Anticipation of Social and Monetary Rewards in Schizophrenia

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Abstract
Numerous behavioural and neuroimaging studies have explored human cognitive processing of various rewards, such as food, monetary or social stimuli. Previous studies with patients suffering from schizophrenia (SZ) used incentive delay tasks with monetary rewards. Apart from slower reaction times in general in SZ, there were no differences in task performance between patients with schizophrenia and healthy controls (HC). Patients with schizophrenia have impaired social functioning and thus may have a disturbed sensitivity to social rewards. 54 schizophrenia patients and 54 matched healthy controls completed a reward paradigm (incentive delay task) with monetary (MID) and social stimuli (SID). Reaction times and hit rates were analysed using a three-way repeated measures ANOVA. Patients demonstrated increased reaction times in both, the MID and the SID tasks compared to healthy controls. Hit rates for healthy controls significantly increased in the MID task, however these results were not found in the SID task with increasing reward level. In both tasks SZ improved their performance as rewards increased. The present findings suggest that patients with SZ are capable to anticipate monetary or social rewards and use this anticipation to guide their behaviour. Extrapolated to social functioning, the capability to anticipate potential reward could be used in therapeutic interventions.

Keywords: Schizophrenia; Monetary incentive delay; Social incentive delay; Reward

Introduction
The ability to anticipate and process rewards is central to everyday live. In recent years, numerous behavioural and neuroimaging studies have explored human processing of various rewards, such as monetary [1] and social stimuli [2–5]. Here a reward is operationalized as a positive and contingent consequence of successful behaviour, which in the long run has potential to increase the probability of a certain behaviour [6]. Reward processing comprises the components “wanting” and "liking". While "liking" describes the feeling of joy during the reward consumption, "wanting" is associated with desire (anticipation) and is fundamental for the motivation to approach a reward [7].

In order to develop the motivation for reward-oriented behaviour individuals must be able to anticipate potential rewards using their experience and learned associations. The learning of associations between environmental stimuli and rewarding events is therefore a crucial ability for goal-directed behaviour and motivation [8].

A considerable number of studies addressed human sensitivity to reward promising cues, for food [9], professional success [10], monetary [1,11] or social stimuli [2,12]. These studies often use incentive delay tasks including explicit cues learned prior to the experiment indicating whether a reward can be expected if a task is performed correctly, or not. Previous results suggest that participants react faster and have higher hit rates with increasing magnitude of the anticipated reward. Thus, reaction times and hit rates reflect the personal reward value and the motivation to achieve the reward.

Reward processing in schizophrenia
Dopamine plays an essential role in reward processing, especially reward anticipation. Irregularities in dopamine transmission are an important part of the pathophysiology of schizophrenia [13–16] and there is ample evidence that reward processing is disturbed in schizophrenia [17]. Motivational deficits often affect patients’ quality of life while the common drug treatment seems to have a limited effect, which has implications for clinical treatment. Motivational disturbances can not only be seen as a result of anhedonia, but as a dissociation between the joyful reaction to a rewarding stimulus and the motivational behavior, for example were patients with schizophrenia found to show relatively intact consummatory pleasure, but a lower motivation to attain a reward [18–20].

In previous studies individuals diagnosed with schizophrenia demonstrated impairments in reward-related learning [21,22], associated with disturbed activation in the brain’s reward system [23,24]. The low activation during reward anticipation was associated with greater negative symptom severity [17]. Furthermore, patients appear to show inappropriately strong activations in reward-associated brain areas in response to neutral stimuli as compared to healthy controls [23,25]. These findings suggest that the discrimination between important and unimportant environmental stimuli may be more difficult for patients suffering from schizophrenia, resulting in decreased reward anticipation and negative symptoms like motivational deficits and avolition. Kapur claims that this ‘aberrant salience’ to irrelevant stimuli underlies psychotic symptoms. Results of several functional neuroimaging studies on monetary reward anticipation in schizophrenic patients are consistent with this interpretation. Unmedicated and drug-naïve patients show significantly reduced activations in the brain’s reward system during the anticipation of monetary gains [26–28], which correlated with negative symptoms.

