

EDITOR'S CHOICE

Is the Lewy body important in the death of neurons?

The relationship between alpha synuclein, Lewy body formation and neurodegenerative processes has always proven slightly elusive. Indeed the normal function of alpha synuclein has always remained somewhat mysterious but is thought to have something to do with normal synaptic function. In the mid 1990's it was discovered that mutations in alpha synuclein could cause parkinsonism and shortly afterwards it was shown that the Lewy body (the pathological hallmark of Parkinson's disease) contained alpha synuclein. This implied that alpha synuclein could have something to do with Parkinson's disease and by inference Parkinson's disease dementia and dementia with Lewy bodies (DLB). In a recent paper in the Journal of Neuroscience, Michael Kramer and Walter Schulz-Schaeffer have investigated this and suggest that it is not the Lewy body formation that is responsible for the neurodegeneration but the presynaptic aggregation of alpha synuclein. They used a technique called paraffin embedded tissue (PET) blot [not to be confused with PET imaging] and a protein aggregation filtration assay so that they could sensitively and accurately detect alpha synuclein aggregates in various tissue sources. They found that they could detect using this technique large amounts of alpha synuclein aggregates in patients with dementia with Lewy body and that this correlated more with the cognitive impairment than Lewy body formation which was relatively limited and not related to any measures of cognitive decline. This suggests that Lewy body formation may be a protective mechanism and not a direct pathogenic pathway and that the aggregation of alpha synuclein presynaptically may be the critical event in triggering neuronal dysfunction leading to neuronal death. It would therefore be this that causes neuronal death in DLB and also presumably in Parkinson's disease. This raises many interesting questions not least of which is what is the role of the Lewy body and in particular should we be targeting therapies to get rid of such structures or would such an approach prove to be more disastrous than helpful. - *RAB*

Kramer ML, Schulz-Schaeffer WJ (2007).

Presynaptic alpha-synuclein aggregates, not Lewy bodies, cause neurodegeneration in dementia with Lewy bodies.

JOURNAL OF NEUROSCIENCE

2007;27:1405-10.

STROKE: Stenting is not inferior to endarterectomy

This is, bless its cotton socks, a preliminary positive non-inferiority trial. For all that, I suspect its conclusions may not be correct. In the Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial, 1183 people within 180 days of a TIA or ischaemic stroke, and with severe symptomatic carotid stenosis, were randomised to stenting or surgery. The headline result is that there is no difference in the early outcome at 30 days. Whilst this may be true statistically, endarterectomy outperformed stenting (non-significantly) on nearly every outcome (for instance the primary outcome measure of recurrent stroke was 4.0% in the carotid-artery stenting group and 2.9% in the carotid endarterectomy-group). I am not entirely sure why the Lancet published this... because the conclusion has to be wait and see what the 6-24 month data shows, but my suspicion is that endarterectomy will win the day. - *AJC*

SPACE Collaborative Group.

30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial.

LANCET

2006 Oct 7;368(9543):1239-47.

MEMORY: working memory dysfunction in subclinical hypothyroidism

Hypothyroidism is often quoted as a cause of reversible dementia, but how many practitioners have ever seen a case? Nonetheless, the possibility that thyroid dysfunction may influence cognitive function remains, and is added to by this study from China. Patients with subclinical hypothyroidism (SCH; = low TSH with normal T3, T4, free T3 and free T4) performed a digit n-back task, a test of working memory, as well as the Wechsler Memory Scale (WMS) as did euthyroid, hyperthyroid, and hypothyroid patients. The former test was also performed whilst undergoing fMRI. The task load of the digit n-back task may be increased: n = 0 is a straight identification task, whereas n = 1 (recall

