The Interaction between Nicotine and Negative Symptoms in Schizophrenia and Bipolar Disorder

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Introduction
• Individuals with psychiatric conditions, such as schizophrenia (SZ) and bipolar disorders (BD), have a higher rate of smoking and have lower quit rates compared to the general population.
• As a dopamine agonist, nicotine may help alleviate negative symptoms by increasing abnormally low levels of dopamine in the prefrontal cortex and mesolimbic system consistent with the dopamine deficit hypothesis.
• The purpose of the study is to further explore the interactions of nicotine and negative symptoms in a diverse population of individuals with serious mental illness.
• Furthermore, research examining interactions of nicotine and negative symptoms for individuals with schizophrenia compared to individuals with bipolar disorder who experience psychotic symptoms has not been conducted to our knowledge.
• Consistent with the continuum of psychosis conceptualizations, the current study will examine rates of smoking in SZ and BP with psychotic features in order to provide additional information about shared symptoms and liabilities that may link schizophrenia and bipolar disorders.

Hypothesis
• Based on the mechanism of nicotine, the current study expected higher rates of nicotine usage in groups experiencing negative symptoms as measured by the the Scale for the Negative Symptoms (SANS).
• Specifically, we expect SZ and BDP to have similar behavioral patterns on our assessments and nicotine usage due to the similarity of their symptomatic features. In contrast, we expect BDN to have a lower rate of nicotine usage due to its lower level of negative symptoms compared to SZ and BDP.

Method
Participants:
• 48 individuals diagnosed with BDN, 47 individuals diagnosed with BDP, and 50 individuals diagnosed with SZ.
• Demographic information for each group can be found in Table 1.

Data Analysis:
• Principal Component Analysis (PCA) with varimax rotation was used to identify groupings of SANS subscales.
• A multivariate ANOVA was used to evaluate differences between groups, smokers, and HDRS on SANS Factor Scores. Differences between smokers on HDRS was also measured.
• Correlation between SANS Factor Scores and HDRS were conducted for the total sample.

Measures and Procedures:
• Structured Clinical Interview for DSM-IV (SCID) was used to confirm diagnoses.
• Participants were then asked if they currently used tobacco; those who endorsed tobacco use were categorized as the nicotine group while those who did not smoke were put in the non-nicotine group.
• Negative Symptoms were evaluated using the Scale for the Negative Symptoms (SANS), which can be divided into two subscales, including motivation/pleasure and emotional expressivity.
• The Hamilton Depression Rating Scale (HDRS) was used to measure symptoms of depression; higher ratings indicate more severe or more frequent symptoms.

Table 1. Demographic Information by Group

<table>
<thead>
<tr>
<th>Total</th>
<th>Bipolar Disorder</th>
<th>Schizophrenia</th>
<th>P</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>38.8(12.8)</td>
<td>38.0(13.3)</td>
<td>36.0(12.6)</td>
<td>40.6(12.8)</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>37.9</td>
<td>29.2</td>
<td>29.8</td>
<td>54.0</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td>0.16</td>
<td>0.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>42.1</td>
<td>39.6</td>
<td>36.2</td>
<td>50.0</td>
</tr>
<tr>
<td>African American</td>
<td>11.0</td>
<td>4.20</td>
<td>2.10</td>
<td>26.0</td>
</tr>
<tr>
<td>Hispanic/ Latino</td>
<td>5.52</td>
<td>2.10</td>
<td>8.0</td>
<td>16.0</td>
</tr>
<tr>
<td>Asian American</td>
<td>1.08</td>
<td>0.00</td>
<td>2.10</td>
<td>2.00</td>
</tr>
<tr>
<td>Bi-racial</td>
<td>4.14</td>
<td>8.33</td>
<td>4.00</td>
<td>8.00</td>
</tr>
</tbody>
</table>

Table 2. Differences Between Groups on SANS Factor Scores Using MANOVA

<table>
<thead>
<tr>
<th>Factor</th>
<th>SZ</th>
<th>BDN</th>
<th>BDP</th>
<th>P</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SANS Factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.27 (1.29)</td>
<td>-0.23 (0.73)</td>
<td>-0.06 (0.84)</td>
<td>3.33</td>
<td>0.04</td>
</tr>
<tr>
<td>2</td>
<td>0.10 (1.14)</td>
<td>0.03 (0.98)</td>
<td>-0.04 (0.81)</td>
<td>0.59</td>
<td>0.56</td>
</tr>
<tr>
<td>3</td>
<td>0.31 (1.27)</td>
<td>-0.27 (0.36)</td>
<td>-0.08 (1.01)</td>
<td>4.13</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.17 (1.14)</td>
<td>-0.21 (0.83)</td>
<td>0.02 (0.95)</td>
<td>1.77</td>
<td>0.18</td>
</tr>
<tr>
<td>5</td>
<td>0.16 (1.32)</td>
<td>-0.15 (0.64)</td>
<td>-0.02 (0.73)</td>
<td>1.14</td>
<td>0.32</td>
</tr>
<tr>
<td>6</td>
<td>0.31 (1.27)</td>
<td>-0.27 (0.85)</td>
<td>-0.03 (0.70)</td>
<td>11.10</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Results
• Based on the criteria of Kaiser-Guttman, PCA indicated that the SANS subscales is composed of six factors:
  • Factor 1 measures Affective Flattening
  • Factor 2 measures Anhedonia-Asociality
  • Factor 3 measures Alogia
  • Factor 4 measures Avolition-Apathy
  • Factor 5 measures Affective Flattening, Alogia, and Avolition-Apathy
  • Factor 6 measures Attention
• Factor scores measuring affective flattening, alogia, and attention were significantly different between groups (see Table 2).
• Attention was significantly different between nicotine and non-nicotine group (see Table 3).
• There were no significant differences between nicotine and non-nicotine group on HDRS total scores.
• SANS Factor Scores measuring anhedonia and avolition significantly correlated with HDRS total scores (see Table 4).

Discussion
• Results suggested that the only difference in negative symptoms among the groups was for attention.
• When the sample is divided into more homogenous subgroups based on diagnostic category and nicotine usage, differential patterns of relationships of nicotine on attention were found. Specifically:
  • In schizophrenia, non-smoking and smoking were associated with attention.
  • In bipolar disorder, non-smoking and smoking were not associated with attention.
• Findings also indicate supporting evidence for the continuum conceptualization of psychosis.
• Similar to schizophrenia, we found bipolar disorder with psychosis to have lower emotional expressivity compared to bipolar disorder without psychosis.
• Findings also indicate that the SANS preserves its ability to measure negative symptoms in a mixed clinical sample.
• Results must be considered in the context of their limitations. First, cause and effect cannot be inferred because no participants were randomly assigned.
• Furthermore, hypotheses regarding long-term vs. short term usage of nicotine could not be examined because past usage was not recorded.
• Additionally, these results were obtained in a population of symptomatically stable out-patients, and therefore do not necessarily extend to individuals with more severe symptoms.
• Future studies should included questionnaire assessing pattern of smoking, such as the Fagerström Test for Nicotine Dependence, when evaluating nicotine usage and may attempt to examine any relationship between nicotine and antipsychotic medications and their interaction on the negative symptoms of schizophrenia and bipolar disorder.