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Revisiting anticipatory hedonic processing in patients with schizophrenia: An examination between representation activation and maintenance

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ABSTRACT

Background: Anticipatory anhedonia is one of the key deficits found in patients with schizophrenia (SCZ). However, the underlying mechanism of this deficit remains unclear. The present study examined whether representation activation and maintenance capacity influenced anticipatory experiences in SCZ patients.
Methods: We recruited 46 SCZ patients (26 males) and 45 matched healthy controls (24 males). The Reward Representation Activation and Maintenance (RRAM) Task was administrated to assess anticipatory experience and representation activation and maintenance capacity.
Results: SCZ patients exhibited lower subjective arousal than controls in anticipation of rewards with high probability when representation activation and maintenance were difficult to accomplish. SCZ patients also tended to reduce their button presses more than HC when they were required to maintain reward representation.
Conclusions: Our findings suggest that representation activation and maintenance may partially account for anticipatory anhedonia observed in SCZ patients.

1. Introduction

Anticipatory anhedonia, the inability to experience pleasure related to future pleasurable activities, is a key deficit that contributes to negative symptoms and poor functional outcome in schizophrenia (SCZ) (Foussias et al., 2011; Loas et al., 2009; Rocca et al., 2014). A large body of research has consistently found impaired anticipatory pleasure in SCZ patients (Kring and Elis, 2013). For example, assessed by the Temporal Experience of Pleasure Scale (TEPS), SCZ patients have been found to score lower on the anticipatory pleasure subscale than healthy controls (HC) (Gard et al., 2007; Kring and Barch, 2014; Li et al., 2015; Lui et al., 2015; Mann et al., 2013; Mote et al., 2014; Schlosser et al., 2014; Wynn et al., 2010), although several studies did find comparable anticipatory pleasure between SCZ patients and HC, which may be related to the influence of negative symptoms severity and antipsychotic medications (Strauss et al., 2011). Moving beyond behavioral indices, two recent imaging meta-analytic studies concluded that SCZ patients exhibit attenuated brain activity in the ventral and dorsal striatum during the anticipation of positive stimuli compared with HC (Radua et al., 2015; Yan et al., 2015). However, the underlying mechanism of the observed anticipatory anhedonia in patients with SCZ remains largely unclear.

One of the key processes involved in the generation of anticipatory pleasure is prospection: the ability to generate mental representation

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of the future by drawing upon memories and present perception (Frost and Strauss, 2016). Thus, as a common construct for prospection and memory, mental representation may play a crucial role in an individual's hedonic reactions towards future events. Some researchers have proposed that reduced anticipatory pleasure in SCZ patients may be attributed to dysfunctional mental representation (Barch, 2005; Barch and Dowd, 2010; Cohen et al., 2011; Kring and Barch, 2014). Specifically, anhedonia measured by self-reported scales may actually reflect impairment in working memory (WM), imagination and retrospective memory (Forbes et al., 2009; Heerey and Gold, 2007). According to the Temporal Experience of Pleasure (TEP) model (Kring and Barch, 2014), before someone experiences anticipatory pleasure, representation of previous similar experience is activated and maintained to form the mental representation of the upcoming event (Schacter et al., 2007). For instance, in a scenario where one is thinking of ordering a pizza, a representation containing the previous experience of having pizza with contextual (i.e. how the pizza looked and smelled) and affective (i.e., how he/she felt while eating it) information would be activated and retained in one's working memory. Successful activation and maintenance of the representation will then lead to the generation and experience of the anticipatory affect. Furthermore, ongoing activation and maintenance of the representation is crucial in motivating individuals to pursue rewarding events. To the extent that anticipatory pleasure depends on the ability to activate and maintain information about the anticipated rewards, deficits in the ability to activate and maintain such representations could contribute to anticipatory pleasure deficits.

However, only a few studies have investigated anticipatory anhedonia in SCZ patients from the perspective of representation activation or maintenance. Although indirectly, several studies have examined the relationships between performance in memory tasks and self-reported anhedonia in SCZ patients and found that the level of anhedonia in SCZ patients was related to their impaired visual (Brébion et al., 2007, 2012; Kemali et al., 1987) and affective memory (Herbener et al., 2008). The above findings support a close relationship between memory and pleasure experience in SCZ. However, to the best of our knowledge, no study has isolated the different components to specifically examine how representation activation and maintenance affect anticipatory pleasure experience in SCZ patients. In this study, we sought to evaluate the effects of representation activation and maintenance on affective responses while anticipating future events. Furthermore, we also sought to strengthen the causal relationship between representation activation/maintenance and anticipatory affect by directly examining the participants' representation activation and maintenance capacity.

The Reward Representation Activation and Maintenance (RRAM) task was developed to address these research goals. Three distinct phases are involved in the RRAM task, including the Learning, Anticipation and Testing phases. The Learning phase embodies the early construct in the circuit of the TEP model (i.e., feedback integration). The purpose is to ensure that participants could build up their representations of the task cues through trial and error. This, in turn, would eventually assign affective/rewarding values to the neutral cues (e.g., participants may learn that one certain cue (e.g., the Tibet character ‘ ’) is associated with high probability of monetary rewards and pleasant experience). The Anticipatory phase covers several constructs in the TEP model (Kring and Barch, 2014), involving “activating/maintaining representation” and “anticipatory affect”. We measured participants' anticipatory pleasure under different levels of activation and maintenance difficulty, resulting in three conditions (i.e., ‘Full Activation’, ‘Partial Activation’ and ‘Maintenance’). The ‘Full Activation’ condition is a control condition with low demand on both representation activation and maintenance dimensions. The ‘Partial Activation’ condition is highly demanding on the activation dimension. The ‘Maintenance’ condition, however, involves high demands on only the maintenance dimension. Participants are required to provide their subjective valence and arousal ratings or objective button pressing during the anticipation of upcoming outcomes under these three conditions. The Testing phase serves as an independent measurement of the activation and maintenance ability beyond the anticipatory context. This phase is designed to ascertain whether these two abilities function well or not.

We tested two hypotheses. First, we hypothesized that SCZ patients would exhibit attenuated anticipatory responses when representation activation and maintenance was difficult to accomplish. It has been proposed that unlike valence, arousal is more sensitive to the interaction between emotion and cognitive processes (Anderson, 2005; Cahill and McGaugh, 1998). Thus, we speculated that degradation would be more prominent in arousal rating and the objective button presses. Secondly, given accumulating evidence suggesting that SCZ patients exhibit difficulties in activating (Green et al., 2000; Kurtz et al., 2001; Rund, 1998) and maintaining stimuli containing various physical (e.g., visual-spatial, Forbes et al., 2009; Lee, 2005) and affective properties (Forbes et al., 2009; Gard et al., 2011; Heerey and Gold, 2007; Lee, 2005; Ursu et al., 2011), we hypothesized that SCZ patients would also exhibit lower percentage of optimal choices under difficult activation and maintenance conditions in the Testing phase.

