A study of physical anhedonia as a trait marker in schizophrenia

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Background: Inability to define the heritable phenotype might be a reason for failure to replicate results in psychiatric genetics. Hence, the use of a candidate symptom approach to identify more homogeneous forms of diseases among affected individuals and subclinical traits among first-degree relatives (FDRs) may increase genetic validity. The objective of the present study was to determine whether physical anhedonia can be used as a marker for individuals at risk of schizophrenia. Materials and Methods: Physical anhedonia scores (measured using Revised Physical Anhedonia Scale [rPAS]) were compared across thirty remitted schizophrenic patients, thirty of their unaffected FDRs, and thirty healthy controls. We compared anhedonia scores among the three main groups using one-way ANOVA. Results: Physical anhedonia (rPAS) scores of the schizophrenic patient group were significantly higher than that of their FDRs and controls both, and physical anhedonia (rPAS) scores of FDRs were significantly higher than that of healthy controls (F = 115.33, P < 0.001). The subgroups did not differ on various other clinical characteristics. Conclusion: Our data suggest that physical anhedonia is a candidate symptom for schizophrenia.

Keywords: Endophenotype, physical anhedonia, schizophrenia, trait marker

Psychiatry is not merely based on etiology, genetics, or response to medications, but also on gross behaviors that have imprecise similarity or correlation with each other; within and between individuals. Obstacles to the identification of genes underlying genetic vulnerability to schizophrenia disorders are largely associated with an inability to define the heritable phenotype.[1,2] Although reliable diagnostic criteria have been used in psychiatric genetics, little is known about how to choose the diagnostic system that best describes the most heritable form of the illness. Among apparently affected patients, various types of phenotypic misclassifications reduce the power of linkage and association studies because of phenocopies or genetic heterogeneity. Thus, unaffected individuals carrying vulnerability genotypes are not identified by the classical nosographical approaches.[3]

The endophenotype strategy uses state-versus-trait comparison of complex behaviors that are reduced into components (neurophysiological, cognitive, or neuropsychological).[3,4] These subclinical quantitative traits minimize the arbitrariness of categorical diagnoses and provide more power in linkage.[1,2] The first step in identifying a potential endophenotype marker is to demonstrate that a trait is more frequent in relatives of schizophrenic individuals than in healthy controls.[5-7]
It has been suggested that anhedonia is a marker for individuals at risk of schizophrenia.\[5-7]\, Moreover, physical anhedonia is known to be a more stable trait in schizophrenic patients than social anhedonia.\[8-10]\, Several studies have used the Chapman self-report questionnaire of physical anhedonia\[11]\, to assess anhedonia among relatives of schizophrenic probands and among relatives of controls. Five of these reports found that anhedonia was significantly more common among relatives of schizophrenic patients,\[12-16]\, whereas the rest did not.\[17,18]\, In the current study, after lifetime diagnostic assessment, along with superior methodology overcoming the limitations, on comparison of anhedonia as measured by Physical Anhedonia Scale (PAS) scores, in schizophrenic patients, their respective unaffected first-degree relatives (FDRs) and healthy controls were assessed.

**MATERIALS AND METHODS**

The present study was conducted at the Central Institute of Psychiatry, Ranchi, Jharkhand, India. It was a hospital-based cross-sectional study. During the study period, 88 patients were screened, of which thirty schizophrenic patients (S group) with their thirty FDRs (R group) fulfilling the inclusion and exclusion criteria were taken up for the study. We also recruited thirty age- and sex-matched healthy individuals in the control group.

**Inclusion criteria**

1. Diagnoses of schizophrenia according to the Diagnostic Criteria of Research, International Classification of Diseases-10\[19]\.
2. Scale for Assessment of Negative Symptoms (SANS) and Scale for Assessment of Positive Symptoms (SAPS) scores of <3 maintained over 6 months for each global item\[20]\.
3. Willing to give consent.

**Exclusion criteria of patients**

1. Any comorbid psychiatric illness
2. Any medical comorbidity or mental retardation.

Healthy FDRs and controls (N group) without any medical or psychiatric illness were selected. All participants were aged between 18 and 60 years and belonged to either sex.

