IN THE NEWS

Man's best friend

Men, next time you see a dog, give them an extra-special pat or treat, because they might be the secret to your success with the opposite sex.

Researchers claim that functional brain imaging has revealed the areas of the female brain that are involved in emotional states, such as anger, happiness and sexual arousal, and have had preliminary success in creating chemicals that can control these emotions.

"'We are stunned by our results,' said Dr Randy Hornmeister, behavioural neuroscientist at the Lowdown Institute for Animal Research. 'If further tests prove what we have found, men may never have to buy chocolates or flowers again'" (*Science Weekly News*, 1 April 2002).

In particular, a synthesized chemical that induces sexual arousal has been a resounding success. "Female dogs that were exposed to this chemical were insatiable … they even attacked cuddly toys."

Hornmeister refused to reveal the identity of this mystery chemical — he calls it Compound X — but did say that it acts on two brainstem nuclei, the nodus operandi (the perceptive–cognitive component of sexual arousal) and the nodus vivendi (which might be related to physical and psychological preparation for sexual activity).

But the big question is, will the researchers be carrying out equivalent experiments to discover the innermost secrets of the male mind. "That probably won't be necessary,' Hornmeister laughed, 'Women have known the answer to that for centuries!'" (*Science Weekly News*).

Simon Frantz
Nature Reviews Molecular Cell Biology

COMPARATIVE NEUROANATOMY

Size isn't everything

Humans differ from our closest relatives, the great apes, in many ways. In particular, our cognitive abilities are much more advanced than theirs, allowing us to undertake such challenging and diverse tasks as building skyscrapers, splitting the atom and composing symphonies. But what is it about our brains that gives us these advanced cognitive abilities? Although overall the human brain is larger than those of the apes, brain size can't be the main factor because animals such as elephants and whales have still larger brains.

A popular explanation for the superior intellectual abilities of humans is that our frontal cortices — which contain areas of cortex that are responsible for many cognitive tasks — are larger than those of the apes when measured as a percentage of total brain size. This oft-repeated claim has, however, been tested and found wanting by Semendeferi *t al.*, as they describe in *Nature Neuroscience*. In the largest study of its type, the authors took detailed magnetic resonance imaging scans of the brains of ten humans, nineteen great apes of various species, and nine lesser apes and monkeys. Surprisingly, they found that the frontal cortices of humans, defined by reference to the central sulcus, were no larger than those of the great apes in relation to the overall size of the brain, although the lesser apes and

RKO (courtesy of the Kobal Collection).

NEURODEGENERATIVE DISORDERS

Not guilty

Mutations in Cu/Zn superoxide dismutase 1 (SOD1) are linked to the development of familial amyotrophic lateral sclerosis (FALS), a neurodegenerative disorder that is characterized by selective motor neuron death. How do these mutations lead to the disease? One leading idea is that the mutations confer toxic properties on SOD1. Specifically, as zinc binding is lost in the mutant enzyme, the copper ion might catalyse aberrant oxidative reactions that could eventually lead to cell death.

A clear prediction of this idea is that reducing the incorporation of copper into the mutant SOD1 should lead to reduced cell death or delayed disease onset. Subramaniam *et al.* have now tested this hypothesis directly. They used mice that express mutant forms of SOD1, and therefore develop motor neuron disease, and ablated the gene that codes for the copper chaperone for SOD1 (CCS) to reduce copper incorporation.

The authors found that the amount of copper that was incorporated into mutant SOD1 was substantially reduced in the doubly mutant mice, a selective effect that did not seem to affect other copper-binding proteins. But despite the reduced incorporation of copper into the mutant SOD1, the development of motor neuron disease was not affected. So, the onset of cell death took place at the same time in the presence or absence of CCS, the probability of survival did not change, and the neuropathological features of the disease were similar in both groups of animals.

The factors that mediate the pathogenesis of FALS remain unknown, but the data obtained by Subramaniam *et al.* make a strong case against the involvement of aberrant copper-mediated oxidative reactions. This finding will allow us to switch our attention to other ideas that have been advanced to explain motor neuron death in FALS, such as other forms of oxidative damage, axonal strangulation from disorganization of neurofilaments, toxicity from intracellular aggregates, and excitotoxic death resulting from mishandling of glutamate.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER
Subramaniam, J. R. *et al.* Mutant SOD1 causes motor neuron disease independent of copper chaperone-mediated copper loading. *Nature Neurosci.* 11 March 2002 (10.1038/nn823)
FURTHER READING Cleveland, D. W. & Rothstein, J. D. From Charcot to Lou Gehrig: deciphering selective motor neuron death in ALS. *Nature Rev. Neurosci.* **2**, 806–819 (2001)
WEB SITES
Encyclopedia of Life Sciences:
http://www.els.net/
amyotrophic lateral sclerosis | motor neuron diseases

monkeys did have relatively smaller frontal cortices.

As Semendeferi and colleagues point out, a more informative analysis would look at the relative sizes of the subdivisions of the frontal cortex, and in particular the prefrontal cortex proper. However, identifying these areas from sulcal anatomy is very difficult, if not impossible, and a detailed cytoarchitectonic study — the only way to analyse these subdivisions definitively — would be extremely costly and very difficult. As a first step, the authors compared the sizes of the frontal cortices when the precentral gyri were excluded, on the grounds that the remaining cortex contains all of the prefrontal cortex and only a few other small cortical areas. Once again, they found no significant difference between the relative sizes of this section of cortex in humans and great apes.

