S20-01

FUNCTIONAL CONSEQUENCES OF GENOME WIDE RISK VARIANTS FOR NEUROPSYCHIATRIC DISORDES IN THE HUMAN BRAIN

T. Lancaster[1], D. Linden[2]
[1]Medical Sciences, Bangor University, Bangor, [2]Psychological Medicine, Cardiff University, Cardiff, UK

Introduction: Recent advances in DNA sequencing have allowed large neuropsychiatric populations to be screened for genetic variants that may influence the progression of mental disorders. Recent GWAS (Genome Wide Association Studies) have identified risk loci for schizophrenia (SZ), Bipolar disorder (BD) and Alzheimer's disease (AD). Objectives

A major concern is to understand how these recently identified risk variants influence vulnerability to neuropsychiatric disorders.

Aims: Common risk variants may contribute to intermediate phenotypes associated with neuropsychiatric disorders. A key aim is to investigate whether individuals expressing susceptibility loci demonstrate similar deficits to those of patients. This may help to elucidate new pharmacological pathways.

Methods: A combination of neuroimaging (fMRI & EEG) and behavioural studies (emotional working memory task, visual encoding efficiency and decision-making ability) were used to probe risk carriers for GWAS validated risk loci associated with SZ, BD and AD. The paradigms were previously validated as methods that neuropsychiatric populations displayed deficits in.

Results: GWAS risk SNP carriers displayed patterns of behavioural/neurophysiology typically seen in their respective neuropsychiatric populations. The risk carrier populations display less overt phenotypes than patients or first-degree relatives, nevertheless displayed small but significant trait effects typically observed in individuals with high levels of genetic risk.

Conclusions: GWAS risk carriers display small but significant effects that reflect a sub-clinical phenotype typically seen in individuals with high genetic risk. Imaging techniques such as fMRI are useful in measuring these subtle differences. Behavioural testing requires larger populations or more penetrant risk alleles for overt phenotypic effects to be witnessed.

https://doi.org/10.1016/S0924-9338(11)73785-3 Published online by Cambridge University Press