participants. We detected subtle deficits in information processing and vigilance in people bearing the low-expressing genotype. Men with the 'low' genotype exhibited additional deficits in executive function.
Conclusions: Study of the genetic contributors to variation in normal brain function will provide insight into normal neurological processes and have direct relevance to our understanding of such disorders as depression, anxiety and Alzheimer's disease. Because the consequences of individual polymorphisms are generally subtle, an integrative approach that allows for large cohorts is essential to assess their effects.

10-02

The neurodevelopmental effects of apolipoprotein E alleles on brain function

DM Alexander[1], JM Gatt[2], S Kuan[2], C Dobson-Stone[3], EG Todd[4], PR Schofield[3], E Gordon[1], LM Williams[2]

[1]The Brain Resource International Database (The Brain Resource Company), Australia; [2]The Brain Dynamics Centre, Westmead Millennium Institute, Westmead Hospital and Western Clinical School, University of Sydney, Australia; [3]Prince of Wales Medical Research and Garvan Institutes, Australia; and [4]Garvan Institute of Medical Research, Australia

Background: Neuroimaging evidence shows the ε4 allele of the apolipoprotein E (*APOE*) gene is related to brain-functional differences during memory tasks in young, middle-aged and elderly adults. Developmental studies, however, indicate that the ε4 allele confers a cognition-enhancing/protective effect in children and young adults. This study uses a new measure of spatiotemporal wave activity that has shown greater sensitivity and larger effect sizes than EEG power measures.
Methods: About 415 normal subjects were genotyped and divided into three *APOE* status groups: ε2 (ε2/ε2 or ε2/ε3), ε3 (ε3/ε3) and ε4 (ε3/ε4 or ε4/ε4) and four age bands: 6–15, 16–30, 31–50 and 51–65 years old. The ε3 'controls' were age and gender matched to the ε2 and ε4 subjects. Subjects were tested on the Brain Resource International Databa cognitive battery. EEG was measured during a visual working-memory task and analyzed using measures of event-related power and spatiotemporal wave activity.
Results: Analysis of covariance (controlling for age) showed no differences for *APOE* status on most cognitive tests. However, the ε4 group had *improved* performance on two tests of verbal fluency, compared with ε3, across all age bands. ε4 subjects showed less spatiotemporal wave activity in the theta band at ~200 ms poststimulus, but no power differences.
Conclusions: This study confirms previous findings of brain-functional differences between ε3 and ε4 subjects across a broad range of ages. However, the verbal fluency results, supported by previous studies showing developmental benefits of ε4, suggest that brain-functional *differences* do not necessarily imply *deficits* prior to the risk period for dementia.

10-03

Identifying pathways to depressed mood and cognitive dysfunction: the BDNF Val66Met polymorphism and early life stress

JM Gatt[1], S Kuan[1], C Dobson-Stone[2], RH Paul[3], PR Schofield[2], E Gordon[4], LM Williams[1]

[1]The Brain Dynamics Centre, Westmead Millennium Institute, Westmead Hospital and Western Clinical School, University of Sydney, Australia; [2]Prince of Wales Medical Research and Garvan Institutes, Australia; [3]Brown Medical School, USA; and [4]The Brain Resource International Database (The Brain Resource Company), Australia

Background: The BDNF Val66Met polymorphism involves a valine (Val) to methionine (Met) substitution, with the Met allele implicated in phenotypes (poor memory, depressed mood) and endophenotypes (abnormal hippocampal-prefrontal function) of depression. Given a well-established link between stress and depression, we examined whether early life stress moderates the depressogenic and related cognitive effects of BDNF Val66Met in humans and whether hippocampal loss and autonomic dysregulation mediate these effects.
Methods: About 374 healthy subjects from the Brain Resource International Database provided data from cheek swabs (for genotyping), cognitive tests, psychometric questionnaires of mood and personality, tonic and phasic measures of autonomic function (average heart rate and variability during resting conditions and during cognitive- and emotion-related tasks) and magnetic resonance imaging.
Results: Path analysis showed that with increasing stress, BDNF Met status predicts direct effects on hippocampal loss and indirect effects on depressed mood and poor cognition (working memory, executive function/processing speed, verbal memory). These effects were mediated by gray matter atrophy, autonomic dysregulation (raised average heart rate, reduced heart rate variability) and neuroticism.
Conclusions: The findings suggest that the BDNF Met allele carriers may show an increased risk for structural brain deficits and autonomic dysregulation if exposed

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to at least three or more stressful early life events. Alterations of this nature may consequently predispose such individuals to emotional and cognitive dysfunctions. These findings may have implications for understanding the pathways to psychiatric disorders of cognition and mood, and may provide some guide to the tailoring of treatment according to the patient's genetic/endophenotypic profile.

