The neuropsychological profile of early-onset Obsessive-Compulsive Disorder

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Introduction

Obsessive-Compulsive Disorder (OCD) occurs in approximately 1% of children and young people, severely disrupts their social and educational functioning and has a marked impact on family burden and stress. The key features of OCD are intrusive, distressing obsessions and disruptive compulsions. Obsessions include thoughts of harming others, contamination, and accidents. Compulsions are varied and idiosyncratic but include behaviours, such as repeated checking or washing, and cognitions that are not observable, such as counting and mental rehearsal. They are often carried out to reduce anxiety associated with obsessions. OCD causes disruption through avoidance (e.g. avoidance of school or friends to prevent possible contamination), the distress and anxiety associated with intrusive thoughts, and the impact of compulsions on the patient and her/his family.

The purpose of the present study is to assess a diversity of cognitive processes (e.g. executive functioning, memory, decision-making, social reasoning) in adolescents with Obsessive-Compulsive Disorder (OCD). Adult OCD is associated with diverse cognitive deficits thought to rely on the integrity of brain regions including the orbitofrontal cortex (OFC) and the striatum.

Previous findings indicate that OCD is associated with cognitive inflexibility. On a visual discrimination task, during which subjects learn by trial-and-error which of two objects is correct, adult OCD patients were slower to inhibit a response that was correct in an earlier phase of the task and to shift their attention away from the feature of the object that used to provide information about which one was correct (Chamberlain,

Fineberg, Blackwell, Robbins, & Sahakian, 2006; Chamberlain, Fineberg, Blackwell, Clark, Robbins, & Sahakian, 2007). On another task, adult OCD patients took longer to inhibit a motor response. Furthermore, a correlation between prolonged inhibition time and reduced grey matter in the OFC has been observed (Menzies et al., 2007). A recent study has identified inhibition processes as a possible OCD endophenotype – or intermediate marker of brain dysfunction that indicates vulnerability for disease development – having observed such deficits in both OCD patients and their unaffected first-degree relatives (Chamberlain et al., 2007). If inhibition processes are similarly impaired in adolescent OCD patients, that would increase their utility as vulnerability markers.

Despite the motor impulsivity observed in the aforementioned study, adult OCD patients did not exhibit increased risk-taking on the Cambridge Gamble Task (Chamberlain et al., 2007). A unique feature of the Cambridge Gamble Task is that it dissociates risk-taking from impulsivity, because the subjects who want to make a risky bet have to wait patiently for it to appear. Even though adult OCD patients do not exhibit increased risk-taking, it is plausible that adolescent OCD patients will, because the OFC, which is the likely substrate for this task, of adolescents has not yet fully matured.

Recently, OCD patients exhibited impaired performance on a task that assesses visuospatial memory and new learning – the Paired Associates Learning task (Morein-Zamir et al., submitted). The PAL task is thought to rely on the integrity of the hippocampus. Previously, the PAL task has been demonstrated to be a very sensitive and specific indicator of preclinical Alzheimer's disease, which is associated with atrophy of the hippocampus (Swainson et al., 2001; Lee, Rahman, Hodges, Sahakian, & Graham,

2003; Blackwell, Sahakian, Vesey, Semple, Robbins, & Hodges, 2004). The brain abnormalities associated with OCD may, therefore, not be limited to the OFC and the striatum.

The present study will seek to establish a neuropsychological profile of adolescent OCD. To that end, several tasks, each designed to assess different cognitive processes, will be administered to adolescents with OCD.

Method

Design

A quantitative between-groups design is planned where performance on each of the neuropsychological tests will be compared between groups. There will be one patient group under investigation in this study, which will consist of adolescents diagnosed with OCD. In addition, we will test an age-matched healthy control group. Correlations between clinical severity scores, personality scales, and the objective performance on the neuropsychological tests will be examined in order to assess whether the cognitive tasks are sensitive to individual variation in clinical characteristics of the patients.

Sample Size

The sample size in each group will be 80. Sample sizes are based on previous neuropsychological testing using the same tasks in adult OCD patients, their first-degree relatives and normal individuals performed by members of the research group (Chamberlain et al., 2006; Chamberlain et al., 2007; Menzies et al., 2007).

