Aberrant salience and reward processing: a comparison of measures in schizophrenia and anxiety

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Abstract

Background. Aberrant salience may contribute to the development of schizophrenia symptoms via alterations in reward processing and motivation. However, tests of this hypothesis have yielded inconsistent results. These inconsistencies may reflect problems with the validity and specificity of measures of aberrant salience in schizophrenia. Therefore, we investigated relationships among measures of aberrant salience, reward, and motivation in schizophrenia and anxiety.

Method. Individuals with schizophrenia ($n = 30$), anxiety ($n = 33$) or unaffected by mental disorder ($n = 30$) completed measures of aberrant salience [Aberrant Salience Inventory (ASI), Salience Attribution Test (SAT)], motivation (Effort Expenditure for Reward Task), and reinforcer sensitivity (Stimulus Chase Task).

Results. Schizophrenia participants scored higher than anxiety ($d = 0.71$) and unaffected ($d = 1.54$) groups on the ASI and exhibited greater aberrant salience ($d = 0.60$) and lower adaptive salience ($d = 0.98$) than anxious participants on the SAT. There was no evidence of a correlation between measures of aberrant salience. Schizophrenia was associated with related deficits in motivated behaviour and maladaptive reward processing. However, these differences in reward processing did not correlate with aberrant salience measures.

Conclusions. The results suggest that key measures of aberrant salience have limited specificity and validity. These problems may account for inconsistent findings reported in the literature.

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Introduction

Aberrant salience is a prominent explanation for the development of psychosis symptoms. According to Kapur (2003), dysregulated dopaminergic firing results in the creation, or exaggeration, of the importance of external objects or events and internal thoughts or perceptions. Dopaminergic firing is associated with motivational salience, the cognitive process of directing attention and behaviour. In the absence of a relevant stimulus context, Kapur (2003) proposed dopaminergic firing leads to impairments in motivational salience and the assignment of importance to irrelevant stimuli. Kapur (2003) suggested delusions serve an explanatory function for patients, explaining the importance of aberrant stimuli, whereas hallucinations manifest from aberrant visual and auditory percepts.

There is some evidence for aberrant salience in schizophrenia, however results are inconsistent. Studies show increased emotional arousal (Haralanova, Haralanov, Beraldi, Moller, & Hennig-Fast, 2012) and neural activation (Horan, Hajcak, Wynn, & Green, 2013) to neutral stimuli in schizophrenia – a pattern that is observed in unaffected individuals who are exposed to negative stimuli. Compared to unaffected individuals, those with schizophrenia rate environmental sounds as more invasive, and artificial abstract sounds as more familiar (Micoulaud-Franchi et al., 2012). Data from measures of aberrant salience, such as the Aberrant Salience Inventory (ASI; Cicero, Kerns, & McCarthy, 2010) and Salience Attribution Test (SAT; Roiser et al., 2009), show heightened aberrant salience in schizophrenia compared to controls (Cicero et al., 2010; Katthagen et al., 2016; Pankow et al., 2015). Additionally, aberrant salience is associated with abnormal beliefs (Roiser, Howes, Chaddock, Joyce, & McGuire, 2013), perceptual aberration, and magical ideation (Cicero et al., 2010; Cicero, Becker, Martin, Docherty, & Kerns, 2013) in individuals with no history of psychosis, suggesting a link between aberrant salience and psychosis risk. Conversely, SAT data from other studies suggest that salience is normal in schizophrenia (Abboud et al., 2016; Roiser et al., 2009).

Reasons for inconsistent findings vary. Aberrant salience may be more prominent during the prodromal phase than other illness phases (Roiser et al., 2013) or be attenuated by medication (Roiser et al., 2009). However, these accounts have not been replicated (Smieskova et al., 2015;

Walter et al., 2016). Alternatively, there is limited evidence of the validity of aberrant salience measures in schizophrenia. ASI scores correlate with psychotic-like experiences, such as magical ideation, in unaffected individuals and discriminate schizophrenia from other psychopathologies, such as bipolar disorder (Cicero et al., 2010). The SAT shows good construct validity in unaffected individuals (Schmidt & Roiser, 2009) and concurrent validity (Katthagen et al., 2016). However, more robust validity studies are needed, examining whether aberrant salience measures correlate with cognitive processes associated with dopamine function, such as motivational salience and reinforcer sensitivity.

Schizophrenia is associated with impairments in motivational salience, such as a reduced ability to unlearn previous associations (Waltz, Frank, Robinson, & Gold, 2007), aberrant reward-related behaviour (Barch, Treadway, & Schoen, 2014; Fervaha et al., 2013; Gold et al., 2013; McCarthy, Treadway, Bennett, & Blanchard, 2016; Reddy et al., 2015; Strauss et al., 2011), and disrupted loss sensitivity (Currie et al., 2017; Scholten, van Honk, Aleman, & Kahn, 2006; Trémeau et al., 2008). Reduced activation of reward-related neural regions in schizophrenia is associated with reward receipt (Gradin et al., 2013; Schlagenhauf et al., 2009), impaired reward anticipation (Radua et al., 2015), and reward-seeking behaviour (Wolf et al., 2014).

Kapur (2003) proposed that motivational salience mediates aberrant salience. However, evidence of an association between motivational salience and measures of aberrant salience is limited. Ceaser and Barch (2016) found incorrect identification of a distractor stimulus as salient was associated with increased dorsal striatal activation in schizophrenia, with the degree of activation positively correlating with ASI score. Boehme et al. (2015) found high SAT implicit aberrant salience in unaffected individuals was associated with reduced ventral striatum activation during reward prediction error.

We previously reported finding no evidence that the ASI and SAT indices are correlated among undergraduates with no history of psychosis (Neumann & Linscott, 2018). At most, the ASI and SAT indices predicted aspects of willingness to expend effort under different task conditions. For example, higher ASI scores predicted greater willingness to expend effort for small, less likely rewards, and the SAT behavioural measure of aberrant salience predicted less effort for large, more likely rewards. The primary finding, that the ASI and SAT were unrelated, may reflect: (a) the effects of range restriction in aberrant salience in unaffected individuals; or (b) a typical pattern of reinforcer sensitivity and motivation in unaffected individuals compared to that seen in individuals with schizophrenia.

