



The misattribution of salience in delusional patients with schizophrenia[☆]

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Abstract

Introduction: Delusions may arise from abnormalities in emotional perception. In this study, we tested the hypothesis that delusional schizophrenia patients are more likely than non-delusional schizophrenia patients and healthy participants to assign affective meanings to neutral stimuli.

Methods: Unpleasant, pleasant, and neutral words were randomly presented to three subject groups—patients with schizophrenia with prominent delusions, patients with schizophrenia without delusions, and healthy participants. Participants performed three tasks: one in which they decided whether a letter string was a word or a non-word (lexical decision) and two affective classification tasks in which they judged whether words were 1) neutral or unpleasant, or 2) neutral or pleasant.

Results: While there were no significant between-group differences in lexical decision performance, patients with delusions showed selective performance deficits in both affective classification tasks. First, delusional patients were significantly more likely than non-delusional patients and healthy participants to classify words as unpleasant. Second, delusional patients took significantly longer than both other groups to correctly classify neutral words in both affective classification tasks.

Conclusions: Taken together, these findings suggest that delusions are associated with the explicit misattribution of salience to neutral stimuli.

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1. Introduction

The nature of the cognitive abnormality underlying delusions in schizophrenia has been much debated (Bentall et al., 2001; Blackwood et al., 2001; Freeman

et al., 2002; Green and Phillips, 2004; Hemsley and Garety, 1986; Maher, 1999). One hypothesis is that delusional patients are highly sensitive to emotionally laden information, exhibiting an “affective attentional bias.” In support of this view, several studies have reported that, relative to non-delusional patients, patients with delusions preferentially attend to emotional (Bentall and Kaney, 1989; Fear et al., 1996; Kinderman, 1994) words. Also, patients with persecutory delusions demonstrate higher recall of threat-related words (Bentall et al., 1995) and propositions (Kaney et al., 1992).

An alternative hypothesis is that delusions stem from the misattribution of affective meaning to neutral or ambiguous information—an “affective misattribution bias.” Consistent with this view is evidence that patients with persecutory delusions have difficulty correctly identifying neutral facial expressions (Kohler et al., 2003) and are slower than patients without persecutory delusions to assess scenes with ambiguous content (Phillips et al., 2000).

The current study was designed to test both of these hypotheses. By using two types of tasks with identical stimuli, we compared measures of incidental and explicit affective processing in the same participants. To focus our study on delusions, we studied three groups: healthy individuals and patients with schizophrenia with and without delusions. This design controlled for the potential confounds of general cognitive impairment and overall slowing of reaction times found in schizophrenia, as well as for the effects of antipsychotic medication. During three experiments, participants viewed affectively valenced and neutral words. In the first experiment, they performed a lexical decision task, deciding whether a letter string (an affectively valenced, neutral or nonsense word) was a real word or nonsense word. In healthy individuals, affective valence facilitates semantic processing of words (Strauss, 1983; Wurm and Vakoch, 2000). An affective attentional bias in delusional patients would predict a further increase of this facilitation, resulting in shorter reaction times for the emotional words in the delusional relative to the comparison groups. In two additional experiments, participants made explicit affective judgments about words; an affective misattribution bias in delusional patients would predict an increased tendency to misclassify neutral

words as affectively valenced (with the potential for longer reaction times for neutral vs. emotional words) in the delusional relative to the non-delusional and healthy groups.

2. Methods

2.1. Participants

In accordance with institutional review boards of the Massachusetts General Hospital (MGH) and the Commonwealth of Massachusetts Department of Mental Health, written informed consent was obtained from all participants.

32 outpatients with schizophrenia, diagnosed using DSM-IV criteria, without histories of major neurological illness, were recruited from the MGH Schizophrenia Program. All patients were on stable doses of antipsychotic medications (5 receiving conventional and 27 receiving atypical antipsychotics). On the day of the study, patients were evaluated using the Schedule for the Assessment of Positive Symptoms (SAPS) (Andreasen et al., 1995), the Schedule for the Assessment of Negative Symptoms (SANS) (Andreasen, 1989) and the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Patients with a score of ≥ 2 on the SAPS global delusion item were assigned to the delusional group; patients with scores of 0 or 1 on this item were assigned to the non-delusional group. 14 of the 16 delusional patients had predominantly persecutory delusions, while one patient had religious delusions and another had the delusion of thought insertion.

16 healthy control participants were recruited from the community via advertisement. Individuals with a first language other than English, a DSM-IV defined psychiatric disorder, or a neurologic disorder were excluded. The three groups were matched with respect to gender, race, and handedness; see Table 1.

The following were assessed in all participants: Premorbid I.Q. (the National Adult Reading Test (NART) (Blair and Spreen, 1989), letter and semantic fluency (Goldberg et al., 1998)), levels of depressive symptoms (the Beck Depression Inventory (BDI) (Beck and Steer, 1993)) and delusional thinking (the Peters et al. Delusions Inventory (PDI) (Peters et al., 1999)).

