outcomes such as mortality, hospitalisations and immunisation rates have been shown to be strongly linked to small area indices (Salmond & Crampton, 2001). However, the small area index of deprivation is only weakly correlated to individual deprivation and hence, although the data can be used as a proxy for individual deprivation, it must be used cautiously (Salmond & Crampton, 2001) to avoid 'the ecological fallacy' (S. Schwartz, 1994) whereby group statistics are inadvertently or inaccurately applied to individuals (White et al., 2008).

1.9. Early childhood development

Early childhood development is an interrelated process of central nervous system development, physical growth and maturation, and the learning that becomes possible with the development of these systems (Segalowitz & Rose-Krasnor, 1992). For example, skill development represented by physical milestones such as coordinated grasping, sitting erect and independent locomotion introduces an increasing array of environmental stimuli and learning opportunities (Aylward, 2009; Hayne, 2006).

A recent increase in information from neuroimaging has provided a detailed understanding of the connection between brain maturation and function (Albright, Kandel, & Posner, 2000). Positron Emission tomography (PET) scans reveal that at birth most of a newborn baby's brain activity is in the

primary sensory and motor cortex, brain stem and cerebellar vermis. By 2 months of age there is an observable increase in activity in the parietal, temporal and primary visual cortices and by 6 to 8 months of age an observable increase in activity in the frontal cortex (Chugani, 1998).

Normal cerebral development includes synaptic pruning, which results in the loss of surplus neuronal pathways (Chugani, 1998) and an increase in brain size, with head circumference and brain size at 9 months being significantly related to Intelligence Quotient (IQ) at 9 years (Gale, O'Callaghan, Godfrey, Law, & Martyn, 2004). Normal cerebral development can be interrupted by adverse events including intrauterine growth restriction and prenatal smoke exposure which can result in a decrease in cerebral volume and poorer cognitive function in later childhood (Ekblad et al., 2010; Geva, Eshel, Leitner, Valevski, & Harel, 2006).

The brain continues to develop and specialise with learning. As an example, the visual cortex develops rapidly in the 6 months after birth, both allowing the development of increasingly targeted physical movements such as grasping and simultaneously developing in response to the information gained (Janette Atkinson & Nardini, 2008). This early development has been conceptualised as a development of basic skills which become functions and then integrated functional units which form the basis of intelligence and can be measured as IQ beyond the age of three (Aylward, 2009). Therefore, developmental assessment requires a corresponding change in emphasis over time from neurologic to motor, sensorimotor, and cognitive function (Aylward, 2009).

Cognitive ability, sometimes referred to as *'g'* or general intelligence, incorporates learned knowledge and processing speed (M. Anderson, 2008) and predicts later outcomes such as education and occupation (Spinath, Ronald, Harlaar, Price, & Plomin, 2003). Heritability accounts for 20 - 30% of phenotypic variation in *'g'* at 2 to 4 years of age. However, by adolescence genetic influence increases to 50% (Spinath et al., 2003). Socioeconomic status significantly influences cognitive ability (Section 1.5, above) and breastfeeding also predicts improved developmental scores at 6 months (Morley, Cole, Powell, & Lucas, 1988) with an even greater difference at 8 years (Lucas, Morley, Cole, Lister, & Leeson-Payne, 1992). This difference in the development of cognitive ability with breastfeeding can be even more pronounced for preterm babies (J. W. Anderson, Johnstone, & Remley, 1999). General intelligence is commonly thought to contain two separate but interrelated aspects: fluid intelligence, or reasoning and problem-solving, and crystallised intelligence or acquired, socially bound knowledge which is contributed to by fluid intelligence (M. Anderson, 2008; Cattell, 1963; Diamond, 2013).

Infancy and childhood are important periods of extended social leaning. However, there is evidence the infant central nervous system is sufficiently mature for learning to begin *in utero*. At 33 weeks gestation babies habituate to sound with male babies habituating more slowly than female babies, apparently because of different information processing systems (Hepper, Dornan, & Lynch, 2012). Prior to birth, babies learn the sound of their mother's voices (DeCasper & Spence, 1986) and preterm babies in NICUs show more rapid language development when exposed to an increase in spoken language by their mother (Caskey, Stephens, Tucker, & Vohr, 2011).

The infant brain has an innate ability to learn language (Chomsky, 2000; Tomasello, Carpenter, Call, Behne, & Moll, 2005) and in its earliest form this may be a primate ability rather than a strictly human ability. Imitation is a powerful form of learning amongst all primates and in human infants it focusses language development so that while babies exposed to all languages respond to and produce the same range of sound at 6 months, by the time they are 12 months old, these sounds are largely restricted to those of their native language (Tamis-LeMonda, Song, Leavell, Kahana-Kalman, & Yoshikawa, 2012).

Proximal environmental influences have a powerful influence on child development (Bronfenbrenner & Ceci, 1994) and this is seen as ethnic differences in verbal and gestural communication by 2 years of age (Tamis-LeMonda et al., 2012). The influence of social environment on language development is further demonstrated by significant relationships between the complexity of children's language and the language of their parents and preschool teachers (Huttenlocher, Vasilyeva, Cymerman, & Levine, 2002). Furthermore, bilingual children show improved executive function scores, especially in managing conflict tasks, supporting the notion that neural development is linked across different cerebral areas (Poulin-Dubois, Blaye, Coutya, & Bialystok, 2011). Conversely, intrinsic processes such as illness and poisoning, and extrinsic factors such as environmental disturbances, social deprivation, and severe neglect can result in serious delays in language development (Dick, Leech, & Richardson, 2008; Hough, 2005).

An infant's receptive language development begins before birth, with word comprehension typically beginning around 9 months of age, several weeks ahead of expressive language (Dick et al., 2008). Between 16 and 20 months children exhibit a 'language burst' where both their vocabulary and language complexity increase (Dick et al., 2008). At this age verbal humour begins to appear (K. E. Johnson & Mervis, 1997) and words reflective of mental state, such as *want*, develop early in the vocabulary of normally developing children (Keenan, 2006). By the age of two, children are beginning to make sense of their world through the use of language and negotiation and a growing sense of self gives rise to a period often referred to as the 'terrible twos' (Carter, Briggs-Gowan, & Davis, 2004).

In addition to language development, imitation is an important aspect of social learning (Hayne, 2006) and toddlers growing up with siblings develop imaginative play at a younger age as a result of imitating what they see (Barr & Hayne, 2003). Babies as young as 6 months can remember new skills and imitate them 24 hours later while at 18 months, imitated skills are remembered for longer and can be generalised to conditions that were not identical to the learning situation (Hayne, Boniface, & Barr, 2000).

The development of a Theory of Mind (TOM) and an understanding of the beliefs, desires, intentions and emotions of self and others are crucial to normal social development (Keenan, 2006). The resulting development of empathy requires multiple components: the emotion detector, intentionality-detector and eye direction detector develop between birth and 9 months and provide inputs for the shared attention mechanism, which develops between 9 and 14 months. The shared attention mechanism provides the input for the development and functioning of the empathising system and

TOM mechanism which develop from approximately 48 months onward (Baron-Cohen & Chakrabarti, 2008). The development of the TOM mechanism depends on brain maturity and normal cortical development and this model has been useful in explaining abnormal development such as Attention Deficit Hyperactivity Disorder (ADHD) and autism (Baron-Cohen & Chakrabarti, 2008).

1.10. Executive function

Executive Function (EF) is commonly thought of as a collective term for "higher order, self-regulatory processes that aid in the monitoring and control of thought and action" (S. M. Carlson, 2005) and has been said to represent the pinnacle of the hierarchy of mental processes (Aron, 2008). The specific skills subsumed within the term include, most commonly, inhibitory control, working memory and planning, and cognitive flexibility (Chevalier et al., 2012; Diamond, 2013; Hughes & Graham, 2008). However, there is, as yet, no single agreed definition (Zelazo et al., 2013) with error correction and detection, resistance to interference and attentional control (P. J. Anderson, 2002; S. M. Carlson, 2005; Diamond, 2013) also included in some definitions of EF. Confirmatory factor analysis appears to indicate that in adults EF is described by three related but separate core EFs: shifting (cognitive flexibility), updating (working memory) and inhibition (Miyake et al., 2000). However, there is still a debate over whether EFs are integrated but separate (P. J. Anderson, 2002) or a singular construct in childhood (Wiebe et al., 2011).

EF has been described as independent of intelligence (Espy, Kaufmann, Glisky, & McDiarmid, 2001), although elsewhere associations between IQ and some EFs have been reported (Arffa, 2007; Friedman et al., 2006; Mahone et al., 2002; Ardila, Pineda & Rosselli, 2000). In particular working memory appears to be associated with intelligence, with age-related improvements in both also asociated with processing speed (Fry & Hale, 2000) and models have been proposed in which descriptions of fluid intelligence incorporate aspects of EF (M. Anderson, 2008; Diamond, 2013). Furthermore, some IQ assessments such as the the Wechsler Intelligence Scale for Children (Wechsler, 2004) and the Wechsler Preschool and Primary Scale of Intelligence (Wechsler, 2002) incorporate aspects of EF, such as working memory, hence separation of the constructs of IQ and EF is not currently possible (Woods et al., 2005).

EF begins to develop in the first few years of life (S. M. Carlson, 2005; Diamond, 1991), continues to mature into adolescence (V. A. Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Zelazo, Carlson, & Kesek, 2008) and decline with normal aging in adulthood (Hughes & Graham, 2008). Preschool EF is a better predictor of school readiness than either IQ or academic progress (Blair & Razza, 2007; Megan M. McClelland, Morrison, & Holmes, 2000) and has been shown to predict school achievement in children at 8 years of age (Bull, Espy, & Wiebe, 2008). Further, EF skills can mediate the social, behavioural and cognitive outcomes for older school children (Scope, Empson, & McHale, 2010). EF at 24 months has been shown to be a predictor of TOM functioning at 39 months (S. M. Carlson, Mandell, & Williams, 2004; Sabbagh, Bowman, Evraire, & Ito, 2009) although cross-cultural studies suggest that at least some aspects of EF develop independently of TOM and at different rates (Sabbagh, Fen, Carlson, Moses, & Kang, 2006).

Early investigations of EF focussed on the impact of frontal cortex damage on cognitive processes such as behaviour regulation and emotions, while other processes such as long term memory, vision and hearing remained unaffected (Aron, 2008). Further research has investigated health related executive dysfunction (EDF) caused by traumatic head injury (Beauchamp et al., 2011; Levin et al., 1996), phenylketonuria (Welsh, Pennington, Ozonoff, Rouse, & McCabe, 1990), hydrocephalus (Fletcher et al., 1996), meningitis (Taylor, Schatschneider, Petrill, Barry, & Owens, 1996), preterm birth (P. J. Anderson, Doyle, & Victorian Infant Collaborative Study Group, 2004; Espy et al., 2002), fetal alcohol syndrome (Mattson, Goodman, Caine, Delis, & Riley, 1999) and ADHD (Fuggetta, 2006; Furman, 2008). Low SES has a detrimental effect on EF and this appears to be the result of altered neural function and development (Hackman & Farah, 2009; Lawson et al., 2013).

Much of the initial research on the development of EF in children was based on assessments adapted from adult EF assessments (Fletcher, 1996), particularly tasks which assessed the ability to inhibit prepotent responses such as the Wisconsin Card Sorting Task, the Stroop word test, and Luria's hand game (Aron, 2008). More recently, assessment tasks have been developed which match infant and child developmental stages (S. M. Carlson, 2005; Espy et al., 2001; Hughes, 1998b). Quantitative assessment of EF is potentially problematic because observed behaviours are typically composed of multiple cognitive factors; hence it is important to isolate the cognitive components of a task to ensure that what is being assessed is a singular construct (Hughes & Graham, 2008). Increasingly EF assessments have employed tasks which focus on singular EF constructs derived from experimental psychology (Aron, 2008; S. M. Carlson, 2005) and age appropriate measures have allowed assessment of EF processes even within the first year after birth (Diamond, 1990, 2013).

Different aspects of EF develop throughout childhood in a sequence which corresponds to brain maturation (Sinclair & Taylor, 2008), with the multiple aspects of attention, which underlies all EF, the most studied and described. The ability to direct attention to events outside of the self is a crucial aspect of adaptive behaviour and although there is no agreed operational definition of attention (Sinclair & Taylor, 2008) it is typically conceived of as a complex, multidimensional process which underpins and contributes to all cognitive activity (Heuer, 1996). To date, developmental research on attention has largely focused on visual attention (Sinclair & Taylor, 2008), although it is thought that findings are applicable to other sensory domains (Richards, 2003) and that there is significant overlap between the sensory processing pathways (Posner & Petersen, 1990).

Neuropsychological and brain imaging studies show that behavioural attention develops in tandem with a wide-spread neural network (Mesulam, 1990). This network lies in the dorsal visual pathway (Posner & Petersen, 1990) and comprises extensive interconnections within and between the posterior parietal cortex, the prefrontal cortex and the anterior cingulate cortex (Mesulam, 1990). From a neuropsychological perspective, different brain regions can be thought to coincide with separate psychological functions, namely the alerting network, the orienting network responsible for reflexive and strategic orienting, and the executive control network in the prefrontal cortex (PFC) which is responsible for conflict detection and resolution (Posner & Petersen, 1990; Posner &

Rothbart, 2007). The executive control network of Posner's model overlaps significantly with descriptions of EF (Zelazo et al., 2013).

An alternate model of attention includes four factors: focussed attention, requiring the ignoring of irrelevant stimuli; sustained attention or maintaining attention and alertness; shifting attention or selectively changing attention to the most salient item or issue; and encoding attention or the ability to maintain information short term (Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991). Impaired attention underlies many learning and behavioural difficulties in school-age children (J. Breslau et al., 2009) and is associated with very preterm birth (P. J. Anderson et al., 2011).

Development of the prefrontal cortex (PFC) allows the developing child to respond to the external world with increasingly complex behaviour. Inhibitory control of behaviour is a skill which develops early in childhood and it has been proposed that it is a dual control process involving 'hot' EF and 'cool' EF (Metcalfe & Mischel, 1999). The hot and cool aspects of inhibitory control have been shown to be separate, but linked, neural pathways in the prefrontal cortex (Hughes & Graham, 2008; Metcalfe & Mischel, 1999). Hot EF or the 'go' system involves an affective response and allows an infant to respond to items of interest. Cool EF or the 'know' system develops later and entails a cognitively controlled response (Bunch & Andrews, 2012; Hongwanishkul, Happaney, Lee, & Zelazo, 2005). Directing attention away from the hot to the cool system, e.g. realising the consequence of an action rather than acting on a prepotent response, provides a means whereby inhibitory control is increased. This ability and the management of more complex tasks increases with age and by the age of six children perform complex cool tasks more successfully than hot tasks (Bunch & Andrews, 2012). Psychological distancing, achieved by the use of symbols to replace desired items such as sweets in a conflict task has been shown to increase inhibitory control in children as young as 3 years of age and it is proposed that symbols allow an increased cooling of 'hot properties' (S. M. Carlson, Davis, & Leach, 2005). Cognitive inhibition is strongly correlated with behavioural inhibition (Friedman & Miyake, 2004) and both behavioural and cognitive inhibition in early childhood predicts later outcomes in health, risk-taking and happiness (Diamond, 2013; Moffitt et al., 2010).

Working memory, or the ability to manipulate information held in mind, develops in tandem with attention and inhibition, relying on these other EF skills for appropriate function (Wiebe et al., 2011), and achieving adult-like modular structure by 6 years of age (Gathercole, Pickering, Ambridge, & Wearing, 2004), although it is measurable in the preschool years (S. M. Carlson, 2005). The prevailing conceptualisation of working memory is the tri-partite model of Baddeley and Hitch (1974), which includes a central executive or control system that regulates attention and inhibition, a visuo-spatial sketch-pad for brief storage of visual and spatial information, and a phonological loop providing brief storage by vocal or sub-vocal rehearsal, with this model recently updated to integrate with long-term memory (Baddeley, 2012). Working memory is correlated with fluid intelligence (Diamond, 2013) and attention, behaviour and cognitive performance (Scope et al., 2010), with preschool working memory predicting later school mathematics achievement (Bull et al., 2008) and reading success (Gathercole, Alloway, Willis, & Adams, 2006; Nevo & Breznitz, 2011). Reduced working memory is associated with impulsivity and risk taking (Hughes, 2011; Romer et al., 2009), although appropriate

training can improve these characteristics in teenagers, including those diagnosed with ADHD (Klingberg et al., 2005).

Cognitive Flexibility, the ability to change perspective and generate novel responses, is the last core EF to develop, and relies on the previously developed EFs (Best & Miller, 2010; Diamond, 2011; Garon, Bryson, & Smith, 2008). It is an important aspect of goal management, develops rapidly in early childhood and is enhanced in young children by stimulating environments and resources and hence, is sensitive to family SES (Chevalier, Wiebe, Huber, & Espy, 2011; C. A. Clark et al., 2013). Impaired cognitive flexibility is characteristic of Autistic Spectrum Disorder and is also associated with very preterm birth (Pennington & Ozonoff, 1996; Pozzetti et al., 2014).

Aspects of EF have been shown to be influenced by environmental factors and there is growing evidence of the importance of skill training in the improvement of some aspects of EF (Diamond, Barnett, Thomas, & Munro, 2007; Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009). Parental and offspring EF scores have been shown to be strongly correlated and independent of IQ scores, with recent studies of EF providing support for the heritability of EF and some externalising psychopathologies such as ADHD (Jester et al., 2009). Studies with preschoolers from the United States and China showed that Chinese children outperformed their US counterparts on all measures of EF, with parental expectations of behaviour possibly a mediating factor in the difference. However, genetic influences may contribute to these findings and although data gathering is still in its infancy in this area, it has already been shown that one of the genes known to be associated with ADHD (7 repeat allele of the dopamine receptor gene - DRD4) is very prevalent in the US (48.3% of the population) but rare in East and South East Asia (1.9% of the population) (Sabbagh et al., 2006). Elsewhere, separate EFs (inhibition, working memory, set shifting) have been shown to have a strong genetic basis (Friedman et al., 2008).

The complexity and interdependence of neural pathways which control executive functions emphasise the vulnerability to neural insults which may occur at different developmental stages. Evidence is accumulating that perinatal events can cause neurological insults which result in subtle but significant developmental impairments (Espy, Senn, Charak, Tyler, & Wiebe, 2007) and increasingly, that EF is one area of neurological development which is vulnerable to early insult (P. J. Anderson et al., 2004; Luu, Ment, Allan, Schneider, & Vohr, 2011; Woodward, Edgin, Thompson, & Inder, 2005).

1.11. Developmental assessment approaches at 2 years of age

It is important that developmental assessment includes the full range of child development and although developmental domains may be assessed separately, they frequently need to be understood together (Aylward, 2002a). Assessment must be appropriate to the age group and include information about the child's home environment (Bronfenbrenner & Ceci, 1994), and be sensitive to cultural and language differences to ensure optimal assessment for each child (Macfarlane, Blampied, & Macfarlane, 2011). Multiple sources of information are especially important in assessing young children as self-report is not an option (Carter et al., 2004). Parent report can be a reliable source of

valid information, especially when not limited to predetermined questions (Dixon, Badawi, French, & Kurinczuk, 2009). However, data pertaining to this are mixed and parent report via the Ages and Stages Questionnaire (ASQ) has been shown to be only mildly to moderately correlated with developmental measurements such as Bayley Scales of Infant Development (BSID-II) (B. J. Woodward et al., 2011), with developmental assessment in infancy only a moderate predictor of later IQ development (M. Anderson, 2008; Hack et al., 2005; G. Roberts, Anderson, & Doyle, 2010; B. J. Woodward et al., 2011).

Standardised assessments must have narrow age ranges for standardised scores as development at this age is very rapid (Carter et al., 2004). For the purposes of research the assessment tools need to be validated and it is an advantage to have data which are standardised and comparable to data from other studies. The Bayley Scales (Bayley, 2006) are commonly used, standardised developmental scales used clinically and in research (Robertson, 2010). The most recent version, the Bayley III, is used to assess development up to 42 months of age; cognitive, language and motor skills by direct assessment and social-emotional development and adaptive behaviour via parent questionnaire (Bayley, 2006). Currently there is a lack of agreement as to whether comparison of results between the different versions of the Bayley scales is possible, with reports of both underestimation by the Bayley II (B. J. Woodward et al., 2011) and overestimation by the Bayley III (P. J. Anderson, De Luca, Hutchinson, Roberts, & Doyle, 2010). The Bayley III technical manual states that there is an expected 7 point increase in score using the Bayley III compared with the Bayley II. The Flynn effect (Flynn, 1999), which describes an approximate 5 point increase in IQ each decade, has also been proposed as an explanation of the difference (Aylward, 2002b). The Bayley III used a more inclusive population in the normative sample and no norms have yet been developed for countries other than the United States (Acton et al., 2011).

Assessment of EF in young children initially relied on the simplification of adult assessments to create a range of developmentally sensitive assessments appropriate for the different stages of EF development observable in preschool children (S. M. Carlson, 2005; Diamond, Carlson, & Beck, 2005). Hence, at 24 months inhibition of prepotent responses can be assessed by sorting coloured blocks of different sizes into buckets of different sizes and the Stroop task will employ shapes such as fruit rather than words in coloured font (S. M. Carlson, 2005). This simplification of tasks has also allowed the development of tests more likely to assess a single process of executive function, thereby avoiding some of the initial problems caused by convergent processes (Hughes & Graham, 2008). To date preschool EF assessments have not been standardised. However, data are available on comparative task difficulty by age (S. M. Carlson, 2005). Standardised assessment of EF via parent report is also available from the Behaviour Rating Inventory of Executive Function – Preschool Version (BRIEF-P) (Gioia, Espy, & Isquith, 2000). Developmentally sensitive, standardised assessment measures are being developed for the collection of longitudinal data which will make possible the gathering of developmental data for individual children and longitudinal cohort studies (S. M. Carlson & Schaefer, 2012; Tulsky et al., 2013; Zelazo et al., 2013). Computer-based assessment

and “game-like” touch screen versions of preschool EF assessment have recently been developed (Baron, Kerns, Muller, Ahronovich, & Litman, 2012; Zelazo et al., 2013).

Imaging investigations have supplemented standard psychometric testing and found neuropsychological differences in the absence of observable assessment differences (Hackman & Farah, 2009). MRI studies are similarly adding to understanding of developmental changes in cerebral structure and function (Casey, Giedd, & Thomas, 2000) particularly in the area of cerebral injury as a result of neonatal events such as hypoglycaemia (Burns et al., 2008; Inder, 2002) where injuries may not be detectable by other means (Kinnala et al., 1999). Electroencephalographic (EEG) studies have elucidated cerebral structure and function relationships and have shown that SES differences may result in different cerebral function even though psychometric performance showed no difference between individuals (Hackman & Farah, 2009). These differences highlight the potential importance of a multifaceted approach to assessment, especially where clinically relevant (Aylward, 2002b; Inder, 2002; Woodward, Anderson, Austin, Howard, & Inder, 2006).

1.12. The Waikato district and population

The Waikato District Health Board (WDHB) provides health services to the Waikato region, which encompasses approximately 21, 220 km^2, or 8% of New Zealand’s total land area, including Waikato Hospital, a 600 bed regional base hospital within a network of community hospitals and clinics. The population of the Waikato region is approximately 339,200 people, or 8% of New Zealand’s population, with a greater proportion of the Waikato population living in rural areas than is found in other regions of New Zealander (Waikato District Health Board, 2010a).

A higher proportion of the Waikato population identify as Māori in comparison to New Zealand’s total population (19% compared with 13%). However, the Pacific population is lower than in the rest of New Zealand (3% compared with 6.4%). The population of the Waikato region is ethnically diverse with more than 20 nationalities represented with a total of 4% of the population being composed of refugees and new migrants (Waikato District Health Board, 2010a). More than 50% of the Māori population is below 24 years of age; a much higher proportion than any other nationality (Waikato District Health Board, 2010a).

Four of the ten territorial authorities in the Waikato region have more than half of their populations living in areas with NZDep scores of 7 – 10. Furthermore, NZDep scores between 7 – 10 include those of Māori and Pacific ethnicity, children between 0 – 14 years and adults over 65 years at a disproportionate rate (Waikato District Health Board, 2010b). Thirteen towns and urban centres in the Waikato district have been identified as having more than 80% of the population living in areas with NZDep scores of 7 – 10 (Waikato District Health Board, 2010b).

Several chronic health conditions are reportedly higher in the Waikato region than in New Zealand as a whole. Census data for 2006 showed that 19.9% of New Zealanders smoked although 22% of the Waikato population smoked. This figure is higher for Māori, especially Māori female. Obesity rates in

New Zealand are increasing and in the 2002-2003 NZ Health Survey were reported as 20.1% in the country overall. However, in the Waikato region the prevalence of obesity is 22.7%. These figures are higher for Māori (31.5%) especially Māori men (33.5%). Total diabetes rates are similar in the Waikato region to the rest of New Zealand (approximately 4.0%). However, there is an increased rate for Māori (approximately 8.0%) and a disparity for Māori men where the national rate is 9.5% but in the Waikato region it reaches 12.3%. The mortality rate for diabetes is higher in the Waikato region and is six times higher for Māori than for non-Māori (Waikato District Health Board, 2010b).

1.13. Summary

Neonatal hypoglycaemia is a common and potentially serious problem for the newborn (Cornblath, 1997) and is known to cause adverse developmental outcomes (Koh, Aynsley-Green, et al., 1988; Lucas et al., 1988). However, controversy still exists over the definition and appropriate operational thresholds for treatment (W. W. Hay, Jr. et al., 2009). The discrepancies in definition first highlighted in Koh's 1988 survey of paediatricians and textbooks (Koh, Eyre, et al., 1988) have been largely replaced with a definition of hypoglycaemia as blood glucose concentration < 2.6 mmol/L. However, not all babies become symptomatic at this concentration (Koh & Vong, 1996) and the uncertainties surrounding the definition are still evidenced clinically by a wide range of treatment responses (Boluyt et al., 2006; D. L. Harris et al., 2009). Uncertainty also exists over whether detrimental effects of hypoglycaemia are caused by the frequency, severity or duration of low blood glucose concentration (Cornblath et al., 2000). Further uncertainty has been created by the number of different techniques used to determine glucose concentrations and the different types of samples used (Boluyt et al., 2006).

In normal term babies the blood glucose concentration decreases over the first 1 to 2 hours after birth during the time that the metabolic processes required for independent life are stabilising (Srinivasan et al., 1986). However, infants of diabetic mothers are at increased risk of hypoglycaemia because of elevated levels of insulin experienced *in utero* (Hawdon & Aynsley-Green, 1994) and preterm babies are at increased risk of hypoglycaemia because of their immature metabolic processes and low level of stored glucose and glycogen. Similarly, babies born after intra-uterine growth restriction or small for gestational age may also be at risk (Armentrout & Caple, 1999). Introducing early feeds and breast feeding appear to be protective against adverse neurodevelopmental outcomes (Ward Platt & Deshpande, 2005).

Early reports of the developmental sequelae of neonatal hypoglycaemia included convulsions (Cornblath et al., 1964) cerebral palsy, developmental delay (Lucas et al., 1988) and even death (Norval et al., 1949). However, neonatal hypoglycaemia is frequently asymptomatic (Koh, Aynsley-Green, et al., 1988) and may be difficult to detect clinically (D. L. Harris et al., 2010). The clinical approach to assessing blood glucose concentration is inherently a potential source of error as timing of sampling may miss periods of hypoglycaemia. Continuous glucose monitoring, which has been shown to be reliable for use with newborn babies at risk for hypoglycaemia, indicates that there are

many more periods of hypoglycaemia in the first week of life than are identified by standard clinical assessments (D. L. Harris et al., 2010).

The developmental significance of the frequency, severity and duration of neonatal hypoglycaemia in different at-risk groups of babies is not known. To assess the significance of these measures of hypoglycaemia in the neonatal period it is necessary to collect longitudinal data from babies whose neonatal glycaemic status was comprehensively recorded. Such a study needs to be of prospective design with methodology to adequately answer the study questions (Boluyt et al., 2006; W. W. Hay, Jr. et al., 2009). Medical procedures need to be clearly defined and the data need to be analysed in a timely fashion to ensure relevance (Aylward, 2002b).

Neuropsychology, imaging techniques and observational psychology have contributed to our understanding of the complex nature of fetal and infant development (Albright et al., 2000; Hackman & Farah, 2009; Inder, 2002). Neuroimaging studies are informing a growing understanding of the brain regions associated with different aspects of EF and simultaneously emphasising the complexity and interdependence of the neural networks involved (Aron, 2008; Rabbitt, 1997). The results from neuropsychology mirror developmental understanding of the ontogeny of cerebral development such as the reliance of attentional control tasks on short term memory (Espy & Bull, 2005). Longitudinal studies of at-risk babies have provided information about the developmental consequences of adverse environments (Poulton et al., 2002) and disturbances to normal development (P. J. Anderson et al., 2011; Engle et al., 2007; Woodward et al., 2005). The development of techniques which allow for the assessment of separate aspects of EF in young children has contributed further to our understanding of developmental processes.

The uncertainty that exists as to the cause of adverse developmental sequelae that can result from neonatal hypoglycaemia and our increased understanding of child development and neuropsychology can direct future research to an appropriately designed, prospective, longitudinal study (W. W. Hay, Jr. et al., 2009). The study we are undertaking is a follow-up at 2 years of a cohort of 600 babies born at risk of neonatal hypoglycaemia. The objective is to determine neurodevelopmental outcome in a cohort of children born at risk of neonatal hypoglycaemia. The prospective design has allowed for the collection of clinical neonatal data in addition to 2 year developmental data. Therefore, we will be able to relate neonatal glycaemic status to the results of developmental assessment.

Chapter 2. Methods

2.1. Introduction

The aim of this study is to investigate the neuropsychological development of young children who were identified around the time of birth as being at risk of developing hypoglycaemia. In addition, we aimed to develop a battery of assessment tasks to assess EF within this cohort.

2.1.1. Study hypothesis

The study hypothesis is that the neuropsychological development of 2 year old children will be better for those whose glucose concentrations were above, in comparison to those whose glucose concentrations were below, 2.6 mmol/L in the neonatal period.

2.1.2. Specific aims

1. To examine relationships between the assessed developmental indicators at 2 years of age and demographics and family characteristics, and health and medical history.

2. To determine the neurodevelopmental outcomes at 2 years of age of children who were identified as being at risk of hypoglycaemia in the neonatal period. Specific outcomes will include:

- Cognitive processes such as concept formation, object relatedness and play development
- Receptive and expressive language ability
- Gross and fine motor skills
- Social and emotional development and communication skills
- Adaptive behaviour
- Executive function including inhibition, attention, working memory and cognitive flexibility

2.2. Ethics

Ethical approval was gained from Northern Y Health and Disability Ethics Committee following consultation with the Kaumātua Kaunihera Research Sub-committee at Waikato Hospital. Ethics Reference: NTY/10/03/021.

2.3. CHYLD Study cohort – The neonatal studies

Participants in the CHYLD Study were the babies who were recruited into one of two clinical studies after being identified as being at risk of neonatal hypoglycaemia: either the BABIES (December 2006 – February 2009) or Sugar Babies (November 2008 – November 2010) studies. Most babies were recruited to one of these two studies antenatally, although a small number were recruited neonatally.

Children were assigned a primary risk factor at birth on the basis of clinical judgment as to the strongest risk predisposing the baby to neonatal hypoglycaemia. Risk factors for hypoglycaemia included:

- Infant of a diabetic mother (IDM)
- Large (≥ 90th percentile or ≥ 4500g)
- Small (≤10th percentile or ≤ 2500g)
- Pre-term (< 37 weeks gestation).
- Other (including poor feeding, sepsis, pre-eclampsia)

Using a hierarchical allocation, infants of diabetic mothers were assigned IDM as their primary risk, then preterm babies were assigned this as their primary risk. Further risk factors were small, large and other. Birth weight percentiles were calculated based on Australian data (Kitchen, Robinson and Dickinson, 1983).

In both neonatal studies hypoglycaemia was defined as a blood glucose concentration < 2.6 mmol/L and was measured by regular heel prick assessment. Blood samples were analysed on a blood gas analyser using the glucose oxidase method. Glucose concentration was also recorded by continuous glucose monitor (CGMS® system gold ™ Medtronic, MiniMed, Northridge,CA, USA) which was attached to the thigh with a small probe inserted subcutaneously. The probe remained in place for 2 to 7 days. The CGMS did not provide a real time read out, meaning that data collected this way did not influence clinical practice. All babies were managed according to standard clinical guidelines and most were breastfed. Babies were not eligible for enrolment if they had a serious congenital abnormality, or a skin condition which meant the continuous glucose monitor could not be attached.

The aim of the BABIES study was to assess the validity and usefulness of CGMS and its relationship with EEG in babies born at risk of neonatal hypoglycaemia. A total of 102 babies born ≥ 32 weeks gestation, and admitted to NICU were recruited to this study. They remained in the study with CGMS monitoring until no longer at risk of hypoglycaemia or a maximum of 7 days.

The Sugar Babies study was a randomised clinical trial designed to assess the efficacy of 40% dextrose gel treatment for babies identified as having hypoglycaemia. A total of 514 babies born ≥ 35 weeks gestation and less than 48 hours old were enrolled in this study. They remained in the study for 48 hours. One half of the babies became hypoglycaemic and were randomised to treatment with either dextrose gel or placebo.

2.4. The recruitment process

Children were assessed at 24 ± 1 months of age. Children born at less than 37 weeks' gestation were assessed and scored according to their corrected age. Approximately 3 months prior to each child's second birthday the family was contacted to discuss recruitment to the CHYLD Study. Initial contact was via a letter and information sheet which was sent to the family at the last known contact address. In some instances families made contact with the Study team via the 0800 number or the e-

mail address to express interest in taking part. Other families were contacted by phone and offered an opportunity to ask questions about the study and the research process. We employed a Māori research nurse to assist with the recruitment and assessment of Māori families. Families who were willing to take part were offered an appointment at that stage or during a second phone call if they preferred to have time for discussion with family/whanau. The Home and Family Questionnaire (Appendix A) was sent with the appointment letter to be completed prior to the assessment.

Families who had changed address were traced through the National Health Identifier (NHI) database, next of kin or General Practitioner (GP).

2.5. CHYLD Study cohort – Exclusion criteria

Children born at less than 35 weeks gestation or older than 25 months at the start of the CHYLD study were excluded from follow-up at 2 years.

2.6. The Assessment Process

2.6.1. Assessor training

The developmental assessments were all conducted by assessors who had been trained to reliability in the Bayley III and EF assessments and were blind to neonatal hypoglycaemic status. Reliability is defined as an experienced stage of assessment whereby the practitioner is able to perform an assessment in accordance with the protocol, with a high degree of inter-rater reliability, as determined by video review by an experienced trainer. This quality assurance process resulted in minimal differences between assessors, and allowed the assessed child to display their best achievement in each domain.

2.6.2. Consent

Written consent was obtained from a parent or legal guardian prior to each assessment.

2.6.3. Video review

Wherever possible, and with written parent consent, the full developmental assessment was recorded on video. This allowed assessment review for quality assurance, scoring verification by the assessor and assisted decision making if an onward referral was indicated. Reasons for onward referral included a Bayley III score in the borderline range (score < 70) on any of the scales, or moderate concern (score < 80) over several domains.

2.6.4. Assessment feedback

Families were provided with a brief written summary of assessments and outcomes and with parent consent a copy was forwarded to their GP. Incidental findings or developmental concerns were discussed with the parents prior to appropriate onward referral, typically via the family GP.

2.6.5. Assessment locations

The majority of families lived within the greater Hamilton area and assessments for these families were conducted at Waikato Hospital or at Kahikatea Research House which was a designated CHYLD Study research facility (Table 2.1). Families living outside Hamilton who could not easily travel to Hamilton were either assessed at a regional hospital outpatient clinic, or were flown to Auckland for assessment at a University of Auckland research clinic. Home assessments were conducted if no other options were practicable. However, these were avoided if possible as control of external distractions was more difficult.

Table 2.1: Summary of locations of CHYLD study developmental assessments completed by each assessor

Assessor	Hamilton Outpatient Clinics	Kahikatea Research House	Tokoroa Hospital	Tauranga Hospital	Auckland University	Thames Hospital	Other Clinics	Home Visits	Total
100	51	6	16	6	5	-	13	1	99
101	23	1	4	3	1	6	4	10	52
102	114	56	-	-	-	-	-	-	170
103	14	3	-	-	-	-	-	-	17
105	14	10	1	-	2	8	1	5	41
106	-	25	-		-	-	-	-	25

Assessor 100 = Judith Ansell (Author); assessors 101 – 106 = trained assessors employed by the CHYLD study

2.7. Working with 2-year-olds

Assessments were scheduled to begin as early as practicable in the morning, whenever possible, and to avoid regular nap times. The assessments were presented in a standard order with breaks as required to maintain toddler cooperation and interest.

2.8. The assessment schedule

The majority of assessments followed a standardised schedule with Bayley III assessment conducted first, followed by the EF assessment (Table 2.2). The caregiver accompanying the child completed

the Bayley III Social-Emotional and Adaptive Behaviour questionnaires and the BRIEF-P in the assessment room while the assessment was being conducted.

The developmental assessment was typically conducted on the same day as the optometry and paediatric assessments. Approximately half of the developmental assessments occurred before and half after the optometry assessment.

Table 2.2: The 2 year assessment schedule in typical order

Assessment	Domains assessed	Details
Bayley Scales of Infant and Toddler Development – 3rd edition (Bayley III)	Cognitive	Reasoning, problem solving, imagination
	Language	Receptive and Expressive communication
	Motor	Fine and Gross Motor skills
	Adaptive Behaviour Questionnaire*	Daily Functional Skills
	Social-Emotional Questionnaire*	Social- Emotional development
Executive Function (EF)	Inhibition	Snack Delay
	Attention & inhibition	Fruit Stroop
	Working memory & cognitive flexibility	Ducks
	Working memory	Multisearch Multilocation
BRIEF-P*	Behavioural manifestations of EF	Parents quantify, on a 3 point scale, the extent to which behaviours have been a problem in the previous 6 months: often, sometimes, never
Home and Family Questionnaire*	Family demographic, health and socioeconomic information (prior to assessment)	Parent age, health, education, socio-economic indicators, drug and alcohol use. Child health, sibling numbers, preschool education

* Parent questionnaire

2.9. The Bayley Scales of Infant and Toddler Development – 3rd edition (Bayley III)

The Bayley Scales of Infant Development has been the most widely used and reported developmental assessment since the first version was released in 1969 (P. J. Anderson et al., 2010; T. Moore, Johnson, Haider, Hennessy, & Marlow, 2012). These scales were designed to assess developmental functioning in infants and young children between 1 and 42 months of age, with the primary aim being to identify developmental delay (Bayley, 2006). A revised and re-standardised second version was released in 1993 and has been used extensively in clinical and research populations, particularly in at-risk populations (Acton et al., 2011; P. J. Anderson et al., 2010; Freeman Duncan et al., 2012; B. J. Woodward et al., 2011). In 2006 a revised version of the Bayley scales, the Bayley Scales of Infant and Toddler Development (Bayley III), was released and included a number of changes including the use of 5 separate developmental scales: cognitive, language (receptive and expressive subtests) and motor (fine and gross subtests), along with social-emotional and adaptive behaviour scales in the form of parent questionnaires (Bayley, 2006). The Bayley III assessment can be administered in any order, but was typically administered as described in Table 2.2.

2.10. Executive Function

2.10.1. Introduction

Assessment of toddler EF is a relatively new domain within developmental psychology and most direct assessments are yet to be standardised (S. M. Carlson & Schaefer, 2012; Diamond, 2013; Zelazo et al., 2013). However, analysis of increasing EF task competence with age amongst preschool children has previously identified age appropriate EF tasks for children as young as 24 months (S. M. Carlson, 2005; Diamond, 2013; Kochanska, Murray, & Harlan, 2000). These tasks assess different aspects of EF and have different probabilities of success (S. M. Carlson, 2005). We aimed to construct a battery of tasks which would assess different aspects of EF and show a range of success rates within the cohort.

Our battery of four EF tasks was developed to include age-appropriate tasks which would provide a range of difficulty, reflecting a span of abilities in each task, thereby providing discrimination and avoiding floor or ceiling effects (Table 2.3). They were based on previously reported assessments (S. M. Carlson, 2005; Kochanska et al., 2000; Woodward et al., 2005; Zelazo, Reznick, & Spinazzola, 1998) although two tasks were modified for portability and increased toddler appeal. The four tasks were offered in a standard order and a standardised script was used (Appendix B). In addition to the four direct assessment tasks, EF was assessed via parent report using the Behaviour Rating Inventory of Executive Function – Preschool version (BRIEF-P) (Gioia et al., 2000).

A scoring schedule was created for the assessments with all tasks being accorded a similar maximum score (range of 6 to 12). This allowed the creation of a combined EF Total score in which all tasks had a similar weighting with a maximum score of 35.

Each of the tasks began with a training task in order to familiarise the child with the task and to assess language competence. Failed trials were recorded and coded differentially to reflect insufficient language or poor behaviour, including refusal. Assessor error was also recorded.

Table 2.3: Assessed EF tasks in order of presentation, showing domains assessed and scoring

Task order	Task	EF Domain	Reference	Maximum Score
1	Snack Delay	Inhibition	Kochanska et al (2000); Carlson (2005)	8
2	Fruit Stroop	Attention, inhibition	Kochanska et al (2000); Carlson (2005)	6
3	Ducks - Reverse Categorisation	Working memory, cognitive flexibility	Carlson et al (2004); Carlson (2005)	12
4	Multisearch Multilocation (MSML)	Working memory, cognitive flexibility	Zelazo (1998)	9

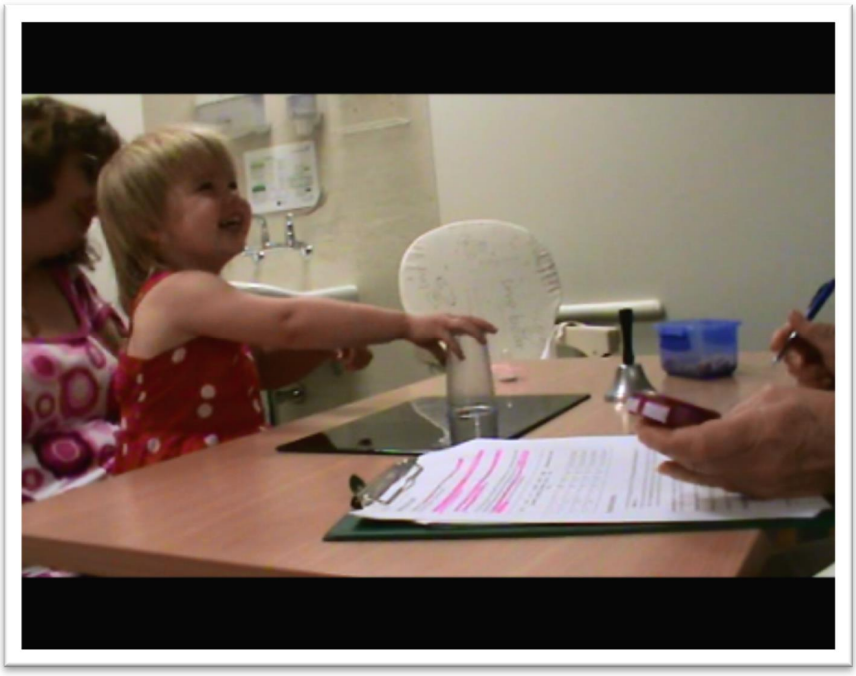
2.10.2. Snack Delay

Equipment: 1 small black mat, a clear plastic cup, food treats, stopwatch, hand bell

Description: The Snack delay task is an assessment of a child's ability to inhibit a prepotent response. In this task the prepotent response is to retrieve the treat, without waiting as instructed.

Method: During the training phase a treat was placed on the mat underneath the upturned cup and the child was encouraged to retrieve it (Fig 2.1). If the criterion of two successful training trials was met, the task instruction of waiting for the bell to be rung before retrieving the sweet was explained to the child. This instruction was repeated between trials. The delay imposed increased with each trial through four trials of 5, 15, 30 and 45 seconds delay.

Figure 2.1: The Snack Delay task



Possible outcomes are:

1. Full wait: Waiting until the bell is rung before lifting the glass and retrieving the treat
2. Partial wait: Lifting or touching the glass, but not the treat, prior to the bell being rung
3. Failed trial: Retrieving the treat or ringing the bell prior to the bell being rung by the assessor

Outcomes were recorded immediately and the assessment continued until all 4 trials were completed or until the first failed trial. Full credit (2 points) was given for each full wait and half credit (1 point) for each partial wait. No credit was given for a failed trial and if failure occurred on the first trial it was recorded as 0 seconds. This 3-tiered points schedule is similar to the original assessment design (Kochanska, 2000) and reflects differential task achievement.

2.10.3. Fruit Stroop

Equipment: Fruit Stroop cards: 1. Cards of big and little apple, orange, banana (Fig 2.2); 2. Cards of big fruit with different little fruit embedded (Fig 2.3)

Description: The Fruit Stroop is an assessment of attention and inhibition. There are no training trials. However, there is a language check during which the child is asked to identify the fruit as they are named. Feedback is provided at this stage for a correct or incorrect response. The child then needs to both attend to the task of finding the little fruit and to inhibit their previous response, which was to point to each big fruit in turn when asked to do so.

Figure 2.2: Fruit Stroop cards showing big and little fruit

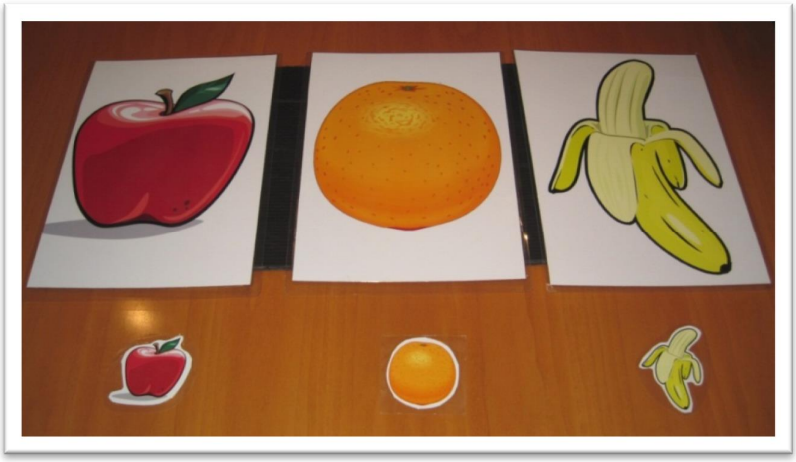


Figure 2.3: Fruit Stroop cards showing big fruit with embedded little fruit

Method: The child was asked to point to each of the little fruit in turn (fig 2.3). Responses were recorded and no feedback was given during the trial.

Scoring for this assessment was a 3-tiered scoring system similar to the original (Kochanska, 2000) and the same as Carlson (2004). Full credit (2 points) was given for each correct response and part credit (1 point) was given if the child attempted to respond correctly and pointed to the big fruit. No credit was given for no or an incorrect response. Separate subset data were presented for 'little apple' responses.

2.10.4. Reverse categorisation (Ducks)

Equipment: 2 children's plastic buckets (1 big, 1 little); 3 little plastic ducks; 3 big plastic ducks

Description: The Ducks task is a two-part task requiring categorization (sorting) of large and small ducks followed by a reverse categorisation task. This is an assessment of working memory, cognitive flexibility and inhibition (Carlson, 2012). It is based on earlier reverse categorisation tasks that used large and small blocks (Carlson, 2005) and was modified for greater appeal to toddlers.

Method: In the training trial of the categorisation task the child was taught to put the big duck in the big bucket and the little duck in the little bucket. Following this there were two rule check trials, one each for big and small, with feedback. In the categorisation task the child was asked to sort a pseudorandom assortment of 3 large and 3 small ducks. Responses were recorded. The criterion for proceeding to the reverse categorization was for the child to correctly sort at least five ducks in the categorization task. Reverse categorization was introduced as a "silly game" in which the big ducks were to go into the little bucket and little ducks into the big bucket. There were two rule check trials

again, during which feedback was provided. The child was asked to reverse sort a pseudorandom assortment of 3 big and 3 little ducks. Carlson (2004) used the proportion of correctly sorted items in the reverse categorisation task as the task score. However, we used a simple scoring system of 1 point for each duck correctly sorted in each part of the assessment, which was more appropriate to the lower success rate we found in our cohort.

Figure 2.4: The categorisation (Ducks) task

2.10.5. Multisearch Multilocation (MSML)

Equipment: 3 drawer MSML equipment; food treats; stopwatch

Description: The MSML task is an assessment of working memory and cognitive flexibility and is an adaptation of Piaget's A not B task (Zelazo, 1998). This task uses a three drawer apparatus to allow assessment of perseverative and non-perseverative errors (Zelazo, 1998). However, modification to a light–weight version was made to create a portable test kit. The apparatus consists of 3 plastic drawers attached to a solid base with a sheet of black felt, large enough to cover the equipment, attached to the board (Fig 2.5).

Elsewhere, a fourth step of removing a barrier has been used with different apparatus (Zelazo, 1998). This fourth step was considered too difficult for very pre-term 2-year-olds who have increased difficulty with some new motor skills (Woodward et al., 2005). Pilot study assessments using similar

apparatus as that used by Zelazo (1998) with a four step process also proved difficult for many of our study children and hence a 3 step process was used.

Method: The MSML task began with training trials during which a food treat was put into the middle drawer, to which a black diamond shape was attached (Fig 2.5). The black felt cover was put over the drawers and the apparatus was then put in front of the child. The assessor told the child there was a treat, demonstrated lifting the black felt, and encouraged the child to open the correct drawer to retrieve the treat. The criterion to proceed to the pre-switch trials was that the child was not excluded for language or behaviour reasons and that after three training trials the child was able to retrieve the food treat without assistance. Training trial outcomes were recorded as success, partial success or fail.

Following training, the black diamond shape was removed and 3 different shapes were attached in a standard order: from the child's left: a yellow circle, blue triangle and green square (Fig 2.6). The first set of trials constituted the pre-switch condition in which the food treat was always hidden in the middle (blue triangle) drawer. The child watched the treat being 'hidden' and was encouraged to retrieve it.

A successful trial was recorded if the child found the treat on their first attempt. If the child opened an incorrect drawer the equipment was withdrawn and a failed trial was recorded. The correct drawer was then opened to reveal the treat and the instructions were repeated. Pre-switch trials continued until the child achieved three consecutive correct trials, which was the criterion for progressing to the post-switch phase, or until six trials were attempted. Failure to respond after 30 seconds was a failed trial.

The post-switch phase was introduced as a "silly game" and the child was encouraged to watch as the food treat was hidden in the green square drawer. A 10 second delay was imposed before the child was presented with the drawers and encouraged to find the treat. Possible outcomes were:

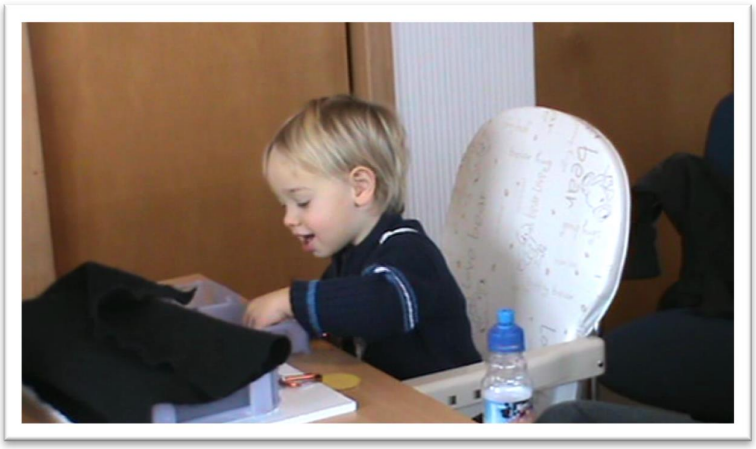
1. Post-switch success: retrieving the treat at the green square drawer
2. Perseverative error: unsuccessfully searching at the blue diamond
3. Non-perseverative error: unsuccessfully searching at the yellow circle

Trials continued until the child had correctly searched on two consecutive trials, or until eight trials had been attempted.

Figure 2.5: The MSML drawers (training mode)

Figure 2.6: The MSML drawers (Pre-switch trial)

Figure 2.7: A 2 year old during the MSML assessment



Scoring was designed to reward correct and efficient searching with fewest attempts. Scores for correct pre-switch searching had a range of 1 to 3 and post-switch searching a range of 1 to 6. Pre-switch success scores indicate the ease with which the child learnt the task and thereby functioned as a proxy for a timed training period as has been used elsewhere (Woodward, 2005). Carlson et al (2004) recorded the number of post-switch perseverative errors which were then reverse scored in analyses. However, assigning a scoring schedule of our design has allowed a meaningful MSML score to be included in the Global EF score.

2.10.6. Behaviour Rating Inventory of Executive Function – Preschool version (BRIEF-P)

The BRIEF-P (Gioia et al., 2000) is a standardised preschool assessment that measures parent report of EF-related behaviour. Questions relate to five scales which combine to produce three indexes and a Global Executive Composite score (Table 2.4). The mean T-score is 50 (10), with higher scores indicating poorer outcome and T-scores greater than 65 indicating potential clinical significance. The BRIEF-P was designed to add ecological validity to assessed EF.

The BRIEF-P has separate standardised scoring for two age bands: 2 & 3 and 4 & 5 year old children; and for girls and boys.

Table 2.4: BRIEF-P scales and indexes and behaviours assessed by each

Scale/Index	Name	Description of behaviour assessed
Scales		
	Inhibit	Inhibitory control and impulsivity
	Shift	Flexibility, ability to change activities as needed
	Emotional Control	Control of emotions and emotional responses
	Working Memory	Holding information in mind to use/manipulate it
	Plan/Organise	Anticipating requirements and completing goal
Indexes		
	Inhibitory Self-control Index (ISCI)	Inhibit plus Emotional Control scales
	Flexibility Index (FI)	Shift plus Emotional Control scales
	Emergent Metacognition Index (EMI)	Working Memory plus Plan/Organise scales
Total		
	Global Executive Composite (GEC)	Combined score from all 5 scales

2.11. Vision Assessment

Included in the battery of vision assessments was an assessment of dorsal visual stream functioning using a computerised random dot kinetogram assessed by optokinetic reflex (OKR). OKR is a psychophysical measure of motion detection that doesn't require a behavioural or cognitive response and has been shown within the CHYLD study to be appropriate for use in 2-year-olds (Yu et al., 2013). OKR is the brief automatic tracking of motion before the eyes return in a saccadic motion to their original position. Random dot kinetograms have two sets of dots, one moving randomly and the other moving coherently in one direction. There is individual variation in the ability to detect movement direction as the proportion of dots moving coherently in one direction is changed. The lowest level at which an OKR was observable in at least 63% of trials presented to a child was defined as their OKR threshold. This OKR threshold was used as a measure of an aspect of dorsal stream function, allowing us to investigate associations between this aspect of visual processing and our measures of EF.

2.12. The Home and Family Questionnaire

The Home and Family Questionnaire was used to collect contact information and alternative contact details via a perforated first page which could be removed and stored separately to ensure confidentiality of the remaining data. Family data reported in the literature to be associated with child development were also collected. Socioeconomic data collected included parent education, employment, income, home and car ownership, ethnicity, language(s) spoken at home and preschool attendance. Health data pertaining to the child were collected and included breastfeeding, hearing, ear infections and grommets, hospitalisations, and specialist referrals. Data were also gathered on maternal prescription drug use during pregnancy, and tobacco, alcohol and other drug use by parents and other household members.

Ethnicities were recorded in accordance with the 'total response' ethnicity classification (Ministry of Health, 2004a), meaning that families were able to nominate multiple ethnicities. These were then prioritised for summary with any nomination of Māori ethnicity resulting in Māori as the primary category, and New Zealand European (NZE) as the primary category for all other multiple nominations in which NZE was included. Broad categories were created to include all Pacific island ethnicities as Pacifica, central and South-East Asian as Asian, and the remainder, if none of the above categories were nominated, as Other. We did not include Other with European as is frequently done in health reporting (Ministry of Health, 2008b) as this category included children recently arrived from African and Middle Eastern countries.

2.13. The Data

2.13.1. Data collection and scoring

Direct assessment data were collected by the assessors during the assessment on standard Bayley III forms and in the CHYLD Study EF booklet. Assessment scoring was completed immediately after the assessment. Calculation of the EF global score was performed from raw data within SAS (SAS Institute Inc., Cary, North Carolina, USA). The Bayley III Adaptive Behaviour and Social-emotional questionnaires, and BRIEF-P were completed by the caregiver during the assessment period. The Home and Family questionnaire was completed prior to the assessment by the primary caregiver, typically the child's mother. The questionnaires were collected and checked by the assessor or research nurse at the assessment. If clarification was needed or questions required completion this was done at the assessment.

2.13.2. Data checking

A Bayley III report was generated for each child using the Bayley III Scoring Assistant (Bayley, 2006) report writer software. At this stage the child's date of birth, gestational age, corrected age, and assessment scoring were double checked by another assessor. EF protocol adherence and scoring was also double checked.

2.13.3. Data entry

Bayley III and EF data was double-entered into an Access™ (Microsoft) Database. The BRIEF-P data was entered into an Access™ (Microsoft) database designed to calculate scale and index scores from the raw data.

2.14. Statistical Analysis

2.14.1. Statistics software

Data were analysed using JMP statistical software (version 9.0.2; SAS Institute Inc., Cary, North Carolina, USA). Results are presented as mean (SD), median (interquartile range) or number (%).

2.14.2. Bayley Scales of Infant and Toddler Development III

Bayley III mean scores and standard deviations for each of the scales and subscales were compared with the standardised test scores using a one-sample *t*-test.

Continuous data were compared between groups using one-way Analysis of Variance (ANOVA) with Tukey's HSD post-hoc correction for multiple comparisons. Interactions were assessed using multiple regression.