Therefore, our aim was to investigate relationships among measures of aberrant salience, motivation, and reinforcer sensitivity in schizophrenia and anxiety groups and in unaffected individuals. We elected to compare schizophrenia to anxiety because of evidence that anxiety results from the conflict of competing goals during reward processing (Corr & McNaughton, 2012; Gray & McNaughton, 2000). That is, although reward processing is associated with anxiety and psychosis, the sources of symptom development are thought to differ between these disorders. If aberrant salience is specific to schizophrenia, predicted relationships between measures should be evident in schizophrenia but not in anxious and unaffected individuals.

Participants with schizophrenia, anxiety, and unaffected individuals completed measures of motivational salience [Effort Expenditure for Rewards Task (EEfRT); Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009] and reinforcer sensitivity

[Stimulus Chase Task (SCT); Hall, Chong, McNaughton, & Corr, 2011] along with the ASI and SAT. We predicted that the schizophrenia group would exhibit greater aberrant salience on the ASI and SAT than would unaffected or anxiety groups (Cicero et al., 2010; Katthagen et al., 2016; Pankow et al., 2015). We expected greater variance of aberrant salience in schizophrenia, resulting in relationships between measures of aberrant salience that would not be present in the unaffected and anxiety groups. We also examined the relationship between measures of motivation and aberrant salience. We hypothesised that, in schizophrenia, aberrant salience would predict comparatively greater and lesser engagement in hard tasks when these were poorly and richly rewarded, respectively (Fervaha et al., 2013). Finally, we predicted that relative sensitivity to gain and loss would correlate with aberrant salience indices (Currie et al., 2017; Scholten et al., 2006; Trémeau et al., 2008). We also explored whether relationships among measures were consistent across groups or specific to schizophrenia.

Methods

Participants and procedures

Patients ($n = 34$) with working diagnoses of schizophrenia, schizoaffective disorder, schizophreniform disorder, or first-episode psychosis were recruited by referral from mental health clinicians. Patients with anxiety ($n = 37$) and individuals with no mental disorder ($n = 31$) were recruited using posters in hospital staff areas and an online advertisement in a local newspaper. Inclusion criteria for the anxiety group were meeting diagnostic criteria for an anxiety disorder and reporting no prior or current psychotic symptoms. The inclusion criterion for the unaffected group was the absence of current or past experience of mental health issues. All participants were aged 18 to 65 years and indicated no history of neurological injury or disease. For the large effects ($f^2 = 0.35$) expected between measures of the same construct, where $\alpha = 0.05$, a sample of 30 per group affords a power of ~0.84. For large effects ($r = 0.5$) between measures within groups, where $\alpha = 0.05$, a sample of 30 affords a power of ~0.83.

In the clinical groups, the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 2010) was used, in conjunction with other measures and clinical evidence, to confirm the current working diagnosis and assess symptom expression. The schizophrenia group included one participant who met criteria for schizoaffective disorder and two who denied any clinically relevant mental health symptoms yet had working diagnoses of schizophrenia and histories of in- and out-patient psychiatric care and treatment for schizophrenia. Five referrals to the schizophrenia group were excluded: one who reported faking symptoms of psychosis; two who met the MINI criteria for primary mood disorder rather than a psychotic disorder; one with current (<3 months) alcohol dependency; and one who was unable to complete the assessment. All anxiety participants met the MINI diagnostic criteria for an anxiety disorder. Two were reassigned to the schizophrenia group as they met the MINI diagnostic criteria for schizophrenia and two others were excluded because of age or current alcohol dependence. One unaffected individual was excluded due to prior diagnosis of mental health issues. Table 1 shows demographic characteristics of participants included in the final analysis. Table 2 shows MINI output and current positive symptom summary for schizophrenia and anxiety participants.

Table 1. Demographics for unaffected, anxiety and schizophrenia groups

Demographic	Unaffected (n = 30)	Anxiety (n = 33)	Schizophrenia (n = 30)
Female n (%)	19 (63)	25 (76)	6 (20)
Age in years M (s.d.)	32 (10)	35 (10)	44 (11)
Ethnicity n (%)			
NZ European	20 (67)	26 (79)	21 (70)
Maori	1 (3)	3 (9)	4 (13)
Other	9 (30)	4 (12)	5 (16)
Currently employed n (%)	22 (73)	20 (61)	6 (20)
Household income n (%)			
>200k	–	1 (3)	–
151–200	2 (7)	2 (6)	–
101–150	3 (10)	5 (15)	–
76–100k	4 (13)	4 (12)	1 (4)
51–75k	5 (17)	3 (9)	2 (8)
26–50k	8 (27)	7 (21)	1 (4)
<25k	8 (27)	11 (33)	21 (84)
First degree relative mental health diagnosis n (%)			
Schizophrenia spectrum	–	1 (3)	4 (13)
Anxiety disorder	2 (7)	8 (24)	2 (7)
Other	3 (10)	4 (12)	3 (10)

Table 2. Clinical characteristics of anxiety and schizophrenia groups

Diagnosis/symptoms[a]	Anxiety (n = 33)	Schizophrenia (n = 30)
Primary diagnosis N (%)		
Psychotic disorder	–	28 (93)
Mood disorder with psychotic features	–	2 (7)[b]
Positive symptoms	–	21 (70)
Delusions	–	14 (47)
Auditory hallucinations	–	12 (40)
Visual hallucinations	–	6 (20)
Anxiety	33 (100)	–
General anxiety disorder	17 (51.5)	–
Social phobia/disorder	5 (15)	–
Panic disorder	3 (9)	–
Non-anxiety primary disorder	7 (21)	–
Inconclusive	1 (3)	–
Secondary diagnosis (current) N		
General anxiety disorder	2	3
Social phobia/disorder	8	3
Panic disorder	14	11
Agoraphobia	14	4
PTSD	1	–
Major depressive disorder	–	1
Bipolar disorder I	–	2
Obsessive compulsive disorder	–	4
Secondary diagnosis (past/recurrent) N		
Major depressive disorder (recurrent)	12	4
Major depressive disorder (past)	7	2
Bipolar disorder I	1	3
Bipolar disorder II	1	–
Manic/hypomanic episode	–	4

[a]Classification based on the MINI.
[b]These patients had working diagnoses of schizophrenia and schizoaffective disorder, respectively.