Table 1
Demographic and clinical information about the subjects

	Healthy (<i>n</i> = 16)		Non-delusional (<i>n</i> = 16)		Delusional (<i>n</i> = 16)	
	Mean	SD	Mean	SD	Mean	SD
Gender (M, F)	13, 3		14, 2		10, 6	
Race (C, A, H)	3, 3, 0		11, 4, 1		10, 6, 0	
Handedness (R, L, B)	14, 0, 2		14, 2, 0		13, 2, 1	
Age (years)	43.9	10.0	43.3	7.9	46.2	7.4
Parental SES*	2.8	1.2	2.8	1.1	3.5	0.9
Premorbid I.Q.**	113.9	12.6	105.5	11	108.6	7.9
Letter fluency	14.9	4.7	11.4 ^a	3.7	12.2	4.3
Semantic fluency	19.0	3.7	13.2 ^a	3.4	14.6 ^b	3.7
Age of onset (years)	–	–	26.2	6.7	24.3	6.6
Duration of illness (years)	–	–	17.1	8.6	21.9	7.4
Chlorpromazine equivalents	–	–	512.7	437.6	507.4	309.3
BDI score	2.8	2.4	7.1 ^a	7.8	13.1 ^{b,c}	7.7
PDI total score	4.1	5.2	5.4	5.7	16.5 ^{b,c}	10.0
SAPS global delusion item	–	–	0.44	0.51	3.31 ^c	1.0
SAPS global hallucination item	–	–	0.94	1.4	2.9 ^c	2.0
SAPS TD subscale	–	–	5.13	7.88	4.18	4.07
PANSS delusion item	–	–	1.81	0.75	4.63 ^c	0.96
PANSS hallucination item	–	–	1.88	1.20	3.44 ^c	1.41
SANS	–	–	21.0	16.31	25.0	22.8

*Estimated using the Hollingshead Index. **Estimated using the American National Adult Reading Test. ^a Significant difference between non-delusional and healthy participants ($p < .05$), ^b significant difference between delusional and healthy participants ($p < .05$), and ^c significant difference between delusional and non-delusional patients ($p < .05$). Abbreviations: M = male, F = female, C = Caucasian, A = African-American, H = Hispanic, R = right, L = left, B = ambidextrous, BDI = Beck Depression Inventory, PDI = Peters et al. Delusions Inventory, SAPS = Scale for the Assessment of Positive Symptoms, TD = thought disorder, PANSS = Positive And Negative Symptom Scale, SANS = Scale for the Assessment of Negative Symptoms.

There were no significant differences among groups in mean age, parental socioeconomic status, and premorbid I.Q. Delusional and non-delusional patient groups did not differ with respect to negative symptoms, thought disorder severity, age of onset of illness, duration of illness, daily antipsychotic exposure (chlorpromazine equivalents (Centorrino et al., 2002; Woods, 2003)), semantic and letter fluency. The delusional and non-delusional group differed, however, with respect to hallucination and depression symptoms levels. The delusional group had significantly higher mean hallucination scores than the non-delusional group. Both patient groups showed significantly higher mean BDI scores than the healthy participants, with a significantly higher mean BDI score in the delusional relative to the non-delusional group. The non-delusional and healthy groups did not differ with respect to severity of delusional thinking (SAPS global delusion item, PANSS delusion item, and PDI score).

2.2. Stimulus materials

The stimuli and experimental paradigms were identical to those used in a parallel study (Long and Titone, in press). 432 words were selected from the Toglia and Battig (1978) word list, normed for affect, concreteness, meaningfulness, and familiarity. Pleasant words (e.g., rose, smooth, triumph; affect ratings $> \text{mean} + 1.3 \text{ SD}$), neutral words (e.g., grocer, preview, cause; affect ratings $< \text{mean} \pm 1.3 \text{ SD}$) and unpleasant words (e.g., tomb, bitter, misery; affect ratings $< \text{mean} - 1.3 \text{ SD}$) were matched for meaningfulness, familiarity, and length. Because the level of abstractness (e.g., *discontent* (abstract) vs. *corpse* (concrete)) of words has been shown to influence response times during word identification tasks (Kounios and Holcomb, 1994; Paivio, 1966; Strain et al., 1995; Strain and Herdman, 1999), the three affect conditions were matched for abstractness, with three levels (abstract, intermediate, concrete) within

each affect condition. For the lexical decision experiment, pronounceable, phonotactically legal letter strings were constructed to match with the target words for length. Target words from each affect category were counterbalanced across all participants and tasks using a Latin square rotation method.

2.3. Overall procedure

Participants performed the three experiments: Lexical Decision (LD), Positive Affective Classification (PosAC) and Negative Affective Classification (NegAC). The explicit affective classification experiments (PosAC and NegAC) followed the LD experiment to minimize strategic effects on lexical decision. The order of the PosAC and NegAC experiments was counterbalanced across participants. All experiments were preceded by short practice sessions.

In the LD experiment, participants pressed one of two buttons depending on whether each target word was a real word or a nonsense word. Of the 432 randomly presented lexical decision trials, 216 were nonsense words and 216 were real words (108 neutral, 54 pleasant and 54 unpleasant). This experiment was conducted in three 5-min blocks.

