IN THE NEWS

A head start on autism

For more than 60 years it has been known that some people with autism have abnormally large heads. Now, a group from the University of California San Diego has described an aberrant pattern of head growth that might provide an early warning of the onset of this increasingly prevalent disorder.

Led by E. Courchesne, the team examined the medical records of normal children and infants with autism between the ages of 6 and 14 months. The head size of 60% of the patients was significantly above average, and the severity of their symptoms was positively correlated with head circumference. Interestingly, head size at birth was below average in the affected group, indicating that a growth spurt of unusual magnitude had occurred during their first year.

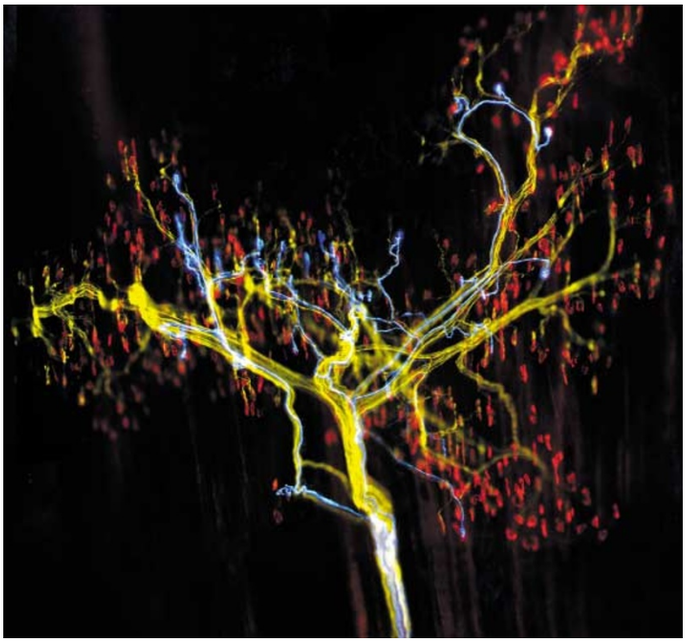
During development, steady brain growth allows synapses to form then be reinforced or eliminated, according to sensory and motor inputs. Courchesne told the *Seattle Post-Intelligencer* (16 July 2003) that rapid enlargement might inhibit "the guidance of experience and learning, [causing] the brain [to create] abnormal connections that make it very hard for autistic children to make sense of the world they live in".

As this pattern of head development can be detected long before the onset of behavioural symptoms, the already routine measurement of the head circumference of infants will yield an early warning to parents of those at risk. As the father of a child with autism, R. Rollens of the MIND Institute is all too aware that "it's better to know as early as possible that something might be wrong" (*Los Angeles Times*, USA, 16 July 2003).

Suzanne Farley

SYNAPTOGENESIS

A process of elimination



Two motor axons expressing different coloured fluorescent proteins (yellow and cyan). Post-synaptic receptor sites are labelled with Alexa-594 conjugated bungarotoxin (red). Reproduced, with permission, from *Nature* © Macmillan Magazines Ltd.

In mammals, the immature neuromuscular junction (NMJ) receives inputs from several motor neurons, but these are gradually whittled away during early postnatal life, so that each muscle fibre in the adult is innervated by a single motor neuron (although each motor neuron can still innervate many muscle fibres). What determines which input will escape elimination? Is the competition mediated by local factors at each NMJ, or by some global property of the motor neuron? Two new studies reported in *Nature* provide some answers to these questions.

Kasthuri and Lichtman generated transgenic mouse lines in which a fraction of motor neurons expressed different fluorescent proteins. They obtained mice in which a single forelimb motor neuron expressed cyan fluorescent protein, whereas another expressed yellow fluorescent protein. In the forelimb muscles of neonatal

ATTENTION

Faster than the eye can see

Visual attention is a demanding task for the brain, owing to the many factors that can affect our attentional capability. A recent paper reports that it is possible to dissociate two aspects of attention — its top–down control and the so-called 'attentional blink' — in people with mild cognitive impairment (MCI). This dissociation indicates that different neural substrates subserve these two processes.

Many studies have established that, when presented with complex visual stimuli, our attention to specific elements of the scene is influenced by 'automatic', stimulus-driven processes (which are referred to as bottom–up) and by task-dependent, goal-directed mechanisms (termed top–down).

At the same time, much effort has gone into finding out how quickly attention can be directed at a stimulus, and how long it takes to disengage from it to attend to a different one. This effort has disclosed a phenomenon known as attentional blink; when we're required to identify two stimuli that are briefly presented in close succession, the first stimulus interferes with our ability to identify the second for a period of up to 500 milliseconds.

In the new paper, Perry and Hodges explored how top–down mechanisms interacted with the attentional blink by sequentially presenting two brief stimuli, and asking subjects to identify both of them, or to ignore one of them and identify the other. In the first case, the interference of the first stimulus with the identification of the second one constituted a measure of the attentional blink; in the second case, the ability to ignore the first stimulus provided a measure of top–down processing. They tested two groups of people — healthy subjects and people with MCI (the preclinical stage of Alzheimer's disease) — and found that, whereas the attentional blink was similar between the groups, top–down processing was impaired in people with MCI.

