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Booij, Sanne H.; Snippe, Evelien; Jeronimus, Bertus F.; Wichers, Marieke; Wigman, Johanna T. W.

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Affective reactivity to daily life stress: relationship to positive psychotic and depressive symptoms in a general population sample

Authors: Sanne H. Booij[1,3*], Evelien Snippe[1], Bertus F. Jeronimus[1,2], Marieke Wichers[1], Johanna T.W. Wigman[1,3]

[1] University of Groningen, University Medical Center Groningen, Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE), The Netherlands.

[2] University of Groningen, Department of Developmental Psychology, The Netherlands.

[3] Mental Health Service (GGZ) Friesland, Leeuwarden, The Netherlands

* Corresponding author

Additional information corresponding author:

Interdisciplinary Center Psychopathology and Emotion regulation (ICPE), Department of Psychiatry, University Medical Center Groningen, CC72, P.O. Box 30001, 9700 RB, The Netherlands. Telephone: +31(0)50-3615733, Fax: +31(0)50-3619722, E-mail: s.h.booij@umcg.nl

Abstract (248 words)

Introduction: Increased affective reactivity to daily life stress has been found in individuals with psychosis and depression, and in those at risk for these conditions. Because depressive and psychotic symptoms often co-occur, increased affective reactivity in these disorders may be explained by the presence of depressive symptoms, psychotic symptoms, or both. Therefore, we examined whether affective reactivity to daily stress is related to positive psychotic symptoms, independently of depressive symptoms, and vice versa.

Methods: We used data from an intensive sampling study in the general population (n=411), with three measurements a day (t=90). The following subjective stressors were assessed: appraisal of activities, appraisal of social interactions, and experienced physical discomfort. Affective reactivity was conceptualized as both the positive affect (PA) and negative affect (NA) response to these stressors. By means of mixed model analyses, it was examined whether affective reactivity was independently related to depressive and/or positive psychotic symptoms.

Results: The PA response to activities and NA response to social interactions were negatively and positively related to depressive symptoms, respectively, independent of psychotic symptoms. In contrast, no (in)dependent association was found between positive psychotic symptoms and affective reactivity to any of the daily life stressors. These findings were confirmed in a subsample with increased symptoms.

Limitations: The prevalence of positive psychotic symptoms was relatively low in this general population sample.

Conclusions: Increased affect reactivity predicts depressive symptoms, but not positive psychotic symptoms. Affective reactivity may still facilitate the development of psychotic symptomatology via its impact on depressive symptoms.

Key words: Depression, Psychosis, Affective reactivity, Experience sampling, General population, Social interaction

Word count: 5394 (excluding tables and reference list)

Introduction

Psychosis and depression are both characterized by affective disturbances. These disturbances have been examined in-depth in daily life in experience sampling (ESM) studies (de Vries and Csikszentmihalyi, 2006). ESM studies have consistently shown that individuals with psychosis display increased responses of positive affect (PA) and negative affect (NA) to daily life stress (as measured by appraisal of negative or stressful situations), sometimes referred to as increased emotional/affective reactivity (Myin-Germeys, et al, 2003; Myin-Germeys, et al, 2005; Myin-Germeys, et al, 2001). Similar patterns have been found in family members of individuals with psychotic illness (Myin-Germeys, et al, 2001). In addition, increased NA reactivity to daily life stress was associated with persistence of psychotic experiences over time (Collip, et al, 2013) and being at ultra-high risk for psychosis (Palmier-Claus, et al, 2012). Increased affective reactivity has therefore been termed an endophenotype of psychosis (Myin-Germeys and van Os, 2007).