Studies of patients treated with atypical antipsychotics showed less hypofunction of reward-related brain areas during reward anticipation compared to untreated patients or patients treated with typical

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antipsychotics. This effect was attributed to the stronger blockade of D2 receptors by typical antipsychotics [27,29–31]. However, previous studies that conducted incentive delay tasks with schizophrenia patients mainly focused on monetary rewards. There was no difference in task performance between schizophrenia patients and healthy controls apart from slower reaction times in patients [26,30–32] and no evidence for reduced discrimination between neutral and reward cues was found [28,31].

There is evidence that disturbed social reward processing is central to the symptomatology of schizophrenia, as demonstrated by well-documented severe impairments in social functioning [33,34], including less engagement in social interactions, having problems to maintain relationships with family and friends, as well as lower performance in the workplace and/or daily activities [34–37].

Therefore, we investigated the response behaviour of patients suffering from schizophrenia during the anticipation of monetary as well as social rewards. We compared the patients’ data to a matched community sample and expect to find greater response differences during the anticipation of social compared to monetary rewards between groups. Furthermore, we examined the impact of psychopathology on the response behaviour. Based on previous findings [1,2] we predict a linear decrease in reaction times and a linear increase in hit rates with increasing level of both, potential monetary and social reward in healthy subjects. We expect worse task performance in schizophrenia patients during the anticipation of social rewards but not during the anticipation of monetary rewards. Furthermore, we predict a correlation between task performance and symptom severity.

Methods

Participants

The sample consisted of 69 participants with a diagnosis within the schizophrenia (SZ) spectrum (schizophrenia and schizoaffective disorder). To obtain a more homogenic sample we excluded six patients suffering from schizoaffective disorder and four outpatients. Five patients had to be excluded due to incomplete data sets, resulting in a final sample of 54 post-acute inpatients suffering from schizophrenia. The SZ sample was recruited from two Psychiatric hospitals in Giessen, Germany. Diagnoses were based on the Structured Clinical Interview for DSM-IV Axis I disorders [38] and available medical records. The community sample (CS) consisted of 54 volunteers matched by age, sex, and education recruited via mailing lists, social media, newspaper ads, and notices in shops at the University of Giessen. Volunteers of the CS were excluded if they were ever treated for schizophrenia during the anticipation of monetary as well as social rewards. For a better characterization of our PANSS data we transformed the original three subscales into the consensus five-factor model suggested by [41]. Measures of social functioning included the Global Assessment of Functioning [42]. Diagnostic assessment was performed by five trained psychiatrists / clinical psychologists. The success of the training was evaluated by computing intra-class correlation coefficients (ICC) for interviews and tutorial videos (ICC1,2 = 0.92; 95% CI [0.87, 0.96]).

Scores of clinical symptoms and functioning scores are shown in Table 1. SZ showed lower levels of positive symptoms and milder levels of negative symptoms. Nevertheless, the average score (54.6 out of 100) of the GAF scale suggests moderate impairment of social functioning. The CGI score indicated a moderate to marked severity of illness.

Stimuli and task

The experiment consisted of two different tasks with 88 trials: the monetary incentive delay task [1] and the social incentive delay task [2].

Participants were asked to perform two MID and two SID tasks, which were presented interleaved with the order of tasks counterbalanced across participants. At the beginning of each session, participants were informed which task would follow the next. Each trial started with a cue (240 ms), followed by a cross-hair (between 2250 and 2750 ms), the target symbol (individually adjusted presentation time; between 170 and 570 ms) and the feedback (1650 ms) (Figure 1). The feedback (reward outcome) depended on participants’ performance in hitting a button within an individually adjusted time window.

