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ORIGINAL ARTICLE

Emotional and symptomatic reactivity to stress in individuals at ultra-high risk of developing psychosis

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Background. The stress–vulnerability model of psychosis continues to be influential. The aim of this study was to compare emotional and symptomatic responses to stress in individuals at ultra-high risk (UHR) of developing psychosis, in age- and gender-matched healthy controls, and in patients with non-affective psychosis.

Method. A total of 27 UHR, 27 psychotic and 27 healthy individuals completed the experience sampling method, an ambulant diary technique, where they were required to fill in self-assessment questions about their emotions, symptoms and perceived stress at semi-random times of the day for 6 days. Questionnaire and interview assessments were also completed.

Results. Multilevel regression analyses showed that individuals at UHR of developing psychosis reported greater negative emotions in response to stress than the healthy individuals. Against the initial hypotheses, the UHR individuals also experienced greater emotional reactivity to stress when compared with the patient group. No significant differences were observed between the patients and the non-clinical sample. Stress measures significantly predicted the intensity of psychotic symptoms in UHR individuals and patients, but the extent of this did not significantly differ between the groups.

Conclusions. Individuals at UHR of developing psychosis may be particularly sensitive to everyday stressors. This effect may diminish after transition to psychosis is made and in periods of stability. Subtle increases in psychotic phenomena occur in response to stressful events across the continuum of psychosis.

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Key words: Prodrome, psychosis, schizophrenia, stress, ultra-high risk.

Introduction

According to stress–vulnerability models of psychosis, life stress may act on an underlying genetic predisposition to trigger the formation of hallucinations and delusions (Zubin & Spring, 1977; Nuechterlein & Dawson, 1984). These theories propose that once an individual has experienced their first psychotic episode, the stress threshold needed to elicit future symptomatic responses becomes substantially reduced. In particular, an individual's sensitivity to everyday stressors (e.g. getting lost, losing one's car keys) may be important in the aetiology of psychosis.

Research has often found an association between minor stressors and subsequent changes in symptom severity across several months (Malla *et al*. 1990; Norman & Malla, 1994). The association between stress and psychosis has also been demonstrated using the experience sampling method (ESM; Csikszentmihalyi & Larson, 1987; Delespaul, 1995). In its typical form, the ESM is a diary technique, where participants are required to complete ambulant self-report questions at pseudo-random times of the day when prompted by the beep of an electronic device (e.g. a wristwatch). This approach holds several advantages over questionnaire- and interview-based studies in that it: (1) reduces the confounding effects of retrospective recall bias and forgetting; (2) produces data with high ecological validity; and (3) allows the context of experiences to be assessed (e.g. places, company; Palmier-Claus *et al*. 2010).

ESM studies have found that individuals with psychosis suffer from greater emotional responses to stress (i.e. shifts in mood in response to adverse everyday events) when compared with relatives, healthy controls (Myin-Germeys *et al*. 2001) and individuals with uni- and bipolar depression (Myin-Germeys *et al*. 2003). Stress sensitization may be the

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consequence of familial vulnerability (Lataster *et al*. 2009, 2010), early childhood trauma (Glaser *et al*. 2006), cognitive processing biases (Lincoln *et al*. 2009) and metacognitive beliefs (Palmier-Claus *et al*. in press *a*). It may provide a common mechanism by which a plethora of risk factors (e.g. urban living, discrimination) for psychosis confer their vulnerability, thereby providing a unifying theory for several areas of research (Collip *et al*. 2008).

In addition to increased affective reactivity to stress, everyday irritations and hassles may trigger subtle increases in the severity and intensity of psychotic symptoms. Myin-Germeys *et al*. (2005) found that this effect occurred in patients and, to a lesser extent, their family members. Morrison (2001) suggests that psychotic symptoms may be the result of a state of cognitive dissonance generated by intrusive thoughts, and triggered by internal or external events. Psychotic symptoms may help to temporarily resolve this dissonant state, which reinforces their occurrence and increases their frequency. Other authors have proposed that affective dysregulation, triggered by anomalous experiences acting on a bio-psycho-social vulnerability, may contribute to the misattribution of anomalous experiences (Garety *et al*. 2001).