Affective reactivity has been studied in relation to depression as well. The available evidence suggests that individuals with depression show increased affective reactivity to daily life stress, to both perceived negative situations and perceived stressful events (Bylsma, et al, 2011; Myin-Germeys, et al, 2003; van Winkel, et al, 2015), especially NA responses. It must be noted that one study did not find this (Peeters, et al, 2003). Furthermore, individuals at increased risk for depression indexed by heightened genetic risk or known risk factors for depression display this characteristic as well (Schneiders, et al, 2006; Suls and Martin, 2005; Wichers, et al, 2007). Finally, increased NA responses to daily life stress predicted the development of depressive symptoms several months later (Wichers, et al, 2009). Based on the available evidence, it seems that affective reactivity, and NA reactivity in particular, is a vulnerability marker for both domains, rather than an endophenotype for either psychosis or depression.

Although affective reactivity is associated with increased symptomatology in both domains, it is not known whether it is associated with subclinical psychotic symptoms, independently of depressive symptoms, and vice versa. The co-occurrence of depressive and psychotic symptoms at both subclinical and clinical level is very high (Gaudiano and Zimmerman, 2013; House, et al, 1987; Sartorius, et al, 1974; Wigman, et al, 2012), and symptoms of one disorder predict development of symptoms of the other disorder, at all levels of severity (Demjaha, et al, 2012; Häfner, et al, 2005; Häfner, et al, 2008; Kaymaz, et al, 2012; Lin, et al, 2015; van Rossum, et al, 2011; Yung, et al, 2004). Hence, the relationship between psychotic and depressive symptoms is bidirectional and complex. Therefore, the pathway from affective reactivity to psychopathology may run specifically via depressive symptoms or psychotic symptoms, instead of both. Results from a study in female twins from the general population indirectly support the idea that increased affective reactivity is facilitating depressive symptoms, which in turn provoke psychotic symptoms (Kramer, et al, 2012). Specifically, the influence of childhood trauma on the development of psychotic-like symptoms was larger in individuals with increased genetic liability for depression, and this effect was mediated by depressive symptoms, not affective reactivity, when these variables were assessed simultaneously.

The present study examined whether the association between affective reactivity to daily life stress and psychotic symptoms (psychotic experiences with clinical impact, Van Os, et al, 2009), was independent of co-occurring depressive symptoms. Conversely, it was examined whether the association between affective reactivity to daily life stress and depressive symptoms was independent of psychotic symptoms. We did so by means of an intensive diary study, in a large sample from the general population. In addition, because symptom levels in the general population may be rather low, we tested the relationship in a subsample of individuals with higher levels of depressive and psychotic symptoms as a

sensitivity analysis. Because of the general population sample, the focus was specifically on the preclinical phase. In this phase, symptoms are hypothesized to be mild and non-specific and symptoms of different domains are thought to more often occur together, compared to more severe levels of expression where psychopathology is assumed to be more crystallized into different clinical disorders, as suggested according to the clinical staging model (e.g. McGorry, et al, 2006). We focused specifically on positive psychotic symptoms (e.g. hallucinations, delusions, paranoia),because research has shown that increased reactivity to daily life stress is particularly associated to the positive symptoms of psychosis (Lataster, et al, 2013; Myin-Germeys and van Os, 2007). Similar to previous studies, the current study focused on affect reactivity to two external stimuli (i.e. activities, social interactions). In addition, we wanted to explore the relevance of affective reactivity to a more internal stimulus as well, specifically physical discomfort. Physical discomfort may be misinterpreted by individuals with psychotic experiences (Reeves and Torres, 2003), who therefore may show increased affective response to this stimulus.

Methods

Procedure and sample

The HowNutsAreTheDutch (HND) sample was recruited from the general population of the Netherlands by means of a crowdsourcing procedure. Using radio broadcasts, television, local podium discussions, newspapers, and magazines, people were invited to participate in our research on mental health as a dimensional and dynamic phenomenon. To do so, people had to visit the website www.HoeGekIs.nl to assess themselves on their mental health in a cross-sectional study and/or in a longitudinal diary study. All details on the aims of the HND study, the procedures, the participants, and the measures are provided elsewhere (van der Krieke, et

al, 2015). The current study concerns the diary study, in which participants completed assessments in their natural environments, thrice a day for 30 days, resulting in a maximum of 90 assessments per individual. Assessments were prompted at equidistant time points with a six-hour interval in between, with the exact time points depending on participants' sleep-wake schedule. Participants received a text message on their mobile phone with a link to a questionnaire. They were asked to fill out the questionnaire immediately after the alert, or, if impossible, within one hour, after which the questionnaire could no longer be accessed.