Data pertaining to SES was recoded to reduce the number of categories and create a more even spread between categories. Household income, NZDep2006 and maternal and paternal education were thus reduced to 3 categories each: high, medium and low. Household income was grouped as: 1. ≥ $70,001, 2. $70,000 - $40,001, 3. ≤ $40,000. NZDep2006 deciles were grouped as: 1. Deciles 1 – 3, 2. Deciles 4 – 6, 3. Deciles 7 – 10. Parent reported highest education level was grouped as: 1. University education, 2. Post-secondary training such as trade certificate or Polytechnic, 3. Secondary education or less. The number of hours per week of preschool attendance was recoded to create 2 categories: ≤ 20 h/wk (n=71) and > 20 h/wk (n=76).

We used multiple regression to develop a model of SES, which incorporated 2-year NZDep2006 deciles, household income and home ownership. This model was used to adjust for SES, as appropriate in subsequent analyses. Relationships between SES and developmental outcome were explored using linear regression, and interactions tested for using multiple regression analysis.

2.14.3. Executive Function assessment

Distribution of the assessed EF tasks and BRIEF-P scores were skewed (Gioia et al., 2000). However, results did not change substantially when non-parametric analyses using log-normal scores were performed and compared with parametric analyses. Results were therefore reported as mean (SD) rather than median (95% CI) as it allowed for easier comparison with the standardised results reported in the BRIEF-P manual and other research reports, and allowed for comparison of absolute differences after adjustment.

Assessed EF scores were calculated and separate task scores were combined to give the EF Total score. In addition, cohort success rates were calculated for each task with children assigned a single rating according to their maximum success. Snack Delay success was divided into four groups: 0 seconds (failure), 5, 15, ≥ 30seconds. Fruit Stroop success rates were divided into three groups for the total number of correct small fruit identifications made. The Ducks success rates were divided into four groups: < 5 ducks correctly sorted, 5-6 ducks correctly sorted, 1-2 ducks correctly reverse sorted, and ≥3 ducks correctly reverse sorted. MSML success rates were a binary outcome in each of two groups: pre-switch success and post-switch success. Chi-square analyses were performed on these ratings and presented as success rates (N, % of cohort).

Rates of clinically significant scores on BRIEF-P T scores were analysed using chi-square after scores were recoded to a binary format (< 65/≥ 65), which is the level at which T-scores are considered to be potentially clinically significant (Gioia et al., 2000). The BRIEF-P includes Inconsistency and Negativity scales which allow an assessment of the validity of responses. Calculation of these scores resulted in no data being removed from the data set.

Linear regression was performed to calculate correlations.

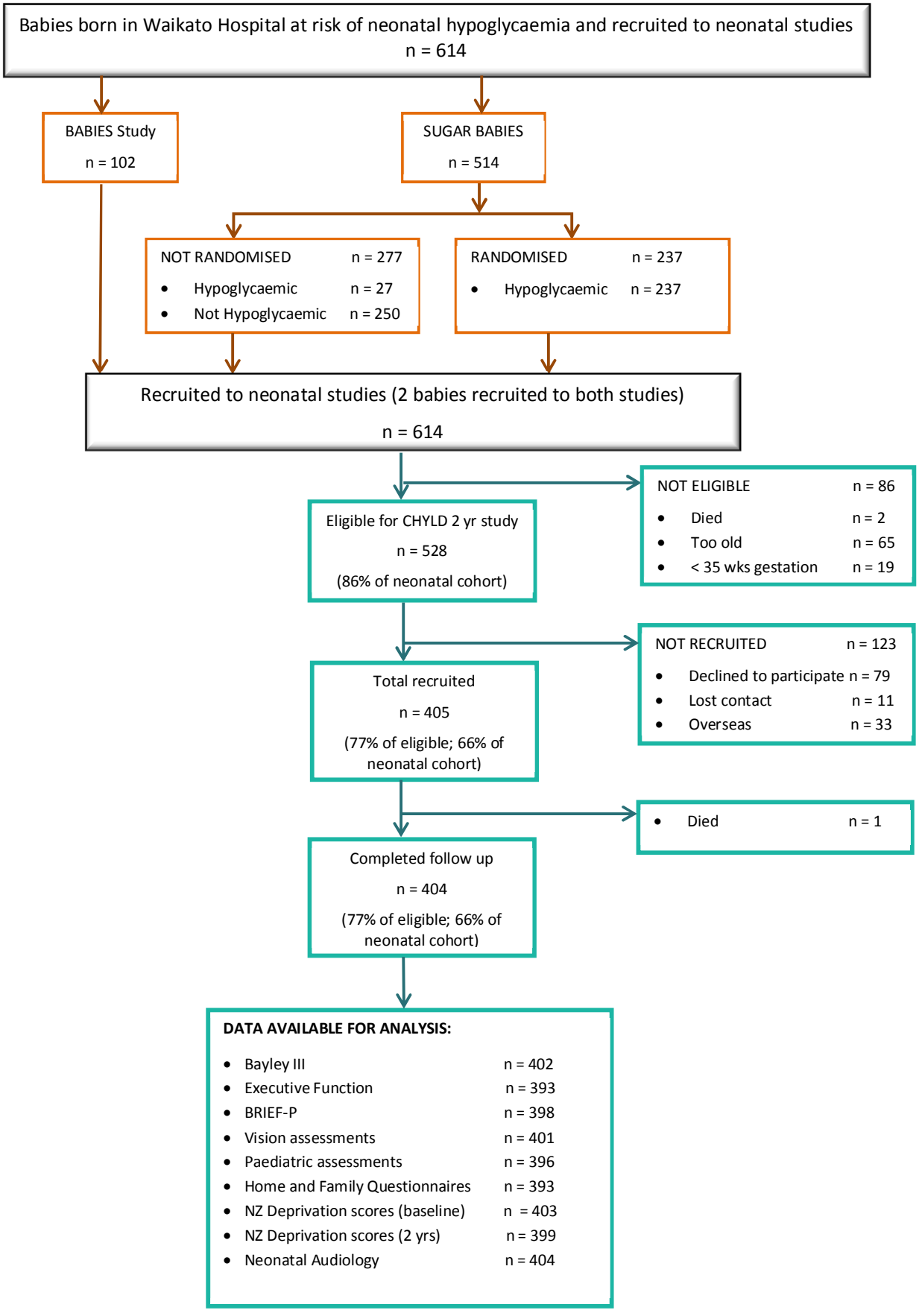
Chapter 3. The CHYLD Study cohort

3.1. The CHYLD Study cohort

The Children with Hypoglycaemia and their Later Development (CHYLD) Study is a follow-up at 2 years of 614 children born at risk of neonatal hypoglycaemia at Waikato Hospital, Hamilton, New Zealand. These children were recruited to either the BABIES or Sugar Babies studies and are described here in accordance with the international guidelines from the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) group (Vandenbroucke et al., 2007; von Elm et al., 2007)(Fig 3.1).

Of the 614 children recruited to the neonatal studies, 86 were not eligible because they were born at less than 35 weeks' gestation or were more than 25 months old at the time of enrolment. The remaining 528 (86%) eligible babies included 44 who were not available (lost or overseas) and 79 whose families declined participation, leaving 404 (77%) who were successfully recruited. The majority of these children completed the full battery of assessments (Fig 3.1).

Figure 3.1: CHYLD Study STROBE statement



3.2. CHYLD Study cohort description

The CHYLD cohort did not differ significantly from the neonatal cohort with respect to family SES, measured as NZDep2006, maternal age, parity, ethnicity or gender (Table 3.1). However, the mean gestational age, birth weight and head circumference for the CHYLD cohort were all greater than for the neonatal cohort, as the youngest babies from the neonatal cohort, those with a gestational age less than 35 weeks, were excluded from the CHYLD study. This is also reflected in the difference in distribution of risk factors between the CHYLD and neonatal cohorts, with a lower percentage of preterm babies in the CHYLD than in the neonatal cohort. These data suggest that the CHYLD cohort was representative of the neonatal data, with the exception of factors related to the gestational age exclusion.

Table 3.1: Characteristics of the 2 year CHYLD cohort and comparison with the neonatal cohort

	Not eligible	Eligible but not included	Total excluded	CHYLD cohort	p
	87	123	210	404	
NZDep2006	7 (4-9)	7 (5-9)	7 (4-9)	7 (4-9)	0.531
Maternal Characteristics					
Age (y)	31.5 (5.9)	29 (6.9)	29.9 (6.3)	29.9 (6.2)	0.904
Parity	1.4 (1.8)	1.2 (1.5)	1.3 (1.6)	1.4 (1.7)	0.498
Ethnicity					
NZEuropean	1 (0.4)	49 (19.9)	50 (40.3)	196 (50.8)	0.062
Māori	1 (0.7)	41 (26.8)	42 (33.9)	111 (28.8)	
Pasifika	1 (7.7)	0 (0)	1 (0.8)	12 (3.0)	
Asian	0 (0)	12 (38.7)	12 (9.7)	19 (4.9)	
Other	0 (0)	19 (28.4)	19 (15.3)	48 (12.4)	
Infant Characteristics					
Female	41 (47.1)	54 (43.9)	95 (45.2)	192 (47.5)	0.590
Gestational age (weeks)	35.1 (2.6)	37.8 (1.8)	36.6 (2.6)	37.8 (1.7)	**<0.001**
Birth weight (g)	2486 (852)	3029 (886)	2804 (60)	3135 (844)	**<0.001**
Head circumference (cm)	32.0 (2.8)	33.8 (2.5)	32.9 (2.8)	34.0 (2.2)	**<0.001**
Neonatal Risk:					
IDM	27 (31.0)	44 (35.8)	71 (33.8)	161 (40.0)	0.055
Preterm	45 (51.7)	42 (34.1)	87 (41.4)	129 (31.8)	
Small	9 (10.4)	18 (14.6)	27 (12.9)	60 (14.8)	
Large	2 (2.3)	12 (9.8)	14 (6.7)	42 (10.4)	
Other	4 (4.6)	7 (5.7)	11 (5.2)	12 (3.0)	

Data are median (interquartile range), mean (SD) or n (%); p value is for comparison between CHYLD cohort and total excluded

3.3. CHYLD Study cohort 2 year follow up

Cohort characteristics data were available from our 'Home and Family' questionnaire for 394 (97.5%) of the 404 children (Table 3.2). The CHYLD cohort was 48% girls with the Small group having more (67%) and Large having fewer (29%) girls ($p<0.05$). As expected, differences in gestational age, body weight and head circumference were found between risk groups both at birth and at 2 years, with children born large or small on average still larger or smaller than the cohort mean at 2 years. The cohort children were predominantly NZ European (NZE: 49.3%) and Māori (34.9%).

No significant differences were found between risk groups on measures of child health, ethnicity, home languages, parental work, household income or drug and alcohol use.

Table 3.2: Physical health, family, ethnicity and measures of socioeconomic status at birth and 2 years for the CHYLD cohort and primary risk groups.

	Cohort	IDM	Preterm	Small	Large	Other	p
Number	404	161 (39.9)	129 (31.9)	60 (14.9)	42 (10.4)	12 (3.0)	
Female	192 (47.5)	80 (49.7)	55 (42.6)	40 (66.7)	12 (28.6)	5 (41.7)	**0.002**
Gestational age (weeks)	37.8 (1.7)	38.2 (1.0)	36.1[aaa] (0.6)	38.3[bbb] (1.3)	40.3[aaabbbccc] (1.3)	38.5[bbbddd] (1.7)	**<0.001**
Birth weight (g)	3135 (844)	3461 (614)	2613[aaa] (417)	2310[aaa] (226)	4684[aaabbbccc] (378)	3063[abcccddd] (396)	**<0.001**
Birth head circumference (cm)	34.0 (2.2)	34.7 (1.6)	33.0[aaa] (1.9)	32.4[aaa] (1.6)	37.7[aaabbbccc] (1.3)	34.5[ccddd] (1.1)	**<0.001**
Mother as primary caregiver	371 (94.4)	149 (92.6)	115 (94.3)	54 (96.4)	41 (97.6)	12 (100.0)	0.928
Assessment age (months)	24.1 (1.8)	24.1 (1.1)	24.1 (0.9)	24.4 (1.2)	23.9 (0.8)	24.2 (1.1)	0.090
Height (cm)	86.5 (3.8)	86.3 (3.4)	87.0 (4.0)	84.1[aaabbb] (3.8)	89.1[aaabccc] (3.4)	86.2 (3.6)	**<0.001**
Weight (kg)	13.0 (1.8)	13.0 (1.7)	13.2 (1.6)	11.7[aaabbb] (1.4)	14.5 [aaabbbccc] (1.8)	13.4[ccc] (1.7)	**<0.001**
Head circumference (cm)	49.0 (1.8)	48.9 (1.6)	49.1 (1.7)	47.9[aaabbb] (1.6)	50.4[aaabbbccc] (2.0)	49.6[ccc] (1.5)	**<0.001**
Arm circumference (cm)	16.4 (1.3)	16.4 (1.2)	16.5 (1.2)	15.9 (1.4)[b]	16.8 (1.2)[cc]	17.0 (1.4)	**0.005**

	Cohort	IDM	Preterm	Small	Large	Other	p
Breastfed	362 (92.6)	148 (92.5)	110 (90.2)	53 (94.6)	40 (97.6)	11 (91.7)	0.578
Ever hospitalised	118 (31.1)	45 (28.9)	39 (33.3)	20 (38.5)	10 (23.8)	4 (33.3)	0.554
Children with ear infections	208 (54.3)	92 (57.8)	62 (52.5)	25 (45.5)	23 (59.0)	6 (50.0)	0.537
Number of siblings	1.5 (1.4)	1.6 (1.6)	1.5 (1.3)	1.5 (1.4)	1.3 (1.3)	1.6 (1.0)	0.772
Number in household	4.5 (1.5)	4.5 (1.5)	4.6 (1.5)	4.3 (1.6)	4.1 (1.4)	5.0 (1.3)	0.293
Attends Preschool	164 (50.8)	64 (47.8)	57 (54.8)	20 (44.4)	16 (55.2)	7 (63.6)	0.585
Primary Ethnicity:							
NZ European	199 (49.3)	77 (47.8)	60 (46.5)	28 (46.7)	27 (64.3)	7 (58.3)	0.129
Māori	143 (35.4)	62 (38.5)	46 (35.7)	19 (31.7)	11 (26.2)	5 (41.7)	
Pasifika	19 (4.7)	7 (4.4)	6 (4.7)	4 (6.7)	2 (4.8)	0 (0.0)	
Asian	24 (5.9)	13 (8.1)	5 (3.9)	5 (8.3)	1 (2.4)	0 (0.0)	
Other	5 (1.2)	2 (1.2)	2 (1.6)	0 (0.0)	1 (2.4)	0 (0.0)	
Unknown	14 (3.5)	0 (0.0)	10 (7.8)	4 (6.7)	0 (0.0)	0 (0.0)	
Home Languages: (n=388)							
English (first language)	361(93.0)	145 (90.1)	113 (96.6)	51 (91.1)	40 (95.2)	12 (100.0)	0.198
Other (first language)	27 (7.0)	16 (9.9)	4 (3.4)	5 (8.9)	2 (4.8)	0 (0.0)	
Bilingual – Māori	50 (12.9)	18 (11.2)	22 (18.8)	5 (8.9)	2 (4.8)	3 (25.0)	
Bilingual – Other	32 (8.2)	15 (9.3)	9 (7.7)	5 (8.9)	3 (7.1)	0 (0.0)	
Māori	70 (18.0)	27 (16.8)	24 (20.5)	11 (19.6)	5 (11.9)	3 (25.0)	
Pasifika	13 (3.3)	5 (3.1)	3 (2.6)	3 (5.4)	1 (8.3)	0 (0.0)	
Asian languages	26 (6.7)	15 (9.3)	5 (4.3)	5 (8.9)	1 (8.3)	1 (8.3)	
Other	4 (1.1)	1 (0.6)	2 (1.7)	0 (0.0)	1 (8.3)	0 (0.0)	

	Cohort	IDM	Preterm	Small	Large	Other	p
Translation required	13 (3.3)	9 (5.6)	1 (0.9)	3 (5.4)	0 (0.0)	0 (0.0)	
Measures of SES							
Median NZDep2006 (birth)	7 (4-9)	7 (5-9)	7 (4-9)	7 (4-10)	7 (4-8)	9 (4-9)	
Median NZDep2006 (2 y)	6 (4-9)	6 (4-9)	7 (4-9)	6 (4-9)	6 (4-8)	5 (4-8)	
Owned home	163 (40.3)	68 (42.2)	54 (41.9)	21 (35.0)	17 (40.5)	3 (25.0)	0.624
Owned transport	351 (86.9)	146 (90.7)	107 (82.9)	44 (73.3)	42 (100.0)	12 (100.0)	**0.002**
Maternal Work: (n=377)							
Employed	140 (37.1)	62 (40.5)	45 (38.1)	14 (26.4)	14 (34.2)	5 (41.7)	**0.022**
Self-employed	30 (8.0)	12 (7.8)	4 (3.4)	5 (9.4)	9 (22.0)	0 (0.0)	
Homemaker	167 (44.3)	60 (39.2)	56 (47.5)	27 (50.9)	18 (43.9)	6 (50.0)	
Unemployed	24 (6.4)	12 (7.8)	5 (4.2)	6 (11.3)	0 (0.0)	1 (8.3)	
Other	16 (4.2)	7 (4.6)	8 (6.8)	1 (1.9)	0 (0.0)	0 (0.0)	
Paternal Work: (n=333)							
Employed	247 (74.2)	112 (77.8)	74 (77.1)	28 (65.1)	26 (68.4)	7 (58.3)	0.492
Self-employed	51 (15.3)	18 (12.5)	13 (13.5)	8 (18.6)	10 (26.3)	2 (16.7)	
Homemaker	9 (2.7)	4 (2.8)	3 (3.1)	2 (4.7)	0 (0.0)	0 (0.0)	
Unemployed	19 (5.7)	8 (5.6)	4 (4.2)	3 (7.0)	2 (5.3)	2 (16.7)	
Other	7 (2.1)	2 (1.4)	2 (2.1)	2 (4.7)	0 (0.0)	1 (8.3)	

	Cohort	IDM	Preterm	Small	Large	Other	p
Annual Household Income (n=327)							
< $10, 000	5 (1.5)	0 (0.0)	2 (1.9)	1 (2.3)	2 (5.4)	0 (0.0)	0.751
$10,001 - $20, 000	26 (8.0)	10 (7.6)	10 (9.6)	4 (9.3)	2 (5.4)	0 (0.0)	
$20,001 - $30,000	45 (13.8)	17 (12.9)	13 (12.5)	8 (18.6)	4 (10.8)	3 (27.3)	
$30,001 - $40,000	45 (13.8)	17 (12.9)	14 (13.5)	6 (14.0)	5 (13.5)	3 (27.3)	
$40,001 - $50,000	47 (14.4)	19 (14.4)	13 (12.5)	8 (18.6)	6 (16.2)	1 (9.1)	
$50,001 - $70,000	52 (15.9)	26 (19.7)	18 (17.3)	3 (7.0)	5 (13.5)	0 (0.0)	
>$70,001	107 (32.7)	43 (32.6)	34 (32.7)	13 (30.2)	13 (35.1)	4 (36.4)	
Government Benefit	119 (34.2)	41 (28.5)	39 (37.9)	22 (42.3)	12 (31.6)	5 (45.5)	0.291
Antenatal Drugs and Alcohol (n=393)							
Maternal smoking	108 (27.5)	39 (24.2)	36 (29.5)	21 (37.5)	8 (19.1)	4 (33.3)	0.061
Maternal alcohol	39 (9.9)	11 (6.8)	14 (11.5)	11 (19.6)	3 (7.1)	0 (0.0)	0.076
Maternal marijuana	15 (3.8)	4 (2.5)	4 (3.3)	5 (8.9)	1 (2.4)	1 (8.3)	0.247
Maternal other drugs	3 (0.8)	1 (0.6)	1 (0.8)	1 (1.8)	0 (0.0)	0 (0.0)	0.840
Paternal smoking	111 (28.2)	47 (29.2)	33 (27.1)	16 (28.6)	10 (9.0)	5 (41.2)	0.274
Paternal alcohol	236 (60.1)	93 (57.8)	73 (59.8)	36 (64.3)	26 (61.9)	8 (66.7)	0.071
Paternal marijuana	35 (8.9)	14 (8.7)	13 (10.7)	5 (8.9)	2 (4.8)	1 (8.3)	0.151
Paternal other drugs	4 (1.0)	2 (1.2)	1 (0.8)	1 (1.8)	0 (0.0)	0 (0.0)	0.131

Data are n (%), mean (SD) or median (interquartile range); [a] p<0.05,[aa] p<0.01, [aaa] p<0.001 for comparison with IDM; [b] p<0.05,[bb] p<0.01, [bbb] p<0.001 for comparison with Preterm; [c] p<0.05,[cc] p<0.01, [ccc] p<0.001 for comparison with Small; [d] p<0.05,[dd] p<0.01, [ddd] p<0.001 for comparison with Large. IDM: Infant of Diabetic Mother, NZDep2006: New Zealand Deprivation Index 2006; p value is for overall comparison between risk groups.

3.4. CHYLD Study cohort socioeconomic status

The distribution of NZDep2006 decile rankings for cohort families at birth and 2 years showed a left skew, indicating more families at higher levels of deprivation than is found in the New Zealand national distribution (Fig 3.2). However, the distribution of births across the NZDep2006 deciles for our cohort is similar to that of the national NZDep2006 birth data for 2008 (Ministry of Health, 2008a) ($p = 0.751$). The overall distribution of NZDep2006 scores changed slightly between birth and the 2 year assessment, with the biggest change being decreases in the number of families living in decile 7 and 9 neighbourhoods. The mean NZDep2006 decile score for the birth cohort was 6.5 (2.7) and median was 7 (interquartile range: 9 – 4). The mean NZDep2006 decile score for the 2 year cohort was 6.3 (2.7) and median was 6 (interquartile range: 9 – 4). However, the overall changes disguise the mobility of the population. During those 2 years 182 (45.7%) families showed a change in NZDep2006 score between 1 and 8 decile rankings (Fig 3.3), with 101 families moving to an area of lower deprivation and 81 families to an area of higher deprivation.

Figure 3.2: Distribution of cohort families across NZDep2006 deciles at birth and 2 year assessment time

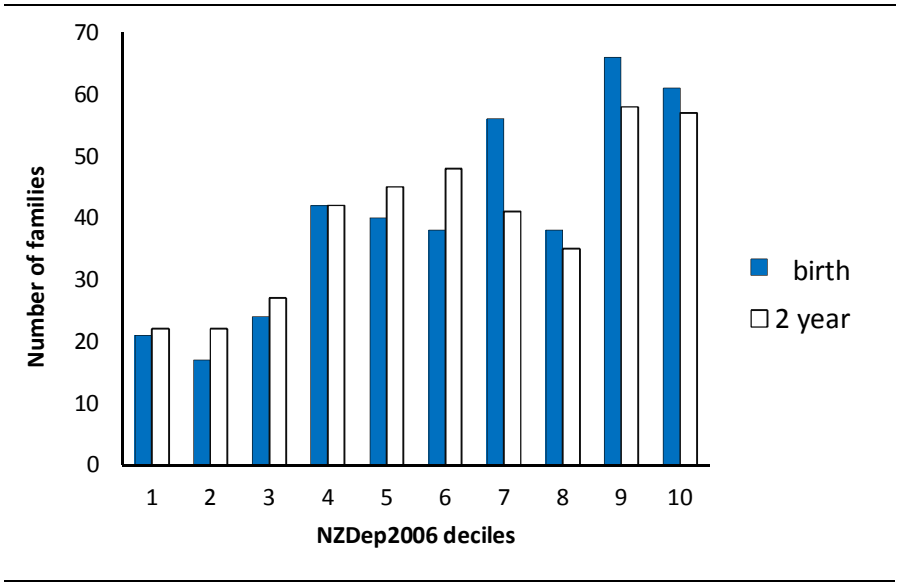
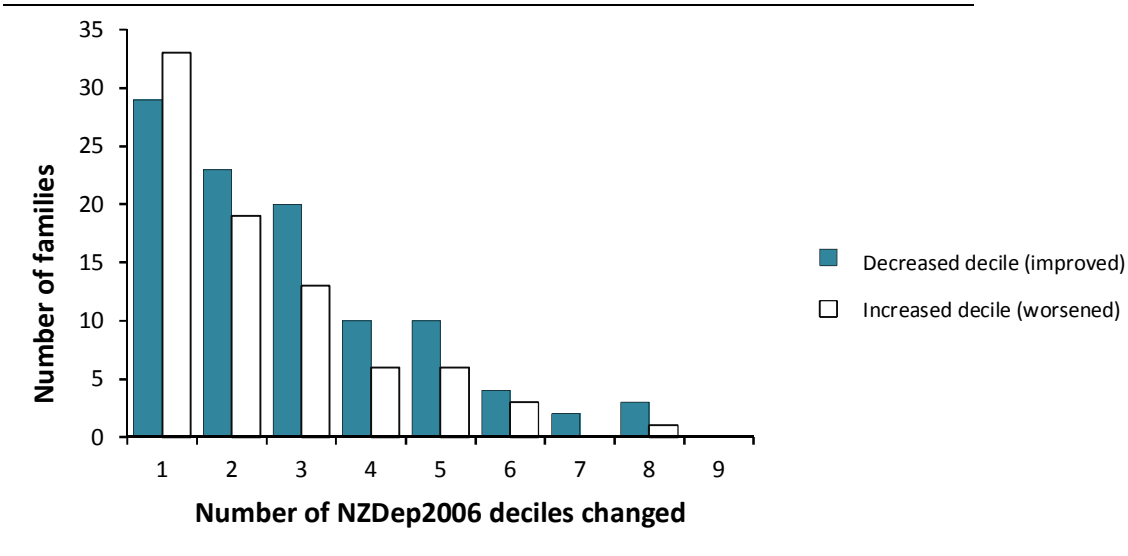


Figure 3.3: Distribution of the number of NZDep2006 decile changes resulting from families moving between birth and 2 year assessment time



3.5. Family resources and health as a function of socioeconomic status

Household income data were available for 326 (80.7%) families and were used as the indication of SES most relevant to individual households. These data were divided into approximately even tertiles with the income for the highest group greater than $70,000, the middle group between $40,001 and $70,000 and the lowest group $40,000 or less (Table 3.3). In the lowest group 31 children were in households with a reported annual income of $20,000 or less.

Household income was associated with NZDep2006 at birth and 2 years (both <0.001) and indicators of wealth such as home and car ownership (both <0.001). Household income was not associated with rates of preschool attendance, reported ear infections, child hospitalisation, size of household or number of siblings. There was a difference in distribution of ethnicity across income tertiles ($p<0.001$) with the largest percentage of New Zealand European families in the highest income group (40.0%), the largest percentage of Māori in the lowest income group (51.8%) and a less skewed distribution of the other ethnicities (Table 3.3).

Maternal and paternal education were both strongly positively associated with household income (both <0.001). Reported maternal and paternal smoking and marijuana use were also strongly positively associated with household income (all $p< 0.001$), although drinking was negatively associated with household income (maternal: $p = 0.015$; paternal: $p<0.001$, Table 3.3).

Table 3.3: Family resources, child health and education and parental drug used according to tertile of household income

	Household Income			
	High	Medium	Low	p
n	107	99	121	
NZDep2006 at birth	5 (3-8)	7 (4-9)	8 (6-9)	**<0.001**
NZDep2006 at 2y	4 (2-7)	6 (5-8)	8 (5-9)	**<0.001**
Child hospitalisation to 2y	30 (28.9)	26 (26.3)	43 (37.4)	0.178
Reported ear infections	63 (59.4)	56 (57.7)	59 (52.2)	0.530
Breastfed	99 (92.5)	95 (96.0)	109 (92.4)	0.496
Preschool attendance	56 (64.4)	43 (53.1)	49 (47.6)	0.065
Owned home	81 (77.9)	52 (53.6)	14 (12.0)	**<0.001**
Owned car	107 (100.0)	98 (99.0)	99 (85.3)	**<0.001**
No. in household	4.2 (1.1)	4.6 (1.6)	4.3 (1.5)	0.081
No. of siblings	1.3 (1.2)	1.7 (1.4)	1.4 (1.4)	0.128
Ethnicity				
NZ European	73 (68.2)	59 (59.6)	48 (39.7)	**<0.001**
Māori	25 (23.4)	29 (29.3)	60 (49.6)	
Pacifica	2 (1.9)	5 (5.1)	4 (3.3)	
Asian	6 (5.6)	4 (4.0)	9 (7.4)	
Other	0 (0.0)	2 (2.0)	0 (0.0)	
Maternal Education				
Secondary School	21 (18.3)	26 (27.1)	63 (58.9)	**<0.001**
Post-secondary	40 (34.8)	45 (46.9)	31 (29.0)	
University	54 (47.0)	25 (26.0)	13 (12.2)	
Paternal Education				
Secondary School	14 (14.9)	21 (22.8)	55 (52.9)	**<0.001**
Post-secondary	31 (33.0)	41 (44.6)	31 (29.8)	
University	49 (52.1)	30 (32.6)	18 (17.3)	

Maternal antenatal smoking, alcohol and drug use				
Smoking	7 (6.5)	26 (26.3)	51 (42.2)	**<0.001**
Alcohol	10 (9.4)	6 (6.1)	13 (10.7)	**0.015**
Marijuana	0 (0.0)	1 (1.0)	12 (9.9)	**<0.001**
Other drugs	0 (0.0)	0 (0.0)	3 (2.5)	0.106
Paternal antenatal smoking, alcohol and drug use				
Smoking	14 (13.1)	25 (25.3)	52 (43.0)	**<0.001**
Alcohol	81 (75.7)	65 (65.7)	61 (50.4)	**<0.001**
Marijuana	4 (3.7)	6 (6.1)	18 (14.9)	**<0.001**
Other drugs	0 (0.0)	0 (0.0)	3 (2.5)	**<0.001**

Data are median (interquartile range), n (%) or mean (SD); High income group: >$70,000, Medium income: between $40,001 and $70,000, Low income group: < $40,000.

3.6. Discussion

The CHYLD study was a follow-up at 2 years of a cohort of babies born at Waikato Hospital. We enrolled 404 (77%) of the eligible children. The assessed CHYLD cohort were similar in gender, neonatal risk, SES, maternal age, parity and ethnicity, to the neonatal cohort from which they were drawn, with the differences in gestational age, birth weight and head circumference likely to have resulted from the exclusion of preterm babies less than 35 weeks' gestation, who were the smallest babies in the neonatal cohort. These babies were excluded in an attempt to avoid the potential confounding effect of low gestational age on developmental outcome.

3.6.1 Factors that influence follow-up rates

Maximising recruitment is an important consideration of follow-up studies, to avoid the risk of attrition bias and to retain statistical power (Dumville, Torgerson, & Hewitt, 2006; Peinemann, Labeit, Thielscher, & Pinkawa, 2014). Bias can be introduced if the follow-up cohort is not representative of the initiation cohort. There is no single criterion which defines the level at which bias may occur, and our 77% follow-up rate falls in the "Unclear risk of bias" range (Higgins, Altman, & Sterne, 2011). However, with the exception of differences related to our exclusion criterion, the profile of the CHYLD cohort does not differ significantly from the eligible group of the neonatal cohort, suggesting that the risk of bias is low.

Maintaining a follow-up cohort large enough to collect valid data over time is important for developmental studies and clinical trials (P. J. Anderson, 2002; Aylward, 2002b; Turner, 2014). Within a follow-up study there are multiple points at which study management may enhance the follow-up rate. Informing participants of the follow-up timescale, and providing contact details and information about the purpose of the study are both practical and ethical requirements (Schulz & Grimes, 2002). It is also important to understand potential barriers to follow-up and to provide options for venue, including the participant's home. Providing culturally competent team members and translation services when required will also increase the likelihood of recruitment (J. Barnett, Aguilar, Brittner, & Bonuck, 2012). As tracing participants can be difficult, collecting alternate contact addresses and the use of a national hospital number in addition to a study ID all provide additional contact routes (Schulz & Grimes, 2002).

Recruitment to the neonatal cohort began prior to planning for the CHYLD follow-up study. Hence, our families were unaware that they were going to be contacted in the future and no planning for maintaining contact had taken place. This may have reduced the number of families we were able to contact at 2 years, whereas continuous contact is known to enhance follow-up rates (Sharps et al., 2013; Tilson et al., 2013). In order to improve follow-up rates at four and a half years, in addition to the information pack which included contact details, we provided our families with fridge magnets with the CHYLD study logo and contact details and asked them to contact us with change of address information. We also gave them a shopping bag and a teddy bear with the CHYLD study logo and sent families an assessment summary, which provided feedback about their child and study

involvement. These measures may help to maintain contact and study awareness for the four and a half year assessment (J. Barnett et al., 2012; Nicholson et al., 2011).

Many of our processes were consistent with recommended approaches for follow-up studies. To increase likelihood of recruitment we offered assessments at clinics as close as practically possible to the child's home, or flights and accommodation in Auckland for assessment at the University clinic, or petrol vouchers to reimburse expenses. Home visits were also offered to families unable to attend clinic assessments. All team members attended two clinical cultural competency training sessions run by the Māori Studies department at the University of Waikato. We also employed a Māori research nurse to assist with the recruitment and assessment of Māori families. Translation services were offered to all families for whom English was not the home language. Elsewhere, monetary incentives were found to increase follow-up rates (Booker, Harding, & Benzeval, 2011; Brueton et al., 2013). However, this was not a realistic option for our study, and is a contentious ethical issue in paediatric studies (Committee on Drugs, 1995; Kimberly, Hoehn, Feudtner, Nelson, & Schreiner, 2006).

Lessons learnt from this study include the need for forward planning and maintaining contact with families after the initial recruitment. Birthday cards sent to the children would be a positive method of contact. Mid-way through the 2-year CHYLD assessment phase we established Kahikatea Research House, which was family-friendly with easy parking. Prior to this we had used three different hospital clinical settings in Hamilton for our assessments. Establishing a non-medical venue for follow-up from the outset may have improved follow-up rates as some parents expressed reluctance to attend a hospital-based clinic.

First contact with the family during recruitment is important and allowing caregivers the chance to ask questions and fully understand the purpose of the study and assessments involved appeared to increase follow-up success. We found it was not uncommon for caregivers to agree to follow-up only once they understood that assessment did not involve blood tests. Training all team members who are likely to approach families to a consistent approach, including open-ended questions and empathetic listening may enhance follow-up in future studies. Supervision sessions and ongoing training to provide support in managing contact with a wide range of families is reported to increase confidence of team members and follow-up success (J. Barnett et al., 2012; Doran et al., 2012; Nicholson et al., 2011; Wilcox et al., 2001). The informative nature of the study, including the use of videos to inform potential participants about the study, has also been reported to increase follow-up rates (J. Barnett et al., 2012; Gesualdo, Ide, Rewers, & Baxter, 2012). A contemporary version of this would be a study website with study information and updates, which may also maintain visibility and later follow-up rates with some families.

SES is one of the strongest factors affecting likelihood of follow-up, with low SES families harder to recruit than high SES families. One important reason for this is the increased difficulty in locating them (Aylward, 2002b; Huizink, 2009; Sharps et al., 2013). Low SES families have an increased rate of household mobility, related to often living in rental accommodation, sometimes with uncertain

tenure, and uncertain employment (Bradley & Corwyn, 2002; Buckett, Jones, & Marston, 2011; Martin, Razza, & Brooks-Gunn, 2012; Ministry of Education, 2011; Statistics New Zealand, 2013).

Families in our neonatal cohort had a high rate of relocation, with approximately 46% moving between different NZDep2006 decile neighbourhoods. This is likely to be an underestimate of the total number of relocations as it does not reflect those families who moved without changing the decile ranking of their neighbourhood, which constitute the majority of moves (Morton et al., 2014). This high rate of mobility created further challenge for tracking some families. The large Growing Up in New Zealand study (N= 6822) reported that 32% of their cohort moved between the 9 month and 2 year assessment times, with families who moved more likely to be single parent than two-parent households, and more likely to be Māori than NZ European (Morton et al., 2014). At the time of CHYLD cohort recruitment NZ experienced a higher than average number of families relocating overseas, primarily to Australia, to find work (Statistics New Zealand, 2012). This migration accounted for 33 (5.4%) families from our potential cohort, and study resources did not allow us to attempt to assess these families.

Low SES families may be reluctant to consent to a follow-up study if it requires them to take time off work, or if the cost of attending is perceived as too high. In addition, parent education is a factor that influences the likelihood of a parent consenting to having a child in a health-related follow-up study (Hense et al., 2013; Svensson, Ramírez, Peres, Barnett, & Claudio, 2012).

Families from ethnic minority groups are also less likely to be successfully recruited to follow-up which may contribute to attrition bias (Baxter et al., 2012; Nicholson et al., 2011; Paskett et al., 2008). They are more likely to belong to low SES groups than families from the predominant cultural group. Unmet specific needs of ethnic groups such as a preference for personal contact, consideration of cost of involvement, personal confidence to attend an appointment, confidence in health-related processes and concerns over language have all been identified as factors which can contribute to lower representation of ethnic minorities enrolled in follow-up studies (Baxter et al., 2012; Coronado et al., 2012; Mendoza, Williams, Chapman, & Powers, 2012; Svensson et al., 2012).

Our cohort comprised 34.9% Māori, higher than the proportion in the Waikato region (19%), with proportions of other ethnic groups similar to those reported in the Waikato region (Waikato District Health Board, 2010a). The higher proportion of Māori children in our cohort is consistent with the comparatively high proportion of births for low SES families and suggests that the measures we adopted were effective in enrolling children from all ethnicities.

Health outcomes of children enrolled in a follow-up study may also affect parent decision to continue in the study, with the most difficult children to enrol in follow-up reported to have higher rates of poor outcome including higher rates of disability and lower IQ in a very low birth-weight cohort (Callanan et al., 2001), and higher rates of obesity in a study of approaches to childhood obesity (Hense et al., 2013). However, elsewhere the opposite has been reported, with the children with greatest morbidity and poorest developmental outcome most likely to continue with follow-up (Aylward, 2002b; Campbell

et al., 1993). These contrasting findings suggest that other factors known to affect follow-up rates such as maternal education, information provided to parents about the study, social support, maternal physical and mental health and family busy-ness may also be important considerations for a family (Ballantyne, 2010; J. Barnett et al., 2012; Gesualdo et al., 2012; Lernmark et al., 2011; Sharps et al., 2013; Wilcox et al., 2001).

3.6.2. The CHYLD cohort

Higher deprivation, indicated by higher NZDep2006 decile is associated with lower household incomes, lower parental education and lower rates of home and car ownership. The mean New Zealand household income, when our data collection began in 2010, was $76,584 and changed little over the next 2 years (Statistics New Zealand, 2011), while the median income in our cohort was within the $40,000 to $50,000 band. The CHYLD cohort is characterised by a distribution of NZDep2006 rankings which shows a distinct left skew, indicating a higher proportion of families living in areas of higher deprivation than is found nationally overall (White et al., 2008). However, this distribution is similar to national birth distribution data available for a similar time period (Ministry of Health, 2008a), suggesting that our results are likely to be generalisable to New Zealand children of a similar age.

The highest income group of our cohort had a home ownership rate of 77.9% which is higher than the New Zealand national average of 64.8% (Morrison, 2008; Statistics New Zealand, 2013). Nationally, this rate falls to 60% for households with an income less than $50, 000, which is similar to the rate for the middle income group in our cohort (53.6%) but considerably higher than that of the lowest income group (12%). This low rate of home ownership in our lowest SES families is likely to have contributed to household mobility. Rental houses in New Zealand are of significantly poorer quality than owner occupied houses in terms of needed repairs, lack of permanent heating, likelihood of having no insulation and presence of mould, with low quality housing a contributing factor to many poor health outcomes (Baker et al., 2012; Buckett et al., 2011).

The higher proportion of low SES families in our cohort reflects the fact that the neonatal risk factors, the inclusion criteria for the CHYLD study, are also associated with low SES. Diabetes is more common in low than high SES communities and rates are disproportionately high amongst Māori, in part as a result of the associated high rates of obesity amongst Māori (Craig, Mantell, Ekeroma, Stewart, & Mitchell, 2004; Ministry of Health, 2013; Robbins et al., 2005; Waikato District Health Board, 2010b). Other health indicators associated with low SES which may increase a mother's chance of delivering a baby which is large, small or preterm include: poor maternal health, inadequate diet, substandard housing, lack of a healthy lifestyle, increased rate of illegal drug use and a lower rate of antenatal care which is begun at a later gestational age (Gao et al., 2006; Hense et al., 2013; Kalk et al., 2009; Ministry of Health, 2013; Rattihalli, Smith, & Field, 2012; Smith et al., 2007; Wouldes & Woodward, 2010).

Our data show that babies born small or large typically remain below or above the cohort mean, respectively, 2 years later with head circumference showing a similar pattern. Elsewhere, data show similar results with differences in size remaining significant for small and large groups through to adulthood (Ornoy, Ratzon, Greenbaum, Wolf, & Dulitzky, 2001; Paz et al., 1993; Strauss, 2000; Strauss & Dietz, 1998; Whitaker & Dietz, 1998), although catch-up growth in childhood may be associated with increased adult height and improved educational outcome (Stein et al., 2013). Small neonatal head circumference has been associated with developmental deficits (Strauss & Dietz, 1998) and again, catch-up growth is associated with improved developmental and academic outcomes (Frisk, Amsel, & Whyte, 2002). Low birth weight appears to be associated with less lean muscle development and the rapid catch-up growth of small infants in the first 6 to 12 months is typically the result of fat deposition, so although potentially an advantage developmentally, may result in a greater risk of obesity and metabolic disorders later in childhood and adulthood (Druet & Ong, 2008; Stein et al., 2013; J. C. K. Wells, 2007).

In our cohort low SES was significantly associated with higher reported smoking and marijuana use, which is a pattern reported previously in New Zealand (Boden, Fergusson, & Horwood, 2006; Ministry of Health, 2013; Poulton et al., 2002) and elsewhere (Baum, Garofalo, & Yali, 1999; Bradley & Corwyn, 2002). In turn, maternal smoking and marijuana use are known risk factors for preterm birth and small babies (Chiolero, Bovet, & Paccaud, 2005; Cnattingius, 2004; Ministry of Health, 2013; Morton et al., 2012). Neighbourhood clustering of marijuana use has been reported in New Zealand, with higher use associated with Māori ethnicity, which in turn is associated with higher rates of early school leaving and unemployment in these communities (Marie, Fergusson, & Boden, 2008; J. E. Wells, Degenhardt, Bohnert, Anthony, & Scott, 2009).

Many aspects of low SES associated with health such as housing, diet, obesity, exercise and smoking are all interlinked and also associated with the increased stress, depression and poor educational outcomes of low SES families (Palmer et al., 2013; Poulton et al., 2002; van den Berg et al., 2012). Child development is strongly influenced by these SES factors along with family access to resources and educational experiences (American Psychological Association task force on socioeconomic status, 2007; Bradley & Corwyn, 2002). Poorer developmental outcomes including cognitive, language, EF and social-emotional development have been reported for children from low SES families (Noble et al., 2007; Palmer et al., 2013; Potijk, Kerstjens, Bos, Reijneveld, & de Winter, 2013). SES was therefore likely to be a critical confounder in the assessment results for our cohort and hence required consideration in all analyses and interpretation of the data.

Chapter 4. Developmental assessment

4.1. Bayley III scores

Bayley III data were available for 402 (99.5%) children. All cohort scores were lower than the standardised mean except the Adaptive Behavior scale and Fine Motor subscale (Table 4.1), with no significant differences between risk groups. There were also no differences in scores between children whose mothers had gestational diabetes (n=130), type 1 diabetes (n = 14) and type 2 diabetes (n = 17). Adjusting for SES (see section 4.2 below) did not alter these findings.

There was a trend for girls to have higher scores than boys, although this only reached significance within the total cohort for the Adaptive Behaviour scale and Fine Motor subscale. There was an interaction between the group assigned to the 'Other' risk category and gender on the Language scale and Receptive communication subscale with boys, but not girls, in the Other risk group having higher scores than those in the remaining risk groups.

4.2. Bayley III scores and socioeconomic status

4.2.1. Bayley III scores and measures of socioeconomic status

We obtained six indices of SES: household income, NZDep2006 scores at birth and at 2 years, maternal and paternal education, and home ownership.

Household income data were available for 327 (81%) children. Overall, Bayley III scores had a graded relationship with household income, with children in the high income group (≥ $70, 001 pa) having Cognitive, Language, and Motor Scale scores 4 to 6 points above those of children in the medium income group ($40,000 - $70,000 pa), and 5 to 13 points above those of children in the low income group (≤ $40,000 pa) ($p < 0.001$) (Table 4.2). Children in the medium income group had Cognitive, Language, and Adaptive Behavior scores between 4 and 8 points above those of the low income group ($p < 0.01$). There was an interaction between gender and household income on the Adaptive Behaviour scale ($p = 0.026$) and Receptive Communication subscale ($p = 0.020$), with boys', but not girls', scores decreasing between each income group.

NZDep2006 decile ratings at birth were available for 403 (100%) children (Table 4.2). Bayley III Cognitive and Language scores had a graded relationship with NZDep2006 ratings, with children in the high decile group (deciles 1 - 3) having Language scale scores 3 points higher than those from the medium group (deciles 4 - 6, $p < 0.05$), and Cognitive scale scores 5 points, and Language scale scores 8 points higher than children in the low group (deciles 7 - 10, both $p < 0.001$). There were significant interaction effects between gender and NZDep2006 at birth on the Cognitive scale ($p = 0.046$), with boys, but not girls, having a lower score with increasing deprivation.

NZDep2006 decile ratings at the time of the 2-year assessment were available for 399 (99%) children (Table 4.2). Children in the high group had Cognitive scale scores 5 points ($p < 0.001$) and Language scale scores 8 points higher ($p < 0.001$) than children in the low group. Children in the medium group had intermediate scores, but these were not significantly different from those of the high group. There were no significant interaction effects between gender and NZDep2006 at 2 years of age.

Maternal education data were available for 377 (93%) and paternal education for 332 (82%) children (Table 4.3). Overall, scores decreased with decreasing number of years of parent education. Children of mothers in the high education group had Cognitive and Language scale scores approximately 8 points (both $p < 0.001$) and Social-Emotional scores 5 points higher ($p < 0.05$) than children of mothers in the low education group. Children of fathers in the high education group had Cognitive, Language, Motor scores and Social-Emotional scores 4 to 9 points higher (all $p < 0.01$) than children of fathers in the low education group. The biggest between-group differences were in boys' language scores, with boys of mothers in the low education group having scores approximately 8 points ($p < 0.01$), and of fathers in the low education group 11 points ($p < 0.001$) below boys of mothers and fathers in the high education group.

There was a significant interaction between gender and maternal education level on the Language and Adaptive Behaviour scales, and Receptive Communication subscales, with boys but not girls having a decreased score between the medium and low maternal education groups. There were no significant interactions between gender and paternal education level.

Home ownership data were available for 377 (93%) children (Table 4.3). Home ownership, in comparison to home rental, was associated with significantly higher Bayley III scores on all scales and subscales ($p < 0.001$) except the Gross Motor subscales. Girls' and boys' scores followed the same overall pattern and there were no significant interactions between gender and home ownership.

Table 4.1: Bayley III scores for total cohort, girls and boys, and risk groups.

		Total Cohort	IDM	Preterm	Small	Large	Other
	Cohort	402	159	129	60	42	12
	Girls	191	79	55	40	12	5
	Boys	211	80	74	20	30	7
Cognitive Composite	Cohort	93.5 (10.2)***	92.7 (10.7)	94.9 (9.3)	91.4 (11.5)	95.0 (9.8)	94.6 (5.4)
	Girls	94.0 (9.4)***	94.6 (10.0)†	95.4 (8.6)	91.3 (9.4)	94.6 (9.4)	92.0 (6.7)
	Boys	93.0 (10.9)***	90.8 (11.1)	94.5 (9.8)	91.8 (15.1)	95.2 (10.0)	96.4 (3.8)
Language Composite	Cohort	94.7 (14.2)***	94.5 (15.5)	94.8 (13.4)	93.3 (13.5)	97.4 (14.5)	94.8 (9.1)
	Girls	95.9(13.8)***	96.1 (15.1)	97.3 (12.9)	93.8 (12.5)	99.3 (14.8)	86.6 (2.5)††
	Boys	93.6 (14.6)***	92.8 (15.8)	92.9 (13.5)	92.5 (15.4)	96.6 (14.5)	100.6 (7.2)i
Receptive Communication (scaled)	Cohort	9.3 (2.7)***	9.2 (3.0)	9.3 (2.6)	9.2 (2.5)	9.6 (2.7)	9.3 (1.9)
	Girls	9.5 (2.6)**	9.6 (3.0)	9.7 (2.5)	9.2 (2.2)	9.8 (2.4)	7.6 (0.5)††
	Boys	9.0 (2.8)***	8.8 (3.0)	8.9 (2.6)	9.2 (3.0)	9.5 (2.8)	10.6 (1.5)i
Expressive Communication (scaled)	Cohort	8.9 (2.6)***	8.8 (2.7)	8.9 (2.5)	8.4 (2.5)	9.4 (2.5)	8.8 (1.5)
	Girls	9.0 (2.5)***	9.0 (2.6)	9.3 (2.5)	8.6 (2.4)	9.8 (2.8)	7.6 (0.5)†
	Boys	8.7 (2.6)***	8.7 (2.8)	8.6 (2.4)	8.2 (2.7)	9.2 (2.5)	9.6 (1.4)

		Total Cohort	IDM	Preterm	Small	Large	Other
Motor Composite	Cohort	98.6 (9.5)*	98.4 (10.9)	99.4 (7.3)	96.7 (9.5)	99.5 (10.9)	99.7 (7.0)
	Girls	99.2 (9.1)	99.8 (11.0)	99.6 (6.8)	97.2 (8.5)	98.6 (6.9)	103.4 (6.0)
	Boys	98.1 (9.9)*	97.0 (10.7)	99.2 (7.6)	96.2 (11.3)	99.8 (12.0)	97.0 (6.7)
Fine Motor (scaled)	Cohort	10.0 (2.1)	9.8 (2.3)	10.4 (1.8)	9.8 (2.2)	10.0 (1.9)	10.5 (1.7)
	Girls	10.4 (2.0)*††	10.4 (2.2)†	10.6 (1.7)	9.9 (2.0)	10.1 (1.2)	11.6 (0.9)†
	Boys	9.8 (2.1)*	9.3 (2.2)	10.2 (1.9)	9.5 (2.4)	10.0 (2.1)	9.7 (1.7)
Gross Motor (scaled)	Cohort	9.5 (1.8)***	9.6 (2.1)	9.4 (1.4)	9.1 (1.7)	9.8 (2.3)	9.3 (1.1)
	Girls	9.3 (1.7)***	9.5 (2.0)	9.3 (1.5)	9.1 (1.5)	9.4 (1.5)	9.4 (1.1)
	Boys	9.6 (1.9)**	9.7 (2.1)	9.5 (1.3)	9.2 (2.0)	9.9 (2.6)	9.3 (1.1)
Social-Emotional	Cohort	102.5 (15.1)***	102.2 (15.1)	104.3 (16.0)*	101.5 (15.7)	101.2 (12.2)	97.9 (11.4)
	Girls	104.0 (15.2)***	103.9 (14.1)	106.0 (16.8)	102.2 (15.4)	105.8 (14.3)	93.0 (10.4)
	Boys	101.2 (15.0)	100.5 (15.9)	103.0 (15.4)	100.3 (16.4)	99.1 (10.8)	101.4 (11.4)
Adaptive Behaviour	Cohort	99.0 (14.9)	98.5 (14.4)	99.3 (14.7)	99.9 (15.2)	98.6 (18.1)	101.2 (9.8)
	Girls	101.5 (13.7)††	101.7 (12.8)††	100.9 (14.7)	102.3 (13.5)	100.2 (16.2)	101.0 (15.1)
	Boys	96.8 (15.6)**	95.2 (15.2)	98.1 (14.8)	95.3 (17.2)	97.9 (19.1)	101.3 (3.1)

Data are n or mean (SD); IDM = Infant of a Diabetic Mother; *p< 0.05; **p<0.01; ***p<0.001 for comparison with standardised mean; †p<.05; †† p<.01 for comparison between genders; [i] p<0.05 for interaction between gender and risk factor.

Table 4.2: The relationship between Bayley III scores and household income and New Zealand Deprivation Index rating at birth and 2 years

		Household income at 2 year assessment			NZDep2006 at birth			NZDep2006 at 2 year assessment		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
	Cohort	107	99	121	62	120	221	71	135	193
	Girls	55	56	50	26	61	104	33	70	88
	Boys	52	43	70	36	59	117	38	65	105
Cognitive	Cohort	99.2 (9.3)	95.2[aa] (8.0)	89.8[aaabbb] (9.7)	97.1 (11.1)	94.1 (10.3)	92.1[aa] (9.7)	96.2 (11.4)	95.6 (10.5)	91.1[aaabbb] (9.1)
	Girls	99.3 (9.3)	95.7 (6.0)	88.6[aaabbb] (10.0)	94.6 (9.7)	95.9 (8.9)	92.7 (9.6)	95.0 (9.3)	96.4 (9.6)	91.9[bb] (8.9)
	Boys	99.0 (9.4)	94.5 (10.0)	90.6[aaa] (9.4)	98.9 (11.8)	92.3[aı] (11.3)	91.6[aa] (9.8)	97.2 (13.0)	94.7 (11.4)	90.5[aab] (9.2)
Language Composite	Cohort	102.3 (13.5)	95.9[aa] (14.1)	89.1[aaabbb] (13.3)	100.4 (15.5)	96.9[a] (13.1)	91.8[aaabb] (13.8)	99.1 (16.4)	98.3 (13.8)	90.9[aaabbb] (12.6)
	Girls	100.4 (7.9)	97.9 (10.0)	89.4[aaabb] (13.1)	101.3 (15.2)	97.3 (11.5)	93.6[a] (14.2)	100.0 (15.0)	99.2 (13.4)	100.4[aabb] (8.8)
	Boys	103.7 (12.5)	92.9[aaa] (15.7)	88.8[aaa] (13.5)	99.8 (15.9)	96.5 (14.6)	90.3[ab] (13.3)	98.3 (17.6)	97.4 (14.3)	90.0 [aabb] (12.6)
Receptive Communication	Cohort	10.7 (2.6)	9.6[aa] (2.6)	8.2[aaabbb] (2.5)	10.5 (2.8)	9.7[a] (2.5)	8.7[aaabb] (2.6)	10.3 (3.1)	10.0 (2.7)	8.5[aaabbb] (2.3)
	Girls	10.3 (2.8)	10.1[††] (2.3)	8.2[aaa bb] (2.3)	10.7 (3.0)	9.8 (2.3)	9.0[aa] (2.6)	10.5 (3.1)	10.0 (2.6)	8.8 [aabb] (2.2)
	Boys	11.1 (2.3)	8.9[aaaı] (2.8)	8.1[aaa] (2.7)	10.3 (2.8)	9.6 (2.7)	8.4[aaab] (2.6)	10.1 (3.2)	9.9 (2.8)	8.2 [aaabbb] (2.4)

		Household income at 2 year assessment			NZDep2006 at birth			NZDep2006 at 2 year assessment		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
Expressive Communication	Cohort	10.0 (2.5)	8.9[aa] (2.7)	8.1[aaa] (2.4)	9.6 (2.9)	9.2 (2.4)	8.4[aab] (2.4)	9.4 (2.9)	9.5 (2.5)	8.3[aabbb] (2.4)
	Girls	9.9 (2.6)	9.2 (2.4)	8.1[aaa] (2.4)	9.7 (2.8)	9.3 (2.2)	8.7 (2.6)	9.5 (2.6)	9.6 (2.4)	8.4[bb] (2.5)
	Boys	10.2 (2.3)	8.6[aa] (2.9)	8.0[aaa] (2.3)	9.6 (3.0)	9.2 (2.7)	8.2[ab] (2.3)	9.3 (3.2)	9.3 (2.5)	8.3[b] (2.3)
Motor Composite	Cohort	102.6 (9.3)	98.8[aa] (8.6)	96.4[aaab] (9.7)	98.5 (9.4)	99.8 (8.9)	98.0 (9.9)	100.4 (9.6)	98.8 (8.3)	97.9 (10.3)
	Girls	103.1 (10.2)	99.3 (7.5)	95.9[aaa] (8.3)	98.9 (9.1)	101.0 (6.9)	98.1 (10.1)	100.4 (8.8)	100.4[†] (7.9)	97.9 (10.0)
	Boys	102.1 (8.2)	98.1 (9.9)	96.8[aa] (10.6)	98.1 (9.6)	98.6 (10.5)	97.8 (9.7)	100.4 (10.4)	97.2 (8.3)	97.8 (10.6)
Fine Motor	Cohort	11.0 (2.1)	10.2[aa] (2.0)	9.5[aaab] (1.8)	10.1 (2.0)	10.3 (2.0)	9.9 (2.1)	10.5 (2.3)	10.1 (1.0)	9.8 (2.1)
	Girls	11.1 (2.0)	10.5 (1.9)	9.4[aaa] (1.7)	10.2 (1.8)	10.7[†] (1.6)	10.2 (2.2)	10.6 (2.1)	10.5[†] (1.7)	10.1 (2.2)
	Boys	10.8 (2.1)	9.7[a] (2.1)	9.5[aa] (1.9)	10.1 (2.2)	9.8 (2.3)	9.6 (2.0)	10.3 (2.4)	9.7 (2.1)	9.6 (2.0)
Gross Motor	Cohort	9.8 (1.9)	9.4 (1.5)	9.3 (2.0)	9.4 (1.7)	9.6 (1.8)	9.4 (1.9)	9.6 (2.0)	9.4 (1.5)	9.4 (2.0)
	Girls	9.8 (2.0)	9.3 (1.3)	9.2 (1.9)	9.5 (1.7)	9.6 (1.7)	9.2 (1.8)	9.5 (1.8)	9.5 (1.7)	9.2 (1.8)
	Boys	9.8 (1.9)	9.6 (1.6)	9.4 (2.1)	9.3 (1.7)	9.7 (1.9)	9.6 (2.0)	9.8 (2.2)	9.3 (1.2)	9.6 (2.2)

		Household income at 2 year assessment			NZDep2006 at birth			NZDep2006 at 2 year assessment		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
Social-Emotional	Cohort	105.1 (15.5)	104.8 (14.2)	100.6 (15.0)	100.9 (14.5)	100.7 (16.0)	97.6 (14.3)	99.8 (14.5)	101.2 (14.9)	97.5 (14.9)
	Girls	105.3 (17.0)	106.7 (14.7)	101.9 (14.0)	105.0 (13.5)	109.2† (15.4)	100.5^{bb} (14.5)	104.5 (16.0)	108.5† (14.2)	100.1^{bb} (14.8)
	Boys	104.9 (13.8)	102.3 (13.3)	99.8 (15.7)	102.4 (11.7)	102.2 (15.9)	100.3 (15.4)	103.1 (13.1)	103.3 (1.9)	99.4 (15.4)
Adaptive Behaviour	Cohort	102.0 (12.3)	100.8 (14.8)	93.0^{aabb} (15.6)	100.8 (14.0)	99.7 (15.8)	97.3 (14.5)	100.7 (14.8)	100.7 (13.9)	96.6 (15.5)
	Girls	101.5 (12.6)	105.0†† (12.5)	98.6^{b} (14.9)	101.8 (14.0)	103.2 (13.2)	100.3†† (13.9)	101.1 (13.3)	102.9 (13.4)	100.8†† (13.9)
	Boys	102.6 (11.9)	95.2^{ai} (16.0)	94.1^{aa} (15.9)	100.3 (15.1)	98.0 (18.1)	95.1 (14.2)	98.7 (15.6)	99.4 (16.2)	94.6 (15.2)

Data are n or mean (SD); †p<.05; ††p<0.01 for comparison between genders; ^{i}p<0.05; ^{ii}p<0.01 for interaction between gender and household income or NZDep2006; ^{a}p<0.05; ^{aa}p<0.01; ^{aaa}p<0.001 for comparison with High group; ^{b}p< 0.05; ^{bb}p<0.01; ^{bbb}p<0.001 for comparison between Medium and Low groups; Household income: High = ≥$70, 001 pa; Medium = $40,001 - $70,000 pa; Low = ≤ $40,000 pa; NZDep2006: High = deciles 1,2,3; Medium =deciles 4,5,6; Low = deciles 7,8,9,10.

