In support of Bleuler: Objective evidence for increased affective ambivalence in schizophrenia based upon evocative testing

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Abstract

Background: Ambivalence and anhedonia have long been identified as schizophrenic symptoms. However, ambivalence has rarely been studied, and in most evocative studies, schizophrenia participants are not anhedonic. Affective neurosciences posit two evaluative systems (one for Positivity and one for Negativity), the coactivation of which produces ambivalence, and point to two asymmetries in affective processing: Positivity Offset (which measures our capacity to explore the environment) and Negativity Bias (a measure of reactivity to intense threat). These characteristics have not received much attention in schizophrenia research.

Methods: Sixty-four individuals with schizophrenia and 32 non-patient control participants completed an evocative emotional task with pictures, sounds and words of various valences and intensities. Following each presentation, participants rated the level of pleasantness, unpleasantness, and arousal elicited by the stimulus. Finally, participants completed questionnaires on anhedonia, and practical life skills were assessed.

Results: Schizophrenia participants showed higher levels of ambivalence, greater arousal, greater Positivity Offset, and non-significantly different hedonic capacities and Negativity Bias. Ambivalence to positive stimuli significantly correlated with duration of illness, current level of psychopathology, anhedonia questionnaires and practical life skills. Schizophrenia patients with negative symptoms did not differ from patients without negative symptoms on computer tasks.

Conclusions: Ambivalence is greater in schizophrenia, and can be understood as a de-differentiation of the activation of the two evaluative systems. Ambivalence to positive stimuli, which may reflect early-stage affective processing is associated with impairments in higher-level emotional processes and in everyday functioning. Future studies should clarify the status of anhedonia in schizophrenia.

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1. Introduction

Kraepelin and Bleuler described symptoms reflecting emotional deficits in schizophrenia including absence of emotions and ambivalence (defined as “the tendency…to endow the most diverse psychisms with both a positive and negative indicator at one and the same time” by Bleuler, 1950, p.53). The fate of these two symptoms diverged in the history of psychiatry (Berrios and Olivares, 1995; Raulin and Brenner, 2000).
The aims and hypotheses of the current study were 1) to compare emotional ambivalence and hedonic capacities between individuals with schizophrenia and non-patient control subjects. Based on previous studies, we hypothesized that ambivalence but not anhedonia would differentiate schizophrenia from healthy participants; 2) to measure and compare other aspects of affect processing. We hypothesized...
that schizophrenia participants would show similar levels of negative emotions. Due to scarce literature on PO and NB, this study explored group differences in PO and NB; 3) to examine associations between these early-stage emotional processes and clinical and everyday functioning measures. More specifically, we hypothesized that self-report measures of anhedonia would be moderately correlated with and predicted by hedonic reactivity and other affective processes; 4) to compare schizophrenia participants with or without negative symptoms. Based on published studies, we hypothesized that hedonic reactivity and ambivalence would not differ between schizophrenia subgroups, and PO would be lower in schizophrenia participants with negative symptoms as motivation is quite impaired in this subpopulation.

2. Methods

2.1. Participants

The present study was part of a larger study on affect processing in schizophrenia. Participants included 64 individuals with schizophrenia and 32 non-patient control participants. Schizophrenia participants were outpatients or inpatients in a research unit at the Nathan S. Kline Institute for Psychiatric Research (NKI), New York. All subjects were English-speaking and between 18 and 65 years of age, and had capacity to give consent. Diagnosis of schizophrenia was assessed using the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1998). Patients with schizoaffective disorder were not included. Healthy control participants were recruited from the NKI Volunteer Recruitment Pool. They were community subjects who responded to advertisement and volunteered to participate in research studies conducted at NKI. They had no psychiatric history and no psychiatric diagnosis as assessed with the Non-patient version of the SCID. The study was approved by the local Institutional Review Board. All participants had a reading level higher than 8th grade, as assessed with the Wide Range Achievement Test.