There is evidence to suggest that psychotic phenomena lie on a continuum which extends to normality (Peters *et al*. 1999; Johns & Van Os, 2001). Healthy individuals who experience these attenuated symptoms may be at increased risk of developing psychosis. Treating psychosis in its early stages may be associated with better outcomes and potentially help to avert oncoming psychopathology (Petersen *et al*. 2005; McGorry *et al*. 2010). Yung *et al*. (1995) have developed a set of criteria which establishes whether someone is at ultra-high risk (UHR) of developing a psychotic disorder. UHR status can be met if an individual possesses subthreshold psychotic symptoms (attenuated group), is overtly psychotic for a short period of time (brief limited intermittent psychotic symptoms group), or has a familial vulnerability (familial group) in conjunction with significant levels of distress and poor functioning. In their original study, Yung *et al*. (1995) found that 40% of UHR individuals made the transition to psychotic disorder over a 1-year period, although lower rates have more recently been observed (Yung *et al*. 2007).

Research in UHR populations may provide insights into the early stages of disorder without the potential confounding influences of long-term institutionalization and medication use. Studies examining the role of stress in this group have generally examined physiological measures as long-term predictors of transition to psychosis. For example, some studies have found that individuals with larger pituitary glands (Garner *et al*. 2005) and higher cortisol levels (Thompson *et al*. 2007), both thought to be associated with an increased stress response, are more likely to develop psychosis.

This study tested the hypothesis that individuals at UHR of developing psychosis would experience an increased affective response to stress when compared with healthy controls. We also predicted that greater emotional responses to stress would be observed in individuals with established psychosis, when compared with UHR and control groups. The third hypothesis of this study was that patients would experience greater symptomatic responses to stress when compared with UHR individuals. Therefore, the primary aim of this study was to establish whether sensitization to stress is heightened in individuals experiencing psychotic phenomena, but greatest in those who have made the transition to a full-blown disorder. These hypotheses were based on the vulnerability–stress model of psychosis, which suggests that an individual's stress threshold is substantially lowered after they make transition to psychosis (Zubin & Spring, 1977).

Method

Participants

A total of 27 UHR individuals were entered into the final analyses. In addition to this, six individuals started the procedure but dropped out ($n=5$) or failed to complete the minimum number of diary entries ($n=1$). Participants were recruited upon exiting a randomized control trial for cognitive behavioural therapy (CBT; $n=15$) or from an early detection and intervention service ($n=12$; Salford and Wigan), where they were also receiving regular CBT sessions. All individuals had met UHR criteria, as determined by the Comprehensive Assessment of Ultra-High Risk Mental State (CAARMS; Yung *et al*. 1998, 2005) within the past year. At the time of taking part in the study, 23 individuals met UHR criteria for the attenuated group, while one of these participants was also eligible for the vulnerability group. Four participants were no longer deemed to be at UHR at the time of taking part in the study, although these still reported some attenuated psychotic phenomena. The inclusion criteria comprised of being aged 16–35 years and not having made the transition to a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of disorder, organic brain disease, or moderate to severe learning disabilities. The demographic information for all groups is presented in Table 1. The only prescribed antipsychotic in the UHR group was promazine ($n=2$; $10+50$ mg), and the most commonly prescribed antidepressant was citalopram

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Table 1. *Demographic information for UHR and patient samples*

	Patients ($n=27$)	UHR ($n=27$)	Controls ($n=27$)
Mean age, years (S.D.)	33.2 (11.0)	22.6 (4.4)	22.6 (5.2)
Gender, *n*			
Male	21	14	14
Female	6	13	13
History of CBT, *n*	3	22	N.A.
Mean age of onset, years (S.D.)	27.0 (9.5)	17.4 (5.7)	N.A.
Ethnicity, *n*			
White British	24	27	24
White other	0	0	1
Asian Indian	1	0	1
Asian Pakistani	1	0	0
Black African	1	0	1
Living status, *n*			
Alone	11	3	0
With child	1	0	0
With parents	5	16	0
With partner	6	3	1
Shared accomodation	1	5	26
Supported living	1	0	0
Hospital ward	2	0	0
Medication type, *n*			
No medication	6	13	27
Typical AP	0	2	0
Atypical AP	12	0	0
Clozapine	7	0	0
Typical and atypical AP	2	0	0
Antidepressant	10	14	0

UHR, ultra-high risk; S.D., standard deviation; CBT, cognitive behavioural therapy; N.A., not applicable; AP, antipsychotic.