Participants

Young people with Obsessive-Compulsive Disorder will be recruited, with the help of the Mental Health Research Network, from ten research sites. The sites from which participants will be recruited are: (1) Cambridgeshire and Peterborough, (2) South Essex Partnership, (3) Hertfordshire Partnership, (4) Norfolk and Waveney Mental Health, (5) East London, (6) West London Mental Health, (7) Central and North West London, (8) Sussex Partnership, (9) Norfolk and Suffolk NHS Foundation Trust, (10) Barnet Enfield and Haringey Mental Health Trust. In addition, we will advertise the study online (on facebook, twitter and websites from charities) and in newsletters. Patients will be diagnosed according to DSM-IV-TR criteria for OCD. All patients will be screened by a psychiatrist or clinician. As comorbid psychiatric disorders are prevalent in the OCD population, this level of screening is essential. During recruitment, it will be made clear to patients that not taking part will not affect their treatment in any way. Patients will be between the ages of 12 and 19.

Healthy volunteers will be recruited from Cambridge via local advertising. Participants will have read the information sheet explaining the study prior to arranging a time for testing, and they will have already expressed interest in participating in the study. All participants will be screened via telephone to ensure that they meet inclusion and do not have exclusion criteria. Likewise, it will be verified that participants are English speakers.

Written consent will be obtained from all participants prior to commencement of testing (see attached information sheet and consent form).

Inclusion criteria

All participating patients of the study will be between ages of 12 and 19 and it will be verified that participants are English speakers. To qualify for the OCD group, all subjects must meet the DSM-IV-TR diagnostic criteria for OCD, OCD must be their primary diagnosis, and they must score 12 or above on the Children's Yale-Brown Obsessive Compulsive Scale (Scahill et al., 1997).

Exclusion criteria

For all participants: excessive drug or alcohol use, neurological deficits or head injury. Apart from OCD, other significant Axis I mental disorders as diagnosed according to DSM-IV-TR criteria including psychosis, bipolar disorder, anxiety disorder other than OCD, Tourette's Syndrome, Attention-Deficit Hyperactivity Disorder, Asperger Syndrome/Autism Spectrum Disorders, and eating disorders will be exclusion criteria for this study. Participants in the OCD group will be excluded if their score on the Beck Depression Inventory for Youth indicates clinically significant depression. Severe physical impairments affecting eyesight or motor performance will also be exclusion criteria, as this may affect performance on the tasks.

Materials

Participants will be assessed by the researcher on the day of testing using the Beck Anxiety Inventory for Youth and the Beck Depression Inventory for Youth from the Beck Youth Inventories Second Edition (Beck, Beck, & Jolly, 2005), the Wechsler Abbreviated Scales of Intelligence – Second Edition (Wechsler, 2011), the Children's

Yale-Brown Obsessive Compulsive Scale (Scahill et al., 1997), and the Yale Global Tic Severity Scale (Leckman et al., 1989). All assessments are brief, requiring 15 to 20 minutes to complete.

We will then administer a cognitive battery consisting of 4 main tests. All tests will be administered on a computer. The first test will be a web-based Wisconsin-Card Sorting Task that has been administered to many patient groups in previous studies, including adolescent ones (Abbruzesse, Ferri and Scarone, 1995; Henry, 2006; Gruner and McKay, 2006).

The second test will be an adapted probabilistic learning task (Eisenegger et al., 2014). Variations of this task have been used on patients with OCD to test cognitive flexibility and probability learning (Chamberlain et al., 2006; Remijnse et al., 2006; Bon-Mi et al., 2008).

The third cognitive task will assess the relationship between decision-making and confidence in participants. This test was originally used by Vaghi et al. (2017) on a cohort of patients with OCD and healthy controls.

The last cognitive task will be a 4-arm bandit task adapted from a study by Daw, O'Doherty, Dayan, Seymour, and Dolan (2006) and Seymour et al. (2012). This will assess decision-making strategies.

This cognitive battery will take 1.5 hours in total to administer to each participant.