Table 4.3: Table 4.3 Relationships between Bayley III scores and maternal and paternal education and home ownership

		Maternal Education			**Paternal Education**			**Home Ownership**	
		High	Medium	Low	High	Medium	Low	Own	Rent
	Cohort	118	128	131	96	117	119	162	215
	Girls	54	67	58	49	62	45	81	98
	Boys	64	61	73	47	55	74	81	117
Cognitive	Cohort	97.5 (9.8)	94. 5[a] (9.3)	90.0[aaabbb] (10.1)	98.3 (9.8)	94.8[a] (8.6)	91.1[aabb] (10.3)	97.6 (10.1)	90.7[aaa] (9.3)
	Girls	98.6 (8.4)	94.6[ab] (8.9)	90.6[aaa] (9.3)	99.4 (7.9)	94.7[a] (8.1)	92.2[aaa] (9.2)	98.5 (8.4)	90.7[aaa] (8.6)
	Boys	96.6 (10.8)	94.3 (9.8)	89.6[aaab] (10.8)	97.1 (11.4)	94.9 (9.2)	90.5[aa] (10.9)	96.7 (11.6)	90.6[aaa] (9.8)
Language Composite	Cohort	99.5 (14.4)	94.9[a] (13.7)	91.6[aaa] (14.2)	100.9 (13.2)	95.9[a] (13.4)	91.9[aa] (15.2)	100.5 (14.2)	90.8[aaa] (12.8)
	Girls	101.6 (12.5)	94.4[a] (13.7)	94.6[†a i] (13.9)	101.2 (11.3)	96.2 (14.0)	95.1 (14.4)	102.1 (14.0)	91.7[aaa] (11.1)
	Boys	97.7 (15.7)	95.5 (13.7)	89.3[aa] (14.1)	100.6 (15.0)	95.5 (12.8)	90.0[aaa] (15.4)	99.0 (14.3)	90.0[aaa] (14.1)
Receptive Communication	Cohort	10.3 (2.7)	9.3 (2.5)	8.6[aaabb] (2.7)	10.6 (2.6)	9.5[aa] (2.5)	8.6[aaab] (2.7)	10.5 (2.7)	8.5[aaa] (2.4)
	Girls	10.7 (2.5)	9.2[aa] (2.4)	9.2[†aa i] (2.6)	10.5 (2.4)	9.6 (2.5)	9.2[a] (2.6)	10.7 (2.7)	8.7[aaa] (2.1)
	Boys	9.9 (2.9)	9.4 (2.6)	8.2[aaab] (2.6)	10.6 (2.8)	9.3 (2.5)	8.3[aaab] (2.8)	10.2 (2.7)	8.3[aaa] (2.6)

		Maternal Education			Paternal Education			Home Ownership	
		High	Medium	Low	High	Medium	Low	High	Medium
Expressive Communication	Cohort	9.5 (2.5)	8.9 (2.6)	8.4 (2.5)	9.8 (2.3)	9.0 (2.5)	8.6 [aa] (2.7)	9.7 (2.6)	8.3[aaa] (2.3)
	Girls	9.8 (2.3)	8.8 (2.7)	8.9 (2.5)	9.9 (2.0)	9.0 (2.7)	9.1 (2.7)	9.9 (2.6)	8.4[aaa] (2.1)
	Boys	9.3 (2.7)	9.0 (2.5)	8.1[a] (2.5)	9.7 (2.7)	9.1 (2.3)	8.2[a] (2.7)	9.4 (2.5)	8.3[aaa] (2.6)
Motor Composite	Cohort	100.9 (8.9)	99.3 (9.5)	96.5 (9.8)	101.5 (8.0)	99.7 (8.5)	97.3 [aa] (11.3)	101.7 (9.6)	96.8[aaa] (8.9)
	Girls	101.4 (8.4)	100.2 (9.6)	97.2[a] (9.0)	102.3 (7.6)	99.4 (8.7)	99.2 (9.8)	102.3 (9.7)	97.3[aaa] (7.7)
	Boys	100.5 (9.3)	98.3 (9.3)	96.0[a] (10.4)	100.6 (8.4)	100.1 (8.3)	96.2 (12.0)	101.1 (9.5)	96.3[aaa] (9.9)
Fine Motor	Cohort	10.6 (1.9)	10.1 (2.0)	9.7[aaa] (2.2)	10.7 (1.7)	10.2 (2.0)	9.7[aa] (2.2)	10.8 (2.1)	9.5[aaa] (1.9)
	Girls	10.9 (1.8)	10.4 (2.1)	10.0[a] (2.0)	11.0 (1.5)	10.4 (2.0)	10.2 (2.0)	11.0 (2.1)	9.9[aaa†] (1.8)
	Boys	10.3 (1.9)	9.8 (2.0)	9.4[a] (2.2)	10.4 (1.9)	10.0 (2.0)	9.5 (2.4)	10.6 (2.2)	9.3[aaa] (1.9)
Gross Motor	Cohort	9.7 (1.9)	9.6 (2.0)	9.1 (1.7)	9.7 (1.8)	9.6 (1.7)	9.4 (2.1)	9.7 (1.9)	9.3 (1.8)
	Girls	9.5 (1.8)	9.6 (1.9)	9.0 (1.5)	9.7 (1.8)	9.4 (1.5)	9.5 (2.0)	9.7 (2.0)	9.2 (1.4)
	Boys	9.8 (2.0)	9.6 (2.0)	9.2 (1.8)	9.8 (1.8)	10.0 (1.9)	9.2 (2.2)	9.7 (1.9)	9.5 (2.0)

		Maternal Education			Paternal Education			Home Ownership	
		High	Medium	Low	High	Medium	Low	High	Medium
Social-Emotional	Cohort	104.8 (15.0)	103.3 (15.2)	99.7[a] (14.7)	106.6 (15.0)	102.0 (13.0)	100.9[a] (16.9)	105.8 (14.8)	100.2[aaa] (14.9)
	Girls	105.8 (14.7)	103.4 (16.4)	103.2[†] (13.7)	108.9 (15.0)	102.5 (14.1)	103.4 (15.8)	107.2 (14.8)	101.1[aa] (14.7)
	Boys	104.0 (15.3)	103.2 (13.9)	97.0[b] (14.9)	104.1 (14.8)	101.3 (11.6)	99.4 (17.4)	104.4 (14.8)	99.4[a] (15.1)
Adaptive Behaviour	Cohort	100.9 (13.0)	99.9 (15.0)	96.7 (16.7)	101.1 (13.3)	102.0 (13.2)	96.8[b] (16.4)	101.2 (14.2)	97.9[a] (15.4)
	Girls	101.8 (12.8)	101.1 (14.5)	102.7[††† i] (13.8)	102.8 (12.7)	103.2 (12.5)	101.7[†] (12.4)	103.2 (13.5)	100.7[†] (13.8)
	Boys	100.2 (13.1)	98.6 (15.7)	92.1[aa] (17.3)	99.4 (13.8)	100.5 (14.0)	93.9 (17.8)	99.1 (14.7)	95.5 (16.3)

Data are n or mean (SD); [a]p< 0.05; [aa]p<0.01; [aaa]p<0.001 for comparison with High group, or between own and rent; [b]p< 0.05; [bb]p<0.01; [bbb]p<0.001 for comparison between Medium and Low groups; [†]p<.05; [††]p<0.01; [†††] p<0.001 for comparison between genders; [i] p<0.05; [ii]p<0.01 for interaction between gender and SES measure; Maternal & Paternal Education: High = University education; Medium = Post-secondary training such as Polytechnic or trade certificate; Low = Up to completion of secondary school.

4.2.2 Deriving a model for adjustment for socio-economic status

We had six indices of SES available to us: NZDep2006 scores at birth and at 2 years, household income, maternal and paternal education, and home ownership. There was a high degree of correlation between these measures ($p<0.001$) although their individual associations with Bayley III scores varied (Table 4.4). Household income was the measure with the strongest association with Cognitive ($R^2 = 0.160$, $\beta = -4.717$), Language ($R^2 = 0.142$, $\beta = -6.600$), Motor ($R^2 = 0.072$, $\beta = -3.070$), and Adaptive Behavior Scores ($R^2 = 0.030$, $\beta = -3.021$). The Social-Emotional scale was most strongly correlated with home ownership ($R^2 = 0.034$, $\beta = 2.890$). The Gross Motor subscale was only significantly correlated with maternal education ($R^2 = 0.014$, $\beta = -0.269$).

Since SES was related to all of the outcomes of interest in this study, we aimed to derive the most appropriate model to take SES into account for all other study analyses. We therefore included in our multivariate analysis all indices that were related to Bayley III scores on univariate analysis with $p<0.10$, and retained those indices with a significance of $p<0.05$ in the final model (Table 4.5). We used stepwise multiple regression run forward and backward to confirm the model with the highest R^2.

The highest predictive values were attained with a model that incorporated the 2-year NZDep2006, household income, and home ownership. This model explained 19% of the variance in Cognitive, 18% of the variance in Language, and Receptive Communication, and 12% of the variance in Expressive Communication and Fine Motor scores. There were small but significant relationships with the Adaptive Behaviour and Social Emotional scores. However, there were no significant relationships with Gross Motor scores. Despite maternal and paternal education levels being significantly correlated with Bayley III scores, neither of these factors was retained in the final model.

Table 4.4: CHYLD Study measures of socioeconomic status and their individual associations with Bayley III scores

Bayley III Scale	Measure	R^2	Estimate	SE	T Ratio	P value
Cognitive	NZDep2006 at birth	0.058	-0.917	0.185	-4.95	**<0.001**
	NZDep2006 at 2 y assessment	0.072	-1.010	0.183	-5.53	**<0.001**
	Household income	0.160	-4.717	0.599	-7.87	**<0.001**
	Maternal Education	0.090	-3.764	0.619	-6.08	**<0.001**
	Paternal Education	0.083	-3.588	0.658	-5.46	**<0.001**
	Home Ownership	0.112	3.459	0.502	6.89	**<0.001**
Language Composite	NZDep2006 at birth	0.095	-1.628	0.253	-6.45	**<0.001**
	NZDep2006 at 2 y assessment	0.099	-1.644	0.259	-6.58	**<0.001**
	Household income	0.142	-6.600	0.901	-7.32	**<0.001**
	Maternal Education	0.049	-3.907	0.894	-4.37	**<0.001**
	Paternal Education	0.061	-4.45	0.963	-4.63	**<0.001**
	Home Ownership	0.116	4.892	0.699	7.00	**<0.001**
Receptive Communication	NZDep2006 at birth	0.107	-0.330	0.048	-6.91	**<0.001**
	NZDep2006 at 2 y assessment	0.110	-0.329	0.047	-6.96	**<0.001**
	Household income	0.142	-1.247	0.171	-7.31	**<0.001**
	Maternal Education	0.062	-0.834	0.168	-4.96	**<0.001**
	Paternal Education	0.080	-0.960	0.180	-5.34	**<0.001**
	Home Ownership	0.133	1.002	0.133	7.56	**<0.001**
Expressive Communication	NZDep2006 at birth	0.058	-0.232	0.046	-5.04	**<0.001**
	NZDep2006 at 2 y assessment	0.064	-0.237	0.046	-5.18	**<0.001**
	Household income	0.101	-0.996	0.165	-6.04	**<0.001**
	Maternal Education	0.029	-0.537	0.162	-3.31	**0.001**
	Paternal Education	0.034	-0.599	0.176	-3.39	**<0.001**
	Home Ownership	0.067	0.660	0.128	5.17	**<0.001**

Bayley III Scale	Measure	R^2	Estimate	SE	T Ratio	P value
Motor Composite	NZDep2006 at birth	0.008	-0.318	0.177	-1.80	0.073
	NZDep2006 at 2 y assessment	0.017	-0.455	0.176	-2.59	**0.010**
	Household income	0.072	-3.070	0.612	-5.02	**<0.001**
	Maternal Education	0.036	-2.213	0.598	-3.70	**<0.001**
	Paternal Education	0.031	-2.092	0.651	-3.22	**0.001**
	Home Ownership	0.067	2.490	0.481	5.18	**<0.001**
Fine Motor	NZDep2006 at birth	0.011	-0.081	0.038	-2.12	**0.035**
	NZDep2006 at 2 y assessment	0.022	-0.114	0.038	-2.98	**0.003**
	Household income	0.095	-0.760	0.130	-5.85	**<0.001**
	Maternal Education	0.035	-0.472	0.129	-3.65	**<0.001**
	Paternal Education	0.038	-0.497	0.139	-3.57	**<0.001**
	Home Ownership	0.089	0.624	0.103	6.04	**<0.001**
Gross Motor	NZDep2006 at birth	0.001	-0.023	0.034	-0.76	0.450
	NZDep2006 at 2 y assessment	0.003	-0.038	0.034	-1.13	0.261
	Household income	0.011	-0.237	0.123	-1.93	0.055
	Maternal Education	0.014	-0.269	0.117	-2.30	**0.022**
	Paternal Education	0.006	-0.188	0.130	-1.44	0.150
	Home Ownership	0.010	0.181	0.095	1.90	0.058
Social-Emotional	NZDep2006 at birth	0.014	-0.684	0.290	-2.36	**0.019**
	NZDep2006 at 2 y assessment	0.017	-0.771	0.283	-2.72	**0.007**
	Household income	0.016	-2.250	1.004	-2.24	**0.026**
	Maternal Education	0.019	-2.567	0.968	-2.65	**0.008**
	Paternal Education	0.022	-2.809	1.047	-2.68	**0.008**
	Home Ownership	0.034	2.890	0.788	3.57	**<0.001**
Adaptive Behaviour	NZDep2006 at birth	0.013	-0.640	0.284	-2.26	**0.025**
	NZDep2006 at 2 y assessment	0.013	-0.617	0.280	-2.20	**0.029**
	Household income	0.030	-3.021	0.963	-3.14	**0.002**
	Maternal Education	0.013	-2.128	0.965	-2.20	**0.028**
	Paternal Education	0.016	-2.281	1.007	-2.7	**0.024**
	Home Ownership	0.012	1.646	0.788	2.09	**0.037**

Table 4.5: Relationship between Bayley III scores and measures of socioeconomic status within the combined model of socioeconomic status

Bayley III Scale	R^2 Adjusted	Measure	Estimate	SE	T Ratio	p value
Cognitive	0.189	Combined model				**<0.001**
		2 y NZDep2006	-0.569	0.196	-2.91	**0.004**
		Household income	-3.03	0.753	-4.02	**<0.001**
		Home ownership	1.467	0.609	2.41	**0.017**
Language	0.180	Combined model				**<0.001**
		2 y NZDep2006	-1.003	0.288	-3.50	**0.001**
		Household income	-3.561	1.103	-3.23	**0.001**
		Home ownership	2.288	0.892	2.56	**0.011**
Receptive Communication	0.186	Combined model				**<0.001**
		2 y NZDep2006	-0.193	0.055	-3.54	**0.001**
		Household income	-0.605	0.210	-2.88	**0.004**
		Home ownership	0.522	0.169	3.08	**0.002**
Expressive Communication	0.122	Combined model				**<0.001**
		2 y NZDep2006	-0.158	0.053	-2.98	**0.031**
		Household income	-0.596	0.203	-2.93	**0.004**
		Home ownership	0.248	0.164	1.51	0.131
Motor Composite	0.086	Combined model				**<0.001**
		2 y NZDep2006	-0.116	0.201	-0.57	0.566
		Household income	-1.791	0.773	-2.32	**0.021**
		Home ownership	1.715	0.625	2.74	**0.006**
Fine Motor	0.118	Combined model				**<0.001**
		2 y NZDep2006	-0.021	0.043	-0.50	0.617
		Household income	-0.432	0.164	-2.64	**0.009**
		Home ownership	0.447	0.132	3.38	**0.001**

Bayley III Scale	R^2 Adjusted	Measure	Estimate	SE	T Ratio	p value
Gross Motor	0.006	Combined model				0.258
		2 y NZDep2006	-0.019	0.041	-0.47	0.638
		Household income	-0.148	0.156	-0.95	0.343
		Home ownership	0.106	0.126	0.84	0.400
Social-Emotional	0.030	Combined model				**<0.001**
		2 y NZDep2006	-0.291	0.331	-0.88	0.381
		Household income	-0.048	1.260	-0.04	0.970
		Home ownership	2.612	1.025	2.55	**0.011**
Adaptive Behaviour	0.023	Combined model				**0.027**
		2 y NZDep2006	-0.231	0.322	-0.72	0.473
		Household income	-1.893	1.226	-1.54	0.124
		Home ownership	1.015	0.991	1.02	0.307

4.3 Bayley III scores, breast feeding and ear infections

Breastfeeding data were available for 389 (96%) children (Table 4.6). Children who had ever been breastfed had scores approximately 7 points higher than those who had not on the Cognitive, Language, and Social-Emotional scales. There was no significant interaction between gender and breastfeeding. Adjusting for SES made little difference to the effect of breastfeeding on Cognitive (adjusted mean difference [95%CI] 6.6 [2.72, 10.46] $p < 0.001$), Language scores (8.0 [2.27, 13.67] $p = 0.006$) Receptive Communication (1.6 [0.51, 2.66] $p=0.004$) and Expressive Communication scores (1.2 [0.16, 2.26] $p = 0.024$) but abolished the effect on the Social-Emotional (4.3 [-2.47, 10.98]) and Fine Motor scores (0.8 [-0.04, 1.66]).

Data on ear infections were available for 363 (90%) children, with 208 (54.3%) reported by parents to have had at least one ear infection (Table 4.6). The mean number of ear infections reported was 2.1 (2.1). Cognitive Scale scores were 3 points higher for those who had ear infections reported than for those who did not. There was no significant interaction between gender and reported ear infections. There was also no significant correlation between Bayley III scores and the number of ear infections reported. Adjusting for SES abolished the association between reported ear infections and Cognitive scores (1.4 [-0.67, 3.42]).

4.4: Bayley III scores, preschool education and language

Data on preschool attendance were recorded for 323 (80%) children (Table 4.7). Children who attended preschool had scores approximately 5 points higher on all Bayley III scales than those who did not attend preschool, although this difference was not significant for the Social-Emotional scale, with similar patterns for girls and boys. There was an interaction between preschool attendance and gender on the Adaptive Behaviour scale, with boys, but not girls, who attended preschool having higher scores than those who did not. Adjusting for SES made little difference to the effect of preschool attendance on the Cognitive (4.0 [1.93, 6.07] $p < 0.001$), Language (3.3 [0.10, 6.53] $p = 0.043$), Motor (4.6 [2.45, 6.66] $p < 0.001$), Expressive Communication (0.8 [0.18, 1.36] $p = 0.011$), Fine Motor (0.8 [0.33, 1.23] $p < 0.001$), and Gross Motor scores (0.7 [0.26, 1.14] $p < 0.002$) but abolished the effect on the Social-Emotional (1.3 [-2.45, 4.99]), Adaptive Behavior (1.4 [-2.12, 4.84]) and Receptive Communication (0.4 [-0.27, 0.96]) scores.

For 149 children (37% of the cohort) data were also available for the reported number of hours per week spent at preschool (Table 4.8). Children spent a median of 24 hours at preschool. However, the distribution was bi-modal with peaks of attendance at 5-10 hours and 40-45 hours per week. Children with high hours of preschool attendance (≥ 24 h/wk) had higher Motor scale and Gross motor subscale scores than those with low hours of attendance (< 24 h/wk) (Table 4.8). There was no significant interaction between gender and hours of preschool attendance. Adjusting for SES did not alter the differences for Motor (4.0 [0.88, 7.03] $p = 0.012$) and Gross Motor (0.8 [0.11, 1.43] $p = 0.023$) scores, but abolished the differences for Fine Motor scores (0.5 [-0.15, 1.16]).

English was reported as being the first language for 361 (89.4%) of the cohort (Table 4.7). Children who had English as their first language had scores 5 points higher than those who did not on the Cognitive and Language scales and 8 points higher on the Social-Emotional and Adaptive Behavior scales. Adjusting for SES abolished the effect of first language on the Cognitive (2.9 [-1.28, 7.07]) and Expressive Communication scales (1.0 [-0.14, 2.10]) but not on the Social-Emotional (7.6 [0.57, 14.66] p=0.034) and Adaptive Behavior scales (7.2 [0.37, 14.05] p=0.039).

Table 4.6: Bayley III scores in children who were and were not ever breastfed and were reported to have had, or not had, ear infection

		Breastfed	Not Breastfed	Ear Infection Reported	No Ear Infection Reported
	Cohort	360	29	208	175
	Girls	175	11	97	88
	Boys	185	18	111	87
Cognitive	Cohort	94.2 (9.7)***	86.9 (14.0)	94.9 (10.6)*	92.3 (9.9)
	Girls	94.6 (9.1)*	87.3 (2.8)	94.9 (9.3)	93.3 (9.7)
	Boys	93.8 (10.3)**	86.7 (15.4)	94.8 (11.6)*	91.3 (10.1)
Language Composite	Cohort	95.5 (14.0)**	88.3 (16.7)	96.3 (15.3)	93.9 (13.0)
	Girls	96.7 (13.5)	88.4 (16.7)	98.1 (14.6)	94.2 (12.6)
	Boys	94.4 (14.5)	88.3 (17.2)	94.7 (15.8)	93.5 (13.6)
Receptive Communication	Cohort	9.4 (2.7)**	8.0 (3.2)	9.5 (3.0)	9.2 (2.4)
	Girls	9.7 (2.5)	8.2 (3.2)	9.9 (2.9)	9.2 (2.2)
	Boys	9.2 (2.8)	7.9 (3.3)	9.1 (3.0)	9.2 (2.6)
Expressive Communication	Cohort	9.0 (2.5)*	7.9 (2.6)	9.2 (2.6)	8.7 (2.5)
	Girls	9.1 (2.5)	7.8 (2.8)	9.4 (2.5)	8.7 (2.6)
	Boys	8.9 (2.6)	8.0 (2.6)	9.0 (2.7)	8.6 (2.4)
Motor Composite	Cohort	99.0 (9.5)	95.5 (10.3)	99.0 (9.8)	98.6 (9.5)
	Girls	99.5 (9.3)	95.8 (6.7)	99.8 (9.0)	98.8 (10.0)
	Boys	98.6 (9.7)	95.3 (12.2)	98.4 (10.5)	98.4 (9.5)

		Breastfed	Not Breastfed	Ear Infection Reported	No Ear Infection Reported
Fine Motor	Cohort	10.2 (2.0)**	9.0 (2.2)	10.1 (2.2)	10.1 (2.0)
	Girls	10.4 (2.0)*†	9.1 (1.8)	10.5 (2.0)	10.3 (2.0)
	Boys	9.9 (2.1)	9.0 (2.4)	9.8 (2.2)	9.9 (2.0)
Gross Motor	Cohort	9.5 (1.8)	9.4 (2.1)	9.5 (1.9)	9.4 (1.9)
	Girls	9.3 (1.8)	9.5 (1.9)	9.4 (1.7)	9.3 (1.8)
	Boys	9.6 (1.9)	9.4 (2.3)	9.6 (2.0)	9.5 (1.9)
Social-Emotional	Cohort	103.0 (14.8)*	96.5 (18.5)	102.8 (15.1)	102.4 (15.6)
	Girls	104.5 (14.7)*	93.5 (20.3)	105.4 (15.2)	102.4 (1.7)
	Boys	101.6 (14.7)	98.4 (17.8)	100.6 (14.7)	102.5 (15.9)
Adaptive Behaviour	Cohort	99.4 (14.6)	96.6 (17.9)	99.5 (14.9)	98.7 (15.0)
	Girls	101.5 (13.8)†	103.5 (11.0)	102.7 (14.0)	100.5 (13.4)
	Boys	97.3 (15.1)	92.2 (20.3)	96.7 (15.1)	96.9 (16.5)

Data are n or mean (SD); *p<.05; **p<0.01; ***p<0.001 for comparison between children who were and were not breastfed, and children who did and did not have ear infections reported; †p<.05 for comparison between genders;

Table 4.7: Bayley III scores for children who did or did not attend preschool and for whom English was or was not their first language

		Attends Preschool	No Preschool	English First Language	Other First Language
	Cohort	164	159	361	27
	Girls	79	74	172	11
	Boys	85	85	18	16
Cognitive	Cohort	96.3 (9.3)*	90.7 (9.7)	93.9 (10.3)*	89.4 (9.2)
	Girls	96.2 (8.5)*	91.3 (9.7)	94.4 (9.5)	89.5 (8.2)
	Boys	96.5 (10.1)*	90.2 (9.8)	93.4 (11.0	89.4 (10.1)
Language Composite	Cohort	97.4 (13.7)*	92.1 (14.7)	95.3 (14.4)	90.0 (13.7)
	Girls	98.4 (13.1)*	93.5 (14.8)	96.5 (13.7)	89.6 (14.3)
	Boys	96.6 (14.2)*	90.8 (14.5)	94.1 (14.9)	90.2 (13.8)
Receptive Communication	Cohort	9.7 (2.6)*	8.9 (2.8)	9.3 (2.7)	8.8 (2.8)
	Girls	9.7 (2.5)	9.3 (2.8)	9.6 (2.6)	8.6 (2.6)
	Boys	9.6 (2.7)*	8.5 (2.8)	9.1 (2.8)	8.9 (3.0)
Expressive Communication	Cohort	9.4 (2.4)*	8.4 (2.6)	9.0 (5.6)*	7.8 (2.3)
	Girls	9.6 (2.3)*	8.4 (2.7)	9.1 (2.5)	7.8 (2.5)
	Boys	9.2 (2.6)*	8.3 (2.5)	8.9 (2.6)	7.7 (2.2)

		Attends Preschool	No Preschool	English First Language	Other First Language
Motor Composite	Cohort	101.5 (9.2)*	97.3 (8.9)	98.9 (9.7)	96.5 (8.4)
	Girls	102.3 (8.7)*	97.5 (8.9)	99.5 (9.1)	97.5 (10.2)
	Boys	100.7 (9.6)*	97.1 (8.9)	98.4 (10.1	95.8 (7.2)
Fine Motor	Cohort	10.7 (2.0)*	9.8 (2.0)	10.1 (2.1)	9.8 (2.0)
	Girls	10.9 (2.0)*	10.0 (2.0)	10.3 (2.0)†	10.5 (2.3)
	Boys	10.4 (2.0)*	9.6 (1.9)	9.8 (2.1)	9.3 (1.7)
Gross Motor	Cohort	9.8 (1.8)*	9.3 (1.8)	9.5 (1.9)	9.0 (1.4)
	Girls	9.8 (1.8)*	9.2 (1.6)	9.4 (1.7)	8.5 (1.5)
	Boys	9.8 (1.8)	9.4 (1.9)	9.6 (2.0)	9.3 (1.4)
Social-Emotional	Cohort	104.2 (12.7)	101.0 (16.8)	103.0 (15.0)**	94.8 (16.2)
	Girls	104.3 (12.0)	102.2 (17.1)	104.1 (15.2)	97.0 (14.9)
	Boys	104.1 (13.3)	99.9 (16.6)	102.0 14.7)	93.3 (17.3)
Adaptive Behaviour	Cohort	100.7 (13.0)*	96.7 (15.8)	99.6 (14.8)*	92.4 (15.8)
	Girls	101.9 (11.8)	101.3(14.9)†††	101.9 (13.5)††	95.8 (16.2)
	Boys	99.5 (14.0)* [i]	92.5 (15.5)	97.4 (15.6)	90.1 (15.7)

Data are n or Mean (SD) *p<.05; **p<0.01; ***p<0.001 for comparison between children who did and did not attend preschool, and children who did and did not have English as their first language; †p<.05; ††p<.001; †††p<.001 for comparison between genders.

Table 4.8: The relationship between Bayley III scores and hours of preschool attendance for the cohort and girls and boys

		Low attendance	High attendance
	Cohort	78	71
	Girls	40	33
	Boys	38	38
Cognitive Scale	Cohort	96.2 (11.1)	96.2 (7.2)
	Girls	96.9 (10.0)	94.8 (6.3)
	Boys	95.4 (12.3)	97.4 (7.9)
Language Scale	Cohort	97.3 (16.0)	97.0 (11.3)
	Girls	98.5 (15.0)	97.2 (9.9)
	Boys	96.1 (17.1)	96.8 (12.4)
Receptive Communication	Cohort	9.7 (3.0)	9.4 (2.1)
	Girls	9.9 (2.8)	9.3 (1.9)
	Boys	9.6 (3.2)	9.6 (2.4)
Expressive Communication	Cohort	9.3 (2.8)	9.5 (2.1)
	Girls	9.5 (2.6)	9.7 (1.8)
	Boys	9.0 (3.1)	9.3 (2.3)
Motor Scale	Cohort	100.1 (8.4)	103.7 (10.2)*
	Girls	101.5 (7.4)	103.8 (10.6)
	Boys	98.6 (9.2)	103.7 (9.9) *
Fine Motor Subscale	Cohort	10.4 (2.0)	10.9 (2.1)
	Girls	10.8 (2.0)	11.0 (2.2)
	Boys	10.0 (2.0)	10.9 (2.0) *
Gross Motor Subscale	Cohort	9.6 (1.3)	10.2 (2.3) *
	Girls	9.6 (1.3)	10.2 (2.3)
	Boys	9.5 (1.4)	10.2 (2.3)
Social-Emotional Scale	Cohort	104.3 (14.0)	104.5 (10.4)
	Girls	105.6 (14.3)	103.3 (8.2)
	Boys	102.9 (13.7)	105.4 (11.9)
Adaptive Behaviour Scale	Cohort	99.8 (14.9)	100.8 (10.3)
	Girls	100.9 (13.4)	102.5 (9.4)
	Boys	98.5 (16.6)	99.4 (11.0)

Data are n or Mean (SD) *p<.05 for comparison between low (< 24 h/wk) and high (≥ 24 h/wk) preschool attendance hours.

4.4. Bayley III scores and family tobacco, alcohol and other drug use

Data were available on maternal and paternal cigarette, alcohol, marijuana and other drug use antenatally and at the 2-year assessment for 393 (97%) children.

Mothers of 108 (27.5%) and fathers of 111 (28.2%) children were reported to smoke antenatally, with the status of 16 (4.1%) mothers and 63 (16.0%) fathers unknown. Smoking rates were very similar at the 2-year assessment with 108 (27.5%) mothers and 90 (22.9%) fathers reported to smoke, and the status of 19 (4.8%) mothers and 75 (19.1%) fathers unknown. There was a strong association between reported maternal antenatal smoking and smoking at the 2-year assessment ($p<0.001$) with 78.7% of mothers who smoked antenatally also smoking at the time of the 2-year assessment.

Children whose mothers reported not smoking antenatally had Cognitive and Language scale scores approximately 5 points higher than those whose mothers reported smoking ($p = 0.002$) and 7 points higher than those whose mothers' smoking status was unknown ($p = 0.033$) (Table 4.9). Children whose fathers were reported as not smoking antenatally had Cognitive and Language scale scores 3 points higher than those whose fathers were reported as having smoked antenatally ($p = 0.028$) and 8 points higher than those whose smoking status was unknown ($p <0.001$). A similar pattern and magnitude of differences was found for the relationship between Cognitive and Language scores and parental smoking status at the time of the 2 year assessment. There were no significant interactions between gender and maternal or paternal antenatal smoking or paternal smoking at 2-years. However, there was an interaction between gender and maternal smoking at 2-years on the Social-Emotional scale with boys' but not girls' scores lower in the unknown status group.

Adjusting for SES reduced the differences in scores between children of mothers who smoked and did not smoke both antenatally and at 2 years to a similar degree and abolished the effect of maternal smoking at both time periods, with the exception of the Receptive Communication score at 2 years (maternal smoking antenatally: Cognitive (0.6 [-2.39, 3.49]), Language (2.8 [-1.55, 7.08]), Motor (0.5 [-3.49, 2.57]), Social-Emotional (1.8 [-3.22, 6.78]), Adaptive Behavior (2.4 [-7.23, 2.43]), Receptive Communication (0.5 [-0.30, 1.34]), Expressive Communication (0.5 [-0.33, 1.26])); (maternal smoking at 2 years: Cognitive (1.5 [-1.38, 4.33]), Language (3.1 [-1.05, 7.32]), Motor (0.3 [-2.67, 3.23]), Social-Emotional (1.6 [-3.26, 6.45]), Adaptive Behavior (4.4 [-9.07, 0.21]), Receptive Communication (0.9 [0.06, 1.64] p=0.032)). Similarly, adjusting for SES abolished the effect of paternal smoking at both time periods (paternal smoking at 2-years: Cognitive (2.8 [-0.29, 5.97]), Language (1.6 [-3.04, 6.18]), Motor (0.3 [-2.96, 3.51]), Social-Emotional (0.1 [-5.41, 5.19]), Adaptive Behavior (3.0 [-2.06, 8.09]), Receptive Communication (0.4[-0.49, 1.26]), Expressive Communication (0.2 [-0.67, 1.03])).

Mothers of 39 (9.9%) and fathers of 236 (60.1%) children were reported to have drunk alcohol antenatally, with the drinking status of 22 (5.6%) mothers and 67 (17.0%) fathers unknown. At the 2 year assessment more mothers (198, 50.4%) but similar numbers of fathers (236, 60.1%) were reported to drink alcohol, and similar numbers of mothers (25, 6.4%) and fathers 80 (20.4%) had

unknown drinking status (Table 4.10). Children's Bayley III scores showed no significant differences with maternal antenatal drinking status. However, children whose fathers were reported to not drink or whose drinking status was unknown before birth and at 2 years, along with children whose mothers were reported to not drink at the 2 year assessment, had Cognitive scale scores 5, Language scale scores 4-8, and Motor scale scores 3-4 points lower than those whose parents were reported to drink alcohol.

There were no significant interaction effects between gender and fathers' antenatal or 2 year alcohol use. However, there was a significant interaction between gender and maternal 2 year alcohol use, with girls whose mothers were reported to not use alcohol having lower Social-Emotional scores ($p<0.05$) than either girls whose mothers did use alcohol or those whose alcohol use status was unknown (Table 4.10). Adjusting for SES abolished the effect of maternal drinking at 2 years on all but the Gross Motor subscale (Cognitive (0.8 [-3.28, 1.65]), Language (1.2 [-4.83, 2.39]), Motor (2.4 [-0.10, 4.93]), Social-Emotional (1.9 [-6.08, 2.21]), Adaptive Behavior (0.0 [-4.06, 4.00]), Expressive Communication (0.4 [-0.29, 1.04]), Gross Motor (0.6 [0.07, 1.08] p=0.020)). Adjusting for SES also abolished the effect of paternal antenatal and 2 year drinking on all scores except antenatal Language and Expressive Communication (paternal drinking antenatally: Cognitive (2.7 [-0.26, 5.64]), Language (4.9 [0.64, 9.24] $p<0.020$), Motor (2.6 [-0.47, 5.59]), Social-Emotional (0.8 [-4.16, 5.73]), Adaptive Behavior (0.4 [-5.17, 4.42]), Receptive Communication (0.6 [-0.19, 1.46]), Expressive Communication (1.0 [0.20, 0.79] p=0.009), Gross Motor (0.6 [-0.03, 1.19])); (paternal drinking at 2 years: Cognitive (2.8 [-0.39, 5.95]), Language (4.5 [-0.11, 9.15]), Motor (2.4 [-0.84, 5.68]), Social-Emotional (0.5 [-4.84, 5.82]), Adaptive Behavior (0.5 [-4.63, 5.69]), Receptive Communication (0.6 [-0.27, 1.50]), Expressive Communication (0.9 [-0.00, 1.71]), Gross Motor (0.5 [-0.14, 1.18])).

Mothers of 15 (3.8%) and fathers of 35 (8.9%) children were reported to have used marijuana antenatally, with the status of 17 (4.3%) mothers and 64 (16.3%) fathers unknown. At the 2 year assessment 7 (1.8%) mothers and 20 (5.1%) fathers were reported to use marijuana with the status of 16 (4.1%) mothers and 74 (18.8%) fathers unknown (Table 4.10). There was a strong association between tobacco and marijuana use ($p<0.001$) with only 2 mothers who reported using marijuana antenatally not using tobacco as well.

Children whose parents reported no antenatal marijuana use had overall higher scores than children whose parents reported marijuana use. In particular they had Cognitive scores 7, Social-Emotional scores 9, and Language scores 12 points higher than those whose mothers reported using marijuana, with associated higher Receptive and Expressive Communication scores (Table 4.11). Scores for children whose mothers' antenatal marijuana use was unknown were similar to those whose mothers reported marijuana use. Children whose fathers were reported to have not used marijuana antenatally had scale scores approximately 3 points higher than those who were reported to have used marijuana, and Cognitive and Language scale scores 7 points higher than those whose marijuana status was unknown (data not shown).

Children whose mothers were reported to not use marijuana at 2 year assessment time had Cognitive and Motor Scale scores 5 points higher, but Adaptive Behavior scale scores 10 points lower than those whose mothers who were reported to use marijuana, although these differences did not reach significance. Children whose mothers' marijuana use at 2 years was unknown had scale scores similar to those whose mothers were reported to use marijuana. Similar effect sizes to these were found for children whose fathers were reported to, and reported to not use marijuana at this time (data not shown). However, children whose fathers' marijuana use status was unknown had scores approximately 5 points lower than those whose fathers were reported to not use marijuana.

There was a significant interaction between gender and marijuana use with girls, but not boys, whose mothers' were reported to use marijuana having lower Fine Motor scores than those whose mothers were reported to not use marijuana, and lower Expressive Communication subscale than girls whose mothers' status was unknown. There was also a significant interaction between gender and paternal marijuana use with boys whose fathers' marijuana use was unknown having lower scores than both other groups on the Language scale and Receptive and Expressive Communication subscales. Adjusting for SES abolished the differences between children whose mothers were reported to use and not use marijuana antenatally: (Cognitive (2.7 [-3.39, 8.896]), Language (7.5 [-1.48, 16.55]), Motor (2.5 [-3.81, 7.66]), Social-Emotional (10.1 [-0.35, 20.51]), Adaptive Behavior (0.21 [-9.70, 10.12]), Receptive Communication (1.1 [-0.58, 2.85]), Expressive Communication (1.5 [-0.13, 3.18]), Fine Motor (0.8 [-0.51, 2.17]). After adjusting for SES, Adaptive Behavior scores for children whose mothers' 2 year marijuana use was unknown became significantly different to both other groups (Maternal non-use: Adaptive Behavior (12.7 [0.65, 24.70] p=0.036); maternal use: (23.5 [5.31, 41.61] p=0.007)).

Adjusting for SES also abolished differences between scores of children whose fathers were reported to use marijuana and those whose fathers' status was unknown at 2 years (Cognitive (0.43 [-3.14, 4.00]), Language (0.61 [-5.84, 4.62]), Motor (0.88 [-2.77, 4.54]), Social-Emotional (3.41 [-2.58, 9.40]), Adaptive Behavior (3.98 [-1.83, 9.79]), Receptive Communication (0.39 [-0.60, 1.39]), Expressive Communication (0.24 [-0.73, 1.20]), Fine Motor (0.16 [-0.62, 0.93])).

Mothers of 3 (1%) and fathers of 4 (1%) children were reported to have used other drugs antenatally, with 19 (4.8%) mothers and 65 (16.5%) fathers of unknown status. No parental use of other drugs was reported at the 2 year assessment. These numbers for reported drug use were too small for further analysis.

Table 4.9: Bayley III scores for children whose mother were reported to smoke antenatally, and whose mothers and fathers were reported to smoke at 2-year assessment time

		Maternal antenatal tobacco			**Maternal tobacco at 2 years**			**Paternal tobacco at 2 years**		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
		269	108	16	266	108	19	228	90	75
Cognitive	Cohort	94.9 (10.2)	90.9** (9.3)	88.4* (11.9)	95.0 (10.5)	90.6*** (8.3)	90.3 (12.3)	95.9 (10.4)	90.8*** (8.9)	90.0*** (9.7)
	Girls	95.6 (8.8)	91.3* (9.7)	87.1* (13.2)	95.5 (9.5)	91.9* (8.0)	86.7 (14.4)	96.5 (8.7)	91.1** (9.1)	89.6*** (9.9)
	Boys	94.3 (11.4)	90.5* (8.9)	89.4 (11.6)	94.6 (11.4)	89.3** (8.6)	91.9 (11.5)	95.2 (11.8)	90.6* (8.8)	90.4* (9.6)
Language Composite	Cohort	96.8 (14.8)	91.0** (12.3)	90.8 (12.6)	96.7 (14.7)	91.0** (12.3)	92.9 (14.7)	97.1 (14.5)	92.5* (14.3)	91.3** (12.6)
	Girls	97.4 (13.9)	93.6 (13.1)	92.6 (13.5)	97.4 (14.2)	94.3†† (12.3)	89.5 (15.9)	97.6 (13.7)	94.6 (14.8)	93.4* (12.6)
	Boys	96.1 (15.6)	88.8** (11.2)	89.3 (12.4)	96.1 (15.3)	87.6*** (11.4)	94.5 (14.5)	96.6 (15.3)	91.0 (13.9)	89.4 (12.5)
Receptive Communication	Cohort	9.7 (2.8)	8.5*** (2.4)	8.8 (2.5)	9.7 (2.8)	8.3*** (2.4)	8.9 (27)	9.8 (2.7)	8.7** (2.6)	8.6** (2.6)
	Girls	9.8 (2.6)	9.0 (2.4)	9.1 (2.9)	9.8 (2.7)	9.1††† (2.3)	8.5 (3.3)	9.9 (2.6)	9.1 (2.6)	9.0 (2.5)
	Boys	9.6 (2.9)	8.0*** (2.2)	8.6 (2.4)	9.6 (2.9)	7.6*** (2.2)	9.1 (2.5)	9.7 (2.8)	8.4* (2.6)	8.3* (2.6)

		Maternal antenatal tobacco			Maternal tobacco at 2 years			Paternal tobacco at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Expressive Communication	Cohort	9.2 (2.6)	8.4* (2.3)	7.9 (2.4)	9.1 (2.6)	8.5 (2.3)	8.6 (2.8)	9.2 (2.6)	8.7 (2.6)	8.3* (2.2)
	Girls	9.2 (2.5)	8.7 (2.5)	8.3 (1.9)	9.2 (2.6)	8.9 (2.4)	7.8 (2.2)	9.2 (2.5)	9.0 (2.8)	8.7 (2.1)
	Boys	9.1 (2.7)	8.1* (2.1)	7.7 (2.7)	9.0 (2.7)	8.1 (2.1)	8.9 (3.0)	9.2 (2.7)	8.4 (2.4)	8.0* (2.2)
Motor Composite	Cohort	99.3 (9.9)	97.7 (8.7)	96.6 (9.3)	99.2 (9.7)	97.7 (9.4)	97.7 (9.2)	99.7 (9.7)	98.4 (9.8)	96.3* (8.6)
	Girls	99.8 (9.4)	98.7 (8.5)	93.7 (8.3)	100.1 (9.7)	98.2 (7.6)	92.7[i] (8.5)	99.8 (9.6)	100.0 (7.7)	96.8 (9.0)
	Boys	98.8 (10.3)	96.8 (8.9)	98.8 (9.9)	98.5 (9.6)	97.2 (1.4)	100.0 (2.8)	99.6 (9.8)	97.2 (11.0)	95.9 (8.4)
Fine Motor	Cohort	10.2 (2.1)	9.7 (2.0)	9.6 (1.8)	10.2 (2.1)	9.8 (2.0)	9.8 (2.2)	10.3 (2.1)	9.9 (2.1)	9.6* (2.0)
	Girls	10.6 (1.9)	10.0 (2.1)	9.6 (1.8)	10.5[†] (2.0)	10.2[†] (2.0)	9.0[i] (2.1)	10.4 (2.0)	10.4 (1.8)	10.1 (2.1)
	Boys	9.9 (2.2)	9.5 (1.9)	9.6 (1.9)	9.9 (2.1)	9.3 (2.0)	10.2 (2.3)	10.1 (2.1)	9.6 (2.2)	9.2 (1.8)
Gross Motor	ohort	9.5 (1.9)	9.5 (1.7)	9.3 (1.8)	9.5 (1.8)	9.5 (2.0)	9.3 (1.5)	9.6 (1.9)	9.5 (1.9)	9.1 (1.5)
	Girls	9. 3 (1.8)	9.6 (1.7)	8.3[i] (1.6)	9.5 (1.9)	9.2 (1.2)	8.5 (1.9)	9.4 (1.9)	9.6 (1.4)	8.8 (1.7)
	Boys	9.6 (2.0)	9.4 (1.8)	10.0 (1.6)	9.5 (1.8)	9.7 (2.5)	9.7 (1.3)	9.7 (2.0)	9.4 (2.2)	9.4 (1.4)

		Maternal antenatal tobacco			Maternal tobacco at 2 years			Paternal tobacco at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Social-Emotional	Cohort	103.5 (14.8)	100.0 (15.3)	102.3 (18.8)	103.4 (15.2)	100.2 (15.1)	101.1 (14.5)	103.5 (15.0)	102.0 (15.7)	100.0 (15.0)
	Girls	105.2 (14.8)	100.2* (15.5)	106.4 (17.7)	104.8 (14.5)	100.7 (16.6)	114.2†i (11.1)	105.0 (15.0)	105.0 (16.4)	99.4 (14.3)
	Boys	101.9 (14.7)	99.7 (15.3)	98.8 (20.1)	102.3 (15.7)	99.6 (13.5)	94.6 (11.4)	102.0 (14.9)	99.9 (15.0)	100.5 (15.8)
Adaptive Behaviour	Cohort	99.1 (15.3)	99.4 (14.1)	97.7 (14.9)	98.4 (15.1)	100.8 (14.5)	99.9 (14.8)	100.7 (14.6)	97.3 (14.7)	96.2 (15.6)
	Girls	100.9 (13.7)	103.6 (14.0)	101.1 (12.0)	100.2 (13.2)	105.7*††† (14.3)	96.8 (10.7)	102.3 (13.2)	101.9†† (12.5)	99.3 (16.4)
	Boys	97.4 (16.5)	95.6 (13.1)	94.8 (17.3)	96.8 (16.5)	95.5 (12.9)	101.5 (16.7)	99.1 (15.9)	94.1 (15.4)	93.4 (14.5)

Data are n or mean (SD). *p< 0.05; **p<0.01; ***p<0.001 for comparison with 'No' (non-use); †p<0.05; †† p<0.01; †††p<0.001 for comparison between genders. i p<0.05 for interaction between gender and maternal tobacco use.

Table 4.10: Bayley III scores for children whose fathers who were reported to drink alcohol antenatally, and whose mothers and fathers were reported to drink alcohol at 2 year assessment time

		Maternal alcohol at 2years			**Paternal antenatal alcohol**			**Paternal alcohol at 2 years**		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
		170	198	25	90	236	67	77	236	80
Cognitive	Cohort	92.5 (10.5)	95.0 (9.6)	89.6* (11.7)	91.1 (10.2)	95.7*** (9.8)	89.4 (9.9)	90.8 (10.3)	95.7*** (9.7)	90.1*** (10.1)
	Girls	93.1 (9.8)	95.2 (9.0)	92.8 (9.7)	92.4 (9.1)	96.0 (8.7)	90.0∞∞ (10.9)	92.3 (8.6)	96.0 (9.2)	90.5** (9.7)
	Boys	91.9 (11.1)	94.8 (10.2)	87.8∞ (12.6)	90.0 (11.0)	95.5** (10.8)	88.8∞∞ (9.0)	89.5 (11.6)	95.4** (10.2)	89.6** (10.6)
Language Composite	Cohort	93.1 (14.7)	97.0* (13.6)	91.8 (15.4)	90.2 (12.9)	98.1*** (14.5)	90.1 (12.3)	90.1 (12.6)	98.0*** (14.6)	90.7*** (12.8)
	Girls	94.0 (15.2)	98.4 (12.1)	94.9 (13.4)	90.0 (12.6)	99.4*** (13.8)	93.0∞ (11.9)	90.1 (12.5)	99.2** (14.1)	93.7† (11.6)
	Boys	92.1 (14.3)	95.8 (14.7)	90.0 (16.6)	90.3 (13.3)	97.0** (15.1)	87.1∞ (12.2)	90.1 (12.9)	96.9** (15.0)	87.9* (13.4)
Receptive Communication	Cohort	9.1 (2.9)	9.6 (2.5)	8.8 (3.0)	8.6 (2.4)	9.8** (2.8)	8.5∞∞ (2.6)	8.6 (2.4)	9.8** (2.8)	8.6** (2.6)
	Girls	9.2 (2.9)	9.9 (2.2)	9.8 (2.9)	8.7 (2.2)	10.1** (2.6)	9.1 (2.5)	8.7 (2.2)	10.0* (2.7)	9.2† (2.5)
	Boys	8.9 (2.9)	9.4 (2.7)	8.3 (3.0)	8.6 (2.6)	9.6 (2.9)	7.9∞∞ (2.6)	8.6 (2.7)	9.6 (2.8)	8.0** (2.7)

		Maternal alcohol at 2 years			Paternal antenatal alcohol			Paternal alcohol at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Expressive Communication	Cohort	8.5 (2.5)	9.3** (2.5)	8.3 (2.9)	8.0 (2.5)	9.5*** (2.6)	8.0∞∞∞ (2.1)	8.0 (2.3)	9.5*** (2.6)	8.2*** (2.2)
	Girls	8.6 (2.7)	9.5* (2.3)	8.4 (2.3)	7.9 (2.5)	9.7*** (2.5)	8.5∞ (2.0)	7.9 (2.5)	9.6*** (2.5)	8.6 (2.0)
	Boys	8.3 (2.3)	9.2 (2.6)	8.2 (3.3)	8.1 (2.4)	9.3* (2.6)	7.6∞∞ (2.0)	8.1 (2.2)	9.3* (2.7)	7.8** (2.4)
Motor Composite	Cohort	97.4 (8.5)	100.3* (9.9)	96.1 (12.2)	96.6 (9.5)	100.3** (9.5)	96.3 (9.1)	97.0 (8.0)	100.3* (9.7)	95.8*** (9.6)
	Girls	97.6 (8.3)	101.2* (9.7)	95.6 (8.4)	96.6 (8.5)	100.8* (9.1)	97.3 (9.5)	96.5 (7.3)	101.0* (9.5)	97.2 (9.1)
	Boys	97.2 (8.6)	99.4 (10.1)	96.4 (14.1)	96.6 (10.4)	99.7 (9.8)	95.3 (8.7)	97.6 (8.7)	99.7 (10.0)	94.5* (10.1)
Fine Motor	Cohort	9.9 (2.0)	10.3 (2.1)	9.4 (2.6)	9.8 (2.2)	10.3 (2.0)	9.6∞ (2.1)	9.9 (1.9)	10.3 (2.1)	9.5** (2.1)
	Girls	10.1 (1.8)	10.6† (2.1)	10.0 (2.1)	10.1 (2.0)	10.5 (1.9)	10.1 (2.2)	10.1 (1.9)	10.6 (2.0)	10.1† (2.0)
	Boys	9.8 (2.1)	10.0 (2.0)	9.1 (2.8)	9.6 (2.3)	10.1 (2.0)	9.1∞ (2.0)	9.8 (2.0)	10.1 (2.1)	8.9** (2.1)
Gross Motor	Cohort	9.2 (1.4)	9.8** (2.0)	9.2 (2.0)	9.0 (1.5)	9.7** (2.0)	9.1∞ (1.5)	9.1 (1.3)	9.7* (2.0)	9.1* (1.7)
	Girls	9.0 (1.5)	9.7* (1.9)	8.4 (1.5)	8.8 (1.4)	9.7* (1.8)	8.9 (1.7)	8.7† (1.2)	9.7** (1.8)	8.9* (1.8)
	Boys	9.3 (1.3)	9.8 (2.3)	9.6 (2.2)	9.3 (1.6)	9.8 (2.2)	9.3 (1.4)	9.4 (1.4)	9.7 (2.2)	9.3 (1.6)

		Maternal alcohol at 2 years			Paternal antenatal alcohol			Paternal alcohol at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Social-Emotional	Cohort	101.6 (16.1)	103.6 (14.4)	99.8 (14.3)	102.4 (16.6)	103.7 (14.8)	98.2$^{\infty}$ (13.8)	101.8 (13.1)	103.6 (14.7)	99.8 (15.4)
	Girls	100.9^{i} (16.0)	106.3† (14.6)	108.9† (7.0)	101.8 (15.2)	106.1† (15.3)	99.2 (14.0)	101.8 (15.1)	106.1† (15.6)	99.7 (13.3)
	Boys	102.3 (16.3)	101.3 (13.8)	94.3 (14.9)	102.9 (17.9)	101.5 (14.0)	97.1 (13.6)	101.8 (17.1)	101.4 (13.5)	99.9 (17.4)
Adaptive Behaviour	Cohort	98.6 (15.5)	99.6 (14.0)	98.4 (17.7)	99.0 (15.6)	100.4 (14.4)	94.8$^{\infty}$ (15.4)	99.2 (14.4)	100.3 (14.6)	95.3* (16.2)
	Girls	100.2 (14.0)	103.1†† (13.5)	100.6 (11.0)	99.9 (13.7)	103.1†† (12.8)	98.8† (16.0)	100.6 (13.4)	102.9† (13.1)	99.2† (15.4)
	Boys	97.0 (16.9)	96.5 (13.8)	97.1 (21.0)	98.3 (17.1)	97.8 (15.3)	90.5 (13.8)	97.8 (14.8)	98.1 (15.5)	91.4 (16.3)

Data are n or mean (SD). *p< 0.05; **p<0.01; ***p<0.001 for comparison with 'No' (non-use); $^{\infty}$ p< 0.05 for between 'Yes' and 'Unknown'; †p<0.05; †p<0.01; †††p<0.001 for comparison between genders; ^{i}p<0.05 for interaction between gender and alcohol use

Table 4.11: Bayley III scores for children whose mothers reported antenatal marijuana use, and whose mothers and fathers were reported to use marijuana at 2 year assessment time

		Maternal antenatal marijuana			**Maternal marijuana at 2 years**			**Paternal marijuana at 2 years**		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
		361	15	17	370	7	16	299	20	74
Cognitive	Cohort	94.1 (10.0)	87.3* (2.6)	87.4* (11.2)	93.9 (10.1)	89.3 (13.4)	87.5* (11.5)	94.6 (10.0)	93.2 (10.7)	89.4*** (10.0)
	Girls	94.6 (9.2)	86.9* (12.8)	90.8 (9.7)	94.5 (9.2)	82.5 * (14.4)	90.8 (9.7)	95.1 (8.8)	95.0 (15.8)	90.0** (9.9)
	Boys	93.7 (10.8)	87.9* (7.0)	85.5 (11.9)	93.4 (10.8)	98.3 (2.9)	85.5 (12.6)	94.2 (11.1)	92.3 (8.1)	88.8* (10.2)
Language Composite	Cohort	95.6 (14.2)	84.0** (3.6)	90.1 (14.8)	95.2 (14.3)	95.0 (12.8)	88.4 (15.4)	96.3 (14.1)	92.4 (17.3)	90.4** (13.4)
	Girls	96.8 (13.8)	84.4* (7.9)	96.2 (12.6)	96.6 (13.8)	86.0†† (6.0)	92.8 (14.8)	97.3 (13.6)	80.8*† (14.5)	94.3† (12.9)
	Boys	94.6 (14.6)	83.6 (14.2)	86.7 (15.4)	94.0 (14.6)	107.0 (7.5)	85.7 (15.9)	95.2 (14.6)	97.8 (16.3)	86.7**∞∞ii (12.9)
Receptive Communication	Cohort	9.4 (2.7)	7.5* (2.4)	8.8 (2.8)	9.3 (2.7)	9.7 (2.1)	8.4 (2.9)	9.5 (2.7)	9.3 (3.4)	8.5* (2.6)
	Girls	9.7 (2.6)	7.8* (2.0)	10.0 (2.7)	9.6 (2.6)	8.5 (1.7)	9.2 (3.1)	9.7 (2.6)	7.8 (3.5)	9.2† (2.5)
	Boys	9.2 (2.8)	7.1 (3.0)	8.1 (2.7)	9.1 (2.8)	11.3 (1.5)	8.0 (2.8)	9.3 (2.8)	10.0 (3.3)	7.8*∞i (2.6)

		Maternal antenatal marijuana			Maternal marijuana at 2 years			Paternal marijuana at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Expressive Communication	Cohort	9.0 (2.5)	7.0** (1.6)	7.8 (2.7)	9.0 (2.5)	8.6 (2.4)	7.5 (2.8)	9.2 (2.5)	8.0 (3.0)	8.1** (2.4)
	Girls	9.2 (2.5)	6.9* (1.1)	8.7 (1.8)	9.1 (2.5)	6.8$^{\dagger\dagger i}$ (1.0)	8.3 (2.1)	9.3 (2.5)	5.5***†† (2.6)	8.8$^{\dagger\infty\infty}$ (2.3)
	Boys	8.9 (2.5)	7.1 (2.0)	7.3 (3.1)	8.8 (2.5)	11.0 (1.0)	7.0* (3.1)	9.0 (2.6)	9.2 (2.4)	7.5**^{ii} (2.3)
Motor Composite	Cohort	99.1 (9.4)	94.1 (7.2)	94.9 (12.8)	99.0 (9.4)	94.0 (8.3)	94.6 (13.1)	99.3 (9.2)	100.3 (12.5)	96.0* (9.9)
	Girls	99.7 (9.2)	94.1 (6.9)	95.7 (8.5)	99.7 (9.2)	90.3 (2.9)	94.2 (8.4)	99.9 (9.3)	95.5 (5.3)	97.4 (9.2)
	Boys	98.6 (9.6)	94.1 (8.0)	94.5 (15.0)	98.4 (9.6)	99.0 (11.4)	94.9 (15.8)	98.8 (9.1)	102.5 (14.3)	94.7$^{\infty}$ (10.5)
Fine Motor	Cohort	10.2 (2.0)	8.7* (1.4)	9.3 (2.6)	10.1 (2.0)	8.7 (2.1)	9.1 (2.7)	10.2 (2.0)	10.2 (2.0)	9.6* (2.2)
	Girls	10.5 (2.0)	8.4** (1.5)	10.2 (1.5)	10.5 (2.0)	7.5 ** (0.6)	9.5 (1.9)	10.4† (2.0)	9.8 (1.7)	10.2† (2.0)
	Boys	9.9 (2.1)	9.1 (1.3)	8.8 (3.0)	9.8 (2.0)	10.3 (2.3)	8.9 (3.1)	10.0 (2.0)	10.4 (2.1)	9.0* (2.2)
Gross Motor	Cohort	9.5 (1.8)	9.3 (1.9)	8.9 (2.0)	9.5 (1.9)	9.3 (1.1)	9.0 (2.1)	9.5 (1.8)	9.8 (3.2)	9.1 (1.7)
	Girls	9.4 (1.7)	9.6 (2.4)	8.3 (1.8)	9.4 (1.8)	9.3 (1.0)	8.5 (1.9)	9.5 (1.8)	8.7 (1.0)	8.9 (1.8)
	Boys	9.6 (1.9)	8.9 (1.3)	9.3 (2.1)	9.6 (1.9)	9.3 (1.5)	9.3 (2.3)	9.6 (1.8)	10.4 (3.7)	9.2 (1.6)

		Maternal antenatal marijuana			Maternal marijuana at 2 years			Paternal marijuana at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Social-Emotional	Cohort	103.2 (14.8)	93.9* (18.0)	94.4 (16.5)	102.9 (15.0)	100.7 (17.9)	94.7 (16.5)	103.4 (14.9)	100.6 (16.9)	99.1 (15.5)
	Girls	104.1 (15.2)	97.9 (17.3)	105.8 (13.2)	103.8 (15.2)	98.8 [i] (24.3)	110.0 (8.4)	104.8 (15.4)	100.0 (16.6)	101.0 (14.4)
	Boys	102.4 (14.4)	90.0 (19.1)	87.5** (14.8)	102.0 (14.8)	103.3 (7.6)	84.4** (11.8)	102.1 (14.4)	100.8 (17.7)	97.1 (16.5)
Adaptive Behaviour	Cohort	99.4 (14.7)	97.7 (15.9)	95.2 (18.4)	99.2 (14.7)	109.1 (15.4)	92.6[∞] (17.8)	100.5 (14.5)	94.3 (13.1)	94.7* (16.2)
	Girls	101.6 (13.7)	102.8 (16.3)	102.7 (12.4)	101.7[†] (13.6)	108.0 (20.5)	96.8 (10.7)	102.6[†] (13.2)	93.8 (7.3)	99.3[†] (15.9)
	Boys	97.3 (15.4)	91.9 (14.4)	90.7 (20.4)	96.9 (15.3)	110.7 (8.6)	89.8 (21.5)	98.5 (15.4)	94.6 (15.35)	90.1* (15.4)

Data are n or mean (SD). *p< 0.05; **p<0.01; ***p<0.001 for comparison with 'No' (non-use); [∞] p< 0.05 for comparison between 'Yes' and 'Unknown'
[†]p<0.05; [††]p<0.01; [†††]p<0.001 for comparison between genders; [i] p<0.05 for interaction between gender and marijuana use

4.5. Discussion

The Bayley Scales (Bayley, 2006) are standardised developmental scales commonly used clinically and in research (Robertson, 2010). The most recent version, the Bayley III, is used for assessment of development up to 42 months; cognitive, language, and motor skills by direct assessment and social-emotional development and adaptive behaviour by parent questionnaire (Bayley, 2006). No Bayley III norms have yet been developed for countries other than the United States (Acton et al., 2011). Therefore, there is no confirmation that the standardisation of the Bayley III is appropriate for New Zealand preschoolers. However, there is no evidence to suggest that the New Zealand preschool population would be expected to perform significantly differently from the preschool population of the United States.

