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Ability of the maze navigation test (MNT) to predict driving performance on a specialist assessment for individuals with dementia

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Background

While it is generally accepted that those with a moderate dementia should not drive, the driving ability of those with early cognitive decline or mild dementia is less clear. With no reliable measure to guide decisions, it is left to the physician's subjective judgment as to whether further on-road testing is necessary, the cost of which is prohibitive for many. The Maze Navigation test (MNT) was developed as a measure of executive functioning and has been shown to predict driving ability.

Objectives

To assess the ability of the MNT to predict driving performance on a specialist driving assessment for individuals with dementia.

Methods

Thirty-five participants recently diagnosed with dementia in the Waikato memory service and still driving were administered the MNT, Montreal Cognitive Assessment (MoCA) and Trail making tests A & B, then completed a specialist occupational therapist on-road driving assessment.

Findings

Of the 23 completed assessments to date, 11 (47.9%) passed without restrictions, 9 (39.1%) passed with restrictions and three (13%) failed the

on-road assessment, with only Trails A ($p=.004$) and Trails B ($p=.012$) and an MNT cutoff of 1.5SD below normal ($p=.019$), correctly predicted driving outcome. When participants were dichotomised into pass or fail, only MNT ($p=.005$) and Trails B ($p=.003$) but not MoCA ($p=.477$) or Trails A ($p=.185$) predicted outcome.

Conclusions

Preliminary results indicate most individuals diagnosed with dementia and still driving are safe to do so, with only the Trails B and MoCA predicting on-road driving outcome.

Investigation into the role of a rare *CDKN1B* germline variant in a patient with acromegaly

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Background

Acromegaly is a rare disorder characterised by overgrowth of most tissues in the body, including the hand, feet and facial features. This condition is usually caused by a sporadically occurring growth hormone-secreting pituitary gland tumour. Rarely, acromegaly may occur as part of a familial syndrome, multiple endocrine neoplasia type 4 (MEN4). MEN4 is characterised by the development of tumours in multiple endocrine glands including the parathyroids and pituitary and is due to a mutation in the tumour suppressor gene *CDKN1B*.

Method

DNA sequencing of a patient with familial acromegaly identified a germline missense mutation (c.356T>C, p.I119T) in the *CDKN1B* gene. *CDKN1B* encodes the protein, p27, which inhibits cell-cycle proteins in the nucleus preventing unrestrained cell growth and consequent tumour formation. While germline *CDKN1B* mutations have been associated with MEN4, the pathogenicity of this particular variant has yet to be determined.

Objectives

To investigate the pathogenicity, the common *in vitro* method of studying genetic mutations by plasmid transfection was used. Human breast cancer (MDA-MB436 and MCF-7) and rat pituitary tumour (GH3) cell lines were transfected with plasmids containing either FLAG-tagged wild-type (WT) or mutant *CDKN1B*. Immunocytochemistry and western blotting experiments were then carried out to investigate the localisation and expression profiles of the protein in each of the cell lines, respectively.

Conclusion

No apparent change in the predominantly cytoplasmic localisation of p27 in the MDA-MB436 cell line between WT and mutant *CDKN1B* was observed. However, the western blot data suggests that the mutant protein (>28kDa) is larger than its WT counterpart (28kDa) in both breast cancer cell lines possibly due to post-translational modification. Further results from mass spectrometry and the GH3 cell line may reveal more information about the pathogenicity of the variant.

Assessment of weight gain following treatment for thyrotoxicosis

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Background

Obesity has reached epidemic proportions in New Zealand, with almost one-third of all adults obese.¹ While weight loss may frequently be reported in patients with thyrotoxicosis, excessive weight gain commonly occurs with successful treatment² and may continue even after restoration to a euthyroid state.³ This is of major concern for many patients and may have significant implications for adherence with medical therapy.⁴ The aim of this study was to assess long-term weight gain in patients receiving treatment for thyrotoxicosis.