### Table 1: Demographic, psychopathological, and medicinal characteristics for SZ and CS.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SZ (N = 54)</th>
<th>CS (N = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (N, male / female)</strong></td>
<td>33 / 21</td>
<td>33 / 21</td>
</tr>
<tr>
<td><strong>Age (in years)</strong></td>
<td>35.6 (9.8)</td>
<td>35.4 (11.3)</td>
</tr>
<tr>
<td><strong>Duration of illness (in years)</strong></td>
<td>11.4 (8.5)</td>
<td>---</td>
</tr>
<tr>
<td><strong>Psychopathology</strong></td>
<td>---</td>
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</tr>
<tr>
<td>GAF</td>
<td>54.6 (10.6)</td>
<td>---</td>
</tr>
<tr>
<td>CGI</td>
<td>4.3 (0.7)</td>
<td>---</td>
</tr>
<tr>
<td><strong>PANSS original scales</strong></td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>PANSS total</td>
<td>62.4 (13.0)</td>
<td>---</td>
</tr>
<tr>
<td>PANSS positive</td>
<td>12.8 (4.5)</td>
<td>---</td>
</tr>
<tr>
<td>PANSS negative</td>
<td>18.1 (5.4)</td>
<td>---</td>
</tr>
<tr>
<td>PANSS general</td>
<td>31.5 (6.5)</td>
<td>---</td>
</tr>
<tr>
<td><strong>PANSS five-factor model</strong></td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Positive</td>
<td>7.6 (3.7)</td>
<td>---</td>
</tr>
<tr>
<td>Negative</td>
<td>16.3 (5.3)</td>
<td>---</td>
</tr>
<tr>
<td>Disorganized/concrete</td>
<td>6.8 (2.5)</td>
<td>---</td>
</tr>
<tr>
<td>Excited</td>
<td>5.5 (1.9)</td>
<td>---</td>
</tr>
<tr>
<td>Depressed</td>
<td>6.6 (2.8)</td>
<td>---</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>CPZ</td>
<td>662.3 mg (425.9 mg)</td>
<td>---</td>
</tr>
<tr>
<td>FGA + SGA</td>
<td>n = 9</td>
<td>---</td>
</tr>
<tr>
<td>FGA + SGA + SGA</td>
<td>n = 6</td>
<td>---</td>
</tr>
<tr>
<td>SGA</td>
<td>n = 25</td>
<td>---</td>
</tr>
<tr>
<td>SGA + SGA</td>
<td>n = 13</td>
<td>---</td>
</tr>
<tr>
<td>No antipsychotics</td>
<td>n = 1</td>
<td>---</td>
</tr>
</tbody>
</table>

Note: Number of participants (N). PANSS=Positive and Negative Syndrome Scale, GAF=Global Assessment of Functioning, CGI=Clinical Global Impression Score, CPZ=chlorpromazine equivalent, FGA=first generation antipsychotic, SGA=second generation antipsychotic, FGA+SGA=combined treatment with FGA and SGA, FGA + SGA + SGA=combined treatment with one FGA and two SGA, SGA + SGA + SGA=combined treatment with two SGA.
-values were reported, and Greenhouse-Geisser corrected p-values were also reported. The between-subject factor was 'group' (SZ, CS) and between-subject factor 'reward type' (monetary, social) and 'reward level' (0.20 Euro, 1.00 Euro, and 3.00 Euro) and the SID task (and three happy face expressions with horizontal lines that were displayed within each circle indicated one of three levels of potential rewards in the MID task (0.20 Euro, 1.00 Euro, and 3.00 Euro) and the SID task (and three happy face expressions with increasing intensity levels [2]. When hitting the target in time, feedback was shown by either pictures of a happy face or a wallet containing the money. When reactions were too slow or were given for 'no outcome' trials, an empty wallet or a graphically dysmorphed face without any facial features [2] were shown. Trial categories were presented in pseudo-random order within the MID and SID sessions. Inter-trial-intervals were jittered between 2500 and 5000 ms (Figure 1).