Our cohort is characterised by scores lower than the standardised mean on all Bayley III measures except the Fine Motor subscale. However, results of parent report for the Social-Emotional scale were higher and the Adaptive Behaviour scale not different from the standardised mean.

The Bayley III used an inclusive United States population in the normative sample and included data from children with cerebral palsy, and those born at risk of developmental delay, small-for-gestational-age and preterm (Bayley, 2006). However, the standardised special population results reported in the Bayley III technical manual state that small-for-gestational-age children scored lower than normal controls on all scales but only significantly so for the Receptive Communication and Gross Motor subscales, and the preterm group scored significantly lower than normal controls only on the Fine Motor scale. The Bayley III results for our cohort do not differ between risk factor groups, which suggests that low Bayley III scores in our cohort are not likely to be explained entirely by primary risk factors at birth. Elsewhere, reduced developmental scores across all domains have been recorded in late preterm and low SES preschool children, and have been found to persist through to school leaving age (Baron et al., 2011; Black, Hess, & Berenson-Howard, 2000; N. Breslau, Dickens, Flynn, Peterson, & Lucia, 2006; Laucht, Esser, & Schmidt, 1997).

SES is a significant predictor of developmental outcome, although its definition and measurement are controversial (American Psychological Association task force on socioeconomic status, 2007; Bradley & Corwyn, 2002). This controversy relates to the number of interrelated factors which contribute to SES and can be measured and then employed in analysis either singly or as a composite (Oakes, 2012). These factors include income, education, work, marital status, neighbourhood, and indicators of wealth such as home and car ownership (Bradley & Corwyn, 2002). From a developmental perspective, SES describes an individual's access to resources including both material resources as diverse as education, health care, books and educational toys, and non-material resources such as social networks and opportunities (American Psychological Association task force on socioeconomic status, 2007). Health, social-emotional, and neurocognitive outcomes are significantly and differentially associated with SES; with language development, including both receptive and expressive communication, the most negatively influenced aspect of development for children in low SES American families (Hackman & Farah, 2009; Noble et al., 2007; Wild et al., 2013). Low SES is

associated with greater stress, heightening the likelihood of maternal depression which is a risk factor in social-emotional development, particularly for boys (Hughes & Ensor, 2009; Palmer et al., 2013).

We assessed family income, maternal and paternal education, and NZDep2006 at birth and at 2 year assessment, and home ownership to assess their relationship to developmental outcome. We also included analysis with the New Zealand Deprivation Index (NZDep), which uses New Zealand census data for nine factors weighted for importance to SES (Crampton et al., 2000). Income is included twice to reflect its importance to overall SES. However, NZDep2006 is a population analysis tool, based on small geographically defined population groups, that was initially intended to support social policy and planning. As such, it can only be used as a proxy for individual SES (Crampton et al., 2000; Oakes, 2004) and even then only cautiously (Bound, Geronimus, & Neidert, 1996). Furthermore, a recent large-scale review by the American Psychological Association suggests that the individual factors contributing to SES need to be assessed separately for their different and relative contributions (American Psychological Association task force on socioeconomic status, 2007).

In our cohort, as previously reported (Bradley & Corwyn, 2002; Duncan & Brooks-Gunn, 2000), household income was the SES factor most strongly related to developmental scores. This accords with Oakes' (2012) contention that despite the effort invested in the development of composite measures, income and education are, alone or together, sufficiently descriptive of SES. Overall, our cohort had scores below the standardised mean. However, children in the high income group had Bayley III scores at the standardised mean, while children in the lower income group showed a graded decrease in scores. This was most marked on the Cognitive and Language scale scores where the low income group had scores two-thirds of a standard deviation below the mean on the Cognitive scale and nearly a full standard deviation below on the Language scale. A similar sized difference was found on the Bayley III Language scales and subscales between high and low SES groups of very preterm American children at 23 months (Wild et al., 2013). Elsewhere, it has been found that SES predicts developmental outcome in all developmental domains, particularly language, but excluding gross motor skills, which may be explained by the gross motor assessment focussing on early skills which are less vulnerable to familial and environmental influences, and also because subtle gross motor deficits may not be apparent until older ages (B. Hart & Risley, 1995; Hoff, 2003; Piek, Dawson, Smith, & Gasson, 2008; Potijk et al.).

The rate of home ownership in New Zealand in 2006 was approximately 67%, with the lowest income quartile much less likely to own their own home (Morrison, 2008). Our cohort reflects this trend of home ownership significantly correlated with income. However, only 43% of the children in our cohort lived in homes owned by a parent or caregiver. This lower rate is partly explained by the higher proportion of our cohort being from areas of higher deprivation than is found nationally, as evidenced by the skewed NZDep2006 distributions. In addition, home ownership is not just a function of household income, as it is also associated with family wealth, job security and parental age. These factors affect, amongst other things, the ability to save for a house deposit (Buckett et al., 2011). Rental housing in New Zealand is associated with a higher household moving rate, poorer housing conditions including less insulation and poorer heating, and higher incidence of damp and mould than

is found in owner-occupier homes (Buckett et al., 2011). Our SES model shows home ownership to be independently related to all Bayley III scores except Gross Motor and Adaptive Behaviour scores. Moreover, children in rental housing in our cohort had a significant disadvantage in cognitive and language development compared to those children living in a family-owned home. Studies from the United States and United Kingdom have found a similar effect, although the detail of the factors underlying the differences and how they function are not fully understood (Boyle, 2002; Brennan, 2010).

Maternal education has been found to be predictive of child intellectual outcomes, independent of other SES indicators (Duncan, Brooks-Gunn, & Maritato, 1997) and to be predictive of language outcome, contributing to an increasing amount of language variation over the preschool years as the influence of biological risk decreases and that of environmental risk increases (Laucht et al., 1997; Noble et al., 2007; Reilly et al., 2010). However, paternal education was the variable most predictive of IQ at 5 years in a group who had been very low birth weight babies, although maternal education was more predictive in the control group (Böhm, Katz-Salamon, Smedler, Lagercrantz, & Forssberg, 2002). In our cohort both maternal and paternal education were similarly correlated with Bayley III scores, predicting approximately 9% of the variation in cognitive and 5% of the variation in language scores. These similar correlations of parental scores may be a result of our cohort being assessed at 2 years of age and may change with children's age (Bradley & Corwyn, 2002). A more comprehensive comparison of maternal and paternal contribution to child development at 2 years is difficult as paternal education is frequently not reported; a reflection of both the number of single-parent households and the problem of missing data (Duncan et al., 1997).

The model we developed to take SES into account for our analyses incorporated NZDep2006 at 2 year assessment, household income, and home ownership. Household income had the strongest single correlation with Bayley III scores but including the other two variables further strengthened the predictions, an effect that has been reported elsewhere (Bradley & Corwyn, 2002). Neither maternal nor paternal education remained significant in our final model, which most likely reflects a high degree of correlation of parent education with other measures of SES.

Approximately 51% of our cohort attended preschool, which is comparable to the national figure of 54% of all preschoolers (Statistics New Zealand, 2010). Developmental scores were significantly higher on all scales amongst children who attend preschool and after adjustment for SES the differences remained significant for the Cognitive, Language and Motor scales, suggesting that preschool attendance is a significant positive contribution to children's learning, independent of SES. Only children's motor scores were related to the number of hours of attendance at preschool. It is possible that increased preschool attendance gives increased access to play equipment and toys that encourage the development of motor skills, such as running, jumping and ball skills, in the presence of trained preschool teachers (Draper, Achmat, Forbes, & Lambert, 2011). This may be occurring in tandem with reduced exposure to passive television watching at home.

Children who were breastfed performed better on all Bayley III scales, except the Adaptive Behaviour scale and Gross Motor subscale, than those who were never breastfed. This is consistent with previous reports of a correlation between breastfeeding and cognitive, language and neural development (Belfort et al., 2013; Herba et al., 2013; Kramer et al., 2008). Unlike previous studies from New Zealand, France and the United States (Horwood & Fergusson, 1998; Rey, 2003; Uauy & Peirano, 1999), in our cohort there was no correlation between breastfeeding and SES or ethnicity. This probably reflects the very high proportion (93%) of mothers in our cohort who breastfed their babies, although this is a lower than the 97% recently reported in a large New Zealand study (Morton et al., 2012). Because breastfeeding remains a significant predictor of Cognitive and Language scores, it is an important item to include in the analysis of our primary study questions.

There was a trend for children who had ear infections reported to have higher scores than those who had no ear infections reported but this only reached significance on the Cognitive Scale score. There is no apparent reason for children with ear infections to have higher developmental scores than those without; in fact the opposite would be expected, (Ucles, Alonso, Aznar, & Lapresta, 2012; Winskel, 2006) with language development being adversely affected by potential hearing loss (Browning, Rovers, Williamson, Lous, & Burton, 2010; J. E. Roberts, Rosenfeld, & Zeisel, 2004). Our data may be capturing parental reporting and hence awareness, rather than the actual occurrence of ear infections. In an at-risk population such as ours, ear infections are likely to be common, and not always recognised or remembered.

Girls in our cohort had higher Fine Motor subscale and Adaptive Behaviour scores than boys; differences that have been widely reported elsewhere (Black et al., 2000; Domínguez, Vitiello, Maier, & Greenfield, 2010; Statistics New Zealand, 2006). These differences are important because Fine Motor and Adaptive Behavior skills positively predict achievement at kindergarten entry (Cameron et al., 2012) along with later cognitive development and academic achievement (A. G. Carlson, Rowe, & Curby, 2013; Dinehart & Manfra, 2013; Megan M. McClelland et al., 2007; McPhillips & Jordan-Black, 2007). However, girls in our cohort did not have significantly higher language scores as has been reported in overseas studies of similar age children (Reilly et al., 2007; Schjolberg, Eadie, Zachrisson, Oyen, & Prior, 2011; Zubrick, Taylor, Rice, & Slegers, 2007). This may suggest that gender differences are not as important in our cohort as the medical risk factors that made these children eligible for the study.

Boy babies have higher rates of mortality and morbidity than girl babies. They are more likely to be still-born or born preterm, to have a poor outcome after brain haemorrhage as a result of preterm birth, to be diagnosed with cerebral palsy (Chounti, Hagglund, Wagner, & Westbom, 2013), and ADHD by the age of four (Ingemarsson, 2003), and to be hospitalised (Hon & Nelson, 2006). This early gender difference in biological vulnerability can have a significant effect on developmental trajectory and in New Zealand, as elsewhere, is associated with lower academic achievement for boys in reading and writing (Liederman, Kantrowitz, & Flannery, 2005), with twice as many boys as girls entering the reading recovery programme, and internationally two to three times as many boys as girls entering special education services (David Mitchell, 2010; Ministry of Education, 2007).

Behaviour and social outcomes are also influenced by gender with 70% of school stand-downs and suspension in New Zealand being boys, and boys more likely to apply for formal early school leaving, to finish school with no formal education and to not continue with tertiary qualification (Ministry of Education, 2007). Differences in early developmental trajectory continue and the increased vulnerability of boys is still seen in the teenage years, at which time in New Zealand boys account for 87% of youth suicides and 75% of youth under the age of 17 with conduct disorder (Fergusson, Donnell, & Slater, 1994; Moller-Leimkuhler, 2003) with the combination of social, economic and family effects cited as the most prevalent underlying cause (Landgren, Pettersson, Kjellman, & Gillberg, 1996).

In addition to differences in scores between girls and boys, we found gender interactions with household income (Adaptive Behavior), NZDep2006 at birth (Cognitive and Social-Emotional), and maternal education (Language scale and subscales; Adaptive Behavior) with boys from the lowest SES group having lower scores than other boys and all girls. However, boys but not girls who attended preschool had higher scores on the Adaptive Behavior scale. Elsewhere, boys' Bayley Mental Development scores have been shown to be more negatively affected than girls' by their mothers' return to work within their first year (Brooks–Gunn, Han, & Waldfogel, 2002), more susceptible to the negative effects of preschool, such as those associated with high child-staff ratios and increasing time in day-care than girls, and more sensitive to family conflict (Bornstein, Hahn, Gist, & Haynes, 2006). These results suggest that boys are more sensitive than girls to adverse environmental conditions and although, with appropriate preschool education, boys from low SES families can learn skills such as those assessed on the Adaptive Behaviour scale, their increased vulnerability to biological and social factors may result in a growing disparity with girls with increasing age (Bornstein et al., 2006; Brooks–Gunn et al., 2002; Megan M. McClelland et al., 2007; Sektnan, McClelland, Acock, & Morrison, 2010).

The interaction between gender and SES in our data may reflect both the biological vulnerability of boy babies, which mediates a sensitivity to environmental disadvantage, and different parenting of girls and boys. Parents respond differently to disruptive behaviour from girls and boys, and boys' but not girls' receptive communication skills at 2 years are positively associated with mothers' sensitive parenting at 3 years of age (M. A. Barnett, Gustafsson, Deng, Mills-Koonce, & Cox, 2012; Wright et al., 2013). In low SES environments warm, supportive relationships with their mothers are more important for boys than girls (Gaylord-Harden, Elmore, & Montes de Oca, 2013). In New Zealand, as elsewhere, there is also a prevalent social attitude amongst both men and women which expects men and boys to be tough and requiring of less nurturing than girls and this may underlie the overlooking of the increased needs of male children, particularly those at biological or social risk (Bannister, 2005; Edwards, McCreanor, Ormsby, Tuwhangai, & Tipene-Leach, 2009; Hammond, 2012).

A large proportion of mothers in our cohort (27%) continued to smoke while pregnant, in keeping with the range reported in Sweden and the United Kingdom (Cnattingius, 2004; Ward, Lewis, & Coleman, 2007) but twice the rate reported in America (Wu et al., 2013). Children in our cohort whose mothers smoked antenatally had lower Cognitive and Language scores than those whose mothers did not

smoke although this difference was abolished after adjusting for SES. This strong correlation with SES, and in particular maternal education, has been reported elsewhere in New Zealand and international studies (Knopik, 2009; van den Berg et al., 2012). Antenatal smoking is also associated with increased risk of preterm birth and being born small, with resulting smaller head circumference (Rivkin et al., 2008; Ward et al., 2007) and behaviour and attention problems in school-age children (El Marroun et al., 2014; Knopik, 2009).

A small number of mothers in our cohort were reported to drink alcohol antenatally (10%), with the number increasing at the 2 year assessment (50%). Elsewhere, maternal antenatal drinking rates as high as 53% have been reported in New Zealand (Wu et al., 2013). However, maternal drinking was not related to Bayley scores at 2 year assessment after correcting for SES. Interestingly, paternal alcohol use was associated with higher scores and this persisted for Cognitive and Language scores after adjustment for SES. Since there is no obvious reason why paternal drinking is beneficial, an alternative explanation may be that not drinking is adversely related to early development, perhaps because some non-drinkers may belong to particularly conservative religious or economically disadvantaged groups and that these contribute to the observed relationship with preschool child development.

Mothers and fathers were both reported to smoke marijuana antenatally and at 2 years (2-5%), although elsewhere higher rates have been reported in New Zealand (Wu et al., 2013). Both maternal and paternal marijuana use was associated with lower scores on most scales, although these differences were abolished after adjustment for SES. Marijuana use in New Zealand is associated with low SES, with the higher use rate associated with poorer outcomes in education, employment and crime rates (Marie et al., 2008). Elsewhere, maternal antenatal marijuana use has been associated with reduced head circumference in school age children, and lower IQ at 3 years, although this effect was negated by preschool attendance for 'white' (sic) and therefore higher SES children (Day et al., 1994; Rivkin et al., 2008). It is also associated with learning and attention problems in 10-year-olds, so these problems may only become apparent at older ages and hence may have been less apparent in our cohort (Goldschmidt, Day, & Richardson, 2000; Richardson, Ryan, Willford, Day, & Goldschmidt, 2002).

Data on parent use of tobacco, alcohol and drugs was collected by questionnaire, and many participants (4-20%) chose not to answer some or all of these questions. The mean Bayley scores of this "Unknown" group tended to be the same as or lower than those of children whose parents reported use of tobacco, alcohol and drugs. In one New Zealand study 54% of pregnant mothers continued to use tobacco, 56% alcohol and 21% marijuana (Wu et al., 2013). These rates, obtained by interview, are considerably higher than our questionnaire responses, suggesting that our data may reflect under-reporting, as has been found elsewhere (Ernhart, Morrow-Tlucak, Sokol, & Martier, 1988; Huizink, 2009; Jacobson et al., 1991; Shipton et al., 2009).

Developmental outcome is mediated by proximal factors such as parenting practices, and health and safety factors, and distal factors such as access to educational and employment opportunities

(American Psychological Association task force on socioeconomic status, 2007; Bronfenbrenner, 1977). Our cohort has developmental scale scores which are related to family income, NZDep scores, maternal and paternal education, and home ownership. These factors are not easily separated; rather they seem to describe different aspects of the complexity that is SES, which also incorporates tobacco, alcohol and marijuana use. Breastfeeding and preschool attendance appear to be associated with improved outcomes at this age and will be included in subsequent analyses, along with SES, which will be adjusted for.

Chapter 5. Executive function

5.1. Executive function and risk factors

EF is an important aspect of child development, affecting both learning and behaviour (Diamond, 2013). Considered to be a better predictor of school readiness and achievement than IQ (Blair & Razza, 2007), it is positively associated with maths (Bull & Scerif, 2001), reading (Swanson & Jerman, 2007) and overall school achievement (Gathercole, Pickering, Knight, & Stegmann, 2004). Impaired EF is a feature of ADHD (Fuggetta, 2006) and autism (Goldberg et al., 2005) and it is associated with neonatal risks such as pre-term birth (Aarnoudse-Moens, Smidts, Oosterlaan, Duivenvoorden, & Weisglas-Kuperus, 2009; P. J. Anderson et al., 2004; Baron et al., 2012), hydrocephalus (Fletcher et al., 1996), phenylketonuria (Welsh et al., 1990) and being born SGA (O'Keeffe, O'Callaghan, Williams, Najman, & Bor, 2003). Low SES impacts negatively on EF development (Hackman & Farah, 2009; Lawson et al., 2013; Noble, Norman, & Farah, 2005). However, improvements in EF are possible with appropriate training (Diamond & Lee, 2011; Weiland & Yoshikawa, 2013). We hypothesised that EF outcome would be negatively associated with neonatal risk for hypoglycaemia and that this association would differ with different risk factors.

EF was measured for 368 (91.1%) children. Age at assessment ranged from 23 to 25 months but EF task scores did not change significantly with age (data not shown).

5.1.1. Snack Delay

Nearly two-thirds of all children (228, 62.0%) were unable to inhibit their pre-potent, or impulsive, response and failed the first test condition (0 seconds, Table 5.1). Of these, 12 children (3.3%) failed for behavioural reasons, which included being unable to stay at the assessment table or indicating their lack of continued interest. Success decreased with increased delay with 72 (19.6%) children achieving maximum success at 5 seconds, 30 (8.2%) at 15, 6 (1.6%) at 30 and 32 (8.7%) at 45 seconds.

There was no overall difference between success rates or Snack Delay score for different risk groups. However, girls had a higher overall success rate than boys (p=0.027), although there was no difference in mean Snack Delay score. There was a significant interaction between gender and risk group with IDM girls having the lowest (33, 45%) and IDM boys having the highest (52, 71%) failure rate at 0 seconds (p = 0.047).

5.1.2. Fruit Stroop

More than half of all children (206, 56.0%) failed to inhibit their pre-potent response and attend sufficiently to identify any of the small fruit (Table 5.1), with 76 (20.7%) children failing for behavioural reasons. The success rate reduced to 37 (10.1%) for 2 and 21 (5.7%) for 3 small fruit identified.

There were no differences between groups in the ability to correctly identify each target fruit. However, Preterm children were more likely than other risk groups to identify the small apple (p=0.011) although not small banana or orange (data not shown).

There were no differences between girls and boys for success rates or Fruit Stroop score and no significant interactions between gender and risk group.

5.1.3. Ducks

A total of 315 (85.6%) children were unable to reach the criterion for the reverse categorisation task by correctly sorting 5 or 6 ducks in the initial categorisation task, although 143 (38.9%) were able to correctly sort 3 or 4 ducks.

Of the 53 children who attempted the reverse categorisation task, 20 (37.7%; 5.4% of cohort) correctly reverse sorted 1 or 2 ducks and 11 (20.8%; 3.0%of cohort) 3 or more. There were no significant differences between risk groups for success rates or the Ducks score. At the categorisation task stage 61 (16.6%) and at the reverse task stage 7 (1.9%) children failed for behavioural reasons.

There was no significant difference in success rates between girls and boys although girls had a higher Ducks score than boys (p=0.022). There were no significant interactions between gender and risk groups.

5.1.4. Multisearch Multilocation

Only a small proportion (56, 15.2%) of the cohort was unable to achieve success for the Pre-switch task, which was the criterion for progressing to the Post-switch task. This included 23 (6.3%) children who failed for behavioural reasons. More than half (216, 58.7%) of the cohort achieved success on the first Post-switch trial. Of those who failed at this stage 108 (29.3%) made a perseverative error and 2 (<1.0 %) a non-perseverative error. There were no differences in success rates between risk groups for the Pre-switch or Post-switch tasks or the MSML score.

There were no significant differences between girls and boys in success or score totals. However, there was a significant interaction between gender and risk group for Post-switch success (p=0.021) with IDM girls having much higher success rates than boys (70.3% vs 50.7%), whereas Other girls had much lower success rates than boys (40.0% vs 100.0%) (Table 5.1).

5.1.5. EF total score

The EF total score, a composite of the 4 task scores, for the cohort did not differ significantly between risk groups or between girls and boys. However, there was a significant interaction between gender and risk group (p=0.043) with IDM girls having high and IDM boys low scores (15.2 vs 11.8) relative to the rest of the cohort.

Table 5.1: Success rates and scores of the four assessed executive function tasks for total cohort, girls and boys, and risk groups

Assessment		Total	IDM	Preterm	Small	Large	Other	P value
	Cohort	368	147	124	50	36	11	
	Girls	175	74	53	33	10	5	
	Boys	193	73	71	17	26	6	
Snack Delay								
0s failure	Cohort	228 (62.0)	85 (57.8)	80 (64.5)	37 (74.0)	20 (55.6)	6 (54.5)	0.374
	Girls	99 (56.6) [†]	33 (44.6) [i]	31 (58.5)	26 (78.8)	5 (50.0)	4 (80.0)	
	Boys	129 (66.8)	52 (71.2)	49 (69.0)	11 (64.7)	15 (57.7)	2 (33.3)	
5s success	Cohort	72 (19.6)	33 (22.4)	22 (17.7)	5 (10.0)	8 (22.2)	4 (36.4)	
	Girls	44 (25.1)	24 (32.4)	12 (22.6)	4 (12.1)	3 (30.0)	1 (20.0)	
	Boys	28 (14.5)	9 (12.3)	10 (14.1)	1 (5.9)	5 (19.2)	3 (50.0)	
15s success	Cohort	30 (8.2)	10 (6.8)	13 (10.5)	2 (4.0)	4 (11.1)	1 (9.1)	
	Girls	11 (6.3)	4 (5.4)	7 (13.2)	0 (0.0)	0 (0.0)	0 (0.0)	
	Boys	19 (9.8)	6 (8.2)	6 (8.5)	2 (11.8)	4 (15.4)	1 (16.6)	
≥ 30s success	Cohort	38 (10.3)	19 (12.9)	9 (7.3)	6 (12.0)	4(11.1)	0 (0.0)	
	Girls	21 (12.0)	13 (17.6)	3 (5.7)	3 (9.1)	2 (20.0)	0 (0.0)	
	Boys	17 (8.8)	6 (8.2)	6 (8.5)	3 (17.7)	2 (7.7)	1 (16.7)	
Snack Delay Score	Cohort	1.4 (2.3)	1.6 (2.5)	1.2 (2.0)	1.1 (2.3)	1.5 (2.1)	1.0 (1.3)	0.466
	Girls	1.5 (2.3)	2.1 (2.7)	1.2 (1.8)	0.9 (2.1)	1.7 (2.4)	0.4 (0.9)	
	Boys	1.2 (2.2)	1.1 (2.2)	1.2 (2.2)	1.6 (2.7)	1.4 (2.1)	1.5 (1.5)	

Fruit Stroop		Total	IDM	Preterm	Small	Large	Other	p value
0 Correct	Cohort	206 (56.0)	88 (59.9)	59 (47.6)	32 (64.0)	21 (58.3)	6 (54.6)	0.130
	Girls	101 (57.7)	42 (56.8)	27 (50.9)	23 (69.7)	6 (60.0)	3 (60.0)	
	Boys	105 (54.4)	46 (63.0)	32 (45.1)	9 (52.9)	15 (57.7)	3 (50.0)	
1 Correct	Cohort	104 (28.3)	41 (27.9)	38 (30.7)	13 (26.0)	7 (19.4)	5 (45.5)	
	Girls	47 (26.9)	20 (27.0)	15 (28.3)	8 (24.2)	2 (20.0)	2 (40.0)	
	Boys	57 (29.5)	21 (28.8)	23 (32.4)	5 (29.4)	5 (19.2)	3 (50.0)	
2 Correct	Cohort	37 (10.1)	12 (8.2)	14 (11.3)	5 (10.0)	6 (16.7)	0 (0.0)	
	Girls	18 (10.3)	7 (9.5)	8 (15.1)	2 (6.1)	1 (10.0)	0 (0.0)	
	Boys	19 (9.8)	5 (6.9)	6 (8.5)	3 (17.7)	5 (19.2)	0 (0.0)	
3 Correct	Cohort	21 (5.7)	6 (4.1)	13 (10.5)	0 (0.0)	2 (5.6)	0 (0.0)	
	Girls	9 (5.1)	5 (6.8)	3 (5.7)	0 (0.0)	1 (10.0)	0 (0.0)	
	Boys	12 (6.2)	1 (1.4)	10 (14.1)	0 (0.0)	1 (3.9)	0 (0.0.)	
Little Apple	Cohort	80 (21.7)	25 (17.0)	39 (31.5)	5 (10.0)[a]	9 (25.0)	2 (18.2)	**0.011**
	Girls	31 (17.7)	14 (18.9)	11 (20.8)	3 (9.1)	2 (20.0)	1 (20.0)	
	Boys	49 (25.4)	11 (15.1)	28 (39.4)	2 (11.8)	7 (26.9)	1 (16.7)	
Fruit Stroop Score *Mean (SD)*	Cohort	2.1 (2.0)	2.0 (1.9)	2.3 (2.1)	1.8 (1.8)	2.0 (2.2)	1.6 (1.7)	0.408
	Girls	2.1 (1.9)	2.3 (2.0)	2.4 (2.0)	1.5 (1.7)	2.2 (2.4)	0.8 (1.1)	
	Boys	2.1 (2.0)	1.8 (1.8)	2.3 (2.2)	2.4 (1.8)	2.0 (2.1)	2.3 (1.9)	

Ducks		Total	IDM	Preterm	Small	Large	Other	p value
<5 Categorised	Cohort	315 (85.6)	124 (84.4)	110 (88.7)	40 (80.0)	30 (83.3)	11 (100.0)	0.667
	Girls	147 (84.0)	58 (78.4)	48 (90.6)	28 (84.9)	8 (80.0)	5 (100.0)	
	Boys	168 (87.1)	66 (90.4)	62 (87.3)	12 (70.6)	22 (84.6)	6 (100.0)	
5-6 Categorised	Cohort	22 (6.0)	10 (6.8)	7 (5.7)	5 (10.0)	3 (8.3)	0 (0.0)	
	Girls	10 (5.7)	6 (8.1)	0 (0.0)	3 (9.1)	1 (10.0)	0 (0.0)	
	Boys	12 (6.2)	4 (5.5)	4 (5.6)	2 (11.8)	2 (7.7)	0 (0.0)	
1-2 Reverse	Cohort	20 (5.4)	8 (5.4)	7 (5.7)	4 (8.0)	1 (2.8)	0 (0.0)	
	Girls	13 (7.4)	6 (8.1)	4 (7.6)	2 (6.1)	1 (10.0)	0 (0.0)	
	Boys	7 (3.6)	2 (2.7)	3 (4.2)	2 (11.8)	0 (0.0)	0 (0.0)	
≥3 Reverse	Cohort	11 (3.0)	5 (3.4)	3 (2.4)	1 (2.0)	2 (5.6)	0 (0.0)	
	Girls	5 (2.9)	4 (5.4)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	
	Boys	6 (3.1)	1 (1.4)	2 (2.8)	1 (5.9)	2 (7.7	0 (0.0)	
Ducks Score	Cohort	2.9 (2.4)	2.9 (2.6)	2.9 (2.3)	3.3 (2.5)	2.8 (2.5)	2.6 (0.8)	0.791
	Girls	3.2 (2.4) †	3.4 (2.7)	3.3 (2.0)	2.9 (2.1)	3.1 (2.2)	3.0 (0.7)	
	Boys	2.7 (2.4)	2.4 (2.2)	2.6 (2.4)	4.1 (3.0)	2.7 (2.7)	2.3 (0.8)	

MSML		Total	IDM	Preterm	Small	Large	Other	p value
Pre-switch success	Cohort	312 (84.8)	117 (79.6)	107 (86.3)	45 (90.0)	32 (88.9)	11 (100.0)	0.148
	Girls	151 (86.3)	62 (83.8)	44 (83.0)	30 (90.9)	10 (100.0)	5 (100.0)	
	Boys	161 (83.4)	55 (75.3)	63 (88.7)	15 (88.2)	22 (84.6)	6 (100.0)	
Post-switch success	Cohort	216 (58.7)	89 (60.5)	68 (54.8)	27 (54.0)	24 (66.7)	8 (72.7)	0.515
	Girls	109 (62.3)	52 (70.3) [ii]	33 (62.3)	16 (48.5)	6 (60.0)	2 (40.0) [i]	
	Boys	107 (55.4)	37 (50.7)	35 (49.3)	11 (64.7)	18 (69.2)	6 (100.0)	
MSML Score	Cohort	8.4 (1.2)	8.4 (1.1)	8.3 (1.2)	8.3 (1.6)	8.4 (1.7)	8.7 (0.5)	0.909
n=323	Girls	8.4 (1.2)	8.6 (0.9)	8.4 (1.3)	8.2 (1.8)	8.3 (0.9)	8.4 (0.5)	
	Boys	8.4 (1.2)	8.1 (1.8)	8.3 (1.2)	8.4 (1.2)	8.4 (1.9)	9.0 (0.0)	
EF Total Score								
n=323	Cohort	14.0 (6.1)	13.7 (7.2)	13.9 (5.3)	14.5 (6.0)	14.6 (5.5)	14.0 (2.4)	0.921
	Girls	14.5 (6.0)	15.2 (7.2) [i]	14.1 (5.1)	13.5 (5.5)	15.3 (4.2)	12.6 (1.1)	
	Boys	13.4 (6.2)	11.8 (6.7)	13.7 (5.5)	16.3 (6.6)	14.3 (6.1)	15.2 (2.7)	

Data are n (%) or mean (SD); p value for comparison of risk group success in each task for cohort, or for ANOVA of Risk Group EF task score or EF Total score; [†]p<0.05 for difference between girls and boys; [i] p<0.05; [ii] p<0.01 for interaction between gender and risk factor; [a]p< 0.05 for difference from Preterm group; IDM = Infant of a Diabetic Mother; MSML = Multisearch Multilocation;.

5.2. EF and SES

Children from low income households had lower scores on all four EF tasks and also EF Total score than those from high income households, with little difference between high and medium income groups (Table 5.2). Similar patterns were seen with NZDep2006 at 2 years.

A low level of parent education was also associated with lower EF scores, with the low maternal education group having significantly lower scores on Ducks and EF Total (Table 5.3), and low paternal education having significantly lower scores on Fruit Stroop (data not shown).

Living in a rented home rather than a family-owned home was also associated with significantly lower scores for all tasks (data not shown).

There were no significant interactions between gender and household income, NZDep2006 at birth or 2 years or parent education for any of the scores.

Table 5.2: Executive function scores for the cohort and girls and boys for high, medium and low groups of household income, NZDep2006 at 2 years and maternal education

		Household income at 2 year assessment			NZDep2006 at 2 year assessment			Maternal Education		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
	Cohort	101	87	116	64	124	184	112	113	127
	Girls	51	49	49	29	66	83	52	59	55
	Boys	50	38	67	35	58	101	60	54	72
Snack Delay	Cohort	1.9 (2.7)	1.8 (2.3)	1.0[ab] (1.9)	1.8 (2.7)	1.8 (2.5)	1.0[abb] (1.9)	1.7 (2.5)	1.3 (2.1)	1.2 (2.1)
	Girls	1.9 (2.7)	2.2[†] (2.5)	0.9[a] (1.8)	2.3 (3.0)	1.7 (2.6)	1.1 (1.8)	2.2 (2.7)	1.3 (2.2)	1.4 (2.2)
	Boys	1.8 (2.7)	1.2 (1.9)	1.0 (2.0)	1.4 (2.5)	1.9 (2.3)	0.9[bb] (2.0)	1.3 (2.2)	1.2 (2.1)	1.1 (2.0)
Fruit Stroop	Cohort	2.6 (2.0)	2.4 (1.9)	1.7[aab] (2.0)	2.5 (2.1)	2.3 (2.0)	1.8 (1.9)	2.2 (2.0)	2.3 (2.0)	1.8 (2.0)
	Girls	2.5 (2.0)	2.6 (1.9)	1.5[ab] (1.8)	2.8 (2.1)	2.3 (1.9)	1.7[a] (1.9)	2.3 (1.9)	2.3 (2.0)	1.9 (2.0)
	Boys	2.7 (2.0)	2.2 (1.9)	1.8 (2.1)	2.2 (2.1)	2.3 (2.1)	1.9 (1.9)	2.1 (2.1)	2.4 (1.9)	1.8 (2.0)

		Household income at 2 year assessment			NZDep2006 at 2 year assessment			Maternal Education		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
Ducks	Cohort	3.9 (2.8)	3.1 (2. 3)	2.4[aaa] (2.0)	3.2 (2.6)	3.3 (2.3)	2.7 (2.4)	3.4 (2.7)	3.2 (2.5)	2.5[ab] (2.0)
	Girls	4.1 (2.5)	3.4 (2.5)	2.6[aa] (2.0)	3.6 (2.3)	3.5 (2.2)	3.0 (2.5)	3.8 (2.3)	3.6 (2.6)	2.7[a] (2.1)
	Boys	3.6 (3.2)	2.6 (2.1)	2.3[a] (2.0)	2.9 (2.8)	3.0 (2.4)	2.5 (2.3)	3.0 (3.0)	2.8 (2.3)	2.3 (1.9)
MSML	Cohort	8.4 (1.0)	8.6 (0.9)	7.9[abb] (2.1)	8.3 (1.7)	8.6 (0.9)	8.2 (1.5)	8.4 (1.3)	8.5 (0.9)	8.2 (1.6)
	Girls	8.5 (0.9)	8.6 (1.1)	8.0 (1.8)	8.2 (2.2)	8.7 (0.9)[†]	8.3 (1.0)	8.5 (1.1)	8.6 (0.7)	8.4 (1.2)
	Boys	8.3 (1.1)	8.7 (0.6)	7.7[b] (2.2)	8.3 (1.5)	8.4 (1.2)	8.1 (1.8)	8.3 (1.3)	8.6 (0.7)	8.2 (1.8)
EF Total	Cohort	15.6 (6.2)	15.0 (6.0)	11.7[aaabbb] (5.9)	14.5 (7.1)	15.2 (5.4)	12.5[bbb] (5.9)	14.6 (6.4)	14.2 (5.8)	12.5[a] (5.9)
	Girls	15.6 (6.4)	16.3 (5.9)[†]	11.8[aabbb] (4.9)	15.1 (7.5)	15.6 (5.2)	13.0[b] (5.7)	15.9 (5.7)	14.6 (6.2)	13.0 (6.1)
	Boys	15.7 (6.1)	13.3 (5.6)	11.6[aa] (6.5)	13.9 (6.8)	14.7 (5.5)	12.1[b] (6.0)	13.4 (6.8)	13.7 (5.4)	12.1 (5.8)

Data are Mean (SD); [†]p<.05; [††]p<0.01 for comparison between genders; [a]p<0.05; [aa]p<0.01; [aaa]p<0.001 for comparison with High group; [b]p< 0.05; [bb]p<0.01; [bbb]p<0.001 for comparison between Medium and Low groups; Household income: High = ≥$70, 001 pa; Medium = $40,001 - $70,000 pa; Low = ≤ $40,000 pa; NZDep2006: High = deciles 1,2,3; Medium = deciles 4,5,6; Low = deciles 7,8,9,10; Maternal Education: High = University education; Medium = Post-secondary training such as Polytechnic or trade certificate; Low = Up to completion of secondary school.

5.3. EF and breastfeeding, preschool attendance and home language

There were no differences in EF scores between children who were and were not ever breastfed, who did or did not attend preschool or between those with low or high hours of preschool attendance. There were also no significant interactions between gender and breastfeeding, preschool attendance or hours of attendance. Adjusting for SES did not change this (data not shown).

There were no differences in EF scores between children who did or did not have English as their first language, and no significant interactions between gender and first language (data not shown). Adjusting for SES decreased the Ducks score of those whose first language was not English, resulting in an increased difference in scores between children who did or did not have English as their first language (Ducks: (1.2 [0.1, 2.4] p=0.038).

5.4. EF and tobacco, alcohol and drugs

Data for family tobacco, alcohol and drug use were available for 359 (88.9%) children who completed the EF assessment.

Reported parental antenatal, but not 2 year, smoking was associated with lower EF scores with maternal smoking associated with lower Fruit Stroop score (0.6, p=0.026) and paternal smoking associated with lower Ducks score (0.9, p=0.008) (Table 5.4). Adjusting for SES abolished these differences: maternal smoking; Fruit Stroop (0.52 [-0.16, 1.21]), paternal smoking; Ducks (0.50 [-0.35, 1.35]).

There were no differences in scores between children whose mothers were reported to drink or not either antenatally or at 2 years (data not shown). Reported paternal antenatal drinking was associated with higher Ducks (0.8, p=0.016) and EF Total scores (3.0, p=0.001) (Table 5.3). Adjusting for SES abolished the difference between scores for Ducks: (0.68 [-0.12, 1.48]) but not for EF Total score (2.3 [0.12, 4.45] p=0.035). Reported 2 year paternal drinking was associated with higher Snack Delay (1.1, p=0.024) and EF Total score (2.8, p=0.004). Adjusting for SES did not abolish the difference for Snack Delay: (0.86 [0.04, 1.68] p=0.036), but did for EF Total: (2.2 [-0.11, 4.48]).

The only difference in EF scores associated with reported parental marijuana use was a lower Fruit Stroop score with maternal antenatal use (1.5, p=0.022). However, these differences were abolished after adjusting for SES: (1.3 [-0.18, 2.73]) (data not shown).

Table 5.3: Executive function scores for children whose mothers and fathers were reported to use tobacco antenatally, and whose fathers were reported to drink alcohol at 2 year assessment time

		Maternal antenatal smoking			**Paternal antenatal smoking**			**Paternal alcohol at 2 years**		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
	Cohort	247	96	16	200	101	58	74	212	76
	Girls	121	42	7	103	39	28	36	100	37
	Boys	126	54	9	97	62	30	38	112	39
Snack Delay	Cohort	1.4 (2.4)	1.2 (2.1)	1.4 (2.5)	1.6 (2.4)	1.2 (2.0)	1.2 (2.2)	0.7 (1.3)	1.7** (2.5)	1.2 (2.2)
	Girls	1.7 (2.5)	1.2 (1.9)	1.1 (3.0)	1.7 (2.5)	1.4 (2.0)	1.3 (2.4)	0.8 (1.1)	1.8 (2.6)	1.5 (2.5)
	Boys	1.3 (2.2)	1.2 (2.2)	1.7 (2.2)	1.4 (2.3)	1.1 (2.1)	1.1 (2.2)	0.5 (1.5)	1.6* (2.4)	0.9 (2.0)
Fruit Stroop	Cohort	2.3 (2.0)	1.7* (1.8)	2.1 (2.3)	2.4 (1.9)	2.0 (2.1)	1.4** (1.8)	1.9 (1.9)	2.4 (2.0)	1.5∞∞ (1.9)
	Girls	2.4 (2.0)	1.5* (1.8)	1.4 (1.9)	2.4 (1.9)	2.0 (2.1)	1.3* (1.9)	2.0 (2.0)	2.5 (1.9)	1.4∞∞ (1.8)
	Boys	2.1 (2.0)	1.8 (1.7)	2.7 (2.5)	2.3 (2.0)	2.0 (2.1)	1.5 (1.8)	1.8 (1.8)	2.3 (2.0)	1.6 (2.0)

		Maternal antenatal smoking			Paternal antenatal smoking			Paternal alcohol at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Ducks	Cohort	3.1 (2.6)	2.7 (1.9)	2.8 (1.8)	3.4 (2.6)	2.5** (2.0)	2.5* (2.1)	2.5 (2.3)	3.2 (2.4)	2.7 (2.5)
	Girls	3.6† (2.5)	2.7 (1.8)	2.3 (2.2)	3.6 (2.4)	2.7 (2.1)	2.9 (2.2)	2.8 (2.3)	3.4 (2.3)	3.4† (2.7)
	Boys	2.7 (2.6)	2.6 (2.0)	3.1 (1.4)	3.1 (2.8)	2.4 (2.0)	2.1 (2.0)	2.2 (2.2)	3.0 (2.5)	2.2 (2.3)
MSML	Cohort	8.4 (1.4)	8.3 (1.1)	7.8 (2.4)	8.5 (1.2)	8.4 (1.0)	7.8 (2.2)	8.2 (1.6)	8.4 (1.2)	8.2 (1.7)
	Girls	8.4 (1.4)	8.5 (0.7)	8.6 (0.8)	8.4 (1.5)	8.7 (0.7)	8.4 (0.8)	8.2 (1.9)	8.5 (1.0)	8.5 (0.8)
	Boys	8.4 (1.4)	8.2 (1.4)	7.0 (3.3)	8.6 (0.6)	8.3 (1.2)	7.3***∞ (2.8)	8.3 (1.2)	8.4 (1.3)	8.0 (2.1)
EF Total	Cohort	14.5 (6.4)	12.9 (5.4)	13.4 (5.5)	15.0 (6.3)	13.2 (5.6)	12.3 (5.8)	12.3 (5.5)	15.1 (6.0)	12.7 (6.4)
	Girls	15.3 (6.3)	13.2 (4.7)	13.4 (6.4)	15.3 (6.2)	14.0 (5.8)	13.2 (5.4)	13.5 (4.5)	15.5 (6.2)	13.5 (6.4)
	Boys	13.7 (6.5)	12.7 (6.0)	13.4 (5.0)	14.6 (6.6)	12.6 (5.4)	11.4 (6.2)	11.1 (6.3)	14.7 (5.9)	12.1* (6.4)

Data are mean (SD). *p< 0.05; **p<0.01; ***p<0.001 for comparison with 'No' (non-use); ∞ p< 0.05, ∞∞p<0.01 for post-hoc comparison between 'Yes' and 'Unknown'; †p<0.05; for comparison between genders.

5.5. EF and behaviour

Data on the order of assessment were available for 366 (99.5%) children. EF assessment occurred either in the first half of the assessment (First), following the Bayley III assessment, or at the end of the assessment (Last) following both the Optometry and Bayley III assessments.

When the EF assessment was conducted last, approximately three times as many children were excluded for behavioural reasons from the Snack Delay (p=0.018) and MSML tasks (p=0.008), but there was no relationship between timing of assessment and behavioural exclusions from the Fruit Stroop or Ducks tasks (Table 5.4). Children whose EF assessment was conducted last had lower scores on the Ducks task (p=0.004) and EF Total score (p=0.013), but not on scores for the other tasks.

There was a significant interaction between gender and assessment order for Multisearch Multilocation with boys, but not girls, whose assessment was conducted last having lower scores (p=0.014).

Table 5.4: Behavioural exclusions and EF task scores for children whose EF assessment was conducted in the first half of the assessment or last

		Excluded for behaviour		Task Score	
		First	Last	First	Last
	Cohort	192	174		
	Girls	87	86		
	Boys	105	88		
Snack Delay					
	Cohort	3 (1.6)	11 (6.3)*	1.4 (2.2)	1.3 (2.3)
	Girls	2 (2.3)	5 (5.8)	1.7 (2.4)	1.4 (2.3)
	Boys	1 (1.0)	6 (6.8)	1.2 (2.1)	1.3 (2.3)
Fruit Stroop					
	Cohort	37 (19.3)	44 (25.3)	2.2 (1.9)	1.9 (2.0)
	Girls	15 (17.2)	24 (27.9)	2.4 (1.9)	1.8 (1.9)
	Boys	22 (21.0)	20 (22.7)	2.0(1.9)	2.1 (2.1)
Ducks					
	Cohort	33 (17.2)	39 (22.4)	3.3 (2.6)	2.5(2.1)***
	Girls	10 (11.5)	16 (18.6)	3.7 (2.6)	2.8(2.0)
	Boys	23 (21.9)	23 (26.1)	3.0 (2.5)	2.3 (2.2)
MSML					
	Cohort	6 (3.4)	16 (11.0)**	8.4 (1.1)	8.4 (1.3)
	Girls	4 (4.7)	7 (9.5)	8.3 (1.4)	8.6 (0.9) [i]
	Boys	2 (2.2)	9 (12.5)	8.5 (0.8)	8.0 (2.1)
EF Total score					
	Cohort			14.7 (5.6)	13.0 (6.6)*
	Girls			15.1 (6.0)	13.8 (6.0)
	Boys			14.3 (5.3)	12.2 (7.1)

Data are N (%) for Excluded for Behaviour and mean (SD) for Task score; *p<0.05, **p<0.01 for comparison with first assessment; [i] p<0.05 for interaction between gender and assessment order; MSML= Multisearch Multilocation

5.6. BRIEF-P scores

BRIEF-P data were collected for 398 (98.5%) children. Mean scores were higher in this cohort on all scales and indices than the standardised mean, potentially indicating more behaviour problems (Table 5.5). Preterm children had scores 5 points lower than the Small group on the Inhibit scale ($p<0.05$), but there were no other differences between risk groups. There were also no differences in scores between children whose mothers had gestational diabetes (n=121), Type 1 diabetes (n = 11) and Type 2 diabetes (n = 16). Adjusting for SES abolished the difference in Inhibit score between the Small and Preterm groups: (4.4 [-0.9, 9.7]).

Girls had higher T-scores than boys on Inhibit, Shift, Plan/Organise, Emergent Metacognition and Global Executive Composite. However, there were no significant interactions between gender and risk group for any of the BRIEF-P scales or indexes. Analysis of raw data was also done to assess possible differences in outcome as a result of different normalisation for girls and boys. Raw scores for girls were lower than boys for Inhibit ($p=0.003$), Inhibitory Self Control ($p=0.006$) and Global Executive Composite ($p=0.038$) (data not shown).

The Cronbach's alpha for the 5 scale scores was 0.872, showing a good level of internal consistency.

Table 5.5: Comparison of BRIEF-P T-scores for total cohort, girls and boys, and risk groups

		Total Cohort	IDM	Preterm	Small	Large	Other
	Cohort	398	157	129	59	41	12
	Girls	188	78	55	39	11	5
	Boys	210	79	74	20	30	7
Inhibit	Cohort	56.6 (10.9)***	56.6 (11.0)	54.7 (10.2)[a]	59.9 (11.7)	56.2 (9.5)	61.5 (13.5)
	Girls	58.2 (11.1)***††	57.3 (10.6)	55.7 (11.3)	62.3 (10.9)	59.2 (10.3)	66.2 (11.3)
	Boys	55.1 (10.5)***	55.9 (11.3)	53.9 (9.2)	55.4 (12.0)	55.2 (9.1)	58.1 (14.7)
Shift	Cohort	52.5 (10.1)***	51.9 (9.1)	53.1 (10.0)	54.5 (12.2)	49.6 (10.0)	55.3 (10.6)
	Girls	54.0 (11.1)***††	52.6 (9.7)	55.2 (10.8)	56.0 (13.4)	50.3 (11.5)	56.0 (14.3)
	Boys	51.2 (8.9)*	51.2 (8.5)	51.5 (9.1)	51.7 (9.1)	49.3 (9.6)	54.7 (8.4)
Emotional Control	Cohort	51.9 (9.9)***	51.7 (10.1)	51.4 (9.8)	53.5 (10.8)	51.3 (8.7)	55.7 (6.9)
	Girls	51.7 (10.1)*	50.8 (9.9)	50.5 (10.5)	54.3 (10.6)	52.4 (7.2)	55.8 (4.1)
	Boys	52.2 (9.7)***	52.5 (10.2)	52.0 (9.2)	52.0 (11.1)	51.0 (9.3)	55.6 (8.7)
Working Memory	Cohort	61.5 (12.0)***	62.3 (11.7)	59.6 (11.7)	64.4 (14.4)	58.9 (9.0)	65.3 (11.5)
	Girls	62.3 (12.3)***	61.8 (11.2)	59.5 (12.2)	67.2 (14.4)	59.6 (7.7)	68.6 (13.2)
	Boys	60.7 (11.7)***	62.8 (12.3)	59.6 (11.4)	58.9 (13.2)	58.6 (9.5)	62.9 (10.4)
Plan/Organise	Cohort	55.5 (11.3)***	56.0 (10.6)	54.3 (11.1)	57.7 (13.2)	53.2 (12.1)	57.8 (9.3)
	Girls	56.6 (11.5)***†	56.4 (10.0)	55.3 (12.1)	59.6 (12.9)	54.7 (13.3)	56.4 (9.8)
	Boys	54.4 (11.1)***	55.6 (11.2)	53.5 (10.2)	54.0 (13.2)	52.6 (11.8)	58.7 (9.6)

		Total Cohort	IDM	Preterm	Small	Large	Other
Inhibitory Self-Control	Cohort	55.1 (10.5)***	54.9 (10.7)	53.6 (10.2)	57.9 (10.9)	54.6 (9.0)	59.9 (11.3)
	Girls	55.9 (10.7)***	54.9 (10.3)	53.8 (11.6)	59.7 (10.3)	56.7 (8.1)	62.8 (8.6)
	Boys	54.3 (10.2)***	55.0 (11.1)	53.5 (9.0)	54.5 (11.6)	53.8 (9.3)	57.9 (13.1)
Flexibility Index	Cohort	52.6 (10.2)***	52.1 (9.8)	52.5 (10.1)	54.7 (12.3)	50.6 (9.2)	56.6 (8.5)
	Girls	53.4 (11.0)***	52.0 (10.0)	53.3 (11.1)	55.5 (13.5)	51.9 (8.9)	57.2 (9.4)
	Boys	51.9 (9.4)**	52.1 (9.6)	51.9 (9.2)	52.0 (10.4)	50.1 (9.4)	56.1 (8.6)
Emergent Metacognition	Cohort	59.8 (12.1)***	60.6 (11.7)	58.0 (11.5)	62.8 (14.8)	57.0 (10.4)	63.1 (10.2)
	Girls	61.0 (12.3)***†	60.7 (11.0)	58.4 (12.4)	65.6 (14.5)	58.5 (9.9)	64.8 (11.5)
	Boys	58.6 (11.8)***	60.5 (12.4)	57.5 (10.8)	57.3 (14.3)	56.5 (10.7)	61.9 (10.0)
Global Executive Composite	Cohort	57.6 (11.6)***	57.8 (11.3)	56.2 (11.1)	60.8 (13.8)	55.4 (9.8)	62.1 (10.5)
	Girls	59.0 (12.1)***†	58.0 (10.8)	57.1 (12.8)	63.4 (13.4)	57.5 (8.7)	64.6 (11.7)
	Boys	56.4 (10.9)***	57.6 (11.8)	55.5 (9.6)	55.9 (13.4)	54.6 (10.2)	60.3 (10.0)

Data are mean (SD); IDM = Infant of a Diabetic Mother; *p< 0.05; **p<0.01; ***p<0.001 for comparison with standardised mean; ^{a}p<0.05; ^{aa}p<0.01; ^{aaa}p<0.001 for comparison with small group; †p<.05; ††p<.01 for comparison between genders.