The present sample is selected from the 975 individuals who took part in the "HowNutsAreTheDutch" diary study between May 22nd, 2014 (launching date of the diary study) and May 22nd, 2016 (end of second-year wave of the diary study). The inclusion criteria for the current study were an age of at least 18, and having filled out cross-sectional questionnaires on depressive symptoms, psychotic experiences, and sociodemographics, . Of these 975 diary participants, 411 (42%) fulfilled these inclusion criteria and were included in the present study.

The HND study protocol was assessed by the Medical Ethical Committee of the University Medical Center Groningen. The committee judged the protocol to be exempted from review by the Medical Research Involving Human Subjects Act (in Dutch: WMO) because it concerned a non-randomized open study targeted at anonymous volunteers in the general public (registration number M13.147422).

Measures

Baseline measures

Sociodemographic factors. Participants provided information on their age (birth year and month), gender, relationship status (No/Yes), relationship duration, and education level. Education was subdivided in the categories: no primary education (=1), primary education (=2 to 4), vocational education (=5 to 6), higher education (=7), master degree and PhD (=8).

Symptoms of depression. Mood over the past week was assessed with the Depression, Anxiety, and Stress Scale (DASS), which is known to be sensitive to subthreshold symptoms (de Beurs, et al, 2001; Lovibond and Lovibond, 1995). The DASS scales consist of 42 self-report items, with 14 items per scale. In the present study, we used the Depression scale, which assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia. Each item was rated on a four-point Likert scale ranging from "Did not apply to me at all" (=0) to "Applied to me very much, or most of the time" (=3). The items were summed, hence possible scores ranged between 0 and 42. The internal consistency of the depression scale proved to be good in this sample (alpha = 0.98, Wardenaar, et al, submitted).

Positive psychotic symptoms. Subclinical psychotic experiences were assessed with the Community Assessment of Psychic Experience (CAPE, Stefanis, et al, 2002). The CAPE is a 42-item self-report questionnaire that measures three symptom dimensions: positive psychotic experiences (20 items), negative psychotic experiences (14 items) and depressive feelings (8 items). We used the positive psychotic experiences dimension only, because increased affective reactivity to daily life stress is particularly associated to the positive symptoms of psychosis. Another reason for not including the depression dimension is that it has much overlap with the depression scale of the DASS. Each item of the CAPE assesses both frequency and secondary distress, which were both rated on a four-point Likert scale. The frequency scale ranged from "Never" (=0) to "Nearly always" (=3), whereas the distress scale ranged from "Not distressed" (=0) to "Very distressed" (=3). Because we were particularly

interested in the manifestation of psychotic experiences with clinical impact, that is, psychotic symptoms (see van Os, et al. 2009), we summed the item scores of the frequency as well as the distress scale, and thereafter averaged the scores on both scales, creating one overall score. Possible scores ranged between 0 and 60.

Diary items

Positive affect and negative affect. Momentary affect was assessed with 12 items from the circumplex model of affect (Feldman Barrett and Russell, 1998; Yik, et al, 1999). Specifically, PA was assessed with the items relaxed, energetic, enthusiastic, content, calm, and cheerful, and NA with the items gloomy, anxious, nervous, irritable, dull, and tired. An example item is "I feel cheerful." All items in the present study were rated on a visual analogue scale (VAS) ranging from "Not at all" (=0) to "Very Much" (=100). Scores on PA and NA items were averaged into a PA and NA scale (range 0 – 100), respectively.