Clinical group participants attended two ~90-min sessions. In the first, participants completed a demographics questionnaire and the ASI, SAT, EEfRT and SCT. The performance task order was counterbalanced across participants. During the second session, conducted within a week of the first, participants completed the screening and symptom measures. Unaffected participants attended one 2-hr session during which they completed all measures except the MINI.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the University of Otago Human Ethics Committee (H16/026). All participants provided written informed consent. Participants were offered a payment of $25 per appointment.

Measures

Screening and symptoms

The Alcohol and Drug Abuse and Dependence Screen (ADDS; Muthén, 1995) was used to screen for problematic substance use. The ADDS contains items that address the quantity and impact of consumption of drugs and alcohol. Outcome scores range from 0 (no use) to 240 (severe dependency).

The Depression Anxiety Stress Scales (DASS; Lovibond and Lovibond, 1995) were used to quantify mood and anxiety symptoms. The DASS contains 42 self-report items that respondents rate from 0 = *did not apply at all* to 3 = *applied most of the time*, with 14 items relating to each of depression, anxiety, and stress.

Nine items comprising the Anxiousness facet of the Personality Inventory for *DSM-5* (PID-5A; American Psychiatric Association, 2013b) were used to assess anxious temperament. Respondents

rate items from 0 = *very false or often false* to 3 = *very true or often true*.

The *DSM-5* Self-Rated Level 1 Cross-Cutting Symptom Measure (L1SM; American Psychiatric Association, 2013a) was used to screen for current mental health issues. The L1SM is a 23-item screen for key features of depression, anger, mania, anxiety, somatic symptoms, suicidal ideation, psychosis, sleep problems, memory impairment, repetitive thoughts and behaviours, dissociation, personality functioning, and substance use experienced in the past 2 weeks. Respondents rate items from 0 = none/*not at all* to 4 = *severe/nearly every day*.

The MINI (Sheehan et al., 2010) was used to evaluate current and past diagnoses. The MINI is a semi-structured brief interview covering *DSM-IV* and ICD-10 Axis I psychiatric disorders.

Aberrant salience

The ASI (Cicero et al., 2010) was used as a self-report measure of aberrant salience. The ASI consists of 29 dichotomous-response items about lifetime experiences and beliefs characterised by aberrant salience. The ASI score is the number of endorsed items. ASI scores have high test-retest reliability over 2 weeks (0.96; Lelli et al., 2015), high internal consistency ($\alpha = 0.89$; Cicero et al., 2010; Lelli et al., 2015), and predict psychotic experiences (Cicero et al., 2010).

The SAT (Roiser et al., 2009) was used as a performance measure of adaptive and aberrant salience. The SAT is a computerised task that uses implicit and explicit associative learning of stimulus-reinforcement contingencies to measure adaptive and aberrant salience. The task comprises two blocks of 64 trials. In each trial, a red or blue line drawing of an animal or household object appears above and below a fixation cross. When the fixation cross is replaced by a black box, respondents are to press a button as fast as possible. Following each trial, feedback indicates whether the trial was reinforced and, if so, the amount of reward.

Participants are informed that response latency determines reward magnitude (*reward*; between 10c and $1) whereas stimulus type determines reward probability (*probability*). For the latter, the stimulus-reward contingencies vary randomly across participants. That is, for a participant, only one of the two dimensions (colour = red or blue; semantic category = household object or animal) is *task relevant*. On the task-relevant dimension, one level has a high reinforcement probability (87.5%) and the other a low reinforcement probability (12.5%); on the task-irrelevant dimension, both levels have a 50% reinforcement probability.

Dependent measures include implicit and explicit indices of adaptive and aberrant salience. Implicit adaptive salience is the mean difference in response latency (ms) between high and low probability trials of the task-relevant dimension; implicit aberrant salience is the absolute between-level difference in response latency on the task-irrelevant dimension. Explicit measures are obtained by asking respondents at the end of each 64-trial block to indicate the probability that each stimulus type was rewarded, with responses given on a visual analogue scale (mm).

Reward processing

The EEfRT (Treadway et al., 2009) was used to assess decision making. The EEfRT is a computerised, multi-trial, fixed-duration task in which willingness to exert effort (determined by task choice) is assumed to reflect motivation. At the start of each trial, respondents are told the rewards for easy (set at $1) and hard (between $1.24 and $4.30) task choices and the probability

of winning (12, 50 or 88%). In the easy task, respondents use the dominant index finger to complete 30 buttons presses whereas in the hard task, the non-dominant little finger to complete 100 buttons presses. After choosing and completing the selected task, trial feedback indicates whether a reward was available and how much was won. The dependent variable is task choice. As the easy task took less time to complete than the hard task, the number of trials completed during the 20-min task varied between participants.

The SCT (Hall et al., 2011) was used to assess relative sensitivities to gain and loss and relative tendencies for approach and avoidance. Respondents begin the task with a nominal balance of $180 (equivalent to NZ$1.80) and are told they will be paid the cash equivalent of their end-of-task balance. The SCT has two phases, each comprising 50 blocks of 5 trials. In each trial the respondent sees a blue box on a computer screen. Gain and loss values (e.g. '+$6, –$2') are displayed alongside the box. The respondent's task is to choose whether to chance a gain or loss (outcome probability = 50%) or to refrain and retain the current balance. If they take the gamble, the trial ends with feedback showing the outcome and the revised balance.

At the start of each block, respondents are told gain and loss values for the block; these do not vary within blocks. Across blocks, gain and loss values follow the sequence, (+8, −8), (+8, −6), (+8, −4), (+8, −2), (+8, −0), (+6, −8), … , (+0, −2), (+0, −0), (+0, −0), (+0, −2), (+0, −4), … , (+8, −6), (+8, −8). At the start of each phase, respondents are told how to enter or refrain from the gamble: In Phase 1, respondents click on the blue box to chance the outcome; in Phase 2, respondents chance the outcome by not clicking. If there is no response, trials end at 3000 ms. Thus, Phases 1 and 2 capture approach and avoidance behaviour, respectively. Decision speed is recorded.