How can we reconcile these results with previous studies that claimed to find large differences in the relative sizes of human and ape frontal cortex? One explanation might be sample size. Previous studies used much smaller groups of subjects and looked at fewer species, whereas Semendeferi and colleagues included several examples of every extant species of great ape. Differences in how the frontal cortex is defined could also have contributed.

Of course, size isn't everything. It is likely that the human frontal cortex differs in other ways from those of apes and monkeys — for example, in being more densely interconnected (as supported by data showing that more white matter underlies the frontal cortices in humans than in apes). In addition, specific areas of the frontal cortex might have evolved to be relatively larger at the expense of other subdivisions, without altering the overall size. But one thing is certain: we will have to consider more than just size if we are to figure out what makes humans so different.

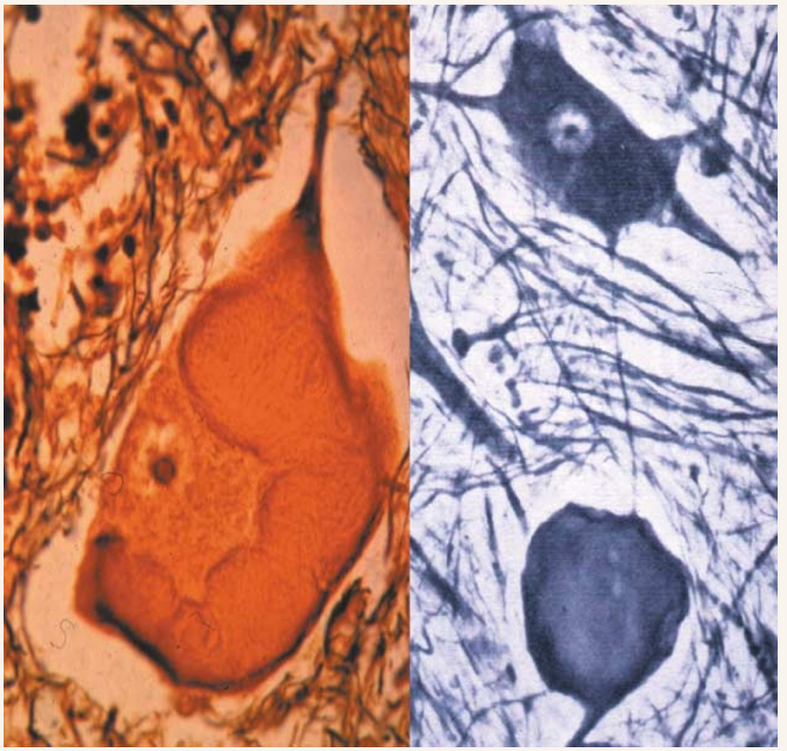
Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Semendeferi, K. *et al*. Humans and great apes share a large frontal cortex. *Nature Neurosci*. 19 February 2002 (10.1038/nn814)

WEB SITES

Semendeferi's laboratory:
http://anthro.ucsd.edu/anthfac/semendeferi.html



Neurofilament aggregates distend a motor neuron in the spinal cord of a patient with ALS (left). A neurofilament-containing spheroidal swelling in the axon of a motor neuron from a patient with ALS (right).

IN BRIEF

DEVELOPMENT

Tangential migration in neocortical development.

Jiménez, D. *et al. Dev. Biol.* 25 February 2002 (10.1006/dbio.2002.0586)

Ventricle-directed migration in the developing cerebral cortex.

Nadarajah, B. *et al. Nature Neurosci.* **5**, 218–224 (2002)

It is known that some cortical neurons migrate tangentially from the basal telencephalon during development, but their precise site of origin has not been clear. Jiménez *et al*. have now shown that distinct populations of cortical neurons are derived from two regions — the medial and lateral ganglionic eminence. Nadarajah *et al*. have addressed a different but related question; namely, how do tangentially migrating cells know where to go once they have reached the cortex? Their data indicate that the cells initially migrate towards the cortical ventricular zone, where they acquire the information that determines their final position in the cortex.

AGEING

Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging.

Logan, J. M. *et al*. *Neuron* **33**, 827–840 (2002)

Using functional magnetic resonance imaging, Logan *et al*. found that older adults showed less recruitment of frontal regions during the self-initiated memory encoding of words than did younger adults. This under-recruitment could be reversed if the memory encoding was supported, for example, by requiring semantic elaboration. A second difference between younger and older adults — nonselective activation of multiple frontal regions for both words and faces — was not reversed by this strategy. The results might have implications for understanding and ameliorating age-related cognitive decline.

ION CHANNELS

Models of the extracellular domain of the nicotinic receptors and of agonist- and Ca^{2+}-binding sites.

Le Novère, N. *et al*. *Proc. Natl Acad. Sci. USA* **99**, 3210–3215 (2002)

Experimentally based model of a complex between a snake toxin and the α7 nicotinic receptor.

Fruchart-Gaillard, C. *et al*. *Proc. Natl Acad. Sci. USA* **99**, 3216–3221 (2002)

These two papers constitute significant progress in the elucidation of the extracellular domain of nicotinic acetylcholine receptors (nAChRs). The authors took advantage of the crystal structure of a molluscan acetylcholine-binding protein (AChBP), which shows substantial homology to nAChRs, and constructed three-dimensional models of the receptor. They identified key differences between AChBP and nAChRs in the binding pocket, and provided a structural basis for previous mutagenesis experiments. In the second paper, the authors model the α7 nAChR subunit in association with a toxin antagonist, identifying the interaction sites and paving the way to the design of new receptor blockers.