Procedure

Participants will be first approached by a Clinical Studies Officer (CSO) from the MHRN or by one of our local collaborators (a psychiatrist or clinician) at the site (see co-investigators) or they will approach the study team themselves after reading the

advertisement. Potential participants who are suitable for the study (see inclusion and exclusion criteria) and their parents/guardians, if under 16, will be asked if they are interested in taking part in a research study. Those who are interested will be given the appropriate Participant Information Sheet(s). After 48 hours, they will be contacted by telephone to address any questions and if they are interested they will be asked a few screening questions to ensure that they are suitable for the study. We will also verify that participants meet the inclusion and exclusion criteria listed above. Following the telephone interview, interested participants who meet the criteria for the study will be invited to participate and an appointment will be set up. Testing will take place: (1) at a pre-arranged, mutually convenient time; (2) in a private room within the Trust facility from which the participant was recruited (i.e. in the same building that the participant normally goes to for her/his clinic visits). Participants will be given the option to travel to Cambridge for testing. In that case, testing would take place in the Behavioural and Clinical Neuroscience Institute, where there are three designated testing rooms. If participants prefer not to travel, then the researcher will travel to the Trust facilities to conduct the testing session. All participants will be paid £24 for each session and will be reimbursed for travel expenses. On the day of testing, participants will be asked to sign the consent form attached. The following clinical scales will be administered in a semi-structured interview to participants by a trained researcher:

- Children's Yale-Brown Obsessive Compulsive Scale
- Yale Global Tic Severity Scale

The researcher will also administer the two-subtest form of the Wechsler Abbreviated Scales of Intelligence Second Edition to estimate general intellectual ability.

Participants will also complete the Beck Anxiety Inventory for Youth and the Beck Depression Inventory for Youth from the Beck Youth Inventories Second Edition. These questionnaires are very short, taking 5 to 10 minutes each.

While participants are seated in front of the computer, the cognitive tests will be administered. These computerized tasks are perceived as simple puzzles or games. For all tasks, performance will be measured by pressing a keyboard, a touchscreen, or a specialized button-box configured to register responses with millisecond accuracy. The computer will record accuracy and response times throughout each task.

At the end of testing, participants will be thanked, paid for their time, reimbursed for travel costs, and will be offered a chance to ask questions regarding the testing procedure and the study. In total, testing will be completed in a single session lasting approximately 3 hours. Participants will be compensated for their time at a rate of £24 for the session. Participants will also be compensated for travel expenses according with the University of Cambridge standard guidelines for travelling by car or the exact value of rail or bus transport.

Analysis

Performance data in all cognitive tasks consists of button presses, the timing of responses (in milliseconds), and the ratings given. Primary analyses will use analysis of variance to test for group differences. In addition, regression analyses will be conducted with cognitive performance measures as predictors of the anxiety, depression scores, and

symptom severity scores from the clinical scales/questionnaires. It is predicted that on some cognitive tests that have shown impairments in adult OCD, impairments will also be found in adolescent OCD. On other cognitive tests that have shown impairments in adult OCD, it may be the case that adolescent OCD will demonstrate performance that does not differ from that of age, gender, and IQ-matched controls.

Data Storage

All paper-and-pencil data together with the results of the computerised tasks will be made anonymous in order to ensure confidentiality, with patients being identified by a participant identification number only. Paper copies with any identifying information, such as names, will be kept to a minimum and stored in a locked filing cabinet in the Behavioural and Clinical Neuroscience Institute, Department of Experimental Psychology, University of Cambridge in accordance with the Data Protection Act and authorized by Derek Matthews, the department data protection officer. Electronic copies with any identifying information will be kept to a minimum and stored on university computers using password-protected encryption known only to key members of the research team.

Potential Benefits and Outcomes

This study may have important long-term consequences in assessing, understanding the development of, and treatment of obsessions and compulsive behaviors. However, the study will not have direct therapeutic benefits for the individual patients.

Finance/Costs

This study poses minimal finance costs. The study is financed by a Wellcome Trust Programme Grant.

Audit Procedures

All questionnaire and computer data will be saved and made available to audit. Behavioural data from the computerized tasks is recorded automatically, with result files including considerable amounts of numerical data. Summary variables are also automatically generated by existing computer programs. A random selection (10%) of the outcome variables will be cross-checked against the raw data by the PI.

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