For the explicit affective classification experiments, participants were instructed to press one of two buttons depending on whether each target word was pleasant or neutral (PosAC) or unpleasant or neutral (NegAC). For each affective classification experiment, 54 affectively valenced (pleasant for PosAC, unpleasant for NegAC) words and 54 neutral words were randomly presented. In each experiment, target words were preceded by a fixation cross (500 ms, random interstimulus interval of 500 or 1000 ms).

2.4. Statistical analyses

2.4.1. Reaction time and error rate

Mean reaction times (RTs) to correct responses were calculated for each target word category. To reduce the effects of outliers, a logarithmic transformation was applied to the RT data prior to calculating means. Data analyses were also performed on the raw data and these results did not substantially differ from those derived from the log-transformed values.

Percentage of response types was calculated for each target word category.

Dependent variables were entered into mixed model ANOVAs with group as the between-subjects factor and affect (LD task: 3 levels: unpleasant, pleasant, neutral; NegAC and PosAC tasks: 2 levels: unpleasant or pleasant, neutral) and abstractness (3 levels: abstract, intermediate, concrete) as within-subject factors.

Significant or near significant affect by group interactions were followed by planned comparisons using Student's *t*-tests. Given that our a priori hypotheses focused on the effects of affect rather than of abstractness, statistical effects involving abstractness are summarized but not explored in detail. Correlations were performed using Pearson's *r* and, for correlations with ratings scales, Spearman's *r*. Significance was set at $p \leq .05$.

2.4.2. Discrimination sensitivity and response bias

For the affective classification experiments, discrimination sensitivity and response bias were measured with the signal detection parameters of d' and C , respectively (Macmillan and Creelman, 1990). D' was calculated by subtracting the false positive rate—the rate of misclassifying a neutral word as pleasant (PosAC) or unpleasant (NegAC)—from the true positive rate—the rate of correctly classifying a pleasant word as pleasant (PosAC) or an unpleasant word as unpleasant (NegAC). Higher values of d' indicate higher discrimination sensitivity. C , a measure of response bias, was calculated by multiplying the sum of the true positive rate and false positive rate by -0.5 . Higher values for C indicate a greater tendency to classify a word as neutral. True positive rates and false positive rates were transformed by adding .5 to the raw values, dividing by $n + 1$ and then performing an inverse-normalization. Between-group comparisons were made using one-way ANOVAs followed by Student's *t*-tests.

3. Results

3.1. LD experiment

3.1.1. Error rate

There was a main effect of affect ($F(2,90)=9.76$, $p < .0003$) due to a lower error rate for pleasant words than unpleasant ($t=3.75$, $df=47$, $p=.0005$) and neutral ($t=3.35$,

$df=47, p<.003$) words (Fig. 1A; also see Table 2 for means and standard deviations of outcome measures of all three experiments). A significant main effect of group ($F(2,45)=3.73, p<.04$) was due to the significantly higher overall error rate in the non-delusional group in comparison with the healthy participants ($t=2.73, df=30, p<.02$).

However, the overall error rate in the delusional patients did not differ from that in the non-delusional ($t=1.19, df=30, p=.24$) and the healthy ($t=1.58, df=30, p=.12$) participants. There was no affect by group interaction ($F(4,90)=1.25, p=.29$).

3.1.2. RT

A main effect of affect ($F(2,90)=28.17, p<4 \times 10^{-10}$) resulted from shorter RTs to pleasant than to unpleasant ($t=6.18, df=47, p<2 \times 10^{-7}$) and neutral ($t=3.27, df=47, p<.002$) words and shorter RTs to neutral than to unpleasant words ($t=3.98, df=47, p<.0003$) (Fig. 1B). A significant main effect of group ($F(2,45)=9.36, p<.0005$) for LD RT was due to longer overall RTs in both patient groups relative to the healthy participants (non-delusional vs. healthy: $t=3.74, df=30, p<.001$; delusional vs. healthy: $t=4.08, df=30, p<.0005$). There were no significant differences in RT between the delusional and non-delusional patients ($t=-1.40, df=30, p=.17$). Also, there was no significant affect by group interaction ($F(4,90)=.11, p=.98$).

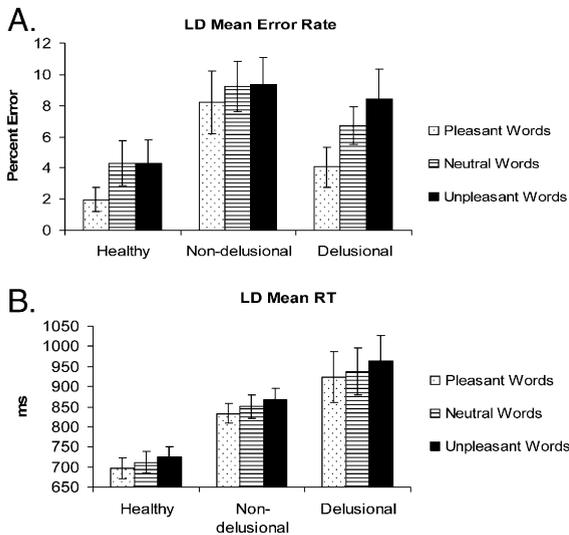


Fig. 1. LD error rate and RT. Mean LD error rates (A) and mean LD RTs (B) for pleasant (bars with dots), unpleasant (solid black bars) and neutral (bars with horizontal stripes) words in the delusional, non-delusional and healthy participants. Error bars represent standard errors of the mean. $N=16$ for each group; ms=milliseconds.