2.2. Clinical ratings, questionnaires and everyday functioning

All participants completed the Revised Physical Anhedonia Scale and the Revised Social Anhedonia Scale (Chapman and Chapman, 1978; Eckblad et al., 1982). Schizophrenia participants were clinically assessed with the following scales: 1) the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), from which the total scores and the Positive Syndrome subscale scores were used; 2) the modified Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1989), the Attention subscale was not used as attention deficits are not specific negative symptoms (Miller et al., 1993); and 3) the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979). In addition, practical life skills were evaluated with the University of California, San Diego, Performance-Based Skills Assessment (UPSA) (Patterson et al., 2008).

In order to identify patients with primary negative symptoms, the following steps were taken. First, participants with a SANS sum score less than 12 were considered as participants without negative symptoms (n = 38). As negative symptoms can be secondary to depression, anxiety, extrapyramidal side effects, or suspicious withdrawal (Kirkpatrick et al., 1989), the following criteria had to be met for primary negative symptoms: 1) a MADRS score less than 8, 2) a Calgary Depression Scale for Schizophrenia (Addington et al., 1992) score less than 6, 3) a Simpson and Angus scale (Simpson and Angus, 1970) score not greater than 5, 4) a PANSS Anxiety score (item G2) not greater than “3” (“mild”), and 5) a PANSS Active Social Avoidance score (item G16) not greater than “3” (“mild”). Twenty-one schizophrenia participants were subsequently classified as participants with primary negative symptoms.

All raters and SCID interviewers met reliability criteria, and were blind to study performances.

2.3. Evocative tasks

One author (JTC) developed a computerized evocative emotional test (psychometric properties discussed in Ito et al., 1998 and Ito and Cacioppo, 2005) with 48 pictures from the International Affective Pictures System (Lang et al., 1999), 48 sounds from the International Affective Digitized Sounds (Bradley and Lang, 1999a) and 48 words from the Affective Norms for English Words (Bradley and Lang, 1999b). Items differed in valence (positive, negative or neutral), intensity (moderate, extreme) and arousal levels (low, high). Visual items were presented on a 16-inch screen. Participants were instructed to attend to each stimulus for its entire duration (6s) and think about how it made them feel. After each item presentation, participants gave three separate ratings: they were asked to rate how pleasant, unpleasant, and arousing the stimulus was for them, on a 1 to 5 point Likert scale. The presentation order of the three subtests was randomized. Answers were not timed.

2.4. Data analysis

For each participant and for each evocative task (visual, auditory and semantic task), the sum scores of all “pleasantness ratings”, “unpleasantness ratings” and “arousal ratings” were calculated. Four primary evocative task variables were defined and classified according to two characteristics: stimulus valence (positive or negative), and valence congruence (positive if same valence in stimulus and ratings; negative if opposite valence in stimulus and ratings). The four primary variables were named and scored as follows: 1) hedonia (positive stimulus valence, positive congruence) was the mean pleasantness rating for positive stimuli (i.e., the sum of pleasantness ratings for all positive stimuli divided by the number of positive stimuli), 2) negative emotion reactivity (negative stimulus valence, positive congruence) was the mean unpleasantness rating for negative stimuli, 3) ambivalence to positive stimuli (positive stimulus valence, negative congruence) was the mean unpleasantness rating for positive stimuli, and 4) ambivalence to negative stimuli (negative stimulus valence, negative congruence) was the mean pleasantness rating for negative stimuli. Three secondary variables were defined: 1) PO was obtained by subtracting the unpleasantness ratings from the pleasantness ratings for all neutral stimuli, divided by the number of neutral stimuli, 2) NB was the difference between the valence ratings for extremely negative stimuli and the valence ratings for extremely positive stimuli (valence ratings are defined as the...
subtraction of unpleasantness score from the pleasantness score for each item), and 3) mean Arousal.