**Assessment tools**

- A semi-structured sociodemographic and clinical data sheet
- Revised Physical Anhedonia Scale\[21]\, The PAS is a self-rating scale of 61 items with yes or no answers rated 0–1 with total ranging from 0 to 61. The PAS includes items concerning the experience of pleasures. In both patient and nonclinical samples, internal consistency and reliability were consistently very good, with alpha coefficients typically exceeding 0.80\[22]\.
- SAPS and SANS\[23]\, The SAPS, a 34-item scale used to assess positive symptoms in schizophrenia, is designed for use in conjunction with the 25-item SANS, which is used to assess negative symptoms; scoring ranges from 0 (no abnormality) to 5 (severe)
- Family Interview of Genetics Studies (FIGS)\[24]\, It was developed by the National Institute of Mental Health for systematically collecting information about relatives in family and genetic studies of the disorders
- Calgary Depression Rating Scale for Schizophrenia (CDSS)\[25]\, It is used specifically for the assessments of level of depression in schizophrenia. The scale has 9 items with scores ranging from 0 to 3. Items are scored on the basis of a semi-structured interview for the first 8 items and the 9th item is rated on the basis of observation during the interview
- Barnes Akathisia Rating Scale (BARS)\[26]\, Is a 4-item scale to assess the presence and severity of drug-induced akathisia. It includes both objective and subjective items. Global assessments are made on a scale of 0–5
- Simpson Angus Scale for Extrapyramidal Side Effects (SAS)\[27]\, It is a 10-item instrument used to measure the symptoms of parkinsonism or side effects related to the use of antipsychotic medications. The scale has items measuring rigidity, tremors, akinesia, etc., This has 10 items rated on a 5-point scale
- General Health Questionnaire-12\[28]\, It is a self-administered screening test which is sensitive to the presence of psychiatric disorders containing 12 items. It is used to screen FDRs and controls.

**Procedure**

Individuals fulfilling inclusion and exclusion criteria and those who gave consent were taken. Participants were assessed on SANS and SAPS, CDSS, BARS, and SAS, and those who had SANS and SAPS scores of <3 maintained over 6 months for each global item\[20]\, were included, whereas those who had scores of 2 or more in BARS or score of >0.3 in SAS were excluded. In addition, patients having current depressive episode as per CDSS were excluded. Following this procedure, thirty individuals were taken and further assessed on PAS.

Familial psychiatric morbidity was assessed by FIGS\[24]\, A complete family history of FDRs was obtained from each proband and from at least one FDR. Healthy controls were assessed on GHQ 12. Then, FDRs and healthy controls were evaluated using the revised PAS (rPAS).
Statistical analysis
Besides descriptive statistics, between-group differences were tested with one-way ANOVA for continuous variables and using a Chi-square test for categorical variables. For correlation analysis, Pearson’s correlation coefficient ($r$) was used.

RESULTS
The comparison of various sociodemographic characteristics is summarized in Table 1. All the variables were comparable except for family type. Table 2 summarizes the clinical characteristics of patients with schizophrenia.

Comparison of anhedonia scores among schizophrenic patients, FDRs, and normal controls, using one-way ANOVA, is shown in Table 3. It was found that there was significant difference between each group, with schizophrenic patients scoring highest, healthy controls scoring the lowest, and scores of FDR group lying in between. Pearson’s correlation of rPAS scores with sociodemographic and clinical variables in patients with schizophrenia showed that BARS scores are positively correlated ($r = 0.506; P = 0.004$) with rPAS scores. Specifically, no significant correlation was found between rPAS score and antipsychotic dose (typical or atypical) ($r = 0.092; P = 0.630$) and between diagnosis (paranoid schizophrenia and other subgroups) and the rPAS scores.

DISCUSSION
As hypothesized, our patient population had higher anhedonia scores than relatives. Anhedonia rPAS (25.83 ± 8.23) scores in our patient population were similar to those for the schizophrenic population tested

Table 1: Comparison of sociodemographic characteristics between schizophrenia patients, FDR’s and normal controls

| Variables       | S* n=30 M±SD(n%) | R† n=30 M±SD(n%) | N‡ n=30 M±SD(n%) | F(χ²) | Df | P     |
|-----------------|------------------|------------------|------------------|--------|----|-------|
| Age             | 33.47±9.09       | 36.8±12.56       | 30.1±10.2        | 2.93   | 87 | 0.059 |
| Sex             |                   |                  |                  |        |    |       |
| Male            | 23 (76.7)         | 26 (86.7)        | 25 (83.3)        | 1.06   | 1  | 0.587 |
| Female          | 7 (23.3)          | 4 (13.3)         | 5 (16.7)         |        |    |       |
| Marital status  |                   |                  |                  |        |    |       |
| Married         | 18 (60)           | 20 (66.5)        | 16 (53.3)        | 1.11   | 1  | 0.574 |
| Single          | 12 (40)           | 10 (33.3)        | 14 (46.7)        |        |    |       |
| Religion        |                   |                  |                  |        |    |       |
| Hindu           | 26 (86.7)         | 26 (86.7)        | 26 (86.7)        | 0.00   | 1  | 1.000 |
| Others          | 4 (13.3)          | 4 (13.3)         | 4 (13.3)         |        |    |       |
| Caste           |                   |                  |                  |        |    |       |
| General         | 23 (76.7)         | 23 (76.7)        | 27 (90)          | 2.32   | 1  | 0.313 |
| Others          | 7 (23.3)          | 7 (23.3)         | 3 (10)           |        |    |       |
| Family set      |                   |                  |                  |        |    |       |
| Rural           | 15 (50)           | 11 (36.7)        | 14 (46.7)        | 1.968  | 2  | 0.742 |
| Suburban        | 5 (16.7)          | 5 (16.7)         | 3 (10)           |        |    |       |
| Urban           | 10 (33.3)         | 14 (46.7)        | 13 (43.3)        |        |    |       |
| Family type     |                   |                  |                  |        |    |       |
| Joint           | 27 (90)           | 27 (90)          | 20 (66.7)        | 7.45   | 1  | 0.024*|
| Nuclear         | 3 (10)            | 3 (10)           | 10 (33.3)        |        |    |       |
| Education       |                   |                  |                  |        |    |       |
| Below matric    | 9 (30)            | 8 (26.7)         | 12 (40)          | 1.32   | 1  | 0.516 |
| Others          | 21 (70)           | 22 (73.3)        | 18 (60)          |        |    |       |
| Occupation      |                   |                  |                  |        |    |       |
| Employed        | 17 (56.7)         | 22 (73.3)        | 20 (66.7)        | 3.79   | 2  | 0.436 |
| Unemployed      | 4 (13.3)          | 3 (10)           | 1 (3)            |        |    |       |
| Housewife student | 9 (30)       | 5 (16.7)         | 9 (30)           |        |    |       |
| Income          |                   |                  |                  |        |    |       |
| Low             | 14 (45.8)         | 11 (45.8)        | 10 (47.6)        | 1.72   | 1  | 0.423 |
| High            | 8 (26.4)          | 13 (45.2)        | 11 (52.4)        |        |    |       |

