University of Birmingham

SCHOOL OF PSYCHOLOGY

MSc Brain Imaging and Cognitive Neuroscience

Assessment and Feedback Template

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Module title:	**Proposing Research in Psychology**
Assessment:	**Methods and Planned Analysis**

Inhibiting the right temporoparietal junction triggers diametric effects of autism and psychosis traits on mentalizing

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Participants

Thirty right-handed adults aged 18+ with no history of neurological disease, psychiatric disorders or epilepsy will be recruited from the Birmingham community. Participants will complete MRI and TMS safety screening questionnaires and will be assessed in autism and psychosis traits. Subjects who meet the inclusion criteria will be invited for an MRI scan and a subsequent TMS session. Participants who complete all three parts of the study will be reimbursed with a £20 Amazon voucher. Students from the University of Birmingham may alternatively choose 2.5 credits as compensation. The University of Birmingham Research Ethics Committee approved the study and written informed consent will be obtained from all subjects.

Resources

Autism traits and psychosis proneness assessment

The positive scale of the Community Assessment of Psychic Experiences (CAPEp) questionnaire (Stefanis et al., 2002) will be used to assess psychosis proneness. Autism tendencies will be assessed using the Autism-Spectrum Quotient (AQ) questionnaire (Baron-Cohen et al., 2001a). Both CAPEp and AQ have shown high internal consistency, test-retest reliability (Baron-Cohen et al., 2001b), and have proven to be, respectively, very effective tools for discriminating between autism and psychosis proneness in neurotypical population (Abu-Akel et al., 2017a; Abu-Akel et al., 2017b; Donaldson et al., 2018). Higher scores on AQ and CAPEp indicate greater degrees of traits expression.

Repetitive Transcranial Magnetic Stimulation (rTMS)

Prior to the TMS session, structural T1-weighted MRI scans will be obtained to localise the target region in each individual brain.

A figure-of-eight coil (70-mm wing diameter) connected to a MagStim Rapid stimulator (MagStim) will be positioned over either Cz (the control site: 10-20 EEG coordinate system) or the right ventral posterior temporoparietal junction (rvpTPJ). The coordinates for the rvpTPJ (in MNI space: x = 54, y = -55, z = 26) will be taken from Mars et al. (2012) and will be used based on a previous study conducted by Abu-Akel et al. (2017b), that found significant activation of this area in psychosis-prone individuals using fMRI during a mentalizing task. The rvpTPJ mask will be transformed from MNI space to each participant's individual space and superimposed on their high-resolution T1-weighted MR image. Coil position will be determined using the Brainsight neuronavigation system (Rogue Research, Montreal, Canada). Stimulation will be given at a frequency of 1 Hz and at 60% of the stimulator's maximum output for a period of 10 minutes. The rTMS train frequency, intensity, and duration will be well within safe limits (Wassermann, 1998).

Movie for the Assessment of Social Cognition (MASC) task

Theory of mind will be assessed with the English version of the MASC (Dziobek et al., 2006). The MASC is a 15-min movie about four people spending an evening together. It presents social situations involving misunderstandings, sarcasm, ambiguous body language and flirtation between the four characters. The video is paused 45 times and participants are presented with multiple choice (4 options) questions about the mental states, emotions, thoughts or intentions of the characters (see Figure 1). There is only one correct answer and three types of errors: overmentalizing errors, undermentalizing errors and absence of mentalizing. Higher scores on the correct response scale indicate increased mentalizing ability, while higher scores on the other three scales represent greater mentalizing difficulties. The instrument has reported adequate psychometric properties (Dziobek et al, 2006, Lahera et al. 2014) and has been shown to discriminate well between healthy controls and patients with schizophrenia (Fretland et al. 2015; Montag et al. 2011), and ASD (Dziobek et al., 2006;

Lahera et al. 2014; Müller et al. 2016); and among neurotypical population with low and high levels of ASD traits (Gökçen, Frederickson and Petrides, 2016).

Figure 1. Item 1 of the MASC task. Option *a* represents absence of mentalizing, option *b* is undermentalizing, option *c* is overmentalizing and option *d* is the correct response.

