Neural Correlates of Variation in Personal Space and Social Functioning in Schizophrenia and Healthy Individuals

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Background: Changes in the regulation of interpersonal distance, or “personal space” (PS), have been repeatedly observed in schizophrenia and, in some studies, linked to negative symptoms. However, the neurobiological basis of these impairments is poorly understood. Methods: Personal space measurements, functional connectivity of a brain network sensitive to intrusions into PS, and symptoms of social withdrawal and anhedonia were assessed, and associations among these outcomes measured, in 33 individuals with a psychotic disorder (primarily schizophrenia [SCZ]) and 36 control subjects (CON). Results: Personal space size was significantly higher (P = .002) and PS permeability (reflecting the capacity to tolerate intrusions into PS) was significantly lower (P = .021) in the SCZ relative to the CON group, and both measures were significantly correlated with social anhedonia and withdrawal in the full sample (all P < .007). Moreover, functional connectivity between the PS and default mode (DM) networks was significantly correlated with the permeability, but not the size, of PS in the full sample and in the SCZ and CON groups separately, and with social withdrawal in the SCZ group. Lastly, the association between PS-DM network connectivity and social withdrawal in the SCZ group was fully mediated by PS permeability. Discussion: Neural and behavioral aspects of PS regulation are linked to social motivation in both healthy individuals and those with psychotic disorders, suggesting that measurements of PS could serve as transdiagnostic markers of social functioning.

Key words: personal space/social anhedonia/negative symptoms/psychotic disorders/parietal cortex/default network

Introduction

Negative symptoms and the impairments in social functioning associated with schizophrenia are strong predictors of the day-to-day disability commonly observed in the disorder. Yet, the neurobiological mechanisms underlying these symptoms are poorly understood, hindering the development of effective treatments for them. However, there is some evidence that relatively automatic behaviors that are involved in social interactions, such as facial expressions, gestures, and eye movements, are altered in schizophrenia and may contribute to these symptoms. Thus, understanding the mechanisms underlying these abnormalities may lead to the development of new treatments that could improve social functioning in people with schizophrenia.

One such easily measurable behavior is the regulation of the physical space or distance maintained between individuals during social interactions, or “personal space” (PS). Numerous studies have shown that PS regulation is altered in some individuals with schizophrenia and may be linked to symptoms of the illness, including negative symptoms. However, it remains unclear whether these changes represent a contributing cause or a long-term consequence of having these symptoms.

The automatic regulation of PS during encounters with others is a form of nonverbal social communication, similar to facial expressions and other types of “body language.” Maintaining a greater distance from another person may signal respect or fear, whereas smaller distances have been linked to greater intimacy and affiliation. These nonverbal messages can also convey an understanding of social norms.

Although features of PS are sensitive to context-dependent or environmental influences, PS size and “permeability” (the capacity to tolerate PS intrusions) also have a relatively fixed, “trait-level” component following adolescence. These stable features of PS vary substantially across individuals and can be measured reliably in controlled laboratory settings.
Although the neurophysiological basis of PS (as defined as the “comfort zone” required when interacting with others) has been little studied, the related concept of “peripersonal space” (PPS), defined as the space surrounding the body in which physical actions of an individual can occur, has been studied extensively in both nonhuman primates and humans. A network of parietal and frontal cortical regions (the PPS network) increases its activity in response to a range of sensory stimuli (visual, tactile, and auditory) near or approaching the body. Also, stimulation of neurons within regions of the PPS network can generate stereotyped, defensive motor responses to such stimuli. Recent studies have also shown that the 2 primary nodes of this PPS network, the dorsal parietal cortex and the ventral premotor cortex, increase their activity in response to images of human faces that appear to cross into PS, suggesting that the regulation of PS boundaries may also rely on the PPS network.

In addition, associations between the magnitude of functional connectivity between the dorsal parietal and ventral premotor cortices (and the connectivity of the dorsal parietal cortex with the anti-correlated default network) and the size and permeability of PS have been observed in healthy subjects as well as in individuals with schizophrenia, and negative symptom severity in schizophrenia has been linked with PS enlargement and the strength of parietal-frontal connectivity.

