Functional connectivity gradients and thought-patterns in schizophrenia - negative symptoms

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Introduction

Ongoing thought-patterns and their association with macroscale neural connectivity patterns known as "gradients" [1] have been investigated in healthy populations [2]. In our study, we characterized thought-patterns and connectivity gradients in patients with schizophrenia (SZP) with predominantly negative symptoms and compared them to healthy controls (HC).

Figure 1: Different thought patterns between SZP and HC

Figure 1: Upper row: Three thought pattern components (TP) that differ between the groups. Lower line: Group differences based on TP scores. TP1: Episodic social thoughts [*t*(141)=-2.18, *p*=.03]. TP2: Intrusive and negative thoughts [*t(141)* = 3.53, *p* =.00]. TP6: Abstract spontaneous thoughts [*t(141)*= -2.45, *p*=.01]. Font size describes the influence; ink color indicates the polarity (red = positive, blue = negative).

Figure 2: Group differences of gradient 1 & 2

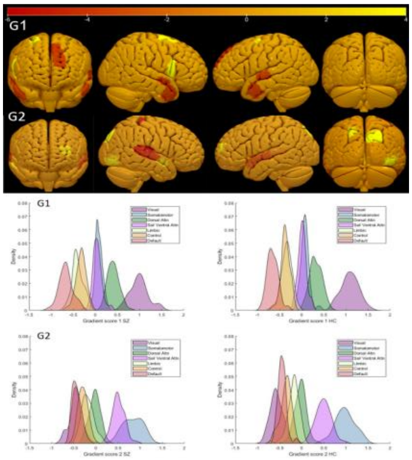

Figure 2: Upper row: surface images of G1 and G2 based on group comparison t-test values. Two lower lines: Density maps (Y-axis; Probability density estimation of participants) of the seven networks in G1 (up) and G2 (down) based on gradient score (X-axis) in the two groups (SZP left, HC right).

Methods

77 SZP and 66 HC matched for age and sex underwent a 9.8-min resting-state fMRI scan followed by Multi-Dimensional Experience Sampling [MDES; 3] to describe their thoughts during the scan. We extracted six thought-pattern components (TPs) using Principal Component Analysis (PCA) and created cortical connectivity gradients with BrainSpace [4] based on Schaefer-400-parcellated resting state data [5]. All TPs and gradients were compared between SZP and HC, controlling for age, motion, and gender. The first three gradient scores for each of the 400 parcels were used as dependent variables in 400 separate linear regression models, corrected for False Discovery Rate. Finally, associations were then examined between the TPs and parcels that differed significantly between SZP and HC.

Results

The SZP had significantly lower scores in TP1 (episodic social thought) [t(141)=-2.18, p=.03] and TP6 (abstract spontaneous thought) [t(141)= -2.45, p=.01], and higher scores in TP2 (intrusive and negative thoughts) [t(141) = 3.53, p =.00] (Fig. 1).

Among the three gradients, 39 parcels differed between the groups [pFDR1200<0.025], mainly from DMN, visual, somatomotor, and attentional networks, particularly from G1 and G2. G1 showed 15 parcels differed between groups, mainly from the DMN, with SZP presenting a more segregated pattern [all pFDR≤.02, t(138)≤ -3.5]. G2 differed for 21 parcels, mainly from DMN, visual, and somatomotor, indicating a shorter gradient for SZP, with less segregation of connectivity patterns between the negative pole of visual parcels (with more positive values in SZP *[all pFDR≤.01, t(138)≥3.54]*), with the DMN parcels (with more negative values in SZP *[all pFDR≤.01, t(138)≤ -3.53]*) (Fig. 2).

Significant correlations between gradient scores in parcels with group differences were observed for G2 with TP1 in the visual network *[all r(143)≤ -.17, p=.04]* and the somatomotor network *[all r(143)≥.18, p≤.03)*, indicating higher values of the visual network and lower values of the somatomotor associated with less episodic social thought and more thoughts about 'here and now.' TP6 presented a positive correlation with G2 with parcels from the DMN *[all (143)≥0.18, p≤ 0.03]* and the somatomotor network *[all r(143)≥.21, p≤ .01]*, i.e., an association between lower scores in the DMN and somatomotor parcels to less abstract spontaneous thoughts.

Discussion

Our findings showed that TPs and brain organization differed between HC and SZP for the first time using gradient analyses in SZ. Among SZP, a pattern of DMN segregation from the rest of the networks, including the visual network at the other edge, was found in G1. A prior study in HC presented more detailed thoughts in different contexts among participants with a stronger coupling of the visual and the DMN [6]. Attentional networks in SZP resemble more the visual network and have less similarity with DMN in G1; this fits findings from SZ studies with a focus on salience network-DMN connectivity [7,8].

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