Preliminary evidence for abnormalities of the peripersonal space network in adolescents with psychosis

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Introduction

- Negative symptoms of psychosis, such as anhedonia and social withdrawal, are some of the most impairing symptoms of psychotic disorders.
- Identifying neurobiological correlates of negative symptoms may be used as objective markers to track symptom emergence and treatment response.
- “Personal space” i.e. greater preferred physical distance from others is enlarged in psychosis and correlated with negative symptoms.
- Functional MRI studies have found that a parietofrontal cortical network of brain regions (the peripersonal space (PPS) network) which is engaged during intrusions into personal space may be overactive in schizophrenia, and the magnitude of this activity correlates with the personal space enlargement seen in these patients.
- The PPS network consists of left and right superior parietal, superior frontal and medial parietal cortices.
- The central question of this ongoing study is: Does increased personal space size and activation of the PPS network emerge over time in psychosis, or is it an early (pre-existing) marker of psychosis pathophysiology?
- Studying individuals with psychotic illness early in their illness course (i.e. in adolescence) may shed light on this question.

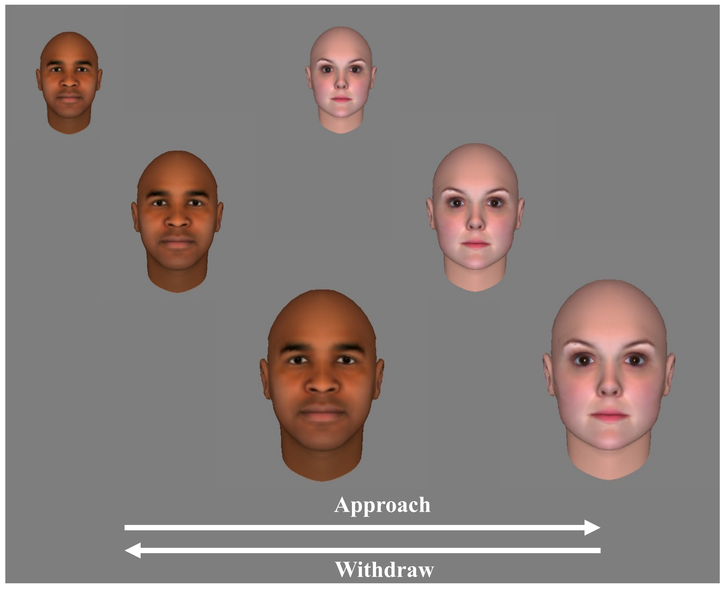
Methods

Sample:

- In a preliminary pilot sample of this ongoing study, data were collected from seven adolescents (ages 14-17, 5 females), including four with diagnoses of psychotic disorders (x with Schizophrenia, y with Psychosis NOS), two healthy controls, and one sibling of an individual with psychosis. We measured responses of the PPS network using fMRI. During the scans, participants viewed images of male and female faces that appeared to either approach or withdraw from them. Personal space was also measured.

fMRI data acquisition:

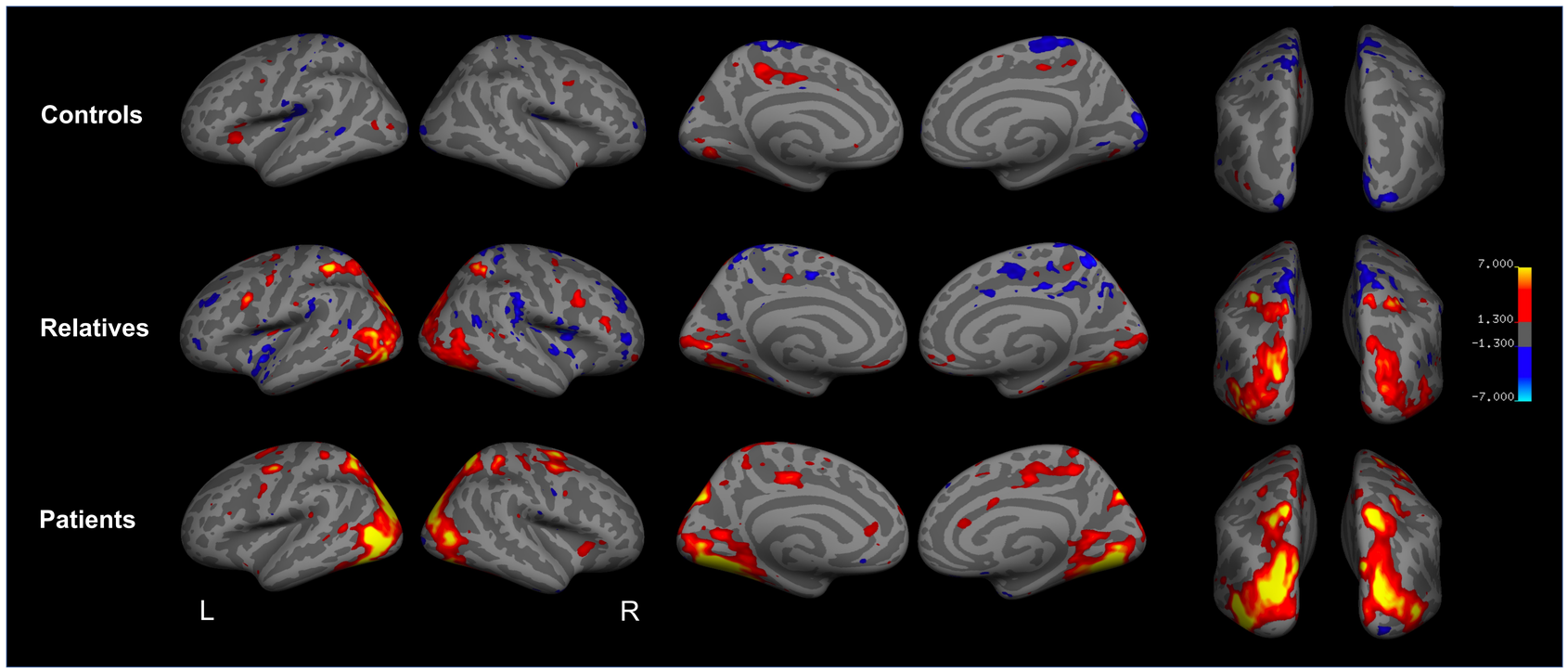
- Eight 4 min, 30-second-long BOLD scans were collected in each subject (with 180 time points, 2.5 mm isotropic voxels, TR = 1600 ms, TE = 30 ms, FA = 65º, FOV = 230 mm) from a 3T Prisma MRI scanner.
- During the collection of BOLD data, subjects viewed computer generated, realistic appearing male and female faces with neutral expressions, that appeared to either approach or withdraw from the subject in 16-seconds blocks, at a rate equivalent to a speed of 112 cm/sec – a typical speed for walking. During these scans, participants performed a dummy attention task (see Holt et al, 2014, 2016 and Nasiriavanaki et al, 2021 for additional details).
- Main effect cortical surface maps were made using the contrast of Face Approach > Face Withdrawal using Freesurfer software.

