WEB WATCH

Mutations galore

The idea of performing genetic screens in mammals, akin to what has been achieved in *Drosophila melanogaster* or in the zebrafish, has always seemed a daunting task to most researchers. Luckily, not everybody has been intimidated by this challenge and a few groups have already embarked on large-scale mammalian mutagenesis projects. They have begun to put together significant collections of mutant mice — the mammal of choice for genetic studies — and their lists of available phenotypes just keep growing and growing.

There are several web sites where you can find all the relevant information on the different mutants screened so far and, more importantly, where you can ask the scientists responsible for the different programmes to share their mice with you. Although not all of the phenotypes are related to defects of the nervous system, many of them do show evident sensory, motor or behavioural abnormalities. It is therefore a good idea to pay a visit to their web sites and see whether a given mutant is capable of feeding your imagination. But visit the sites periodically because the list of available mice changes quite frequently.

The ENU mutagenesis programme at Harwell (UK) and the ENU-mouse mutagenesis screen project in the Deutsches Humangenomprojekt (Germany) are just two of the centres that have taken on the Herculean task of screening the mouse genome. If you know about any other sites, please let us know so that we include them in our list of recommended links.

Juan Carlos López

GENES AND DISEASE

Hip, hip, array

Searching for the aetiology of a complex, multifaceted disorder such as schizophrenia can be like searching for the proverbial needle in a haystack. Just where do you begin? Not only does the disorder present as a constellation of symptoms, including delusions, hallucinations, disorganized thoughts and emotional and motivational deficits, but the reported pathophysiology includes several brain regions, such as the hippocampus, thalamus, superior temporal gyrus and prefrontal cortex. Add to this evidence implicating genetic, environmental and developmental factors, and the fact that most patients have been treated with a range of neuroleptic drugs, and the problem can seem to be insurmountable.

A report in *Neuron* provides an intriguing hint that help may be at hand in the form of microarrray gene-expression profiling. Karoly Mirnics and colleagues from David Lewis's and Pat Levitt's groups narrowed their search to one region of the brain, the dorsal prefrontal cortex. This area of the brain has been implicated in the cognitive disturbances associated with schizophrenia and has also been shown to have altered expression of gene products linked to neurotransmission and second messenger systems. Applying microarray technology to this disease, the authors took a three-step approach. First, they used high-density cDNA microarrays to compare the levels of over 7,000 gene transcripts in the prefrontal cortex of matched pairs of schizophrenic patients and controls. A data-mining technique revealed that transcripts encoding a specific set of proteins that regulate presynaptic function were decreased in all subjects with schizophrenia, with a different pattern across patients. The results for the most consistently altered genes were then verified using *in situ* hybridization in both the original tissue and a new cohort of patients. Two of the most commonly changed transcripts were *N*-ethylmaleimide sensitive factor and synapsin II. Although the changes were modest compared to those reported for cancer with this approach, the results do demonstrate a consistent abnormality in schizophrenic patients.

Even though this complex analysis will need to be mirrored in other brain areas and will need to be extended to a wider variety of gene transcripts that encode proteins that regulate for example, specific neurotransmitter systems, this approach should provide some much needed raw data. It seems equally likely that bioinformatics will be a vital tool in the search for the aetiology of such a complex disorder.

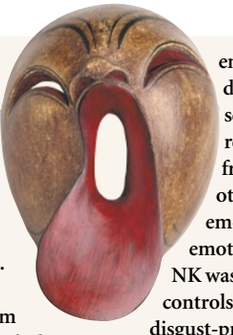
Peter Collins

References and links

ORIGINAL RESEARCH PAPER Mirnics, K. *et al*. Molecular characterization of schizophrenia viewed by microarray analysis of gene expression in prefrontal cortex. *Neuron* **28**, 53–67 (2000)
ENCYCLOPEDIA OF LIFE SCIENCES Schizophrenia
WEB SITE David Lewis | Pat Levitt | PittArray

EMOTION

I'll second that emotion



We've all been there. You sit down after a hard day in the lab and open a bottle of wine to relax. Offering the first glass to a friend, you watch in horror as their first sip turns into a facial grimace of disgust — the wine has corked. Without even tasting your own glass, you consign the offending liquor to the bin and pull another from your wine rack. In a sense, that is the purpose of the readily recognizable facial expression of disgust — to prevent you from experiencing unpleasantness, such as food or drink that has turned and may be harmful to your health. But what is the neural basis of your reaction to recognition of disgust in others?

Functional neuroimaging studies have shown that facial expressions of disgust involve a range of brain areas. However, just two areas are consistently identified by these studies — the insula and the putamen. These results are consistent with data from patients with Huntington's disease who are impaired at the recognition of disgust from the facial expression of others, and have damage to the striatal regions (which include the putamen) and insula. However, these patients have damage to other brain systems, and the functional neuroimaging data provide correlational rather than causal evidence for the role of these structures.

Andrew Calder and colleagues now report the first analysis of a patient (NK) with selective and specific damage to the insula and putamen on various aspects of the processing of disgust and other emotions. Patient NK demonstrated a largely selective deficit in the recognition of disgust from facial expressions of others, non-verbal emotional sounds, and emotional prosody. Moreover NK was less disgusted than controls when presented with disgust-provoking scenarios.

These data support the idea that the neural substrates of emotional experience are recruited during the recognition of the expression of emotion by others and indicate that an insular-striatal network may be involved in disgust across all sensory modalities.

Peter Collins

References and links

ORIGINAL RESEARCH PAPER Calder, A. J. *et al*. Impaired recognition and experience of disgust following brain injury. *Nature Neurosci.* **3**, 1077–1078 (2000)
FURTHER READING Philips, M. L. *et al*. A specific neural substrate for perceiving facial expression of disgust. *Nature* **389**, 495–498 (1997)
WEB SITE Andrew Calder's laboratory