Thus, based on these previous findings, in the current study, we examined clinical, behavioral, and resting-state connectivity functional magnetic resonance imaging (fMRI) data in order to test the hypothesis that characteristics of PS (ie, its size and permeability) in humans are linked to variation in (1) functional connectivity of a network of parietal and frontal regions sensitive to PS intrusions and (2) social functioning. Because we found similar relationships among these measures in healthy and schizophrenia groups previously, we used a transdiagnostic (Research Domain Criteria [RDoC]-informed) dimensional approach in our primary analysis, testing our main hypotheses in the combined schizophrenia and healthy sample. We tested the prediction that a greater size and lower permeability of PS are linked to: (1) greater impairment in social functioning (ie, higher levels of social anhedonia and withdrawal) and (2) poorer connectivity of a PS-sensitive network.

**Methods**

**Participants**

Healthy control subjects without psychiatric illnesses were recruited via advertisement, and patients treated in the Massachusetts General Hospital (MGH) Psychosis Clinical and Research Program who met diagnostic criteria for schizophrenia, schizoaffective disorder, or another non-affective psychotic disorder were invited to participate in this study. For all subjects, exclusion criteria included having any chronic medical or neurological illness, an IQ lower than 80, active substance abuse within the previous 3 months, or any contraindications for having an MRI scan. Written informed consent was obtained from all subjects prior to enrollment, and all procedures were approved by the Mass General Brigham Institutional Review Board. The healthy control group (CON) and the psychotic disorder/schizophrenia spectrum group (SCZ) were matched for sex, age, and socioeconomic status (table 1).

**Measures**

**Symptoms.** We focused on social withdrawal and social anhedonia as indicators of social functioning and motivation. In all participants, social withdrawal was measured using the self-report Time Alone Questionnaire (TAQ), and social anhedonia was measured using the Chapman Social Anhedonia Scale-Revised (SAS-R). In addition, in the SCZ group, the Positive and Negative Syndrome Scale (PANSS) was used to assess the positive and negative symptoms of schizophrenia and social withdrawal specifically (with the passive social withdrawal item). See Supplementary Methods for additional details.

**Personal Space.** The size and permeability of PS size were measured using the well-validated and reliable (kappa ~0.8) Stop Distance Procedure (SDP) (supplementary figure 1). This procedure begins with the subject and an “experimenter” (typically a research assistant) standing 3 meters apart. The experimenter walks slowly toward the subject while maintaining eye contact and a neutral facial expression. The subject is instructed to say “stop” at 2 different distances. The first is when the experimenter reaches the distance preferred by the subject when encountering someone they have not met previously, distance 1 (D1, PS size). The experimenter then continues to walk slowly toward the subject, who says “stop” again when their PS boundary has been crossed, at distance 2 (D2). The ratio of D1 and D2 (100 − ((D2 * 100)/D1)) is a measure of the subject's level of reactivity to PS intrusions, the “permeability” of PS. The SDP was conducted with both male and female experimenters (in a counterbalanced order across subjects).

**MRI Data Collection and Analysis Procedures**

**Data Collection.** In total, 34 individuals with a DSM-V diagnosis of a non-affective psychotic disorder (31 with schizophrenia, 1 with schizoaffective disorder, and 2 with Psychosis not otherwise specified [NOS], referred to as the “schizophrenia group” [SCZ]) and 36 healthy control subjects participated in a single scan session. MRI data were collected using a 3T Siemens Tim Trio MRI scanner (Erlangen) with a 32-channel head coil. Among other scans, one T1 anatomical scan (spatial resolution 1 mm isotropic, repetition time (TR) = 2530 ms, echo
Table 1. Demographic and Clinical Characteristics of the Subjects