5.7. BRIEF-P scores and SES

Children from low income households had higher scores on all scales and indexes than those from high income households, with little difference between scores for children from medium and high income households (Table 5.6). There were no significant interactions between gender and household income.

Similarly, children in the low SES group, as measured by NZDep2006 at birth and at 2 years, had higher scores than the high SES group for Inhibit, Emotional Control and Inhibitory Self Control Index and at 2 years also for Flexibility Index and Global Executive Composite (Table 5.7). There was an interaction between gender and NZDep2006 at 2 years for Shift with girls' but not boys' scores being higher in the lowest NZDep2006 group.

Children of mothers in the low education group had higher scores than those of mothers in the high education group for all scales and indexes except Shift (Table 5.6). There was a similar pattern with paternal education (data not shown). There were no significant interactions between gender and maternal or paternal education.

Scale and index scores were approximately 5 points higher on all scales for children who lived in rented rather than family owned homes ($p<0.001$). There were no significant interactions between gender and home ownership (data not shown).

Table 5.6: Comparison between BRIEF-P scores and household income, NZDep2006 at 2 years and maternal education

		Household income at 2 year assessment			NZDep2006 at 2 year assessment			Maternal Education		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
	Cohort	100	86	116	63	123	181	112	109	127
	Girls	50	49	49	28	65	82	52	57	55
	Boys	50	37	67	35	58	99	60	52	72
Inhibit	Cohort	54.4 (10.5)	56.3 (10.6)	58.6[aa] (10.9)	53.5 (10.3)	56.5 (10.4)	57.6[a] (11.1)	54.7 (10.3)	56.5 (10.7)	58.4[a] (11.6)
	Girls	56.5 (11.9)	57.8 (11.0)	58.8 (10.4)	55.8 (11.0)	58.2 (11.1)	59.1 (11.2)	56.2 (10.6)	57.6 (11.7)	60.2 (11.0)
	Boys	52.2 (8.4)	54.3 (9.8)	58.5[aa] (11.2)	51.6 (9.4)	54.7 (9.3)	56.3[a] (10.9)	53.3 (10.0)	55.2 (9.5)	57.1 (12.0)
Shift	Cohort	50.3 (10.2)	50.3 (9.5)	55.1[aabb] (10.5)	51.2 (10.4)	51.1 (8.6)	53.7 (10.8)	51.3 (11.7)	51.4 (9.6)	54.1 (9.0)
	Girls	52.6 (12.2)	50.9 (10.1)	56.6[b] (10.8)	53.0 (11.3)	51.0 (9.5)	56.7[bb††† i] (11.7)	52.0 (13.3)	52.7 (10.4)	55.9[†] (9.5)
	Boys	48.0 (7.1)	49.5 (8.6)	54.1[aaab] (10.1)	49.7 (9.4)	51.3 (7.7)	51.2 (9.2)	50.6 (10.2)	50.0 (8.5)	52.7 (8.3)
Emotional Control	Cohort	50.0 (10.0)	51.4 (9.4)	53.2[a] (10.0)	49.6 (10.0)	50.9 (9.2)	53.2[a] (9.9)	50.6 (10.5)	50.6 (8.7)	53.9[ab] (10.1)
	Girls	50.2 (10.3)	51.6 (9.8)	51.7 (9.1)	49.5 (9.7)	50.4 (9.0)	53.4 (10.8)	50.5 (10.3)	50.2 (9.5)	53.4 (10.0)
	Boys	49.7 (9.7)	51.0 (8.9)	54.3[a] (10.5)	49.7 (10.4)	51.4 (9.4)	53.0 (9.1)	50.6 (10.8)	51.0 (7.7)	54.3 (10.1)

		Household income at 2 year assessment			NZDep2006 at 2 year assessment			Maternal Education		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
Working Memory	Cohort	59.0 (10.9)	60.1 (11.2)	63.5[a] (13.0)	59.5 (12.3)	60.9 (12.0)	62.5 (11.8)	59.9 (12.3)	59.5 (11.7)	64.8[aabb] (11.9)
	Girls	60.5 (12.0)	60.4 (11.8)	63.8 (12.6)	61.6 (13.7)	61.9 (13.0)	62.9 (11.4)	60 (12.6)	60.8 (12.2)	65.6[a] (11.9)
	Boys	57.3 (9.3)	59.7 (10.5)	63.2[a] (13.4)	57.8 (10.9)	59.8 (10.9)	62.1 (12.1)	59.9 (12.0)	58.1 (11.0)	64.2[bb] (12.0)
Plan/ Organise	Cohort	52.6 (11.0)	54.8 (10.7)	56.8[a] (11.2)	54.8 (12.0)	54.9 (12.0)	55.8 (10.5)	54.0 (11.8)	54.1 (10.6)	57.5[ab] (11.3)
	Girls	54.8 (11.8)	55.3 (11.2)	58.1 (10.8)	57.3 (12.4)	55.7 (12.7)	57.0 (10.2)	55.1 (12.1)	56.1[†] (10.9)	57.6 (11.4)
	Boys	50.3 (9.7)	54.1 (10.1)	55.8[a] (11.4)	52.7 (11.3)	54.0 (11.3)	54.8 (10.6)	53.1 (11.6)	51.8 (9.8)	57.4[b] (11.4)
Inhibitory Self Control	Cohort	52.8 (10.3)	54.6 (10.1)	57.0[aa] (10.4)	52.0 (10.1)	54.5 (9.9)	56.3[aa] (10.6)	53.2 (10.5)	54.4 (9.7)	57.1[a] (11.1)
	Girls	54.2 (11.6)	55.6 (10.4)	56.3 (9.2)	53.4 (10.6)	55.2 (10.3)	57.3 (11.1)	54.1 (10.7)	54.9 (10.6)	57.9 (10.8)
	Boys	51.3 (8.6)	53.3 (9.6)	57.5[aa] (11.1)	50.9 (9.6)	53.7 (9.5)	55.5[a] (10.2)	52.5 (10.4)	53.9 (8.7)	56.5 (11.4)

		Household income at 2 year assessment			NZDep2006 at 2 year assessment			Maternal Education		
		High	Medium	Low	High	Medium	Low	High	Medium	Low
Flexibility Index	Cohort	50.2 (10.1)	51. 1 (9.8)	54.8[aab] (10.4)	50.5 (10.5)	51.3 (9.1)	54.0[ab] (10.5)	51.1 (11.5)	51.2 (9.3)	54.6[ab] (9.6)
	Girls	51.7 (11.7)	51.7 (10.4)	54.8 (10.4)	51.5 (11.0)	51.0 (9.3)	55.8[b†] (11.8)	51.6 (12.5)	51.8 (10.2)	55.4 (9.9)
	Boys	48.6 (7.9)	50.2 (9.1)	54.8[aab] (10.4)	49.7 (10.1)	51.5 (8.9)	52.4 (9.0)	50.7 (10.8)	50.6 (8.1)	54.0 (9.3)
Emergent Metacognition	Cohort	56.9 (11.1)	58.6 (11.5)	61.6[aa] (12.6)	58.2 (12.7)	59.1 (12.5)	60.6 (11.4)	58.2 (12.5)	57.9 (11.6)	62.8[aabb] (12.0)
	Girls	59.1 (12.1)	59.2 (12.0)	62.6 (12.0)	60.8 (13.6)	60.4 (13.6)	61.6 (10.9)	58.9 (12.9)	59.8 (12.0)	63.6 (11.9)
	Boys	54.6 (9.6)	57.9 (10.7)	60.9[aa] (13.1)	55.9 (11.5)	57.8 (11.3)	59.7 (11.9)	57.5 (12.3)	55.8 (10.8)	62.1[bb] (12.1)
Global Executive Composite	Cohort	54.6 (10.9)	56.4 (10.9)	60.0[aab] (11.7)	55.1 (11.6)	56.7 (11.1)	58.9[a] (11.5)	55.7 (12.2)	56.2 (10.6)	60.4[aab] (11.7)
	Girls	56.9 (12.9)	57.3 (11.4)	60.5 (10.8)	57.5 (12.5)	57.7 (12.1)	60.5 (11.8)	56.7 (12.8)	57.6 (11.5)	61.6 (11.7)
	Boys	52.3 (7.9)	55.0 (10.2)	59.6[aaa] (12.4)	53.1 (10.5)	55.7 (10.0)	57.4 (11.1)	54.8 (11.8)	54.5 (9.3)	59.4[ab] (11.6)

Data are Mean (SD); [i] $p<0.05$ for interaction between gender and NZDep2006; [a] $p<0.05$; [aa] $p<0.01$; [aaa] $p<0.001$ for comparison with High group; [b] $p< 0.05$; [bb] $p<0.01$ for comparison between Medium and Low groups; Household income: High = ≥$70, 001 pa; Medium = $40,001 - $70,000 pa; Low = ≤ $40,000 pa; NZDep2006: High = deciles 1,2,3; Medium = deciles 4,5,6; Low = deciles 7,8,9,10; Maternal Education: High = University education; Medium = Post-secondary training such as Polytechnic or trade certificate; Low = Up to completion of secondary school.

5.8. BRIEF-P and breastfeeding, preschool and language

There were no differences in BRIEF-P scores between children who were and were not ever breastfed (Table 5.7), who did or did not attend preschool or between those with low or high hours of preschool attendance (Data not shown). There were no significant interactions between gender and breastfeeding, preschool attendance or hours of attendance. Adjusting for SES did not change these findings.

There were no differences in BRIEF-P scores between children who did and did not have English as their first language (Table 5.8). However, there were interactions between gender and first language for Shift and Flexibility Index with scores lower in girls, but not boys, whose first language was not English.

Adjusting for SES approximately doubled the difference between scores of children who did and did not have English as their first language, resulting in differences becoming significant for Emotional Control (5.0 [0.5, 9.5] p=0.029) and Flexibility Index (5.4 [0.7, 10.0] p=0.024).

Table 5.7: Comparison of BRIEF-P T-scores, for the cohort and girls and boys who were and were not breastfed and did and did not have English as their first language

		Breastfed		English 1st Language	
		Yes	No	Yes	No
	Cohort	357	29	332	26
	Girls	173	11	170	11
	Boys	184	18	187	15
Inhibit	Cohort	56.6 (10.9)	56.6 (12.2)	56.6 (10.8)	54.9 (9.6)
	Girls	58.4 (11.1)[††]	55.2 (10.6)	58.4 (11.1)[††]	56.1 (11.7)
	Boys	55.0 (10.4)	57.5 (13.3)	55.3 (10.8)	54.0 (8.0)
Shift	Cohort	52.2 (10.1)	54.6 (10.7)	52.7 (10.4)	50.0 (7.4)
	Girls	53.7 (11.1)[††]	57.2 (11.4)	54.2 (11.3) [††]	46.8 (4.7) [ai]
	Boys	50.9 (8.9)	53.0 (10.2)	51.1 (9.1)	52.3 (8.3)
Emotional Control	Cohort	51.7 (9.8)	53.7 (11.2)	51.9 (9.8)	49.4 (8.9)
	Girls	51.6 (10.0)	51.5 (11.8)	51.9 (10.2)	45.6 (5.6) [a]
	Boys	51.9 (9.6)	55.1 (10.9)	52.1 (9.8)	52.1 (10.0)
Working Memory	Cohort	61.5 (12.1)	61.3 (11.8)	61.5 (14.7)	61.5 (11.8)
	Girls	62.5 (12.5)	57.8 (9.9)	62.2 (12.0)	60.9 (18.1)
	Boys	60.5 (11.8)	63.5 (12.7)	60.7 (11.8)	62.0 (12.4)
Plan/Organise	Cohort	55.2 (11.2)	57.8 (13.7)	55.3 (11.1)	54.3 (11.4)
	Girls	56.6 (11.7)[†]	55.8 (7.4)	56.7 (11.3)[†]	53.7 (13.7)
	Boys	53.9 (10.5)	59.0 (16.5)	54.2 (11.2)	54.8 (9.9)

		Breastfed		English 1st Language	
		Yes	No	Yes	No
Inhibitory Self Control Index	Cohort	55.0 (10.4)	56.0 (12.0)	55.1 (10.4)	52.6 (8.7)
	Girls	56.0 (10.7)	54.2 (11.9)	56.1 (10.8)	51.4 (9.2)
	Boys	54.1 (10.1)	57.2 (12.3)	54.4 (10.5)	53.5 (8.6)
Flexibility Index	Cohort	52.3 (10.1)	54.7 (11.6)	52.7 (10.3)	49.7 (8.9)
	Girls	53.2 (10.9)	54.8 (12.7)	53.7 (11.1)	45.7 (5.5)[ai]
	Boys	51.5 (9.3)	54.6 (11.3)	51.7 (9.5)	52.5 (9.9)
Emergent Metacognition Index	Cohort	59.7 (12.1)	60.7 (13.1)	59.7 (11.8)	59.3 (14.2)
	Girls	61.2 (12.5)[†]	57.7 (9.2)	61.0 (12.0)	58.8 (17.4)
	Boys	58.3 (11.6)	62.4 (15.0)	58.5 (12.0)	59.6 (11.8)
Global Executive Composite	Cohort	57.5 (11.5)	58.9 (13.1)	57.6 (11.4)	55.6 (11.7)
	Girls	59.0 (12.1)[†]	57.2 (11.5)	59.2 (12.0)[†]	54.2 (13.1)
	Boys	56.0 (10.8)	59.9 (14.2)	56.3 (11.1)	56.6 (10.9)

Data are Mean (SD); [a]p<0.05; [aa]p<0.01; [aaa]p<0.001 for comparison with Yes group; [†]p<.05; [††] p<.01 for comparison between genders; [i] p<0.05 for interaction between gender and first language; ISCI=Inhibitory Self Control Index; FI=Flexibility Index; EMI=Emergent Metacognition Index; GEC=Global Executive Composite.

5.9. BRIEF-P scores and family tobacco, alcohol and other drug use

Data for family tobacco, alcohol and drug use were available for 388 (96%) children.

The BRIEF-P scores for children whose parents were reported to smoke antenatally and at 2 years were significantly higher on all scales than those of children whose parents were reported to not smoke (Maternal 2 year data; Table 5.8). There were no significant interactions between gender and maternal or paternal smoking at either time period (Data not shown).

Adjusting for SES abolished all differences between scores for children of both mothers and fathers who did and did not smoke antenatally, and of fathers who did and did not smoke at 2 years. For children of mothers who did and did not smoke at 2 years, adjusting for SES abolished differences for Shift, Working Memory, Plan/Organise and EMI, and reduced differences on the other scores by approximately 60%: Inhibit (3.9 [0.6, 7.2] p=0.015), Shift (2.4 [-0.8, 5.6]), Emotional Control (3.8 [0.8, 6.8] p=0.008) Working Memory (2.0 [-1.7, 5.7]), Plan/Organise (2.3 [-1.2, 5.8]), ISCI (4.3 [1.2, 7.4] p=0.004), FI (3.6 [0.5, 6.7] p=0.018), EMI (2.3 [-1.5, 6.0]), GEC (3.7 [0.3, 7.2] p=0.031).

The BRIEF-P scores for children whose mothers were reported to drink antenatally were higher than those of mothers reported not drinking antenatally on all scales except Shift, Emotional Control, Working Memory and Flexibility Index (Table 5.9), whereas there were no differences between scores of children of mothers reported to drink and not drink at 2 years (data not shown). Scores of children whose fathers were reported to drink were higher than those of children whose fathers were reported to not drink antenatally on the Emotional Control scale (data not shown), but there were no differences between scores of children whose fathers were reported to drink or not drink at 2 years (Table 5.9). There were no significant interactions between gender and maternal alcohol use. However, there was a significant interaction between gender and paternal alcohol use, with girls, but not boys, whose fathers were reported to use alcohol having significantly higher scores for Plan/Organise than those whose fathers were reported to not use alcohol at 2 years.

Adjusting for SES abolished score differences between children whose mothers did and did not drink alcohol antenatally: Inhibit (3.8 [-1.0, 8.6]), Shift (0.3 [-4.9, 4.4]), Emotional Control (2.7 [-1.6, 7.1]) Working Memory (2.2 [-3.2, 7.6]), Plan/Organise (4.3 [-0.7, 9.4]), ISCI (3.7 [-0.8, 8.3]), FI (1.5 [-3.0, 6.0]), EMI (3.3 [-2.1, 8.8]), GEC (3.4 [-1.6, 8.5]). In contrast, adjusting for SES decreased scores for children whose fathers were reported to not drink which increased score differences between children whose fathers were reported to drink and not drink antenatally: (Emotional Control (4.5 [1.4, 7.5] p=0.002), ISCI (4.1 [0.8, 7.3] p=0.010)) and at 2 years: Emotional Control (4.8 [1.5, 8.1] p=0.002), ISCI (4.5 [1.1, 8.0] p=0.007), FI (3.6 [0.2, 7.1] p=0.039), GEC (4.4 [0.5, 8.3] p=0.022).

There were no score differences associated with maternal antenatal or maternal or paternal 2 year marijuana use. However, Inhibit scale scores were 6 points higher for children whose fathers were reported to use marijuana than those whose fathers were reported to not use marijuana antenatally. Adjusting for SES abolished this difference: Inhibit (4.8 [-0.69, 9.65]) (data not shown).

Table 5.8: BRIEF-P scores for children whose mothers reported using tobacco and drinking alcohol, and whose fathers were reported to drink alcohol at 2 year assessment time

		Maternal tobacco at 2 years			**Maternal antenatal alcohol**			**Paternal alcohol at 2 years**		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
	Cohort	264	105	19	327	39	22	76	232	80
	Girls	125	53	6	152	22	10	37	108	39
	Boys	139	52	13	175	17	12	39	124	41
Inhibit	Cohort	55.2 (10.5)	61.1*** (11.0)	52.2$^{\infty\infty}$ (8.8)	56.1 (10.8)	61.5** (11.5)	56.0 (9.8)	54.9 (9.6)	56.5 (11.0)	58.6 (11.5)
	Girls	56.6† (10.5)	62.4** (11.6)	53.3 (10.5)	57.9†† (11.1)	60.5 (11.5)	56.8 (11.1)	55.2 (10.0)	59.0†† (11.5)	58.7 (10.7)
	Boys	53.8 (10.4)	59.8** (10.4)	51.7$^{\infty}$ (8.3)	54.4 (10.3)	62.9** (11.8)	55.4 (9.2)	54.6 (9.5)	54.3 (10.2)	58.4 (12.4)
Shift	Cohort	51.3 (9.4)	55.2** (11.6)	53.5 (7.9)	52.1 (10.1)	53.5 (11.1)	55.4 (8.5)	51.4 (8.5)	51.2 (10.4)	56.8**$^{\infty\infty}$ (9.7)
	Girls	52.4 (10.5)	57.0* (12.4)	57.3 (4.9)	53.5† (11.1)	54.9 (12.7)	56.8 (7.9)	51.2 (9.0)	52.8† (11.8)	59.5**$^{\infty\infty\dagger}$ (9.2)
	Boys	50.2 (8.2)	53.4 (10.6)	51.7 (8.5)	50.9 (9.0)	51.7 (8.8)	54.2 (9.1)	51.7 (8.2)	49.9 (8.8)	54.2$^{\infty}$ (9.6)
Emotional Control	Cohort	50.4 (9.6)	55.5*** (10.0)	53.4 (8.2)	51.4 (9.7)	55.3 (10.7)	53.5 (10.0)	49.7 (8.7)	51.9 (10.0)	54.1* (10.1)
	Girls	49.9 (9.5)	55.5** (10.6)	52.2 (8.6)	51.2 (9..5)	54.6 (12.9)	51.8 (11.7)	48.7 (8.7)	52.1 (10.3)	53.1 (10.2)
	Boys	50.7 (9.7)	55.4** (9.3)	53.9 (8.3)	51.6 (9.9)	56.1 (7.2)	54.9 (8.6)	50.4 (8.8)	51.7 (9.8)	55.0 (10.0)

		Maternal tobacco at 2 years			Maternal antenatal alcohol			Paternal alcohol at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Working Memory	Cohort	60.6 (12.3)	64.9** (11.0)	55.5$^{\infty\infty}$ (10.4)	61.8 (12.3)	65.2 (13.1)	62.2 (12.7)	60.3 (11.5)	61.2 (12.0)	63.5 (12.6)
	Girls	61.2 (12.3)	65.5 (11.9)	56.0 (14.1)	62.8 (12.6)	61.7 (12.4)	62.3 (11.0)	58.0 (11.0)	63.0† (12.7)	64.3 (12.1)
	Boys	60.0 (12.3)	64.4 (10.2)	55.2$^{\infty}$ (9.0)	60.5 (11.9)	65.3 (11.2)	58.5 (10.6)	62.5 (11.6)	59.6 (11.3)	62.8 (13.3)
Plan/ Organise	Cohort	54.3 (11.2)	58.3** (11.1)	54.7 (11.2)	54.8 (11.1)	59.8* (12.4)	56.6 (11.2)	53.1 (9.4)	55.3 (11.6)	57.8* (11.9)
	Girls	55.4 (11.1)	59.8* (11.5)	53.3 (14.3)	56.0 (11.1)	61.0 (12.7)	56.3 (12.4)	50.8† (8.6)	57.7**$^{\dagger\dagger\,i}$ (11.9)	59.2** (10.9)
	Boys	53.3 (11.2)	56.8 (10.5)	55.4 (11.9)	53.8 (11.1)	58.2 (12.2)	56.8 (10.5)	55.3 (9.6)	53.3 (11.0)	56.5 (12.8)
Inhibitory Self Control	Cohort	53.4 (10.1)	59.6*** (10.6)	53.1$^{\infty}$ (8.9)	55.5 (10.8)	59.9** (10.4)	55.5 (11.7)	52.8 (9.4)	55.0 (10.6)	57.4* (9.4)
	Girls	54.1 (10.0)	60.4*** (11.4)	53.3 (10.3)	55.5 (10.4)	58.9 (12.4)	55.2 (11.8)	52.5 (9.8)	56.6† (10.9)	57.0 (10.6)
	Boys	52.9 (9.6)	58.7** (9.7)	52.9 (8.6)	53.6 (10.2)	61.2* (9.9)	55.8 (8.8)	53.1 (9.2)	53.6 (10.0)	57.8 (11.5)

		Maternal tobacco at 2 years			Maternal antenatal alcohol			Paternal alcohol at 2 years		
		No	Yes	Unknown	No	Yes	Unknown	No	Yes	Unknown
Flexibility Index	Cohort	51.0 (9.6)	56.2*** (11.2)	53.9 (7.9)	52.0 (10.1)	55.1 (11.5)	55.1 (9.5)	50.6 (9.1)	51.9 (10.4)	56.1**$^{\infty\infty}$ (9.9)
	Girls	51.4 (10.1)	57.4** (12.3)	55.5 (6.5)	52.8 (10.6)	55.6 (13.8)	55.0 (10.7)	49.9 (9.4)	53.0 (11.5)	57.1* (10.0)
	Boys	50.5 (9.2)	55.0* (9.9)	53.2 (8.6)	51.3 (9.6)	54.5 (8.0)	55.2 (9.0)	51.2 (8.9)	50.9 (9.3)	55.3$^{\infty}$ (9.9)
Emergent Metacognition	Cohort	58.7 (12.3)	63.4** (11.3)	55.4$^{\infty}$ (11.2)	59.3 (12.1)	64.1* (12.6)	59.3 (11.6)	58.0 (10.8)	59.5 (12.3)	62.1 (12.7)
	Girls	59.8 (12.2)	64.4 (11.9)	55.3 (14.7)	60.4 (12.1)	64.8 (13.4)	60.7 (13.3)	55.6 (9.9)	61.9*†† (12.9)	63.4* (11.8)
	Boys	57.7 (12.4)	62.0 (10.5)	55.4 (9.9)	58.3 (12.0)	63.2 (11.8)	58.2 (10.6)	60.2 (11.2)	57.5 (11.5)	60.9 (13.6)
Global Executive Control	Cohort	56.0 (11.3)	62.3*** (11.5)	54.7$^{\infty}$ (9.8)	57.0 (11.4)	62.3* (12.5)	58.2 (10.8)	55.4 (10.1)	57.2 (11.7)	60.8* (12.2)
	Girls	57.1 (11.3)	63.5** (12.7)	55.7 (11.8)	58.4† (11.8)	62.5 (13.5)	59.1 (12.6)	54.1 (10.2)	59.5*†† (12.5)	61.7** (11.5)
	Boys	54.9 (11.1)	60.7** (10.4)	54.3 (9.2)	55.7 (11.0)	62.1 (11.5)	57.5 (9.6)	56.5 (10.1)	55.2 (10.6)	59.9 (12.9)

Data are mean (SD). *p< 0.05; **p<0.01; ***p<0.001 for comparison with 'No' (non-use); $^{\infty}$ p< 0.05, $^{\infty\infty}$p<0.01 for post-hoc comparison between 'Yes' and 'Unknown'; †p<0.05; †† p<0.01 for comparison between genders. ^{i}p<0.05 for interaction between gender and parental tobacco or alcohol use; ISCI=Inhibitory Self Control Index; FI=Flexibility Index; EMI=Emergent Metacognition Index; GEC=Global Executive Composite.

5.10. Clinically significant BRIEF-P results

The proportion of children with T-scores in the clinically significant range (≥ 65) on the different BRIEF-P scales and indexes is expected to be 8 -14% (Gioia, Isquith, Guy, & Kenworthy, 2000). Our cohort had elevated rates of clinically significant scores on the Inhibit scale (20%) and Inhibitory Self Control Index (18%), and greatly increased rate on the Working Memory scale (37%), which contributed to the high rate of clinically significant scores on the Emergent Metacognition Index (33%) (Table 5.9). Thus the proportion of children with clinically significant Global Executive Composite scores for the cohort was 25% compared with the expected rate of 10%.

Rates of clinically significant scores differed between groups, with Small and IDM having the highest rates (38-46%), and Large groups the lowest rates (17%) for both Working Memory (p=0.005) and Emergent Metacognition Index (p=0.024).

Girls had higher rates of clinically significant scores than boys for Inhibit (p=0.003), Shift (p=0.012) Working Memory (p=0.016), Emergent Metacognition (p=0.023) and Global Executive Composite (p=0.043). However, there were no significant interactions between gender and risk group.

Table 5.9: Comparison of the children with different risk factors for neonatal hypoglycaemia who had clinically significant BRIEF-P scores

		Total Cohort	IDM	Preterm	Small	Large	Other	p
	Cohort	398	157	129	59	41	12	
	Girls	188	78	55	39	11	5	
	Boys	210	79	74	20	30	7	
Inhibit	Cohort	81 (20.4)	29 (18.5)	22 (17.1)	17 (28.8)	8 (19.5)	5 (41.7)	0.126
	Girls	50 (26.6)††	17 (21.8)	13 (23.6)	15 (38.5)	2 (18.2)	3 (60.0)	
	Boys	31 (14.8)	12 (15.2)	9 (12.2)	2 (10.0)	6 (20.0)	2 (28.6)	
Shift	Cohort	52 (13.1)	18 (11.5)	17 (13.2)	12 (20.3)	3 (7.3)	2 (16.7)	0.351
	Girls	33 (17.6)†	11 (14.1)	9 (16.4)	10 (25.6)	1 (9.1)	2 (40.0)	
	Boys	19 (9.1)	7 (8.9)	8 (10.8)	2 (10.0)	2 (6.7)	0 (0.0)	
Emotional Control	Cohort	45 (11.3)	17 (10.8)	16 (12.4)	8 (13.6)	3 (7.3)	1 (8.3)	0.871
	Girls	18 (9.6)	6 (7.7)	6 (10.9)	6 (15.4)	0 (0.0)	0 (0.0)	
	Boys	27 (12.9)	11 (13.9)	10 (13.5)	2 (10.0)	3 (10.0)	1 (14.3)	
Working Memory	Cohort	149 (37.4)	70 (44.6)	40 (31.0)	27 (45.8)	7 (17.1)	5 (41.7)	**0.005**
	Girls	82 (43.6)†	37 (47.4)	17 (30.9)	22 (56.4)	2 (18.2)	4 (80.0)	
	Boys	67 (31.9)	33 (41.8)	23 (31.1)	5 (25.0)	5 (16.7)	1 (14.3)	
Plan/Organise	Cohort	69 (17.3)	28 (17.8)	22 (17.1)	12 (20.3)	4 (9.8)	3 (25.0)	0.637
	Girls	39 (20.7)	14 (18.0)	12 (21.8)	10 (25.6)	2 (18.2)	1 (20.0)	
	Boys	30 (14.3)	14 (17.7)	10 (13.5)	2 (10.0)	2 (6.7)	2 (28.6)	

		Total Cohort	IDM	Preterm	Small	Large	Other	p
Inhibitory Self Control	Cohort	71 (17.8)	28 (17.8)	17 (13.2)	15 (25.4)	7 (17.1)	4 (33.3)	0.184
	Girls	39 (20.7)	14 (18.0)	9 (16.4)	12 (30.8)	2 (18.2)	2 (40.0)	
	Boys	32 (15.2)	14 (17.7)	8 (10.8)	3 (15.0)	5 (16.7)	2 (28.6)	
Flexibility Index	Cohort	54 (13.6)	21 (13.4)	16 (12.4)	12 (20.3)	3 (7.3)	2 (16.7)	0.416
	Girls	32 (17.0)	13 (16.7)	7 (12.7)	10 (25.6)	1 (9.1)	1 (20.0)	
	Boys	22 (10.5)	8 (10.1)	9 (12.2)	2 (10.0)	2 (6.7)	1 (14.3)	
Emergent Metacognition	Cohort	130 (32.7)	60 (38.2)	34 (26.4)	24 (40.7)	7 (17.1)	5 (41.7)	**0.024**
	Girls	72 (38.3)†	32 (41.0)	16 (29.1)	19 (48.7)	2 (18.2)	3 (60.0)	
	Boys	58 (27.6)	28 (35.4)	18 (24.3)	5 (25.0)	5 (16.7)	2 (28.6)	
Global Executive Composite	Cohort	100 (25.1)	41 (26.1)	32 (24.8)	19 (32.2)	4 (9.8)	4 (33.3)	0.124
	Girls	56 (29.8)†	21 (26.9)	15 (27.3)	16 (41.0)†	1 (9.1)	3 (60.0)	
	Boys	44 (21.0)	20 (25.3)	17 (23.0)	3 (15.0)	3 (10.0)	1 (14.3)	

Data are N (%);p for comparison of rates of clinically significant scores in different risk groups; IDM = Infant of a Diabetic Mother; †p<.05, †† p<.001 for comparison between genders; ^{i} p<0.05 for interaction between gender and risk factor.

5.11. Relationships between assessed EF measures

The Snack Delay, Fruit Stroop and Ducks task scores were each significantly correlated with those of other tasks, with only a small amount of variation (4-8%) in each score accounted for by the scores in other tasks. Scores on the Multisearch Multilocation task were not correlated with scores on any of the other tasks (Table 5.11), and nor were scores on the Post-switch task (data not shown).

The scores of individual children on Snack Delay showed little association with scores on other tasks, with children on each level of Snack Delay being represented at all levels of success in the other three tasks (Fig 5.1). However, approximately half of the children who achieved level 2 success on Snack Delay, indicating a good level of inhibitory control, also achieved level 2 success on Ducks, whereas very few of them were represented at level 0 for Multisearch Multilocation.

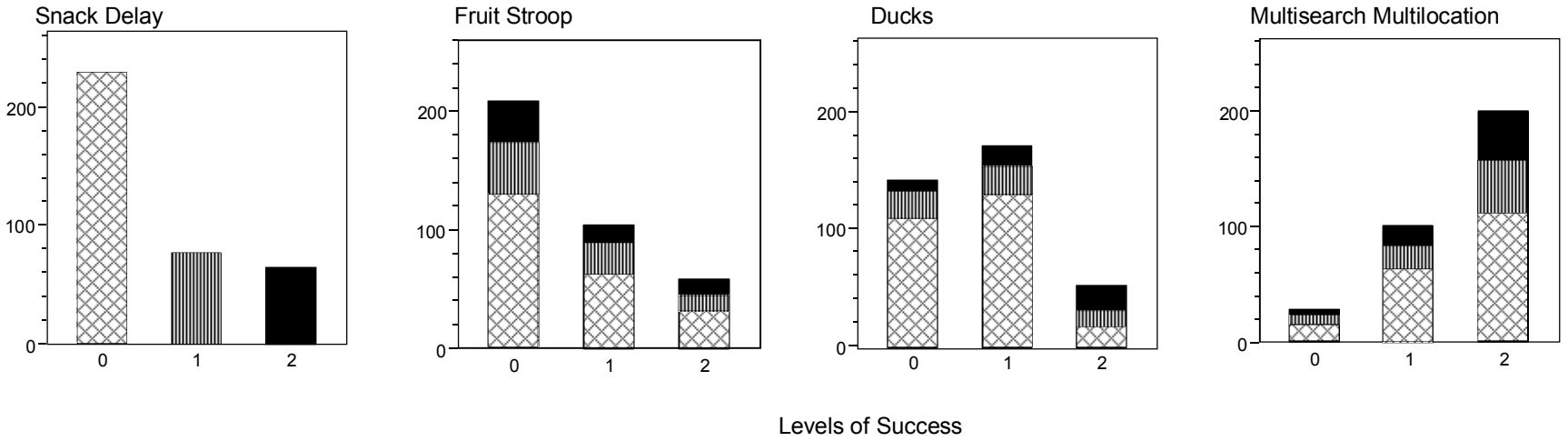
Cronbach's alpha for all 4 tasks was 0.429, and omitting MSML was 0.491.

Table 5.10: Relationships between assessed executive function task scores

	Snack Delay	Fruit Stroop	Ducks	Multisearch Multilocation
Snack Delay	-	R^2 = 0.040 β = 0.229*** [0.113, 0.344]	R^2 = 0.077 β = 0.262*** [0.169, 0.355]	R^2 = 0.003 β = 0.103 [-0.094, 0.299]
Fruit Stroop		-	R^2 =0.064 β =0.209*** [0.127, 0.291]	R^2 = 0.0001 β = 0.017 [-0.151, 0.185]
Ducks			-	R^2 = 0.004 β = 0.111 [-0.095, 0.317]
Multisearch Multilocation				-

Data are R^2, β [95%CI]; ***p<0.001

Figure 5.1: Distribution of results in all EF tasks showing number of children who failed, succeeded partially and succeeded fully in the Snack Delay task



Fruit Stroop success 1= 1 correct, 2= >1 correct; Ducks success 1=3 or 4 correct, 2= >5 correct; Multisearch Multilocation success 1= >3 attempts for pre-switch success, 2= 3 attempts for pre-switch success.

5.12. Relationships between assessed EF task and BRIEF-P scores

There were small but significant negative correlations between assessed EF scores and BRIEF-P scores (Table 5.12). Scores on Snack Delay, an assessment of Inhibition, were significantly associated with all scales and Indexes except Shift, Emotional Control and Flexibility Index. Most notably they were correlated with Inhibit (R^2 = 0.022, β = -0.032), Working Memory ((R^2 = 0.024, β = -0.030) and Emergent Metacognition (R^2 = 0.023, β = -0.029). Fruit Stroop primarily assesses attention and inhibition, and scores on this task showed highest correlation with Inhibit (R^2 = 0.013, β = -0.022) and the Inhibitory Self-Control scale (R^2 = 0.015, β = -0.024). Scores on the Ducks task and Multisearch Multilocation were not significantly correlated with any of the BRIEF-P scales or indexes.

EF Total scores were significantly correlated with all BRIEF-P scales and indexes. The highest correlations with scale scores were Working Memory (R^2 = 0.038, β = -0.099) and Plan/Organise (R^2 = 0.032, β = -0.097). The strongest association for EF Total score was with the Global Executive Composite score (R^2 = 0.040, β = -0.105). However, each of these assessed EF skills explained only 1.1 – 2.4% of the variation in BRIEF-P scores, and the EF Total score explained only 4% of the variation in BRIEF-P Global Executive Composite score.

Table 5.11: Relationship between assessed Executive Function tasks with BRIEF-P scales and indexes

Assessed EF	BRIEF-P	R^2	β	Lower 95% CI	Upper 95% CI	P value
Snack Delay						
	Inhibit	0.022	-0.032	-0.054	-0.010	**0.004**
	Shift	0.003	-0.013	-0.036	0.010	0.262
	Emotional Control	0.005	-0.017	-0.041	0.007	0.168
	Working Memory	0.024	-0.030	-0.050	-0.010	**0.003**
	Plan/Organise	0.015	-0.025	-0.046	-0.004	**0.020**
	Inhibitory Self-Control Index	0.016	-0.028	-0.051	-0.005	**0.015**
	Flexibility Index	0.005	-0.017	-0.040	0.007	0.160
	Emergent Metacognition Index	0.023	-0.029	-0.049	-0.010	**0.004**
	Global Executive Composite	0.021	-0.029	-0.050	-0.008	**0.006**
Fruit Stroop						
	Inhibit	0.013	-0.022	-0.041	-0.002	**0.028**
	Shift	0.008	-0.017	-0.037	0.003	0.093
	Emotional Control	0.011	-0.022	-0.042	-0.001	**0.043**
	Working Memory	0.010	-0.017	-0.034	0.001	0.061
	Plan/Organise	0.009	-0.017	-0.036	0.001	0.071
	Inhibitory Self-Control Index	0.015	-0.024	-0.044	-0.004	**0.020**
	Flexibility Index	0.011	-0.021	-0.041	-0.001	**0.041**
	Emergent Metacognition Index	0.011	-0.017	-0.035	0.000	0.051
	Global Executive Composite	0.014	-0.021	-0.040	-0.003	**0.022**
Ducks						
	Inhibit	0.005	-0.016	-0.039	0.008	0.187
	Shift	0.001	-0.008	-0.033	0.016	0.510
	Emotional Control	0.008	-0.023	-0.048	0.003	0.080
	Working Memory	0.009	-0.019	-0.041	0.002	0.074
	Plan/Organise	0.007	-0.018	-0.040	0.005	0.121
	Inhibitory Self-Control Index	0.007	-0.020	-0.044	0.005	0.112
	Flexibility Index	0.005	-0.017	-0.042	0.007	0.168
	Emergent Metacognition Index	0.008	-0.019	-0.040	0.002	0.079
	Global Executive Composite	0.008	-0.019	-0.042	0.003	0.087

Assessed EF	BRIEF-P	R^2	β	Lower 95%	Upper 95%	P value
MultiSearch MultiLocation						
	Inhibit	0.000	0.001	-0.015	0.017	0.896
	Shift	0.013	-0.016	-0.032	0.001	0.062
	Emotional Control	0.001	-0.005	-0.022	0.012	0.583
	Working Memory	0.001	-0.003	-0.018	0.011	0.665
	Plan/Organise	0.001	-0.004	-0.019	0.011	0.626
	Inhibitory Self-Control Index	0.000	-0.001	-0.018	0.015	0.874
	Flexibility Index	0.006	-0.011	-0.027	0.005	0.188
	Emergent Metacognition Index	0.001	-0.003	-0.017	0.011	0.686
	Global Executive Composite	0.002	-0.005	-0.020	0.010	0.504
EF Total Score						
	Inhibit	0.030	-0.097	-0.159	-0.035	**0.002**
	Shift	0.013	-0.067	-0.133	-0.002	**0.043**
	Emotional Control	0.025	-0.097	-0.166	-0.029	**0.005**
	Working Memory	0.038	-0.099	-0.154	-0.043	**0.001**
	Plan/Organise	0.032	-0.097	-0.157	-0.037	**0.002**
	Inhibitory Self-Control Index	0.032	-0.103	-0.166	-0.039	**0.002**
	Flexibility Index	0.023	-0.088	-0.153	-0.023	**0.008**
	Emergent Metacognition Index	0.039	-0.100	-0.155	-0.044	**0.001**
	Global Executive Composite	0.040	-0.105	-0.163	-0.047	**<0.001**

5.13. Discussion

EF is an important aspect of child development which contributes to both behaviour and learning (Diamond, 2013). It develops in tandem with neurological maturation, particularly of the prefrontal cortex, and so may be impacted by processes which affect neurological development (P. J. Anderson, 2002). In adulthood EF components are moderately correlated but clearly separable, although in early childhood they are less clearly separable with separate components developing in a hierarchical and interrelated manner (Garon et al., 2008; Miyake et al., 2000). Attention and inhibition are the earliest EF skills to emerge and underlie the later development of working memory and cognitive flexibility (P. J. Anderson, 2002; Kochanska et al., 2000).

Our hypotheses that EF outcome would be negatively associated with neonatal risk, with different outcomes for different risk groups were supported by our results. Parent report suggests that our cohort performed more poorly than expected in comparison to the standardised mean, with a higher rate of potentially clinically significant scores. The most striking difference between risk groups was the gender interaction with IDM status on assessed EF measures, which resulted in boys performing worse and girls better, than the rest of the cohort. We also found differences between risk groups in the strength of association between EF scores and other developmental domains.

5.13.1. Assessed executive function

The importance of EF to child development meant it was imperative to include assessed EF along with parent report in our data collection. However, EF assessment of preschoolers is a developing science, and despite studies which showed the validity and sensitivity of then-current methods, there were no standardised assessed EF measures for this age group when our study started (S. M. Carlson, 2005; Zelazo et al., 2013). Reports that it was possible to assess EF at this age provided us with guidelines from which to design a developmentally appropriate and practical EF assessment battery (S. M. Carlson, 2005; Kochanska et al., 2000; Woodward et al., 2005; Zelazo et al., 1998) with further details provided by Stephanie Carlson (S.M. Carlson, personal communication, June 26, 2010).

The assessment battery was designed to include the principal components of preschool EF: attention, inhibition, working memory and cognitive flexibility; and to provide a range of difficulties and distribution scores within each task while avoiding floor and ceiling effects (Miyake et al., 2000; Zelazo et al., 2013). Binary measures such as the first Snack Delay trial and the first Post-switch attempt of the MSML added useful data about specific EF-related behaviours such as which children could inhibit a behavioural response or switch their search to a different location (S. M. Carlson, 2005). The importance of this detailed, so-called 'micro-analytic' data which enhances the utility of continuously distributed task score data, has been emphasised elsewhere (P. J. Anderson, 2002).

Of the four assessed EF measures we used, Multisearch Multilocation had the highest success rate, followed by Snack Delay, Fruit Stroop and Ducks /Reverse categorisation. This is similar to the range

of task difficulties previously reported by Carlson (2005). There was a range of scores in each task, with none of the tasks showing floor or ceiling effects. Children engaged readily with the tasks, even when the EF assessment was the final phase of the entire assessment, with the play-style presentation of the tasks providing a finish to the psychological assessment that children appeared to enjoy. Thus, the assessment tasks we used were age-appropriate and met the requirements for this study.

Emerging EF and other developmental domains including language and behaviour are inter-related, highlighting the difficulties of developing preschool EF measures with a single focus (M. A. Barnett et al., 2012; S. M. Carlson & Moses, 2001; Noble et al., 2005). The Multisearch Multilocation task had a higher rate of success than the other assessed tasks and is, arguably, the easiest because it can be learnt by imitation and hence, requires the least receptive language for instruction. Snack Delay had simple instructions and was also conceptually simple, even though the task itself was not easy for all children. The Ducks task, on the other hand has a more complicated set of verbal instructions and the lowest success rate. This task can only be completed by children with adequate working memory, inhibition and cognitive flexibility and so is a valid assessment of EF. However, it was also the only assessment where scores were lower for children whose first language was not English which suggests that the language used in this task may have been difficult for some children in this cohort. Further development of this assessment would include simplifying and reducing the language component and incorporating more modelling of behaviour. The strong relationships between EF skills required in categorisation tasks was an important factor in the choice of a similar sorting task being chosen as the basis of standardised preschool and childhood EF assessment currently being developed (S. M. Carlson & Schaefer, 2012; Zelazo et al., 2013).

Although the Fruit Stroop assessment is primarily one of inhibition and attention, other cognitive and behavioural features are also important. The task required children to be able to identify each of the three fruit and to know the words ‘big’ and ‘little’, so in addition to knowing these specific words this task required children to have developed the concept of comparative size. The importance of language development to this task is emphasised by the fact that while 28% of children correctly identified one little fruit, most of these (22%) were in response to the apple, the most commonly available fruit in New Zealand. Behavioural requirements included attending sufficiently to the pictures to focus on a subdominant visual feature, inhibiting a response to the dominant visual feature, and responding as requested (Kochanska et al., 2000).

EF assessments are likely to be more challenging and frustrating than other psychological assessments, and apparently simple tasks can be frustrating and even evoke emotional reaction from particiapnts, child and adult alike, which may result in reduced performance (Golden & Hines, 2011). Children who had their EF assessment last in the sequence of assessments were three times more likely to be excluded from the Snack Delay and Multisearch Multilocation tasks for behavioural reasons than those children who had the EF assessment in the first half of the session. They also had lower scores for Ducks, leading to lower EF Total scores. Since Snack Delay and Multisearch Multilocation both required some patience before a treat was received, it is possible that poor

behaviour may have been influenced by both tiredness and hunger, especially given that they were both 'Hot' or emotionally charged rather than 'Cool' or abstract tasks (Bunch & Andrews, 2012; Hongwanishkul et al., 2005). Fruit Stroop and Ducks had high behavioural exclusion rates (Stroop: 19.3%, Ducks 17.2%) but these were not higher in children whose EF assessment was last, although scores for the Ducks task were lower for them. This suggests that even for children who were able to manage their behaviour, the task became significantly more demanding with tiredness. Inhibiting inappropriate behaviour is a component of EF so a zero score for excluded children whose behaviour prevented them from completing the task still contributes to the assessment of EF in those children.

Our findings suggest that to achieve optimal assessment of 2-year-olds practical considerations such as language used, length of assessment, scheduling of assessments within the assessment battery, and timing of assessment in relation to sleep times need to be included.

5.13.2. BRIEF-P

Parent report is considered to be an essential contribution to the ecological validity of EF assessment as it provides data on children's everyday functioning (Golden & Hines, 2011; Isquith, Crawford, Espy, & Gioia, 2005). We used the BRIEF-P for this data collection as it is commonly accepted to be an appropriate assessment measure for parent report of preschool EF (Ezpeleta, Granero, Penelo, de la Osa, & Domènech, 2013; Gioia et al., 2000; Wittke, Spaulding, & Schechtman, 2013).

Cohort mean scores for BRIEF-P on all scales and indices were significantly higher than the standardised scores, which is not unexpected in a cohort born at risk of morbidity and with a higher proportion of low SES families than the general population (Farah et al., 2006; Noble et al., 2007). The overall cohort score was highest for the Working Memory Scale (61.5), and as a result the Emergent Metacognition Index (59.8) and Global Executive Composite score (57.6) were correspondingly higher. The mean score for the Inhibit scale was the next highest cohort score (56.6). A cohort of normally developing, regionally representative Christchurch 4-year-olds had BRIEF-P results in line with the standardised scores, suggesting the standardisation is appropriate for New Zealand (C. A. C. Clark, Pritchard, Woodward, & García Coll, 2010). Elsewhere, an Australian cohort of very preterm and extremely low birth weight babies at early school age follow-up were found to have higher mean scores than normal birth weight babies on all scales of the BRIEF (P. J. Anderson et al., 2004). Thus the high scores in our cohort are likely to reflect the at-risk nature of this group of children.

5.13.3. Correlations between assessed executive function measures and BRIEF-P

Examiner assessment of EF in young children allows for the gathering of objective information which is detailed data typically timed in seconds. By contrast, the BRIEF-P reflects parents' perceptions of behaviour during the 6 months prior to data collection. It is, therefore, unsurprising that parent report and assessed EF are often not closely related, as while examiner assessments of EF measure specific skills or behaviour, parent reports appear to assess the every-day implementation of these

skills (P. J. Anderson, 2002; Bodnar, Prahme, Cutting, Denckla, & Mahone, 2007; McAuley, Chen, Goos, Schachar, & Crosbie, 2010; Silver, 2012; Wittke et al., 2013).

Our assessed EF scores, except for the Ducks task, had significant but low levels of correlation with BRIEF-P scale and index scores, with only a small percentage of variability explained by the BRIEF-P scores. It is likely that lack of significant correlation between the Ducks task scores and the BRIEF-P was due to the low level of success on the Ducks task, resulting in insufficient power for adequate analysis of results. The Snack Delay and Fruit Stroop were both correlated with Inhibit, Inhibitory Self Control and Global Executive Composite score, thus supporting the theoretical basis of these two tasks as assessments of preschool inhibition (S. M. Carlson, 2005; Kochanska et al., 2000).

The Multisearch Multilocation task was developed from Piaget's A-not-B task and is considered to assess a child's developing understanding of object permanence, perseverative errors and working memory (Zelazo et al., 1998). Poorer performance of very preterm children than term controls on the Multisearch Multilocation task at 2 years has been associated with reduced total cerebral volume and the extent of neonatal white matter injury observed on neonatal MRI (Woodward et al., 2005). At 4 years the very preterm children of the same cohort were found to have poorer performance than term controls on measures of selective attention, planning, inhibitory control and cognitive flexibility, with performance inversely associated with the extent of neonatal white matter injury (Woodward, Clark, Pritchard, Anderson, & Inder, 2011). Together these studies suggest that Multisearch Multilocation performance at 2 years was predictive of later EF of children born very preterm, and related to neonatal brain structure. In our cohort, scores on the Multisearch Multilocation post-switch task, which provided the first opportunity to display working memory, but not the Multisearch Multilocation score which also scored speed of learning the task, was correlated with the BRIEF-P Working Memory, Emergent Metacognition Index and Global Executive Composite. Our results support previous reports that the Multisearch Multilocation task was a measure of preschool working memory (Woodward et al., 2005; Zelazo et al., 1998), and follow-up of our cohort will provide further data as to the predictive value of this task for subsequent EF development.

The EF Total score was significantly correlated with all BRIEF-P scales and indexes except the Shift scale. This suggests that despite only small amounts of variance in the score being explained by behaviours measured by the BRIEF-P, our assessed EF measures and the BRIEF-P are both assessing aspects of the same construct. Our results suggest that assessed EF measures can provide information about specific EF behaviours that contribute to an overall pattern of behaviour as measured on the BRIEF-P.

5.13.4. EF assessments as a unitary or composite construct

The BRIEF-P scale scores had a good level of internal consistency, as shown by the high Cronbach's alpha, but the assessed EF measures did not, showing only a low level of internal consistency. Therefore, while BRIEF-P results are concordant with the literature reporting that emergent EF at 2 years of age can be thought of as a single construct which differentiates with age, the assessed EF

results do not support this concept (P. J. Anderson, 2002; McAuley & White, 2011; Miyake et al., 2000; Wiebe, Espy, & Charak, 2008; Wiebe et al., 2011; Zelazo et al., 2013).

There was a small degree of correlation between scores on Snack Delay, Fruit Stroop and Ducks, but the Multisearch Multilocation scores had no correlation with those on the other three assessed EF tasks. These results are more consistent with the alternate view that the functions which compose EF - inhibition, working memory, cognitive flexibility and attention – are separate but interrelated at 2 years (Best & Miller, 2010; Hughes, 1998a; Senn, Espy, & Kaufmann, 2004) and thus the results of the assessed EF tasks reflect the numerous possible responses within EF performance, likely served by separate neural pathways which differentiate with increasing age and cognitive development (Aron, 2008; Senn et al., 2004; Wiebe et al., 2011). The difference between the unitary and component theories of preschool EF appear to be a reflection of the measurements used, with different assessed EF tasks assessing specific actions which are observably different yet interlinked components of EF.

5.13.5. Risk Groups

There were no differences in assessed EF scores between risk groups, although Preterm children performed better than others on the little apple task of the Fruit Stroop. This was not a general pattern, and data from the Bayley III assessment also show no differences between the Preterm and other risk groups.

The only significant difference in BRIEF-P scores between risk groups was a lower Inhibit scale score for the Preterm in comparison to the Small group, which suggests that at 2 years children born late preterm are reported by their parents to exhibit better inhibitory control than are children born small, although both groups had BRIEF-P scores above the standardised mean. Limited EF results have been reported for late preterm and small children at preschool age. However, children born SGA were found to have reduced attention and inhibition, when compared to AGA peers, which persisted into teenage years (Kulseng et al., 2006). Thus inhibition may be an ongoing concern for children born small, and an early indication of this in our cohort may be that 29% of our Small group had Inhibit scale scores that were potentially clinically significant.

Although our Late Preterm group had a lower Inhibit scale score than the Small group, it was higher than the standardised mean and 17% of the group had Inhibit scale scores in the clinically significant range. Others have reported that children born late preterm had reduced complex working memory scores, but not inhibition, when compared with full term children in a touch screen battery of assessments at 3 years of age (Baron et al., 2012), and had reduced verbal inhibitory control at 4 years of age, although parent report on the BRIEF-P did not differ (Brumbaugh, Hodel, & Thomas, 2013). This suggests that the elevated scores in our Late Preterm group for all BRIEF-P scales and indexes may reflect SES and co-morbid neonatal health factors rather than gestational age alone.

Working Memory is the aspect of EF that was reported by parents as being the most problematic for our cohort, particularly for Other, Small and IDM children, with 42-45% of children in these groups

scoring in the clinically significant range. Others have reported poorer working memory on a delayed imitation task in IDM compared with non-IDM children at 12 months, and on the working memory subtests of the Wechsler Intelligence Scale for Children - version 4 (Wechsler, 2004) when compared with United Kingdom normative data at school age (DeBoer, Wewerka, Bauer, Georgieff, & Nelson, 2005; Temple, Hardiman, Pellegrini, Horrocks, & Martinez-Cengotitabengoa, 2011). Similarly, at 40 weeks term-born SGA babies have poorer neurobehavioral development including attention, habituation and state regulation, with lower IQ, and memory and subtle attention deficits persisting into adulthood (Figueras et al., 2009; Kulseng et al., 2006; O'Keeffe et al., 2003; Viggedal, Lundälv, Carlsson, & Kjellmer, 2004). Our results add to the body of work identifying working memory as an area of neuropsychological impairment for children in both the neonatal and socioeconomic risk groups included in our cohort.

5.13.6. Gender and EF

Girls were more successful than boys in completing the Snack Delay and Ducks tasks, indicating a greater ability to inhibit a prepotent response, and successfully employ working memory. This gender difference in inhibitory control and EF skills has been previously reported for preschoolers (Kochanska, Murray, & Coy, 1997; Kochanska et al., 2000; Wiebe et al., 2008). In contrast, girls had higher BRIEF-P T-scores than boys for Inhibit, Shift, Plan/Organise, Emergent Metacognition and Global Executive Composite, although their raw scores were several points lower than boys for Inhibit, Inhibitory Self-Control Index and Global Executive Composite. These results suggest that girls in our cohort perform better on assessed measures of inhibition but less well on parent reported inhibitory behaviour than do the boys. There are several possible reasons for these findings.

It is possible that normalisation for 2-year-old girls and boys in New Zealand is not appropriate because their behaviour is more alike than 2-year-old girls and boys in the United States was 10 years ago when normalisation of the BRIEF-P was undertaken. However, previous studies of a normal population of New Zealand 4-year-olds and a cohort of 3-year-olds in Spain have supported the internal validity and standardisation of the BRIEF-P, with high Cronbach's alpha results, and T-scores in the expected range (C. A. C. Clark et al., 2010; Ezpeleta et al., 2013).

Further, the Strength and Difficulties questionnaire (SDQ), a parent report of behaviour which can be used for children from the age of 3 years, has been reported to show a similar level of problem identification within New Zealand, the United States, Australia and Great Britain and a good level of reliability and validity for Australian 4 – 9 year old children (Goodman, Ford, Simmons, Gatward, & Meltzer, 2000; Hawes & Dadds, 2004; Tuohy, 2010). Thus it seems unlikely that parental reports of preschool behaviour differ widely between New Zealand and other societies. However, there are no reports addressing the question of whether they are equally and separately valid for girls and boys.

A related but alternate explanation for the gender differences we found is that while EF gender differences can be observed at three and older they are less apparent at 2 years (Granie, 2010; D. F. Hay, 2007) and hence separate standardisation for girls and boys at 2 years may not be required.

This would explain why girls' assessed EF and raw scores indicate better EF performance than boys, but the opposite is true for T-score results. There appear to be no reported studies addressing this issue in 2-year-olds assessed with the BRIEF-P.

A third possible explanation is that New Zealand parents have higher expectations of girls' behaviour in comparison to boys' than is the case for parents in the United States. However, girls in this cohort had a significantly higher mean score than boys on the Adaptive Behavior scale parent questionnaire from the Bayley III (see 4.1), suggesting that overall parents have a positive perception of their daughters' development. Furthermore, a previously reported New Zealand cohort showed no difference between levels of behaviour problems for girls and boys as reported by parents on the Behaviour Check List, in a study which also reported a good level of validity and reliability for that assessment Pavuluri, Luk, Clarkson, & McGee, 1995; Pavuluri & Luk, 1996). Therefore, it seems unlikely that a difference in parental expectations of girls' and boys' behaviour explains our findings of girls having better inhibition scores on assessed EF tasks and worse on parent report. Further assessment of EF development in a population of normal New Zealand 2-year-olds, along with New Zealand standardisation of the BRIEF-P, may help address this finding.

IDM children in our cohort did not differ from other risk groups in their performance on assessed EF tasks, although their parents did report high Working Memory and Emergent Metacognition Index scores on the BRIEF-P. One previous study of IDM reported impaired memory networks, as demonstrated by event related potentials at 6 and 8 months, that were not reflected in either behavioural assessment at the same time or Bayley Scales of Infant Development assessment at 12 months (deRegnier, Long, Georgieff, & Nelson, 2007; Nelson et al., 2000), suggesting subtle early neurocognitive deficits in IDM children. School-age IDM were shown to have impaired attention and neurocognitive development and poorer school outcomes than non-IDM children (Dahlquist & Källén, 2007; Ornoy et al., 1998; Ornoy et al., 2001; Stenninger et al., 1998).