3.2. Affect classification experiments (NegAC and PosAC)

3.2.1. Discrimination sensitivity

For both affect classification experiments, a significant main effect of group for discrimination sensitivity (NegAC: $F(2,45)=3.58, p<.04$; PosAC: ($F(2,45)=10.78, p<.0002$) was due to a lower discrimination sensitivity in both patient groups relative to the healthy group (NegAC: non-delusional vs. healthy: $t=2.58, df=30, p<.02$; delusional vs. healthy: $t=2.41, df=30, p=.02$. PosAC: non-delusional vs. healthy: $t=5.17, df=30, p<2 \times 10^{-5}$; delusional vs. healthy: $t=2.82, df=30, p<.01$). There were no significant differences in discrimination sensitivity between the delusional and non-delusional patients in either the NegAC ($t=.22, df=30, p=.83$) or the PosAC experiment ($t=1.63, df=30, p=.11$).

3.2.2. Response bias

In the NegAC experiment, there was a significant main effect of group ($F(2,45)=3.91, p<.04$) because delusional patients were more likely than non-delusional patients ($t=2.00, df=30, p=.05$) and healthy individuals ($t=2.68, df=30, p<.02$) to classify words as unpleasant, as indicated by their lower mean C values (Fig. 2A). In contrast, the mean C value of the non-delusional and healthy participants did not differ ($t=.59, df=30, p=.56$). In the PosAC experiment, there was a significant main effect of group ($F(2,45)=4.74, p<.02$) because the delusional patients were more likely than the healthy participants to classify a word as pleasant ($t=2.91, df=30, p<.008$) (Fig. 2B). The difference in response bias between the non-delusional and healthy participants approached significance ($t=1.94, df=30, p=.06$). However, unlike in the NegAC experiment, there was no significant difference in response bias between the delusional and non-delusional patients ($t=1.91, df=30, p=.24$).

3.2.3. RT

There were no main effects of affect in the NegAC ($F(2,45)=.003, p=.96$) or PosAC ($F(1,45)=1.68, p=.17$) experiments. However, there were significant main effects of group in both the NegAC ($F(2,45)=13.27, p<3 \times 10^{-5}$) and the PosAC ($F(2,45)=8.38, p<.001$) experiments because of significantly longer RTs in both patient groups relative to the healthy participants for all word categories (Fig. 3A, B).

Of most interest, there were significant affect by group interactions in both the NegAC ($F(2,45)=5.0, p<.02$) and the PosAC ($F(2,45)=3.14, p=.05$) experiments. Follow-up within-group comparisons in the NegAC experiment revealed longer RTs to neutral words than to unpleasant words in the delusional patients ($t=2.39, df=15, p<.04$) but shorter RTs to neutral words than to unpleasant words in the

Table 2
Means and standard deviations for all outcome measures

	Healthy (<i>n</i> = 16)		Non-delusional (<i>n</i> = 16)		Delusional (<i>n</i> = 16)	
	Mean	SD	Mean	SD	Mean	SD
<i>LD:</i>						
Pleasant word mean RT (s)	723.92	107.71	868.13	110.86	963.81	249.02
Unpleasant word mean RT (s)	696.42	100.88	832.74	98.82	923.76	249.81
Neutral word mean RT (s)	711.54	108.64	850.42	119.91	937.92	237.35
Overall RT (s)	731.98	103.10	872.85	113.16	974.06	247.30
Pleasant word mean ER (%)	4	6	9	7	9	8
Unpleasant word mean ER (%)	2	3	8	8	4	5
Neutral word mean ER (%)	4	6	9	6	7	5
Overall ER (%)	12	14	27	19	19	17
<i>NegAC:</i>						
Unpleasant word mean RT (s)	537.98	96.74	677.33	139.27	711.37	152.33
Neutral word mean RT (s)	511.68	111.15	665.18	150.92	772.94	182.77
Overall RT (s)	524.83	100.29	671.26	137.94	742.16	158.60
Discrimination sensitivity (<i>d'</i>)	2.52	0.57	1.87	0.83	1.80	1.06
Response bias (<i>C</i>)	0.47	0.33	0.40	0.37	0.13	0.39
Unpleasant word mean ER (%)	23	11	32	18	24	19
Neutral word mean ER (%)	5	5	12	10	19	22
Overall ER (%)	14	6	22	11	22	16
<i>PosAC:</i>						
Pleasant word mean RT (s)	934.12	189.27	1078.07	212.57	1077.35	273.19
Neutral word mean RT (s)	912.37	266.11	1148.17	430.49	1364.69	312.59
Overall RT (s)	923.24	213.38	1113.12	306.11	1292.28	300.23
Discrimination sensitivity (<i>d'</i>)	1.89	0.42	0.98	0.56	1.34	0.66
Response bias (<i>C</i>)	0.59	0.63	0.18	0.55	-0.07	0.64
Pleasant word mean ER (%)	38	20	39	17	26	17
Neutral word mean ER (%)	11	13	29	22	32	25
Overall ER (%)	24	7	34	9	29	10