|                        | CON (n = 36) | SCZ (n = 33) | Group Comparison Test P-value |
|------------------------|--------------|--------------|-------------------------------|
| Sex (% male)           | 61.10        | 66.70        | .632                          |
| Age (y)                | 28.94 (5.83) | 29.97 (6.02) | .475                          |
| Parental education (y) | 15.96 (2.75) | 14.92 (3.74) | .194                          |
| IQ                     | 107.21 (9.81)| 103.69 (10.51)| .185                          |
| Personal space size (cm)| 52.53 (25.75)| 78.61 (41.69)| .003                          |
| Personal space permeability (%)| 67.12 (17.54)| 57.84 (14.82)| .021                          |
| Social anhedonia       | 5.75 (3.70)  | 12.70 (8.10) | <.001                         |
| Social withdrawal (%)  | 35.61 (17.27)| 58.54 (24.75)| <.001                         |
| PANSS total            |              | 66.91 (2.76) |                               |
| PANSS Positive Symptom Subscale |       | 16.30 (0.99) |                               |
| PANSS Negative Symptom Subscale |       | 18.24 (0.91) |                               |
| PANSS Passive Social Withdrawal |       | 3.30 (1.65)  |                               |
| PANSS General Symptom Subscale |       | 32.36 (1.34) |                               |
| CPZ equivalents        |              | 470.0 (57.90)|                               |

Note: Variables listed include gender (percentage of males) in the control and schizophrenia groups, with the P-value of the between-group comparison (chi-square), and average (mean (standard deviation)) age (y), parental education (y), IQ (the American National Adult Reading Test score), personal space size (centimeters), personal space permeability (percentage), social anhedonia (the Chapman Social Anhedonia Scale-Revised Total Score), and social withdrawal (the Time Alone Questionnaire score (percentage of time preferred alone)) of the 2 groups, with P-values of the between-group comparisons (independent t-tests) of these measures. Average (mean (standard deviation)) scores of the Positive and Negative Syndrome Scale (Total and Positive, Negative, and General subscales, and the Social Withdrawal item score) and chlorpromazine equivalents for the schizophrenia group are also listed. CON, control group; SCZ, schizophrenia group; PANSS, Positive and Negative Syndrome Scale; CPZ, chlorpromazine equivalents.

Correlational and Mediation Analyses

Independent samples t-tests were used to test for differences between the two groups. Pearson’s correlations were used to assess associations between the PS, symptom, and connectivity measures. Correlations were first assessed in the full cohort, followed by separate analyses in the 2 subject groups, given prior evidence for the predicted associations in both schizophrenia and healthy populations and our primary dimensional hypothesis. In follow-up sensitivity analyses using linear regressions, we controlled for group membership to assess whether the effects in the full cohort were driven by group differences. Pearson correlation coefficients (r) are reported for bivariate analyses, and standardized beta coefficients (β) are reported for multivariate sensitivity analyses.

In addition, based on the correlations identified, a simple mediation model was tested using the PROCESS macro for SPSS. This approach employs bias-corrected bootstrap confidence intervals as a measure of the indirect effect of a mediation. With this approach, if zero is not contained in the confidence interval, the indirect effect is considered significant.

Results

Behavioral and Symptom Measures

Between-Group Comparisons. Means for each group are listed in Table 1. The size of PS was significantly larger (t(52.4) = −3.093, P = .003), and the permeability of PS was significantly lower (t(67) = 2.363, P = .021) in the SCZ compared with the CON group, and there was

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time (TE) = 1.64 ms, flip angle 7°) and one 6-minute, 20-second-long resting-state blood oxygenation level-dependent (BOLD) scan (3 mm isotropic, 124 slices, TR = 3000 ms, TE = 30 ms, flip angle 85°) were collected and used in the current analyses.