We also found significant gender effects with IDM in our cohort, with girls being more successful on the Snack Delay and Multisearch Multilocation tasks and having a higher EF Total score than cohort girls overall while IDM boys were less successful on these tasks with a lower EF Total score than cohort boys overall. These gender differences were not reflected in the BRIEF-P results, which is likely a reflection of the assessments themselves. The 17 items that comprise the BRIEF-P Working Memory scale relate to generally observable behaviour rather than the discrete behavioural differences on the assessed EF tasks. The narrow focus on specific tasks, as presented in our assessed EF tasks, appears to have been useful in identifying differences in performance ability on tasks requiring inhibition and working memory.

It has also been reported that IDM boys are more vulnerable to morbidity, including neonatal hypoglycaemia, and show a greater physiological response to maternal antenatal treatment of gestational diabetes (Bahado-Singh et al., 2012; Bracero, Cassidy, & Byrne, 1996). Taken together with our findings, this suggests that in IDM, boys are more vulnerable and more likely to display impairment in neurocognitive development, including EF.

There were also significant interactions between gender and English as a first language, with girls, but not boys, whose first language was not English having lower scores for Shift and Flexibility Index than those whose first language was English. This result may be explained by a cultural difference in EF performance, expectation of obedience and increased shyness in girls, which have been reported elsewhere (Chen et al., 1998; Sabbagh et al., 2006) resulting in a decreased Shift score only for girls. This finding appears to contrast with the interaction between gender and NZDep2006 at 2 years, with girls, but not boys in the lowest SES group having a significantly higher Shift score than other SES groups. Harsher and less empathetic parenting practices, reported in lower SES families with lower maternal education, are associated with less secure attachment which in turn is associated with poorer responses to unfamiliar situations. These factors, intersecting with a general increased shyness for girls, may underlie the gender interactions found on the Shift scale for girls from the low SES group (Bowlby, 1982; Chen et al., 1998; Sherry et al., 2013; Valenzuela, 1997).

5.13.7. SES and family effects on EF

SES was related to both assessed EF and BRIEF-P results, with low household income and home rental rather than ownership associated with much lower assessed EF and higher BRIEF-P scores on all assessments and scales. Low maternal education was the other main variable most consistently associated with lower EF results, with differences in BRIEF-P scores between high and low maternal education groups that were similar in magnitude to those for high and low household income groups. Interestingly, the high and low groups on the NZDep 2006 differed only in the low group having a lower score on the Snack Delay and higher scores on Inhibition, Emotional Control, Inhibitory Self Control Index, Flexibility Index and Global Executive Composite. Elsewhere, low SES has been associated with reduced success on the A-not-B task at 6 -14 month olds (Lipina, Martelli, Vuelta, & Colombo, 2005), impaired set-shifting and ADHD in 3 – 6 year olds (Martel, 2013), and reduced problem-solving in 4-year-olds (Potijk et al., 2013). At school age the effect of childhood poverty has been found to have a greater effect on the development of neurocognitive systems underlying language, cognitive control and working memory than other systems (Farah et al., 2006; Hackman & Farah, 2009). Some of these differences are already seen in our cohort with differences between high and low SES groups greatest on Bayley III Language score (see Chapter 4). However, poorer EF outcomes associated with low SES were seen on all measures.

Our results suggest that household income and maternal education are stronger predictors of EF at 2 years than NZDep2006, with these results showing the same pattern as that found for SES associations with Bayley III scores (Chapter 4). Other reports differ as to whether household income or maternal education is a stronger predictor of EF, with both considered more predictive than neighbourhood effects (Noble et al., 2007; Oakes, 2012). The strong correlation between education levels of the mothers and fathers, also seen in our cohort, has been termed the ‘home effect’ to emphasise the additive advantage or disadvantage this may represent (Ardila et al., 2005). In early childhood day-to-day interactions with care-givers are more important to development than distal influences such as neighbourhood, although in the preshool years how children play and spend their

time will influence behaviour (Lillard & Peterson, 2011). The 'home effect' may reflect a myriad of factors that can interact to influence EF development, including parental availability, sensitivity, style, language, mental health and understanding of child development and availability of toys, books and social learning opportunities (Bradley & Corwyn, 2002; Farah et al., 2006; Hughes & Ensor, 2009; Valenzuela, 1997).

After adjustment for SES, children who did not have English as a first language had lower Emotional Control and Flexibility Index scores than those whose first language was English. The majority of children who did not have English as a first language were in the broad category 'Asian'. These results may be consistent with previous reports that family expectations vary with culture and influence EF outcomes, with obedience and emotional control being behaviours expected and desired to a greater extent in Asian than in Western families (Chen et al., 1998; Sabbagh et al., 2006).

5.13.8. Parental tobacco, alcohol and marijuana use

Maternal smoking at 2 years, but no other measure of parental smoking, was associated with higher BRIEF-P scores for Inhibit, Emotional Control, Flexibility Index and Global Executive Composite after adjustment for SES. Maternal antenatal smoking has previously been associated with reduced brain volume, increased affective, hyperactivity and conduct problems, and poorer inhibitory control (El Marroun et al., 2014; Huijbregts, Warren, de Sonneville, & Swaab-Barneveld, 2008). It is possible that we did not see this in our cohort because maternal antenatal smoking was underreported, since the rate in our cohort (27%) was much lower than the estimated maternal antenatal tobacco use rate in New Zealand (54%) (Shipton et al., 2009; Wu et al., 2013). Further, there was a high correlation between maternal smoking antenatally and at 2 years, which may explain why the children whose mothers were reported to smoke at 2 years had similar EF problems to those seen elsewhere in children whose mothers smoked antenatally. In addition, developmental outcomes associated with maternal smoking have complex associations with other family factors and also environmental tobacco smoke, and these influences may also be reflected in the results in our cohort (Knopik, 2009; Pagani, 2013).

There were no associations between EF outcomes and reported maternal alcohol use. This contrasts with other reports that maternal antenatal alcohol use is associated with poorer preschool EF, particularly performance on inhibition tasks (Noland et al., 2003), although no association between low to moderate maternal antenatal alcohol consumption and poor developmental outcomes was found in a large Danish cohort at 5 years (Kesmodel & Frydenberg, 2004). The reported rates of maternal antenatal alcohol use in our cohort (9.9%) are much lower than in a recent New Zealand report (56.3%) (Wu et al., 2013) suggesting under-reporting in our cohort, and thus it is difficult to draw conclusions. Children whose fathers were reported to not drink antenatally had lower assessed EF Total score, after adjustment for SES, than children whose fathers were reported to drink. However, they had lower Emotional Control and Inhibitory Self Control scores on BRIEF-P, and children whose fathers were reported to not drink at 2 years also had lower Flexibility Index and Global Executive Composite scores. These results appear to suggest that children whose fathers do

not drink alcohol do not perform as well on specific EF tasks but are perceived by their parents as having fewer problem behaviours. This may reflect parenting differences between families who do and those who, for religious, health, or financial reasons do not drink alcohol (see also 4.5).

Although antenatal marijuana use has been associated with childhood attention, learning and memory problems and impulsivity (Fried & Smith, 2001; Richardson et al., 2002), we found that associations between parental marijuana use either antenatally or at 2 year assessment and EF scores were abolished after adjusting for SES. The levels of reported marijuana use in our cohort (3-5%) are much lower than estimated use in the New Zealand adult population (13-18%) (J. E. Wells et al., 2009; Wilkins & Sweetsur, 2008) and hence, are likely to be underreported. Because the numbers are so small we did not have the power to detect EF problems related to marijuana in our cohort (Danette, Fergusson, & Boden, 2008; Wu et al., 2013).

5.13.9. EF assessment in the future

Overall, different neonatal risk factors did not predict differences in EF development of the same magnitude as factors such as family income and parental education. Our results indicate that assessed EF, with a narrow focus on a target behaviour, can identify children with EF deficits such as lack of inhibitory control or poor working memory, children with observable EF skills and those who have a high level of EF skills such as very good inhibitory control. However, the extent that these separate skills at 2 years contribute to EF skills at a later age, and whether separate skills or an EF composite measure is the more predictive of later EF and behavioural outcomes, remains to be determined. On-going follow-up of this cohort will provide valuable data on how predictive the 2 year EF results are of later outcomes, including whether results such as high BRIEF-P scores reflect EF developmental delay or executive dysfunction.

Ideally, the assessed EF measures reported here would be standardised with a larger, representative population of New Zealand children as this would allow comparison of results between at-risk cohorts such as ours and expected New Zealand preschool performance. Such standardisation would also provide a greater clinical usefulness for individual preschool children requiring assessment. In addition, standardisation of the BRIEF-P for New Zealand children would address outstanding questions as to whether our cohort scores, which are higher than the expected mean, may be in part due to cultural differences between New Zealand and the United States and whether the current separate normalisation for girls and boys is valid or appropriate for New Zealand 2-year-olds.

EF skills can be taught, even to preschool children with challenging behaviour such as ADHD, raising the possibility that children from low SES homes, who are more likely to have EF deficits, could be taught EF skills that would improve their ability to cope with the demands of a primary school classroom (Diamond et al., 2007; Diamond & Lee, 2011; Halperin et al., 2013; Noble et al., 2005). The assessments reported here have the potential to identify impairments and indicate appropriate remedial support requirements for children in high risk groups such as IDM boys and children in low

SES families who appear to be at a developmental disadvantage. These assessments supplement parent report as they can provide data on both the learning and execution of novel EF tasks.

Chapter 6. Executive function and developmental outcomes

Infant and toddler development across all domains increases with neurological maturation, with integrated simultaneous development allowing further skill development (Fry & Hale, 2000), as is observed with cognitive and language skills. Because EF is a relatively new area of developmental studies, particularly preschool EF, the extent to which emerging cognitive, language, motor and processing skills are associated with EF skills is unclear. It is also unclear if perinatal health issues may disrupt the developmental process and thus result in altered association between EF and other developmental domains. Therefore, we tested the hypotheses that EF is associated with other developmental domains, including cognition, language, motor and vision, and that this association is influenced differently by different perinatal health issues.

Global motion coherence or the ability to discern directional motion is a measure of the functioning of the dorsal visual stream. The optokinetic reflex (OKR) is a measure of global motion coherence, and can be assessed using a random dot kinetogram. This dorsal visual stream is vulnerable to disruption as a result of certain syndromes and developmental disruptions (Braddick, Atkinson, & Wattam-Bell, 2003; Ridder, Borsting, & Banton, 2001; Spencer et al., 2000) including very preterm birth (MacKay et al., 2005) and because it is also associated with attention (Janette Atkinson & Braddick, 2012) we hypothesised that it would be related to EF at 2 years of age.

6.1. Executive function and cognitive development

EF was moderately associated with cognitive development in our cohort, with assessed EF Total score having a stronger association with Bayley III Cognitive score than did the BRIEF-P Global Executive Composite score (R^2 = 0.185, β = 0.254, vs R^2 = 0.058, β = -0.269,) (Table 6.1). The EF task assessing working memory and cognitive flexibility (Ducks) was more strongly related to Bayley III Cognitive scores (R^2 = 0.141, β = 0.089) than Snack Delay, a measure of inhibition (R^2 = 0.058, β = 0.054). A similar pattern was seen on the BRIEF-P with the Working Memory scale (R^2 = 0.066, β = -0.301) more strongly related to Bayley III Cognitive scores than the Inhibit scale (R^2 = 0.020, β = -0.147). Consistent with this, the Bayley III Cognitive score explained a small to moderate amount of the different EF task scores (R^2= 0.021 – 0.141), and only a small amount of the different BRIEF-P scores (R^2= 0.020 – 0.069) (Table 6.1).

The relationship between assessed EF Total score and cognitive development was similar in all risk groups, with the 95% confidence interval overlapping for all β coefficients. This relationship accounted for a larger proportion of the variance in the Small (R^2 = 0.384) and Large (R^2 = 0.304) groups, than IDM (R^2 = 0.248) and was not statistically significant for the Preterm or Other groups (Fig 6.1). However, the small number of children in the Other group (n=12) meant that significant relationships were unlikely. The relationship between BRIEF-P and cognitive development showed a similar pattern (Fig 6.2), being similar in all risk groups, although accounting for a larger proportion of

the variance in the Large (R^2 = 0.173) and Small (R^2 = 0.111) groups, less for Preterm (R^2 = 0.054), and was not statistically significant in the IDM or Other groups (Fig 6.2). There were no significant interactions between cognitive score and risk factor for either the EF Total score or the BRIEF-P Global Executive Composite score.

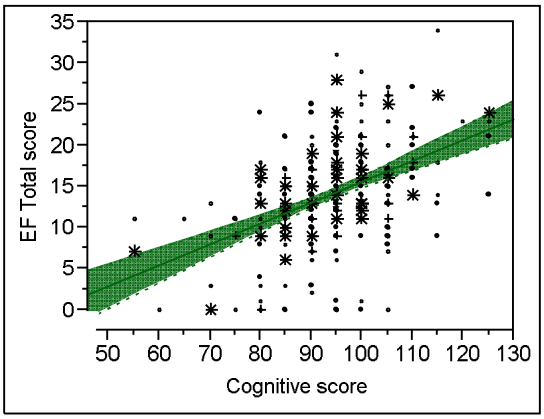
Children of school age with high cognitive skills but poor EF may be identified as having learning disabilities. We therefore attempted to identify whether this developmental profile was present in our cohort. There were 11 children with high Cognitive scores (1 SD or more above mean) but poor EF performance (Snack Delay and Fruit Stroop scores = 0; Ducks ≤2; Multisearch Multilocation ≤6; BRIEF-P score ≥ 65). Of these, 6 were IDM, 4 Preterm and 1 Small, with 8 boys and 3 girls. The small number of children precludes drawing conclusions. However, the low EF scores in this group showed no relationship with low SES factors, as measured by NZDep2006 and home ownership, suggesting that antenatal or perinatal health factors rather than SES, which is a known moderator of child development, may be contributing to this developmental profile.

Table 6.1: Associations between measures of executive function and Bayley III Cognitive score

EF Measure	Score	R^2	β	Lower 95% CI	Upper 95% CI	P value
Assessed EF						
	Snack Delay	0.058	0.054	0.031	0.076	**<0.001**
	Fruit Stroop	0.063	0.049	0.030	0.069	**<0.001**
	Ducks	0.141	0.089	0.067	0.112	**<0.001**
	MSML	0.021	0.020	0.004	0.037	**0.017**
	EF Total	0.185	0.254	0.194	0.314	**<0.001**
BRIEF-P						
	Inhibit	0.020	-0.147	-0.250	-0.044	**0.005**
	Shift	0.034	-0.181	-0.277	-0.085	**<0.001**
	Emotional Control	0.029	-0.163	-0.257	-0.070	**<0.001**
	Working Memory	0.066	-0.301	-0.412	-0.189	**<0.001**
	Plan/Organise	0.060	-0.269	-0.374	-0.163	**<0.001**
	Inhibitory Self-Control Index	0.026	-0.165	-0.265	-0.066	**0.001**
	Flexibility Index	0.037	-0.192	-0.289	-0.096	**<0.001**
	Emergent Metacognition	0.069	-0.310	-0.423	-0.198	**<0.001**
	Global Executive Composite	0.058	-0.269	-0.377	-0.162	**<0.001**

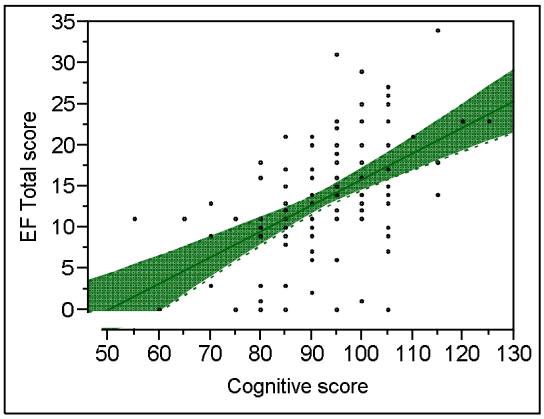
Figure 6.1: Assessed EF Total and Bayley III Cognitive scores for cohort and risk groups

Cohort



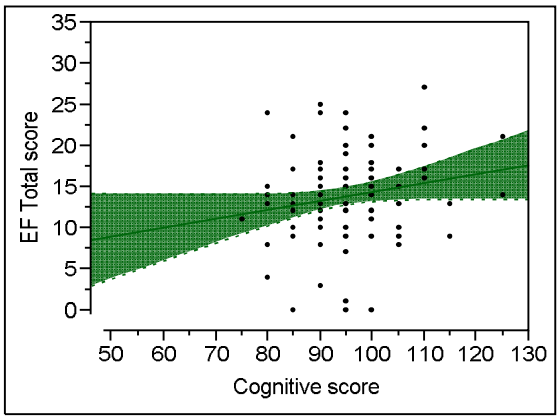
R^2=0.185; β = 0.254; [0.194, 0.314]; **p<.0001**

IDM



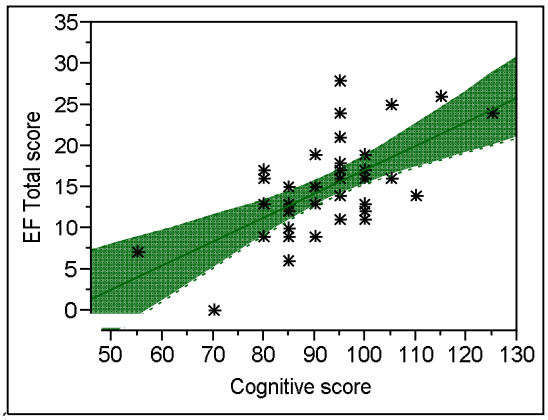
R^2=0.248; β = 0.317; [0.219, 0.416]; **p<.0001**

Preterm



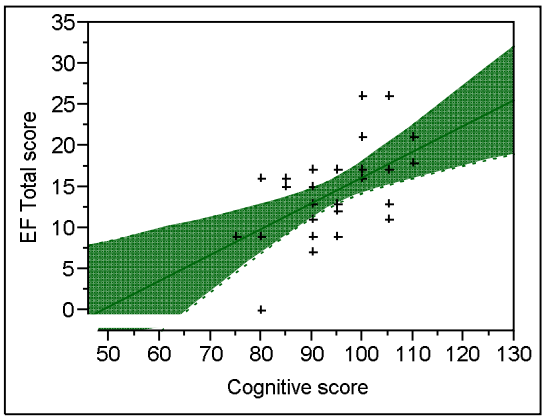
R^2=0.034; β = 0.108; [-0.005, 0.221]; p=0.062

Small



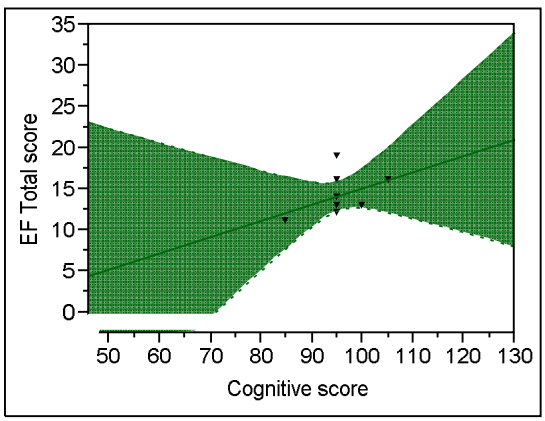
R^2=0.384; β = 0.292; [0.167, 0.417]; **p<.0001**

Large



R^2=0.304; β = 0.314; [0.136, 0.491]; **p=0.001**

Other

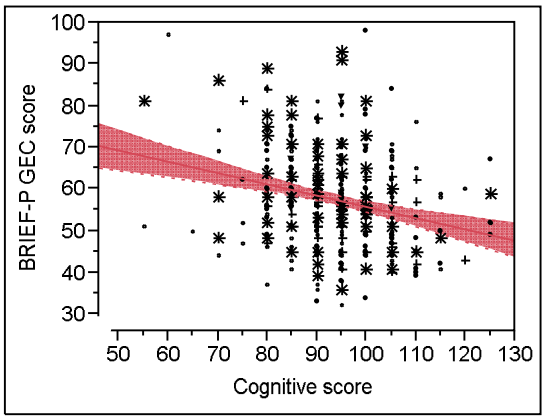


R^2=0.156; β = 0.198; [-0.176, 0.572]; p=0.258

Data are: R^2; β [95% confidence intervals]; p for interaction between EF Total score and cognitive score.

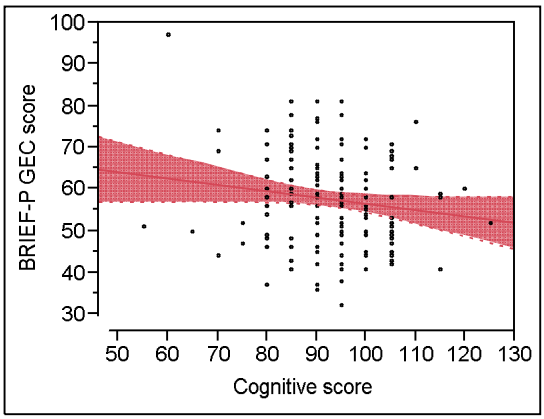
Figure 6.2: BRIEF-P Global Executive Composite (GEC) and Bayley III Cognitive scores for cohort and risk groups

Cohort



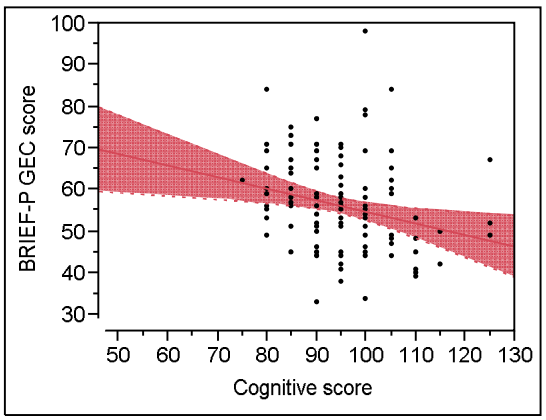
R^2=0.058; β =-0.269; [-0.377,-0.162]; **p<.0001**;

IDM



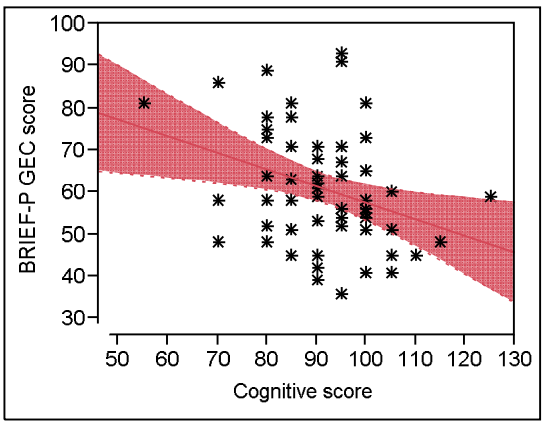
R^2=0.022; β =-0.153; [-0.316, 0.010]; p=0.066

Preterm



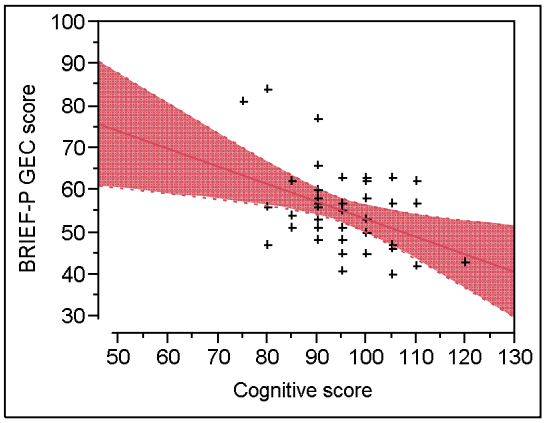
R^2=0.054; β =-0.277; [-0.481,-0.074]; **p=0.008**

Small



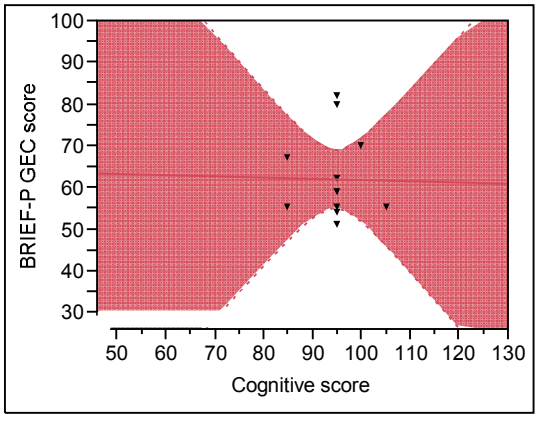
R^2=0.111; β =-0.395; [-0.691,-0.099]; p**=0.010**

Large



R^2=0.173; β =-0.419; [-0.716,-0.122]; p=0.007

Other



R^2=0.002; β =-0.030; [-1.389, 1.330]; p=0.962

Data are: R^2; β [95% confidence intervals]; p for interaction between BRIEF-P GEC score and cognitive score.

6.2. Executive function and language development

EF was moderately associated with language development in our cohort, with assessed EF Total score having a stronger association with Bayley III Language score than did the BRIEF-P Global Executive Composite (R^2 = 0.318, β = 0.235 vs R^2 = 0.071, β = -0.215) (Table 6.2). The EF task assessing working memory and cognitive flexibility (Ducks) was more strongly correlated to Bayley III Language scores (R^2 = 0.165, β = 0.068) than Snack Delay, a measure of inhibition (R^2 = 0.132, β = 0.058). A similar pattern was seen on the BRIEF-P with the Working Memory scale more strongly related to Bayley III Language scores than the Inhibit scale (R^2 = 0.075, β = -0.231 vs R^2 = 0.038, β = -0.147). Consistent with this, the Bayley III Language score explained a small to moderate amount of the variance in different EF task scores (R^2= 0.054 – 0.194), whereas it explained only a small amount of the variance in different BRIEF-P scores (R^2= 0.031 – 0.078) (Table 6.2). This pattern was similar to that seen for Cognitive scores, although a greater degree of variance in assessed EF scores was explained by Bayley III Language scores than by Bayley III Cognitive scores.

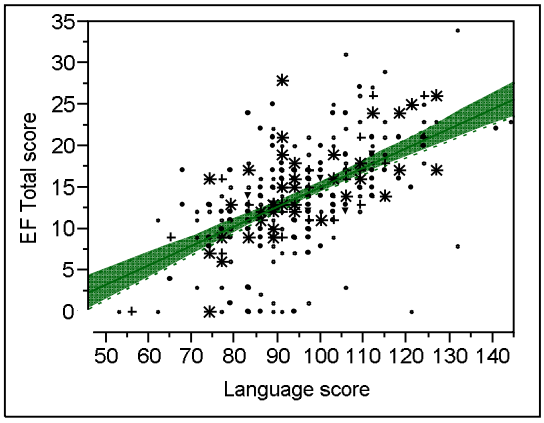
The relationship between assessed EF Total score and language development was similar for all risk groups, with the 95% confidence interval overlapping for all β coefficients (Fig 6.3). This relationship accounted for a larger proportion of the variance in the Large (R^2 = 0.664) and Small (R^2 = 0.412) groups than the IDM (R^2 = 0.316) and Preterm (R^2 = 0.206) groups, and was not significant for the Other group (Fig 6.3). The relationship between BRIEF-P and language development was also similar in all risk groups (Fig 6.4) but, as with the EF Total score, it accounted for more variance in the Large (R^2 = 0.166) and Small (R^2 = 0.138) groups, than in the Preterm (R^2 = 0.054) and IDM (R^2 = 0.045) groups, and was not statistically significant in the Other group (Fig 6.4). There were no significant interactions between language score and risk factor for either the EF Total score or the BRIEF-P Global Executive Composite score.

Table 6.2: Associations between measures of executive function and Bayley III Language score

EF Measure	Score	R^2	β	Lower 95% CI	Upper 95% CI	P value
Assessed EF						
	Snack Delay	0.132	0.058	0.042	0.073	**<0.001**
	Fruit Stroop	0.194	0.061	0.048	0.074	**<0.001**
	Ducks	0.165	0.068	0.052	0.084	**<0.001**
	MSML	0.054	0.023	0.011	0.034	**<0.001**
	EF Total	0.318	0.235	0.197	0.274	**<0.001**
BRIEF-P						
	Inhibit	0.038	-0.147	-0.221	-0.074	**<0.001**
	Shift	0.037	-0.136	-0.205	-0.068	**<0.001**
	Emotional Control	0.031	-0.123	-0.190	-0.055	**<0.001**
	Working Memory	0.075	-0.231	-0.311	-0.151	**<0.001**
	Plan/Organise	0.063	-0.199	-0.275	-0.123	**<0.001**
	Inhibitory Self-Control Index	0.042	-0.149	-0.220	-0.078	**<0.001**
	Flexibility Index	0.041	-0.145	-0.215	-0.076	**<0.001**
	Emergent Metacognition	0.078	-0.236	-0.317	-0.156	**<0.001**
	Global Executive Composite (GEC)	0.071	-0.215	-0.292	-0.138	**<0.001**

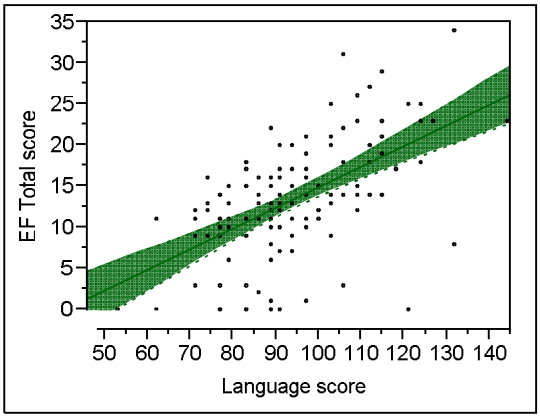
Figure 6.3: Assessed EF Total and Bayley III Language scores for cohort and each risk group

Cohort



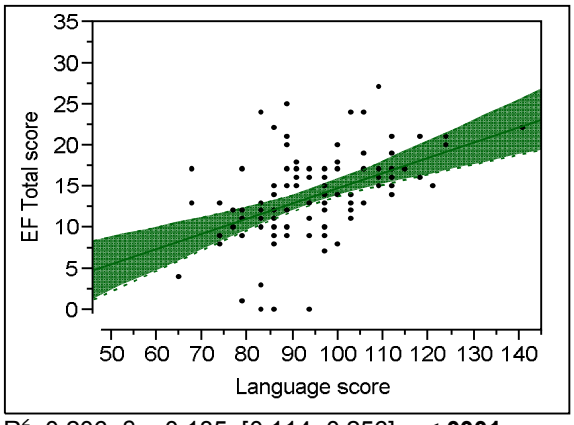
R^2=0.318; β = 0.235; [0.197, 0.274]; **p<.0001**

IDM



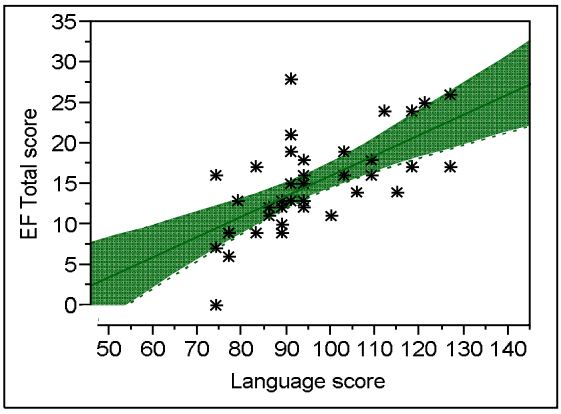
R^2=0.316; β = 0.251; [0.185, 0.317]; **p<.0001**

Preterm



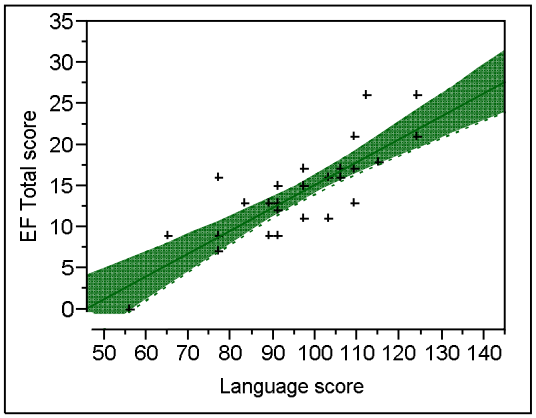
R^2=0.206; β = 0.185; [0.114, 0.256]; **p<.0001**

Small



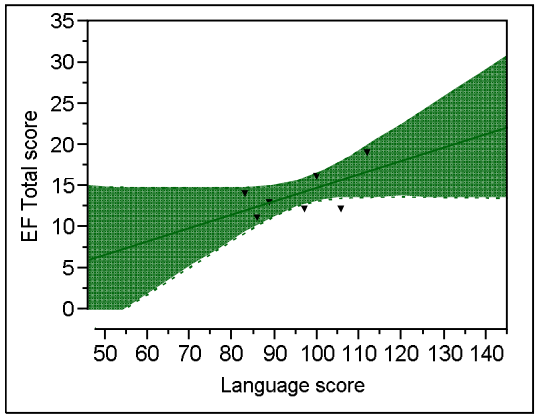
R^2=0.412 β = 0.251; [0.150, 0.353]; **p<.0001**

Large



R^2=0.664; β = 0.278; [0.205, 0.352]; **p<.0001**

Other

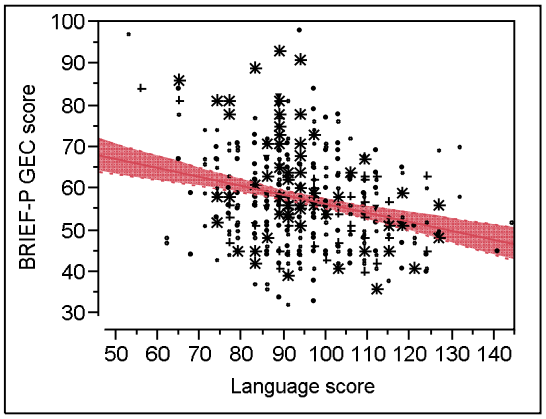


R^2=0.368; β =0.163; [-0.011, 0.337]; p=0.063

Data are: R^2; β [95% confidence intervals]; p for interaction between EF Total score and language score.

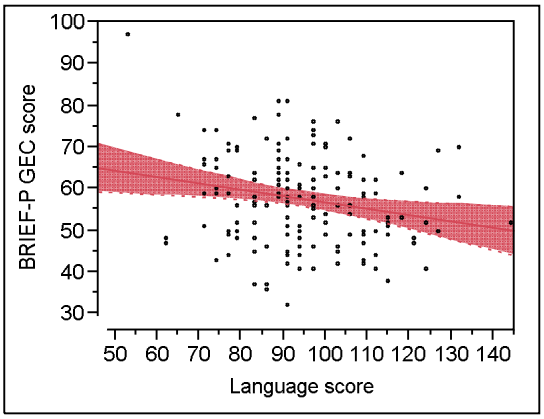
Figure 6.4: BRIEF-P Global Executive Composite (GEC) and Bayley III Language scores for cohort and each risk group

Cohort



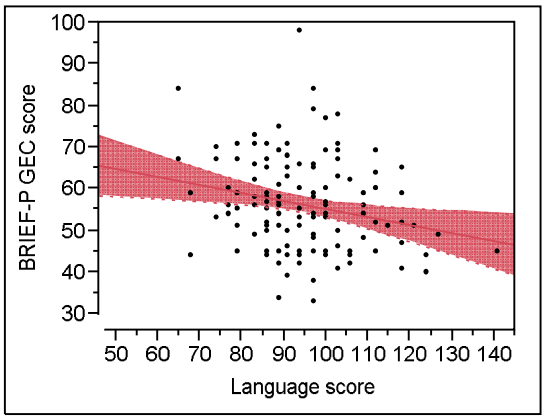
R^2=0.071; β =-0.215; [-0.292, -0.138]; **p<.0001**

IDM



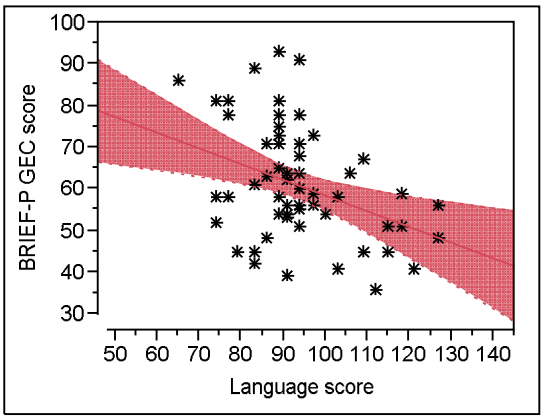
R^2=0.045; β =-0.153; [-0.265, -0.41]; **p=0.008**

Preterm



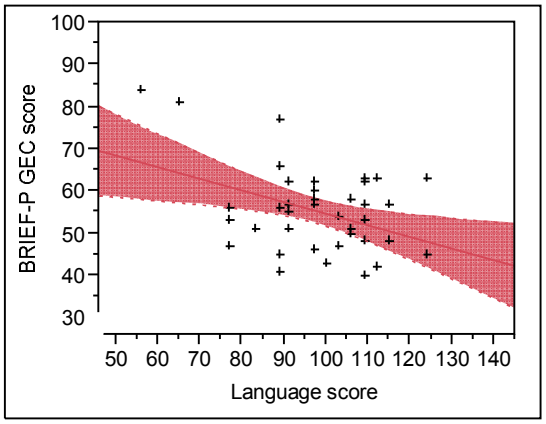
R^2=0.054; β =-0.192; [-0.333, -0.050]; **p=0.008**

Small



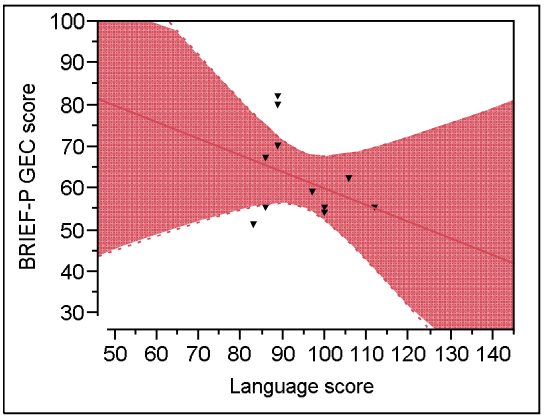
R^2=0.138; β =-0.377; [-0.626, -0.127]; **p=0.004**

Large



R^2=0.166; β =-0.276; [-0.475 -0.076]; **p=0.008**

Other



R^2=0.120; β =-0.400; [-1.16, 0.36]; p=0.270

Data are: R^2; β [95% confidence intervals]; p for interaction between BRIEF-P GEC score and language score.

6.3. Motor development and executive function

EF had a weak association with motor development in our cohort, with assessed EF Total score having a stronger association with Bayley III Motor scores than did the BRIEF-P Global Executive Composite (R^2 = 0.163, β = 0.250 vs R^2 = 0.029, β = -0.205) (Table 6.3). Again, the EF task assessing working memory and cognitive flexibility (Ducks) was more strongly related to Bayley III Motor scores (R^2 = 0.088, β = 0.075) than Snack Delay, a measure of inhibition (R^2 = 0.065, β = 0.061). A similar pattern was also seen on the BRIEF-P with the Working Memory scale most strongly associated with Bayley III Motor scores (R^2 = 0.038, β = -0.242) and the Inhibit scale not significantly related to the Bayley III Motor scores. Consistent with this, the Bayley III Motor score explained a small proportion of the variance in different EF task scores (R^2= 0.019 – 0.088), and an even smaller proportion of the variance in different BRIEF-P scale and index scores (R^2= 0.011 – 0.038) (Table 6.3).

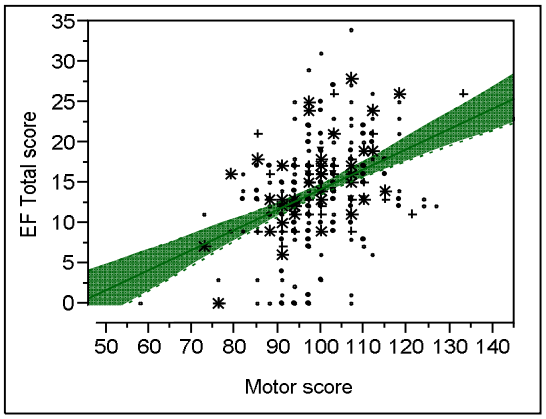
The relationship between EF Total score and motor development was similar in all risk groups (Fig 6.5) with the 95% confidence interval overlapping for all β coefficients. This relationship accounted for a larger proportion of variance in the Small (R^2= 0.307) and Large (R^2= 0.247) groups than in the IDM (R^2= 0.175) and Preterm (R^2= 0.076) groups (Fig 6.5). The relationship between BRIEF-P and motor development showed a different pattern (Fig 6.6), accounting for a larger amount of variance in the Large (R^2= 0.104) group than in the Small (R^2= 0.085) and was not statistically significant in the other groups. There were no significant interactions between motor score and risk factor for either the EF Total score or the BRIEF-P Global Executive Composite score.

Table 6.3: Associations between measures of executive function and Bayley III Motor score

EF Measure	Score	R^2	β	Lower 95% CI	Upper 95% CI	P value
Assessed EF						
	Snack Delay	0.065	0.061	0.037	0.085	**<0.001**
	Fruit Stroop	0.060	0.051	0.030	0.072	**<0.001**
	Ducks	0.088	0.075	0.050	0.100	**<0.001**
	MSML	0.019	0.020	0.003	0.038	**0.020**
	EF Total	0.163	0.250	0.187	0.314	**<0.001**
BRIEF-P						
	Inhibit	0.007	-0.096	-0.208	0.015	0.091
	Shift	0.027	-0.175	-0.278	-0.072	**0.001**
	Emotional Control	0.011	-0.110	-0.212	-0.008	**0.035**
	Working Memory	0.038	-0.242	-0.364	-0.121	**<0.001**
	Plan/Organise	0.021	-0.172	-0.288	-0.057	**0.004**
	Inhibitory Self-Control Index	0.011	-0.112	-0.220	-0.005	**0.041**
	Flexibility Index	0.022	-0.160	-0.265	-0.055	**0.003**
	Emergent Metacognition	0.035	-0.235	-0.357	-0.112	**<0.001**
	Global Executive Composite	0.029	-0.205	-0.322	-0.087	**<0.001**

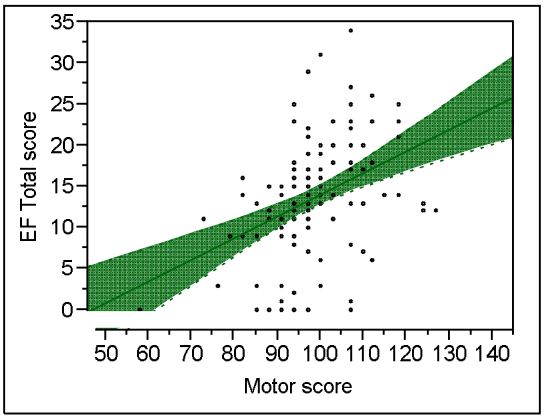
Figure 6.5: Assessed EF Total and Bayley III Motor scores for cohort and each risk group

Cohort



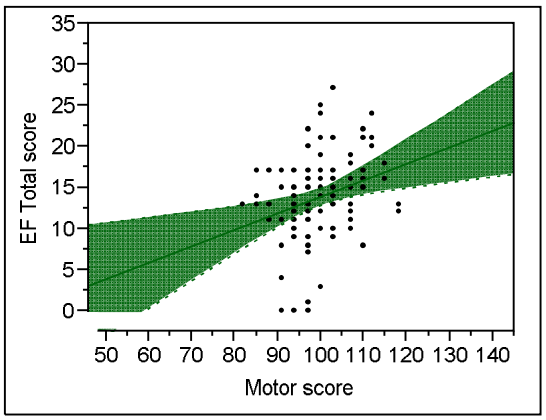
R^2=0.163; β = 0.250; [0.190, 0.314]; **p<.0001**

IDM



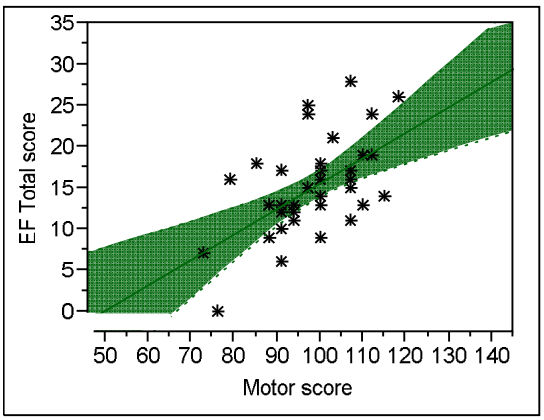
R^2=0.175; β =0.264; [0.161, 0.366]; **p<.001**

Preterm



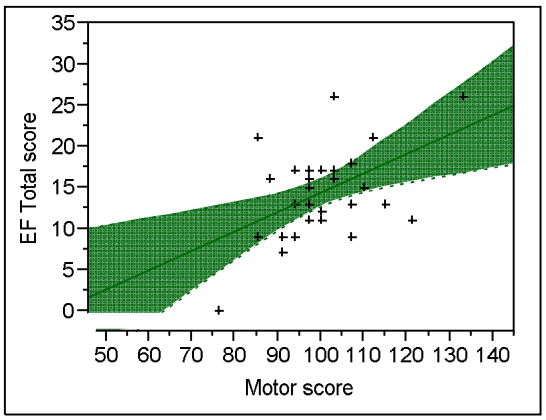
R^2=0.076; β = 0.200; [0.064, 0.337]; **p=0.005**

Small



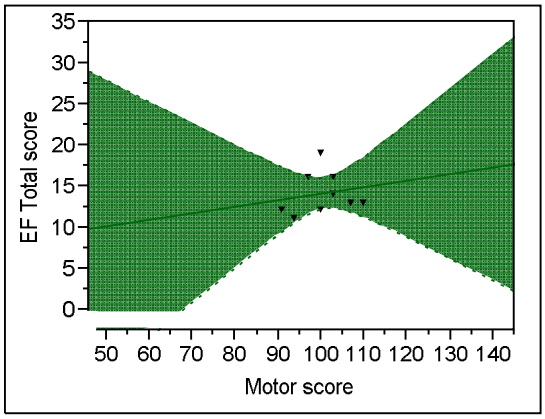
R^2=0.307; β = 0.309; [0.152, 0.466]; **p<0.001**

Large



R^2=0.247; β = 0.236; [0.082, 0.390]; **p=0.004**

Other

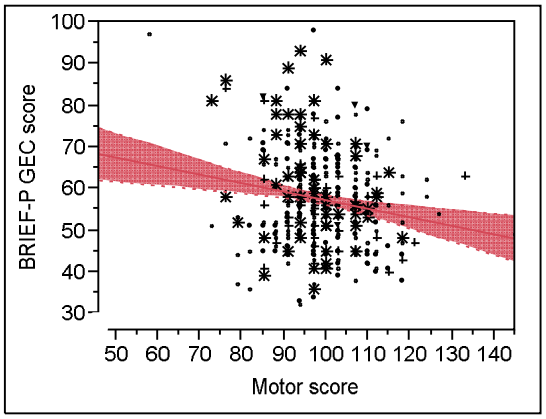


R^2=0.033; β = 0.079; [-0.268, 0.427]; p=0.614

Data are: R^2; β [95% confidence intervals]; p for interaction between EF Total score and motor score.

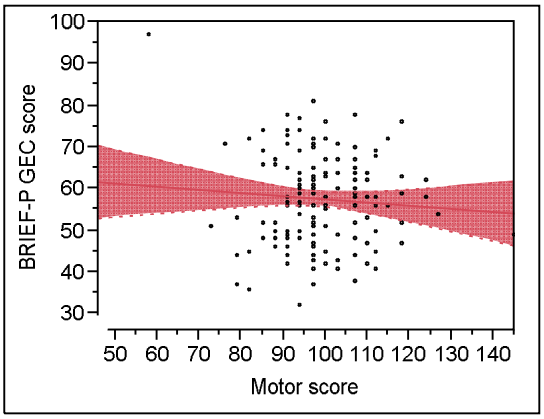
Figure 6.6: BRIEF-P Global Executive Composite (GEC) and Bayley III Motor scores for cohort and each risk group

Cohort



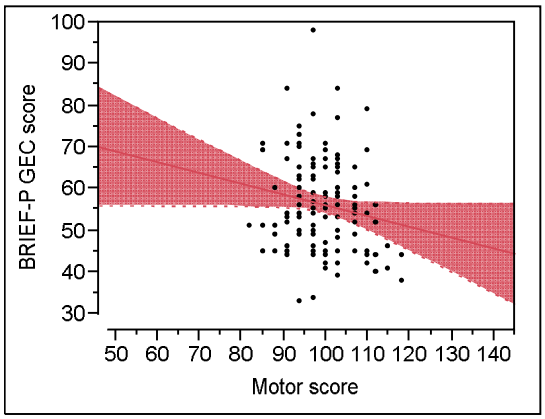
R^2=0.029; β =-0.205; [-0.322, -0.087]; **p<0.001**

IDM



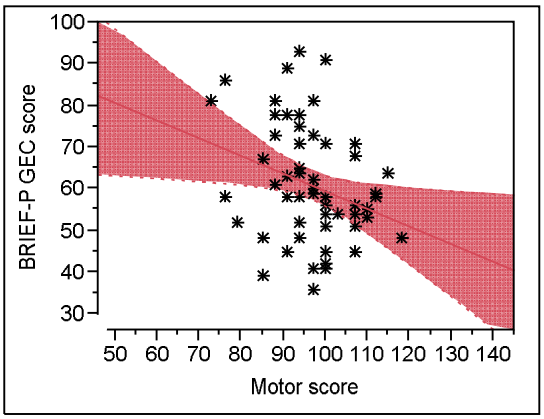
R^2=0.006; β =-0.077; [-0.239, 0.086]; p=0.353

Preterm



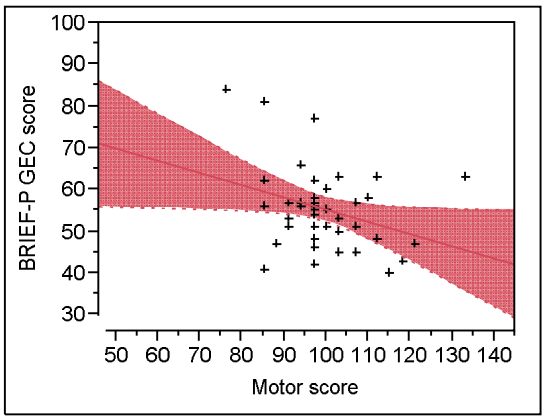
R^2=0.029; β =-0.259; [-0.522, 0.003]; p=0.052

Small



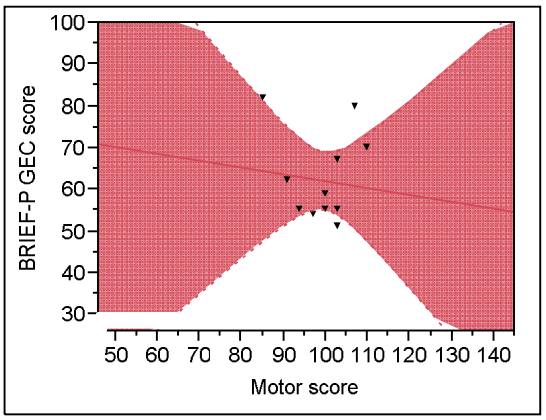
R^2=0.085; β =-0.424; [-0.793, -0.056]; **p=0.025**

Large



R^2=0.104; β =-0.292; [-0.569, -0.015]; **p=0.040**

Other



R^2=0.012; β =-0.164; [-1.21, 0.887]; p=0.735

Data are: R^2; β [95% confidence intervals]; p for interaction between BRIEF-P GEC score and motor score.

6.4. Vision development and EF

OKR threshold data was collected for 397 (98.3%) children. The OKR threshold was normally distributed (Mean: 42.2 ± 13.8) with a lower score indicating better function. There were no significant differences in mean OKR thresholds between risk groups or between girls and boys and there was no association between OKR threshold and birth weight, length or head circumference (data not shown).

OKR threshold was weakly associated with EF Total score (R^2 = 0.051, β = -0.098) but was not significantly associated with the BRIEF-P Global Executive Composite score or any of the BRIEF-P scales or indexes (Table 6.4). The EF task assessing working memory and cognitive flexibility (Ducks) was more strongly related to OKR threshold (R^2 = 0.030, β = -0.030) than Snack Delay, a measure of inhibition (R^2 = 0.014, β = -0.019) and Fruit Stroop, a measure of attention and inhibition (R^2= 0.014, β = -0.017), suggesting a stronger association with cognitive flexibility and working memory than other EFs. OKR threshold was not significantly related to the Multisearch Multilocation score. However, it was associated with Multisearch Multilocation post-switch success with the mean OKR threshold score for children who achieved post-switch success significantly lower than those who did not (p=0.042).

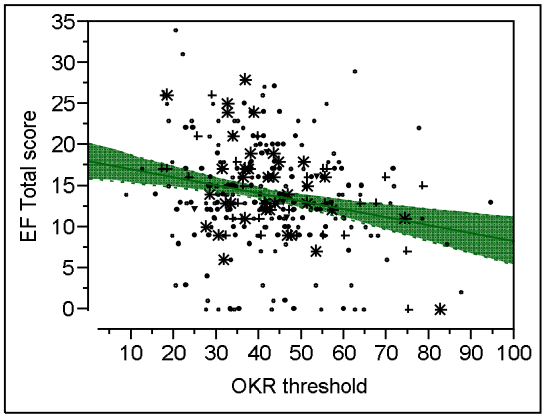
The relationship between EF Total score and OKR threshold was similar in all risk groups, with the 95% confidence interval overlapping for all β coefficients. This relationship accounted for a larger proportion of the variance in the Large (R^2= 0.285) and Small (R^2= 0.232) groups than the IDM (R^2= 0.047) and was not statistically significant in the Preterm and Other groups (Fig 6.7). There were no significant interactions between OKR threshold and risk factor for the EF Total score.

Table 6.4: Associations between measures of executive function and optokinetic reflex threshold

EF Measure	Score	R^2	β	Lower 95% CI	Upper 95% CI	P value
Assessed EF						
	Snack Delay	0.014	-0.019	-0.037	-0.002	**0.026**
	Fruit Stroop	0.014	-0.017	-0.032	-0.002	**0.025**
	Ducks	0.030	-0.030	-0.048	-0.011	**0.001**
	MSML	0.004	-0.006	-0.019	0.006	0.319
	EF Total	0.051	-0.098	-0.146	-0.049	**0.001**
BRIEF-P						
	Inhibit	0.000	0.009	-0.070	0.088	0.824
	Shift	0.005	0.052	-0.022	0.127	0.170
	Emotional Control	0.002	0.035	-0.037	0.108	0.342
	Working Memory	0.001	0.030	-0.118	0.057	0.495
	Plan/Organise	0.002	-0.041	-0.124	0.042	0.335
	Inhibitory Self-Control Index	0.001	0.021	-0.055	0.098	0.578
	Flexibility Index	0.005	0.050	-0.025	0.125	0.194
	Emergent Metacognition	0.002	-0.036	-0.125	0.052	0.418
	Global Executive Composite	0.000	-0.008	-0.076	0.092	0.855

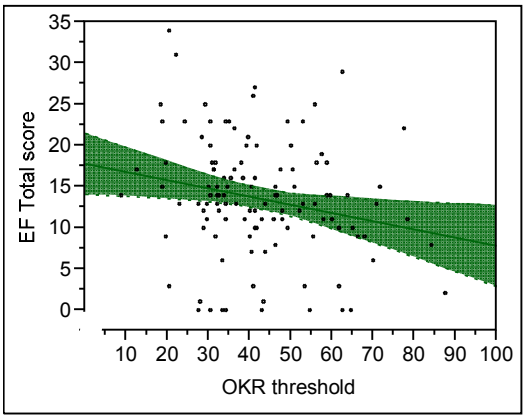
Figure 6.7: Assessed EF Total score and optokinetic reflex threshold for cohort and each risk group

Cohort



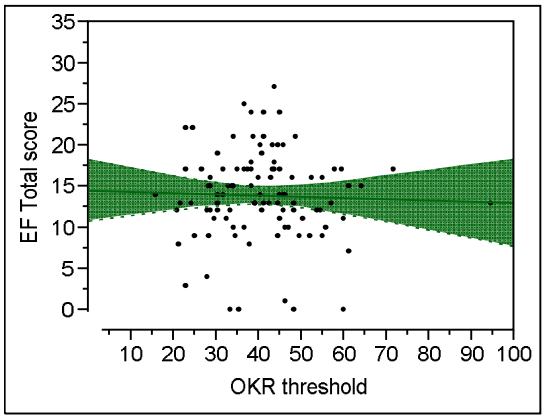
R^2=0.051; β =-0.098; [-0.146, -0.049]; **p<.001**

IDM



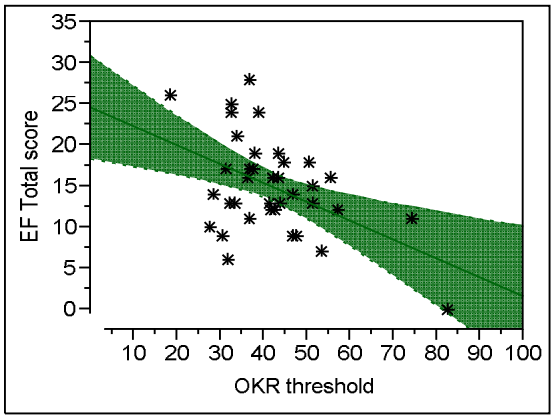
R^2=0.047; β = -0.100; [-0.183, -0.017]; **p=0.019**

Preterm



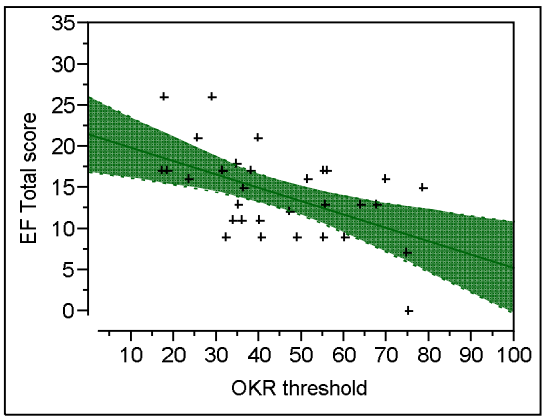
R^2=0.001; β = -0.015; [-0.102, 0.072]; p=0.734

Small



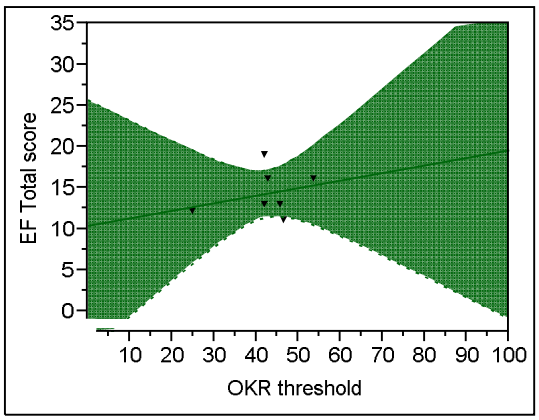
R^2=0.232; β = -0.230; [-0.373, -0.086]; **p=0.003**

Large



R^2=0.285; β = -0.162; [-0.258, -0.066]; **p=0.002**

Other



R^2=0.082; β = 0.092; [-0.262, 0.446]; p=0.533

Data are: R^2; β [95% confidence intervals]; p for interaction between EF Total score and OKR threshold.

