

# **M45. EXPLORING THE EFFECTS OF MUSCARINIC M1 RECEPTOR SEQUENCE VARIATION ON EXECUTIVE FUNCTIONING IN SCHIZOPHRENIA AND HEALTHY CONTROLS**

Sean Carruthers<sup>1</sup>, Vanessa Cropley<sup>2</sup>, Caroline Gurvich<sup>3</sup>, Kiymet Bozaoglu<sup>4</sup>, Christos Pantellis<sup>5</sup>, Susan Rossell<sup>6</sup>

<sup>1</sup>Swinburne University of Technology, <sup>2</sup>Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne and Melbourne Health; Department of Psychiatry, The University of Melbourne, <sup>3</sup>Monash Alfred Psychiatry Research Centre (MAPrc), The Alfred Hospital and Central Clinical School, Monash University, Melbourne, Australia, <sup>4</sup>Baker IDI Heart and Diabetes Institute, Melbourne, Australia, <sup>5</sup>Melbourne Neuropsychiatry Centre, The University of Melbourne & Melbourne Health, Melbourne, Australia, <sup>6</sup>Monash Alfred Psychiatry Research Centre (MAPrc), The Alfred Hospital and Central Clinical School, Monash University, Melbourne, Australia; Brain and Psychological Sciences Research Centre (BPsyC), Faculty of Health, Arts and Design, School of Health Sciences, Swinburne University, Melbourne, Australia; St Vincent's Mental Health, Melbourne, Australia

**Background** Despite cognitive deficits being recognised as a core feature of schizophrenia (Sz), comprehensive understanding of the underlying aetiology remains elusive. Evidence has implicated a dysfunctional muscarinic system in contributing to the executive functioning (EF) deficits prevalent in Sz. Two independent investigations have investigated a SNP at the M1 receptor gene c.267C (rs2067477) that reportedly spares EF capabilities in Sz. Both studies indicated that patients who were heterozygous at c.267C made less perseverative errors on the Wisconsin Card Sorting Test (WCST) as compared to the homozygous group. This SNP has not been investigated beyond the WCST nor has the influence on cognition been explored in a healthy population. In both a Sz and healthy control sample, the current study sought to determine whether the rs2067477 genotype influences EF outside of that documented using the WCST. To provide a more holistic understanding of the influence M1 receptor sequence variation is having in Sz, the present study explored if differences in the genotype is associated with differential changes in cortical thickness of a number of EF-critical brain regions.

**Methods** Study 1: Genotype and neuropsychological data were obtained from 70 Sz/schizoaffective (SzA) patients and 165 healthy controls. Participants completed the Mazes and Spatial Span Backwards sub-tests of the MATRICS consensus cognitive battery as part of an ongoing investigation.

Study 2: Imaging and genotype data were obtained from 176 Sz/SzA patients and 109 healthy controls from the Australian Schizophrenia Research Bank. Image pre-processing and Surface-based morphometry was performed using the FreeSurfer analysis suite.

**Results** Study 1: For the Mazes, only a significant main effect of group was returned, with healthy controls outperforming patients. Furthermore, a significant main effect of group and significant group by genotype interaction was returned for Spatial Span Backwards performance. In contrast to previous findings patients who were homozygous outperformed the heterozygous group, whilst homozygous and heterozygous healthy controls both equally outperformed the patient group.

Study 2: Group-based statistical analysis across left and right hemispheres for five brain regions (anterior cingulate, rostral middle frontal gyrus, pars opercularis/triangularis/orbitalis) revealed no significant differences in grey matter thickness across genotype. Similarly, no significant group by genotype interactions

were returned for any of the five brain regions included in the analysis. An additional exploratory analysis was performed using all 33 bilateral brain regions produced by the FreeSurfer analysis suite, with no significant results being returned.

**Discussion** These preliminary results suggest that our current understanding of the rs2067477 genotype variation is not comprehensive enough, revealing a conflicting pattern of EF-rs2067477 genotype in schizophrenia compared to that previously documented. Furthermore, whilst this is the first study to investigate M1 receptor gene variation effects on EF in healthy controls, it appears that the association is disease specific, however more comprehensive investigations are required and recommended. Additional studies are likewise required to examine if rs2067477 genotype variation is associated with differential changes in brain structure in schizophrenia, as the present study was unable to identify any changes in cortical grey matter thickness.

**Disclosure:** Nothing to Disclose.