SD = standard deviation. s = seconds. % = percentage.

healthy participants ($t=2.15$, $df=15$, $p<.05$), and no differences between conditions in the non-delusional patients ($t=.68$, $df=15$, $p=.50$). In the PosAC experiment, follow-up within-group comparisons again revealed significantly longer RTs to neutral words than to pleasant words in the delusional patients ($t=2.55$, $df=15$, $p<.03$), but no significant differences between RTs to neutral and unpleasant words in the non-delusional ($t=.6$, $df=15$, $p=.56$) or healthy participants ($t=.91$, $df=15$, $p=.37$). Follow-up between-group comparisons revealed longer RTs to neutral words in the delusional patients relative to the non-delusional patients (approaching significance in the NegAC experiment ($t=1.91$, $df=30.00$, $p=.06$ and reaching significance in the PosAC experiment ($t=2.03$, $df=27.38$, $p=.05$), but no significant difference between the two patient groups in their RTs to unpleasant words ($t=.64$, $df=30$, $p=.52$) or pleasant words ($t=1.37$, $df=30$, $p=.17$) (Fig. 3A, B).

3.2.4. Correlations between neutral word RT and response bias

For the NegAC experiment, response bias was significantly correlated with mean RT to neutral words ($r=-.41$, $p<.03$, $n=32$) but not with mean RT to unpleasant words ($r=.01$, $p=.95$, $n=32$). Similarly, in the PosAC experiment, response bias was significantly correlated with mean RT to neutral words ($r=-.61$, $p<.0003$, $n=32$) but not with mean RT to pleasant words ($r=-.13$, $p=.46$, $n=32$).

3.3. Correlations with delusion severity and potential confounds

We correlated scores on the delusion items of the SAPS and PANSS with each experimental measure that showed differences in the delusional patients relative to the non-delusional and healthy participants: NegAC response bias, and NegAC and PosAC neutral word RTs. There was a

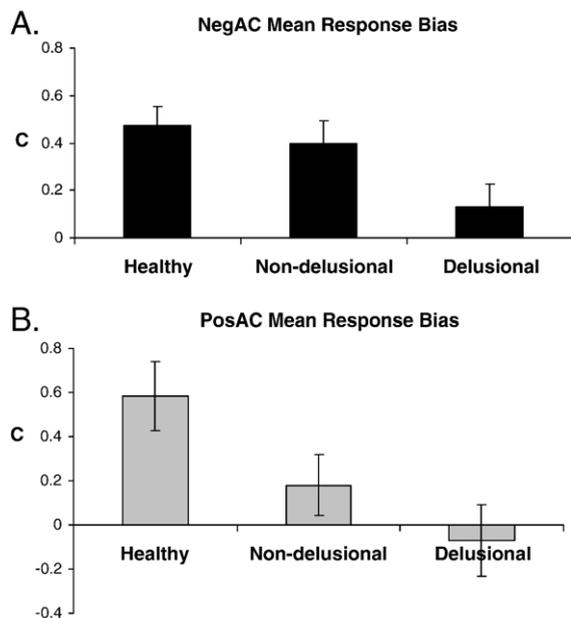


Fig. 2. NegAC and PosAC response bias. Mean NegAC (A, black bars) and PosAC (B, gray bars) response bias in the healthy, non-delusional and delusional participants. Error bars represent standard errors of the mean. $N=16$ for each group; C =response bias.

significant inverse correlation between mean NegAC response bias and the PANSS delusion item score ($r=-.36, p<.05, n=32$), with trends towards significant inverse correlations between mean NegAC response bias and the SAPS global delusion item score ($r=-.34, p=.06, n=32$) and between PosAC neutral word RT and the PANSS delusion item score ($r=.33, p=.06, n=32$). However, there were no significant correlations between these measures and BDI score or scores on the hallucination items of the SAPS and PANSS. Also, no significant correlations were found between the three experimental measures of interest and magnitude of daily antipsychotic exposure, age of onset, or duration of illness.

Finally, three multiple regression analyses were performed with premorbid I.Q., letter fluency, semantic fluency, BDI score, SAPS global delusion item score and SAPS global hallucination item score as independent variables; each of the three outcome measures of interest (NegAC response bias, and NegAC and PosAC neutral word RTs) served as a dependent variable. For each of the three analyses, only the SAPS global delusion item significantly predicted each of the three outcome measures in the expected direction, i.e. a higher score on the SAPS global delusion item predicted higher NegAC and PosAC neutral

RTs and a lower NegAC response bias (p values of .01, .002 and .005, respectively ($n=32$)). Additionally, a lower BDI score significantly predicted a higher PosAC neutral word RT ($p=.03$) and a higher premorbid I.Q. predicted a higher NegAC response bias ($p=.02$).