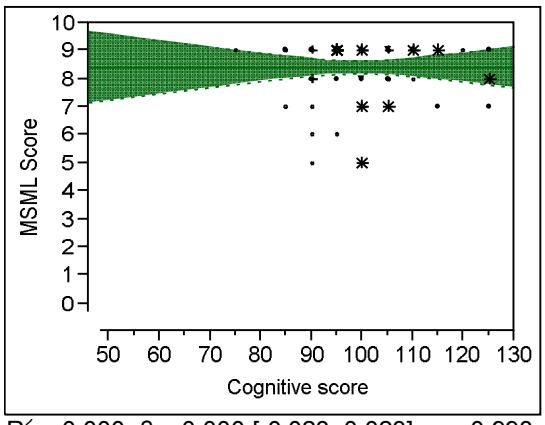
6.5. The influence of socioeconomic status on associations between executive function and cognitive and language development

There were significant interactions between household income and developmental scores for two measures of EF. Firstly, significant relationships between the Multisearch Multilocation task score, a measure of working memory, and Bayley III Cognitive ($p = 0.007$), Language ($p = 0.002$) and Motor scores ($p<0.001$) were seen only in the low income group (Fig 6.6 and for motor scores for the low income group $R^2 = 0.110$, $\beta = 0.073$, $p = 0.002$, data not shown).

Secondly, significant relationships between the BRIEF-P Shift scale, a measure of cognitive and behavioural flexibility and cognitive ($p = 0.038$), language ($p = 0.039$), and motor scores ($p = 0.004$) were seen only in the low income group (Fig 6.7) and for motor scores for the low income group $R^2 = 0.125$, $\beta = -0.384$, $p = <0.001$, (data not shown).

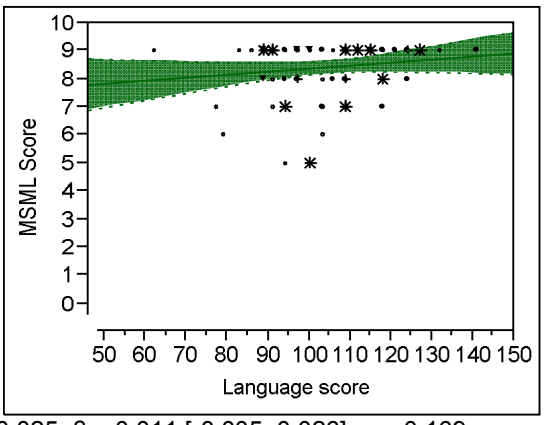
Figure 6.8: The interaction between household income and the relationship between Multisearch Multilocation (MSML) scores and Bayley III Cognitive (left) and Language scores (right)

High Income



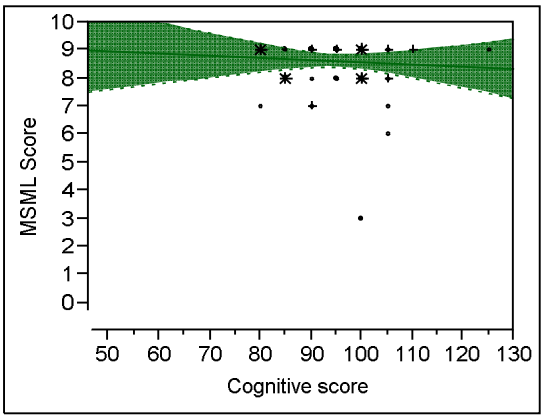
R^2 = 0.000, β = 0.000 [-0.023, 0.023], p = 0.998

High Income



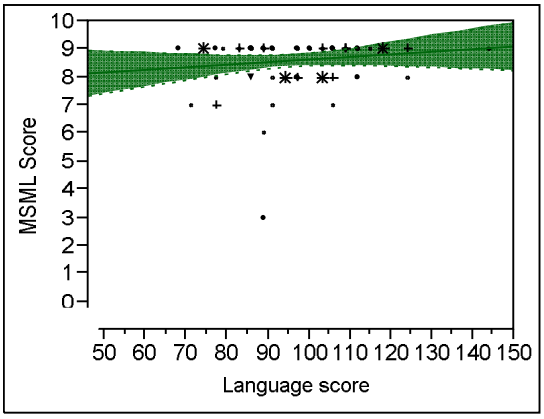
R^2 = 0.025, β = 0.011 [-0.005, 0.026], p = 0.169

Medium Income



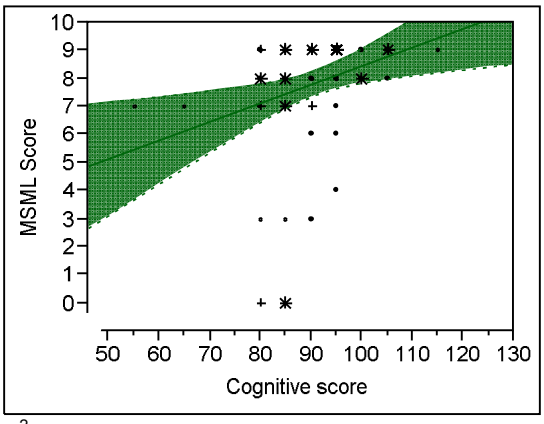
R^2 = 0.004, β = -0.008 [-0.038, 0.220], p = 0.596

Medium Income



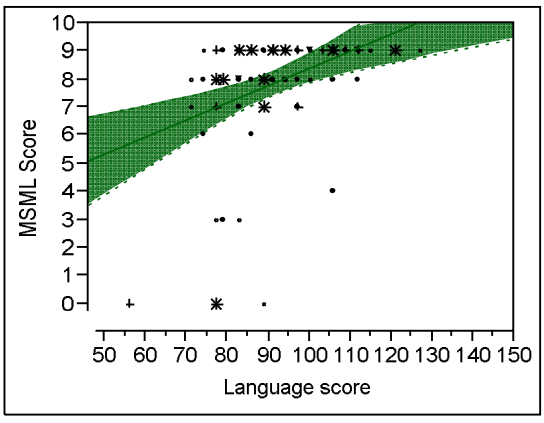
R^2 = 0.020, β = 0.009 [-0.006, 0.025], p = 0.241

Low Income



R^2 = 0.086, β = 0.066 [0.018, 0.115], **p = 0.008**

Low Income

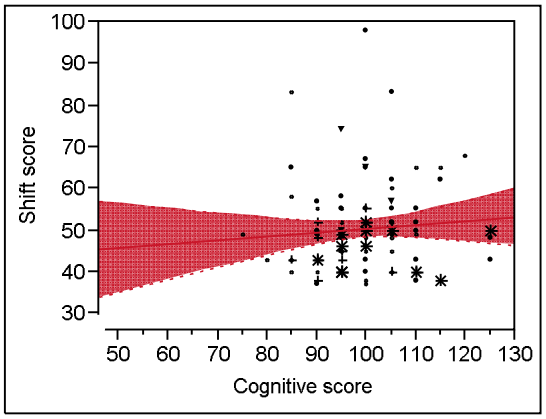


R^2 = 0.142, β = 0.061 [0.028, 0.095], **p < 0.001**

Data are R^2; β [95% confidence intervals]; p= 0.007 for interaction between SES and the relationship between MSML and cognitive scores and p = 0.002 for interaction between SES and the relationship between MSML and language scores.

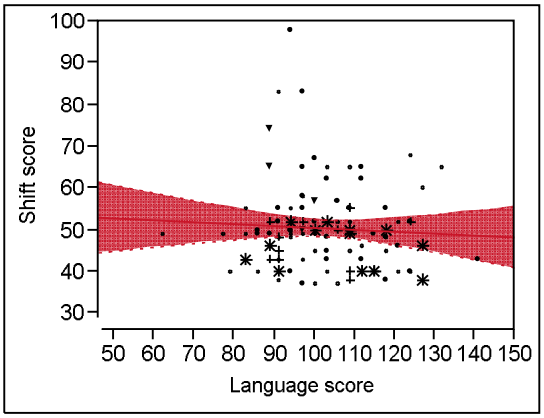
Figure 6.9: The interaction between household income and the relationship between BRIEF-P Shift scale scores and Bayley III cognitive (left) and language scores (right)

High Income



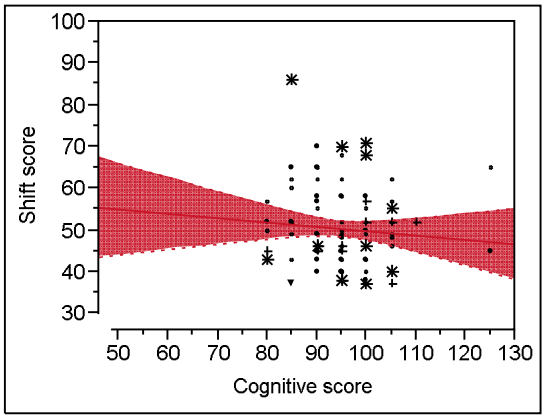
R^2 = 0.007, β = 0.092 [-0.120, 0.305], p = 0.392

High Income



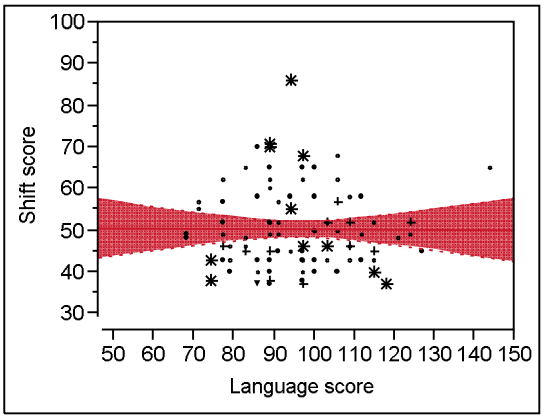
R^2 = 0.004, β = -0.046 [-0.192, 0.100], p = 0.535

Medium Income



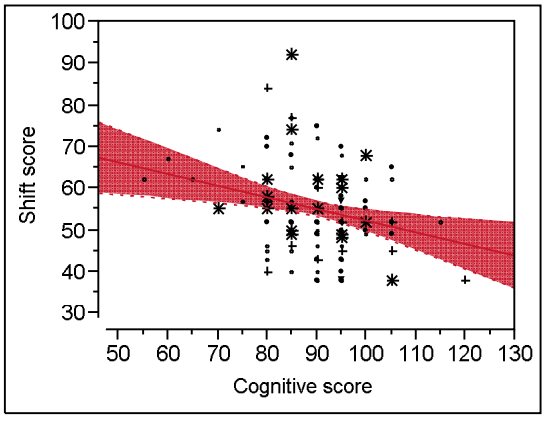
R^2 = 0.008, β = -0.104 [-0.343, 0.135], p = 0.389

Medium Income



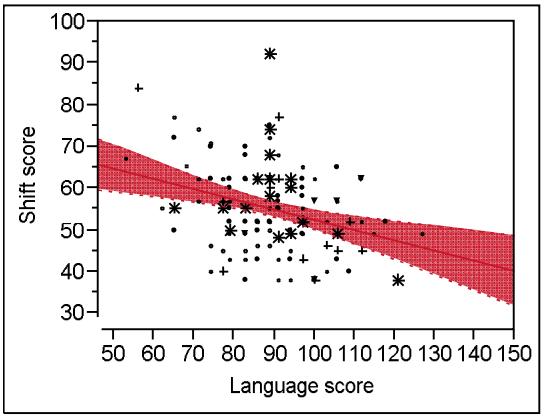
R^2 = 0.000, β = -0.003 [-0.139, 0.132], p = 0.962

Low income



R^2 = 0.067, β = -0.280 [-0.470, -0.090], **p = 0.004**

Low income



R^2 = 0.097, β = -0.245 [-0.381, -0.110], **p < 0.001**

Data are $R^{2;}$ β [95% confidence intervals]; p= 0.0.38 for interaction between SES and the relationship between MSML and cognitive scores and p = 0.039 for interaction between SES and the relationship between Shift and language scores.

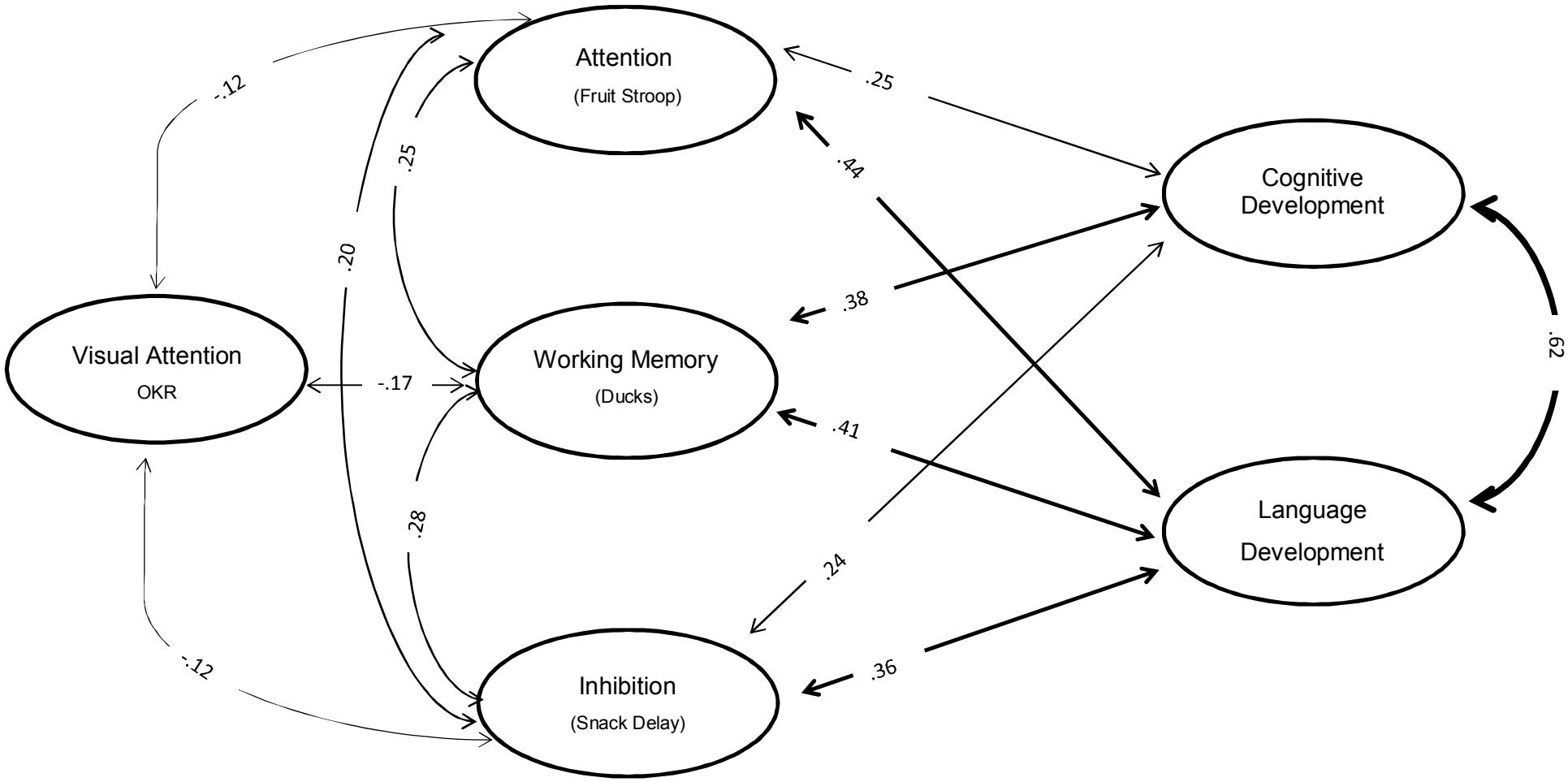
6.6. A summary schema integrating EF, cognitive and language development and optokinetic reflex

We reported in Chapter 5 that scores of three EF tasks (Snack Delay, Fruit Stroop, Ducks) were moderately correlated with each other, and in this chapter that there were significant associations between EF and other developmental domains, including cognitive and language, and also optokinetic reflex, which is known to be associated with attention. These relationships are now presented as a proposed schema of neuropsychological development at 2 years of age.

The strongest association was between cognitive and language development (r = 0.62), with the correlation between language and EF stronger than the correlation between cognition and EF (r = 0.44 – 0.36 vs r = 0.38 – 0.24). The EF task most strongly correlated with cognitive development was the working memory task (Ducks, r = 0.38), although this task and the attention/inhibition task were similarly correlated with Language development (Ducks, r = 0.41; Fruit Stroop, r = 0.44).

The three EF tasks were moderately correlated with each other (r = 0.20 – 0.28) and with OKR reflex (r = -0.12 – -0.17).

Figure 6.10: Summary schema of neuropsychological development showing associations between cognitive and language development, three assessed executive functions and optokinetic reflex



Data are *r* (Pearson correlations)

6.7. Discussion

The data presented in this chapter supported our hypothesis that EF development is significantly associated with development in other domains including cognitive, language, and motor and global motion coherence. However, there were differences in strength of association between EF and developmental domains for different risk groups, with a greater variation in EF explained by cognitive, language, motor and OKR scores for children born in Large and Small primary risk groups than for children from other groups.

We found that all assessed EF and BRIEF-P scores were associated with cognitive development. No evaluations of correlations between any versions of the Bayley assessment and EF have been found in the literature. However, measures of EF at 5 years have been reported to be positively correlated with IQ as measured on the Wechsler Preschool and Primary Scale of Intelligence, revised edition (WPPSI-R) (Wechsler, 1989) and in early adulthood with IQ measured on the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1997) (Böhm, Smedler, & Forssberg, 2004; Friedman et al., 2006). Between 28 and 42 months Bayley III language and cognitive scores correlate highly with scores of the Wechsler Preschool and Primary Scale of Intelligence (3rd edition) (WPPSI-III) (Wechsler, 2002), so although the Bayley III does not purport to be a measure of general intellectual ability as measured and reported at older ages as an IQ score, the language and cognitive scales appear to measure similar abilities (Bayley, 2006).

All assessed EF scores and BRIEF-P scores were also associated with language development; with language development explaining more variance in EF Total and task scores than did cognitive development. In the preschool years language development underlies much cognitive development, and has been shown to be an important mediator of cognitive outcome in children from low SES families (Noble et al., 2007; Noble et al., 2005). Verbal ability was a significant predictor of EF development for preschoolers enrolled in the United States Head Start programme, particularly in the area of inhibitory control and self-regulation (Fuhs & Day, 2011) and improved working memory, inhibitory control, and attention shifting was identified in preschoolers enrolled in a kindergarten program of mathematics, language and literacy coaching (Weiland & Yoshikawa, 2013). BRIEF-P scores for Emergent Metacognition and Flexibility indexes were correlated with language ability for preschool children with specific language impairment (Wittke et al., 2013). In adulthood verbal fluency is associated with executive function and is commonly used as an EF assessment measure (Woods et al., 2005). Baron (2009) found poorer verbal fluency at 3 years for late preterm children who required NICU admission, in comparison to term-born control children, leading her to suggest that verbal fluency may make a useful early predictor of later executive dysfunction. Our results appear to be consistent with these previous findings regarding the importance of language, with 31.8% of the variation in EF Total score explained by Bayley III Language score in our cohort, and language development associated with all EF scores.

Motor development was only weakly associated with EF and, again, assessed EF was more strongly associated than parent report. The assessed EF tasks all had an element of physical manipulation as part of the assessment. However, in addition to this obvious link these results appear to support the view that at 2 years development involves coherent and overlapping neural networks (Herschkowitz, 2000; Jung & Haier, 2007; Mesulam, 1990).

OKR threshold, an indication of the intactness of the vision-related dorsal stream, is related to attention (Braddick et al., 2003; Yu et al., 2013). Disruption in dorsal stream function, as identified from increased global motion coherence threshold, has been reported in children with disabilities such as Williams' and Down syndrome and those born very preterm and very low birth weight (Braddick et al., 2003, 2011; MacKay et al., 2005). This increased likelihood of disruption in some populations has been referred to as 'dorsal stream vulnerability' (Braddick et al., 2003). Our data showed that assessed EF but not parent report was related to OKR threshold. There was no significant relationship between EF Total score and OKR threshold for our preterm group, which had a mean gestational age of 36.1 (± 0.6) weeks, in contrast to the very preterm group reported by MacKay (2005) which had a gestational age of 29 (± 1.8) weeks. However, there was a significant relationship between EF Total score and OKR threshold for the Small group even though the mean birth weight for this group (2310g ± 226) was heavier than the group reported by MacKay (2005)(1198g ±245).

Our data support those reported elsewhere that dorsal stream function is associated with measures of attention and inhibitory control in children as young as three (Janette Atkinson et al., 2003). We found that global motion perception was associated with cognitive flexibility and even more strongly with working memory; apparently the first report of an association between global motion processing and EF abilities other than attention and inhibition. In addition, our results are consistent with those which include attention and attentional control as a core EF (P. J. Anderson, 2002), rather than an aspect of inhibition (Diamond, 2013).

Assessing 2 year olds is not easy. However, because the random dot kinetogram using OKR assessment does not require a behavioural response and is readily engaged with by 2 year olds, it can be successfully used in young children (Yu et al., 2013) to obtain data which could prove to be useful in early neuropsychological screening. Because OKR threshold was significantly associated with assessed EF, it could be particularly valuable in the assessment of at-risk populations where early intervention may be warranted. These data also support previous calls for early assessment to include areas of subtle deficit which are associated with later academic underachievement (P. J. Anderson et al., 2004; Aylward, 2002a; Baron et al., 2009).

General intelligence (*g*) is typically thought to consist of two interrelated aspects: fluid and crystallised intelligence, where fluid intelligence includes reasoning and problem solving and crystallised intelligence is knowledge acquired via learning and exercising fluid intelligence (M. Anderson, 2008; Cattell, 1963). The EF model presented by Diamond (2013) and previously reported (M. Anderson, 2008) defines fluid intelligence as synonymous with the reasoning and problem-solving aspects of EF, and relying heavily on working memory for development. Our results appear to conform to this model

as the Ducks assessment, measuring cognitive flexibility and working memory, was the EF task most strongly related to cognitive development domains, although Fruit Stroop was also strongly related to language. BRIEF-P Working Memory and Emergent Metacognition scores were also the most strongly associated with cognitive, language and motor development scores, with Inhibit scale and Inhibitory Self Control index having scores with the weakest association. Inhibit and Inhibitory Self Control scores were also weakly related to Bayley III language scores, with Emotional Control the least related. These results conform to Anderson's (1992) model of 'minimal cognitive architecture' which includes perception of three dimensional space and inhibition as two of a range of dedicated information-processing modules that underlie EFs and contribute to knowledge acquisition and intelligence. Hence, our results are in line with current, albeit limited in scope and number, theoretical descriptions of the relationship between EF and intelligence.

The summary schema presented here expands on these models, describing relationships between the three main EFs, cognitive and language scores and OKR threshold, and showing that the strongest relationships are with Working Memory. Another feature of the schema is the relationship between language and EF, which is expected at 2 years of age as development progresses across multiple areas in a so-called "cognitive developmental cascade" (Fry & Hale, 2000). There appear to be no other reports that present correlations between these developmental domains at 2 years, possibly due to the fact that only the most recent version of the Bayley III (Bayley, 2006), the most commonly used preschool developmental assessment, has included separate cognitive and language scores.

The associations between developmental and EF scores for children in our cohort suggest that children with greater cognitive and language development are also likely to have better working memory skills, and to a lesser extent better inhibitory skills than children with poorer developmental scores. Because EF, and working memory in particular, is associated with later school outcomes in maths and reading, these results appear to be an early glimpse of one of the components contributing to the 'Matthew Effect' (Stanovich, 1986). This term refers to the Bible passage in the book of Matthew that describes the rich getting richer and the poor getting poorer and was coined to describe the advantageous school pathway experienced by able children, for whom success builds on success, in comparison to the less able.

Despite the association between cognitive and EF development there was one group of children who did not appear to be developing as expected. This group of 11 (2.7%) children had high cognitive scores and poor EF scores. This group may be an early reflection of the developmental trajectory that results in learning disabilities including dyslexia and Attention Deficit Hyperactivity Disorder (ADHD) (Ferrer, Shaywitz, Holahan, Marchione, & Shaywitz, 2010; Gooch, Snowling, & Hulme, 2011; Hughes & Graham, 2008; Menghini, Finzi, Carlesimo, & Vicari, 2011). The definition of learning disability depends on a mismatch between intelligence and specific abilities; hence these disabilities are only defined in children of above average intelligence (M. Anderson, 2008). The group we identified may be children who have delayed EF development in comparison to the rest of the cohort or, alternatively, these results may be an early indication of executive dysfunction. Re-assessment of

these children will be important in establishing an aetiology of this divergent development and if assessment is early it makes EF training possible prior to beginning school. Early intervention is successful and important in at risk groups of children, particularly for working memory training, as it underlies early academic and school success (Diamond et al., 2007; Diamond & Lee, 2011). Hence, there is an emerging international trend for working memory research and training intervention (P. C. Entwistle & Shinaver, 2014; Pascoe et al., 2013).

Associations between EF and intelligence in adults have been shown to be stronger in populations with compromised frontal lobe function such as clinical populations and the elderly (Friedman et al., 2006; Salthouse, Atkinson, & Berish, 2003). It has been suggested that general compromised frontal lobe function, resulting from a reduction in neurons, neurotransmitters and myelination, affects all EFs generally, resulting in higher correlations between EFs and thus leading to a higher correlation with intelligence (Rabbitt, Lowe, & Shilling, 2001; Salthouse et al., 2003). Therefore, it is possible that at the other end of life when neural development is still occurring that disruptions to this development may also be reflected in variations in associations between EF and intelligence or cognitive development. We hypothesised that primary risk factor would alter the relationship between EF and developmental domains, although there appear to be no reported results of associations between EF and domains other than intelligence with which to compare our results. Our data showed a difference between risk groups in the amount of variance in EF score explained by developmental scores, with the Large and Small groups consistently having the highest R^2 results. The slope and direction of the relationships between EF and each developmental domain did not differ between risk groups. However, this relationship was only consistently significant for the Large and Small groups. The Large group achieved higher Bayley III scores, assessed EF success and lower BRIEF-P scores than other groups (see Chapters 4 & 5). That is to say, they appeared to approximate 'typical' development on standardised assessments. However, the opposite results were found for the Small group who achieved the poorest results, except for the BRIEF-P where the Other group of 12 children performed marginally more poorly. These differences in associations between developmental domains and EF suggest that development of EF and cognitive, language, motor and dorsal-stream related vision overlap at 2 years but develop independently. These results for the different risk groups also suggest that the neonatal risks may affect developmental pathways in different ways.

The detrimental effects of low SES on child development, including cognitive and language development have been previously documented (American Psychological Association task force on socioeconomic status, 2007; Bradley & Corwyn, 2002; Brooks-Gunn & Duncan, 1997; B. Hart & Risley, 1995). More recently the impact of low SES on EF (Farah, Hackman, & Meaney, 2010), including working memory (Lipina et al., 2005), cognitive control (Farah et al., 2006; Noble et al., 2007) and verbal fluency (Ardila et al., 2005) have also been reported. In addition, development of the prefrontal cortex in infancy has been associated with quality of environment and SES (Als et al., 2004), and MRI studies have shown that cortical thickness in frontal brain regions is associated with parent education, providing an insight into how SES may alter cognitive development (Lawson et al., 2013). Interactions have also been found between SES and other aspects of development.

Interactions between SES and genes have been reported to alter cognitive development in children (Turkheimer, Haley, Waldron, D'Onofrio, & Gottesman, 2003), including development between 10 months and 2 years of age (Tucker-Drob et al., 2011), and to separately influence school readiness and mathematics ability in 4-year-olds (Rhemtulla & Tucker-Drob, 2012), prompting these authors to propose a model of "recurring disadvantage" to describe the repeated effects of gene - SES interaction on cognitive development. These results appear to provide evidence in support of Bronfenbrenner and Ceci's (1994) Bioecological model which emphasises the importance of proximal environmental effects and demonstrates that inherited genetic potential contributes significantly to the development of children from high and medium SES families, but that SES and environment constrain this influence in children from low SES families (Rhemtulla & Tucker-Drob, 2012; Tucker-Drob et al., 2011; Turkheimer et al., 2003).

Our results showed significant interactions between household income and the relationship between cognitive and language scores and an assessed measure of working memory (Multisearch Multilocation) and a parent-reported scale of cognitive and behavioural flexibility (Shift scale), suggesting a different developmental pathway for working memory and cognitive flexibility in children from low SES households than for children from medium and high SES households. Previous reports suggest that SES constrains cognitive, language and EF development differentially for children from low SES families (Farah et al., 2006; Noble et al., 2007; Raizada & Kishiyama, 2010). Our results suggest that, because of the relationship between cognitive and language development and EF development, this SES constraint can then lead to impairment in the development of EF as well. The long term consequence of this for children from low SES families is likely to be that the development of cognition, language and EF continue on a different trajectory than for children from middle and high SES families, in another example of recurrent disadvantage. There appear to be no other reports identifying an interaction between SES and the relationships between both cognitive and language development on the one hand and EF development on the other.

Cognitive, language, and motor development, along with global motion coherence perception are all associated with EF development, with language development the strongest predictor at 2 years of age. However, EF appears to develop separately to these other developmental domains and to be affected by both perinatal risk factors and SES.

Chapter 7. Neonatal hypoglycaemia in the CHYLD Study cohort

7.1. Neonatal hypoglycaemia in the CHYLD Study cohort

Neonatal hypoglycaemia is associated with poor developmental outcome, including cerebral palsy, epilepsy and developmental delay, with a blood glucose concentration of <2.6 mmol/L having been proposed as a definition of neonatal hypoglycaemia (Koh, Aynsley-Green, et al., 1988; Lucas et al., 1988). However, this definition is based on very limited evidence (Cornblath et al., 2000; W. W. Hay, Jr. et al., 2009) and there are no reports of the developmental outcomes of children who were treated for neonatal hypoglycaemia at this blood glucose concentration. We hypothesised that children in the CHYLD cohort who experienced neonatal hypoglycaemia, defined as a blood glucose concentration <2.6mmol/L within the first 48 hours after birth, would have poorer developmental outcomes at 2 years than those who did not experience neonatal hypoglycaemia.

7.1.1. Hypoglycaemia, neonatal measurements and breastfeeding

Approximately half of the CHYLD cohort (213; 53.7%) were identified as having experienced neonatal hypoglycaemia, with a greater proportion of girls (59.9%) than boys (46.2%) identified as having experienced neonatal hypoglycaemia ($p<0.006$) (Table 7.1). There was no significant difference in the percentage of babies in the different risk groups who were identified as having had hypoglycaemia and no significant interaction between gender and risk group. There were no significant differences in birth weight, length, head circumference or gestational age between babies who were and were not identified as having had neonatal hypoglycaemia (Table 7.1). None of the babies in our cohort displayed recognised symptoms of hypoglycaemia.

Within the group of babies identified as having had neonatal hypoglycaemia the mean minimum blood glucose concentration was 2.08 (± 0.39) mmol/L, with 62 (15%) babies experiencing at least one recorded blood glucose concentration < 2.0 mmol/L. Recurrent hypoglycaemia, defined as more than one blood glucose concentration < 2.6 mmol/L was reported for 78 (19%) babies.

Data for the number of children who were or were not breastfed at any stage were available for 390 (96.5%) children and showed a high rate of breastfeeding in this cohort (92.8%). Amongst children who were ever breastfed 197 (54.4%) were reported to have experienced hypoglycaemia. However, amongst children who were never breastfed only 9 (32.1%) were reported to have experienced hypoglycaemia ($p = 0.030$).

Table 7.1: Neonatal data for babies who did and did not experience neonatal hypoglycaemia

	Neonatal hypoglycaemia	No hypoglycaemia	p
n =	213	191	
Girls	115 (54.0)	77 (40.3)	**0.006**
Boys	98 (46.0)	114 (59.7)	
Risk Groups			
IDM	80 (37.6)	81 (42.4)	0.083
Preterm	69 (32.4)	60 (31.4)	
Small	38 (17.8)	22 (11.5)	
Large	17 (8.0)	25 (13.1)	
Other	9 (4.2)	3 (1.6)	
Birth data			
Weight (g)	3100 (810)	3173 (882)	0.382
Length (cm)	51.1 (4.2)	51.8 (3.7)	0.372
Head circumference (cm)	34.0 (2.3)	34.0 (2.2)	0.991
Gestational age (weeks)	37.7 (1.6)	37.8 (1.7)	0.667
Breastfeeding			
n =	206	185	
Ever breastfed	197 (95.6)	165 (89.2)	**0.015**

Data are n (%) or mean (SD). IDM: Infant of a diabetic mother

7.1.2. Hypoglycaemia, ethnicity and indicators of socioeconomic status

There were no significant differences in ethnic distribution between babies who were and were not identified as having experienced neonatal hypoglycaemia (Table 7.2). However, there was a significant interaction between gender and ethnicity ($p = 0.043$) with Māori girls being identified with the highest rate (61.8%) and Pacifica girls the lowest rate (25.0%) of neonatal hypoglycaemia.

Babies who were and were not identified as having had neonatal hypoglycaemia had similar distributions of NZDep2006, household income, maternal education (Table 7.2) and paternal education (data not shown). They also had similar distributions of reported parental antenatal smoking, drinking or drug use (data not shown).

Table 7.2: Neonatal ethnicity and socioeconomic status data for children who did and did not experience neonatal hypoglycaemia

	Neonatal hypoglycaemia	No hypoglycaemia	p
Ethnicity			
n =	213	191	
NZ European	106 (49.8)	93 (48.7)	0.638
Māori	78 (36.6)	65 (34.0)	
Pacifica	8 (3.8)	11 (5.8)	
Asian	12 (5.6)	12 (6.3)	
Other	1 (0.5)	4 (2.1)	
Unknown	8 (3.8)	6 (3.1)	
Birth NZDep2006			
n =	212	191	
High	117 (55.2)	104 (54.5)	0.867
Medium	61 (28.8)	59 (30.9)	
Low	34 (16.0)	28 (14.7)	
Household income			
n =	175	152	
High	62 (35.4)	59 (38.8)	0.816
Medium	54 (30.9)	45 (29.6)	
Low	59 (33.7)	48 (31.6)	
Maternal education			
n =	198	179	
High	64 (32.3)	67 (37.4)	0.321
Medium	74 (37.4)	54 (30.2)	
Low	60 (30.3)	58 (32.4)	

Data are n (%). NZDep2006: High: deciles 10 – 7, Medium: 6 – 4, Low: 3-1; Household Income High: ≥$70,001, Medium: $40,001 - $70,000, Low: ≤$40,000; Maternal Education High: University, Medium: Post-secondary, Low: up to 5 years of secondary schooling

7.1.3. Multiple risk factors

It was possible for babies to be identified as having more than one risk factor for hypoglycaemia at the time of birth (Fig. 7.1) with 275 (68.1%) having one, 116 (28.7%) having two, and 13 (3.2%) having three risk factors. The proportion of babies identified as having neonatal hypoglycaemia was similar in each of these groups (54.9%, 45.7% and 69.2% respectively, $p = 0.119$) (Table 7.3).

The IDM group comprised babies whose mothers had gestational, Type 1 and Type 2 diabetes. More children whose mother had gestational diabetes had just one risk factor than those whose mothers had Type 1 or Type 2 diabetes ($p<0.0001$). However, the incidence of neonatal hypoglycaemia was similar in babies whose mothers had different types of diabetes (Table 7.3). In the Preterm group a higher percentage (62.9%) of the babies who had one risk factor were identified with neonatal hypoglycaemia than those who had two risk factors (44.8%) ($p = 0.039$).

Figure 7.1: Venn diagram showing the primary risk factors and numbers of children in each group with single and multiple risk factors

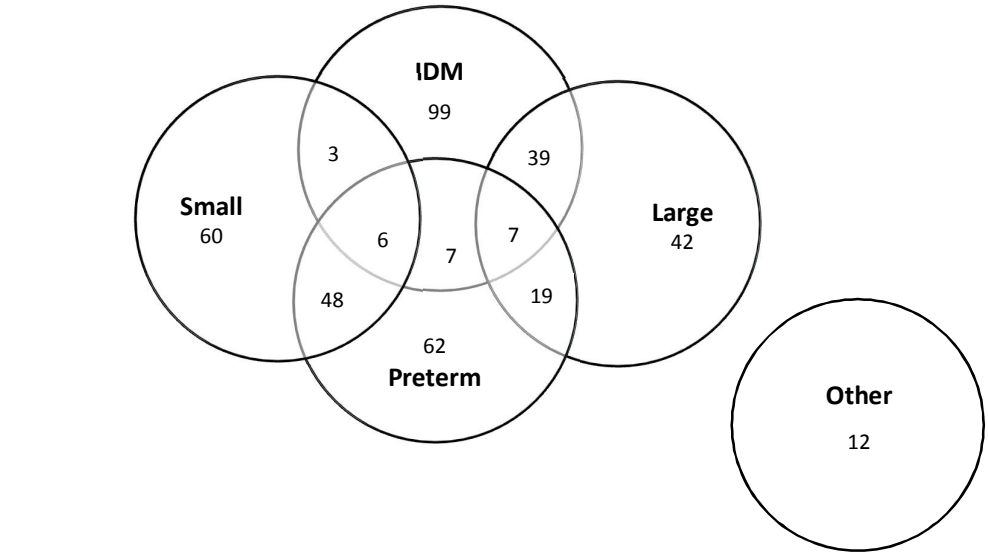


Table 7.3: Number and percentage of babies identified as having neonatal hypoglycaemia in the CHYLD cohort and each primary risk group and according to the different numbers of risk factors

Risk group		Cohort	1 risk	2 risks	3 risks	p
		213/404 (52.7)	151/275 (54.9)	53/116 (45.7)	9/13 (69.2)	0.119
IDM		80/161 (49.7)	48/99 (48.5)	23/49 (46.9)	9/13 (69.2)	0.334
	Gestational	59/130 (45.4)	38/85 (44.7)	17/39 (43.6)	4/6 (66.7)	0.559
	Type 1	11/14 (78.6)	4/6 (66.7)	4/5 (80.0)	3/3 (100.0)	0.515
	Type 2	10/17 (58.8)	6/8 (75.0)	2/5 (40.0)	2/4 (50.0)	0.422
Preterm		69/129 (53.5)	39/62 (62.9)	30/67 (44.8)	0 (0) (0, 0)	**0.039**
Small		38/60 (63.3)	38/60 (63.3)	0	0	
Large		17/42 (40.5)	17/42 (40.5)	0	0	
Other		9/12 (75.0)	9/12 (75.0)	0	0	

Data are: n with hypoglycaemia/N in group (%); IDM: Infant of a Diabetic Mother. P value is for comparison between groups with 1, 2 and 3 risk factors

7.2. Hypoglycaemia and Bayley III developmental scores

Bayley III data were available for 401 children (99.3%). The Social-Emotional score was 3.4 points higher in children who had experienced hypoglycaemia than those who had not (p = 0.029) (Table 7.4). However, after adjusting for SES this difference was no longer significant (3.1 [-6.5, 0.3]). There were no other differences in Bayley III scores between groups, and no significant interactions between gender or risk factor and hypoglycaemia for Bayley III scores.

Bayley III scores did not differ significantly with the number of risk factors for hypoglycaemia.

Table 7.4: Comparison of Bayley III scores for children who did and did not experience hypoglycaemia in the first 48 hours after birth

	Neonatal hypoglycaemia	**No hypoglycaemia**	**p**
n =	213	191	
Cognitive	93.9 (9.9)	93.2 (10.6)	0.498
Language	95.5 (13.2)	93.9 (15.2)	0.246
Receptive Communication	9.4 (2.5)	9.2 (2.9)	0.420
Expressive Communication	9.0 (2.5)	8.7 (2.6)	0.182
Motor	98.6 (9.3)	98.8 (9.7)	0.779
Fine Motor	10.0 (2.1)	10.1 (2.1)	0.901
Gross Motor	9.4 (1.9)	9.5 (1.8)	0.780
Social-Emotional	104.2(15.1)	100.8 (14.9)	**0.029**
Adaptive Behaviour	99.7 (14.1)	98.3 (15.8)	0.351

Data are Mean (SD).

7.3. Hypoglycaemia, assessed EF and BRIEF-P results

There were no significant differences in success rates for assessed EF for Snack Delay, Fruit Stroop, Ducks or Multisearch Multilocation, or EF Total score between children who were and were not identified as having had neonatal hypoglycaemia (Table7.5). There were also no significant differences between BRIEF-P scale and index scores for children who were or were not identified as having had neonatal hypoglycaemia. There were no significant interactions between either gender, or risk group, and hypoglycaemic status for any assessed EF outcomes or BRIEF-P scale or index scores.

Scores for assessed EF and BRIEF-P did not differ significantly with the number of risk factors for hypoglycaemia (data not shown).

Table 7.5: Comparison of assessed EF success rates and BRIEF-P scores for children who did and did not experience neonatal hypoglycaemia

		Neonatal hypoglycaemia	No hypoglycaemia	p
Assessed EF				
n =		193	175	
Snack Delay	Failure at 0 secs	118 (61.1)	110 (63.9)	0.844
	Success at 5 secs	38 (19.7)	34 (19.4)	
	Success 15 secs	18 (9.3)	12 (6.9)	
	Success ≥ 30 secs	19 (9.8)	19 (10.9)	
Fruit Stroop	0 correct	107 (55.4)	99 (56.6)	0.521
	1 correct	58 (30.1)	46 (26.3)	
	2 correct	20 (10.4)	17 (9.7)	
	3 correct	8 (4.2)	13 (7.4)	
Ducks	< 5 categorised	161 (83.4)	154 (88.0)	0.207
	5-6 categorised	12 (6.2)	10 (5.7)	
	1 -2 reverse	15 (7.8)	5 (2.9)	
	≥3 Reverse	5 (2.6)	6 (3.4)	
MSML	Pre-switch success	165 (85.5)	147 (84.0)	0.691
	Post-switch success	122 (63.2)	94 (53.7)	0.065
EF Total score		14.1 (5.9)	13.8 (6.3)	0.677
BRIEF-P				
n =		211	186	
	Inhibit	56.4 (10.7)	56.6 (10.9)	0.699
	Shift	52.5 (10.0)	52.5 (10.2)	0.998
	Emotional Control	52.0 (10.1)	51.7 (9.5)	0.881
	Working Memory	61.1 (11.7)	61.8 (12.3)	0.468
	Plan/Organise	55.4 (10.6)	55.3 (12.0)	0.971
	ISCI	55.0 (10.3)	55.0 (10.5)	0.875
	FI	52.7 (10.2)	52.4 (10.3)	0.872
	EMI	59.5 (11.6)	59.9 (12.6)	0.657
	GEC	57.5 (11.0)	57.6 (12.0)	0.789

Data are n (%) or mean (SD). MSML: Multisearch Multilocation; ISCI: Inhibitory Self Control Index; FI: Flexibility Index; EMI: Emergent Metacognition Index; GEC: Global Executive Composite

7.4. Discussion

Children who experience severe hypoglycaemia have a higher risk of morbidity, mortality and brain injury than those who do not (Burns et al., 2008; Hartmann & Jaudon, 1937; Kinnala et al., 2000). However, controversy continues to surround the definition of neonatal hypoglycaemia, and whether a single 'safe level' should be the standard for all babies regardless of risk (Boluyt et al., 2006; Cornblath et al., 2000; W. W. Hay, Jr. et al., 2009). Previously, it has been reported that Bayley developmental scores were lower for very preterm children who had blood glucose concentrations less than 2.6 mmol/L on five or more days, and separately, that normal neural function was maintained in babies whose blood glucose remained above this level (Koh, Aynsley-Green, et al., 1988; Lucas et al., 1988). These two studies of Lucas and Koh were seminal in establishing the prevailing definition of neonatal hypoglycaemia as a blood glucose concentration less than 2.6 mmol/L (Marlow, 2013).

Our hypothesis, that children in the CHYLD cohort who experienced neonatal hypoglycaemia would have poorer developmental outcomes at 2 years than those who did not, was not supported by the data, as there were no significant differences in Bayley III, assessed EF or BRIEF-P scores between children who did and those who did not experience hypoglycaemia in the first 48 hours after birth. Similar results have been found elsewhere, with a recent attempt to repeat the study of Lucas et al (1988) showing that at 15 years WISC-III IQ, reading, mathematics and behaviour scores did not differ between the children who experienced repeated neonatal hypoglycaemia and a normoglycaemic control group (Tin, Brunskill, Kelly, & Fritz, 2012).

We found no difference in likelihood of hypoglycaemia or developmental outcomes between different neonatal risk groups. Similar results have been reported elsewhere with large and small size found to not be a reliable indicator of risk of hypoglycaemia (T. S. Johnson et al., 2006; Kernaghan, Ola, Fraser, Farrell, & Owen, 2007). Furthermore, no significant IQ or behavioural differences were found between 4 year old term-born large for gestational age (LGA) children who did and those who did not experience neonatal hypoglycaemia (Brand et al., 2005). We found no association between the number of risk factors and developmental outcome for any risk group. More babies in the Preterm group who had one risk factor were identified with hypoglycaemia than those who had two risk factors. It is not clear why this should be the case, and it is possible that it is a chance finding due to large numbers of comparisons being undertaken (a type 1 error).

There are a number of possible reasons why our hypothesis was not supported. Firstly, because the children in the CHYLD cohort were all born at risk of neonatal hypoglycaemia they were monitored regularly and, if identified as having blood glucose less than 2.6 mmol/L, were treated according to the standard clinical guidelines. It is possible that regular screening and prompt treatment resulted in no evidence of poorer developmental outcome in those babies who were identified as being hypoglycaemic than those who were not. This would support the adoption of a blood glucose concentration of 2.6 mmol/L as a safe threshold for treatment.

A second possible reason we found no developmental differences between children who had and had not been identified as having hypoglycaemia is that while severity, frequency and duration of hypoglycaemia are all associated with neurodevelopmental outcome (Duvanel et al., 1999; Hawdon, 1999; Lucas et al., 1988; Montassir et al., 2009), none of the babies in our cohort suffered severe or prolonged, recurrent hypoglycaemia. Recurrent episodes of neonatal hypoglycaemia have been associated with poorer developmental outcome (Armentrout & Caple, 1999; Cornblath & Ichord, 2000), in particular for babies born small (Duvanel et al., 1999). It is possible that some instances of hypoglycaemia were not identified because of the timing of heel-prick blood glucose tests (D. L. Harris et al., 2010). Therefore, our data for frequency of hypoglycaemia may be an underestimate, but available data shows very few babies experienced recurrent hypoglycaemia. Longer duration of hypoglycaemia in neonates suffering from hyperinsulinaemic or persistent hypoglycaemia is associated with the highest rates of mortality, morbidity and poor developmental outcome (Cornblath & Ichord, 2000; Steinkrauss et al., 2005), with the length of time that a newborn can experience hypoglycaemia without experiencing developmental disadvantage not yet established. We do not currently have data for the duration of each hypoglycaemic event. However, the small numbers of babies who experienced recurrent hypoglycaemia in our cohort may be a result of timely intervention which may have prevented long-term adverse developmental outcomes.

A further possible reason that we found no differences between children who had and had not experienced neonatal hypoglycaemia may relate to the fact that babies in our cohort who experienced neonatal hypoglycaemia were asymptomatic. The adverse developmental effects of asymptomatic hypoglycaemia, if present, may be more subtle and less frequent than those identified for children with severe hypoglycaemia (Armentrout & Caple, 1999; Williams, 2005). However, uncertainty still surrounds the significance of asymptomatic hypoglycaemia (W. W. Hay, Jr. et al., 2009), with reports variously stating that it does not result in poorer outcome (Committee on Fetus and Newborn, 1993) and that similar proportions of babies were found to have neural dysfunction in the asymptomatic group of babies as the symptomatic group (Koh, Aynsley-Green, et al., 1988). In addition, changing approaches to management of hypoglycaemia mean that it is difficult to compare results between studies (D. L. Harris et al., 2009; R. Schwartz & Teramo, 2000). Elsewhere, increased rates of 'minimal brain dysfunction' were found in 8 year old children who experienced asymptomatic hypoglycaemia than in the normoglycaemic control group (Stenninger et al., 1998). These differences included a lower total development score and increased hyperactivity, impulsiveness and distractibility, all of which are now likely to be described as executive dysfunction. However, no studies of the neurodevelopmental sequelae of neonatal hypoglycaemia have included 2 year follow-up of EF measures so there is no similar research with which to compare our findings.

Another possible reason why we found no differences between the groups of children who had and had not experienced neonatal hypoglycaemia may be that at 2 years of age many areas of development, such as EF skills, are only beginning to emerge, and assessment measures for children of this age are still developing (S. M. Carlson, 2005; Diamond, 2013). It may be that children who experienced neonatal hypoglycaemia do have different developmental trajectories from those who did

not, but that, as with preterm infants, these differences will be more readily observable at older ages as outcomes worsen in comparison to typically developing children (Annaz, 2008; Aylward, 2002a). Long-term neurological dysfunction including poorer attention, perception and fine motor skills have been reported at 8 years for IDM who experienced neonatal hypoglycaemia, when compared to IDM without neonatal hypoglycaemia and non-IDM controls (Stenninger et al., 1998). Elsewhere 6 – 12 year old children who were born to mothers with Type 1 diabetes were found to have normal cognitive functioning but poorer working memory than control children (Temple et al., 2011). Therefore, developmental differences between children who were and were not identified as experiencing neonatal hypoglycaemia cannot be definitively ruled out as some of the important yet subtle, developmental differences may not be observable until these children are older (P. J. Anderson et al., 2004; Aylward, 2002a).

One further possible reason why our results do not show developmental differences between children who had and those who had not been identified with neonatal hypoglycaemia may be that with the numbers we recruited to follow-up and the numbers experiencing hypoglycaemia, we did not have the statistical power to detect small differences. However, retrospective power calculations indicated that a cohort of 404 children would give us 98% power to detect differences between groups of 3 points for Bayley scores, and differences smaller than this are unlikely to be of clinical significance.

The relationship between glucose concentration and developmental outcome appears to not be linear, with brain injury identified by MRI more predictive of neurodevelopmental outcomes at 18 months than either the severity or duration of the neonatal hypoglycaemia experienced (Burns et al., 2008). This suggests that factors other than glucose concentration alone may influence developmental outcome. It has also been proposed that alternative cerebral fuels, namely ketones from the oxidation of fatty acids derived from adipose stores and milk, and lactate may allow normal cerebral function in the presence of low glucose concentrations (Hawdon, 1999; Hawdon & Ward Platt, 1993). This suggests that developmental outcome of at risk babies may be associated with the total cerebral fuels available in the neonatal period rather than glucose alone. Assessment of all available cerebral fuels is thus, potentially, an important future investigation. However, the babies recruited to the BABIES study, 14 of whom were followed up in the CHYLD cohort, were found to have very low levels of non-glucose cerebral fuels that were unlikely to be metabolically significant (D. L. Harris et al., 2011).

Boys have been reported to be at greater risk than girls of experiencing neonatal hypoglycaemia after diabetic pregnancy (Bracero et al., 1996). However, in our cohort girls had a higher rate of hypoglycaemia than boys. As expected, girls in our cohort had lower birth weight than boys. However, birth weight alone does not show a simple association with hypoglycaemia (T. S. Johnson et al., 2006) so this is unlikely to explain the difference between our results and those reported elsewhere.

A higher percentage of children who were breastfed were identified as having had neonatal hypoglycaemia than of those who were formula fed. Elsewhere, breastfed newborn babies have been found to have lower blood glucose concentrations than formula fed babies, including one study

showing a mean blood glucose concentration for breast fed babies of 2.10 (±0.53) mmol/L, which is within the hypoglycaemic range as defined in our study (Deshpande & Ward Platt, 2005; Swenne, Ewald, Gustafsson, Sandberg, & Östenson, 1994). In the first 48 hours formula fed babies have a more reliable and plentiful supply of milk than those who are breastfed, since the amount of breast milk available initially is small (Eidelman, 2001). In addition, the amount of mother's milk taken at each feed is unknown whereas the amount of formula taken from a bottle is a known amount (T. S. Johnson, 2002) and mothers observing small bottle feeds may continue encouraging their babies to take more than breastfeeding mothers who do not have this information. Thus babies who were formula fed are likely to have had a higher caloric intake than breastfed babies, which may contribute to their lower incidence of neonatal hypoglycaemia. Indeed, formula feeding is common practice in managing new born babies identified with hypoglycaemia (Deshpande & Ward Platt, 2005; D. L. Harris et al., 2009).

The glucose concentration that defines neonatal hypoglycaemia remains uncertain. Our results may suggest that when 2.6 mmol/L was used as the threshold to trigger intervention this has prevented significant adverse developmental outcome in children who experienced neonatal hypoglycaemia. At 2 years of age risk factor does not appear to be significantly related to developmental outcome after neonatal hypoglycaemia. However, it is possible that differences will emerge when our cohort reaches school age because at that time a higher demand is placed on cognitive skills, and EF differences which are not recognisable until school age, begin to emerge (Aylward, 2002b; Doyle, Roberts, & Anderson, 2010).

Chapter 8. Conclusions

Neonatal hypoglycaemia is a common metabolic problem in newborn babies (Cornblath et al., 2000) and can result in white matter injury and long-term morbidities including cerebral palsy, epilepsy, developmental delay (Burns et al., 2008; Rozance & Hay, 2006) and even death (Aynsley-Green, 1996). The blood glucose concentration that defines neonatal hypoglycaemia remains uncertain (W. W. Hay, Jr. et al., 2009), although two studies in 1988 reported data indicating that maintaining blood glucose concentrations above 2.6 mmol/L in newborn babies was associated with better neuropsychological outcomes (Koh, Aynsley-Green, et al., 1988; Lucas et al., 1988). Despite this apparent support for establishing 2.6 mmol/L as the threshold for intervention in neonatal hypoglycaemia, uncertainty persists in practice (Bonacruz et al., 1996; D. L. Harris et al., 2009).

In 2008 the Eunice Kennedy Shriver National Institute of Child Health and Human Development convened a workshop with the key objective being to identify major knowledge gaps in the understanding of neonatal hypoglycaemia, and resulted in a list of 5 'general knowledge gaps' and 18 'research agenda' items (W. W. Hay, Jr. et al., 2009). They identified a need to establish an understanding of the link between neonatal blood glucose concentrations and neurodevelopmental outcomes, including the subtle long-term outcomes including EF, for children who experienced asymptomatic neonatal hypoglycaemia, and for babies from different perinatal risk groups. In our prospective cohort study we aimed to describe the neuropsychological outcomes of children born at risk of neonatal hypoglycaemia and to compare the outcomes for those who were and were not identified as having experienced neonatal hypoglycaemia, defined as a blood glucose concentration of 2.6 mmol/L.

8.1. Neonatal Hypoglycaemia

We found no differences in developmental outcome at 2 years of age between children who were and were not identified as having experienced neonatal hypoglycaemia. Our findings do not support previous reports which indicated that neonatal blood glucose concentrations below 2.6 mmol/L were associated with poorer neurodevelopmental outcome at 18 months in very low birth weight, very preterm babies (Lucas et al., 1988) and with neural dysfunction in newborn babies (Koh, Aynsley-Green, et al., 1988). Our cohort was neither as small nor as preterm as those reported by Lucas and colleagues (1988), and our assessments were not of acute neurological events as were Koh and colleagues (1988). However, these findings were the basis for the widespread practice of intervening clinically when blood glucose falls below 2.6 mmol/L (Cornblath et al., 2000; D. L. Harris et al., 2009) so our results raise questions as to why we did not find outcome differences between children who had and had not experienced neonatal hypoglycaemia.

One possibility is that the results we present here may indicate that the effective treatment of neonatal hypoglycaemia (D. L. Harris, Weston, Signal, Chase, & Harding, 2013) was also effective in

preventing adverse neuropsychological sequelae at 2 years of age. If this were the case, we would also expect to see no higher rate of adverse neurodevelopmental outcomes at any stage in the future amongst those children in our cohort who did experience neonatal hypoglycaemia than amongst those who did not. Therefore, ongoing monitoring of this cohort will be vital to confirm these findings.