The SCT yields two dependent measures based on the response time: the ratios of gain to loss sensitivities and of approach to avoidance tendencies. Sensitivity and tendency parameters are modelled with the matching law (Hall et al., 2011) using Microsoft® Excel Solver. If the model fit is poor (i.e. $r^2 < 0.7$), participant's SCT data are excluded.

Analysis

Planned comparisons and ANOVA with Games-Howell post hoc analysis were used to test group differences in measures. Pearson's correlation coefficient (2-tailed unless otherwise stated), with the Holm adjusted significance level, was used to assess relationships among measures within each group. Holm correction for multiple comparisons was carried out on each within-group measure pair. For planned comparisons, ANOVA, and correlations, bias-corrected and accelerated bootstrapped confidence intervals (95%, 10 000 samples) were computed using SPSS version 25 (IBM Corp, 2017). SCT ratios were log-transformed for analysis. Holm's correction was applied to families of hypotheses using R psycho package (Makowski, 2018).

EEfRT trials were categorised by probability (12, 50 and 88%) and reward (low <$2, medium $2 to $2.99, high ⩾$3), yielding 9 trial types, and the proportion of hard task choices (effort) was obtained for each trial type. Mixed-effects modelling was used to calculate the effects of probability, reward, and reward × probability on task choice. Models included random slopes and intercepts. Mixed-effects analyses were conducted using R (R Development Core Team, 2016) with the Hmisc (Harrell,

Table 3. Means and their bootstrapped (BCa) 95% confidence intervals (CI) for the ASI, SAT, SCT and EEfRT

Measure	Group mean (CI)		
	Unaffected	Anxiety	Schizophrenia
ASI	*n* = 30	*n* = 33	*n* = 30
	9.5 (7.34, 11.73)	13.6 (11.10, 15.89)	17.7 (16.11, 19.12)
SAT	*n* = 30	*n* = 33	*n* = 30
Implicit AS	17.3 (13.32, 21.84)	14.5 (11.24, 18.16)	24.0 (17.80, 30.72)
Explicit AS	7.8 (5.20, 11.25)	10.2 (7.42, 13.33)	8.8 (5.63, 12.33)
Implicit AdS	9.2 (3.58, 14.63)	10.1 (3.97, 16.33)	1.5 (−5.78, 8.76)
Explicit AdS	40.3 (30.26, 50.58)	39.2 (28.15, 49.84)	12.8 (5.73, 20.75)
SCT	*n* = 17	*n* = 23	*n* = 12
A:A ratio	.50 (.45, .55)	.54 (.50, .58)	.65 (.58, .73)
G:L ratio	−.34 (−.45, −.25)	−.34 (−.41, −.27)	−.53 (−.70, −.38)
EEfRT	*n* = 30	*n* = 33	*n* = 30
Hard choices	.42 (.37, .47)	.38 (.34, .43)	.26 (.20, .33)
L Pr	.18 (.12, .25)	.13 (.10, .18)	.21 (.15, .28)
M Pr	.43 (.37, .49)	.35 (.28, .42)	.24 (.18, .31)
H Pr	.63 (.56, .70)	.66 (.58, .73)	.33 (.24, .42)
L $	.14 (.09, .19)	.17 (.12, .22)	.18 (.11, .26)
M $	.36 (.30, .42)	.34 (.29, .40)	.24 (.18, .31)
H $	.59 (.53, .66)	.53 (.47, .60)	.31 (.24, .38)
L Pr L $	.06 (.02, .10)	.07 (.02, .13)	.19 (.11, .29)
L Pr M $	.19 (.12, .27)	.13 (.09, .18)	.20 (.14, .27)
L Pr H $	.25 (.17, .35)	.18 (.12, .25)	.23 (.15, .31)
M Pr L $	.13 (.07, .20)	.12 (.08, .16)	.12 (.06, .18)
M Pr M $	.38 (.29, .48)	.34 (.24, .45)	.26 (.17, .34)
M Pr H $	.66 (.57, .74)	.50 (.40, .61)	.32 (.24, .41)
H Pr L $	.24 (.16, .33)	.31 (.22, .42)	.24 (.14, .36)
H Pr M $	.60 (.48, .73)	.65 (.54, .76)	.30 (.20, .41)
H Pr H $	.86 (.78, .93)	.86 (.77, .93)	.39 (.30, .49)

ASI, Aberrant Salience Inventory; SAT, Salience Attribution Test; SCT, Stimulus Chase Task; EEfRT, Effort Expenditure for Reward Task; AS, aberrant salience; AdS, adaptive salience; A:A, approach-avoid; G:L, gain-loss; L, low; M, medium; H, high; Pr, probability; $, reward.

2016), lme4 (Bates, Maechler, Bolker, & Walker, 2015), and psych (Revelle, 2016) packages.
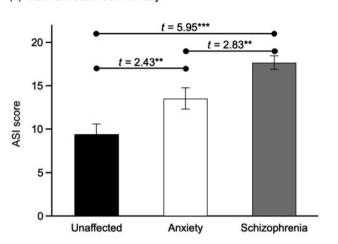
Results

One outlier in the schizophrenia group fell above 1.5 × the inter-quartile range and singularly skewed results, creating a correlation between ASI and SAT aberrant salience. Data from this outlier were excluded. SCT data from *n* = 41 participants did not fit the matching law. There was no difference between SCT fit and non-fit group means for other indices (all *p* > 0.10) and non-fitting behaviour was not associated with the group, $\chi^2(2) = 5.63$, *p* = 0.06. SCT data were analysed for: schizophrenia, *n* = 12; anxiety, *n* = 23 and unaffected, *n* = 17. The mean number of trials completed during the EEfRT was: schizophrenia, *m* = 65; anxiety, *m* = 68 and unaffected, *m* = 67.
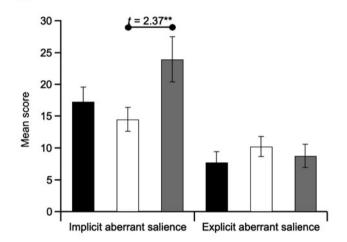
Group differences