Method

A prospective review of all thyrotoxic patients referred with the first presentation of either Graves' disease or toxic multinodular goitre (TMNG) between 1 March 2013 and 31 October 2014 in Waikato, New Zealand. Weight and thyroid hormone (TSH, FT₄ and FT₃) levels at baseline, six weeks, and three, six and twelve months were recorded.

Results

A total of 215 patients were included of whom 178 had Graves' disease and 37 TMNG; 147 receiving medication (carbimazole or propylthiouracil), 39 undergoing surgery and 29 receiving radioiodine. At 12 months after first specialist appointment, 68% of patients were euthyroid, 13% were hyperthyroid and 5% were hypothyroid. 21% were lost to follow-up. There was a mean percent increase in body weight of 8.07% (95% CI 6.55%, 9.01%), with incremental increase at all time-points. Males gained more weight than females (12.3% vs 7.2%, p=0.0001) and patients with Graves' disease gained more weight than those with TMNG (8.5% vs 5.5%, p=0.0374). Patients who reported weight loss at initial presentation gained significantly more

weight at 12 months than those without initial weight loss (8.9% vs 5.5%, p=0.011). There were no differences in weight gain over time between ethnicity or treatment type.

Conclusion

Treatment of thyrotoxicosis is associated with weight gain within the first 12 months of treatment. There is an increased percentage weight gain with Graves' disease, males and in those who had weight loss at presentation. Overall, patients should expect to gain weight with the restoration of thyroid hormone levels.

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Waikato hospital longitudinal surveillance of abdominal aortic aneurysm

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Purpose

To characterise the size, growth, management and outcomes of abdominal aortic aneurysm (AAA) patients seen at Waikato Hospital over a ten-year period. Data was further analysed with respect to ethnicity. This was done to provide preliminary data to inform a national screening initiative.

Methods

Patients who presented with AAA of greater than 3cm were offered biannual surveillance using abdominal ultrasound.

Results

A total of 608 patients were enrolled in 10 years. The mean age for entry into the study was 72 years (s.d. 8.7) for Māori and 76 years (s.d. 8.2) for Pakeha. 86% (516) of patients were Pakeha and 9% (59) were Māori. Māori spent less time on the study (mean 2.5 years) compared to Pakeha (mean 3.1 years). Rates of aneurysm expansion were similar for both Pakeha and Māori patients. In terms of outcomes; Pakeha were over-represented in repair patients and Māori are over-represented in deceased patients.

Conclusions

There are disparities in age, participation and outcomes between Māori and Pakeha AAA patients. The cause of these disparities is unknown, but an awareness of them is important.

Diagnosing mild cognitive impairment (MCI) in the general population using four different methods

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Background

Mild cognitive impairment (MCI) has been recognised as a risk factor in developing dementia (Peterson et al, 1997). Some research has also shown that people have reverted back to normal cognition. The diagnosis of MCI is complex and different methods have been used based on neuropsychological testing. These methods differ among clinicians. The method of diagnosis of MCI would directly impact on people deserving of appropriate support and services causing either false diagnosis or some people missing out on help completely.

Aim

The study aims to compare four different methods of diagnosing MCI-liberal, comprehensive, conventional and conservative methods.

Methods

Ninety-four participants, recruited from the community, who met inclusion criteria

(absence of dementia, other neurological conditions, alcohol abuse or psychiatric disorder) were assessed on a wide range of neuropsychological tests and the Test of Premorbid Functioning (TOPF).

Findings

Seventy-five participants were diagnosed using the liberal method, 21 using the comprehensive method, 47 using the conventional method and three using the conservative method. There were significant differences in the number of people diagnosed with MCI with conventional methods and when their performance was based on their premorbid IQ.

Conclusions

There is a need for consensus on diagnosing MCI to improve the delivery of services for people who need them. The participants were predominantly from a healthy older population sample and data is now being collected from the Waikato District Health Board.