Two preliminary analyses were conducted. First, a regression analysis for each evocative test variable, with group and sensory modality (visual, auditory or semantic) as two independent variables. The interaction term, group by sensory modality, was never significant. Therefore, scores of all three sensory modalities were combined in further analyses. Second, manipulation check was analyzed. A regression analysis was conducted with rating scores (pleasantness and unpleasantness scores) as the dependent factor, and three independent factors were entered: group (schizophrenia versus control group), stimulus valence, and valence congruence. Regression analysis showed that group ($F(1, 377) = 7, p = 0.008$), stimulus valence ($F(1, 377) = 16, p < 0.0001$), valence congruence ($F(1, 377) = 436, p < 0.0001$), group by valence congruence ($F(1, 377) = 5.8, p = 0.017$), stimulus valence by valence congruence ($F(1, 377) = 33, p < 0.0001$) significantly contributed to the model, whereas group by stimulus valence, and the three way interaction term were not significant. Post-hoc analyses showed that congruent ratings were greater than non-congruent ratings for positive and negative stimuli and for both groups, confirming the validity of our evocative test.

Schizophrenia participants were compared to non-patient control participants with univariate general linear model. For each study variable (evocative task variables and questionnaire scores) a separate regression analysis was conducted. Study scores were the dependent factor, and “group” was the principal independent factor. For the six evocative task variables, the following confounding factors were considered: gender, age and education. Effect sizes were measured with Cohen’s $d$, and for non-significant analyses, observed power was also reported.

To compare schizophrenia participants with primary negative symptoms and patients without negative symptoms, a new set of regression analyses was conducted with the evocative task variables.

Pearson correlation coefficients were obtained between the primary evocative task variables and other variables. As PO offers a novel objective way to measure emotional motivation, and as motivation is considered a core negative symptom, we conducted correlation analyses between PO and clinical ratings of negative symptoms, and we measured PO in participants with and without negative symptoms. All tests were two-tailed, and the alpha level was set at 0.05. No correction for multiple comparisons was applied.

## 3. Results

### 3.1. Demographics and questionnaires

Groups did not differ significantly for age and gender. Individuals with schizophrenia had a lower educational level (Table 1). On questionnaires, schizophrenia participants self-
reported greater physical and social anhedonia than controls (Table 1).

3.2. Between group analyses

Results for the four main variables are represented in Fig. 1. Compared to healthy control participants, schizophrenia participants had greater ambivalence to positive stimuli (mean in schizophrenia group: 1.7, SD: 0.5; and 1.3, SD: 0.3 in controls; F(1, 94) = 13.6, p < 0.0001; d = 0.81) and greater ambivalence to negative stimuli (mean in schizophrenia group: 2.2, SD: 0.6; and 2.0, SD: 0.6 in controls; F(1, 94) = 5.2, p = 0.02; d = 0.5). Hedonia (mean in schizophrenia group: 3.3, SD: 0.8; and 3.1, SD: 0.6 in controls; F(1, 94) = 1.3, p = 0.26; d = 0.25; observed power = 0.20) and negative emotion reactivity (mean in schizophrenia group: 3.1, SD: 0.7; and 3.2, SD: 0.6 in controls; F(1, 94) = 1.1, p = 0.30; d = 0.23; observed power = 0.18) did not significantly differ between groups.

Among the secondary variables, PO and arousal were significantly higher in schizophrenia (mean PO in schizophrenia group: 0.7, SD: 0.9; and 0.3, SD: 0.4 in controls; F(1, 94) = 6.1, p = 0.015; d = 0.54) (mean arousal in schizophrenia group: 2.9, SD: 0.8; and 2.4 SD: 0.6 in controls; F(1, 94) = 8.1, p = 0.005; d = 0.62), and NB did not significantly differ between groups (mean in schizophrenia group: −0.7, SD: 3.1; and 0.3, SD: 3.4 in controls; F(1, 94) = 2, p = 0.16; d = 0.31; observed power = 0.29). Confounding factors (gender, age and education) were never a significant factor for any evocative test variables. For the four variables of main interest, “intensity” (moderate versus high) was a significant independent factor (higher intensity predicted higher scores on all four variables), and the interaction term, group by intensity, was never significant. Within the schizophrenia group, outpatients did not differ from inpatients on any study variables.