Compared to anxiety, schizophrenia was associated with higher ASI and SAT implicit aberrant salience scores and lower explicit adaptive salience scores (Table 3, Fig. 1 and online Supplementary Fig. S1). The schizophrenia group also had higher ASI scores and lower explicit adaptive salience scores than the unaffected group. The anxiety group had higher on ASI scores than the unaffected group.
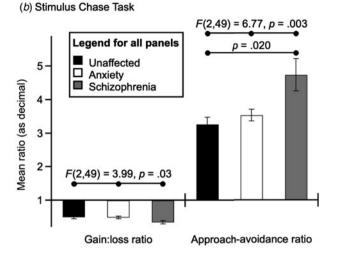
Both SCT ratios differed across groups (Fig. 1b). Ratios over 1 indicate greater sensitivity to gain than loss and greater tendency to approach than avoid, respectively. Compared to the unaffected group, schizophrenia was associated with a higher approach-avoidance ratio.

During the EEfRT task, the schizophrenia group chose the hard task more often with lower less likely rewards; and less often for higher, more certain rewards and for medium and high combinations of probability and reward (Fig. 1). There was also an effect of
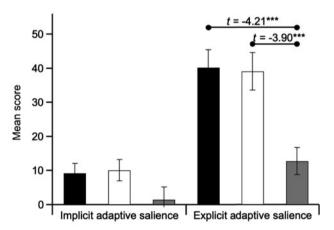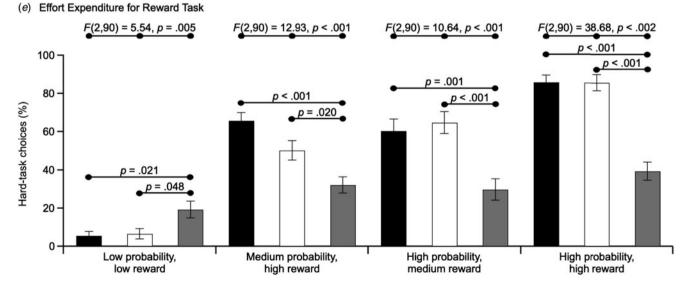
Fig. 1. Mean group scores showing significant differences in planned comparisons for (*a*) ASI, (*b*) Stimulus Chase Task gain-loss and approach-avoidance ratios, (*c*) SAT Attribution Test implicit and explicit aberrant salience and (*d*) Salience Attribution Test implicit and explicit adaptive salience; and ANOVA and *post hoc* differences for significant group differences in (*e*) reward × probability combinations of the Effort Expenditure for Reward Task. Error bars show standard error of the mean.

Table 4. Effect of reward, probability and reward × probability on task choice[a]

	B	S.E.	95% CI Lower	95% CI Upper
Intercept	−4.62***	0.67	−5.92	−3.31
Reward	0.77***	0.19	0.39	1.14
Probability	0.21	0.88	−1.51	1.93
Anxiety group	0.81	0.90	−0.95	2.57
Schizophrenia group	2.42**	0.88	0.70	4.15
Reward × probability	1.30***	0.27	0.77	1.81
Reward × anxiety group	−0.48	0.27	−1.00	0.04
Reward × schizophrenia group	−0.63*	0.26	−1.13	−0.13
Probability × anxiety group	0.12	1.19	−2.20	2.45
Probability × schizophrenia group	−0.73	1.15	−3.00	1.53
Reward × probability × anxiety	0.23	0.36	−0.49	0.94
Reward × probability × schizophrenia	−0.78*	0.34	−1.45	−0.11

[a]Unaffected individuals and hard task choice are baseline.
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

group, with the schizophrenia group selecting the hard task less often than the unaffected and anxiety groups. The effects of reward and reward × probability were also significantly lower in the schizophrenia group compared to the unaffected and anxiety groups (Table 4). There were no main effects of probability.

The number of males and females differed across groups, $\chi^2(2) = 21.29$, $p < 0.001$. Additionally, the mean age of the psychosis group ($M = 43.5$, S.E. $= 2.06$) was higher than the unaffected ($M = 32.10$, S.E. $= 1.83$), $t(58) = −4.14$, $p < 0.001$, $r = 0.47$, and anxiety ($M = 34.82$, S.E. $= 1.83$) groups, $t(59.37) = −3.16$, $p = 0.003$, $r = 0.37$. Multiple regression with bootstrapped confidence intervals (95%, 10 000 samples) were computed to investigate the effect of age and sex covariates on group differences. Controlling for age and sex did not make any substantive difference except that there was no longer any evidence of a schizophrenia group difference on low-probability low-reward EEfRT scores ($\beta = 0.07$, 95% CI −.02, .16)

Within-group relationships between measures

There was no evidence that the ASI correlated with any other measure in the schizophrenia group. SAT implicit and explicit adaptive salience positively correlated, however correlations between SAT, EEfRT, and SCT indices did not survive the Holm correction (online Supplementary Table S1). Similarly, none of the correlations between measures in the anxiety group survived the Holm correction (online Supplementary Table S2). In the unaffected group, ASI and explicit aberrant salience predicted relatively lower gain:loss sensitivity (online Supplementary Table S3). No other correlations survived Holm correction.

Discussion

There was partial support for the idea that, compared to anxiety, schizophrenia is associated with greater expressed aberrant salience. Schizophrenia was associated with higher ASI and higher

SAT implicit aberrant salience scores. However, contrary to our hypotheses, the ASI and SAT aberrant salience indices were negatively correlated, albeit not significantly. We found no evidence for a relationship between aberrant salience indices and reinforcer sensitivity in schizophrenia and correlations between aberrant salience and motivational salience did not survive corrections for multiple testing. Support for the construct validity of aberrant salience indices against reward processing measures was also limited in unaffected and anxiety groups.