($n=6$; 20–100 mg). The mean length of time since the onset of first noticeable attenuated symptoms in the UHR group was 4.7 years (S.D. = 3.6). Other analyses of this dataset are reported in Palmier-Claus *et al*. (in press *b*).

The 27 individuals who had met or were currently meeting the criteria for a DSM-IV diagnosis for non-affective psychosis (schizophrenia, schizo-affective, schizophreniform disorder) were recruited from in-patient and out-patient services, rehabilitation homes and charity groups from around the Greater Manchester area. The inclusion criteria for this group were being younger than age 55 years upon first episode of psychosis. Individuals with organic brain disease, moderate to severe learning disabilities and depression with some psychotic features were excluded from the study. The most commonly prescribed antipsychotics for this group were clozapine (50–700 mg; $n=7$), aripiprazole (5–30 mg; $n=5$) and rispiridone (2–8 mg; $n=4$). Drop-out for this group was high ($n=24$), and the sample over-represented individuals who were stressed and under-represented individuals with negative symptoms (see J. Palmier-Claus *et al*. unpublished observations). The mean length of time since the onset of first-episode psychosis in the patient group was 6.5 years (S.D. = 8.2).

The 27 healthy controls, matched for age and gender with the UHR group, were selected through University of Manchester recruitment emails and psychiatry participation pools. The exclusion criteria were having a history of mental illness and previous use of psychotropic medication.

Measures

Questionnaire

The Perceived Stress Scale (PSS; Cohen *et al*. 1983) is a general measure of perceived stress, which includes 14 items scoring on five-point Likert scales. It has been validated in a variety of languages (Cole, 1999; Remor, 2006) and correlates with measures of life hassles in individuals with non-affective psychosis (Norman & Malla, 1991). Principal components analysis (PCA) has shown one- and two-factor solutions to adequately fit this scale in data from a diagnostically mixed

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psychiatric sample (Hewitt *et al*. 1992). In this study, the PSS was used to validate the ESM measures of stress, and ascertain whether there were group differences in a retrospective, global measure of perceived stress in addition to the diary scales.

ESM diary

The researcher met with the participant to instruct them in the experience sampling procedure. They were asked to fill in a paper diary when prompted by the beep of the electronic wristwatch (Timex Ironman; Timex, USA) and not to backfill or misreport the times of entry. There were 10 diary entries per day which commenced on the morning after briefing at semi-random intervals between 07.30 and 22.30 hours, and continued for 6 days. All entry times were pre-programmed into the watches by the lead researcher and were subsequently locked to the participant (password protected) so that they could not alter the sampling schedule. Participants were required to enter the time of completion at the end of each entry, and only those entries completed 5 min before or 15 min after the alarm going off were included in the analyses (Delespaul, 1995). Upon completion of the sample procedure the lead researcher met with the participant to conduct debriefing questionnaires and an interview. Individuals who completed less than 15 entries at debriefing were asked to complete one additional day of diary assessment. Those who still completed less than 15 entries were excluded from the analysis. A full summary of the procedure is provided by Palmier-Claus *et al*. (2010).

Participants were asked to report on the strength of a variety of experiences and emotions prior to the watch beeping. All of the items used in this study were taken or adapted from past ESM research. Although most items were created and originally employed by researchers at the University of Maastricht (Myin-Germeys *et al*. 2001, 2003, 2005; Lataster *et al*. 2009), they have also been used in studies conducted in the UK (Varese *et al*. 2011). Analyses attesting to the validity and reliability of many of the items used in this study have been published by Delespaul (1995). The validity of the perceived stress items has also been supported through the confirmation of hypothesized associations with mood (Myin-Germeys *et al*. 2001) and dopamine response (Myin-Germeys *et al*. 2005). Reliability (see α levels) and PCA were performed on the pooled data from across all three groups to ensure that the factors were reliable and well fitting in the data collected for this study, the results of which are displayed below.

Emotion items. At each entry the participant was required to rate the extent to which they felt cheerful, excited, relaxed, satisfied, lonely, anxious, irritated, sad and guilty, prior to the alarm sounding, on seven-point Likert scales (1 = not, 7 = very). Past studies have examined this scale as two separate factors: positive and negative affect (Myin-Germeys *et al*. 2001; Palmier-Claus *et al*. in press *b*). However, there is much debate in the literature as to whether this is a meaningful distinction (Russell & Carroll, 1999). In order to reduce the possibility of false-positive findings resulting from multiple hypotheses testing, the mood items were treated as a single factor in this set of analyses (i.e. positive items were reversed and a total score was derived). PCA on affect items revealed that one factor explained an adequate proportion of the variance (47.6%) with an eigenvalue of 4.284 (Cronbach's $\alpha = 0.86$). Total scores were used for all analyses.