3.3. Correlation analyses

Correlation analyses (Table 2) revealed that in the schizophrenia group, ambivalence to positive stimuli was significantly associated with age, duration of illness, PANSS total scores, anhedonia questionnaires and practical life skills. As age and duration of illness were highly correlated (r = 0.71, p < 0.0001), we conducted partial correlations to identify which variable was driving the association with ambivalence to positive stimuli. The correlation between ambivalence to positive stimuli and duration of illness remained significant even after controlling for age (r = 0.29, p = 0.02), whereas the correlation between ambivalence to positive stimuli and age lost significance after controlling for duration of illness (r = 0.09, p = 0.48).

In the schizophrenia group, hedonia, negative emotion reactivity, and ambivalence to positive stimuli were significantly correlated with anhedonia questionnaires. Subsequently, we used regression analyses with a forward selection to test the hypothesis that these three affective processes were predictors of anhedonia scales. The Revised Physical Anhedonia Scale was significantly predicted by ambivalence to positive stimuli and negative emotion reactivity (β = 6.4, F = 16.7, p = 0.0001; and β = −3.5, F = 7.6, p = 0.008 respectively), but not by hedonia (p = 0.40), explaining 28% of the variance. The Revised Social Anhedonia Scale was significantly predicted by ambivalence to positive stimuli and negative emotion reactivity (β = 3.9, F = 9.9, p = 0.003; and β = −2.5, F = 6.4, p = 0.01 respectively), but
not by hedonia ($p = 0.48$), explaining 20% of the variance. Collinearity analyses showed that variance inflation factors were always below 2.

Positivity Offset was significantly correlated with the PANSS Negative Symptom subscale scores ($r = -0.26, p = 0.04$), and the SANS total scores ($r = -0.25, p = 0.049$), but not with any SANS subscales.

### Table 2

Correlations between primary evocative task variables and clinical variables, anhedonia questionnaires and practical life skills in schizophrenia (in bold if $p<0.05$)

<table>
<thead>
<tr>
<th></th>
<th>Hedonia</th>
<th>Negative emotion reactivity</th>
<th>Ambivalence to positive stimuli</th>
<th>Ambivalence to negative stimuli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.07</td>
<td>-0.06</td>
<td>0.38 ($p=0.002$)</td>
<td>0.10</td>
</tr>
<tr>
<td>Education</td>
<td>-0.03</td>
<td>-0.09</td>
<td>-0.18</td>
<td>-0.15</td>
</tr>
<tr>
<td>Duration of illness</td>
<td>-0.09</td>
<td>-0.01</td>
<td>0.46 ($p&lt;0.0001$)</td>
<td>0.12</td>
</tr>
<tr>
<td>PANSS Total score</td>
<td>-0.25</td>
<td>-0.11</td>
<td>0.30 ($p=0.018$)</td>
<td>-0.11</td>
</tr>
<tr>
<td>PANSS Positive score</td>
<td>-0.03</td>
<td>0.03</td>
<td>0.18</td>
<td>0.006</td>
</tr>
<tr>
<td>SANS</td>
<td>-0.19</td>
<td>-0.20</td>
<td>0.20</td>
<td>-0.01</td>
</tr>
<tr>
<td>MADRS</td>
<td>0.08</td>
<td>0.22</td>
<td>0.13</td>
<td>0.04</td>
</tr>
<tr>
<td>Revised Physical Anhedonia Scale</td>
<td>-0.36</td>
<td>-0.26</td>
<td>0.42 ($p=0.001$)</td>
<td>-0.06</td>
</tr>
<tr>
<td>Revised Social Anhedonia Scale</td>
<td>-0.32</td>
<td>-0.26</td>
<td>0.34</td>
<td>-0.11</td>
</tr>
<tr>
<td>UPSA</td>
<td>0.15</td>
<td>0.004</td>
<td>-0.35 ($p=0.005$)</td>
<td>-0.02</td>
</tr>
</tbody>
</table>

PANSS: Positive and Negative Syndrome Scale.
SANS: Scale for the Assessment of Negative Symptoms.
MADRS: Montgomery-Asberg Depression Rating Scale.
UPSA: The University of San Diego Performance-Based Skills Assessment.