The results have several implications for the interpretation of ASI and SAT data. First, they cast doubt on the validity of the ASI and, to a lesser extent, the SAT. The intermediate rating of the anxiety group suggests the ASI measures a trait that is not unique to schizophrenia. Furthermore, the failure to find a relationship between the ASI and EEfRT indicates that the construct measured with the ASI is not related to motivational salience. There was no evidence that implicit aberrant salience predicted effortful decision-making in the schizophrenia group. These findings rest in stark contrast to what would be expected given even modest construct validity and specificity. The lack of relationship could be due to construct validity issues with the EEfRT. However, this is unlikely given the current data from the EEfRT are consistent with evidence suggesting maladaptive behaviour in schizophrenia and contrast with the adaptive behaviour found in unaffected individuals (Barch et al., 2014; Fervaha et al., 2013; McCarthy et al., 2016; Strauss, Waltz, & Gold, 2014).

This notwithstanding, the schizophrenia group did exhibit a pattern of inefficient, maladaptive behaviour not seen in the anxiety or unaffected groups. Schizophrenia was associated with lower adaptive but higher aberrant reinforcement learning. During the EEfRT, the schizophrenia group exhibited less adaptive behaviour, pursuing the hard task when it was less likely to yield higher rewards but not when higher more likely rewards were available.

Several mechanisms may underlie this pattern of behaviour in schizophrenia. Impaired cost and effort computations in schizophrenia have previously been linked to impairments in working memory, value representations, and cost calculations (Strauss et al., 2014). The current findings indicate reduced cognitive effort during cost and effort computations in schizophrenia. Specifically, stimuli that required greater cognitive effort (e.g. determining reward value from a scale and calculating the reward by probability interaction) had less effect on task choice in the schizophrenia compared to other groups. These findings are in line with evidence suggesting reduced activation in the striatum, a region associated with acquired salience (Esslinger et al., 2013), contributes to impaired reward processing (Gradin et al., 2013; Radua et al., 2015; Roiser, Stephan, den Ouden, Friston, & Joyce, 2010; Schlagenhauf et al., 2009) and effortful behaviour (Wolf et al., 2014) in schizophrenia.

However, alternative accounts for these findings should also be considered. First, aberrant salience may be more evident in the prodromal phase but dampened in subsequent illness phases due to medication or symptom development (Abboud et al., 2016). If that were the case, the relationship between aberrant salience and motivational salience may also reduce. Secondly, it may be that the schizophrenia participants here exhibited intact reinforcement learning and motivational salience. However, in line with previous findings (Fervaha et al., 2013), the schizophrenia group exhibited aberrant effortful behaviour.

The findings should be considered in light of several limitations. First, given we examined aberrant salience indices obtained using different measurement methods, our expectation of

obtaining large effects may have been unreasonable or a larger sample should have been used. However, we are confident our expectations were reasonable and our key interpretation is safe for several reasons. The SAT implicit and explicit measures, which involve performance and global judgement methodologies (respectively), did show some evidence of significant within-group relationships; even though we used common methods for the SAT explicit and ASI measures, the magnitude of observed relationships was no greater than those for the SAT implicit measures; and the SAT implicit aberrant salience measure was negatively related to ASI ratings, albeit not significantly.

We did not record information on current medication for schizophrenia or anxiety group participants. A large proportion of the current schizophrenia group, however, reported current psychotic symptoms. Antipsychotic medication is not universally effective (e.g. Gotfredsen et al., 2017) and, among those for whom it is effective, is often not completely effective. However, future research should examine the effect of antipsychotics. All but one participant in the schizophrenia group were receiving treatment within a health care system at the time of participation whereas the anxiety group were not recruited via health services and many had not sought formal treatment. Furthermore, whereas unaffected participants underwent screening for current mental health experiences and asked about past mental health in the demographic questionnaire, there may have been undiagnosed or unreported mental health issues.

The implications of data loss due to chaotic behaviour, resulting in exclusion from SCT analysis, are also worth considering. Higher than expected exclusion rates may be explained if these had been observed in individuals with schizophrenia only. In that case, non-fitting behaviour could have been attributed to impairments in reward processing and motivational salience leading to chaotic behaviour (e.g. Currie et al., 2017; Gold et al., 2013; Reddy et al., 2015; Strauss et al., 2011). However, all groups had high SCT exclusion rates. Given this, we are now exploring whether and how to use non-fitting behaviour as an SCT task outcome. Finally, the groups were not well matched on age and sex. Although there was little evidence that the pattern of effects seen in the schizophrenia group was attributable to sex or age, matching would allow more accurate analysis of the effect.

The current findings suggest a variance in construct definition among measures of aberrant salience and challenge the construct validity of the measures. Therefore, caution should be applied when interpreting findings from currently available measures of aberrant salience. These implications, which rest in part on the failure to reject null hypotheses, should be addressed in future research. In addition to attending to limitations of power and effects of medication, it is critical that in future research investigators continue to develop and test new and diverse approaches to operationalising and measuring aberrant salience.

References

Abboud, R., Roiser, J. P., Khalifeh, H., Ali, S., Harrison, I., Killaspy, H. T., & Joyce, E. M. (2016). Are persistent delusions in schizophrenia associated with aberrant salience? *Schizophrenia Research: Cognition*, 4, 32–38. doi:10.1016/j.scog.2016.04.002.

American Psychiatric Association (2013a). DSM-5: Online assessment measures. Retrieved from http://www.psychiatry.org/practice/dsm/dsm5/online-assessment-measures.

American Psychiatric Association (2013b). The personality inventory for DSM-5 (PID-5) anxiety component. Retrieved from http://www.psychiatry.org/practice/dsm/dsm5/online-assessment-measures.

Barch, D. M., Treadway, M. T., & Schoen, N. (2014). Effort, anhedonia, and function in schizophrenia: Reduced effort allocation predicts amotivation and functional impairment. *Journal of Abnormal Psychology*, 123(2), 387–397. doi: 10.1037/a0036299.supp.

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). Lme4 package in R. *Journal of Statistical Software*, 67(1), 1–48. doi: 10.18637/jss.v067.i01.