Analyses

Statistical analyses were performed using SPSS version 22 [43]. Mean reaction times were calculated averaging the medians of the responses of each single subject. Mean hit rates resulted from the number of correct trials (responses in time) of each subject. Reaction times and hit rates were analysed using a 2x2x4-analyses of variance (ANOVA). The between-subject factor was 'group' (SZ, CS) and the within-subject factors were 'reward type' (monetary, social) and 'reward level' (no reward, low, medium, and high reward). F-values and Greenhouse-Geisser corrected p-values were reported, and squared eta-correlation coefficients (η²) refer to effect sizes. In case of statistically significant interactions, post-hoc analyses between reward levels within each group were performed. In addition, slope coefficients were computed for every subject, reflecting the linear increase of hit rates and the linear decrease of reaction time with increasing level of social and monetary rewards. Slope coefficients were then analysed in separate analyses of variance with the within-subject factor 'reward type' and between-subject factor 'group'. Furthermore, the relationships between the PANSS scores (consensus five-factor model) and SZ slope coefficients of reaction times and hit rates were analysed using one tailed bivariate Pearson's product-moment correlation coefficients (r), for negative correlations (reaction times) and for positive correlations (hit rates).

Results

Reaction times

An ANOVA was conducted to compare the effects of reward level and reward type on reaction times for both groups. There was a significant main effect of the factor reward type [F(1, 0, 106.0)=15.5, p<0.001, η²=0.13], implying faster reaction times in the SID compared to the MID task. Furthermore, a significant main effect of reward level [F(2, 56, 271.3)=7.3, p<0.001, η²=0.07] was found. For the between-subject group a significant effect was observed [F(1, 0, 106.0)=19.0, p<0.001, η²=0.15], suggesting significantly faster reaction times of CS. For the interaction reward type x reward level a significant effect could be shown [F(2.78, 294.7)=4.6, p<0.05, η²=0.04] resulting from the absence of a linear decrease of reaction times in the MID task for CS. There was no significant interaction between reward type x group and reward level x group. Post hoc analysis showed that the main effect of reward level resulted from significant differences throughout the four reward levels in both MID and SID for SZ as well as the significant differences throughout the reward levels in the SID tasks for CS (Figure 2a).

The ANOVA of reaction times' slope coefficients yielded a significant difference between SZ and CS [F(1, 0, 106.0)=5.33, p<0.05, η²=0.05], reflecting stronger decreases of what in SZ compared to CS but no difference between reward types. There was no significant interaction effect. The reaction times and their standard deviations are listed in (Table 2 and Figure 2).

Further analysis of the PANSS scores according to the consensus five-factor model suggest a significant negative correlation coefficient between the computed slope coefficients for the reaction times of MID (r=−0.30, p<0.05) as well as SID (r=−0.30, p<0.05) and the PANSS negative factor (Table 3).

Hit rates

An ANOVA was conducted to compare the effects of reward type and reward level between the PANSS scores (consensus five-factor model) and SZ slope coefficients of reaction times and hit rates were analysed using one tailed bivariate Pearson's product-moment correlation coefficients (r), for negative correlations (reaction times) and for positive correlations (hit rates).
and reward type on hit rates for x groups. There was a significant main effect of reward level $F(2,53, 267.93)=9.16, p<0.01, \eta^2=0.08$, reflecting higher hit rates with increasing reward level, independent of reward type. There was no significant main effect of reward type and no significant main effect of group, suggesting comparable hit rates in both SZ and CS. There were no significant interactions between reward type and reward level, reward type and group, and reward level and group. Post hoc analysis showed that the main effect of reward level resulted from differences throughout the four reward levels in both MID and SID. In our study, SZ were able to discriminate between the different levels of reward - in both, the MID and the SID. Thus, a close link between reaction times and hit rates could only be observed in SZ but not in CS.

Further analysis of the PANSS scores according to the consensus five-factor model suggests a significant positive correlation coefficient between the computed slope coefficient for the hit rates of MID ($r=0.236, p<0.05$) and the PANSS positive factor (Table 3).