3.4. Summary of effects of abstractness

For the LD experiment, a concreteness by affect interaction arose because of shorter RTs to the concrete and abstract unpleasant words relative to the intermediate level (p 's<.002), and longer RTs to the abstract neutral words relative to the intermediate and concrete neutral words (p 's<.004). A similar interaction was found for PosAC experiment, with longer RTs to abstract neutral words than to intermediate ($p<.05$) and concrete ($p=.09$) neutral words. There were no interactions between abstractness and group except in the LD experiment which revealed a significant abstractness by group interaction because the delusional patients made significantly more errors than the healthy participants to the concrete words ($p<.02$), but not to the intermediate or abstract words. There were no differences between the delusional and non-delusional groups in LD errors to concrete, intermediate or abstract words.

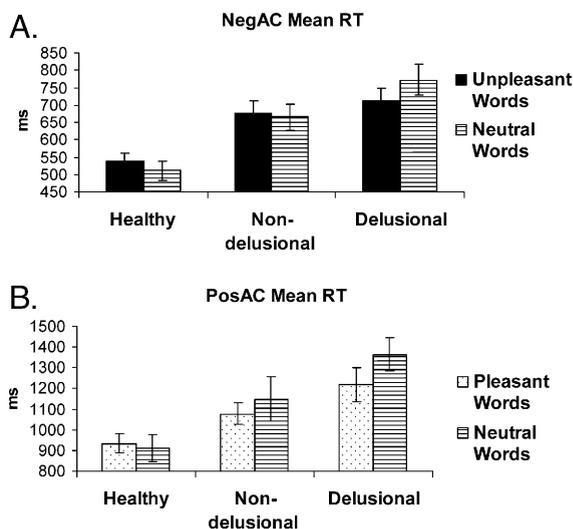


Fig. 3. NegAC and PosAC RT. For the NegAC experiment (A), mean RTs for unpleasant (solid black bars) and neutral (bars with horizontal stripes) words, and for the PosAC experiment (B), mean RTs for pleasant (bars with dots) and neutral (bars with horizontal stripes) words, in the healthy, non-delusional and delusional participants. Error bars represent standard errors of the mean. $N=16$ for each group; ms=milliseconds.

4. Discussion

This study tested two hypotheses: 1) delusions are related to increased attention to affective information—an affective attentional bias, and 2) delusions arise from misattributions of affective meanings to neutral information—an affective misattribution bias. Our findings support the second, but not the first, hypothesis.

While explicitly classifying words as neutral or unpleasant, delusional patients with schizophrenia demonstrated a specific response bias: they were more likely than non-delusional and healthy participants to classify words as unpleasant. The magnitude of this response bias correlated with delusion severity. Moreover, delusional patients took longer than non-delusional and healthy participants to correctly classify neutral words. In the patients, the affective misattribution bias correlated with the RTs to correctly classify neutral words, suggesting that these two abnormalities are linked. On the other hand, in the lexical decision experiment in which affective processing was incidental, there were no differences between the two patient groups in error rates or RTs to neutral words, suggesting that the affective misattribution bias in delusional patients is manifested behaviorally only during explicit affective evaluation.

These results do not provide evidence for an affective attentional bias in delusional patients; in none of the tasks did the delusional patients exhibit response patterns or RTs to the unpleasant or pleasant words that were different from the non-delusional group. This is inconsistent with the findings of studies that used the emotional Stroop task (Bentall and Kaney, 1989; Fear et al., 1996; Kinderman, 1994) in which delusional patients were slower than non-delusional patients to name the print color of words with emotional content. Task-related differences may account for the discrepancy between our results and those of the emotional Stroop studies; an affective attentional bias in delusional patients would have led to facilitated responses to emotional words in the current experiments, while resulting in prolonged RTs for emotional words in the emotional Stroop experiments. Longer overall response times in patients with schizophrenia may have confounded the results of the emotional Stroop studies or, in the

current study, diminished our ability to detect facilitation.

The delusional patients had more severe depressive symptoms and hallucinations than the non-delusional patients. Indeed, some have speculated that covariation between psychosis and affective symptoms may reflect common neurocognitive mechanisms (Bentall and Kaney, 1989; Freeman et al., 2005; Freeman and Garety, 2003; Krabbendam and van Os, 2005). However, in the current study, there were no significant correlations between depression or hallucination severity and the magnitude of any of our findings. Also, multiple regression analyses demonstrated that depression and hallucination levels did not account for our results; in fact, the only significant predictor of the outcome measures of interest was delusion severity. These findings suggest some specificity of the affective misattribution bias to delusions.

The mechanism by which an affective misattribution bias might arise in delusional patients is unclear. Our findings are consistent with an inappropriate activation of a stimulus-independent, internal “salience detector” (Kapur, 2003). This, together with an impairment in the use of context (Cohen and Servan-Schreiber, 1992; Hemsley, 2005; Kuperberg et al., 1998) might lead to the misassignment of emotional salience to neutral, ambiguous stimuli in the real world and, ultimately, to the formation and maintenance of delusions. This theory is consistent with evidence that delusional patients require less information than non-delusional patients to make decisions (Garety et al., 2005; Huq et al., 1988), as they may be guided less by a logical assessment of facts and probabilities than an internal “gut” feeling. Future studies should explore the relative roles and interactions of emotional perception and other neurocognitive processes in delusional patients. In particular, it will be important to examine whether any abnormalities in the interaction of emotional perception and cognitive evaluation of incoming stimuli occur at the earliest stages of stimulus perception or at a later stage of monitoring, during feedback about salience assessments during ongoing stimulus evaluation (Bates et al., 2004; Kopp and Rist, 1999).