2. Methods

2.1. Participants

A sample of 46 patients, diagnosed with SCZ using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (APA, 1994), were recruited from the Shanghai Mental Health Centre, China. None of the SCZ patients had received electroconvulsive therapy in the past eight weeks or had a history of other Axis I mental, neurological, or substance abuse disorders. All patients were taking antipsychotic medications without any change in the preceding six weeks. All of them were taking second-generation antipsychotics (risperidone: 14%; olanzapine: 44%; amisulpride: 53%; aripiprazole: 33%; quetiapine: 7%; paliperidone: 2%; clozapine: 5%) except for one who was taking a first-generation antipsychotic (penfluridol). Forty-five HC who were matched with the patients in age, gender and IQ were recruited from the local community through advertisements via social media platforms. Participants in the HC group had no personal or family history of any psychiatric disorders. The study was approved by the Ethics Committees of the Shanghai Mental Health Centre and the East China Normal University. Written informed consent was obtained from all the participants before the commencement of the study.

2.2. Reward representation activation and maintenance task

The RRAM task was designed using *E*-Prime 2.0.1 (Psychology Software Tools, http://www.pstnet.com), including three distinct phases: the Learning, Anticipation, and Testing phases.

To ensure that both SCZ patients and HC could build up comparable representations, we designed the Learning Phase which involved gradual learning to allow sufficient representation formation since SCZ patients have been found to have relatively intact ability in gradual learning (i.e., integrating longer-term reinforcement outcomes) (Chang et al., 2016). Practically, participants learned the association between cues (i.e., the Tibetan characters, “ ”) and outcomes (i.e., Probability–80% vs. 20% and Valence–Reward vs. Loss) (see Fig. 1 and Supplementary Materials for details). They were first presented with one pair of cues, followed by a choice window in which they were required to select one optimal cue (i.e., the cue associated with maximum rewards or minimum losses) with no time limit. Feedbacks regarding the outcome were then delivered for 2000 ms (see Fig. 1a). There were two runs involving four blocks in each run and 20 trials in each block. To facilitate the learning process, probability and valence properties were separately acquired in these two runs. For example, in the first run, which required participants to learn probability,

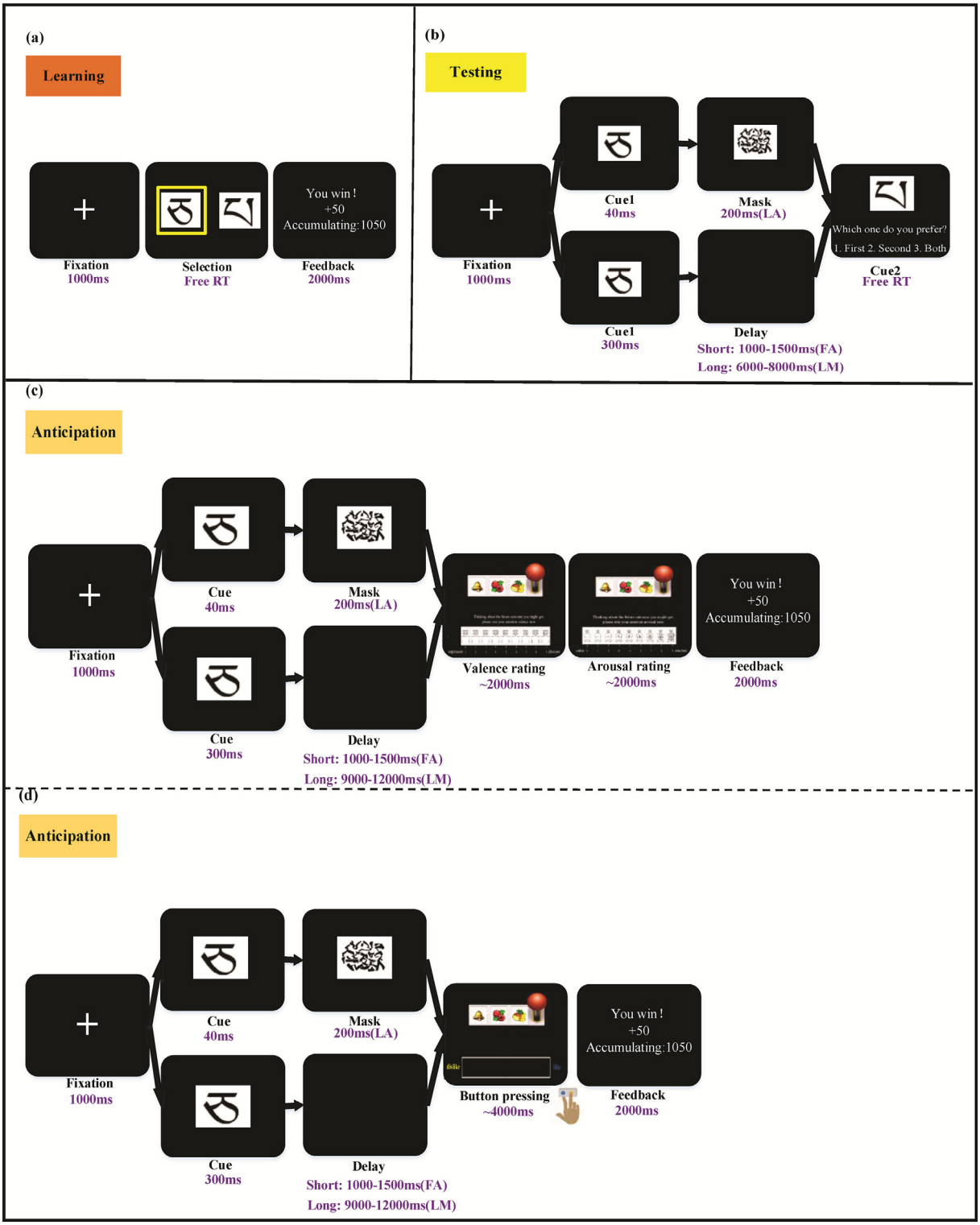

Fig. 1. Task design for the RRAM task. There are three phases in the RRAM task. Participants build representations for cues in the Learning phase. The Anticipation phase was aimed at observing the pattern of anticipatory affect in the context of representation activation and maintenance. In the Testing phase, representation activation and maintenance ability were tested. PA = Partial Activation; FA = Full Activation; M = Maintenance.

participants were presented with two pairs of cues and outcomes with different probability but the same valence (i.e., Frequent Win (FW, 80% win) vs. Infrequent Win (IW, 20% win) and Frequent Loss (FL, 80% loss) vs. Infrequent Loss (IL, 20% loss)). The second run (i.e., acquiring valence property), on the other hand, involved two pairs of cues and outcomes with different valences but the same probability (i.e., FW vs. FL and IW vs. IL). The Learning phase ended when accuracy reached 65% for the first run and 75% for the second run. Otherwise, participants had to complete all four blocks within a run.

In the Anticipation Phase, one of the four previously-learned cues (e.g., , 80% chance to receive reward) was presented to

indicate the potential reward or loss at stake. After a delay, a slot machine with three white panels appeared and began rolling for around 6000 ms. Finally, feedback was shown for 4000 ms to inform whether the participants received rewards or losses. During the rolling period (i.e., the Anticipation period), participants were instructed either to rate their affective experience in terms of valence and arousal on a nine-point Self-Assessment Manikin (SAM) scale or to press the corresponding buttons as much as they wanted to show the extent of their willingness (press 'j') or unwillingness (press 'f') of seeing that cue again in the following trials (see Fig. 1c and d). To set up the conditions targeting distinct representation dimensions (i.e., Activation and Maintenance), we manipulated the presentation length of the cues and the delay duration after its display, which resulted in three conditions, namely the "Full-Activation", "Partial-Activation" and "Maintenance" conditions (see Supplementary materials for the details). The accumulated rewards in this phase were given to the participants after the experiment as monetary payment.