Daily life stress We used three measures for (perceived) daily stress: activity-related stress, social interaction-related stress and physical discomfort. *Activity-related stress* was evaluated by asking how participants appraised the activity that they had spent most of their time on since the last measurement, ranging from "Very unpleasant" (=0) to "Very pleasant" (=100). *Social-interaction-related stress* was evaluated by asking whether participants spent most of their time alone or in company. If mostly in company, they were asked how they appraised their company, again ranging from "Very unpleasant" (=0) to "Very pleasant" (=100). Measurements for which participants designated that they were mostly alone, were left out of the analysis. *Physical discomfort* (i.e., somatic complaints) was evaluated by asking the extent to which participants currently experience physical discomfort, ranging from "Not at all" (=0) to "Very much" (=100). All items were (re)coded so that higher scores reflect higher daily life

stress, ranging from 0 (low negative appraisal) to 100 (high negative appraisal). It must be noted that, although negatively appraised situations are not necessarily the same as stressful situations, in daily life, the two overlap: the more intense/life threatening an event is, the more it is perceived as negative, and the more it is perceived as uncontrollable and unpredictable (Koolhaas, et al, 2011; van Eck, et al, 1998). Therefore, we consider/treat daily life stress and negatively appraised situations as equivalent.

Affective reactivity. Affective reactivity was conceptualized as the PA or NA reaction to the above described daily life stressors. This response was measured by the strength of the association between subjective daily life stress during a six-hour interval (reported at the end of the interval) and momentary PA/NA at the end of that interval. In addition, we controlled for PA/NA at the previous time point to be able to assess how an event contributed to changes in affect.

Statistical analysis

Comorbidity between positive psychotic and depressive symptoms were estimated by means of bivariate Spearman correlations.

The ESM data on PA, NA, and daily life stress variables have a hierarchical structure. In this study, multiple observations (level 1) were nested within individuals (level 2). This requires the use of multi-level modelling procedures, which take the clustering of data into account and are able to handle missing data without excluding cases (Snijders and Bosker, 2012).

Multilevel analyses were performed in a stepwise manner, and separately for every daily life stress variable (i.e. activity-related stress, social interaction-related stress and

physical discomfort). First, we established whether there was significant affective reactivity to daily life stress, by examining for each daily life stress variable (predictor) its association to PA and NA (outcome), respectively (model 1). If an association was significant, it was subsequently examined whether positive psychotic symptoms predicted affective reactivity to daily life stress (model 2), and the same was done for depressive symptoms (model 3). These models both included the following predictors: daily life stress, positive psychotic symptoms, depressive symptoms, depressive symptoms*positive psychotic symptoms. In addition, for model 2, positive psychotic symptoms*daily life stress was added, and for model 3 depressive symptoms*daily life stress was added. Next, to assess whether positive psychotic symptoms were associated with affective reactivity, independent of depressive symptoms, and vice versa, a model was run with the same predictors now including both positive psychotic symptoms*daily life stress and depressive symptoms*daily life stress (model 4).

Because an increase or a decrease in variables over time may induce spurious correlations among variables, all time-varying (level 1) variables were detrended (Rovine and Walls, 2006). In addition, time-varying predictors were person-mean centred, by taking the deviation from the mean of each individual (Curran and Bauer, 2011). All models were controlled for gender, age and dummy variables for morning and evening (reference category: afternoon) by including them as fixed effects. In addition, lag1 (i.e. scores of the previous measurement) PA and NA variables were included as fixed effects in models with PA and NA as the dependent variable to prevent autocorrelation of the residuals and to account for a potential bias of stress appraisal due to prevailing NA (van der Stouwe et al. submitted). All models included a random slope of NA, PA, lag1 NA/PA, morning, evening, and daily life stress to account for between-subject variability in the fixed effects.