*P<.05 (2-tailed); *S=Schizophrenia patient; †R=FDR: First Degree Relative group; ‡N=Healthy control group
Table 3: Comparison of rPAS Scores between schizophrenia patients, FDR’s and normal controls

| Variables | S* n=30 M±SD | R † n=30 M±SD | N‡ n=30 M±SD | F | df | P | Post hoc (Bonferroni) |
|-----------|--------------|--------------|--------------|---|----|---|----------------------|
| rPAS      | 25.8±8.23    | 9.9±4.16     | 4.9±4.72     | 115.33 | 2,87 | <.001 | S>R>N |

***P<.001 (2-tailed); *S=Schizophrenia patient; †R=FDR. First Degree Relative group; ‡N=Healthy control group. \( rPAS. \) Revised Physical Anhedonia Score; FDR: first degree relatives

This finding could have been influenced by the presence of depressive symptoms or due to neuroleptic induction or exaggeration. Our patients were euthymic and did not have any depressive symptoms as evaluated by CDSS. Thus, anhedonia cannot be explained by the presence of depressive symptoms. In addition, in our study, there was no correlation found between rPAS score and antipsychotic dose, which is supported by a similar finding by other studies. This is supported by several prospective studies which have shown that anhedonia is a stable trait in schizophrenia and is independent of the treatment.

We found a positive correlation between BARS and rPAS scores. This finding implies that antipsychotic-induced akathisia may indeed be related to anhedonia. This finding does not gather support from other previous studies such as those by Kontaxakis et al. However, as explained by Alpert and Friedhoff and Freedman (1961), antipsychotic-induced dysfunction of the excitatory mechanisms (striatal dopamine excitatory receptors) is thought to be involved in hypertonic motor manifestations, whereas dysfunction of the inhibitory mechanisms (striatal dopamine inhibitory receptors) is thought to be involved in akathisia, dyskinesia, etc. More recent literature suggests that dopamine systems in the limbic system (excitatory) and frontal cortex (inhibitory) are involved in akathisia.

Gorwood, in his review, reports that anhedonia also has a pivotal role of dopamine and that it is associated with a deficit of activity of the ventral striatum and an excess of activity of ventral prefrontal cortex. As similar mechanisms have been proposed for both these entities – anhedonia and akathisia, a correlation between them is plausible.

We found no correlation between the diagnosis (paranoid schizophrenia and other subgroups) and the rPAS scores. Studies report contradictory results. Possible explanation could be that, in our study, only remitted schizophrenic patients were taken.

We found higher levels of anhedonia scores in FDRs than healthy controls as replicated in previous studies, whereas other studies did not get the similar finding.

A possible reason for this discrepancy could be the heterogeneous population as shown by the bimodal distribution of anhedonia in the schizophrenia proband group, which is in contrast to our study where we have homogeneous distribution of anhedonia scores. Thus, the groups of patients in the previous studies may have contained various proportions of these two subgroups, leading to conflicting results about the relatives.

Our results suggest that physical anhedonia is more common in patients than relatives and more common in relatives than healthy controls. Therefore, our study reiterates that physical anhedonia can be a potential vulnerability marker, an endophenotype in schizophrenia. Future genetic studies could focus on anhedonia in schizophrenia in the context of candidate genes that encode proteins that are involved in dopaminergic neurotransmission and, if the familial nature of genetic studies is confirmed, phenotypic strategy as a quantitative trait in genetic studies might be conducted for patients with schizophrenia.

CONCLUSION

We conclude that physical anhedonia might be used as a trait marker in schizophrenia.

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Conflicts of interest
There are no conflicts of interest.

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Garg, et al.: Is physical anhedonia a schizophrenia trait maker?

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