During the Testing Phase, two previously-acquired cues were presented successively, followed by a choice window where participants were required to choose their favorite one by pressing the corresponding button (1 for the former, 2 for the latter, 3 for both (if two identical cues were presented)). To avoid secondary learning, no feedback was given during this phase. Three conditions were formed similar to the Anticipation Phase (see Fig. 1b and supplementary materials for the details). There were 10 pairs of cues and outcomes in the Testing Phase, involving four pairs of cues presented in the Learning phase and six novel pairs of cues (please see Supplementary Materials for details). Each pair had its own optimal choice. The total number of optimal choice s was calculated as the percentage of optimal choices (POC), which was taken as a proxy of their representation activation/maintenance capacity.

2.3. Clinical and neuropsychological assessment

To estimate general intelligence, participants were administrated the short form (information, arithmetic, similarity, and digit span) of the Chinese version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R). The Letter Number Span (LNS) test was used to assess participants' WM performance. Clinical symptoms of SCZ patients were evaluated by experienced psychiatrists using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and the Scale for the Assessment of Negative Symptom (SANS) (Andreasen, 1989). The Abnormal Involuntary Movements Scale (AIMS) (Guy, 1976) and the Barnes Akathisia Rating Scale (BARS) (Barnes, 1989) were used to evaluate side effects of antipsychotic medications. The TEPS (Gard et al., 2006; Chinese version, Chan et al., 2012a, 2012b) and the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS) (Gooding and Pflum, 2014; Chinese version, Chan et al., 2016) were used to measure trait dispositions in anticipatory and consummatory pleasure experience in physical and social interactions respectively. Physical and social anhedonia were evaluated using the Chapman Scales for Physical Anhedonia (CPAS) and Social Anhedonia (CSAS) (Chapman et al., 1976; Chinese version, Chan et al., 2012b). Finally, the Beck Depression Inventory (BDI-IA) (Beck, 1979; Chinese version, Zheng et al., 1988) was used to measure the severity of depressive symptoms.

2.4. Statistical analysis

Demographic data such as gender, age, educational level and IQ estimates were compared between the two groups using chi-square tests and independent sample *t*-tests. To determine the group difference in representation formation, a Group × Pairs mixed ANOVA was conducted for accuracy in the Learning Phase.

To evaluate the manipulation validity of representation activation and maintenance of our task, a series of repeated-measure ANOVAs were performed on four dependent variables (valence/arousal rating and number of button presses (NBP) in the Anticipation Phase, POC in the Testing Phase) in the HC sample to see if there were significant between-condition effects.

To evaluate the influence of representation processes on anticipatory affect, the following analyses were conducted on three dependent variables: valence, arousal rating and NBP. For activation processes, the main independent variable was Activation level ('Full Activation' vs. 'Partial Activation') with different activation difficulties. Mixed ANOVA with two within-subject factors (Activation level and Probability) and one between-subject factor (Group) were conducted. For maintenance processes, a similar procedure was applied with the only difference of one within-subject variable being the Maintenance Level ('Full Activation' vs. 'Maintenance').

For the Testing Phase, a mixed ANOVA with the same three independent variables in the Anticipation Phase was conducted on POC to test the group difference in representation activation/maintenance capacity.

Pearson correlation analyses were conducted to assess the relationships between anticipatory affect and symptom severity, anticipatory anhedonia severity, and medication doses in SCZ patients. Bonferroni correction was applied to correct for multiple comparisons for both the ANOVA and correlation analyses. Cohen's d was calculated to estimate the effect size.

3. Results

3.1. Demographic characteristics, scale scores, and neuropsychological performances

As shown in Table 1, SCZ patients did not differ from HC in age, length of education, gender and IQ estimates ($ps > .08$). As expected, significant group differences were observed for the total correct numbers ($t_{87} = 2.12$, $p = .04$, d = 0.45) and the longest item passed ($t_{87} = 2.23$, $p = .03$, d = 0.47) in the LNS task. For self-reported questionnaires, SCZ patients scored significantly lower on the anticipatory subscale of the ACIPS ($t_{71.603} = 3.52$, $p = .001$, d = 0.74) and the TEPS ($t_{87} = 2.19$, $p = .03$, d = 0.46). In particular, SCZ patients scored significantly lower in the abstract subscales for both anticipatory ($t_{79.45} = 3.03$, $p = .003$, d = 0.64) and consummatory pleasure ($t_{87} = 2.78$, $p = .007$, d = 0.58) on the TEPS. SCZ patients scored significantly higher on the CSAS and the CPAS compared with HC (CSAS: $t_{87} = -2.65$, $p = .01$, d = −0.56; CPAS: $t_{67.89} = -3.07$, $p = .003$, d = −0.65). No significant group difference was observed for BDI scores ($t_{87} = -1.57$, $p = .12$, d = −0.33).

3.2. Validity of the RRAM task

In terms of manipulation of representation activation, a significant main effect of Activation Level was observed on all dependent variables for both rewarding (Valence: $F_{1,44} = 15.85$, $p < .001$, partial $\eta^2 = 0.27$; NBP: $F_{1,44} = 35.82$, $p < .001$, partial $\eta^2 = 0.45$) and losing trials (Valence: $F_{1,44} = 15.61$, $p < .001$, partial $\eta^2 = 0.26$; NBP: $F_{1,44} = 22.3$, $p < .001$, partial $\eta^2 = 0.34$) except for arousal rating ($ps > 0.05$). In the Testing Phase, HC made more optimal choices in 'Full Activation' conditions than 'Partial Activation' conditions as reflected by the significant main effect of Activation Level for rewarding ($F_{1,44} = 172.41$, $p < .001$, partial $\eta^2 = 0.79$) and losing trials ($F_{1,44} = 45.08$, $p < .001$, partial $\eta^2 = 0.51$).

Regarding representation maintenance, HC reported higher arousal experience in response to FW trials under the 'Maintenance' condition than under the 'Full Activation' condition ($p = .03$). No other results were significant. The main effect of Maintenance Level in the Testing Phase was significant for POC in reward trials ($F_{1,44} = 3.93$, $p = .05$, partial $\eta^2 = 0.08$), indicating lower accuracy in HC under the 'Maintenance' condition than the 'Full Activation' condition. These significant between-condition effects together suggested acceptable validity in

Table 1
Demographic characteristics and neuropsychological test data for SCZ patients and HC.