Data Analyses. All brain images were visually inspected for brain coverage and proper registration. Only resting-state BOLD data with a signal-to-noise (SNR) ratio >125 were included in the analyses. All the MRI data were analyzed using FreeSurfer version 6.0 (http://surfer.nmr.mgh.harvard.edu). The regions of interest used in the functional connectivity analyses were delineated in an independent dataset (n = 130), in which fMRI data were collected using a paradigm in which human faces appearing to move toward or away from the subject are presented.43,50 Areas of the brain that responded preferentially to the faces that approach (vs withdraw from) the subject were identified as nodes of a PS-intrusion sensitive network. This network is highly overlapping with the well-characterized PPS network that has been characterized by its responses to multisensory stimuli close to, approaching, or on the body.42,43,50 See Supplementary Methods for further details about the quality control procedures, preprocessing stream, and the construction of the regions of interest/seeds used in the functional connectivity analyses (also see supplementary figure 2 and supplementary tables 1 and 2). Based on previous work,10,42 3 functional connectivity measurements were calculated: (1) within-PS and (2) within-default mode (DM) network connectivity, and (3) connectivity between the PS and DM networks.
much variation in these measures within each group, as expected. Also, levels of social withdrawal and social anhedonia were significantly higher in the SCZ compared with the CON group ($t(67) = -4.495$, $P < .001$; $t(44.0) = -4.513$, $P < .001$, respectively).

Correlations in the Full Sample. In the full sample of subjects ($n = 69$), both the size and the permeability of PS were significantly correlated with both social withdrawal (size: $r = .408$, $P < .001$; permeability: $r = -.326$, $P = .006$) and social anhedonia (size: $r = .423$, $P < .001$; permeability: $r = -.380$, $P = .001$; figure 1; supplementary table 3). When controlling for group membership, these associations remained significant or near significant ($P = .012$ - .061; supplementary table 4).

Correlations in the Separate SCZ and CON Groups. In the CON group alone ($n = 36$), the size, but not the permeability, of PS correlated with social withdrawal (size: $r = .446$, $P = .006$; permeability: $r = -.253$, $P = .137$) but not with social anhedonia (size: $r = .278$, $P = .100$; permeability: $r = -.085$, $P = .623$).

In the SCZ group alone ($n = 33$), the permeability, but not the size, of PS correlated with: (1) social anhedonia (size: $r = .314$, $P = .076$; permeability: $r = -.463$, $P = .007$), (2) social withdrawal measured by the PANSS passive social withdrawal item (size: $r = .089$, $P = .622$; permeability: $r = -.503$, $P = .003$), and (3) total negative symptom severity (size: $r = .118$, $P = .51$; permeability: $r = -.501$, $P = .003$). See supplementary table 5 for additional details.

Lastly, additional secondary analyses conducted in the SCZ group revealed that there were no correlations between PS measures and positive symptom severity (size: $r = .083$, $P = .645$; permeability: $r = -.169$, $P = .348$), antipsychotic dose (size: $r = .024$, $P = .896$; permeability: $r = -.149$, $P = .407$), or duration of illness (size: $r = .218$, $P = .224$; permeability: $r = -.212$, $P = .235$).

PS and DM Network Resting-State Functional Connectivity

General Patterns of Within- and Between-Network Connectivity for the PS and DM Networks. In all groups,
significant within-PS or within-DM resting-state functional connectivity was reflected by positive correlations among the resting BOLD activity of regions within the PS or the DM network. However, the resting BOLD activity of the PS and DM networks were negatively correlated with one another (anti-correlated), as observed in previous studies\textsuperscript{10,42} (see figure 2A).

**Between-Group Comparisons.** There were no significant differences between the SCZ and CON groups in the overall average magnitude of within-network PS ($t(53.6) = −.537, P = .593$), within-network DM ($t(45.2) = 1.031, P = .308$), or between-network PS-DM ($t(67) = −.530, P = .598$) functional connectivity.

**Correlations.** The magnitude of the within-network connectivity of both the PS and the DM networks was not significantly correlated with either PS size or permeability, nor with social withdrawal or anhedonia in any of the 3 analyses (supplementary table 6).

However, in all 3 analyses (i.e., conducted in the full sample and the separate SCZ and CON samples), PS-DM between-network connectivity was significantly negatively correlated with PS permeability (full sample: $r = −.372, P = .002$; CON: $r = −.382, P = .02$; SCZ: $r = −.360, P = .04$; figures 2B–D). Specifically, since the resting-state activity of the PS and DM networks were anti-correlated overall, weaker PS-DM anti-correlations (resulting in a net positive correlation in a few cases) were linked to lower permeability of PS. When controlling for group membership, the association in the full sample remained significant ($P = .002$).