10-04

Identifying markers of negative mood: the gender-specific influence of COMT and MAO-A polymorphisms on emotion processing

SA Kuan[1], JM Gatt[1], C Dobson-Stone[2], RH Paul[3], PR Schofield[2], E Gordon[4], LM Williams[1]

[1]The Brain Dynamics Centre, Westmead Millennium Institute, Westmead Hospital and Western Clinical School, University of Sydney, Australia; [2]Prince of Wales Medical Research and Garvan Institutes, Australia; [3]Brown Medical School, Rhode Island, USA; and [4]The Brain Resource International Database (The Brain Resource Company), Australia

Background: Our integrative neuroscience model of emotion processing proposes that the effects of genetic polymorphisms on emotional function and risk for disorders of negative affect may vary with gender. The COMT Met allele has been related to anxiety traits (in women), while MAO-A genotypes have been linked to anxiety and phobic disorders (in women) and increased aggression (in men). Using a facial emotion perception task, we examined the role of neuroimaging endophenotypes in the association between COMT, MAO-A and negative mood, and the moderating effects of gender.
Methods: About 273 healthy subjects from the Brain Resource International Database provided data from cheek swabs (for genotyping). We assessed mood and temperament (using DASS and NEO), and emotion-related brain function (using event-related potential recording).
Results: COMT heterozygotes (V/M) were associated with higher neuroticism, and reduced and delayed neural responses to emotion in women. By contrast, while the MAO-A genotype showed no direct effects on negative mood, the high-activity alleles were associated with faster and greater responses to emotion in men.
Conclusions: The gender-related dissociation in the impact of COMT and MAO-A on emotion processing and negative mood suggests that these variants contribute to the differential expression of mood disorders in men and women. Integrative genotype-endophenotype makers may offer promise as a tool to aid in early identification of vulnerability to mood disorder and the selection of optimal treatments.

10-05

Genotypes and neural binding in negative affect: the contribution of genetic polymorphisms to 40 Hz gamma phase synchrony

JM Gatt[1], S Kuan[1], C Dobson-Stone[2], RH Paul[3], PR Schofield[2], E Gordon[4], LM Williams[1]

[1]The Brain Dynamics Centre, Westmead Millennium Institute, Westmead Hospital and Western Clinical School, University of Sydney, Australia; [2]Prince of Wales Medical Research and Garvan Institutes, Australia; [3]Brown Medical School, Rhode Island, USA; and [4]The Brain Resource International Database (The Brain Resource Company), Australia

Objective: Binding of diverse neural activity is essential for complex cognitive and emotional functions. There is increasing evidence for the contribution of genetic polymorphisms to these functions, but their role in neural binding is unknown. We explored differences in 40 Hz gamma synchrony (an index of high-frequency binding) according to COMT Val108/158Met, BDNF Val66Met, MAOA and 5HTT-LPR genotypes, and their combined role in negative mood.
Methods: About 155 healthy subjects from the Brain Resource International Database provided cheek swabs (for genotyping) and were assessed for level of depressed mood and anxiety and early life stress. Gamma phase synchrony was extracted from EEG recordings during perception of facial emotion stimuli, pertinent to eliciting biases in negative affect states.
Results: Reduced synchrony to emotional expressions was related to higher depression, and enhanced synchrony to higher anxiety, suggesting distinct biases in binding with these aspects of mood. Consistent with this pattern, the 5HTT-LPR SS allele was linked to reduced frontal and parieto-occipital synchrony to fear with higher stress. The COMT Met allele was linked to similarly reduced frontotemporal synchrony to fear and happiness. By contrast, the BDNF Met allele was related to enhanced synchrony to both fear and happiness with higher stress, suggesting heightened sensitivity to emotion. Synchrony was also enhanced, right parietally and frontotemporally, for the MAO-A low-activity allele, particularly later in the time course.
Conclusion: Polymorphisms that influence brain function may have distinct effects on neural binding associated with processing salient signals of emotion,

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