Variable	HC group (n = 45)	SCZ group (n = 46)	t/χ^2	p	Cohen'd
Demographic and clinical characteristics					
Age, mean(SD), year	23.64(8.68)	23.78(7.63)	−0.08	0.94	−0.02
Education, mean(SD), year	13.07(2.67)	13.59(2.90)	−0.89	0.38	−0.19
IQ Estimates	115.93 (15.49)	110.54 (13.43)	1.78	0.08	0.37
Sex (Male:Female)	26:19	24:22	−0.29	0.59	−0.11
DUI, mean(SD), year		2.53(3.87)			
CPZ		243.18 (282.98)			
PANSS positive[1]		12.67(5.10)			
PANSS negative[1]		17.11(6.79)			
PANSS general[1]		32.60(9.13)			
SANS total[1]		28.33(16.22)			
SANS affective flattening[1]		7.79(5.40)			
SANS alogia[1]		4.77(3.98)			
SANS avolition[1]		6.53(3.96)			
SANS anhedonia[1]		7.05(3.86)			
SANS attention[1]		2.19(2.59)			
BARS[2]		0.70(1.35)			
AIMS[2]		2.32(3.15)			
Questionnaire scores and neuropsychological assessments performances					
TEPS_consummatory[3]	45.38(6.75)	41.98(8.40)	2.11	0.04	0.45
TEPS_con_abstract[3]	28.82(4.15)	25.93(5.61)	2.78	0.007	0.58
TEPS_con_concrete[3]	16.56(3.52)	16.04(4.09)	0.63	0.53	0.13
TEPS_anticipatory[3]	38.33(6.76)	35.16(6.90)	2.19	0.03	0.46
TEPS_ant_abstract[3]	20.22(2.62)	18.23(3.52)	3.03	0.003	0.64
TEPS_ant_concrete[3]	18.11(4.96)	16.93(4.45)	1.18	0.24	0.25
TEPS_total[3]	86.33(12.08)	79.95(13.48)	2.35	0.02	0.50
ACIPS_total[3]	77.49(9.38)	68.27(14.27)	3.59	0.001	0.76
CSAS[3]	9.96(5.45)	13.77(7.93)	−2.65	0.01	−0.56
CPAS[3]	14.11(6.47)	20.16(11.38)	−3.07	0.003	−0.65
BDI[3]	8.67(6.73)	11.59(10.51)	−1.57	0.12	−0.33
LNS_CorN	16.87(4.87)	14.80(4.34)	2.12	0.04	0.45
LNS_Litem	6.51(1.55)	5.84(1.28)	2.23	0.03	0.47

Note. SCZ = Schizophrenia; HC = Healthy control; DUI = Duration of illness; CPZ = Chlorpromazine dosage; PANSS = Positive and Negative Syndrome Scale; Scale for the Assessment of Negative Symptoms; BARS = Barnes Akathisia Rating Scale; AIMS = Abnormal Involuntary Movement; TEPS = Temporal Experience Pleasure Scale, ant = anticipatory pleasure, con = consummatory pleasure, CSAS = Chapman Social Anhedonia Scale, CPAS = Chapman Physical Anhedonia Scale; ACIPS = Anticipatory and Consummatory Interpersonal Pleasure Scale; BDI = Beck Depression Inventory; LNS = Letter Number Span task (Chinese version), CorN = Correct number; Litem = the Largest item; 1: sample size of SCZ patients was 43; 2: sample size of SCZ patients was 37; 3: sample size of SCZ patients was 44.

the manipulation of representation activation and maintenance difficulty.

3.3. Group difference in building representation

In the Learning Phase, both the main effect of Group ($F_{1,89} = 1.52$, $p = .22$, partial $\eta^2 = 0.02$) and the Group × Pairs interaction ($F_{3,267} = 2.14$, $p = .10$, partial $\eta^2 = 0.02$) were not significant for accuracy.

3.4. Group differences in the effect of representation activation on anticipatory responses

3.4.1. Rewarding trials

The Group × Activation Level × Probability interaction ($F_{1,88} = 6.58$, $p = .01$, partial $\eta^2 = 0.07$) was significant for arousal rating, indicating that SCZ patients' reports of arousal were significantly lower than HC for FW trials when representation activation was difficult to accomplish ($p = .008$ in 'Partial Activation' condition, Fig. 2b). We did not observe any significant main effect of Group or interactions involving Group on valence rating or NBP.

3.4.2. Losing trials

Patients with SCZ reported lower arousal compared with HC in all conditions, as reflected by a significant main effect for Group ($F_{1,88} = 11.42$, $p = .001$, partial $\eta^2 = 0.12$, see Fig. S1b in Supplementary Material). No significant group difference was observed for other variables in losing trials.

3.5. Group differences in the effect of representation maintenance on anticipatory responses

3.5.1. Rewarding trials

A significant Probability × Maintenance Level × Group interaction effect was again found for arousal ratings ($F_{1,88} = 3.89$, $p = .05$, partial $\eta^2 = 0.04$). Simple effect analysis showed that SCZ patients tended to report lower levels of arousal than HC for FW trials under the 'Maintenance' conditions ($p = .08$) (see Fig. 3b). There was no significant group difference in valence ratings. For NBP, only SCZ patients displayed a tendency for a decrease in NBP under the 'Maintenance' conditions compared with 'Full Activation' conditions, as reflected by the marginally significant Maintenance Level × Group interaction ($F_{1,89} = 3.68$, $p = .06$, partial $\eta^2 = 0.04$) and simple effect analysis (SCZ: $p = .09$; HC: $p = .32$, Fig. 3c).

3.5.2. Losing trials

For arousal ratings, a significant main effect of Group was observed ($F_{1,88} = 9.07$, $p = .003$, partial $\eta^2 = 0.09$, See Fig. S2b), indicating that SCZ patients showed lower arousal experience than HC. No significant group difference was found for valence ratings, but the Probability × Maintenance Level × Group interaction was marginally significant for NBP ($F_{1,89} = 3.79$, $p = .06$, partial $\eta^2 = 0.04$). The SCZ group failed to differentiate their NBP towards FL from the IL cue under the 'Maintenance' conditions ($p = .66$), whereas HCs were able to do so ($p = .05$, See Fig. S2c).

3.6. Relationship between anticipatory affect, symptom severity, anticipatory anhedonia and antipsychotic doses

In SCZ patients, the scores on the anticipatory subscale of the ACIPS was significantly correlated with the arousal rating for FW trials under the 'Partial Activation' ($r_{45} = 0.32$, $p = .03$) and 'Maintenance' conditions ($r_{44} = 0.34$, $p = .02$). We also observed significant negative correlations between the anhedonia subscale score on the SANS and arousal ratings for FW trials under the 'Partial Activation' condition ($r_{42} = -0.35$, $p = .02$), and a trend correlation with the 'Maintenance' condition ($r_{42} = -0.27$, $p = .08$). None of them remained significant after Bonferroni correction. Significant correlations between antipsychotic dosage and arousal ratings were found for Frequent-loser (FL, 80% loss, $r_{42} = 0.33$, $p = .03$) and Infrequent-loser (IL, 20% loss, $r_{42} = 0.32$, $p = .04$) cues under the 'Partial activation' condition, but neither of them survived Bonferroni correction.

3.7. Group differences in representation activation/maintenance ability

In the Testing Phase, we did not observe any significant main effect for Group or any significant interactions involving Group in POC in both the rewarding or losing trials ($ps > 0.15$).