Chemotherapy for early breast cancer in patients with comorbidity: a systematic review and meta-analysis

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Background

Early breast cancer patients with co-existent comorbidities generally receive less guideline concordant curative treatment and experience worse prognosis. Depending on disease subtype, chemotherapy can be an important treatment modality to reduce risk of recurrence and improve survival. Randomised trial data on chemotherapy use and tolerance in comorbid patients is limited.

Methods

A systematic search of databases was performed for English-language articles evaluating the impact of comorbidity on chemotherapy use in early breast cancer. Comorbidity was assessed as a specific condition, summary count or index. Outcomes of interest were receipt of chemotherapy, quality of chemotherapy delivery and occurrence of toxicity. Odds ratios (ORs) strat-

ified by level of comorbidity severity were derived where possible and results presented by narrative synthesis and meta-analysis.

Results

Sixty studies met inclusion criteria for systematic review. Most were observational cohorts and study populations were heterogeneous. Thirty-three studies evaluated receipt of chemotherapy, with 58% reporting reduced treatment, particularly with higher levels of comorbidity. Meta-analysis of 10 eligible studies returned ORs of 0.88 (95% CI: 0.81–0.96) and 0.62 (95% CI: 0.50–0.78) for receipt of chemotherapy in patients with comorbidity scores of 1 and ≥ 2 respectively, compared with no comorbidity. Comorbidity had a generally adverse impact on the quality of chemotherapy delivery, although the 23 studies reported on greatly heterogeneous outcomes. Toxicity was also greater in patients with comorbidity, with two out of seven studies demonstrating higher non-completion of treatment and 10 out of 13 studies reporting greater odds of toxicity/hospitalisation during chemotherapy. Meta-analysis of three eligible studies reporting on chemotherapy-associated hospitalisation resulted in ORs of 1.42 (95% CI: 1.20–1.67) and 2.23 (95% CI: 1.46–3.39) for comorbidity scores of 1 and ≥ 2 respectively.

Conclusions

Compared with their non-comorbid counterparts, early breast cancer patients with comorbidity receive less adjuvant chemotherapy. Furthermore, if chemotherapy is received, treatment is of lower quality and greater levels of toxicity are incurred.

Effects of wave shape on EEG analysis

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Background

EEGs are generally analysed using the power spectral density, which assumes that the EEG is made up of a combination of pure sine waves, but some patients can have waves

with triangular or square components. These differently shaped waves increase the power at odd harmonics of the fundamental frequency, which increases the power of higher frequencies in the power spectral density of the EEG. This could cause EEG monitors such as BIS (Bispectral Index, Covidien, WIS, USA), which examine the ratio of high frequency to low frequency power, to report the patient is more conscious than they actually are. At light levels of anaesthesia the BIS relies mainly on an index called the Beta Ratio ($=\log[\text{power}(30\text{--}47\text{Hz})/\text{power}(11\text{--}20\text{Hz})]$).

Method

The Alpha waves were isolated from 20 EEGs recorded during general anaesthesia. They were then modified to be triangular or square before being reconstituted with the rest of the waves.

Results

Modification of the Alpha waves lead to significant changes in the power spectral density. The mean Beta Ratio increased from -1.9294 to -1.1993 in the triangular wave modification, and to -0.5281 in the square wave modification. The mean slope of the power spectral densities increased from -0.9319 to -0.3634 and to -0.1174 respectively. The mean spectral entropy of the unaltered EEG was 0.6072 and did not change with wave modification.

Conclusion

The large changes in Beta Ratio and the power spectral density slope may suggest the accuracy of BIS suffers in patients with waves with non-sinusoid components.

Treatment choice and satisfaction in thyrotoxicosis

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Background

Thyrotoxicosis is an important cause of morbidity, which when treated inadequately, may result in premature mortality. Graves' disease (GD) and toxic multi-

nodular goitre (TMNG) are the most common causes of thyrotoxicosis. There are three treatment options available—antithyroid medication (ATD), radioactive iodine (RAI) and surgery, with little consensus as to which option is better.