We interpreted our results as a de-differentiation between these two affective evaluative systems, that is, they are more frequently activated simultaneously. However, other explanations should be examined. The evaluative system for Negativity and/or the evaluative system for Positivity could be hyperactive. For example, schizophrenia participants may experience more negative emotions because of the cognitive demands of the tasks, or they may show differences in the temporal activation of these evaluative systems. Consequently, schizophrenia participants would give higher unpleasantness ratings for non-congruent and congruent stimuli. In our study, group differences were evidenced with non-congruent stimuli, not with congruent stimuli, which does not support the hypothesis of hyperactive evaluative system. Impairment in early emotion regulation is also a potential explanation. In order to explain a high level of unpleasant emotion with positive stimuli, Horan et al. (2006a) suggested that individuals with schizophrenia are “deficient in their ability to downregulate unpleasant emotions in the context of putatively enjoyable experiences” (p506). Our results gave some support for the existence of such a regulatory process: ambivalence to positive stimuli was lower than ambivalence to negative stimuli (the degree of negative affect induced by positive stimuli was lower than the degree of positive affect induced by negative stimuli) in both groups. However, such a regulation process cannot explain the existence of ambivalence to negative stimuli, which is best explained by a de-differentiation in early stages in emotion processing. However, these two explanations are not mutually exclusive: they both lead to a higher degree of ambivalence to positive stimuli in schizophrenia, and they may act in synergy.

Experiencing negative emotions from positive stimuli was correlated with various aspects of this illness, such as duration of illness and PANSS scores, suggesting that ambivalence to positive stimuli is an indicator of illness severity.
Pleasure or displeasure experiences reflect early stages of emotion processing (Frijda, 1999), and disruptions at these levels may lead to impairments in later-stage processes. This explains the correlations found between ambivalence to positive stimuli and anhedonia questionnaires: experiencing displeasure from positive stimuli may lead to a global impression of less pleasant experiences. Even though the process of positive stimuli is linked to well-being and social competence (Lyubomirsky et al., 2005), the correlation found in our study between ambivalence to positive stimuli and practical life skills is rather intriguing, particularly when taking into account that UPSA performances do not rely on emotional information. These results add to the existing literature on the influence of affect on social cognition/skills (Winkielman and Cacioppo, 2006), and invite for further research in schizophrenia.

4.2. Anhedonia

In accord with previous studies, 1) schizophrenia participants were not anhedonic when their emotional experiences were rated on-line, 2) schizophrenia participants had higher physical and social anhedonia with self-report questionnaires, and 3) on-line hedonia was only moderately correlated with self-report anhedonia questionnaires. Among the explanations that have been advanced for this discrepancy between evocative studies and self-report questionnaires, we tested the hypothesis that self-report questionnaires are sensitive to and predicted by other-than-hedonia affective processes. Ambivalence to positive stimuli was the best predictor for self-report anhedonia, followed by negative emotion reactivity. Surprisingly and contrary to our hypothesis, on-line hedonia was not a significant predictor for physical and social anhedonia (after the other predictors were entered).

As in previous studies (e.g., Earnst and Kring, 1999), schizophrenia participants with primary negative symptoms reported the same level of pleasure as participants without negative symptoms and control subjects. Taken together, these results mean that anhedonia as a global deficit in pleasure reactivity may not be a schizophrenic symptom, nor a negative syndrome characteristic, and different approaches and novel anhedonia subclassifications may bring interesting results (see Gard et al., 2007).