Symptoms items. PCA, conducted on those items which assessed psychotic symptoms, revealed two factors with eigenvalues greater than 1 (1.10 and 3.20), which together explained 71.6% of the variance. The first related to hallucinations (Cronbach's $\alpha = 0.67$) and consisted of the items 'I am hearing voices' and 'I am seeing things that are not real'. The second represented delusional or dissociative thoughts (Cronbach's $\alpha = 0.84$) and was comprised of the items 'My thoughts are suspicious', 'My thoughts are being influenced', 'I feel threatened' and 'I feel unreal'.

Activity-related stress. This scale assessed times where the individual's current activity was causing discomfort or was taxing. PCA showed the items, 'I'd rather be doing something else', 'this activity is difficult' and 'I feel confident about this activity' (reversed) to explain one factor, explaining 51.3% of the variance with an eigenvalue of 1.54 (Cronbach's $\alpha = 0.52$). This scale corresponded well with the written content of the diaries, and the mean score for each participant significantly correlated with the PSS (Pearson's $r = 0.37$, $p < 0.001$).

Social stress. This scale assesses times where an individual's current social environment is inducing some degree of disturbance or dissatisfaction. It consists of three items: 'I'm enjoying myself' (reversed), 'I like this company' (reversed) and 'Right now, I'd rather be alone'. PCA identified a single factor explaining 66.1% of the variance (eigenvalue = 1.684, Cronbach's $\alpha = 0.59$). The aggregate score for this measure was significantly correlated with the PSS ($r = 0.42$, $p < 0.001$).

Event-related stress. This scale asks individuals to state and rate the most important event to occur since

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the last beep from 'very unpleasant' to 'very pleasant' (–3 to 3). This item asks individuals to report events that can be scored as a stressor through a negative appraisal. Again, this scale demonstrated high face validity by corresponding well with the written content of the diaries and the mean score (within each participant) of a dichotomized version of the variable (see below) significantly correlated with the PSS ($\rho = 0.33$, $p = 0.003$). Jacobs *et al*. (2007) found that versions of these stress scales predicted salivary cortisol levels, suggesting that they are associated with a physiological response.

Statistics

Stata 10.0 (StataCorp LP, USA; 2007) and SPSS 15.0 (SPSS Inc., USA; 1998) were used for the analyses. First, visual inspection of a histogram of the hallucination stress scales suggested a heavy skew onto the lowest number of responding. This was also observed in the event-related stress scale when initial transformations were made to remove the effects of positive appraisals of events consistent with past research (see Myin-Germeys *et al*. 2001). Therefore, the event-related stress scale was transformed into a binary variable so that all positive and neutral appraisals of events (scores of 0, 1, 2 or 3) were coded as 0, and negative appraisals (scores of –1, –2, or –3) coded as 1. The hallucination variable was transformed to represent the absence (a score of 2) or presence (greater than 2) of perceptual abnormalities. The emotion and delusion variables were also negatively skewed, but there was no conceptually meaningful cut off point from which to transform these into binary form (MacCallum *et al*. 2002; Altman & Royston, 2006). The analyses were checked with bootstrapping (percentile method, 1000 iterations), which has been proposed as a suitable alternative when parametric assumptions are not met (Mooney & Duval, 1993). There were no major differences in the findings when this was carried out.

Second, one-way analyses of variance were used to assess the differences between the three groups using aggregated ESM scores and the PSS. For significant results, independent t tests were used to identify where this difference lay. Due to data not meeting the assumption of normal distribution, robust standard errors were used in the latter analysis.

Third, in ESM data the assumption of independent observations necessary for most types of statistical analysis (e.g. regression) is almost certainly violated. For example, an individual's emotions at one time-point will probably show stronger correlations with other emotion scores on the same day, than to scores on different days. Multilevel analysis accounts for this by explicitly modelling the random error. In this study, multilevel regression analysis ('XTMIXED'), with the maximum likelihood estimation option ('MLE'), was used to assess whether the stress measures predict affect scores in the combined data from all three groups. Participant number was included as a random effect to control for the nested structure of the data. Although some ESM studies include more than one level (e.g. days) as a random effect in the model, only entering the highest should provide equivalent results (Froot, 1989; Rogers, 1993) with robust standard errors (Huber, 1967; White, 1980). B, S.E. and p values are reported for each of these analyses.