4. Discussion

The present study examined whether attenuated anticipatory pleasure in SCZ patients could be explained by impaired reward representation activation and maintenance. We found that patients with SCZ showed lower arousal intensity than HC for high probability future rewards when representation activation and maintenance were difficult to accomplish. SCZ patients also tended to reduce their button presses compared to HC when they were required to maintain reward

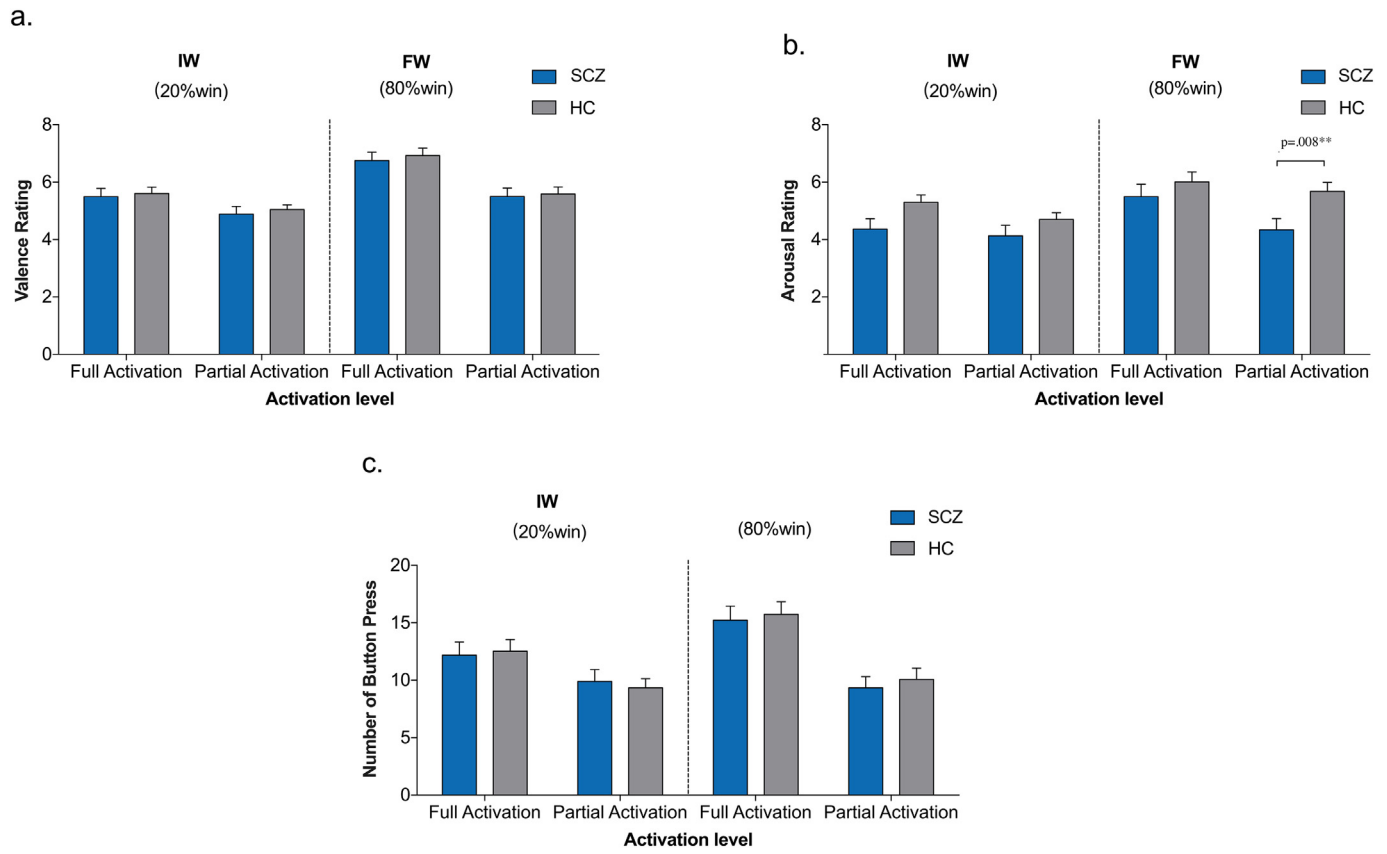

Fig. 2. Group differences in the anticipatory affect towards the rewarding trials under different activation levels. (a.) Valence rating; (b.) Arousal rating; (c.) Number of button press. IW = Infrequent Winner; FW = Frequent Winner; SCZ = Schizophrenia; HC = Healthy control.

representation. We also found significant correlations between arousal ratings under the partial activation and maintenance conditions and anticipatory anhedonia assessed by the ACIPS as well as anhedonia assessed by the SANS anhedonia subscale. Unexpectedly, we did not find any group differences in representation activation and maintenance capacity.

Previous research has found that there is a significant correlation between anhedonia scores on the CSAS and 'in the moment' experience ratings for affective stimuli in SCZ patients with better WM. Results from the neuroimaging literature using affective or reward tasks which involve representation activation have revealed decreased activation in the ventromedial prefrontal cortex, the dorsolateral prefrontal cortex and the orbitofrontal cortex, which are correlated with higher levels of anhedonia in SCZ patients (Dowd and Barch, 2012; Park et al., 2009, 2015; Ursu et al., 2011; Wang et al., 2003). Consistent with these studies, our findings on representation activation also linked cognitive function with affective disruption. Our findings on representation maintenance are also consistent with results from several studies reporting impaired affective experience in SCZ patients after a delay (Gard et al., 2011; Heerey and Gold, 2007), along with decreased activation in the dorsolateral, ventromedial prefrontal and orbitofrontal cortex during affect maintenance (Ursu et al., 2011), albeit in a non-anticipation context.

Additionally, the association we found between self-reported anticipatory anhedonia and arousal rating under the 'Partial Activation' and 'Maintenance' conditions for rewards again consolidates the potential role of reward representation activation and maintenance in anticipatory pleasure. Intriguingly, the significant results were in the social domain of anticipatory anhedonia assessed by the ACIPS rather than in the physical domain measured by the TEPS. Consistent with our findings, some studies have also reported that social anhedonia but not physical anhedonia is predictive of the development of schizophrenia spectrum disorders (Blanchard et al., 2000, 2001; Chapman et al., 1994; Kwapil, 1998).

Unexpectedly, despite the impaired anticipatory experience observed during the Anticipation Phase, we did not find any significant group difference in representation activation or maintenance capacity during the Testing Phase. One possible explanation may be that different processes are involved in these two phases. In the Testing Phase, participants were instructed to activate and maintain previous representations of reward value to guide their decision making without receiving any feedbacks. In contrast, in the Anticipation Phase, both reward value and affective experience may be activated and maintained simultaneously since the participants were asked to respond according to their anticipatory affect. Indeed, one study using the selective interference approach has found that secondary emotion-regulation tasks could block affective intensity maintenance, whereas secondary cognitive tasks disrupt brightness intensity maintenance, but facilitate affect maintenance (Mikels et al., 2008). This supports the unique role of affective maintenance in WM, separable from the representation maintenance of non-affective information. This suggests that SCZ patients' impairment in representation activation and maintenance may be due specifically to deficits in activating and maintaining affective representations. Related to this, Gold and colleagues used a color recall task to measure the precision and stability of WM representations in SCZ patients (Gold et al., 2010) and found that their WM representations were as precise and stable as those in HC even with longer delays, although SCZ patients retained fewer items in their WM. In other words, WM representations may be stable in SCZ patients when the memory load is low, which might be the case in our study in which they only needed to deal with one cue at a time. Our findings thus offer a new perspective on the nature of representation deficits of SCZ patients to show that it may mainly be due to deficits in maintaining affective representations. Future studies are needed to confirm this.