the digit before the current one) and n = 2 (recall the second digit before the current one) require more "online manipulation", such that subjects with hypothyroidism may disengage from the task if it becomes too difficult. SCH patients proved less accurate than euthyroid and hyperthyroid patients at the 2-back task, but better than hypothyroid patients, whilst the WMS showed no significant differences across the groups, suggesting that working memory is impaired in SCH and hypothyroidism but not other memory functions. fMRI activation of a common frontoparietal network known to underpin performance of the n-back task was not seen in SCH subjects, in whom frontal activation was abnormal, suggesting impairment of executive function. Interestingly, a subgroup of the SCH subjects who were retested after 6 months treatment with thyroxine showed recovery in both task performance and fMRI parameters. Hence this study shows impairment of working memory in SCH with clues to the neural substrate for this dysfunction, and also provides some tentative evidence for the use of thyroxine in SCH. - *AJL*

Zhu DF, Wang ZX, Zhang DR, Pan ZL, He S, Hu XP, Chen XC, Zhou JN.

fMRI revealed neural substrate for reversible working memory dysfunction in subclinical hypothyroidism.

BRAIN

2006;129(11):2923-30.

STROKE: Therapy time in stroke units: what are we doing with it?

*** RECOMMENDED

Intensive task specific exercise has a significant positive effect on the functional recovery of stroke patients. The evidence for this is very strong. However, stroke rehabilitation units in the UK are not organized to optimise the amount of therapy given to patients. Indeed, a recent investigation of therapy time allocated to therapeutic activities in four stroke units in different European countries showed the UK unit was for the most times poorest. Physiotherapists and occupational therapists spent only 46% and 33% of their time doing therapeutic activity with patients in the UK unit. This compared with 54%, 66% and 62% for physiotherapists in the Swiss, German and Belgian Units and 45%, 63% and 50% for occupational therapists. More time was spent on patient related co-ordination activities (e.g., administration, ward rounds) in the UK unit. The units involved in the study all have a long tradition of stroke rehabilitation. The survey was carried out by asking therapists to document their activities in 15-minute periods for two weeks. Diaries from 95 physiotherapists and 51 occupational therapists were collected and a total of 20,421 periods of 15 minutes encoded. The lack of time spent in therapeutic activity in the British unit was not due to lower staffing levels. The reason is more likely to be due to differences in priorities of the unit managers. This study is part of a larger European project, Collaborative Evaluation of Rehabilitation in Stroke across Europe (CERISE) comparing the outcome after stroke between SRUs and it remains to be seen whether outcome is any worse in the UK unit than the others, or indeed if the increased time spent communicating with the rest of the team in the UK unit leads to better discharge management and patient satisfaction. However, given the evidence for the benefits of task specific training, it would seem wise to explore ways in which we can increase opportunities for patients to practice. Perhaps some therapy could be given in groups. The survey also showed that most treatments were delivered on a one to one basis (91.2% of physiotherapy treatments and 86% Occupational therapy). It's time for a culture change in British stroke rehabilitation. - *AJT*

Putman K, De Wit L, Schupp W, Ilse B, Berman P, Connell L, Dejaeger E, De Meyer A-M, De Weerd W, Feys H, Walter J, Lincoln N, Louckx F, Anneleen M, Birgit S, Bozena Smith B, Leys M.

Use of time by physiotherapists and occupational therapists in a stroke rehabilitation unit: A comparison between four European rehabilitation centres.

DISABILITY AND REHABILITATION

2006;28:1417-24.

MULTIPLE SCLEROSIS: Treated by carbon monoxide poisoning?

In this paper, Soares' group in Portugal examine the role of hemeoxygenase-1 and carbon monoxide as treatments of EAE. This all arises from the finding of raised levels of hemeoxygenase-1 (HMOX1/HO-1) in the CNS during the course of MS and EAE, where it is the rate-limiting enzyme in the catabolism of heme. They showed first that HO-1 knock-outs get much worse disease than normal animals, and induction of HO-1, by cobalt protoporphyrin IX, reduced the severity of EAE -both when given prophylactically and therapeutically- in healthy animals. Based on their experience in other