Fourth, binary variables representing group status [controls (0) or UHR (1); controls (0) or patients (1); UHR (0) and patients (1)] were generated and independently added to the models as interactions with stress measures. Their main effects were also included in each set of analyses. Significant interactions would suggest that one of the groups is experiencing greater emotional responses to stress than another. Previous research has suggested that females suffer from greater affective responses to stress than males. Therefore, gender and its interaction with stress were controlled for in all analyses including the patient group where there were fewer females. Additionally, whether someone was on a psychotropic medication (antidepressant or antipsychotic) was controlled for in all of the analyses. Due to a lack of statistical power we could not specifically control for the effects of antipsychotic medication alone.

Fifth, the analyses were repeated with delusions as the outcome variable in only the data from the UHR and patient groups. Additionally, multilevel binary logistic regression analyses ('XTMELOGIT'), also with maximum likelihood estimation, was used to see if stress measures, group, or an interaction between the two, predicted hallucinations.

Results

Are there significant differences in the measured variables across the three groups?

The mean and standard deviation scores (in parentheses) for all variables considered in this paper are reported in Table 2. This table also shows the results to group comparison analyses (t tests with robust standard errors). The UHR and patient groups experienced significantly greater social stress, general levels of perceived stress (PSS score), hallucinations and delusions when compared with the healthy controls. The patient group experienced significantly greater hallucinations than the UHR group, but no other significant differences were observed.

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Table 2. *Assessment scores for stress, mood and symptoms*

	Minimum	Maximum	Patients ($n=27$)	UHR ($n=27$)	Controls ($n=27$)
Stress					
Activity	3.9	12.2	8.2 (3.4)	8.2 (2.0)	7.5 (1.8)
Social	3.8	21.0	9.4 (3.4)	9.6 (3.8)	7.0 (2.3)*††
Event	0.0	0.7	0.2 (0.2)	0.1 (0.1)	0.1 (0.1)
PSS	27.0	64.0	46.1 (5.8)	48.1 (7.2)	39.6 (6.6)****†††
Mood	11.5	41.9	26.3 (6.1)	27.8 (6.8)	20.6 (4.1)****†††
Symptom					
Hallucinations	2.0	10.3	3.9 (2.6)	2.3 (0.7)**	2.0 (0.03)***†
Delusions	4.0	20.2	7.8 (5.0)	7.1 (3.9)	4.2 (0.3)****†††

Data are given as minimum and maximum, and as mean (standard deviation) for the three groups based on data averaged for each participant.

UHR, Ultra-high risk; PSS, Perceived Stress Scale.

Mean value was significantly different from that of the patient group: * $p=0.006$, ** $p=0.005$, *** $p=0.001$, **** $p<0.001$.

Mean value was significantly different from that of the UHR group: † $p=0.013$, †† $p=0.005$, ††† $p<0.001$.

Table 3. *Stress × group interactions as predictors of mood*

Groups	IV	*B*	S.E.	*p*	95% CI
UHR: controls	Activity	0.253	0.070	<0.001	0.115 to 0.390
	Social	0.259	0.094	0.006	0.075 to 0.442
	Event	0.796	0.858	0.353	−0.885 to 2.477
Patients: UHR	Activity	−0.349	0.090	<0.001	−0.525 to −0.173
	Social	−0.334	0.131	0.011	−0.591 to −0.077
	Event	−1.992	1.070	0.063	−4.088 to 0.105
Patients: controls	Activity	−0.146	0.077	0.059	−0.298 to 0.005
	Social	−0.152	0.107	0.157	−0.362 to 0.059
	Event	−1.558	0.813	0.055	−3.152 to 0.036

IV, Independent variable; S.E., standard error; CI, confidence interval; UHR, ultra-high risk.

Do individuals at UHR risk of developing psychosis suffer from greater affective reactivity to stress than patients with psychosis and healthy controls?

Multilevel regression analysis showed that social ($B=1.093$, S.E. $=0.043$, $p<0.001$), activity-related ($B=0.686$, S.E. $=0.030$, $p<0.001$) and event-related ($B=4.810$, S.E. $=0.364$, $p<0.001$) stress significantly predicted higher negative emotions across all three groups.