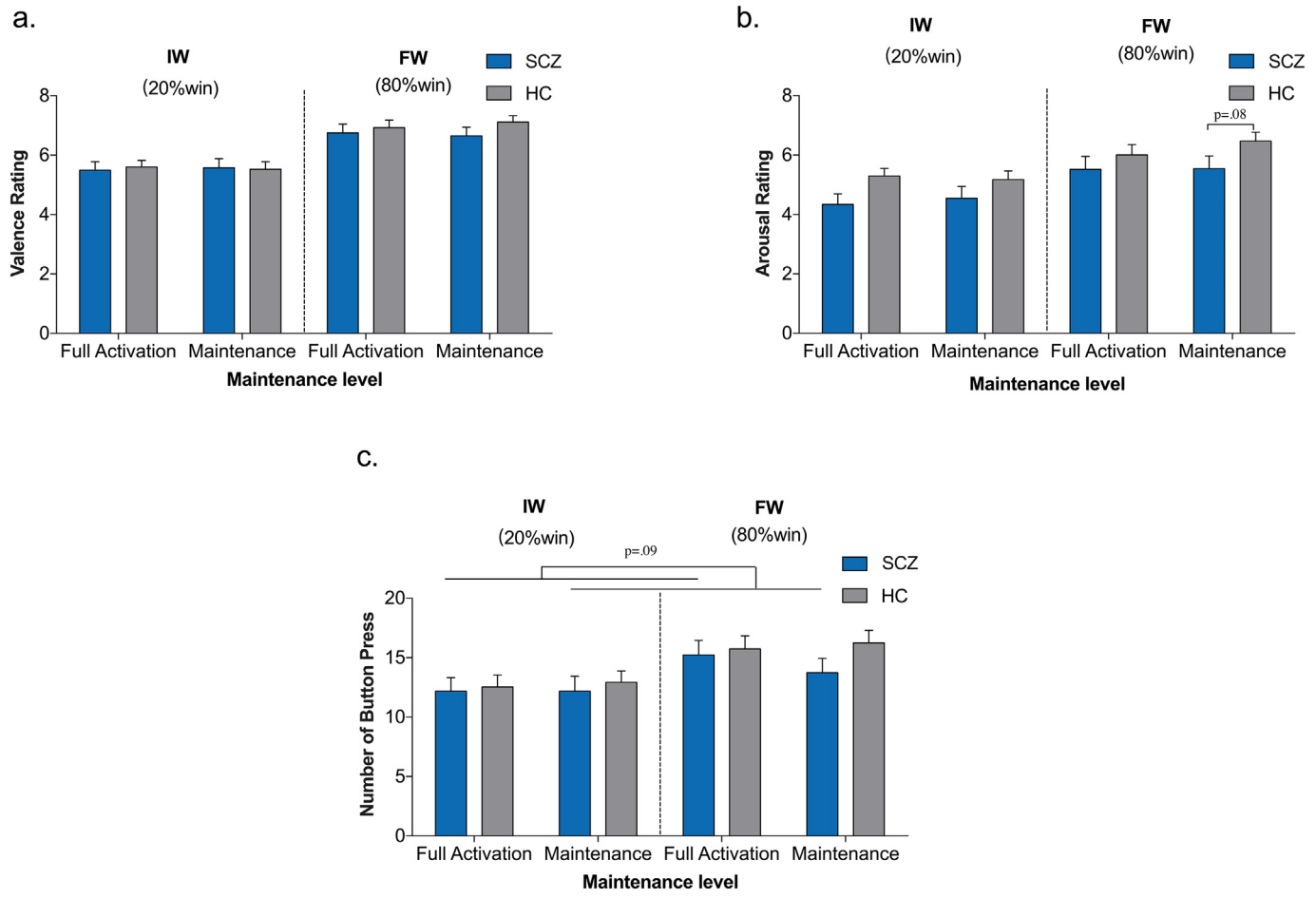

Fig. 3. Group differences in the anticipatory affect towards the rewarding trials under different maintenance levels. (a.) Valence rating; (b.) Arousal rating; (c.) Number of button press. IW = Infrequent Winner; FW = Frequent Winner; SCZ = Schizophrenia; HC = Healthy control.

In conditions involving loss cues, SCZ patients failed to differentiate two loss cues with different probabilities when they were required to maintain the representation online, even though no significant group difference was observed. It appears that the representation maintenance requirement does not exert an obvious influence on aversive outcomes. One possible explanation may be the confounding effects of antipsychotic medications. All SCZ patients except one in our study were taking second-generation antipsychotics. It is known that many second-generation antipsychotic medications act on the D2 dopamine receptor, which is more related to negative stimuli coding. In fact, numerous studies have shown that increased D2 receptor blockade may enhance loss processing in animals and healthy individuals (Amtage and Schmidt, 2003; Centonze et al., 2004; Wiecki et al., 2009). Consistent with the previous findings that SCZ patients taking a higher dose of antipsychotic medication are more likely to respond to negative feedback (Insel et al., 2014), we also found significant positive correlations between antipsychotic dosage and arousal rating for Frequent-loser (FL, 80% loss) and Infrequent-loser (IL, 20% loss) cues under the 'partial activation' condition. As such, negative outcomes may become less salient than positive ones, thus restricting the range of variation (Heerey and Gold, 2007).

In this study, degradation was mainly found in the arousal rating and NBP towards high-probability rewards, but not in valence among SCZ patients. A similar result was reported by Kring et al. (2011) showing that male patients with SCZ showed comparable levels of valence rating but reduced arousal experience on the Self-Assessment Manikin (SAM) scale during the maintenance period compared with HC. These results suggest that valence and arousal may play different roles. As two separate dimensions within emotion, valence and arousal have been proposed to be crucial for motivation activation. Valence determines whether the appetitive or defensive system is activated, while arousal reflects the intensity of that activation. In other words, arousal ratings could be much more sensitive to task outcomes than valence. This could partly explain why most of the differences were found on arousal rating and NBP, as both allowed for more elaborate differentiation of participants' affective responses.

This study had several limitations. First, all the SCZ patients were taking antipsychotic medications, which might have confounded our results. Future studies should minimize this effect by recruiting medication-naïve patients. Secondly, the Anticipation and Testing Phases appear to target different processes as suggested by our results; the Anticipation Phase seems to target affective representation, whereas the Testing Phase appears to target representation for rewarding value. A more direct test of affect maintenance capacity is therefore needed. Thirdly, in the RRAM task, only monetary stimuli were used to invoke anticipatory affect, but monetary reward is only one part of real-life enjoyable experiences. Other domains like social interactions are also highly relevant in the manifestation of negative symptoms in SCZ patients, which affects prognosis and social functioning. Future studies should develop more refined paradigms to incorporate social interactions.

5. Conclusions

Our results suggest that affective representation activation and maintenance processes in SCZ patients may partially contribute to their anticipatory anhedonia, thereby offering a new perspective on the nature of anticipatory anhedonia in SCZ patients. The present

study also adds to a growing body of research exploring the critical interactions between affect and cognition in SCZ. Given the extent to which anticipatory anhedonia can be induced by cognitive impairment in representation activation and maintenance, future intervention protocols may benefit from this finding and could attempt to alleviate anticipatory anhedonia by targeting affective representation activation and maintenance processes in SCZ patients.

Contributors

LLW and CY designed the study, analyzed the data, and wrote up the first manuscript. QYL and ZHY recruited clinical cases and made clinical diagnoses and clinical ratings on patients with schizophrenia. LLW and SYX conducted the assessments to all clinical cases and healthy controls. DN, UE, ZHY and EFCC made critical comments to the drafts of the manuscript. CY and RCKC generated the idea, interpreted the findings and commented critically to the drafts of the manuscript. All authors read and approved the final version of manuscript for submission.

Role of funding source

The funding agents had no further role in the study design; in the collection, analysis and interpretation of the data; in the writing of the manuscript; and in the decision to submit the paper for publication.

Declaration of competing interest

The authors reported no conflicts of interest with this work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2019.12.013.

