Nature and Nurture: Gene-environment interactions related to social cognition in schizophrenia

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Abstract

Recent breakthroughs in schizophrenia research have uncovered over one hundred genetic variants related to disorder incidence (Ripke et al., 2014), with the largest correlation presented in a risk variant coding for immune health. This study aims to uncover mediators of the relationship between this highly correlated gene and impaired social cognition in SZ, as well as uncovering possible biological and neuroanatomical mechanisms associated with this impairment.

1. Introduction

Although the etiology of schizophrenia (SZ) is largely unknown, it is increasingly clear that genetic and environmental interactions contribute to cognitive deficits associated with this disorder. Recent Genome wide association studies (GWAS) have indicated a link between SZ and immune dysregulation, especially genetic mutations related to the major histocompatibility complex (MHC) (McAllister, 2014). Social cognitive deficits are core features of Schizophrenia and related disorders, which relate to genetic risk (Mothershill et al., 2014). This study aims to explore the relationship between MHC risk variants for SZ and social cognitive deficits, while also relating findings to brain activity. Furthermore, a number of environmental risk factors will be examined as possible contributors to the relationship between MHC and impairments in SZ.

2. Method

To test if MHC risk variants impair social cognition, a series of ANCOVAs are performed on genetics data previously collected in a GWAS. Social cognition measures are compared in groups with and without MHC genetic risk, in a population of SZ sufferers and healthy controls. In study 2, environmental factors will be examined as possible mediators of the relationship between MHC risk variants and cognitive impairment. Environmental factors include cannabis use, urbanicity, birthorder and smoking, each with empirical support to suggest as risk contributors (McAllister, 2014). Finally, Functional MRI imaging will also be performed to test if this genetic risk relates to altered neural activity.

2.1 Participants

A total of 1013 participants from previously collected GWAS data will be included in this study. Participants include a case group, with schizophrenic and schizoaffective participants, and a control group of healthy volunteers.

2.2 Materials

Four social cognition measures were used to test for differences in social understanding between case and control populations: Reading the mind in the eyes task, Hinting task, an externalizing bias measure and a personalizing bias measure. Environmental risk factors were also measured using pen and paper questionnaires. fMRI scanning will be performed using BOLD fMRI, acquired with a Philips Intera Achieva 3 Tesla scanner (Philips Medical Systems, Best, The Netherlands). Genetics data was made available via an on-going genome wide study.

3. Results

Preliminary analyses suggest that MHC risk variants contribute to impairments in social cognition on three out of four measures examined. Further analysis will be performed to test for environmental mediators of this relationship, looking at cannabis use, urbanicity, birthorder and smoking as modulators. BOLD fMRI will also be used to test for a relationship between MHC risk and altered neural activity, and this will be examined using MATLAB SPM.

4. Conclusions

The MHC genetic variant may serve as a significant risk marker for schizophrenia, and further elucidate etiology of this neurodevelopmental disorder. By looking at this genetic risk in combination with possible environmental risks, a clearer picture of SZ susceptibility could be tailored for patients and clinicians alike. Future studies on neurobiology of social cognition, and greater knowledge of genetic risk may establish targets for interventions.

5. References

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