Reinforcement-related behaviour in normal brain function and psychopathology

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Objective

A fundamental function of the brain is to evaluate motivational and emotional significance of stimuli and to adapt behaviour accordingly. We hypothesize that genetically influenced individual differences in brain responses to reward, punishment and emotional cues in adolescents mediate risk for mental disorders with a major public health impact. Neuroimaging permits the measurement of specific brain functions implicated in the etiology of mental disorders and link them to genetic variations and behavioural characteristics relevant to disease processes. The goal of the present study is to identify the neurobiological and genetic basis of these traits and to assess their relevance for mental disorder. To this end, we will perform the first multicentre functional and structural genetic-neuroimaging study of a cohort of 2000+ 14 year old adolescents. Intermediate phenotypes of risk for adolescent mental illness will be explored based on cognitive, behavioural, clinical and neuroimaging data. To determine the predictive value of intermediate phenotypes and genetics for development of mental disorders, our cohort will be psychometrically assessed during recruitment and longitudinally at year 4 (age 16-18) of this proposal. DNA samples and phenotype database for the cohort will create a powerful resource for present and future genetic investigations.

In the present study, we will assess association with markers of genes chosen from existing genomic information and from our studies of animals selected for extreme phenotypes of impulsivity and other relevant behavioural traits. Results obtained will be validated in 1000 siblings from the Canadian Saguenay youth neuroimaging study. The IMAGEN study will help elucidate the neural basis of mental disorders and will lay the groundwork for development of treatments that target specific pathological processes across mental disorders rather than heterogeneous categories of mental illness.
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