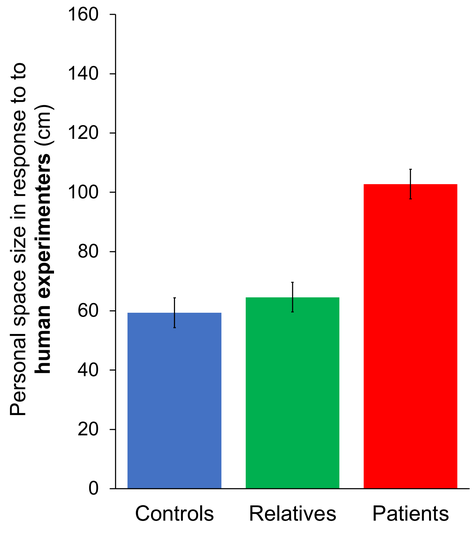


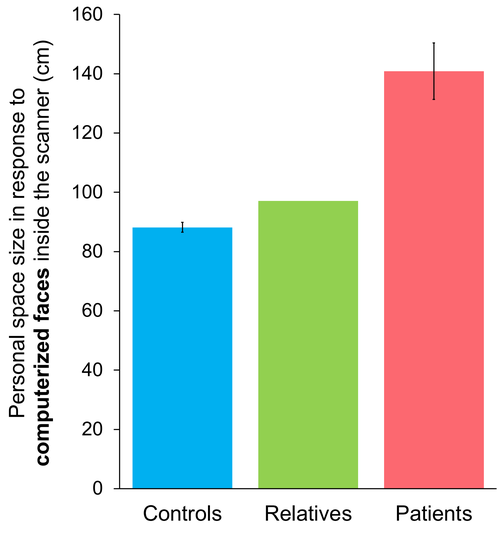
Examples of the female and male face stimuli in the fMRI experiment.

Results

Main effect cortical surface maps showing areas of significant ($p < 0.05$) activation in response to Faces Approach versus Faces Withdrawal.
As shown in the maps, the adolescents with psychosis (n=4) appeared to show greater activation of the PPS network compared to the healthy control adolescents (n=2).
The adolescent sibling (n=1) appeared to show an intermediate level of activation (with greater activation than the controls but lower activation than the patients).







- In this pilot, preliminary sample, the adolescents with psychosis showed a larger personal space size in response to real humans (Distance 1, D1), compared to the healthy control adolescents (mean $D1_{\text{psychosis patients}}$ = 102.76 cm vs. mean $D1_{\text{controls}}$ = 59.37 cm). The adolescent sibling had intermediate values, with a larger personal space size than the control means but lower values than the patient means (mean $D1_{\text{sibling}}$= 64.62 cm).
- Response to computerized faces insides the scanner showed a similar pattern of response (mean $D1_{\text{psychosis patients}}$ = 140.87 cm vs. mean $D1_{\text{controls}}$ = 88.16 cm vs. mean $D1_{\text{sibling}}$= 97.02 cm).

Conclusions and Future Directions

- These preliminary results suggest that adolescents with psychosis exhibit enlargement of personal space and overactivity of the PPS network to personal space intrusions, similar to adults with psychosis.
- Evidence of increased activation of the PPS network early in the course of psychotic disorders suggests that PPS network alterations may underlie early social deficits in psychotic disorders.
- Future analyses will examine the relationships between personal space, activity of the PPS network and the emergence or worsening of negative symptoms, using a longitudinal design.

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