Boehme, R., Deserno, L., Gleich, T., Katthagen, T., Pankow, A., Behr, J., … Schlagenhauf, F. (2015). Aberrant salience is related to reduced reinforcement learning signals and elevated dopamine synthesis capacity in healthy adults. *Journal of Neuroscience*, 35(28), 10103–10111. doi: 10.1523/JNEUROSCI.0805-15.2015.

Ceaser, A. E., & Barch, D. M. (2016). Striatal activity is associated with deficits of cognitive control and aberrant salience for patients with schizophrenia. *Frontiers in Human Neuroscience*, 9, 1–17. doi: 10.3389/fnhum.2015.00687.

Cicero, D. C., Becker, T. M., Martin, E. A., Docherty, A. R., & Kerns, J. G. (2013). The role of aberrant salience and self-concept clarity in psychotic-like experiences. *Personality Disorders: Theory. Research, and Treatment*, 4(1), 33–42. doi: 10.1037/a0027361.

Cicero, D. C., Kerns, J. G., & McCarthy, D. M. (2010). The Aberrant Salience Inventory: A new measure of psychosis proneness. *Psychological Assessment*, 22(3), 688–701. doi: 10.1037/a0019913.

Corr, P. J., & McNaughton, N. (2012). Neuroscience and approach/avoidance personality traits: A two stage (valuation-motivation) approach. *Neuroscience & Biobehavioral Reviews*, 36(10), 2339–2354. doi: 10.1016/j.neubiorev.2012.09.013.

Currie, J., Buruju, D., Perrin, J. S., Reid, I., Steele, J. D., & Feltovich, N. (2017). Schizophrenia illness severity is associated with reduced loss aversion. *Brain Research*, 1664, 9–16. doi: 10.1016/j.brainres.2017.03.006.

Esslinger, C., Braun, U., Schirmbeck, F., Santos, A., Meyer-Lindenberg, A., Zink, M., & Kirsch, P. (2013). Activation of midbrain and ventral striatal regions implicates salience processing during a modified beads task. *PLoS One*, 8(3), e58536. doi: 10.1371/journal.pone.0058536.

Fervaha, G., Graff-Guerrero, A., Zakzanis, K. K., Foussias, G., Agid, O., & Remington, G. (2013). Incentive motivation deficits in schizophrenia reflect effort computation impairments during cost-benefit decision-making. *Journal of Psychiatric Research*, 47(11), 1590–1596. doi: 10.1016/j.jpsychires.2013.08.003.

Gold, J. M., Strauss, G. P., Waltz, J. A., Robinson, B. M., Brown, J. K., & Frank, M. J. (2013). Negative symptoms of schizophrenia are associated with abnormal effort-cost computations. *Biological Psychiatry*, 74(2), 130–3223. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703817/pdf/nihms-434975.pdf.

Gotfredsen, D. R., Wils, R. S., Hjorthoj, C., Austin, S. F., Albert, N., … Nordentoft, M. (2017). Stability and development of psychotic symptoms and the use of antipsychotic medication – Long-term follow-up. *Psychological Medicine*, 47(12), 2118–2129. doi: 10.1017/S0033291717000563.

Gradin, V. B., Waiter, G., O'Connor, A., Romaniuk, L., Stickle, C., Matthews, K., … Steele, J. D. (2013). Salience network-midbrain dysconnectivity and blunted reward signals in schizophrenia. *Psychiatry Research: Neuroimaging*, 211(2), 104–111. doi: 10.1016/j.pscychresns.2012.06.003.

Gray, J. A., & McNaughton, N. (2000). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system* (2nd ed.). Oxford: Oxford University Press.

Hall, P. J., Chong, C. W., McNaughton, N., & Corr, P. J. (2011). An economic perspective on the reinforcement sensitivity theory of personality. *Personality and Individual Differences*, 51(3), 242–247. doi: 10.1016/j.paid.2010.06.023.

Haralanova, E., Haralanov, S., Beraldi, A., Moller, H. J., & Hennig-Fast, K. (2012). Subjective emotional over-arousal to neutral social scenes in paranoid schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience*, 262(1), 59–68. doi: 10.1007/s00406-011-0227-1.

Harrell, F. E., Jr. (2016). Hmisc: Harrell miscellaneous. R package version 3.3.1.

Horan, W. P., Hajcak, G., Wynn, J. K., & Green, M. F. (2013). Impaired emotion regulation in schizophrenia: Evidence from event-related potentials. *Psychological Medicine*, 43(11), 2377–2391. doi: 10.1017/S0033291713000019.

IBM Corp (2017). IBM SPSS Statistics for Mac. Armonk, N.Y., USA.

Kapur, S. (2003). Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, 160(1), 13–23.

Katthagen, T., Dammering, F., Kathmann, N., Kaminski, J., Walter, H., Heinz, A., & Schlagenhauf, F. (2016). Validating the construct of aberrant salience in schizophrenia – behavioral evidence for an automatic process. *Schizophrenia Research: Cognition*, 6, 22–27. doi: 10.1016/j.scog.2016.10.001.

Lelli, L., Godini, L., Lo Sauro, C., Pietrini, F., Spadafora, M., Talamba, G. A., & Ballerini, A. (2015). Validation of the Italian version of the aberrant salience inventory (ASI): A new measure of psychosis proneness. *Journal of Psychopathology*, 21(3), 281–286.

Lovibond, S. H. H., & Lovibond, P. F. F. (1995). *Manual for the depression anxiety stress scales* (2nd ed.). Sydney: Psychology Foundation.

Makowski, D. (2018). The psycho package: An efficient and publishing-oriented workflow for psychological science. *Journal of Open Source Software*, 3(22), 470.

McCarthy, J., Treadway, M. T., Bennett, M. E., & Blanchard, J. J. (2016). Inefficient effort allocation and negative symptoms in individuals with schizophrenia. *Schizophrenia Research*, 170(2–3), 278–284. doi: 10.1016/j.schres.2015.12.017.

Micoulaud-Franchi, J. A., Aramaki, M., Merer, A., Cermolacce, M., Ystad, S., Kronland-Martinet, R., … Vion-Dury, J. (2012). Toward an exploration of feeling of strangeness in schizophrenia: Perspectives on acousmatic and everyday listening. *Journal of Abnormal Psychology*, 121(3), 628–640. doi: 10.1037/a0026411.