### Discussion

The aim of this study was to investigate the response behaviour of SZ compared to matched CS whilst anticipating monetary and social rewards. The results demonstrated that the response pattern of the SZ compared to the response pattern of CS did not differ as predicted.

In SZ, slower reaction times and lower hit rates are well-documented. Slower reaction times for SZ were found as predicted in line with previous research [44,45], while we did not find a significant difference for the hit rates between both groups.

SZ showed a significant decrease of reaction times with increasing level of reward (monetary and social). In contrast, CS displayed different reaction times for different reward levels during the SID, however not during MID which is contrary to previous predictions [1].

There was a significant main effect for hit rates and reward level for both groups. Higher hit rates were associated with higher levels of reward. Additional analyses showed that this effect can be attributed to the linear increase of hit rates with increasing reward levels in SZ in both tasks, MID and SID. Thus, a close link between reaction times and hit rates could only be observed in SZ but not in CS.

The absence of acceleration in reaction times in the MID cannot be a ceiling effect because individuals could react faster in the SID. Furthermore, a reverse pattern in hit rates could be observed. Despite no increase in hit rates in the SID, a ceiling effect could not be assumed as the individuals showed higher hit rates in the MID. Despite these intersecting results the participants generally demonstrated the expected patterns in both paradigms; therefore it can be assumed that they could follow the instructions correctly as well as not showing a motivational deficit.

Apart from faster reaction times in the SID, the SZ response patterns differed in both tasks. In our study, SZ were able to discriminate between the different levels of reward - in both, the MID and the SID task. There was no observable impairment on a behavioural level. This may indicate no motivational deficits in SZ however it does not account for the dysfunctions found on a neural level [17]. Therefore, possible neuro-functional impairments of social and monetary reward processing should be investigated further.
According to the hypothesis of 'dopaminergic noise', and dopamine overload in the reward system, patients suffering from schizophrenia are considered to have difficulties in discriminating between reward stimuli and, have difficulties using reward stimuli for goal-directed behaviour, show limited motivation to achieve a reward [17–20,46]. However, [27,47] report that patients treated with second generation antipsychotics who performed a MID task showed similar response patterns as healthy volunteers. Similarly, in the present study the observed increase in hit rates and decrease in reaction times suggests that SZ are capable to process reward stimuli and adapting their behaviour, as well as they seem able to discriminate between relevant and irrelevant information. This finding is of relevance as a higher dopaminergic activity in the limbic system, particularly the ventral striatal pathways, is assumed in patients suffering from schizophrenia.

Thus, we provide additional evidence that SZ treated with second generation antipsychotics do not exhibit significant deficits in 'wanting' on a behavioural level, understood as the desire and longing to gain a reward.

The observed decrease in reaction times could be a consequence of a less severe and less acute psychopathology of the included patients, e.g. regarding the PANSS score, and therefore their behaviour is guided by the reward levels. Nevertheless, the average chlorpromazine equivalent intake (679.5 mg/d) and the lower severity and acuity of SZ must be seen as a result of appropriate medical and psychiatric treatment and does not indicate a lower severity of the course of illness itself.

The negative correlation between the negative subscale of the PANSS five factor model and the improvement in reaction times for both reward tasks as well as the positive correlation between the positive subscale of the PANSS five factor model and the improvement of hit rates in MID with increasing reward should be interpreted carefully. It does not follow, that patients with serious negative or positive symptoms show an undisturbed reward anticipation in terms of a linear decrease in reaction times or linear increase in hit rates, with increasing level of both, potential monetary and social reward. What does follow?

In our sample, patients suffered from only mild negative and mild positive symptoms resulting in low statistical variance in both symptom groups. Therefore, it remains unclear to what extent psychopathology (negative/positive symptoms) correlates with reaction times and hit rates in reward paradigms. Above these results no further significant correlation between psychopathology and hit rates or reactions times was found.