What are the neural systems that subserve these attentional processes? The prefrontal cortex has been implicated in top–down processing, and the authors propose that the attentional blink might depend on perceptual processes

mice, the authors studied NMJs that contained one input from each labelled neuron. Interestingly, they found that if the 'cyan' input won the competition against a 'yellow' axon at one NMJ, it also beat the yellow input at all the other NMJs that were co-innervated by these two neurons. However, this did not mean that the outcome for these two axons would be the same against all competitors, and by bringing a third neuron into the equation, the authors could establish a competitive hierarchy.

So what gives a motor neuron the competitive edge? In a second study, Buffelli and colleagues showed that synaptic efficacy might be a defining factor. They reduced neurotransmission in some motor neurons by conditionally knocking out the gene for choline acetyltransferase (*ChAT*). In the absence of competition, the ChAT-negative axons could readily make synapses with muscle fibres, but their inputs were always eliminated when they were pitted against wild-type inputs.

In addition, Kasthuri and Lichtman showed that the ranking of a motor neuron in the competitive hierarchy was inversely proportional to the size of its axonal tree. Taken together with the findings of Buffelli *et al.*, this might imply that each neuron has a finite supply of neurotransmitter, which is spread more thinly as the size of the motor unit increases.

These findings highlight the benefits of looking at the bigger picture to make sense of events at individual synapses. Manipulations such as knocking out the *ChAT* gene create abnormally large imbalances in synaptic efficacy, and it remains to be seen whether natural variations in neurotransmission are sufficient to drive competition at the NMJ, or whether it requires additional factors that are globally distributed in motor neurons.

Heather Wood

References and links

ORIGINAL RESEARCH PAPERS Kasthuri, N. & Lichtman, J. W. The role of neuronal identity in synaptic competition. *Nature* **424**, 426–430 (2003) | Buffelli, M. *et al.* Genetic evidence that relative synaptic efficacy biases the outcome of synaptic competition. *Nature* **424**, 430–434 (2003)

FURTHER READING Sanes, J. R. & Lichtman, J. W. Development of the vertebrate neuromuscular junction. *Annu. Rev. Neurosci.* **22**, 389–442 (1999) | Sanes, J. R. & Lichtman, J. W. Induction, assembly, maturation and maintenance of a postsynaptic apparatus. *Nature Rev. Neurosci.* **2**, 791–805 (2001)

early in the visual pathway, although more experiments will be needed to support this idea. More importantly, the data indicate that mnemonic problems are not the only feature of the preclinical stage of Alzheimer's disease, but that attentional deficits, which might have diagnostic implications, are also present.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Perry, R. J. & Hodges, J. R. Dissociation between top–down attentional control and the time course of visual attention as measured by attentional dwell time in patients with mild cognitive impairment. *Eur. J. Neurosci.* **18**, 221–226 (2003)

FURTHER READING Corbetta, M. & Shulman, G. L. Control of goal-directed and stimulus-driven attention in the brain. *Nature Rev. Neurosci.* **3**, 201–215 (2002)

IN BRIEF

ION CHANNELS

Atomic proximity between S4 segment and pore domain in Shaker potassium channels.

Lainé, M. *et al*. *Neuron* **39**, 467–481 (2003)

Crystallographic data on the structure of the bacterial channel KvAP indicated that S4 — the voltage-sensing domain — is at the periphery of the channel and moves through the membrane in response to voltage changes. Here, Lainé *et al*. present a different model for Shaker K^+ channels; on the basis of disulphide-bond formation between engineered pairs of cysteines and molecular modelling, they argue that S4 is located between pore domains.

NEURODEGENERATIVE DISEASE

Neurodegeneration and defective neurotransmission in a *Caenorhabditis elegans* model of tauopathy.

Kraemer, B. C. *et al*. *Proc. Natl Acad. Sci. USA* 18 Jul 2003 (doi:10.1073/pnas.1533448100)

Kraemer *et al*. created a new transgenic model of tau-induced neurodegeneration by expressing wild-type and mutant forms of human tau in *C. elegans*. The expression of wild-type tau led to uncoordinated locomotor behaviour, accumulation of tau and neurodegeneration. These phenotypes were exacerbated in worms that expressed the mutant protein.

NEUROIMMUNOLOGY

Polyamines play a critical role in the control of the innate immune response in the mouse central nervous system.

Soulet, D. & Rivest, S. *J. Cell Biol.* **162**, 257–268 (2003)

The authors found a link between polyamines and the innate immune response in the nervous system. Challenging mice with systemic lipopolysaccharide increased the neuronal and glial levels of ornithine decarboxylase — the rate-limiting enzyme for the synthesis of polyamines. This treatment also elicited an increase in the production of pro-inflammatory cytokines, which was abolished by inhibiting polyamine synthesis. Similarly, the inhibition of polyamine synthesis prevented neuronal death in a mouse model of innate immune reactivity in the brain.

NEUROPHYSIOLOGY

Passive transport disrupts directional path integration by rat head direction cells.

Stackman, R. W. *et al*. *J. Neurophysiol.* 30 July 2003 (doi:10.1152/jn.00346.2003)

Head-direction cells discharge when the head of a rat points in a preferred direction. Here, the authors manipulated different interoceptive cues to test their importance for maintaining the preferred firing direction under conditions in which external cues were unavailable. Altering proprioceptive cues by passively transporting the rat between locations elicited the most significant shift of the preferred direction, highlighting the relevance of proprioception for spatial navigation under conditions that require path integration.