In addition, in the SCZ group alone, PS-DM connectivity correlated with levels of passive social withdrawal ($r = .362, P = .039$; supplementary figure 3). Thus, the weaker the PS-DM anti-correlation, the higher the level of passive social withdrawal in the SCZ subjects.

Lastly, there were no correlations between PS-DM connectivity and PS size, levels of positive symptoms, antipsychotic dose, or duration of illness (supplementary table 7).

**Mediation Model**

Given the significant correlations in the SCZ group among PS-DM connectivity, permeability, and passive social withdrawal, we tested the hypothesis that PS permeability mediates (M) the relationship between PS-DM connectivity.
connectivity (X) and passive social withdrawal (Y) in schizophrenia. Specifically, we tested for an indirect effect of PS-DM connectivity on passive social withdrawal, mediated by permeability.

Greater PS-DM connectivity (or weaker anti-correlations between these 2 networks) predicted lower PS permeability \((a = -15.112, P = .040)\), which then predicted greater social withdrawal \((b = -.050, P = .014)\) (figure 3). A bias-corrected bootstrap 95% confidence interval for this indirect effect \((ab = .7556)\) based on 5000 bootstrap samples did not contain zero \((.0395-.1.7628)\). Furthermore, there was a nonsignificant direct effect of PS-DM connectivity on passive social withdrawal \((c' = .970, P = .218)\), suggesting that PS permeability fully mediates the relationship between PS-DM connectivity and passive social withdrawal (supplementary table 8).

Discussion

Summary of Main Findings

In this study, PS was found to be, on average, larger and less permeable in individuals with schizophrenia compared with controls, generally consistent with previous findings.9–11,16 In addition, significant associations between both the size and permeability of PS and levels of social withdrawal and anhedonia were observed in the full (schizophrenia plus control) sample. Moreover, partially consistent with this pattern, the permeability, but not the size, of PS correlated with social withdrawal and social anhedonia, as well as overall negative symptom severity, in the schizophrenia group.

In addition, we found that weaker anti-correlations between a PS-sensitive network and the DM network were linked with lower PS permeability in the full sample and both groups separately, and with greater social withdrawal in the schizophrenia group. A subsequent mediation analysis revealed that the association between PS-DM network anti-correlations and social withdrawal in the schizophrenia group was fully mediated by PS permeability.

Taken together, these results suggest that variation in PS regulation may contribute to (or represent markers of) social withdrawal and social anhedonia. Moreover, the associations found here across the full sample are consistent with our previous findings of correlations among social withdrawal, PS-DM network connectivity, and PS permeability in an independent sample of healthy subjects.42 Thus, associations between PS regulation, the function of related neural circuitry, and social behavior and drive may be present in both healthy and clinical populations, although these relationships may differ across groups in magnitude and in their specific behavioral manifestations.

Abnormalities in PS in Schizophrenia

Our finding of a significantly larger size and lower permeability of PS in the schizophrenia group, compared with controls, is broadly consistent with previous findings,9,11,16 although, in our earlier, smaller study, group differences were only observed in PS size (not permeability).10 Given that the size and permeability of PS tend to be moderately negatively correlated across subjects, and there is a high degree of variation in PS measurements within both healthy and clinical populations, the specific effects detected in each sample may depend in part on other (eg, neurocognitive and clinical) characteristics of the individuals of that sample.

