

EDITOR'S CHOICE

Myelin and madness

Neuregulin 1 (NRG1) is a growth factor which binds to its receptor, erbB4, and by so doing mediates of its effects on normal development, especially of oligodendrocytes. Interestingly this system has been linked genetically to schizophrenia and bipolar disorders – disorders which some have considered to be neurodevelopmental in origin. In this study Roy et al have used mice in which erbB signalling in oligodendrocytes is blocked by expression of a dominant negative erbB receptor. These mice were then shown to:

- have alterations in oligodendrocyte morphology, number and function including thickness of myelin sheath, which was less in transgenic mice but with increasing numbers of smaller less branched cells, all of which reduced the conduction velocity of action potentials (at least in the optic nerve anyway);
- have increased levels of functional dopamine transporters and D1 receptors as evidenced by direct measurement and response to injections of amphetamines;
- exhibit behavioural alterations suggestive of neuropsychiatric disorders, such as hypoactivity in open field testing, with more time spent in the periphery suggestive of increased anxiety. Furthermore, using a social interaction test they found abnormalities in transgenic mice compared to wildtype.

This all suggests that abnormalities in normal oligodendrocyte development leads to subtle changes in defined neurochemical pathways with behavioural consequences and as such the problem in psychiatric disorders is as much to do with the white matter as anything else. Obviously this paper has focused on NRG1 erbB4 effects on oligodendrocytes and inferred its link to the other abnormalities when of course they may all be primarily affected by an abnormality in this pathway. It does though raise many interesting questions about how different neural elements speak to and affect each other and in particular how oligodendrocytes may instruct the dopaminergic system to behave normally. - **RAB**

Roy K, Murtie JC, El-Khodor BF, Edgar N, Sardi SP, Hooks BM, Benoit-Marand M, Chen C, Moore H, O'Donnell P, Brunner D, Corfas G.

Loss of erbB signalling in oligodendrocytes alters myelin and dopaminergic function, a potential mechanism for neuropsychiatric disorders.

PNAS

2007;104:8131-6.

COGNITION: The Green-eyed monster

*** RECOMMENDED

When a colleague does well (gets a grant, merit award, paper published) do you feel pleased or jealous? And if he or she does badly, do you gloat or commiserate? These 'social competitive emotions' have been studied by a group from Haifa, Israel. 48 subjects with focal brain damage and 35 age-matched controls were asked to judge whether a picture showed a face that was envious, gloating or sympathising with a person. The character in question was a little cartoon head called 'Yoni' for no clear reason. He was surrounded by photos of four different young women with various facial expressions. If Yoni smiled, whilst the woman he was looking at was sad, he was said to be gloating; if Yoni was sad when the woman he started at was happy, he was envious; and if Yoni shared the facial expression of the woman, he was identifying with her. The main result was that patients with ventromedial frontal brain damage lost the ability to work out when Yoni was being jealous or gloating, but could spot when he was identifying with the woman. And those with right-sided lesions had more trouble recognising envy, whereas those with bilateral or left-sided damage could not identify gloating. At p values of 0.074 (which ordinary people call non-significant, but this group describe as 'marginally significant') patient with left inferior parietal damage had impaired gloating recognition, but could identify envy easily. The authors says this fits with Davidson's 'valence theory' which seems altogether improbable to me, that the left hemisphere is dominant for 'positive' emotions (in the sense that gloating is pleasurable) whereas the right is domi-

nant for 'negative' emotions. The anatomical details are beside the point. What is remarkable is that the cognitive kits for recognising identification, envy and gloating are different. Should we read any moral 'design' into the fact that empathising seems to be a distributed function, difficult to disrupt, whereas envy, and even more so gloating, require complex intact pathways? -**AJC**

Shamay-Tsoory SG, Tibi-Elhanany Y, Aharon-Peretz J.

The green-eyed monster and malicious joy: the neuroanatomical bases of envy and gloating (schadenfreude).

BRAIN

2007 Jun;130(Pt 6):1663-78.

REHABILITATION: research of research on efficacy

Those working in the field of brain injury rehabilitation can sometimes feel as if the dominant force in research focuses on the efficacy of the intervention as a whole rather than an analysis of what particular aspects of rehabilitation work and why. Unfortunately as rehabilitation is often perceived as an optional attachment to good medical care rather than a core service, there is an ongoing anxiety on the part of those working in the field of brain injury rehabilitation to prove that what they do 'works' in the same way as a drug for hypertension or a new surgical technique. The variability in type of brain injury, the state of the pre-injured brain and the individual circumstances of the brain-injured individual mean that trying to pin down evidence-based conclusions in this population has proven very difficult. The large meta-analysis illustrates this point very well. As well as looking at the efficacy of inpatient rehabilitation per se, the authors have examined the available research surrounding some of the thorny questions that provoke such debate amongst rehabilitation professionals. When should rehabilitation start? how long should it go on for?, what should its intensity be? and does community or vocational rehabilitation work? Not surprisingly, the authors found that one of the main difficulties in answering these questions comes from the variability in outcome measures adopted by different research groups. In terms of measuring the effectiveness of inpatient rehabilitation, different groups had used the Barthel index, the FIM, the Ranchos Los Amigos level of Cognitive Functioning Scale, Glasgow Outcome Scale, length of hospital stay and return to work. The trials were almost all retrospective or single group intervention and indicated limited evidence for the effectiveness of inpatient rehabilitation, while the one randomised controlled trial demonstrated moderate evidence. The authors rightly state that there is a great variability of the programs and patient populations. This makes meaningful comparisons difficult. As one could probably predict, the other conclusions from the analysis revealed that there was evidence, albeit limited, to support earlier, more intense rehabilitation that continued in the community and was supported by a vocational element. The authors conclude that standardisation of outcome measures would allow more meaningful comparisons between studies. Perhaps more pertinently, however, they speculate that "...further research may well find that optimal timing and duration of rehabilitation is unique to each patient..." - **LB**

Cullen N, Chundamala J, Bayley M, Jutai J.

The efficacy of acquired brain injury rehabilitation.

BRAIN INJURY

2007 Feb;21(2):113-32.

PARKINSON'S DISEASE: Falling asleep with PD

There has been a great deal of interest in the prevalence, type and cause of sleep disturbance in Parkinson's disease, perhaps triggered by the issues of somnolence with dopamine agonists some 5-10 years ago. Whilst abnormalities of sleep are now recognised and may even precede the onset of Parkinson's disease, the aetiology underlying it is not fully understood, although the role of hypocretin/orexin in this has been an active area of research. It is therefore timely that two papers in Brain have recently reported on the loss of orexin in Parkinson's disease. In both papers the authors demonstrate that there is a loss of orexin neurons in the hypothalamus. In addition Fronczek et al showed that there are Lewy bodies in the hypothalamus and reductions in CSF as well as prefrontal orexin levels, whilst Thannickal et al have shown that the loss of orexin neurons increases with disease progression and is associated with the loss of melanocyte stimulating hormone producing neurons in the hypothalamus as well. This latter population of neurons has also been associated with actions in controlling

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