To determine the best fitting covariance matrix, full models were run with several different covariance matrices, using restricted maximum likelihood (REML). The Bayesian

Information Criterion (BIC) was used to determine the best model fit. For all six models, a variance components covariance matrix fitted best and was therefore used in all analyses. Maximum likelihood (ML) estimation was used when models including different fixed effects were compared (e.g., models with or without depressive symptoms). All final (reported) models were run with REML. The analyses were performed using SPSS Statistics 22. A p-value <.05 was considered statistically significant.

Sensitivity analyses. After running the analyses on the complete sample, they were rerun with only extra-compliant participants who filled out 67 or more of the diary assessments as a sensitivity check (n=190). Additionally, because this study concerns a general population sample, levels of depression and especially positive psychotic symptom scores may be very low, and hence, their potential (interaction) effects may not be picked up. The analyses were therefore rerun with participants with the 20% highest scores on either positive psychotic or depressive symptoms (n=123) as a second sensitivity analysis. We refrained from a correction for multiple testing, but considered findings significant only if they replicated across at least two of the three samples or across different daily life stressors.

Two of our measures of daily life stress include both positively and negatively appraised events, namely social interactions and daily activities; they can range from very unpleasant to very pleasant. In previous papers, a discrepancy between affective reactivity to positive and negative events has been found (e.g. Peeters, et al, 2003). Furthermore, in our general population sample, individuals may have experienced relatively many positive social interactions and activities, which may have resulted in more significant results for altered affective reactivity to positive events, while we were most interested in the negative / stressful events. Therefore, in case of significant associations between depressive or psychotic symptoms and affective reactivity, we repeated the analysis for positive and negative appraised activities/social interactions, respectively.

Results

Descriptive statistics

Of the 411 participants (total sample), 40 participants were dropped from the mixed model analyses, because of insufficient (useable) observations (only 0 or 1). Thus, the main analyses included 371 participants. Another 9 participants were dropped from the analysis of social interaction-related stress, because they never spent most of their time in social company, and hence, did not have any data on unpleasantness of their social company.

The first sensitivity analysis comprised 190 participants with >67 valid measurements. The second sensitivity analysis comprised 109 participants who scored above the 80th percentile (from the total sample) on either the DASS depression or the CAPE (N=85 for depressive symptoms, N=74 for positive psychotic symptoms), after 14 participants were dropped because of too few observations. Again, for the analysis of social interaction-related stress, some individuals were dropped (n=5) because they never spent most of their time in social company.

Descriptive statistics are presented in Table 1. Participants with t>67 measurements did not significantly differ from the remaining participants on sex, age, education level or partner status. They also did not differ on psychopathology measures, except for depressive symptom levels, which were lower in the t>67 group (Mann-Whitney test: U=36681.00, z=-2.056, p=0.04). Participants scoring above the 80th percentile on symptoms did not differ significantly from the remaining participants on sex or age. However, they had a lower education level (U=13558.50, z=1009.91, p<0.01) and where less often in a steady romantic relationship (χ^2(2, N=411) = 8.17, p<0.01). They also, by definition, reported higher levels of

psychotic experiences (frequency: U=28329.00, z=9.68, p=<0.01; distress: U=29222.00, z=10.61, p=<0.01) and depressive symptoms (U=31830.00, z=12.85, p<0.01).

Prevalence of psychotic and depressive symptoms

Of the 74 individuals scoring above the 80th percentile on positive psychotic symptoms (i.e. a score of 6.5 or higher), 36 (49%) also scored above the 80th percentile on depressive symptoms, while 7 (9%) of them scored below the 20th percentile for depressive symptoms. Similarly, of the 85 individuals scoring above the 80th percentile on depressive symptoms (i.e. a score of 13.0 or higher), 36 (42%) also scored above the 80th percentile for positive psychotic symptoms, while 12 (14%) of them scored below the 20th percentile on positive psychotic symptoms. The correlation between psychotic and depressive symptoms in the total sample was 0.32 (p<0.01).

Please insert Table 1 here.

Affective reactivity to daily life stress

Increases in all three daily life stress measures were significantly associated with decreases in PA and increases in NA (Table 2).