The permeability of PS is thought to represent a behavioral index of the arousal response that occurs as a person’s PS boundary is crossed.27 The current findings

![Fig. 3. Personal space permeability mediates the relationship between PS-DM network connectivity and social withdrawal in schizophrenia. Unstandardized coefficients and P-values of the hypothesized mediation model in the SCZ group \((n = 33)\) are shown. Path \(a\) shows the significant negative effect of PS-DM network connectivity on personal space permeability; path \(b\) shows the significant negative effect of personal space permeability on passive social withdrawal, after controlling for PS-DM network connectivity; and path \(c\) shows the significant positive total effect of PS-DM network connectivity on passive social withdrawal. Path \(c'\) shows the nonsignificant direct effect of this relationship after accounting for personal space permeability. Note: PS, personal space; DM, default mode; SCZ, schizophrenia group.](image-url)
suggest that some individuals with schizophrenia may exhibit elevated arousal responses during PS intrusions and have a more rigid PS boundary than control subjects. Higher arousal responses to PS intrusions could also reflect a less well-defined PS boundary.52

Some previous studies have used tasks that identify the boundaries of peri-personal space (PPS), often defined experimentally as the area around the body where multisensory facilitation of stimulus detection occurs,34,37 in individuals with schizophrenia and controls. Some of these studies have found evidence for a smaller PPS in schizophrenia relative to control subjects52,53 (but also see Noel et al.).54 One potential explanation for this apparent discrepancy with the evidence for enlarged PS in schizophrenia9–16 comes from several studies in healthy subjects which suggest that the size of PS and PPS may be influenced by situational factors (such as external threats and tool use) in opposite ways.55–57 One integrated model has proposed that PPS represents a “working space,” whereas PS serves as a “protective space”,58 and the mechanisms defining these spaces may be reciprocally regulated. For example, the size of the working space in which one can physically act (ie, PPS) may decrease when there is a need for a larger, protective zone of safety around the body (ie, PS). Additional studies in which these 2 constructs are measured in the same subjects under similar conditions will shed further light on how they are related to each other and affected in schizophrenia.

Links Between PS Permeability, Resting-State Functional Connectivity, and Social Withdrawal

The correlations between PS permeability and connectivity between the PS and DM networks were robust and highly consistent (ie, found in all cohorts), suggesting that interactions between these 2 networks play a central role in the generation of arousal responses to PS intrusions. Moreover, the mediation of the association between PS-DM network connectivity and social withdrawal in the schizophrenia group by PS permeability suggests that one way that the interactions between these 2 networks impact social behavior is via PS regulation. Moreover, changes in PS observed in autism-spectrum conditions59,60 and in association with loneliness in healthy subjects61 suggest that a wide range of social impairments may be linked to altered PS regulation and the associated neural manifestations.

Coupling Between the PS-Sensitive and DM Networks

The activity of “task-positive” networks involved in attending to the environment is diminished when attention is directed toward internally generated information, when the reciprocally engaged DM network increases its activity.62–64 Consistent with this overall pattern, the magnitude of activity of the PS and DM networks is negatively correlated during both tasks and resting states.10,42,43

The degree of anti-correlated activity between task-positive and task-negative networks has been linked to cognitive functioning in previous studies. For example, greater deactivation of the DM network during attention-demanding tasks has been associated with better task performance.55,66 Reduced task-related suppression of the DM network and correspondingly poorer task performance67,68 and weaker anti-correlations between the DM and task-positive networks69,70 have been observed in people with schizophrenia and in those who are at risk for developing psychosis.71 Also, weaker anti-correlations between the DM and task-positive networks have been observed in first-degree relatives of people with schizophrenia,70 suggesting that poorer differentiation of these reciprocally opposing systems in psychotic disorders may have a genetic basis and could serve as a marker of risk for psychosis.

Limitations and Future Directions

The interpretation of these findings must be considered in light of several limitations of this study, such as its cross-sectional design, which limits the inferences that can be drawn from the mediation analysis. Also, in future work, measurements of the functioning of parieto-frontal circuits that are anatomically near to the network involved in PS regulation, such as those involved in eye movements72–75 and gestures,76 which are behaviors that are also affected in schizophrenia,77–79 could be assessed in parallel to PS-related behaviors, to investigate the specificity of the effects observed in the current study. In addition, other processes that may contribute to the ability to distinguish the self from others and from the surrounding environment could be measured, since a wide range of abnormalities in this overall domain have been observed in psychotic individuals.80–83

Supplementary Material

Supplementary material is available at https://academic.oup.com/schizophreniabulletin/.

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