Muthén, B. O. (1995). Factor analysis of alcohol abuse and dependence symptom items in the 1988 National Health Interview Survey. *Addiction*, 90(5), 637–645.

Neumann, S. R., & Linscott, R. J. (2018). The relationships among aberrant salience, reward motivation, and reward sensitivity. *International Journal of Methods in Psychiatric Research*, 27(e1615), 1–8. doi: 10.1002/mpr.1615.

Pankow, A., Katthagen, T., Diner, S., Deserno, L., Boehme, R., Kathmann, N., … Schlagenhauf, F. (2015). Aberrant salience is related to dysfunctional self-referential processing in psychosis. *Schizophrenia Bulletin*, 42, 67–76. doi: 10.1093/schbul/sbv098.

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*, 72(12), 1243–1251. doi: 10.1001/jamapsychiatry.2015.2196.

R Development Core Team (2016). R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.r-project.org/.

Reddy, L. F., Horan, W. P., Barch, D. M., Buchanan, R. W., Dunayevich, E., Gold, J. M., … Green, M. F. (2015). Effort-based decision-making paradigms for clinical trials in schizophrenia: Part 1 – Psychometric characteristics of 5 paradigms. *Schizophrenia Bulletin*, 41(5), 1045–1054. doi: 10.1093/schbul/sbv089.

Revelle, W. (2016). psych: Procedures for personality and psychological research. Evanston, Illinois: Northwestern University. Retrieved from https://cran.r-project.org/package=psych.

Roiser, J. P., Howes, O. D., Chaddock, C. A., Joyce, E. M., & McGuire, P. (2013). Neural and behavioral correlates of aberrant salience in individuals at risk for psychosis. *Schizophrenia Bulletin*, 39(6), 1328–1336. doi: 10.1093/schbul/sbs147.

Roiser, J. P., Stephan, K. E., den Ouden, H. E., Barnes, T. R., Friston, K. J., & Joyce, E. M. (2009). Do patients with schizophrenia exhibit aberrant salience? *Psychological Medicine*, 39(2), 199–209. doi: 10.1017/S0033291708003863.

Roiser, J. P., Stephan, K. E., den Ouden, H. E., Friston, K. J., & Joyce, E. M. (2010). Adaptive and aberrant reward prediction signals in the human brain. *Neuroimage*, 50(2), 657–664. doi: 10.1016/j.neuroimage.2009.11.075.

Schlagenhauf, F., Sterzer, P., Schmack, K., Ballmaier, M., Rapp, M., Wrase, J., … Heinz, A. (2009). Reward feedback alterations in unmedicated schizophrenia patients: Relevance for delusions. *Biological Psychiatry*, 65(12), 1032–1039. doi: 10.1016/j.biopsych.2008.12.016.

Schmidt, K., & Roiser, J. P. (2009). Assessing the construct validity of aberrant salience. *Frontiers in Behavioral Neuroscience*, 3, 58. doi: 10.3389/neuro.08.058.2009.

Scholten, M. R., van Honk, J., Aleman, A., & Kahn, R. S. (2006). Behavioral inhibition system (BIS), behavioral activation system (BAS) and schizophrenia: Relationship with psychopathology and physiology. *Journal of Psychiatric Research*, 40(7), 638–645. doi: 10.1016/j.jpsychires.2006.03.005.

Sheehan, D., Lecrubier, Y., Janavs, J., Harnett-Sheehan, K., Sheeha, M., & Gray, C. (2010). Mini International Neuropsychiatric Interview (MINI): English Versions 6.0.0.

Smieskova, R., Roiser, J. P., Chaddock, C. A., Schmidt, A., Harrisberger, F., Bendfeldt, K., … Borgwardt, S. (2015). Modulation of motivational salience processing during the early stages of psychosis. *Schizophrenia Research*, 166 (1–3), 17–23. doi: 10.1016/j.schres.2015.04.036.

Strauss, G. P., Frank, M. J., Waltz, J. A., Kasanova, Z., Herbener, E. S., & Gold, J. M. (2011). Deficits in positive reinforcement learning and uncertainty-driven exploration are associated with distinct aspects of negative symptoms in schizophrenia. *Biological Psychiatry*, 69(5), 424–431. doi: 10.1016/j.biopsych.2010.10.015.

Strauss, G. P., Waltz, J. A., & Gold, J. M. (2014). A review of reward processing and motivational impairment in schizophrenia. *Schizophrenia Bulletin*, 40 (Suppl. 2), 107–116. doi: 10.1093/schbul/sbt197.

Treadway, M. T., Buckholtz, J. W., Schwartzman, A. N., Lambert, W. E., & Zald, D. H. (2009). Worth the "EEfRT"? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PLoS One*, 4(8), 1–9. 10.1371/journal.pone.0006598.

Trémeau, F., Brady, M., Saccente, E., Moreno, A., Epstein, H., Citrome, L., … Javitt, D. C. (2008). Loss aversion in schizophrenia. *Schizophrenia Research*, 103(1–3), 121–128. doi: 10.1016/j.schres.2008.03.027.

Walter, A., Suenderhauf, C., Smieskova, R., Lenz, C., Harrisberger, F., Schmidt, A., … Borgwardt, S. (2016). Altered insular function during aberrant salience processing in relation to the severity of psychotic symptoms. *Frontiers in Psychiatry*, 7(189), 1–10. doi: 10.3389/fpsyt.2016.00189.

Waltz, J. A., Frank, M. J., Robinson, B. M., & Gold, J. M. (2007). Selective reinforcement learning deficits in schizophrenia support predictions from computational models of striatal-cortical dysfunction. *Biological Psychiatry*, 62(7), 756–764. doi: 10.1016/j.biopsych.2006.09.042.

Wolf, D. H., Satterthwaite, T. D., Kantrowitz, J. J., Katchmar, N., Vandekar, L., Elliott, M. A., & Ruparel, K. (2014). Amotivation in schizophrenia: Integrated assessment with behavioral, clinical, and imaging measures. *Schizophrenia Bulletin*, 40(6), 1328–1337. doi: 10.1093/schbul/sbu026.