Please insert Table 2 here.

The association between positive psychotic experience and affective reactivity to stress

No significant interaction effects were found between any of the daily life stress measures and psychotic experiences in predicting PA or NA (Table 3) in the uncontrolled condition (models 2), except for one trend for a positive interaction between positive psychotic symptoms and physical discomfort in predicting NA (p=0.06). However, this effect was not significant in either of the sensitivity analyses (Supplementary Table B; T>67: p=0.37, >80th percentile: p=0.42). and therefore, we did not consider this a robust result. Thus, affective reactivity did not seem to be higher in individuals with higher levels of psychotic experiences and there was no reason to further assess whether these effects were independent from depressive symptoms.

The association between depressive symptoms and affective reactivity to stress

In the uncontrolled condition (models 3) there was a significant interaction between depressive symptoms and activity-related stress in predicting PA in the total sample (Table 3, B=0.003, p=0.04). This interaction was significant in the sample with increased symptoms as well (B=0.005, p=0.02), but not in the sample with T>67 diary measurements (B=0.003, p=0.11) (see Supplementary Table B). Thus, the negative association between unpleasant activities and PA was weaker in individuals with higher levels of depressive symptoms. The effect remained (trend) significant after controlling for positive psychotic symptoms (models 4, total sample: B=0.002, p=0.08; >80th percentile: B=0.005, p=0.02). When splitting up positive and negative activities in the total sample, the interaction effect remained positive, and remained significant for negative interactions (pos: B=0.003, p=0.34; neg: B=0.012, p<0.01). When predicting NA, there was no significant interaction between depressive symptoms and activity-related stress.

In addition, there was a significant interaction between depressive symptoms and social interaction-related stress in predicting NA in the total sample (Table 3, B=0.003, p=0.04) in the uncontrolled condition (models 3). This effect was significant (B=0.005, p=0.02) in the group with T>67 diary measurements, but not in the group with increased symptoms scores (B=-0.001, p=0.56) (Supplementary Table B). Hence, individuals with higher levels of depressive symptoms displayed increased NA after unpleasant social interactions. Again, these effects remained (trend) significant after controlling for positive psychotic symptoms (models 4, total sample: B=0.003, p=0.07; T>67: B=0.004, p=0.05). The interaction effect remained positive when separately examining positive and negative social interactions in the total sample, but was no longer significant (pos: B=0.004, p=0.14; neg: B=0.002, p=0.35). When predicting PA, there was not significant interaction between depressive symptoms and social interaction-related stress (see Table 3), neither in the uncontrolled condition, nor in the controlled condition.

Finally, no significant interaction effects were found between physical discomfort and depressive symptoms in predicting PA or NA (Table 3), neither in the uncontrolled condition, nor in the controlled condition.

Please insert Table 3 here.

Discussion

The main purpose of this study was to examine whether the co-occurrence of positive psychotic and depressive symptoms could explain their shared (negative) affective reactivity. Although co-occurrence of psychotic and depressive symptoms was relatively common in our

sample, no overlap in their effects were found. Specifically, the results suggest increased NA reactivity to social interactions and decreased PA reactivity to activity-related stress in individuals with increased depressive symptoms. These effects remained trend significant when controlling for positive psychotic symptoms. In contrast, no increased affective reactivity was found to any of the daily life stressors for individuals with increased psychotic symptoms.

Affective reactivity and psychotic symptoms

Several explanations can be discerned for why individuals with increased psychotic symptoms did not show increased affective reactivity. A first possibility is that affective reactivity is a consequence of the affliction rather than a vulnerability marker. However, this possibility cannot explain all null-findings, because increased affective reactivity has been found in individuals who have not had a full-blown psychosis yet, such as family members of individuals with psychosis (Myin-Germeys, et al, 2001), and individuals with persistent subclinical psychotic experiences (Collip, et al, 2013).