Design and Procedure

Participants will complete the AQ and CAPE questionnaires, as well as the TMS and MRI safety screening questionnaires. Eligible subjects will be assigned to the ASD-prone or SSD-prone groups and will be invited for the MRI scan and the two TMS sessions. The order of stimulation sites (Cz and rvpTPJ) will be counterbalanced across participants and the sessions will be separated by a minimum of 24 hours.

The MASC task needs to be adapted to the TMS protocol. To this end, the task will be split into two parts. The first 23 (out of 45) items will be presented in the first TMS session and the remaining 22 will be presented in the second session. In addition, the response time for each item will be restricted to a maximum of 20 seconds, to ensure that subjects respond to the questions while the effects of the rvpTPJ stimulation are still present in the brain. As a result, each part of the task will last approximately 8 minutes.

Participants will undergo 10 minutes of stimulation and immediately after will be given headphones and will complete the adapted version of the MASC task in a PC. The responses will be automatically recorded.

Data analysis

MRI data analysis will be carried out using FSL (FMRIBS's Software Library, fsl.fmrib.ox.ac.uk, version 6.0.1; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). The T1-weighted structural image will be transformed from each participant's native space to standard MNI space using FLIRT (FMRIB's Linear Image Registration Tool; Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001). The mask of the rvpTPJ (fig. X) will be added and finally the T1 image and mask will be transformed back to native space to be used during the neuronavigation process.

A power analysis will be carried out using G*Power version 3.1 to deal with type II errors and determine the minimum sample size needed.

A bias score between the standardised total AQ and CAPEp scores will be calculated (zAQ – zCAPEp) and obtaining a minimum value of |0.7| will be set as inclusion criteria. Participants with a bias towards AQ (> 0.7) will be assigned to the ASD-prone group and those with a bias towards CAPEp (< -0.7) will be part of the SSD-prone group.

SPSS version 26 (IBM Corporation) will be used to analyse the data and to contrast the proposed hypotheses. First, the scores on the four scales of the MASC (correct scale and three types of error) will be obtained for each participant. Descriptive statistics (Mean, Standard Deviation, minimum and maximum) of the scales and the internal consistency of the MASC (cronbach's alpha) will be calculated; and outliers (2.5 SD) will be removed. Parametric assumptions will be assessed with Kolmogorov-Smirnov test for normal

distribution and Levene's test for homoscedasticity. In case they are not violated[1], four mixed ANOVAs will be carried out, one for each MASC scale (dependent variable), with the TMS condition (Cz vs rvpTPJ stimulation) as the within-subject factor and the bias score (< -0.7 vs > 0.7) as the between-subject factor; to check if there is an interaction between this two factors on the dependent variable. If statistically significant interactions are found post-hoc Games-Howell test will be carried out for multiple comparisons.

Predicted Results

The diametric model of ASD and SSD places this two disorders in opposite extremes of the theory-of-mind continuum, where ASD is associated with undermentalizing (Gökçen et al., 2016) and SSD with overmentalizing (Crespi & Badcock, 2008; Fretland et al., 2015). In addition, several studies have shown that subjects with high levels of traits in one disorder and low on the other disorder (i.e. bias scores used in this study) experience more difficulties on social cognition tasks performance (Abu-Akel et al., 2015; Abu-Akel et al., 2017b, Crespi & Badcock, 2008). In consonance with the diametric model it will be hypothesised, in the first place, that the SSD group will have significantly higher scores on the overmentalizing scale of the MASC compare to the ASD group. The second hypothesis will be that the ASD group will have significantly higher scores on the undermentalizing and absence of mentalizing scales. It will also be proposed that the SSD group will have significantly higher scores on the overmentalizing and correct responses scales in the Cz condition compare to the rvpTPJ condition (supporting the role of the rvpTPJ during mentalizing in psychosis prone individuals), while there will be no significant differences in the ASD group. Predicted results for each scale are shown in Figures 2 to 5.

[1] In case the parametric assumptions are violated non-parametric Kruskal-Wallis test will be performed.