References

Amtage, J., Schmidt, W.J., 2003. Context-dependent catalepsy intensification is due to classical conditioning and sensitization. Behav. Pharmacol. https://doi.org/10.1097/00008877-200311000-00009.
Anderson, A.K., 2005. Affective influences on the attentional dynamics supporting awareness. J. Exp. Psychol. Gen. https://doi.org/10.1037/0096-3445.134.2.258.
Andreasen, N.C., 1989. Scale for the Assessment of Negative Symptoms (SANS). Br. J. Psychiatry 155, 49–52.
APA, 1994. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. .
Barch, D.M., 2005. The relationships among cognition, motivation, and emotion in schizophrenia: how much and how little we know. Schizophr. Bull. 31, 875–881. https://doi.org/10.1093/schbul/sbi040.
Barch, D.M., Dowd, E.C., 2010. Goal representations and motivational drive in schizophrenia: the role of prefrontal-striatal interactions. Schizophr. Bull. https://doi.org/10.1093/schbul/sbq068.
Barnes, T.R.E., 1989. A rating scale for drug-induced akathisia. Br. J. Psychiatry 154, 672–676.
Beck, A., 1979. Cognitive Therapy of Depression.
Blanchard, J.J., Gangestad, S.W., Brown, S.A., Horan, W.P., 2000. Hedonic capacity and schizotypy revisited: a taxometric analysis of social anhedonia. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.109.1.87.
Blanchard, J.J., Horan, W.P., Brown, S.A., 2001. Diagnostic differences in social anhedonia: a longitudinal study of schizophrenia and major depressive disorder. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.110.3.363.
Brébion, G., David, A.S., Ohlsen, R., Jones, H.M., Pilowsky, L.S., 2007. Visual memory errors in schizophrenic patients with auditory and visual hallucinations. J. Int. Neuropsychol. Soc. https://doi.org/10.1017/S135561770707107X.
Brébion, G., Ohlsen, R.I., Bressan, R.A., David, A.S., 2012. Source memory errors in schizophrenia, hallucinations and negative symptoms: a synthesis of research findings. Psychol. Med. https://doi.org/10.1017/S003329171200075X.
Cahill, L., McGaugh, J.L., 1998. Mechanisms of emotional arousal and lasting declarative memory. Trends Neurosci. https://doi.org/10.1016/S0166-2236(97)01214-9.
Centonze, D., Usiello, A., Costa, C., Picconi, B., Erbs, E., Bernardi, G., Borrelli, E., Calabresi, P., 2004. Chronic haloperidol promotes corticostriatal long-term potentiation by targeting dopamine D2L receptors. J. Neurosci. https://doi.org/10.1523/JNEUROSCI.1274-04.2004.
Chan, R.C.K., Shi, Y. fang, Lai, M. kin, Wang, Y. na, Wang, Y., Kring, A.M., 2012a. The temporal experience of pleasure scale (TEPS): exploration and confirmation of factor structure in a healthy Chinese sample. PLoS One https://doi.org/10.1371/journal.pone.0035352.
Chan, R.C.K., Wang, Y., Yan, C., Zhao, Q., McGrath, J., Hsi, X., Stone, W.S., 2012b. A study of trait anhedonia in non-clinical chinese samples: evidence from the chapman scales for physical and social anhedonia. PLoS One https://doi.org/10.1371/journal.pone.0034275.
Chan, R.C.K., Yang, Z.Y., Li, Z., Xie, D.J., Gooding, D.C., 2016. Validation of the Chinese version of the Anticipatory and Consummatory Interpersonal Pleasure Scale. PsyCh J https://doi.org/10.1002/pchj.139.
Chang, W.C., Waltz, J.A., Gold, J.M., Chan, T.C.W., Chen, E.Y.H., 2016. Mild reinforcement learning deficits in patients with first-episode psychosis. Schizophr. Bull. https://doi.org/10.1093/schbul/sbw060.
Chapman, L.J., Chapman, J.P., Raulin, M.L., 1976. Scales for physical and social anhedonia. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.85.4.374.
Chapman, L.J., Chapman, J.P., Kwapil, T.R., Eckblad, M., Zinser, M.C., 1994. Putatively psychosis-prone subjects 10 years later. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.103.2.171.
Cohen, A.S., Najolia, G.M., Brown, L.A., Minor, K.S., 2011. The state-trait disjunction of anhedonia in schizophrenia: potential affective, cognitive and social-based mechanisms. Clin. Psychol. Rev. https://doi.org/10.1016/j.cpr.2010.11.001.
Dowd, E.C., Barch, D.M., 2012. Pavlovian reward prediction and receipt in schizophrenia: relationship to anhedonia. PLoS One https://doi.org/10.1371/journal.pone.0035622.
Forbes, N.F., Carrick, L.A., McIntosh, A.M., Lawrie, S.M., 2009. Working memory in schizophrenia: a meta-analysis. Psychol. Med. https://doi.org/10.1017/S0033291708004558.
Foussias, G., Mann, S., Zakzanis, K.K., van Reekum, R., Agid, O., Remington, G., 2011. Prediction of longitudinal functional outcomes in schizophrenia: the impact of baseline motivational deficits. Schizophr. Res. https://doi.org/10.1016/j.schres.2011.06.026.
Frost, K.H., Strauss, G.P., 2016. A review of anticipatory pleasure in schizophrenia. Curr. Behav. Neurosci. Reports. https://doi.org/10.1007/s40473-016-0082-5.
Gard, D.E., Gard, M.G., Kring, A.M., John, O.P., 2006. Anticipatory and consummatory components of the experience of pleasure: a scale development study. J. Res. Pers. https://doi.org/10.1016/j.jrp.2005.11.001.
Gard, D.E., Kring, A.M., Gard, M.G., Horan, W.P., Green, M.F., 2007. Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. Schizophr. Res. https://doi.org/10.1016/j.schres.2007.03.008.
Gard, D.E., Cooper, S., Fisher, M., Genevsky, A., Mikels, J.A., Vinogradov, S., 2011. Evidence for an emotion maintenance deficit in schizophrenia. Psychiatry Res. https://doi.org/10.1016/j.psychres.2010.12.018.
Gold, J.M., Hahn, B., Zhang, W.W., Robinson, B.M., Kappenman, E.S., Beck, V.M., Luck, S.J., 2010. Reduced capacity but spared precision and maintenance of working memory representations in schizophrenia. Arch. Gen. Psychiatry https://doi.org/10.1001/archgenpsychiatry.2010.65.
Gooding, D.C., Pflum, M.J., 2014. The assessment of interpersonal pleasure: introduction of the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS) and preliminary findings. Psychiatry Res. https://doi.org/10.1016/j.psychres.2013.10.012.
Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr. Bull. https://doi.org/10.1093/oxfordjournals.schbul.a033430.
Guy, W., 1976. ECDEU Assessment Manual for Psychopharmacology. National Institute of Mental Health, Rockville,MD, pp. 534–537.
Heerey, E.A., Gold, J.M., 2007. Patients with schizophrenia demonstrate dissociation between affective experience and motivated behavior. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.116.2.268.
Herbener, E.S., Song, W., Khine, T.T., Sweeney, J.A., 2008. What aspects of emotional functioning are impaired in schizophrenia? Schizophr. Res. https://doi.org/10.1016/j.schres.2007.06.025.
Insel, C., Reinen, J., Weber, J., Wager, T.D., Jarskog, L.F., Shohamy, D., Smith, E.E., 2014. Antipsychotic dose modulates behavioral and neural responses to feedback during reinforcement learning in schizophrenia. Cogn. Affect. Behav. Neurosci. 14, 189–201. https://doi.org/10.3758/s13415-014-0261-3.
Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. https://doi.org/10.1093/schbul/13.2.261.
Kemali, D., Maj, M., Galderisi, S., Monteleone, P., Mucci, A., 1987. Conditional associative learning in drug–free schizophrenic patients. Neuropsychobiology https://doi.org/10.1159/000118337.
Kring, A.M., Barch, D.M., 2014. The motivation and pleasure dimension of negative symptoms: neural substrates and behavioral outputs. Eur. Neuropsychopharmacol. 24, 725–736. https://doi.org/10.1016/j.euroneuro.2013.06.007.
Kring, A.M., Elis, O., 2013. Emotion deficits in people with schizophrenia. Annu. Rev. Clin. Psychol. https://doi.org/10.1146/annurev-clinpsy-050212-185538.
Kring, A.M., Germans Gard, M., Gard, D.E., 2011. Emotion deficits in schizophrenia: timing matters. J. Abnorm. Psychol. https://doi.org/10.1037/a0021402.
Kurtz, M.M., Moberg, P.J., Gur, R.C., Gur, R.E., 2001. Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis. Neuropsychol. Rev. https://doi.org/10.1023/A:1012953108158.
Kwapil, T.R., 1998. Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.107.4.558.
Lee, J., 2005. Working memory impairments in schizophrenia: a meta-analysis. Artic. J. Abnorm. Psychol. https://doi.org/10.1037/0021-843X.114.4.599.
Li, Z., Lui, S.S.Y., Geng, F. lei, Li, Y., Li, W. xiu, Wang, C. yue, Tan, S. ping, Cheung, E.F.C., Kring, A.M., Chan, R.C.K., 2015. Experiential pleasure deficits in different stages of schizophrenia. Schizophr. Res. https://doi.org/10.1016/j.schres.2015.05.041.

