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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