The current findings also have implications for the interpretation of functional neuroimaging studies. Several such studies have demonstrated abnormally

reduced differential responses of the amygdala to emotional relative to neutral facial expressions in paranoid (relative to non-paranoid) patients (Phillips et al., 1999; Williams et al., 2004). The findings of the current study and evidence for elevated amygdala (Holt et al., 2006) and peripheral arousal (Williams et al., 2004) responses to neutral facial expressions in schizophrenia suggest that misassignment of affective meaning to neutral stimuli in delusional patients may, in part, account for these neuroimaging findings—an affective misattribution bias may be associated with elevated activity of brain regions involved in emotional perception.

In summary, we have provided evidence for an explicit affective judgment bias associated with delusions—a tendency to misattribute affective meaning to neutral information. Additional studies are needed to determine if this bias is linked to the formation and maintenance of false beliefs in patients with schizophrenia.

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References

- Andreasen, N.C., 1989. The Scale for the Assessment of Negative Symptoms (SANS): conceptual and theoretical foundations. *Br. J. Psychiatry* 49–58.
- Andreasen, N.C., Arndt, S., Alliger, R., Miller, D., Flaum, M., 1995. Symptoms of schizophrenia. Methods, meanings, and mechanisms. *Arch. Gen. Psychiatry* 52, 341–351.
- Bates, A.T., Liddle, P.F., Kiehl, K.A., Ngan, E.T., 2004. State dependent changes in error monitoring in schizophrenia. *J. Psychiatr. Res.* 38, 347–356.
- Beck, A.T., Steer, R.A., 1993. Manual for the Beck Depression Inventory. Psychological Cooperation, San Antonio, TX.
- Bentall, R.P., Kaney, S., 1989. Content specific information processing and persecutory delusions: an investigation using the emotional Stroop test. *Br. J. Med. Psychol.* 62 (Pt 4), 355–364.
- Bentall, R.P., Kaney, S., Bowen-Jones, K., 1995. Persecutory delusions and recall of threat-related, depression-related, and neutral words. *Cogn. Ther. Res.* 19, 445–457.
- Bentall, R.P., Corcoran, R., Howard, R., Blackwood, N., Kinderman, P., 2001. Persecutory delusions: a review and theoretical integration. *Clin. Psychol. Rev.* 21, 1143–1192.
- Blackwood, N.J., Howard, R.J., Bentall, R.P., Murray, R.M., 2001. Cognitive neuropsychiatric models of persecutory delusions. *Am. J. Psychiatry* 158, 527–539.
- Blair, J.R., Spreen, O., 1989. Predicting premorbid IQ: a revision of the National Adult Reading Test. *Clin. Neuropsychol.* 3, 129–136.
- Centorrino, F., Eakin, M., Bahk, W.M., Kelleher, J.P., Goren, J., Salvatore, P., Egli, S., Baldessarini, R.J., 2002. Inpatient antipsychotic drug use in 1998, 1993, and 1989. *Am. J. Psychiatry* 159, 1932–1935.
- Cohen, J.D., Servan-Schreiber, D., 1992. Context, cortex, and dopamine: a connectionist approach to behavior and biology in schizophrenia. *Psychol. Rev.* 99, 45–77.
- Fear, C., Sharp, H., Healy, D., 1996. Cognitive processes in delusional disorders. *Br. J. Psychiatry* 168, 61–67.
- Freeman, D., Garety, P.A., 2003. Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations. *Behav. Res. Ther.* 41, 923–947.
- Freeman, D., Garety, P.A., Kuipers, E., Fowler, D., Bebbington, P.E., 2002. A cognitive model of persecutory delusions. *Br. J. Clin. Psychol.* 41, 331–347.
- Freeman, D., Dunn, G., Garety, P.A., Bebbington, P., Slater, M., Kuipers, E., Fowler, D., Green, C., Jordan, J., Ray, K., 2005. The psychology of persecutory ideation I: a questionnaire survey. *J. of Nerv. Ment. Dis.* 193, 302–308.
- Garety, P.A., Freeman, D., Jolley, S., Dunn, G., Bebbington, P.E., Fowler, D.G., Kuipers, E., Dudley, R., 2005. Reasoning, emotions, and delusional conviction in psychosis. *J. Abnorm. Psychology* 114, 373–384.
- Goldberg, T.E., Aloia, M.S., Gourovitch, M.L., Missar, D., Pickar, D., Weinberger, D.R., 1998. Cognitive substrates of thought disorder: I. The semantic system. *Am. J. Psychiatry* 155, 1671–1676.
- Green, M.J., Phillips, M.L., 2004. Social threat perception and the evolution of paranoia. *Neurosci. Biobehav. Rev.* 28, 333–342.
- Hemsley, D.R., 2005. The development of a cognitive model of schizophrenia: placing it in context. *Neurosci. Biobehav. Rev.* 29, 977–988.
- Hemsley, D.R., Garety, P.A., 1986. The formation and maintenance of delusions: a Bayesian analysis. *Br. J. Psychiatry* 149, 51–56.
- Holt, D.J., Kunkel, L., Weiss, A.P., Goff, D.C., Wright, C.I., Shin, L.M., Rauch, S.L., Hootnick, J., Heckers, S., 2006. Increased

- medial temporal lobe activation during the passive viewing of emotional and neutral facial expressions in schizophrenia. *Schizophr. Res.* 82, 153–162.
- Huq, S.F., Garety, P.A., Hemsley, D.R., 1988. Probabilistic judgements in deluded and non-deluded subjects. *Q. J. Exp. Psychol.*, A 40, 801–812.
- Kaney, S., Wolfenden, M., Dewey, M.E., Bentall, R.P., 1992. Persecutory delusions and recall of threatening propositions. *Br. J. Clin. Psychol.* 31 (Pt 1), 85–87.
- Kapur, S., 2003. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am. J. Psychiatry* 160, 13–23.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261–276.
- Kinderman, P., 1994. Attentional bias, persecutory delusions and the self-concept. *Br. J. Med. Psychol.* 67 (Pt 1), 53–66.
- Kohler, C.G., Turner, T.H., Bilker, W.B., Brensinger, C.M., Siegel, S.J., Kanes, S.J., Gur, R.E., Gur, R.C., 2003. Facial emotion recognition in schizophrenia: intensity effects and error pattern. *Am. J. Psychiatry* 160, 1768–1774.
- Kopp, B., Rist, F., 1999. An event-related brain potential substrate of disturbed response monitoring in paranoid schizophrenic patients. *J. Abnorm. Psychol.* 108, 337–346.
- Kounios, J., Holcomb, P.J., 1994. Concreteness effects in semantic processing: ERP evidence supporting dual-coding theory. *J. Exp. Psychol. Learn. Mem. Cogn.* 20, 804–823.
- Krabbendam, L., van Os, J., 2005. Affective processes in the onset and persistence of psychosis. *Eur. Arch. Psychiatry Clin. Neurosci.* 255, 185–189.
- Kuperberg, G.R., McGuire, P.K., David, A.S., 1998. Reduced sensitivity to linguistic context in schizophrenic thought disorder: evidence from on-line monitoring for words in linguistically anomalous sentences. *J. Abnorm. Psychol.* 107, 423–434.
- Long, L.S., Titone, D. (in press). Psychopathy and verbal emotional processing in non-incarcerated males. *Emotion and Cognition*.
- Macmillan, N.E., Creelman, C.D., 1990. Response bias: characteristics of detection theory, threshold theory and “nonparametric” indexes. *Psychol. Bull.* 107, 401–413.
- Maher, B., 1999. Anomalous experience in everyday life: its significance for psychopathology. *Monist* 82, 547–570.
- Paivio, A., 1966. Latency of verbal associations and imagery to noun stimuli as a function of abstractness and generality. *Can. J. Psychol.* 20, 378–387.
- Peters, E.R., Joseph, S.A., Garety, P.A., 1999. Measurement of delusional ideation in the normal population: introducing the PDI (Peters et al. Delusions Inventory). *Schizophr. Bull.* 25, 553–576.
- Phillips, M.L., Williams, L., Senior, C., Bullmore, E.T., Brammer, M.J., Andrew, C., Williams, S.C., David, A.S., 1999. A differential neural response to threatening and non-threatening negative facial expressions in paranoid and non-paranoid schizophrenics. *Psychiatry Res.* 92, 11–31.
- Phillips, M.L., Senior, C., David, A.S., 2000. Perception of threat in schizophrenics with persecutory delusions: an investigation using visual scan paths. *Psychol. Med.* 30, 157–167.
- Strain, E., Herdman, C.M., 1999. Imageability effects in word naming: an individual differences analysis. *Can. J. Exp. Psychol.* 53, 347–359.
- Strain, E., Patterson, K., Seidenberg, M.S., 1995. Semantic effects in single-word naming. *J. Exp. Psychol. Learn. Mem. Cogn.* 21, 1140–1154.
- Strauss, E., 1983. Perception of emotional words. *Neuropsychologia* 21, 99–103.
- Toglia, M., Battig, W., 1978. *Handbook of Semantic Word Norms*. Erlbaum, Hillsdale, NJ.
- Williams, L.M., Das, P., Harris, A.W., Liddell, B.B., Brammer, M.J., Olivieri, G., Skerrett, D., Phillips, M.L., David, A.S., Peduto, A., Gordon, E., 2004. Dysregulation of arousal and amygdala–prefrontal systems in paranoid schizophrenia. *Am. J. Psychiatry* 161, 480–489.
- Woods, S.W., 2003. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J. Clin. Psychiatry* 64, 663–667.
- Wurm, L.E., Vakoch, D.A., 2000. The adaptive value of lexical connotation in speech perception. *Cogn. Emot.* 14, 177–191.