A second possibility is that affective reactivity is a genuine vulnerability marker, but we did not capture risk for psychosis accurately. The current study deviates from most other studies (e.g. Collip, et al, 2013; Myin-Germeys, et al, 2003; Myin-Germeys, et al, 2001; Myin-Germeys, et al, 2004) by using the level of positive psychotic symptoms in the general population as an indicator of vulnerability. The level of psychotic symptoms in our sample may have been too low to detect significant effects. Therefore, we also tested associations in a sample with increased symptom levels, which yielded similar results. It should be noted that the average CAPE score in this sample was still lower than the cut-off for ultra-high risk (UHR) of psychosis (Mossaheb, et al, 2012). Hence, our increased risk sample was intermediate between the general population and UHR populations (Wigman et al., 2016).

Still, psychosis can be regarded as a dimensional construct and there is ample evidence that subclinical psychotic experiences are continuous with psychotic disorders (Van Os, et al, 2000; Van Os, et al, 2009).

Despite the dimensional nature of psychosis symptoms, research indicates that not all psychotic experiences are equally strong indicators for psychosis risk. Vulnerability seems to be larger for individuals who suffer a certain amount of distress from their experiences (Van Os, et al, 2009; Yung, et al, 2009). By including a distress score in our measure, we reduced the possibility that the relationship between affective reactivity and psychotic symptoms was 'diluted' by neutral or pleasant psychotic experiences, which do not infer risk. Also, a post-hoc test with only those individuals who experienced secondary distress from at least one experience (n=130, at least a score ≤2, indicating 'quite distressed') yielded similar results.

A final possibility is that affective reactivity reflects an increased risk of depressive symptoms, which in turn predict psychosis. There have been several studies that support the view of an affective pathway to psychosis. One study in female twins from the general population showed that the influence of childhood trauma on the development of psychotic-like symptoms is moderated by genetic liability for depression; individuals with genetic liability for depression had a greater chance of developing psychotic-like symptoms in the context of childhood trauma. Furthermore, although affective reactivity was increased in these individuals, the effect was mediated by the presence of depressive symptoms, not affective reactivity (when both variables were assessed simultaneously (Kramer, et al, 2012). This suggests that affective reactivity influences psychotic outcome only indirectly, by promoting the development of depressive symptoms.

On a macro-level, it has been shown that depressive symptoms indeed precede and predict the onset of psychotic disorders (Demjaha, et al, 2012; Häfner, et al, 2005; Häfner, et

al, 2008; Yung, et al, 2004). On a micro-level, an experience-sampling study has shown that the presence of depressive symptoms increased the persistence of paranoid feelings after an increase in NA, which may result in an increased chance to develop more serious psychotic symptoms (Kramer, et al, 2014). Hence, tentatively, our results may also indicate that heightened reactivity to stress in individuals with/at risk for psychosis works through a mediating affective pathway.

In addition to activity- and social-interaction related stress, we explored affective responses to physical discomfort, which were not associated with the level psychotic symptoms either. We included this variable because individuals with body-related psychotic experiences may experience bodily discomfort differently, and therefore show an increased affective response compared to individuals without these symptoms (Reeves and Torres, 2003). The current sample may not have experienced many of these body-related psychotic experiences, because they are not very prevalent in the general population (e.g. Wigman, et al, 2016). Future studies in samples with more severe psychotic symptoms may determine more definitive whether the affective response to physical discomfort is related to psychotic experiences.

Affective reactivity and depressive symptoms

We replicated previous studies by showing that individuals with increased depressive symptoms have increased affective reactivity to daily life stress. Specifically, we found increased NA reactivity to social interactions (but not to daily life activities or physical discomfort). Studies with clinically depressed individuals have found both activity and social-interaction related increases in NA (e.g. Myin-Germeys, et al, 2003; van Winkel, et al, 2015). However, in samples at risk for depression or community samples, which resemble our study population, increased reactivity to social interactions is the most robust finding. For example,

van Winkel et al. (2015) examined individuals with Major Depressive Disorder (MDD) and remitted individuals. They found an increased NA response to both activity and social-interaction related stress in individuals with MDD. Remitted individuals, who still carry a vulnerability, displayed increased NA reactions to social interactions only. In another daily diary study, an increased end-of-day negative mood after interpersonal stressors, but not other stressors, predicted an increased chance of developing depressive symptoms two months later (O'Neill, et al, 2004). This suggests that increased NA reactivity to social interactions is a specific vulnerability factor for MDD.

