

## Poster 4.8

### Lithium Treatment *in vitro* has Direct and Adaptive Effects on Neuronal Excitability

C. BUTLER-MUNRO and P. HEYWARD

*Department of Physiology, University of Otago, Dunedin, New Zealand*

For over fifty years the elemental cation lithium has been used in the treatment and prophylaxis of Bipolar Disorder; however its therapeutic mechanism of action remains unknown. We have investigated the effects of lithium on the activity of brain neurons, mitral cells of the mouse olfactory bulb *in vitro*, using whole cell and extracellular recording techniques. Lithium (0.5-10mM) caused a dose dependent increase in the excitability of mitral cells, depolarizing resting membrane potential, increasing action potential firing rate, and increasing the time constant of action potential repolarization. These effects are consistent with a reduction of outward membrane current. Lithium washout was associated with a significant decrease in action potential frequency below pre-treatment firing rates which persisted for at least twenty minutes. These results suggest that lithium treatment has direct and indirect, possibly adaptive, effects on neuronal membrane properties. We hypothesise that lithium treatment decreases activation of a sodium dependent potassium current ( $IK_{Na}$ ), known to be abundant in mitral cells and regulates action potential firing. Decreased  $IK_{Na}$  during lithium treatment may lead to increased neuronal excitability, and be associated with persistent adaptive changes in membrane properties that lead to reduced excitability when lithium is removed. We are characterizing the membrane currents acutely affected by lithium treatment, and following lithium washout.

## Poster 4.9

### Afferent Axonal Pathfinding in Developing Chicken Rhombencephalon

M. F. KUBKE and J M. WILD

*Department of Anatomy with Radiology, University of Auckland, Auckland, New Zealand*

The developing hindbrain of vertebrates is organized in a series of rhombomeres, each giving rise to specific nuclei. The role of this segmentation has been extensively studied with respect to the origin of motor nuclei. The development of afferent innervation, however, has received little attention. Afferent axons enter the brainstem prior to the migration of their central targets and must therefore navigate in the absence of target derived information. Since the target nuclei for each afferent component originates within discrete rhombomeric boundaries, it is possible that the same positional information that is used by neuronal progenitors to define their final fate, may be available to afferent axons to direct them through their initial growth. This study was aimed at determining the normal sequence that characterises the growth of afferent axons in the hindbrain within the context of the site of origin and of the organisation of second order sensory neurons within specific rhombomere boundaries. Afferent axons were labelled at different embryonic ages using fluorescent lipophilic dyes. Crystals of DiI and/or DiO were placed on specific exposed nerves or nerve branches of fixed embryos. Embryos were incubated at 30 C for 18 hrs, after which the hindbrains were dissected, cleared in glycerol and analysed as whole-mount preparations with confocal microscopy. Afferent axons formed a series of fascicles that extended longitudinally along the alar plate, beyond the rhombomeric boundaries that give rise to their target nuclei. At early stages, the degree of organization and segregation of afferent axons did not appear to reflect the adult patterns. Thus, it appears that the appropriate pathfinding and final segregation of the afferent components involves an initial profuse growth into the hindbrain, and that proper afferent patterning involves axon retraction and may require the initiation of migration if the central targets towards their final position.