Loas, G., Monestes, J.L., Ingelaere, A., Noisette, C., Herbener, E.S., 2009. Stability and relationships between trait or state anhedonia and schizophrenic symptoms in schizophrenia: a 13-year follow-up study. Psychiatry Res. https://doi.org/10.1016/j.psychres.2008.02.010.

Lui, S.S.Y., Wang, Y., Shi, Y. fang, Au, A.C.W., Wong, P.T.Y., Chu, Z.L.S., Kring, A.M., Cheung, E.F.C., Chan, R.C.K., 2015. Subjective pleasure experience in patients with recent-onset schizophrenia: a preliminary report. Psychiatry Res. https://doi.org/10.1016/j.psychres.2015.04.013.

Mann, C.L., Footer, O., Chung, Y.S., Driscoll, L.L., Barch, D.M., 2013. Spared and impaired aspects of motivated cognitive control in schizophrenia. J. Abnorm. Psychol. https://doi.org/10.1037/a0033069.

Mikels, J.A., Reuter-Lorenz, P., Beyer, J., 2008. Emotion and working memory: evidence for domain-specific processes for affective maintenance. Emotion https://doi.org/10.1037/1528-3542.8.2.256.

Mote, J., Minzenberg, M.J., Carter, C.S., Kring, A.M., 2014. Deficits in anticipatory but not consummatory pleasure in people with recent-onset schizophrenia spectrum disorders. Schizophr. Res. https://doi.org/10.1016/j.schres.2014.07.048.

Park, K.M., Kim, J.J., Jeong, H.S., Ji, W.C., Park, H.J., Jong, D.L., 2009. Anhedonia and ambivalence in schizophrenic patients with fronto-cerebellar metabolic abnormalities: a fluoro-D-glucose positron emission tomography study. Psychiatry Investig. https://doi.org/10.4306/pi.2009.6.2.72.

Park, I.H., Chun, J.W., Park, H.J., Koo, M.S., Park, S., Kim, S.H., Kim, J.J., 2015. Altered cingulostriatal function underlies reward drive deficits in schizophrenia. Schizophr. Res. https://doi.org/10.1016/j.schres.2014.11.005.

Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P., 2015. Ventral striatal activation during reward processing in psychosis a neurofunctional meta-analysis. JAMA Psychiatry https://doi.org/10.1001/jamapsychiatry.2015.2196.

Rocca, P., Montemagni, C., Zappia, S., Piterà, R., Sigaudo, M., Bogetto, F., 2014. Negative symptoms and everyday functioning in schizophrenia: a cross-sectional study in a real world-setting. Psychiatry Res. https://doi.org/10.1016/j.psychres.2014.04.018.

Rund, B.R., 1998. A review of longitudinal studies of cognitive functions in schizophrenia patients. Schizophr. Bull. https://doi.org/10.1093/oxfordjournals.schbul.a033337.

Schacter, D.L., Addis, D.R., Buckner, R.L., 2007. Remembering the past to imagine the future: the prospective brain. Nat. Rev. Neurosci. https://doi.org/10.1038/nrn2213.

Schlosser, D.A., Fisher, M., Gard, D., Fulford, D., Loewy, R.L., Vinogradov, S., 2014. Motivational deficits in individuals at-risk for psychosis and across the course of schizophrenia. Schizophr. Res. https://doi.org/10.1016/j.schres.2014.06.024.

Strauss, G.P., Wilbur, R.C., Warren, K.R., August, S.M., Gold, J.M., 2011. Anticipatory vs. consummatory pleasure: what is the nature of hedonic deficits in schizophrenia? Psychiatry Res. https://doi.org/10.1016/j.psychres.2011.01.012.

Ursu, S., Kring, A.M., Gard, M.G., Minzenberg, M.J., Yoon, J.H., Ragland, J.D., Solomon, M., Carter, C.S., 2011. Prefrontal cortical deficits and impaired cognition-emotion interactions in schizophrenia. Am. J. Psychiatry https://doi.org/10.1176/appi.ajp.2010.09081215.

Wang, C., Yang, Y., Chen, M., Chiu, N., ... T.Y.-T.K. journal, 2003. Negative symptoms and regional cerebral blood flow in patients with schizophrenia: a single photon emission computed tomography study. Elsevier undefined, n.d.

Wiecki, T.V., Riedinger, K., Von Ameln-Mayerhofer, A., Schmidt, W.J., Frank, M.J., 2009. A neurocomputational account of catalepsy sensitization induced by D2 receptor blockade in rats: Context dependency, extinction, and renewal. Psychopharmacology (Berl) https://doi.org/10.1007/s00213-008-1457-4.

Wynn, J.K., Horan, W.P., Kring, A.M., Simons, R.F., Green, M.F., 2010. Impaired anticipatory event-related potentials in schizophrenia. Int. J. Psychophysiol. https://doi.org/10.1016/j.ijpsycho.2010.05.009.

Yan, C., Yang, T., Yu, Q. jing, Jin, Z., Cheung, E.F.C., Liu, X., Chan, R.C.K., 2015. Rostral medial prefrontal dysfunctions and consummatory pleasure in schizophrenia: a meta-analysis of functional imaging studies. Psychiatry Res. - Neuroimaging. https://doi.org/10.1016/j.pscychresns.2015.01.001.

Zheng, Y., Wei, L., Lianggue, G., Guochen, Z., Chenggue, W., 1988. Applicability of the Chinese beck depression inventory. Compr. Psychiatry https://doi.org/10.1016/0010-440X(88)90063-6.