Aims

Locally patients are offered three types of treatment, and explanations of the advantages and disadvantages of each. There are no reported studies of patients' views of these treatments, how their quality of life is impacted by the treatments or what their levels of satisfaction with treatment are once that treatment is completed. In this pilot study we assessed factors involved in treatment choice and patient treatment satisfaction in those treated for thyrotoxicosis.

Method

Participants in a Waikato prospective study assessing ethnic differences in thyrotoxicosis incidence and severity were invited to participate. Those who agreed to be involved completed a questionnaire detailing factors involved in treatment choice, QoL and satisfaction with their treatment.

Results

One hundred and forty-six participants comprised of 84% Graves' and 16% TMNG patients participated, a return rate of 74% of those eligible for the study. The impact of treatment on recovery time, activities of daily living, possibility of depression or anxiety and doctor's recommendations were identified as the most important factors in choosing a treatment, with some variation by ethnicity. Fifty-eight percent of patients had received antithyroid medication (ATD), 19% RAI, and 22% thyroid surgery, the latter two groups usually following a period of ATD. Satisfaction levels were high across all three treatment types. There

were no identified ethnic differences in treatments offered, satisfaction with treatment reported or whether participants would recommend their treatments to another person.

Conclusions

This New Zealand study found no ethnic difference in what was offered patients or how satisfied they were with their treatment, but these current results indicate that the service offered appears to have no unconscious bias in treatments explained and offered to the range of patients seen with thyroid disease.

The safety of anaesthetising hyperthyroid patients undergoing thyroidectomy—a retrospective cohort study

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Background

Traditional teaching recommends that when possible, hyperthyroid patients be rendered euthyroid prior to thyroidectomy.¹⁻⁵ Limited evidence supports or quantifies this risk.⁶⁻⁸ Small observational studies have found no increase in adverse events among hyperthyroid patients undergoing thyroidectomy.⁹⁻¹¹ The aim of this study was to assess the outcome of patients undergoing thyroidectomy for thyrotoxicosis comparing those who were thyrotoxic at the time of surgery to those who were euthyroid.

Methods

Patients with a recent history of hyperthyroidism undergoing a thyroidectomy between January 2012 and February 2016 in Waikato, New Zealand were identified from hospital coding and an endocrine surgery database. The cohort included patients

with biochemical evidence of hyperthyroidism on pre-operative tests (high FT₃ or high FT₄ and low TSH) and medically-treated patients with normal or subclinical hyperthyroidism (normal FT₃/FT₄ but and a low or normal TSH). Patients were excluded if perioperative thyroid function tests were not available. Primary outcomes were 30-day mortality, hospital stay and evidence of intra-operative thyrotoxicosis (defined as one or more of: HR>100 bpm, systolic blood pressure>180 or <60mmHg, temperature >38°C). Secondary outcomes were use of intra-operative beta-blocker and level of care post-operatively.

Results

Of the 228 patients who underwent thyroidectomy for thyrotoxicosis during the study period, 149 met the inclusion criteria. Of these, 54 patients (36.2%) were thyrotoxic on perioperative blood tests. The remaining 95 patients served as controls. The 30 day mortality for all study participants was zero. Length of hospital stay was not different between the groups. There was no difference in rates of intra-operative thyrotoxicosis. Intra-operative beta-blocker use was higher among thyrotoxic patients (29.6%) compared with controls (8.40%) (p=0.001). Thyrotoxic patients were more likely to receive a higher level of care post-operatively, with five patients (9.30%) receiving HDU/ICU post-operatively compared with one (1.10%) in the control group (p=0.024).

Conclusion

Pre-operative hyperthyroidism was associated with increased intra-operative beta-blocker administration and a higher level of care post-operatively in patients undergoing thyroidectomy but there were no differences in mortality, length of hospital stay or features of intra-operative thyrotoxicosis.

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