A second possibility is that assessment at 2 years is too early to detect differences between those children who did and did not experience neonatal hypoglycaemia. EF is assessable in the preschool years (S. M. Carlson, 2005) and continues to develop throughout childhood with new skills building on those previously gained (P. J. Anderson, 2002; Diamond, 2013). Therefore, it is possible that subtle impairments resulting from neonatal hypoglycaemia may be more apparent at school age when further development of EF has occurred and there are greater demands placed on EF skills. Data supporting this possibility comes from follow-up of children who experienced neonatal hypoglycaemia and were found at school age to have subtle deficits in attention and motor skills (Stenninger et al., 1998). Furthermore, the Bayley III developmental assessment does not purport to be predictive of later IQ development (Bayley, 2006) and mild cognitive delays are difficult to detect with preschool assessments (S. R. Harris, 1994). The possibility that differences in IQ and complex EF may develop at school age between those children who did and did not experience neonatal hypoglycaemia can only be addressed with continued follow-up at school-age (Boluyt et al., 2006; Pildes et al., 1974). Moreover, longitudinal follow-up of this cohort will allow us to describe the trajectories of different aspects of development following neonatal hypoglycaemia, an important aspect of understanding the development of at-risk children (Annaz et al., 2008), especially if differences are found between children who did and did not experience neonatal hypoglycaemia.

Our results suggest that babies who were treated when their blood glucose concentrations fall below 2.6 mmol/L have no evidence of neurodevelopmental impairment at 2 years. However, our results do not establish this as the level of “pathologic hypoglycaemia” (W. W. Hay, Jr. et al., 2009) and it is possible that although this concentration appears to be safe it does not define the minimum safe level. Previously, a distinction was proposed for babies born at-risk but asymptomatic for neonatal hypoglycaemia between an operational blood glucose level of 2.5 mmol/L which provided “a significant margin of safety” (p1144) above a proposed operational threshold of 2.0 mmol/L (Cornblath et al., 2000). With our study appearing to demonstrate the safety of a treatment protocol involving a threshold of 2.6mmol/L, it may now be possible to consider a prospective study which includes the monitoring of a similar cohort of at-risk babies, randomised to 2.6 mmol/L or a lower level of blood glucose concentration defining hypoglycaemia. Cohort studies of babies born at greater risk and who typically experience more severe hypoglycaemia such as very preterm and very low birth weight babies could also potentially provide data relating severity of neonatal hypoglycaemia to type and severity of later developmental impairment.

8.2. Risk factors for neonatal hypoglycaemia

Our at-risk cohort performed more poorly in cognitive, language and motor development and all scores of EF behaviours than would be expected in comparison with the standardised scores of the

Bayley III and BRIEF-P. In particular, they had lower cognitive scores and a higher rate of potentially clinically significant scores on the Inhibit and Working Memory scales, Inhibitory Self-Control Index and the Global Executive Composite score.

These results agree with those reported elsewhere, although few studies have reported preschool EF outcomes (Baron et al., 2012). In comparison to babies with birth weight in the normal range, small babies are reported to have lower Bayley III scores on all scales (Savchev et al., 2013), subtle impairments in full-scale, performance and verbal IQ at 5 years (Sommerfelt et al., 2000), reduced full-scale IQ, verbal IQ, working memory (Viggedal et al., 2004), poorer reading scores and behaviour at 15 years (Pryor, Silva, & Brooke, 1995), and reduced cognitive flexibility, inhibition (Kulseng et al., 2006) and academic achievement (Strauss, 2000) in young adulthood. IDM have been reported to have working memory deficits at 12 months (DeBoer et al., 2005), increased risk of intellectual disability at 3 years (Mann, Pan, Rao, McDermott, & Hardin, 2013), poorer attention at school age (Ornoy et al., 2001) and poorer overall school achievement at leaving age (Dahlquist & Källén, 2007). School-age WISC-R IQ scores have also been shown to be correlated to indices of maternal metabolic control in IDM (Rizzo, Metzger, Dooley, & Cho, 1997).

Similarly, late preterm children have been reported to have poorer performance on tasks of complex working memory (Baron et al., 2012) and verbal inhibitory control (Brumbaugh et al., 2013) and to have widespread reduced neuropsychological performance at 3 years in comparison to term controls (Baron et al., 2014).

Our results suggest that while late preterm birth is a risk for poor developmental outcome in comparison to standardized assessment norms, it appears to be associated with less later impairment than being born small or IDM. Our findings that large babies seem to experience fewest neuropsychological impairments are in agreement with those reported elsewhere (Brand et al., 2005; Gale et al., 2004). Although the rate of hypoglycaemia was similar in all risk groups, it is likely that being born large is an indication that the baby received sufficient nutrition *in utero* and is therefore at less risk of neuropsychological impairment than babies born small.

We found no significant differences between risk groups for Bayley III scale scores. However, there were BRIEF-P score differences between risk groups, with the Large and Preterm groups having the lowest, and Small and IDM groups having the highest (worse) BRIEF-P scores. Thus, Small and IDM groups had the highest rates of clinically significant scores on the Working Memory scale and Emergent Metacognition Index, suggesting that they were most at risk of EF-related behaviour problems. These findings suggest that babies born small or IDM may benefit from being monitored for developmental impairment through to school age so that timely intervention could be offered to children found to be performing below age expectation. The neurodevelopmental impairment observed in late preterm children in our cohort suggests that although their risk is not as severe as that experienced by Small or IDM babies they may also benefit from monitoring and access to early intervention.

Breastfed babies in our cohort were more likely to experience neonatal hypoglycaemia than those who were not breastfed. However, despite this, breastfed babies achieved significantly higher scores on all Bayley III scales except Motor, Gross Motor and Adaptive Behaviour than babies who were not breastfed. This increased risk of hypoglycaemia for breastfed babies but no association with neurodevelopmental impairment has been previously attributed to an increased supply of alternative cerebral fuels (Hawdon, 1999; Ward Platt & Deshpande, 2005). However, babies in our cohort were reported to have little availability of alternative cerebral fuels (D. L. Harris et al., 2011). In particular, ketone levels were low, although lactate may potentially be an alternative fuel for hypoglycaemic babies (D. L. Harris, Weston, & Harding, 2014). Nevertheless, our results agree with previous reports of better receptive language at 3 years and higher IQ at 7 years for breastfed in comparison to non-breastfed babies (Belfort et al., 2013), and better cognitive and wide ranging academic achievement at 6 (Kramer et al., 2008) and 18 years (Horwood & Fergusson, 1998). It is possible that the improved early neural development associated with breastfeeding (Herba et al., 2013) has a more significant effect than transient hypoglycaemia for most babies. However, as 93% of our cohort were breastfed we had limited power to detect differences in outcome had they been present.

8.3. Gender differences

In our cohort, girls had higher Bayley III scores than boys on all scales except the Gross Motor subscale, although these differences only reached significance for the Adaptive Behaviour and Fine Motor scores. Higher preschool development scores for girls than boys have been previously reported and include higher language scores at 2 years (Reilly et al., 2007), receptive and expressive communication at 4 years (Reilly et al., 2010) and fine motor scores at 3 – 4 years (Cameron et al., 2012). Higher Bayley scale scores for girls than boys have been reported in cohorts of preterm children (Aylward, 2002a; Cho, Holditch-Davis, & Miles, 2010; Romeo et al., 2010). The association between preschool language, fine motor development and early school reading success (A. G. Carlson et al., 2013; Liederman et al., 2005) means that boys' lower preschool achievement in these areas has the potential to impact school achievement. Elsewhere, boys have been shown to be at least twice as likely as girls to be identified with a reading disability (Flannery, Liederman, Daly, & Schultz, 2000).

Girls also performed better than boys on some EF tasks, with a higher success rate on the assessed inhibition task (Snack Delay), and a higher score on the cognitive flexibility/working memory task (Ducks). Similar results have been reported elsewhere with girls having higher scores than boys on measures of inhibitory control at 2 - 4 years (S. M. Carlson & Moses, 2001; Kochanska et al., 2000), inhibition, working memory and verbal fluency at 5 years (Böhm et al., 2004) and wide ranging parent-reported EF differences in the preschool years (Isquith, Gioia, & Epsy, 2004). Boys are more likely than girls to be diagnosed with ADHD (Ben Amor et al., 2005), which is strongly associated with EF impairments including poor inhibition and executive control (Fuggetta, 2006).

In contrast to assessed EF, girls in our cohort had higher (worse) BRIEF-P scores for half of the scales and indexes and for the Global Executive Composite score. The BRIEF-P provides separate

normative data for girls and boys although the rationale for this is not provided (Gioia et al., 2000). Elsewhere, it is reported that sex effects are found for parent report on the Inhibit scale, with boys performing more poorly (Sherman & Brooks, 2010). Separate normative data is not provided for development on the Bayley III (Bayley, 2006) and it is unclear from our results whether separate normalisation at 2 years is appropriate for the BRIEF-P. Assessment at a later stage may reveal whether this was a reflection of parent perceived poorer behaviour or whether this difference arose from separate standardisation for girls and boys at 2 years.

We found a number of interactions between gender and assessed variables which indicated an increased sensitivity to environmental and health factors in boys. There were significant interactions between gender and risk group with IDM boys performing worse and IDM girls better than other risk groups on an assessed inhibition task (Snack Delay) and on an assessed working memory task (Multisearch Multilocation). A higher rate of hypoglycaemia in and morbidity of IDM boys has been previously reported (Bracero et al., 1996) and suggests that boys of diabetic mothers warrant special attention for continued monitoring, with appropriate preschool intervention for those assessed as having poor EF skills. The neurodevelopmental vulnerability of boy babies has been previously reported (Peacock, Marston, Marlow, Calvert, & Greenough, 2012), with biological sex posited as the underlying cause for different pathways of neurological damage (Chounti et al., 2013). However, the physiological reasons for the apparent vulnerability of boys of diabetic mothers are unclear.

There were also gender interactions with SES measures with boys' scores on the various Bayley III scales showing a graded decrease with household income, NZDep2006 at birth and maternal education, suggesting that the development of boys from low SES families is likely to be more impaired than that of girls across all major developmental domains: cognition, language and motor. A positive association has previously been reported between boys' academic achievement (D. R. Entwistle, Alexander, & Olson, 1994) and maths success (DeGarmo, Forgatch, & Martinez, 1999) and measures of SES, but our findings suggest that these associations are already present as early as 2 years of age. Interestingly, we also found that boys, but not girls, who attended preschool had higher Adaptive Behaviour scores than those who did not, suggesting that boys' development can be improved by exposure to an enriched environment and, conversely, is negatively impacted by the lack of it. In New Zealand, as elsewhere, boys are over-represented in special education and reading support classes, and are more likely to leave school early without qualifications, with this likelihood increasing for boys from low SES families (Learning Policy Frameworks, 2007; Piechura-Couture, Heins, & Tichenor, 2011). Our results are important because they suggest that some of the risk factors for poor school outcome are identifiable at 2 years, and hence support the idea that appropriate monitoring could allow for early and targeted support.

In contrast to the apparent vulnerability of boys to the effects of SES and preschool education, girls appeared to be more vulnerable to factors that may have affected or reflected maternal behaviour. Girls, but not boys, whose mothers did not use alcohol had lower Social-Emotional scores than those whose mothers did use alcohol and girls, but not boys, whose mothers used marijuana had lower Expressive Communication and Social-Emotional scores than those who did not report marijuana

use. As the interactions found were with maternal alcohol and marijuana use at 2 years, they may be related to mother-child interactions rather than antenatal development. There appear to be no reports of preschool interactions with postnatal maternal alcohol and marijuana use, and why these interactions indicated poorer outcome for girls is unknown. However, maternal mental health makes an important contribution to child development (Koutra et al., 2013; Vänskä et al., 2011) and maternal sensitivity (Brooks–Gunn et al., 2002) and parenting style (Rubin, Hastings, Chen, Stewart, & McNichol, 1998) have differential effects on girls than boys. Mothers who have been using marijuana may as a consequence of the drug-use, or the underlying reasons for its use, be less communicative and show less warmth, which may affect girls to a greater extent than boys at 2 years.

There was a higher rate of hypoglycaemia in girls than in boys in our cohort, but despite this, girls had better developmental outcomes at 2 years. This is contrary to reports elsewhere that both the risk of and morbidity associated with hypoglycaemia are higher in boys (Bracero et al., 1996; Cornblath et al., 2000). It is not clear from our cohort whether this simply reflects a difference in development between girls and boys, or whether it further supports an absence of association between hypoglycaemia and developmental outcome. In either case, longitudinal follow-up may provide useful data.

8.4. Socioeconomic status and CHYLD cohort outcomes

SES is a complex notion of interacting aspects of a person's life: income, neighbourhood, education, access to resources such as health services, transport, and communication services (American Psychological Association task force on socioeconomic status, 2007; Bradley & Corwyn, 2002). Child development is also influenced by family SES as a result of health-related behaviours (American Psychological Association task force on socioeconomic status, 2007), housing (Baker et al., 2012), educational opportunities (Gibb et al., 2012) and less tangible factors such as family stress (Cohen et al., 2006), maternal depression (Hughes & Ensor, 2009) and family chaos (S. A. Hart et al., 2007; Petrill et al., 2004). Reported results differ on the most relevant measure, and whether income, maternal or parent education, or a scale incorporating these is the best predictor of child developmental outcome (Oakes, 2012). Our results show neighbourhood factors as measured by the New Zealand Deprivation Index 2006, household income and home ownership combined to form the model with the strongest prediction of outcomes. However, as reported elsewhere, individual measures of household income and parent education were also strongly predictive of outcome (Brooks-Gunn & Duncan, 1997; Oakes, 2012).

Confirming previous reports that SES is a significant factor in child development (Bradley & Corwyn, 2002) we found that the 2 year developmental outcome of the CHYLD cohort was strongly influenced by SES, although the extent was different for different variables. Household income had the strongest association with Bayley III Cognitive and Language scores, being close to the standardised mean for children in the high household income tertile, and 10 and 12 points lower, respectively, in the low tertile. In comparison, maternal and paternal education both accounted for an approximate 8 point difference and NZDep2006 at birth and at 2 years for a 5 point difference between high and low

tertiles on both scales. All assessed EF and BRIEF-P scores were also significantly associated with household income; with the Global Executive Composite score 1 standard deviation higher for the low than the high income group. There were less consistent and weaker associations found with NZDep2006 and maternal education.

What is typically meant when SES is included in analyses of child development is the effect of *low* SES on developmental outcomes. Low SES impacts developmental domains and EF singly and via interrelated developmental pathways (Farah et al., 2010). Farah and colleagues (2006) have commented on the impact that poorer working memory and cognitive control may have on the development of general intelligence for children from low SES families, and our developmental and EF results appear to confirm that this concern is warranted. This developmental difference for children from low SES families is likely to contribute to poorer educational achievement, EF development, increased risk of behavioural problems and early school leaving; a particular problem for those who experience low family income during the preschool years (Brooks-Gunn & Duncan, 1997; Evans & English, 2002; Raizada & Kishiyama, 2010; Tucker-Drob et al., 2011).

EF and working memory training have been reported to be successful interventions for improving these skills, especially for the children with the poorest initial performance, hence inclusion of targeted EF training at preschool is likely to be of benefit (Diamond et al., 2007; P. C. Entwistle & Shinaver, 2014). Similarly, preschool coaching for academic readiness has been reported to show largest improvements for low SES children (Weiland & Yoshikawa, 2013), and programmes that support increased mother-child reading in low-income families during the preschool years are associated with improved child language and cognitive skills (Raikes et al., 2006). However, because of the widespread and interrelated nature of child development deficits associated with low SES, addressing outcomes alone is likely to result in limited success. It would appear that a national welfare policy is required that would provide free access to healthcare, preschool and language promotion activities (Duncan & Brooks-Gunn, 2000; Reilly et al., 2007). In addition, healthy and affordable housing, and equitable social support for all low income families may decrease family psychosocial health concerns which contribute to disadvantageous outcome for children from the lowest SES families (Dale et al., 2011).

8.5. Executive function assessment in the CHYLD cohort

Our results confirm that it is possible to usefully assess EF in children as young as 2 years (S. M. Carlson, 2005; Zelazo et al., 1998). This is an important addition to the more traditional developmental assessments because preschool EF is significantly associated with school readiness, academic achievement including reading and mathematics (Blair & Razza, 2007; Bull & Scerif, 2001), rule learning and behaviour (Espy & Bull, 2005; Espy, Sheffield, Wiebe, Clark, & Moehr, 2011). EF appears to be vulnerable to perinatal insult (Mulder, Pitchford, & Marlow, 2010) and hence, assessment at 2 years is important because the impact of perinatal events is more likely to be detected at this stage than it would by assessment at older age when the influence of environmental variables is greater. Furthermore, to understand the neuropsychological sequelae of the neonatal risk

factors and differences in glycaemic status experienced by our cohort it is important to understand the developmental trajectories associated with these risk factors (Annaz et al., 2008; Best & Miller, 2010; C. A. Clark et al., 2013). It has been reported that EF differences between children born term and those born preterm may reflect a difference in rate of development between the two groups (Mulder, Pitchford, Hagger, & Marlow, 2009). Longitudinal data would also allow us to address this issue in our cohort.

We found that the assessed EF Total score was significantly associated with all BRIEF-P scale and index scores, although they explained only a small amount of the variation. Therefore, our results support previous reports that assessed EF and BRIEF-P are accessing related, but different aspects of EF development (P. J. Anderson, 2002). This difference is inherent in the two assessments, with assessed EF assessing short, discrete and novel tasks whereas the BRIEF-P reports parents' perceptions of problem behaviours in the previous 6 months. We found the highest rate of clinically significant BRIEF-P scores to be on the Working Memory scale, which may support a previous report that this was the most sensitive of the BRIEF scales across a range of patient groups at school age (Mahone, Martin, Kates, Hay, & Horska, 2009). However, there is also evidence that working memory is particularly vulnerable to perinatal risk such as preterm birth (Baron et al., 2012; Beauchamp et al., 2008), with both of these possibilities potentially contributing to our findings. We included the BRIEF-P in our assessment because it provides important ecological data (P. J. Anderson, 2002; Bronfenbrenner & Ceci, 1994; Hines, 2013) and also allowed us to compare results for our cohort with normalised T-scores. Working Memory scale scores of the BRIEF have been reported to correlate significantly with frontal gray matter volume, adding support to the validity of parent report as a measure of EF (Mahone et al., 2009).

Currently there is no agreement on whether preschool EFs are related but separate skills (P. J. Anderson, 2002; Fuggetta, 2006; Miyake et al., 2000) or whether preschool EF is a unitary concept that differentiates with age (Brydges, Reid, Fox, & Anderson, 2012; Wiebe et al., 2008). We found significant correlations between three of our four EF assessments. However, the Cronbach's alpha was only moderate suggesting low coherence, and assessment of success rates between tasks indicated that there was little association between success on the different tasks. Hence, our data support the hypothesis that at 2 years EFs are related but separate. A hierarchical progression has been posited from the development of attention, inhibition, working memory and then cognitive flexibility (P. J. Anderson, 2002; Best & Miller, 2010; Romine & Reynolds, 2005), and analysis of longitudinal results from our cohort may provide further evidence for this. Our results appear to indicate that early assessment of EF function requires wide-ranging assessment as separate EFs are related and interdependent; hence disruption to any one EF may impair the future development of others. Further investigation is needed of the extent to which preschool EF training programmes can improve EF skills in children showing impairment and the extent to which targeting one area of EF may contribute to improvement in other areas (P. C. Entwistle & Shinaver, 2014; Gray et al., 2012; van der Donk, Hiemstra-Beernink, Tjeenk-Kalff, van der Leij, & Lindauer, 2013). The apparently

separate but related nature of developing EFs may explain, in part, why improvements after EF training appear to be largely restricted to the target EF (Thorell et al., 2009).

We have demonstrated associations between EF and cognitive, language, and motor development, and between assessed EF and global motion coherence which differed for different perinatal risk groups and SES groups. Hence our results support models proposing that EF, particularly working memory and cognitive flexibility, develops in tandem with other domains of development including cognitive, language and motor domains, and aspects of vision (M. Anderson, 2008; Diamond, 2013). Our results emphasise the importance of language development to EF; a relationship revealed, in part, because of the continued development of preschool EF assessment measures (S. M. Carlson, 2005) and the separation of developmental domains into separate Cognitive and Language scales in the Bayley III (Bayley, 2006). To date, there do not appear to be other reports of this detail of the association between EF and other developmental domains as early as 2 years of age.

8.6. Strengths and issues

This study was a large (n=404) prospective study with a reasonably good follow-up rate (77%). In addition, our cohort was representative of the ethnic and SES distribution of the initial neonatal cohort, with significant effort invested in tracing the 'hard to find' families. We employed a Māori research nurse who was an integral part of recruiting to ensure a good follow-up rate of Māori families and, it is anticipated, will contribute to a similar follow-up rate for the 4½ year follow-up. Our cohort was also broadly representative of the ethnic and SES distribution of the New Zealand newborn population and hence, our results are generalisable to the wider New Zealand population.

Few studies have reported 2 year EF with the cohort size that we have, which makes this a valuable cohort deserving of longitudinal follow-up. A further strength of our study is the multidisciplinary assessment which provided neonatal, optometric and paediatric data in addition to the developmental data. This has allowed us to compare relevant data across disciplines, such as psychology and optometry and to develop a broader view of developmental processes.

One potential weakness of this study is that while we were able to compare developmental outcomes between risk groups and between those children who did and did not experience neonatal hypoglycaemia, we did not have a normal control group with which to compare our at risk population. All of the babies in our cohort were born at risk of neonatal hypoglycaemia and a control group of normal term-born babies would have allowed us to further determine the differences in development between normal term-born babies and those born at risk. A normal control group would also have allowed us to investigate the rate of hypoglycaemia in apparently normal babies.

A control group could have been prospectively and simultaneously recruited with the added explanation to parents that their child was not at increased risk of poor outcome and that their agreement to take part was purely altruistic. However, many parents (perhaps most) would be unlikely to consent to invasive procedures such as heel prick blood tests and the insertion of a

continuous glucose monitor without very good medical reason, and obtaining ethical approval for this approach is likely to have been difficult for the same reasons. In practical terms, recruiting a control group of similar size to our cohort would have doubled the workload and cost of the study. Recruiting a control group of 2-year-olds could have been undertaken, either using birth records from Waikato Hospital where our cohort was born, or by asking parents of our cohort children to recruit families they knew. However, it is unlikely neonatal health records for the control group would be as comprehensive as the current cohort, particularly regarding neonatal glycaemia, and the issues of workload and cost remained a significant barrier.

Another potential weakness of this study is that with the large number of comparisons reported it is likely that some of these could have reached statistical significance by chance (Type 1 error). While continuous data were compared between groups using one-way Analysis of Variance (ANOVA) with Tukey's HSD post-hoc correction for multiple comparisons to reduce Type 1 error, this correction was not done for other analyses. The possibility of Type 1 error could have been reduced by the use of a more stringent (lower) p value, such as p=0.01. However, the exploratory, hypothesis generating rather than hypothesis testing nature of this study meant that a broader, less stringent definition of significance was appropriate. The 2081 comparisons performed resulted in 457 significant at the 1% or lower level of significance and an additional 289 significant at the 5% level of significance. Only 104 would have been expected by chance at the traditional 5% level, suggesting that most of the findings reported were unlikely to have been Type 1 errors. Further, because many of the p values reported were much lower than p = 0.01, reducing the significance threshold to this level is unlikely to have greatly altered our findings or conclusions.

8.7. In conclusion

We have described the 2 year neurodevelopmental outcomes of a large cohort of children born at risk of neonatal hypoglycaemia. Neonatal hypoglycaemia, when treated below the threshold of 2.6 mmol/L, was not associated with a poorer neurodevelopmental outcome at 2 years. However, overall children in this cohort appeared to be at higher risk of poor outcome than would be expected from test norms. Within the cohort, children born small or to diabetic mothers were at increased risk, as were those who were not breastfed, and those from low SES families. Interactions were found between gender and risk group, SES and preschool attendance showing that boys born to diabetic mothers and low SES families were at particular risk of poor outcome, while those who attended preschool had better outcomes, suggesting that boys may be more sensitive than girls to environmental effects on development. EF assessment results suggested that at 2 years different EFs are related but separable and are associated with other developmental domains, with more variation explained by language than cognitive development. Our findings suggest that children born at risk of neonatal hypoglycaemia may benefit from continued monitoring with early intervention services provided where appropriate.

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Appendices

Appendix A: CHYLD Study 2 year Home and Family questionnaire

Appendix B: EF assessment and scoring schedule

LIGGINS INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

Office use only	
Study ID #	
Initials	
Date Assessed	
Checked	
Queries Resolved	
Data Entered	

CHYLD STUDY

Children with Hypoglycaemia and their Later Development

Thank you again for taking the time to fill in this questionnaire.
We realise that this questionnaire requires time and effort, but the information that you provide is very valuable.

0800 CHYLDS (0800 249 537)
021 980 913
CHYLD@auckland.ac.nz

OFFICE USE ONLY
Study No.: _____
NHI No.: _____

Home and Family questionnaire

Child's first name:_____Child's middle name(s): _____
Child's last name: _____
Date of Birth: dd /mm / yyyy Sex: M/F
Street Address: _____
City: _____ Area code: _ _ _ _
Person completing this form:
First name: _____ Last name: _____
Relationship to child:_____

Thank you for agreeing to take part in this important child health study. The information you provide about your child's everyday world is important in helping us to understand their development. Please answer these questions as fully and honestly as you can. Your answers are *strictly confidential* and will not be used in any way that will identify you, your child or your household. If you would like help to answer these questions please contact us.

SECTION A. CONTACT INFORMATION

1. The main caregiver is: (tick one)
   - ☐ Mother
   - ☐ Father
   - ☐ Grandparent
   - ☐ Other (specify)_____

   Caregiver's first name:_____ Last name:_____
   Date of Birth: dd /mm / yyyy
   If the main caregiver is not the child's parent, how long have you/they been the main caregiver?_____years_____months
   Phone: (__)_____Mob: (_____)_____
   Email: _____
   Address: Tick if same as Child's ☐
   OR Street: _____
   City: _____ Area code: _ _ _ _

2. The main caregiver's partner is: (tick one)
   - ☐ Biological mother/father
   - ☐ Stepfather/stepmother
   - ☐ Adoptive father/mother
   - ☐ Boyfriend/girlfriend
   - ☐ Caregiver is a solo parent

   Caregiver's Partner's first name:_____Last name: _____
   Date of Birth: dd /mm / yyyy
   Phone: (__)_____Mob: (__)_____
   Email: _____

3. Grandparents

Mother's parents:	Father's parents:
a. Name(s): _____	e. Name(s): _____
b. Address: _____	f. Address: _____
_____	_____
_____ _ _ _ _	_____ _ _ _ _
c. Phone: ( ) _____	g. Phone: ( ) _____
d. Email: _____	h. Email: _____

4. Other ways we can contact you:
   a. First name: _____ Last name: _____
   b. Relationship (e.g. aunty, neighbour, friend): _____
   c. Address: _____
      _____
      _____ _ _ _ _
   d. Phone: ( ) _____
   e. Email: _____

5. Child's GP:
   a. Doctor's Name: _____
   b. Clinic Name: _____
   c. Address: _____
   d. Phone: ( ) _____

6. Daycare:
   a. Daycare name: _____
   b. Address: _____
   c. Phone: ( ) _____
   e. Daycare days/hours that child attends: _____

This Contact information is for the use of CHYLD study team members only and will be removed from the questionnaire to ensure that your answers to the questionnaire remain completely confidential.

SECTION B. HOME INFORMATION

1. Child's ethnicity:
   Which ethnic group does this child belong to? *(Mark the space or spaces which apply to him/her).*
   - ☐ 1. New Zealand European
   - ☐ 2. Māori
   - ☐ 3. Samoan
   - ☐ 4. Cook Island Maori
   - ☐ 5. Tongan
   - ☐ 6. Niuean
   - ☐ 7. Chinese
   - ☐ 8. Indian
   - ☐ 9. Other such as Dutch, Japanese, Tokelauan. Please state:

8. Family/whānau information:
   a. Total number of people living in the household: _____
   b. Number of brothers and sisters in the household: _____
   c. Ages of other children in the household: (child 1) (child 2)_____
      (child 3)_____(child 4)_____(child 5)_____(child 6)_____
   d. Does the child attend daycare? Yes ☐ No ☐ Hours each week: _____
   e. Does the child attend Kōhanga Reo? Yes ☐ No ☐ Hours each week: _____

9. Languages spoken at home:
   a. Is English the main language spoken at home: Yes ☐ No ☐
   b. If yes, are there other languages other than English spoken at home? Yes ☐ No ☐
   c. Please specify: _____
   d. If English is not the main language, please specify the main language spoken at home:
      _____

10. Do you own or rent the home you live in?
    - ☐ 1. Own
    - ☐ 2. Rent

11. Do you own a car, van, truck or similar vehicle
    (please do not include motorcycles)? Yes ☐ No ☐

12. What is the highest level of education that the child's parents have received? *(Tick <u>one for</u> each parent)*

a. Mother /Primary Caregiver	b. Father/ Caregiver's Partner	
☐	☐	1. Never attended school
☐	☐	2. Primary school/intermediate school
☐	☐	3. High school/secondary school
		i. How many years did mother spend at high school?_____yrs
		ii. How many years did father spend at high school?_____yrs
☐	☐	4. Polytechnic or similar (e.g. trade certificate)
☐	☐	5. University

13. Which of the following categories best describes the **Mother's (or primary caregiver's)** current work situation? Please answer all questions and be as specific as possible (e.g. fitter, secretary, lawyer)

a. A worker for pay Yes ☐ No ☐

i. What is your/her **main** job? _____
ii. How many hours per week do you (does she) work in this job?_____hours

b. Self-employed Yes ☐ No ☐

i. What is your/her **main** job? _____
ii. How many hours per week do you (does she) work in this job?_____hours

c. A homemaker Yes ☐ No ☐

i. What was your/her **main** job **before** becoming a homemaker? _____
ii. How many hours per week did you/she work in this job?_____hours

d. Unemployed Yes ☐ No ☐

i. What was your/her **main** job before becoming unemployed? _____
ii. How many hours per week did you/she work in this job?_____hours

e. Other Yes ☐ No ☐

i. Please specify _____
ii. How many hours a week?_____hours

14. Which of the following categories best describes the **Father's (or primary caregiver's partner's)** current work situation? Please answer all questions and be as specific as possible.

f. A worker for pay Yes ☐ No ☐

i. What is his **main** job?_____
ii. How many hours per week does he work in this job?_____hours

g. Self-employed Yes ☐ No ☐

i. What is his **main** job? _____
ii. How many hours per week does he work in this job?_____hours

h. A homemaker Yes ☐ No ☐

i. What was his **main** job **before** becoming a homemaker?_____
ii. How many hours per week did he work in this job?_____hours

i. Unemployed Yes ☐ No ☐

i. What was his **main** job before becoming unemployed?_____
ii. How many hours per week did he work in this job?_____hours

j. Other Yes ☐ No ☐

i. Please specify _____
ii. How many hours a week?_____hours

15. Are you or any members of your household receiving a benefit? Yes ☐ No ☐

16. What was the household's total income before tax during the past 12 months? *(tick one)*

- ☐ 1. No income
- ☐ 2. $10,000 or less per year (less than $192 per week)
- ☐ 3. $10,001 - $20,000 per year ($144 to $384 per week)
- ☐ 4. $20,001 - $30,000 per year ($385 t0 $576 per week)
- ☐ 5. $30,001 - $40,000 per year ($577 to $768 per week)
- ☐ 6. $40,001 - $50,000 per year ($769 to $961 per week)
- ☐ 7. $50,001 - $70,000 per year ($962 to $1,345 per week)
- ☐ 8. $70,001 and over per year ($1,346 and over per week)
- ☐ 9. Don't know
- ☐ 10.Decline to answer

SECTION C. HEALTH INFORMATION (1)

17. Has this child been referred to, and/or received care from any of the following?
Please tick the appropriate boxes

a. Referred to:	b. Received care from:	
☐	☐	**1 Physiotherapy**
☐	☐	**2 Occupational therapy**
☐	☐	**3 Speech therapy**
☐	☐	**4 Special education service**
☐	☐	**5 Psychology**
☐	☐	**6 Eye-care provider**
☐	☐	**7 Audiology (ears and hearing)**
☐	☐	**8 Other e.g. parenting support, Parents as First Teachers.** **Please specify: _____**
☐	☐	**9 None of the above**

18. Hospitalisation:
Has this child been hospitalised since discharge from hospital after birth? Yes ☐ No ☐

i. If Yes, please complete the section below as best you can:

Age in months at admission	Reason for admission	Duration of admission (specify if in days or weeks)	Name of Hospital

19. Medications

Is this child currently taking medicine of any kind? Yes ☐ No ☐

i. If yes, what is the medicine? _____

ii. What is it for? _____

20. Ear infections

a. Has this child had any ear infections at all? Yes ☐ No ☐

i. If yes, how many up to 12 months old? _____

ii. How many between 12 and 24 months old? _____

b. Does this child have grommets? Yes ☐ No ☐

i. If no, has anyone suggested this child might need them? Yes ☐ No ☐

c. Does this child use simple words yet? Yes ☐ No ☐

d. Does this child respond to sounds like other children? Yes ☐ No ☐

21. Feeding

a. Was this child ever breastfed? Yes ☐ No ☐

b. When did he/she stop receiving breast milk? _____(weeks/months)
please circle one.

c. Of all the liquids this child has had, estimate how much was from breast milk at the following ages (tick one box for each age):

		1. None (0%)	2. Some (1 – 24%)	3. About half (26 – 74%)	4. Most (75 – 99%)	5. All (100%)
i.	Birth					
ii.	1 month					
iii.	3 months					
iv.	6 months					
v.	9 months					
vi.	12 months					
vii.	18 months					
viii.	24 months					

d. At what age did this child begin solid foods? _____ (weeks/months)
please circle one.

22. Prescription Drugs.

Was the child's mother taking medication prescribed by a doctor during this pregnancy e.g for blood pressure, depression, seizures etc? Yes ☐ No ☐

If yes, what were the medicines?

i _____ ii_____

iii _____ iv_____

SECTION D. HEALTH INFORMATION (2)

In this section you are asked to give information about what happened while the mother was pregnant with this child, and also about what is happening now in the household the child lives in. Please answer each of these questions for the mother, father or partner, and other people living in the household.

23. Smoking.
Has the child's mother ever smoked cigarettes once a week or more? Yes ☐ No ☐

24. Smoking. **During this child's pregnancy**.
About how often did people in the household smoke during this pregnancy?

a. Mother	b. Father	c. Others	
☐	☐	☐	1. more than once a week
☐	☐	☐	2. once a week
☐	☐	☐	3. once every 2 weeks
☐	☐	☐	4. once a month
☐	☐	☐	5. don't smoke

25. Smoking. **In the household where the child lives now.**
About how often do people in the household smoke now?

a. Mother	b. Father	c. Others	
☐	☐	☐	1. more than once a week
☐	☐	☐	2. once a week
☐	☐	☐	3. once every 2 weeks
☐	☐	☐	4. once a month
☐	☐	☐	5. don't smoke

26. Alcohol consumption.
Has the child's mother ever drunk alcohol once a month or more? Yes ☐ No ☐

27. Alcohol consumption. **During this child's pregnancy**
About how often did people in the household drink alcohol during this child's pregnancy?

a. Mother	b. Father	c. Others	
☐	☐	☐	1. more than once a week
☐	☐	☐	2. once a week
☐	☐	☐	3. once every 2 weeks
☐	☐	☐	4. once a month
☐	☐	☐	5. don't use alcohol

28. Alcohol consumption. **In the household where the child lives now.**
About how often do people in the household currently drink alcohol?

a. Mother	b. Father	c. Others
☐	☐	☐ 1.more than once a week
☐	☐	☐ 2.once a week
☐	☐	☐ 3.once every 2 weeks
☐	☐	☐ 4.once a month
☐	☐	☐ 5.don't use alcohol

29. Marijuana use.
Has the child's mother ever used marijuana once a month or more? Yes☐ No☐

30. Marijuana use. **During this child's pregnancy.**
About how often did people in the household use marijuana during this child's pregnancy?

a. Mother	b. Father	c. Others
☐	☐	☐ 1.more than once a week
☐	☐	☐ 2.once a week
☐	☐	☐ 3.once every 2 weeks 4.
☐	☐	☐ once a month
☐	☐	☐ 5.don't use marijuana

31. Marijuana use. **In the household where the child lives now.**
About how often do people in the household use marijuana now?

a. Mother	b. Father	c. Others
☐	☐	☐ 1.more than once a week
☐	☐	☐ 2.once a week
☐	☐	☐ 3.once every 2 weeks
☐	☐	☐ 4.once a month
☐	☐	☐ 5.don't use marijuana

32. Other drug use. Other drugs include those, not prescribed by your doctor or bought from a pharmacy, such as cocaine, LSD, speed, P, ecstasy etc.
Has the child's mother ever used other drugs once a month or more? Yes☐ No☐

33. Other drug use. **During this child's pregnancy.**
About how often did people in the household use other drugs during this child's pregnancy?

a. Mother	b. Father	c. Others
☐	☐	☐ 1.more than once a week
☐	☐	☐ 2.once a week
☐	☐	☐ 3.once every 2 weeks
☐	☐	☐ 4.once a month
☐	☐	☐ 5.don't use other drugs

34. Other drug use. **In the household where the child lives now.**
About how often do people in the household use other drugs now?

a. Mother	b. Father	c. Others	
☐	☐	☐	1.more than once a week
☐	☐	☐	2.once a week
☐	☐	☐	3.once every 2 weeks
☐	☐	☐	4.once a month
☐	☐	☐	5.don't use other drugs

35. Is there anything else you would like us to know about you, your child or household?
If so, please let us know about them in the space below.

……

……

……

……

Thank you for your participation in this important study and for taking the time to complete this questionnaire.

Please bring this questionnaire with you when you come for the assessment appointment.

The CHYLD study is continuing and we will let you know the results of the study after all children complete their 2 year assessment. Please let us know if you change your address so that we can maintain contact with you.

Judith Ansell, CHYLD Study,
Liggins Institute, University of Auckland, Private Bag 92019, Auckland Mail Centre, Auckland 1142.
Phone 0800 CHYLDS (0800 249 537) or e-mail chyld@auckland.ac.nz

Study ID:	**Birth Date:**
Examiner's No.	**Date of Assessment:**

CHYLD STUDY

Executive Function Summary Score Sheet

Snack Delay	**Trial Error**	☐ (97) Examiner ☐ (98) Child B ☐ (99) Child L			
	Trial	**Completed/Incompleted**		**Time to Treat**	Retrieved
	Practice 1				☐ N ☐ Y
	Practice 2				☐ N ☐ Y
	0	No Trials Completed		< 5 Seconds	☐ N ☐ Y
	5 seconds	**Full** ☐ Yes ☐ No	**Part** ☐ Yes ☐ No	RT Seconds	☐ N ☐ Y
	15 seconds	**Full** ☐ Yes ☐ No	**Part** ☐ Yes ☐ No	RT Seconds	☐ N ☐ Y
	30 seconds	**Full** ☐ Yes ☐ No	**Part** ☐ Yes ☐ No	RT Seconds	☐ N ☐ Y
	45 seconds	**Full** ☐ Yes ☐ No	**Part** ☐ Yes ☐ No	RT Seconds	☐ N ☐ Y
Fruit Stroop Task	**Trial Error**	☐ (97) Examiner ☐ (98) Child B ☐ (99) Child L			
	Trial	**Correct/Incorrect**			
	Identifies	Apple	☐ (1) Correct	☐ (0) Incorrect	
	Identifies	Orange	☐ (1) Correct	☐ (0) Incorrect	
	Identifies	Banana	☐ (1) Correct	☐ (0) Incorrect	
	Little Apple	☐ (1) Little Apple	☐ (0) Big Apple	☐ (0) Other	
	Little Banana	☐ (1) Little Banana	☐ (0) Big Banana	☐ (0) Other	
	Little Orange	☐ (1) Little Orange	☐ (0) Big Orange	☐ (0) Other	
Categorisation Ducks & Buckets	**Trial Error**	☐ (97) Examiner ☐ (98) Child B ☐ (99) Child L			
	Trial		**(1) Correct**	**(0) Incorrect**	
	Rule Check	Can you show me where <u>big</u> ducks go?	☐ (1) BIG	☐ (0) Little	
	Rule Check	Can you show me where <u>little</u> ducks go?	☐ (1) Little	☐ (0) BIG	
	1	Here is a LITTLE duck.	☐ (1) little	☐ (0) BIG	
	2	Here is a BIG duck.	☐ (1) BIG	☐ (0) Little	
	3	Here is a LITTLE duck.	☐ (1) little	☐ (0) BIG	
	4	Here is a BIG duck.	☐ (1) BIG	☐ (0) Little	
	5	Here is a BIG duck.	☐ (1) BIG	☐ (0) Little	
	6	Here is a LITTLE duck.	☐ (1) little	☐ (0) BIG	

MUST CATEGORISE 5 OUT OF 6 CORRECTLY TO CONTINUE				
Reverse Categorisation Ducks & Buckets	**Trial Error**	☐ (97) Examiner ☐ (98) Child B ☐ (99) Child L		
	Trial		**(1) Correct**	**(0) Incorrect**
	Rule Check	Where <u>big</u> ducks go in silly game?	☐ (1) Little	☐ (0) BIG
	Rule Check	Where <u>little</u> ducks go in silly game?	☐ (1) BIG	☐ (0) Little
		Here is a LITTLE duck.	☐ (1) BIG	☐ (0) Little
		Here is a BIG duck.	☐ (1) Little	☐ (0) BIG
		Here is a LITTLE duck.	☐ (1) BIG	☐ (0) Little
		Here is a LITTLE duck.	☐ (1) BIG	☐ (0) Little
		Here is a BIG duck.	☐ (1) Little	☐ (0) BIG
		Here is a BIG duck.	☐ (1) Little	☐ (0) BIG

Multi-Search Multi-Location Task	**Trial Error**	☐ (97) Examiner ☐ (98) Child B ☐ (99) Child L				
	Trial	Black Diamond	No Response 98 or 99	Full Credit (2)	Part Credit (1)	No Credit (0)
	Training	1	☐	☐	☐	☐
	Training	2	☐	☐	☐	☐
	Training	3	☐	☐	☐	☐
PRE-SWITCH	**Pre-Switch Trials**	No Response 98 or 99		Yellow Circle Error (0)	**Blue Triangle Correct (1)**	Green Square Error (0)
	1	☐		☐	☐	☐
	2	☐		☐	☐	☐
	3	☐		☐	☐	☐
	4	☐		☐	☐	☐
	5	☐		☐	☐	☐
	6	☐		☐	☐	☐
MUST HAVE 3 CONSECUTIVE CORRECT RESPONSES TO CONTINUE						

Multi-Search Multi-Location Task **POST-SWITCH**	**Post Switch Trials**	No Response 98 or 99	Yellow Circle Non-Perseverative Error (0)	Blue Triangle Perseverative Error (0)	**Green Square Correct (1)**
	1	☐	☐	☐	☐
	2	☐	☐	☐	☐
	3	☐	☐	☐	☐
	4	☐	☐	☐	☐
	5	☐	☐	☐	☐
	6	☐	☐	☐	☐
	7	☐	☐	☐	☐
	8	☐	☐	☐	☐

NOTES:

SNACK DELAY

Examiner error during trial makes trial unscorable ☐ (97)
Child refused to do whole task – Behaviour problem ☐ (98)
Child didn't understand task—Language ☐ (99)

Introduction:

Check with parent as to acceptable treat. Confirm what child would call it e.g. M&Ms may be lollies. ***Tick the treat used.***

Fruit Loops_____ M&Ms _____ Cheerios _____ Raisins _____ Popcorn_____ Other_____

I have a special treat for you!

Warm-up (no delay):

Place black mat on table---Place treat under clear cup on top of black mat)

E: I have this yummy *(name treat)* **for you! You can have it. Get the** *(name treat)* .

Practice 1 ☐ **Retrieved snack**

☐ No retrieval (explain) _____

_____

Mmm. That's yummy, huh? *(allow Child to eat treat)*

Let's do it again. *(place another treat under cup)*

You can have it. Get the *(name treat)* .

Practice 2 ☐ **Retrieved snack**

☐ No retrieval (explain) _____

_____

That's fun, huh?

SNACK DELAY Trials:

Examiner: OK. Now we're going to play a game. I have some more (*name treat***) for you!**
(place bell on table for remainder of task)

But you have to wait until I ring this bell *(ring bell)* **before you can go get it. Don't get the (***name treat***)** (*shake head*) **until I ring the bell.**

OK. Let's try it. Remember, you have to wait until I ring this bell before you can go get it. Don't get it until you hear the bell. *(Say before each trial)*

Place treat under cup with one hand, begin timing immediately with timer in other hand, place free hand above bell throughout waiting period; say **OK** *after each trial, then give* reminder--
Remember, you have to wait until I ring this bell before you can go get it. Don't get it until you hear the bell. *Repeat for each trial. Stop trials after* ***one*** *failure.*

Trial	Time (seconds)	R T (seconds)	Full Wait Successful Trial	Partial Success	Failed Trial	Retrieved the Treat
1	5		☐	☐	☐	☐ (0)No ☐ (1) Yes
2	15		☐	☐	☐	☐ (0)No ☐ (1) Yes
3	30		☐	☐	☐	☐ (0)No ☐ (1) Yes
4	45		☐	☐	☐	☐ (0)No ☐ (1) Yes

Directions for Scoring:

1. *Record RT and tick only one trial outcome. =* **Full Wait-Successful trial, Partial Success,** *or* **Failed Trial**
2. *Wait 30 seconds for child to retrieve treat and eat it. If child doesn't retrieve the treat put a tick "No" in* **Retrieved the Treat** *column and move on to next trial. If child retrieves the treat, wait for the child to eat it before you move to next trial or task.*

Response Time (RT) = Time delay from end of wait period (5, 15, 30 or 45) to retrieving treat or child touching treat. Record the number of seconds from when bell rings and child picks up treat.

Full Wait – Successful Trial = Child waits to retrieve treat without touching the glass.

Partial Success = Child does not retrieve treat but touches the glass during the wait period.

Failed Trial = (1) Child retrieving the treat before the bell is rung; or (2) **child** ringing the bell.

END TRIALS AFTER CHILD FAILS ONE TRIAL.

FRUIT STROOP TASK

Examiner error during trial makes trial unscorable ☐ (97)
Child refused to do whole task – Behaviour problem ☐ (98)
Child didn't undrstand task—Language ☐ (99)

Look here! *Place BIG apple, orange, and banana in a row in front of Child---then LITTLE apple, orange, and banana below them. (Place pictures starting at Child's left)*

I have a BIG APPLE (big voice) **and a LITTLE APPLE** (little voice).
A BIG ORANGE (big voice) **and a LITTLE ORANGE** (little voice)
And a BIG BANANA (big voice) **and a LITTLE BANANA** (little voice).

Remove the row of little pictures and ask child to identify large pictures of fruit.

Identification:

Correct child if he/she does not point to the correct picture. Tick child's response.

1. **Show me the APPLE** ☐ **Apple** ☐ Other
2. **Show me the ORANGE** ☐ **Orange** ☐ Other
3. **Show me the BANANA** ☐ **Banana** ☐ Other

OK! *Remove row of big pictures---place embedded fruit cards in front of Child – large banana, large apple, large orange - left to right and begin Stroop Trials.*

Stroop Trials:

Provide no verbal feedback---tick picture child points to.

1. **Now show me the LITTLE apple**

   ☐ **Little apple** ☐ Big apple ☐ Other
2. **Now show me the LITTLE banana**

   ☐ **Little banana** ☐ Big banana ☐ Other
3. **Now show me the LITTLE orange**

   ☐ **Little Orange** ☐ Big Orange ☐ Other

DUCKS AND BUCKETS--CATERGORISATION

Examiner error during trial makes trial unscorable ☐ (97)
Child refused to do whole task – Behaviour problem ☐ (98)
Child didn't understand task—Language ☐ (99)

Categorisation Training:

Introduction of Stimuli:
Use different voices for big ducks and buckets (regular voice) and little ducks and buckets (higher pitch) throughout.

Look what I have here! I have a big duck, and a little duck.
(show child big and little blue ducks)

Practice Trials:
Now, I have these buckets here. (*Place big bucket on child's left and little bucket on child's right. Place buckets approximately 20cm from child's edge of table and approximately 10cm apart*.)

I'm going to put the big ducks in the big buckets and the little ducks in the little bucket. *(pointing to each bucket, slowly)*.

Here's a big duck. It goes in the big bucket. *(put it in)*
Here's a little duck. It goes in the little bucket. *(put it in)*

Now it's your turn to put the big ducks in the big bucket and the little ducks in the little bucket.

Rule Check:

1. **Can you show me where the big ducks go?**

If Correct: **Very good, that's right.** Then proceed to Rule Check 2.
If Incorrect: **Uh oh. Remember, in this game, all the big ducks go in the big bucket and all the little ducks go in the little buckets.** *Point to appropriate buckets. Tick response.*

Response: ☐ **Correct (1)** ☐ **Incorrect (0)**

2. **Can you show me where the little ducks go?**

If Correct: **Very good, that's right.** *Then go to*… **Okay, so let's put all of these ducks in their buckets.**
If Incorrect: **Uh oh. Remember, in this game, all the big ducks go in the big bucket and all the little ducks go in the little buckets.** *(Point to appropriate buckets). Tick response.*

Response: ☐ **Correct (1)** ☐ **Incorrect (0)**

Okay, so let's put all of these ducks in their buckets.

Categorisation Trials: Duck Sorting

1. *If child doesn't like you repeating the rules on each trial, say* **"I have to say it every time, it's the rule."**
2. *If the child points to the bucket Experimenter may sort the duck for him/her.*
3. *Do not say* ***"okay"*** *in response to sort. Say* **, "Let's do another one," "Let's do it again,"** *etc.*
4. *If child asks for help, respond* **"whatever you think", "you choose",** *etc.*
5. *Point to buckets by touching the top with a finger. Do not bring out the duck until the rule statement is complete. (e.g. Big ducks go here, little ducks go here-→ here is a big duck (while simultaneously bringing out big duck)*
6. *Once duck has been presented, Experimenter CANNOT repeat the rule.*
7. *Say the identifying statement while simultaneously displaying the duck.*
8. *Present ducks above and between buckets.*

On *each* trial, say: **If it is a big duck, then put it here, but if it is a little duck, put it here.**

Tick big or little bucket that child puts duck in on each trial

Trial		**(1) Correct Responses**	**(0) Incorrect Responses**
1	**Here is a LITTLE duck.**	☐ **little**	☐ BIG
2	**Here is a BIG duck.**	☐ **BIG**	☐ little
3	**Here is a LITTLE duck.**	☐ **little**	☐ BIG
4	**Here is a BIG duck.**	☐ **BIG**	☐ little
5	**Here is a BIG duck.**	☐ **BIG**	☐ little
6	**Here is a LITTLE duck.**	☐ **little**	☐ BIG
	Response Totals		

GO ON TO REVERSE CATEGORISATION if child gets at least 5 out of 6 correct. If child DOES NOT get 5 out of 6 correct GO TO MULTILOCATION TASK.

DUCKS AND BUCKETS—REVERSE CATEGORISATION

Examiner error during trial makes trial unscorable ☐ (97)
Child refused to do whole task – Behaviour problem ☐ (98)
Child didn't understand task—Language ☐ (99)

OK, now let's play a "silly" game. Let's put all the big ducks in the little bucket *(point, slowly)* **and put all the little ducks in the big bucket** *(point, slowly)*. **This is a silly game**.

Rule Check:

1. Can you show me where the big ducks go in this silly game?

If Correct: **Very good, that's right.**

If Incorrect: **Uh oh. Remember, in this silly game, all the big ducks go in the little bucket and all the little ducks go in the big bucket.** *Tick response.*

Response: ☐ (1) **Correct** ☐ (0) **Incorrect**

2. Can you show me where the little ducks go in this silly game?

If Correct: **Very good, that's right.**

If Incorrect: **Uh oh. Remember, in this silly game, all the big ducks go in the little bucket and all the little ducks go in the big buckets.** *Tick response.*

Response: ☐ (1) **Correct** ☐ (0) **Incorrect**

Okay, let's try this silly game!

Reverse Categorisation Trials:

1. *If the child points to the bucket Examiner may sort the duck for him/her.*
2. *Do not say "okay" in response to sort. Say,* **"Let's do another one," "Let's do it again,"** *etc.*
3. *If child asks for help, respond* **"whatever you think", "you choose",** *etc.*
4. *Point to buckets by touching the top with a finger. Do not bring out the duck until the rule statement is complete. (Example***: Big ducks go here, little ducks go here-→ here is a big duck** *while simultaneously bringing out big duck).*
5. *Once duck has been presented, Experimenter CANNOT repeat the rule.*
6. Say the identifying statement while simultaneously displaying the duck.
7. Present ducks above and between buckets.

On each trial, say: **If it is a big duck, then put it here, but if it is a little duck, put it here.** *Tick big or little bucket that child puts duck in on each trial.*

Trial		(1) Correct Responses	(0) Incorrect Responses
1	**Here is a LITTLE duck.**	☐ **BIG**	☐ little
2	**Here is a BIG duck.**	☐ **little**	☐ BIG
3	**Here is a LITTLE duck.**	☐ **BIG**	☐ little
4	**Here is a LITTLE duck.**	☐ **BIG**	☐ little
5	**Here is a BIG duck.**	☐ **little**	☐ BIG
6	**Here is a BIG duck.**	☐ **little**	☐ BIG
	Response Totals		

MULTI-SEARCH MULTI-LOCATION

Examiner error during trial makes trial unscorable ☐ (97)

Child refused to do whole task – Behaviour problem ☐ (98)

Child didn't understand task—Language ☐ (99)

Materials:

1. Testing apparatus
2. Treats
3. Scoring sheets
4. Stopwatch

Introduction:

Check with parent as to acceptable treat. Confirm what child would call it e.g. M&Ms may be lollies. Tick the treat used.

Fruit Loops _____M&Ms _____ Cheerios _____ Raisins _____ Popcorn_____ Other_____

Training:

Look what I have here!

1. *Examiner presents apparatus within reach of child with only the black diamond shape attached to the center drawer.*
2. *Examiner demonstrates the following steps a) lifting the felt cover, b) pulling on the black diamond, and c) revealing the treat. When treat is revealed say…**There's a (**name treat**) in there. You can have it.***
3. *Examiner allows child to retrieve treat---then slides apparatus slightly away from the child back towards examiner and completes the following steps while child is attending: a) places new treat in center drawer; b) closes the drawer; c) covers the apparatus with the black felt cover; d) pushes apparatus to within child's easy reach, and says…**Can you find the (**name treat**)?***
4. *Record highest credit achieved over three trials:*

1 2 3
☐ ☐ ☐ (2) Full credit = removes cover, pulls black diamond, retrieves treat without assistance.
1 2 3
☐ ☐ ☐ (1) Partial credit = completed some but not all steps. Explain _____
_____
1 2 3
☐ ☐ ☐ (0) No credit = child did not complete any of the steps. Explain_____
_____

5. *Repeat step 3 if necessary, with modeling, up to **3** times.*
6. *Prepare apparatus for trials…. Say… **Alright!** Then move the apparatus out of child's reach, remove the black diamond shape on middle drawer, and position the yellow circle, blue triangle, and green square onto the drawers in order starting from Child's left to right.*

Test--Pre-switch Directions:

1. *Hold treat above blue triangle drawer until Child is attending---then place it in drawer and say…**Here's the (**name treat) while pointing to the blue triangle.*
2. *Point to the yellow circle attached to the drawer and say…* **There's no (**name treat**) here.**
3. *Point to the green square attached to the drawer and say…* **There's no (**name treat**) here.**
4. *Return to blue triangle drawer, point to blue triangle and say…* **Here's the (**name treat**).**
5. *Slide the apparatus back towards Examiner out of Child's reach and cover with felt cover.*
6. *Once the cover is in place slide the apparatus back towards Child and say…* ***Can you find the (**name treat **)?** Allow up to 30 sec for response. If child does not choose a drawer, then repeat instructions. Allow only 1 attempt to choose the correct drawer. If they open an incorrect drawer before choosing the correct drawer put a tick in their first choice. If they do not respond at all put " 98" or "99" in No Response column.*
7. *Record result by placing a tick in appropriate column in the result box below---repeat until achieves **3** consecutive correct trials at the blue triangle location.*

Trial	Yellow Circle	**Blue Triangle**	Green Square	No Response
1				
2				
3				
4				
5				
6				
Total Trials:				

IF CHILD DOES NOT REACH CRITERION BY THE END OF 6 TRIALS DO NOT GO ON TO POST-SWITCH.

Test: Post-switch Directions:

Now we are going to play a silly game. Watch what I do!

1. *Hold treat above the green square drawer until Child is attending, then place it in the drawer. Say...**Here's the (**name treat**)** while pointing to the green square.*
2. *Point to yellow circle attached to drawer saying…* **There's no (**name treat**) here.**
3. *Point to blue triangle attached to drawer saying…***There's no (**name treat**) here.**
4. *Return to green square attached to drawer saying…* **Here's the (**name treat**).**
8. *Pull apparatus slightly away from child's reach toward's examiner. Slowly cover the apparatus with felt allowing a 10 second delay, before sliding the apparatus back towards the child and saying…* ***Can you find the (**name treat**)?** Allow up to 30 sec for response. If child does not choose a drawer, then repeat instructions. Allow only 1 attempt to choose the correct drawer. If they open an incorrect drawer before choosing the correct drawer put a tick in their first choice. If they do not respond at all put " 98" or "99" in No Response column.*
5. Record result by placing a tick in appropriate column in the result box.
6. *Repeat until **2** consecutive correct trials—Child chooses green square first.*

Trial	Response Time	Yellow Circle Non-perseverative Error	Blue Triangle Perseverative Error	**Green Square Correct**	No Response
1					
2					
3					
4					
5					
6					
7					
8					
		Total:	Total:	Total:	Total: