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Changes in delusional dimensions and emotions over eight weeks of antipsychotic treatment in acute patients

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Abstract

Delusional experiences can be considered on a range of dimensions including conviction, distress, preoccupation, and disruption, which have been shown to be related to depression and anxiety. This study aimed to test the hypotheses that delusional conviction is less responsive to antipsychotic treatment than delusional distress and preoccupation, and that depression and anxiety reduce alongside improvements in delusional dimensions. Forty acutely ill inpatients with delusions were assessed during their early stage of antipsychotic treatment. Interview data were analysed using mixed models for repeated measures. There was a significant reduction in psychotic symptoms over eight weeks, after controlling for baseline dosage of antipsychotics. We found no differential rate of improvement across delusional dimensions, and all dimensions improved over time. However, conviction ratings remained relatively high throughout the eight weeks. There was no significant improvement in anxiety and depression, and delusional preoccupation covaried with anxiety and depression throughout eight weeks, suggesting a relationship between emotional and delusional processes during the early recovery phase of psychosis.

Keywords:

Delusions; psychosis; antipsychotics; conviction; distress; depression; anxiety

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1. Introduction

Delusional experience has been conceptualised as consisting of various dimensions, with conviction, distress, preoccupation and disruption to life being commonly identified (Peters et al., 2004; Lincoln, 2007). Studies of psychological interventions have reported differential changes in these delusional dimensions (Chadwick and Lowe, 1990, 1994; Sharp et al., 1996), with newer psychological interventions being developed to specifically target delusional conviction and distress (Garety et al., 2014; Moritz et al., 2014; Freeman et al., 2015). Investigations of how delusional dimensions respond to different treatment modalities, such as pharmacological interventions, should increase our understanding of their psychological mechanisms of action in reducing delusional symptoms. A more sophisticated understanding of the medication effects on patients' subjective delusional experience over time may in turn inform discussions about treatment between patients and physicians.

Mizrahi et al. (2006) and So et al. (2014) examined multidimensional symptom changes over the first six weeks and two weeks of antipsychotic treatment respectively. Mizrahi et al. (2006) found a reduction in the behavioural impact of psychotic symptoms within the first two weeks of treatment, whereas conviction in psychotic experiences decreased later (at six weeks). Using an experience-sampling method, So et al. (2014) found improvement in delusional distress and disruption, but not in delusional conviction and preoccupation, during the first two weeks of treatment. These two studies indicated the possibility of a differential treatment response on aspects of psychotic symptoms (including delusions), with distress improving more and more quickly than conviction during initial treatment. However, Mizrahi et al. (2006) measured 'principal psychotic experience' which included both delusions and hallucinations. So et al. (2014) assessed change in delusional dimensions specifically, but covered two weeks only. We therefore aimed to examine how delusional dimensions respond to antipsychotics in a larger sample over a longer period.

Symptoms of anxiety and depression are highly prevalent in psychosis. Recent reviews (Hafner, 2010; Garety and Freeman, 2013; Hartley et al., 2013; Freeman and Garety, 2014) have argued that emotional processes, including a worry thinking style, negative self-perception, and interpersonal sensitivity, are associated with delusional formation and persistence, especially persecutory delusions. This has been supported by experimental studies (Ellett et al., 2008; Lincoln et al., 2010; Freeman et al., 2014) and longitudinal investigations (Thewissen et al., 2011; Fowler et al., 2012; Vorontsova et al., 2013). In addition, depression and anxiety have been found to be exacerbated during and after delusions, especially following negative appraisals (Iqbal et al., 2000; Freeman et al., 2001; Birchwood et al., 2005; Green et al., 2006). Therefore, it seems that emotional processes can be both triggers and consequences of delusions. However, the association of depression and anxiety with delusional dimensions has only been examined in a few studies, yielding inconsistent results (Freeman & Garety, 1999; Smith et al., 2006; Startup et al., 2007). In view of the evidence that antipsychotics can alleviate depressive and anxiety symptoms (Tollefson et al., 1997, 1998a, 1998b; and review by Möller, 2005), the present study aimed to investigate both changes in delusional dimensions and negative emotions in patients with delusions during the early phase of antipsychotic treatment. More specifically, this study concerns whether depression and anxiety improve in step with delusional dimensions in response to antipsychotics.

The major hypotheses were as follows:

1. Delusional distress, preoccupation and disruption will reduce prior to delusional conviction
2. Depression and anxiety will reduce alongside improvements in delusional dimensions

2. Method

2.1 Participants

Ethical approval was granted by the Camden and Islington Community Research Ethics Committee (ref. 08/H0722/76). Patients were recruited from acute psychiatric wards of the South London and Maudsley NHS Foundation Trust. Inclusion criteria were as follows: (i) aged 15-65 years; (ii) a case note diagnosis of a psychotic disorder; (iii) current experience of delusions, (iv) drug-naïve or drug-free for at least a month prior to admission, and (v) prescription of antipsychotics for less than four weeks before study participation. Patients with drug-induced psychosis, organic psychosis or a primary diagnosis of substance misuse were excluded. Fulfilment of the study criteria was determined by the treating psychiatrist, with presence of delusions further confirmed using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987).

Our sample consisted of 40 in-patients, with a mean age of 32.2 years (range 18-62) and 62% female ($n=25$). Major psychiatric diagnoses were Schizophrenia (25.0%), Bipolar disorder (20.0%), Unspecified psychosis (17.5%), Schizoaffective disorder (10.0%), Depression with psychotic features (10.0%), Brief psychotic disorder (10.0%), Delusional disorder (5.0%) and Schizophreniform disorder (2.5%). Mean age of psychotic onset was 30.4 years (range 18-58). Participants had an average of 2.4 psychiatric admissions ($SD= 2.73$, range 1-15), with 26 patients (65%) being hospitalised for the first time due to psychosis. Out of the 40 patients, 38 (95%) rated ≥ 4 on the suspiciousness item of the PANSS (Kay et al., 1987), whereas 10 (25%) rated ≥ 4 on the grandiosity item.

Eight participants (20.5%) were antipsychotic-free at their first interview, whereas 19 participants (47.5%) had received antipsychotics for less than 14 days. On average, patients were assessed 5.90 days (range 0-27) after the beginning of treatment. The majority (92.3%) were on atypical antipsychotics (Olanzapine, Risperidone, Aripiprazole, Amisulpiride, and Quetiapine); one (2.56%) was on a typical antipsychotic (Trifluoperazine) and two (5.13%) were on both typical and atypical antipsychotics. The mean dose of antipsychotics at the time of the initial interview, in chlorpromazine equivalents (Andreasen et al., 2010), was 195.6mg/day ($SD = 119.1$).

2.2 Measures

2.2.1 Clinical symptom severity

Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) is a 30-item, 7-point (1-7) rating scale developed for assessing symptoms associated with schizophrenia over the past week. Good inter-rater reliability (0.83-0.87 for the four scales) had been reported (Kay et al., 1988).

2.2.2 Dimensions of delusions

Delusional dimensions (conviction, distress, preoccupation and disruption) were assessed

using self-reported VAS¹ (Brett-Jones et al., 1987; Sharp et al., 1996).

At baseline interview, the interviewer elicited the major delusional belief. The statement that participants chose to describe their delusion was then incorporated into the dimension questions for subsequent assessments. The dimension questions were as follows: “To what extent do you believe that (the delusional belief) is true?” (conviction); “How (distressed/angry/fearful/worried/restless) do you feel about (the delusional belief)” (distress); “How much have you been thinking/worrying about (the delusional belief)?” (preoccupation); “How much has (the delusional belief) been affecting/getting in the way of your daily life?” (disruption to life). The participant rated the intensity of each of the four dimensions on a 0-100 VAS.

2.2.4 Emotion

Beck Depression Inventory – II (BDI-II) (Beck et al., 1996) and Beck Anxiety Inventory (BAI) (Beck et al., 1988) are 21-item self-report inventories that assess symptoms of depression and anxiety respectively (score range 0-63). Both scales had high internal consistency and test-retest reliability, adequate validity and diagnostic discrimination.

2.3 Procedures

Consenting participants were interviewed by a qualified clinical psychologist five times over eight weeks (week 0, week 1, week 2, week 4, and week 8). The first interview took place as soon as patients were hospitalized, and within one month of the start of antipsychotic treatment. Only delusional dimensions were assessed at every assessment. PANSS was assessed at baseline, 2 weeks, 4 weeks and 8 weeks. BDI-II and BAI were completed at baseline, 4 weeks and 8 weeks.

2.4. Statistical analysis

Statistical analyses were conducted using SPSS 16.0 for Windows (SPSS, 2007).

For hypotheses 1-2, a series of mixed models for repeated measures (Twisk, 2006) were tested and their model fit indices were compared. The model with the lowest Akaike’s Information Criterion (AIC) and Schwarz’s Bayesian Criterion (BIC) was chosen as the best model for that hypothesis. The mixed model approach was used because: (a) it includes fixed and random effects of modelling; (b) it models the effect of time as a continuous predictor, which is of importance due to irregular assessment intervals; (c) it can handle unbalanced datasets (e.g. when missing values appear in some but not all dimensions within each individual); and (d) it allows a flexible way to model error correlations. The mixed model method makes use of all the data available in the whole sample ($N=40$).

¹ Three measures of delusional dimensions were included in this study- Psychotic Symptom Rating Scale (PSYRATS) (Haddock et al., 1999), Personal Questionnaire (PQ) (Shapiro, 1961) and VAS. Since changes in delusional dimensions were highly correlated across measures ($r= 0.60-0.82$ between VAS and PSYRATS, and $r= 0.44-0.85$ between VAS and PQs), the analyses reported in this paper pertain to VAS only for the sake of succinctness. Parallel analyses were conducted for the other two measures, and are available from the first author.

3. Results

Twenty-nine participants (72.5%) attended all five interviews, four (10.0%) attended four interviews, five (12.5%) attended three interviews and two (5.0%) attended one interview. There was no difference ($p>0.05$) in age or baseline symptom scores between completers and participants with missing data.

3.1 Overall clinical change

Changes in PANSS scores (Kay et al., 1987) are shown in Table 1. Mixed models revealed a significant reduction over 8 weeks in PANSS total score, positive score and delusions score ($p< 0.001$). The effect of time on changes in PANSS scores remained significant after controlling for baseline dosage of antipsychotic and treatment duration ($p<0.05$).

Table 1 Mean (SD) PANSS scores across time points

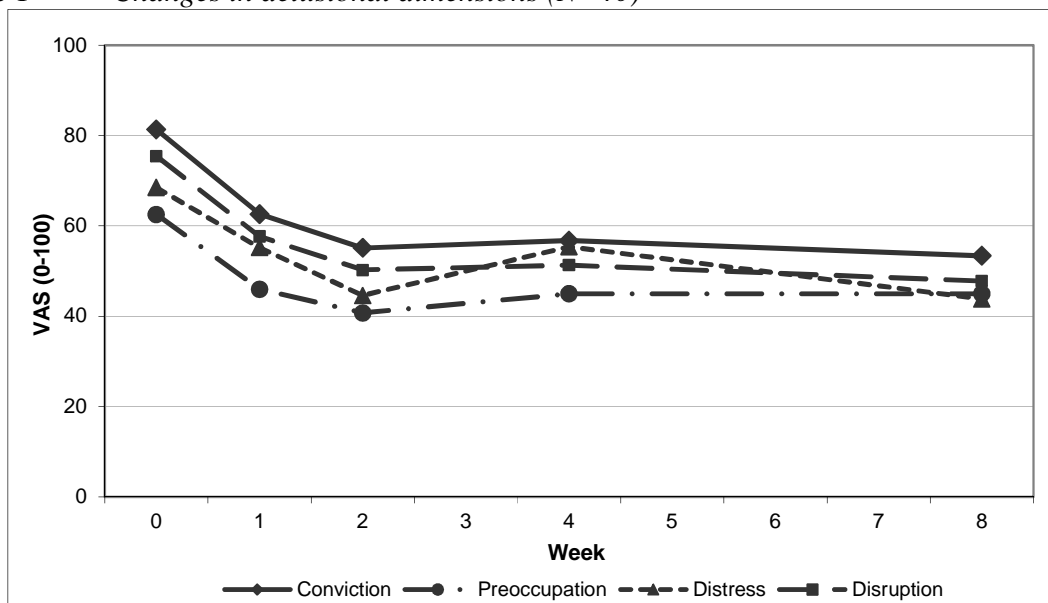
	Week 0 (n=40)	Week 2 (n=38)	Week 4 (n=31)	Week 8 (n=33)	Mixed model (Time as IV and PANSS score as DV)
PANSS total score	69.30 (17.78)	54.32 (15.09)	54.29 (15.96)	51.70 (20.19)	$F[3,142]=8.41, p<0.001$
PANSS positive score	21.75 (5.40)	16.08 (4.81)	15.71 (5.31)	13.45 (4.57)	$F[3,142]=18.93, p<0.001$
PANSS delusions score	4.75 (1.10)	4.00 (1.36)	3.52 (1.39)	3.18 (1.63)	$F[3,142]=9.32, p<0.001$

3.2 Hypothesis 1: Delusional distress, preoccupation and impact on functioning will reduce prior to delusional conviction

3.2.1 Delusional dimensions at each time point

VAS scores of delusional dimensions across time points are shown in Figure 1.

Figure 1 Changes in delusional dimensions (N=40)



3.2.2 Changes in delusional dimensions

Table 2 *Linear mixed models for changes in delusional dimensions*

Model	DV	IV	Model fit indices
1	VAS score	Time ($F[1,28.98]= 9.22, p= 0.005$) Dimension ($F[3,165.95]= 8.87, p< 0.001$) Time x Dimension ($F[3,165.16]= 1.08, p= 0.36$)	AIC=6323.38 BIC=6417.75
2	VAS score	Time ($F[1,29.06]= 9.01, p= 0.005$) Dimension ($F[3,165.41]= 10.57, p< 0.001$)	AIC=6320.60 BIC=6401.48
3	VAS score	Time ($F[1,114.61]= 15.79, p< 0.001$) Dimension ($F[3,165.45]= 10.55, p< 0.001$) Squared time ($F[1,96.20]= 10.00, p= 0.002$)	AIC=6313.10 BIC=6398.48

Using the maximum likelihood estimate of model testing, the effects of Time and Dimension on VAS scores were tested in a series of linear mixed models. In Model 1, with Time, Dimension and Time x Dimension as IVs, the Time x Dimension interaction effect was not significant ($p= 0.36$). Therefore, the interaction effect was removed to form Model 2, which yielded a better model fit than Model 1. In Model 2, the effects of Time and Dimension were both significant predictors of VAS score ($p< 0.01$).

To check whether the effect of Time is non-linear, a third model with the effects of Dimension, Time, and a quadratic term of time (squared Time) was tested. The model fit indices of Model 3 indicated a better fit with the data than the previous two models. In Model 3, the effects of Time, Squared Time, and Dimension were all significant ($p< 0.01$). Based on Model 3, additional models with baseline dosage and duration of antipsychotics as covariates also revealed significant effects of Time, Dimension and Squared Time.

Therefore, all dimensions declined over time, and the reduction became smaller over time. As there was no interaction between dimensions and time, the hypothesis that delusional conviction reduces more slowly or to a lesser degree than the other dimensions was not supported.

There was, however, a significant difference between dimensions, with Bonferroni adjusted pair-wise comparisons revealing a higher overall score on Conviction than Preoccupation (difference= 13.715, $SE= 2.534, df= 164.978, p< 0.01$) and Distress (difference= 8.04, $SE= 2.78, df= 166.01, p= 0.03$) throughout eight weeks.

In order to compare with Mizrahi et al (2006), a follow-up analysis was included with percentage change in the first week as IV and percentage change over eight weeks as DV. Linear regression analyses revealed that first-week change predicted overall change in delusional preoccupation ($B= 0.47, SE= 0.20, p= 0.03$), distress ($B= 0.47, SE= 0.15, p< 0.01$), and disruption ($B= 0.40, SE= 0.11, p< 0.01$).

3.3 Hypothesis 2: Depression and anxiety will reduce over eight weeks of antipsychotic treatment via improvements in delusional dimensions

BDI-II and BAI scores across time points are shown in Table 3.

Table 3 *BDI-II and BAI scores across time points*

	Week 0 (n = 39)	Week 4 (n = 28)	Week 8 (n = 29)
BDI-II	20.38 (15.22)	19.14 (13.81)	17.14 (13.61)
BAI	21.59 (15.11)	16.79 (12.98)	14.24 (12.98)

The relationships between change in BDI-II and BAI, with change in delusional dimensions over time, were tested using linear mixed modelling, with the ML estimation.

Models 1-2 tested the effect of Time on BDI-II and BAI, respectively, without any covariates. Change over time was not significant for depression or anxiety ($p > 0.05$).

Models 3-4 tested the effect of Time on BDI-II and BAI, respectively, with four delusional dimensions included as fixed covariates. These models yielded better model fit than Models 1-2, indicating that including delusional dimensions helped explain the data better. Again, there was no significant change in depression or anxiety ($p > 0.05$). However, the effect of delusional preoccupation as a covariate was significant for both depression and anxiety ($p < 0.05$), whereas Conviction was significant for anxiety only ($p = 0.04$). Distress and Disruption were not significant predictors of either BDI-II or BAI ($p > 0.05$).

To further examine changes of individual dimensions in predicting emotional changes, four more models were tested with BDI-II as the DV, Time as the IV, and each dimension as a covariate (Models 5a-d). Among these four models, the model with Preoccupation as a covariate in predicting the effect of time on BDI-II (Model 5b) was the best fit with the data, which was also better than Model 3 (with all dimensions). In Model 5b, Preoccupation ($p < 0.01$) but not Time predicted BDI-II significantly. An additional model with both Preoccupation and Preoccupation x Time interaction as covariates was also tested, but it showed a poorer fit of the data (AIC= 727.68, BIC= 745.10) than Model 5b. In summary, delusional preoccupation was associated with depression; this association did not change over time.

For anxiety, four models were tested with BAI as the DV, Time as IV, and each dimension as a covariate (Models 6a-d). Among these four models, the model with Preoccupation as a covariate in predicting the effect of time on BAI (Model 6b) was the best model. In this model, Preoccupation ($p < 0.001$) but not Time predicted BAI significantly. An additional model with both Preoccupation and Preoccupation x Time interaction as covariates was also tested, but it showed a poorer fit of the data (AIC= 711.70, BIC= 729.12) than Model 6b. While Model 6b was the best model for explaining variance of BAI, the model with four dimensions as covariates (Model 4) should also be discussed as its AIC almost equalled Model bb and its BIC was only seven units greater than Model 6b. In summary, delusional preoccupation (and conviction) was associated with anxiety; their association did not change over time.

Table 4 *Linear mixed models for co-variation of delusional dimensions and emotions*

Model	DV	IV	Model fit indices
1	BDI-II	Time ($F[2,96] = 0.44, p = 0.645$)	AIC=788.74 BIC=798.99
2	BAI	Time ($F[2,96] = 2.55, p = 0.083$)	AIC=782.57 BIC=792.82
3	BDI-II	Time ($F[2,89] = 0.34, p = 0.710$)	AIC=727.76

		Preoccupation ($F[1,89]= 4.61, p= 0.034$) Conviction ($F[1,89]= 3.29, p= 0.073$) Distress ($F[1,89]= 0.17, p= 0.679$) Disruption ($F[1,89]= 1.16, p= 0.283$)	BIC=747.66
4	BAI	Time ($F[2,89]= 2.11, p= 0.127$) Preoccupation ($F[1,89]= 6.46, p= 0.013$) Conviction ($F[1,89]= 4.25, p= 0.042$) Distress ($F[1,89]= 3.28, p= 0.073$) Disruption ($F[1,89]= 0.003, p= 0.956$)	AIC=707.83 BIC=727.74
5a	BDI-II	Time ($F[2,91]= 0.55, p= 0.579$) Conviction ($F[1,91]= 0.66, p= 0.418$)	AIC=749.27 BIC=761.83
5b	BDI-II	Time ($F[2,89]= 0.35, p= 0.706$) Preoccupation ($F[1,89]= 9.96, p= 0.002$)	AIC=725.45 BIC=737.90
5c	BDI-II	Time ($F[2,90]= 0.27, p= 0.764$) Distress ($F[1,90]= 6.44, p= 0.013$)	AIC=735.84 BIC=748.34
5d	BDI-II	Time ($F[2,91]= 0.23, p= 0.797$) Disruption ($F[1,91]= 5.11, p= 0.026$)	AIC=744.96 BIC=757.52
6a	BAI	Time ($F[2,91]= 1.94, p= 0.150$) Conviction ($F[2,91]= 1.52, p= 0.221$)	AIC=739.77 BIC=752.33
6b	BAI	Time ($F[2,89]= 1.80, p= 0.172$) Preoccupation ($F[1,89]= 18.71, p< 0.001$)	AIC=707.97 BIC=720.41
6c	BAI	Time ($F[2,90]= 1.35, p= 0.265$) Distress ($F[1,90]= 16.88, p< 0.001$)	AIC=717.21 BIC=729.71
4d	BAI	Time ($F[2,91]= 1.46, p= 0.238$) Disruption ($F[1,91]= 5.06, p= 0.027$)	AIC=736.36 BIC=748.91

4. Discussion

This study assessed changes in dimensions of delusions and negative emotions over eight weeks in patients who were recently hospitalised and prescribed medication. The hypothesis that conviction reduces more slowly or to a lesser degree than other dimensions of delusions, namely distress, preoccupation and disruption, was not supported. Although depression and anxiety did not improve significantly after eight weeks of antipsychotic treatment, they were associated with delusional preoccupation longitudinally.

We found that delusional dimensions (including conviction) did not differ in their improvement rate during the first few weeks of antipsychotic treatment. Over the first two weeks of treatment, Mizrahi et al. (2006) and So et al. (2014) reported a reduction in conviction of 6.4% and 3.8% on Dimensions of Psychosis Instrument (DIPI) and PSYRATS respectively, whereas we found a notable improvement of 26.1% in conviction using visual analogue scales (VAS) in the present study. However, over the subsequent weeks, change in conviction in Mizrahi et al. (2006) and the present study became comparable. Improvement in conviction was 24.9% at six weeks in Mizrahi *et al.*, (2006) and 25.5% at eight weeks in our study.

One possible reason for the differences in findings is difference in measures of conviction used. One of the two conviction items on the DIPI is more related to insight than to conviction,

while the PSYRATS is less sensitive to change than VAS ratings. However, we found similar results with the PSYRATS², suggesting that the use of measures is unlikely to account fully for the differences.

There may also have been sample differences between the studies. Unlike Mizrahi et al. (2006) and So et al. (2014), where patients were assessed when they began antipsychotic treatment, our patients were recruited within four weeks of antipsychotic prescription, and around 30% had been on antipsychotics for more than 14 days. Inclusion of patients with a varied medication experience renders our sample not entirely comparable to the drug-free sample in Mizrahi et al. (2006). However, our results remained the same after controlling for duration of treatment at baseline. Furthermore, consistent with Mizrahi et al. (2006), we found a bigger reduction in delusions in the earlier weeks and that improvements in the first week predicted overall 8-week changes..

Despite the current evidence of a decrease in all delusional dimensions, the conviction score remained relatively high across time points (from >80% at baseline to >50% at eight weeks). According to Kapur, patients with psychosis assign salience and novelty to external objects and internal representations abnormally, and delusions are a ‘top-down’ cognitive explanation that one imposes on these aberrant experiences to help make sense of the experiences and to resolve anxiety (Kapur et al., 2005). According to this theory, antipsychotics block dopamine and reduce emotional distress as well as aberrant salience without modifying the appraisals of experiences, while patients work through their symptoms towards a “psychological resolution” (Kapur, 2004; p. 404; Kapur et al., 2006). Our data suggest that the ‘psychological resolution’ may begin to occur in the early weeks of antipsychotics, together with improvement in other dimensions. However, such a process of resolution is unlikely to be complete within the period covered in our study and also may require more active intervention to aid reappraisal, such as concurrent psychological therapy.

We found a longitudinal association between delusional preoccupation and depression, and between delusional preoccupation (and conviction) and anxiety. Individuals with greater delusional preoccupation were also more depressed and anxious. This finding fits with and extends recent work on persecutory delusions and emotional processes, supporting the proposal that anxiety and depression follows and maintains delusions (see reviews by Garety and Freeman, 2013; Freeman and Garety, 2014). There is much evidence that repetitive thought processes (rumination in depression, and worry in anxiety) may maintain emotional disorders (see review by Watkins, 2008). Our finding suggests a possibility that delusional preoccupation, as a form of a repetitive thought, may relate to emotional processes in ways that are reported in emotional disorders. This suggestion would be consistent with the rationale behind a recent intervention for delusions that focused specifically on worry reduction (Foster et al., 2010; Freeman et al., 2015). Future research using an interventional-empirical approach or a longitudinal design such as experience-sampling may further examine the direction of association between change in depression and anxiety and change in delusional preoccupation.

One major limitation of this study was the heterogeneous sample. A proportion of patients had had previous psychiatric admissions, some with affective psychosis, and not all were drug-free at study participation. Although we controlled for variance in medication dosage and duration, a more homogeneous sample would have been preferred. Secondly, the lack of a

² Analyses obtainable from first author

control group or baseline phase makes it difficult to infer that the reported changes are due to medication, as they could reflect a spontaneous symptom improvement, effect of hospitalisation, or other unmeasured effects. Thirdly, there was some attrition in this longitudinal study, with just over 25% of the sample completing fewer than the five assessments, although we made efforts to minimise the impact of attrition using mixed modelling, which takes into account all available data points. Lastly, detail about other psychiatric medications such as anti-depressants and anxiolytics was not available. Against these caveats, this study demonstrated that improvement rates across delusional dimensions did not differ over eight weeks during an early phase of antipsychotic treatment. Despite little change in negative emotions over time, delusional preoccupation co-varied with both anxiety and depression, confirming a relationship between emotional and at least some delusional processes during an early recovery phase.

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