Interactions between stress measures and group were then added to the models, with their main effects, whilst controlling for whether someone was currently on psychotropic medication. Age, gender and gender × stress interactions were controlled for in the analyses on data from the patient group. The output for all interactions scores is displayed in Table 3. The UHR group experienced greater negative emotions in response to activity-related and social, but not event-related, stress than the healthy controls and patients with psychosis. There were, however, no significant differences in emotional responses to stress when comparing the patient and control samples.

Are there differences in symptomatic reactions to stress in UHR and patient samples?

The results of multilevel regression analyses on both the patient and UHR groups showed a significant effect of activity-related ($B=0.151$, S.E. $=0.017$, $p<0.001$), social ($B=0.099$, S.E. $=0.021$, $p<0.001$) and event-related ($B=0.846$, S.E. $=0.183$, $p=0.001$) stress on delusional and dissociative thoughts. When multilevel mixed-effect logistic regression analysis was carried out on the presence of hallucinations, only activity-related stress [odds ratio (OR) $=1.109$, S.E. $=0.032$, $p<0.001$] and event-related stress (OR $=3.180$, S.E. $=0.991$, $p<0.001$) were significant predictors. The association between social stress and hallucinations was, however, non-significant (OR $=1.081$, S.E. $=0.058$, $p=0.146$). The findings were the same when the UHR

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Table 4. *Interactions between stress measures and group (UHR and patient) as predictors of delusions and hallucinations*[a]

	Delusions				Hallucinations			
	B	S.E.	*p*	95% CI	OR	S.E.	*p*	95% CI
Group × activity-related stress	0.013	0.034	0.709	−0.053 to 0.079	1.020	0.063	0.751	0.903–1.152
Group × social stress	−0.023	0.043	0.585	−0.107 to 0.060	1.061	0.132	0.635	0.832–1.353
Group × event-related stress	−0.532	0.368	0.148	−1.253 to 0.188	2.035	1.408	0.304	0.524–7.901

UHR, Ultra-high risk; S.E., standard error; CI, confidence interval; OR, odds ratio.

[a] Output represents analyses when not controlling for medication or gender.

and patient groups were examined separately. The main effect of group and an interaction between group and stress measures were then added to each of the aforementioned analyses. No significant interactions between groups and stress measures were observed in the prediction of delusional or dissociative thoughts, nor hallucinations, as is displayed in Table 4.

Discussion

This study tested the hypothesis that individuals at UHR of developing psychosis would suffer a greater emotional response to stress than age- and gender-matched healthy controls. It also examined the prediction that patients would experience greater emotional responses than UHR and control groups, and greater symptomatic responses to stress when compared to UHR individuals.

The data support the first prediction that individuals at UHR of developing psychosis experienced greater negative emotions in response to stress than healthy controls. Stress sensitization may be an important factor influencing the development of psychotic experiences, and related distress and impairment, increasing an individual's vulnerability to psychotic disorder. Indeed, other studies have observed that stress-related brain changes are associated with a greater risk of transition to psychopathology (e.g. Thompson *et al*. 2007). The data also suggest that stress sensitization is not just the consequence of a chronic and disabling illness, which may explain the findings of research in patient populations (e.g. Myin-Germeys *et al*. 2001). This supports the notion that changes in emotional processing lead to external appraisals of anomalous experiences early in the course of disorder (Garety *et al*. 2001). Understanding an affective pathway to psychosis is an important step if we are to develop effective, evidence-based forms of intervention. Worthy of note is that emotional reactivity may also be a consequence of aberrant thoughts, experiences and beliefs, which sensitize UHR individuals to stress in a circular relationship. Additionally, it is possible that stress sensitivity is associated with help-seeking behaviour, increasing the likelihood that UHR individuals will be detected and entered into clinical services.

Intriguingly, the second hypothesis of this study was rejected: UHR status was a better predictor of negative emotional responses to stressful events than the patient group. Furthermore, negative emotional responses to stress were not significantly different between the patient and healthy samples. There are several possible explanations for these findings. First, stress sensitization may be more involved with the generation, rather than the maintenance, of psychosis, and therefore greater in the early stages of disorder. In a review of dopamine activation studies, Laruelle (2000) has argued that sensitization to stress becomes less acute in periods of remission and stability. Indeed, stressful life events appear to play a more prominent role in the onset of disorder rather than the persistence of symptoms (Bebbington *et al*. 1993). These findings may explain why CBT, which aims at reducing distress by targeting maladaptive cognitions, has been found to be particularly effective in UHR populations (Morrison *et al*. 2004).