4.3. Other affective measures

Positivity Offset measures the emotional incentive salience of neutral stimuli, and is interpreted as the tendency to explore the environment and novel stimuli. In our study, schizophrenia participants had a higher PO than controls. Two other studies (Heerey and Gold, 2007; Murray et al., 2008) reported that schizophrenia participants showed higher motivation for neutral stimuli than controls, even when neutral stimuli were defined as neutral by the participants themselves. Moreover, our results are in accord with studies showing that Novelty Seeking is not impaired in schizophrenia (reviewed in Horan et al., 2008). However, these results seem in contrast with the clinical observation that motivation and social engagement are quite impaired in schizophrenia and more specifically in negative schizophrenia. PO reflects only one motivational process, but other motivational components may be impaired leading to a global deficit in motivation. For example, Herbener et al. (2007) have shown that positive emotional memories lose their incentive salience over time in schizophrenia. Therefore, lack of motivation in schizophrenia may be secondary to impairments in emotional memory and not in early-stage emotional processes.

Higher PO in schizophrenia may represent a primary difference or a compensatory mechanism. The second hypothesis is favored by our correlation analyses: PO was significantly and inversely correlated with negative symptom scores, and was highest in patients without negative symptoms. This lends support to the interpretation that the incentive salience of neutral stimuli is upregulated in schizophrenia, and more so in individuals without negative symptoms. In negative schizophrenia, this upregulation seems minimal and less efficient, not leading to a normalized level of motor activity and social engagement.

Negative emotion reactivity was comparable in schizophrenia and control participants. The emotional evaluative system for Negativity was as reactive in schizophrenia as in controls. Authors have pointed out that experiencing negative emotions from negative stimuli can represent healthy emotional reactions (Lyubomirsky et al., 2005). In our study, also found by Schlenker et al. (1995), schizophrenia participants reported a higher degree of arousal. Even though a few patients had difficulty understanding the concept of affective arousal in our study, future studies adding neurophysiological and cortical measures of arousal to these subjective evaluations may reveal new findings.

Negativity bias was positive in control participants, indicating a NB effect, whereas NB was negative in schizophrenia, indicating that on average, schizophrenia participants did not show a NB effect. However, this difference was not significant. Another study with a different approach (Lee et al., 2006) concluded that NB is absent in schizophrenia. As multiple paradigms can be used to test NB, other studies with different approaches would help to clarify the status of NB in schizophrenia.

4.4. Limitations

1) Groups differed in education level. However, a) study stimuli were not cognitively demanding, b) early emotional processes such as those tested in the present study, do not require extensive cognitive processes (Frijda, 1999), and c) education was not correlated with any study measures. 2) In the literature, different SANS criteria have been used to define negative syndrome. Comparison with recently published studies (e.g., Buchanan et al., 2007) shows that our SANS criteria were more selective. 3) We used operationalized criteria to differentiate primary from secondary negative symptoms, which differs from the criteria proposed by Kirkpatrick et al. (1989) in their definition of primary and deficit negative symptoms.

4.5. Conclusions

In schizophrenia, the emotional evaluative systems for Positivity and for Negativity do not appear hypo-responsive (individuals with schizophrenia are not globally anhedonic), but they are less differentiated, and get activated from opposite-
valence stimuli (individuals with schizophrenia are more ambivalent). Activation of the evaluative system for Negativity from positive stimuli is associated with clinical aspects and functional deficits of schizophrenia. The evaluative system for Positivity is relatively more activated from neutral stimuli in schizophrenia participants than in non-patient control subjects (individuals with schizophrenia have a higher PD). This can be interpreted as an upregulation of some early-stage emotional processes linked to motivation. These results further our understanding of the emotional and motivational deficits in schizophrenia, and they open the door to additional studies of early-stage emotion processing in schizophrenia.

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Contributors
Fabien Trémeau in collaboration with John Cacioppo, Pamela Butler and Daniel Javitt designed the study and wrote the protocol. Fabien Trémeau, Daniel Antonius, Rachel Ziwich, Maria Jalbrzikowski, and Erica Saccente conducted the study and collected the data. Gail Silipo helped in subject recruitment. Fabien Trémeau and John Cacioppo undertook the statistical analysis. Fabien Trémeau, Daniel Antonius and Daniel Javitt wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest
All authors declare that they have no conflict of interest relevant to this study.

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