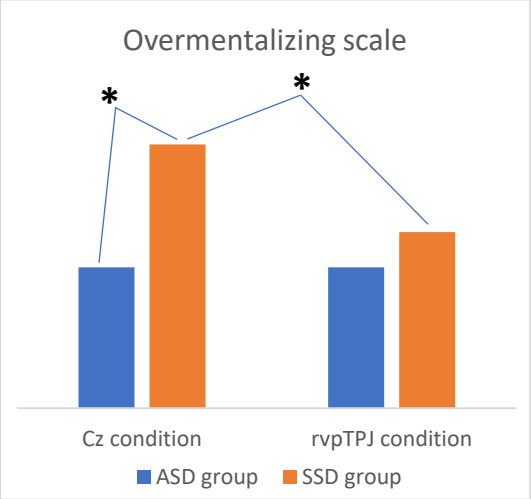

Figure 2. Predicted interactions between groups and stimulation condition on the overmentalizing scale. Significantly different scores represented with: *

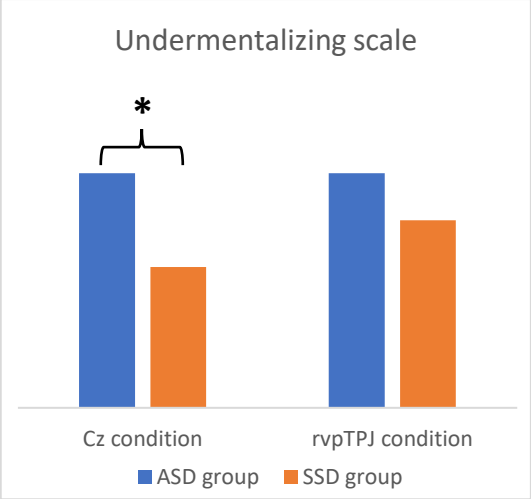

Figure 3. Predicted interactions between groups and stimulation condition on the undermentalizing scale.

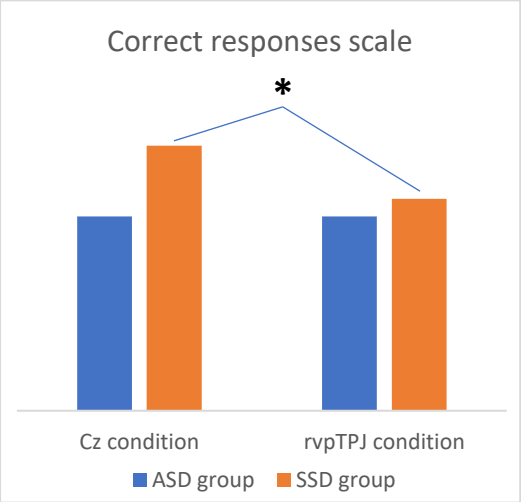

Figure 4. Predicted interactions between groups and stimulation condition on the correct responses scale.

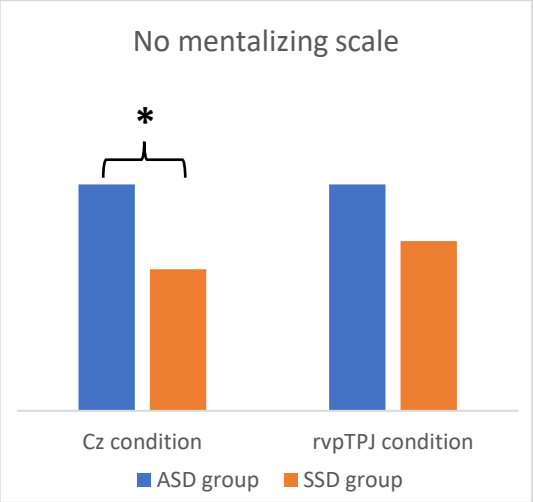

Figure 5. Predicted interactions between groups and stimulation condition on the absence of mentalizing scale.

This study aims to expand the available literature on the brain activity underpinning ToM in ASD and SSD. The potential findings would provide scientific evidence to support the relatively young diametric model. Moreover, this type of research has substantial long-term implications, as it lays the groundwork for more accurate diagnosis and more effective treatments for these disorders.

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