Second, UHR status may not be entirely specific to psychosis, potentially including individuals who would go on to develop affective disorders, which might cause an exaggerated stress response (Meyer *et al*. 2005). However, Myin-Germeys *et al*. (2003) found that individuals with psychosis suffered greater emotional reactions to stress than individuals with diagnoses of either bipolar disorder or depression. Third, it is possible that the types of stressors observed in the UHR and control groups may be more severe than the patient group. Patients may deliberately avoid exposure to situations that elicit an emotional response. Indeed, in has been widely theorized that maladaptive avoidance coping strategies may contribute to psychological dysfunction (e.g. Wells & Matthews, 1996). Potentially discrediting this interpretation is that no significant differences in activity and event-related stress measures were observed

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between the groups. Rather, it was their emotional responses that differed. Fourth, subjects in the patient group were highly medicated, which may have dampened their stress response. Nicolo *et al*. (2010) found that antipsychotic use protected an individual from brain changes associated with chronic exposure to stress. Too few unmedicated patients and medicated UHR individuals were recruited in this study to effectively test this theory in the data, and further research is needed to examine this interpretation.

Heightened symptomatic responses to stress were not observed in the patients when compared with the UHR individuals. Indeed, the UHR group appeared to experience similar increases in the intensity of their symptoms in response to stress. Thus symptoms across the psychosis continuum appear to be triggered by everyday adverse events. The emergence of psychotic phenomena may help to resolve a state of cognitive dissonance, triggered by negative events (Morrison *et al*. 1994). In agreement with this, Kapur (2003) suggests that delusions are a consequence of a patient attempting to make sense of heightened and environmentally incongruent emotional reactions to environmental stimuli, which are caused by dopamine hypersensitivity.

There are several limitations of this research which should be taken into consideration. First, the study was cross-sectional and causation cannot be established. Longitudinal research is required to establish whether stress sensitization is an adequate predictor of transition to psychosis in the UHR group. Second, the ESM measures used in this study failed to take into account important aspects of stress such as controllability over and ability to cope with a situation (Lazarus & Folkman, 1984). Some of the items may not have accurately ascertained whether a situation was undesirable, but rather only suggested that it was taxing (e.g. 'this activity is difficult'). The stress scales may have also been confounded by symptom severity. For example, an argument with a friend could be triggered by persecutory delusions. Nevertheless, the items used in this study are widely used in the literature, appeared to correspond well with the open-ended content of the diaries, correlated with the PSS, and have received some validation in the research literature (Myin-Germeys *et al*. 2001, 2005). Furthermore, symptom severity would have been expected to increase stress sensitivity in the patient group against the direction of the findings. Third, there was greater exposure to CBT in the UHR when compared with the patient group, which would have been expected to desensitize these individuals to stress. This would also have acted against the direction of the results. Fourth, the number of participants included in each group was small and may have increased the possibility of false-negative findings. Fifth, it is difficult to be certain that participants are not misreporting the times of their diary entries. However, a great emphasis was placed on not misreporting entries during the briefing session and the participant would have had to have recorded the time of the beep in order to convincingly deceive the researcher. Sixth, the ESM is demanding on participants, and may lead to sample biases, which limits the extent to which the results can be generalized (J. Palmier-Claus *et al*. unpublished observations).

Clinically, it may be useful to identify reoccurring stressors in UHR individuals' lives in order to improve their mood and symptoms. For example, family interventions operate by identifying maladaptive relationships between patients and their relatives, which could be a source of distress (Lobban & Barrowclough, 2009). CBT and mindfulness training may also equip individuals with stress management skills, which could help to prevent transition to disorder. Alternatively, stress inoculation techniques (Meichenbaum & Deffenbacher, 1988), more widely used in the treatment of anxiety, may be useful in the UHR group. Establishing the psychological processes contributing to the initial stages of psychosis is a vital step in developing interventions effective at averting oncoming psychopathology and bettering long-term outcome.

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Declaration of Interest

S.W.L. has received occasional honoraria for advisory work and speaking engagements from pharmaceutical companies. The other authors have no financial declarations of interest.

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