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Body mass index and brain white matter structure in young adults at risk for psychosis – The Oulu Brain and Mind Study

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ABSTRACT

Antipsychotic medications and psychotic illness related factors may affect both weight and brain structure in people with psychosis. Genetically high-risk individuals offer an opportunity to study the relationship between body mass index (BMI) and brain structure free from these potential confounds. We examined the effect of BMI on white matter (WM) microstructure in subjects with familial risk for psychosis (FR). We used diffusion tensor imaging and tract-based spatial statistics to explore the effect of BMI on whole brain FA in 42 (13 males) participants with FR and 46 (16 males) control participants aged 20–25 years drawn from general population-based Northern Finland Birth Cohort 1986. We also measured axial, radial and mean diffusivities. Most of the participants were normal weight rather than obese. In the FR group, decrease in fractional anisotropy and increase in radial diffusivity were associated with an increase in BMI in several brain areas. In controls the opposite pattern was seen in participants with higher BMI. There was a statistically significant interaction between group and BMI on FA and radial and mean diffusivities. Our results suggest that the effect of BMI on WM differs between individuals with FR for psychosis and controls.

1. Introduction

Brain white matter (WM) abnormalities have consistently been reported in patients with schizophrenia (Ellison-Wright and Bullmore, 2009; Bora et al., 2011). WM alterations have also been found in family members of patients with schizophrenia. Arat et al. (2015) concluded in their review that the most significant abnormalities were seen in the frontal and temporal areas and corpus callosum.

Unhealthy lifestyle and metabolic abnormalities are common among patients with schizophrenia (Mitchell et al., 2013). Individuals with a high risk for psychosis have also been reported to have an overall unhealthier lifestyle than subjects with no risk for psychosis: on average, they smoke more cigarettes and have

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poorer dietary habits (Manzanares et al., 2014) and reduced physical activity (Koivukangas et al., 2010; Manzanares et al., 2014).

In normal population adiposity is associated with abnormalities in WM integrity, e.g. in corpus callosum (Mueller et al., 2011; Stanek et al., 2011; Xu et al., 2013). There are several biological pathways which are disrupted in both weight-related processes and psychiatric disorders (Lopresti and Drummond, 2013). External factors, such as the systemic inflammation associated with obesity, may disturb immunological processes of the brain. Abnormal inflammatory activation plays a role in disturbed WM development in schizophrenia (Hotamisligil, 2006; Chew et al., 2013; Bakhshi and Chance, 2015; Najjar and Pearlman, 2015). Literature exploring the effect of adiposity on WM microstructure in individuals with mental disorder is scarce. Tang et al. (2011) found no association between elevated body mass index (BMI) and fractional anisotropy (FA) in patients with schizophrenia or in controls with no psychosis when using region of interest (ROI) analysis. Overweight or obese individuals with first episode mania showed decreased FA in the right parietal and occipital lobes when compared to normal weight first episode mania subjects, and in the right parietal, temporal, and occipital regions when overweight patients were compared to overweight controls (Kuswanto et al., 2014).

Antipsychotic medications and psychiatric illness-related factors may affect both weight (Lopresti and Drummond, 2013) and brain WM structure in schizophrenia (Samartzis et al., 2014). Studying unaffected family members is important because brain findings may be independent of psychosis-related factors. Non-psychotic family members are also free from antipsychotic medications. We assessed whether BMI has an effect on brain WM structure in individuals with familial risk for psychosis (FR) in young adulthood, at the age of high risk for developing schizophrenia (DeLisi, 1992; Häfner et al., 1994).

Little is known about how weight and genetic liability for psychosis interact in the brain. We hypothesised that increased BMI and FR for psychosis would together cause a more robust effect on FA than increased BMI on its own. We hypothesised that FA would be lower in participants with higher BMI in both controls and the FR group, and that FR participants with higher BMI would have more robust changes in WM than controls. All participants were free from antipsychotic medications. As far as we know, this is the first study exploring the association between BMI and WM microstructure in individuals with FR for psychosis.