There is evidence that patients in our sample demonstrated a surprising response patterns on a behavioural level, which is reflecting their ability to represent the value of different choices. Accordingly, they were able to respond differently depending on the level of the next reward. Furthermore, in both MID and SID, we could not find convincing support for a lack of motivated goal-directed behaviour, because patients in our sample seemed to be able to evaluate representations of affective value. Thus, whether motivation deficits should not be regarded as central to the SZ symptomatology or are no longer detectable in medicated patients continues to be unresolved. However, motivated goal-directed behaviour is hardly examinable in unmedicated patients, since patients’ behaviour is then confounded by positive symptoms and severe psychotic stress caused by the disease itself.

Based on the exaggerated release of dopamine leading to 'aberrant salience' to external and internal stimuli [46] a severe impairment of the motivated goal-directed behaviour in unmedicated patients should be expected [27].

Once the medication starts to influence symptoms of schizophrenia, the effects of the disease on reward behaviour are no longer clearly assessable. Clinical stability based on medical treatment offers a mix of iatrogenic and trait features of the illness.

The treatment with dopamine-blocking medications might be a critical confound. It is assumed, that antipsychotic treatment 'dampens' aberrant salience due to dopamine receptor blockade [46], however it may also impair incentive salience attributions [7]. Although antipsychotics do not decrease normal salience to the same degree they effect aberrant salience in the mesolimbic and the mesocortical pathways, because it cannot be assumed that antipsychotics selectively effect one but not the other [46].

Second generation antipsychotics are more appropriate to reduce aberrant salience without disturbing or even by enhancing salience by developing a ‘pseudo limbic selectivity’ in terms of a lower degree of striatal D2 receptor blockade, showing 5-HT\textsubscript{1A} receptor antagonism, 5-HT\textsubscript{1A} receptor agonism or relatively low D2 receptor affinity and fast dissociation from the receptor ('loose-binding'), or even by showing a partial agonism, leading to a functional agonist activity in the mesocortical pathway [48]. In this case reward-processing impairments on a behavioural level might be less than expected.

In our study, patients were mainly treated with second generation antipsychotics and showed reaction patterns that were guided by monetary as well as social rewards. Regarding the predominantly atypical medication of the sample this could be seen in line with the results of Schlagenhauf and colleagues [30,31] who found a less affected reward system in patients suffering from schizophrenia compared to patients being medicated with second generation antipsychotics. During treatment with atypical antipsychotics there was no difference in the task-associated BOLD response in the ventral striatum of schizophrenia patients compared to healthy controls [31,47]. Furthermore, there was a decrease in reaction times with increasing reward intensity comparable to healthy controls [27-31,47].

In line with Schlagenhauf et al. [30,31] there was no correlation between psychopathology and task performance in patients treated with second generation antipsychotics. There was no deficit of 'wanting' a monetary or social reward, which may have implications for treatment including the importance of social functioning, its maintenance and its improvement for the recovery and the course of schizophrenia [33,34,49,50]. It can be assumed that patients suffering from schizophrenia do not only appreciate having social relationships ("liking") but despite their illness have the potential to seek friendships, establish social relationships or other social reinforcers ("wanting"). Therefore, during therapeutic interventions such as consultations or skills-trainings particular attention should be paid on (re-)establishing social connections. Although these interventions are already part of good clinical practice, despite recurrent social withdrawal of patients suffering from schizophrenia our data provide additional support for the importance of improving social functioning in patients suffering from schizophrenia.

Conclusion

To our knowledge, this study was the first to examine a social incentive delay task in patients suffering from schizophrenia. As expected, reaction times differ significantly for both MID and SID groups. Reward type with increasing level of reward seems to lead to faster reaction times in the SID compared to the MID task. The impact of reward level in SZ on reaction times and the hit rates indicates that
partially remitted patients mainly treated with second antipsychotics are able to show reward-oriented behaviour and anticipate the occurrence of potential rewards in both, monetary and social incentive delays. Further investigations could focus on neuronal activation during reward anticipation to social and monetary rewards in SZ to elucidate the underlying compounds of these findings.

References