2. Materials and methods

2.1. Northern Finland Birth Cohort 1986 (NFBC 1986)

The NFBC 1986 comprises live-born children (n=9432) with the expected date of birth between 1st July 1985 and 30th June 1986 in the two northernmost provinces of Finland (Järvelin et al., 1993). The Oulu Brain and Mind Study, a substudy of the NFBC 1986, was conducted between 2007 and 2010.

2.2. Invitation

The study procedure, details of subject selection and the field study have been described by Veijola et al. (2013). All cohort members who had one or more parents who had experienced a psychotic episode and was treated in hospital (ICD-8, and ICD-9 codes 295–299 and ICD-10 codes F20–33, except for non-psychotic mood disorders) between 1972 and 2005 according to the Care Register for Health Care (CRHC, previously the Finnish Hospital Discharge Register) were invited to participate. Subjects were excluded in the invitation phase if they had a history of any psychotic episodes according to the CRHC until the end of 2008, or the right to reimbursable medication due to a psychotic disorder detected using the Registers of the Social Insurance Institute. After exclusions, 272 cohort members with a parental history of psychosis were identified. Of them, one had died, five were living abroad, and for four no address was available; 262 FR subjects were thus invited to the study (Fig. 1).

Members of the NFBC 1986 who did not have a history of psychosis, familial risk for psychosis or symptomatic risk for psychosis were potential controls. Symptomatic risk was defined as having attenuated psychosis-like experiences and some degree of functional impairment in the educational, social or health domain at age 16, when the last field study for the whole NFBC 1986 was conducted. Of the 8763 subjects, 193 (2.2%) were selected randomly. Of them one had died, and for one no address was available. Invitation letters were therefore sent to 191 potential controls.

2.3. The Oulu Brain and Mind field study

At the time of the study, participants were 20–25 years old. DTI brain scanning was performed during the field study. The participants completed background questionnaires and took part in psychiatric interviews and cognitive tests. The structured Interview for Prodromal Syndromes (SIPS) (McGlashan et al., 2001) was used to determine possible lifetime psychotic episodes, previous prodromal syndromes and current prodromal symptoms and the Structured Interview for DSM-IV disorders, SCID-I (First et al., 2002) to assess current axis-I disorders. Written informed consent was obtained from all participants.

2.4. Variables used in the study

The following data were gathered from the questionnaires during the field study: handedness based on the question which one of the hands the participants preferred to use when writing; educational level categorised into two classes (elementary school and matriculation), and BMI defined by asking weight and height and calculated using the formula BMI = mass (kg) / (height (m))^2. Participants were also asked about cigarette smoking and alcohol use.

IQ was estimated using the Matrix Reasoning and Vocabulary subtests of the WAIS-III (Wechsler Adult Intelligence Scale III Edition; (Wechsler, 1997); Finnish Version; (Mukkala et al., 2011). Global Assessment of Functioning, GAF (American Psychiatric Association, 1994) was used by the interviewer to rate occupational, social and psychological functioning on a numeric scale from 0 to 100.

2.5. Final study groups

We included in our analysis all FR and control participants who had data on DTI scanning. Participants were excluded for any of the following: 1) missing BMI data; 2) history of psychosis; 3) history of head trauma with loss of consciousness for 30 min or more; 4) severe neurological illness; 5) diabetes or arterial hypertension with medication; 6) low quality scan. Four subjects in the FR group and six in the control group had missing information on weight or height and therefore BMI could not be calculated. According to the SIPS interview, one participant in the FR group and one in the control group had a history of psychotic episodes. One participant in the FR group reported arterial hypertension and used medication for it. One participant in the control group had a history of head trauma with 30 min of unconsciousness. Five participants in the FR group and two in the control group had a low-quality scan.