Other studies have examined NA reactivity to stressful events in daily life, which can encompass both social interactions and daily life activities. They found increased NA responses in depressed individuals (e.g. van Winkel, et al, 2015) as well as vulnerable ones (Wichers, et al, 2007), except one study (Peeters, et al, 2003). A slightly different methodology was adopted in this one study; (un)pleasantness of events was not recorded at every assessment, but only when participants reported a positive or negative event. In another study, increased NA responses to stressful events predicted increased depressive symptoms and transition to a full-blown disorder more than one year later in women with no history of depression (Wichers, et al, 2009). To summarize, the available evidence indicates that NA reactivity is a vulnerability marker for depression. The current study adds to the current literature that this effect is independent of co-occurring positive psychotic symptoms, and that it is particularly the NA response to interpersonal stressors that marks this vulnerability.

Our finding that depressive symptoms are related to blunted PA responses to unpleasant daily life activities has, to our knowledge, not been examined often. Peeters et al. (2003), who examined the PA response to daily life stressful events, also found blunted PA responses in individuals with MDD, but, as mentioned, with a slightly different methodological design. Myin-Germeys et al. (2003), did not find a relationship between PA

and daily life activities in MDD. Further research is needed to draw more firm conclusions about whether a reduced PA response is a vulnerability marker for depression.

PA reactivity has also been examined in relation to positive events in daily life (reward experience). Because activities in our study could be rated from very pleasant to very unpleasant, the relationship could potentially also be interpreted reversely, i.e., depressive symptoms are related to smaller increases in PA after a pleasant activity (decreased reward sensitivity). A sensitivity analysis to assess the PA response to positive and negative activities separately, was inconclusive. Although the interaction effect was in the expected direction (i.e. smaller increases in PA after positive activities for individuals with higher levels of depressive symptoms), it was not significant (while it was for negative activities). Other studies could not find differences in baseline reward experience between depressed and non-depressed individuals either (Geschwind, et al, 2010; Wichers, et al, 2009), although several studies have found that increasing reward experiences may help to protect against the detrimental effects of stress on mental health (Geschwind, et al, 2010; Geschwind, et al, 2011). These findings do not necessarily contradict each other, since treatment may improve or prevent depression via different mechanisms than how it develops.

Strengths and limitations

A great strength of the study is the large sample size, especially for ESM studies. In addition, we had many within-person measurements (mean=75). This means that we had enough power to detect both between- and within-individual associations. A limitation is that our sample may not be representative of the general population, given the voluntary nature of the study (self-selection), and the relatively high educational levels and high proportion of females in our sample. Furthermore, regarding the ESM design, there was a relatively large time window over which events could be reported (6 hours). Therefore, we might have missed affective

reactivity if the events happened early during those six hours and the affective response was quick/short-lasting. Conversely, a higher sampling frequency might also dilute the effects of stressful events by including more events of relatively minor importance. In addition, although previous studies have shown that increased affective reactivity predicts the development of depression and psychosis, the current study was of cross-sectional nature. Hence, we cannot rule out that the association is reversed as well, i.e. depressive symptoms predicting increased affective reactivity. Longitudinal studies are needed to provide more definite proof that increased affective reactivity increases depressive symptoms, and that they subsequently incite psychotic symptoms. These studies may also assess whether this pathway holds for psychotic symptoms in general or only for symptoms in the context of specific disorders of the psychosis spectrum. Moreover, while our social interaction-related stress measure (for a large part) resembled measures used in most other ESM studies, the activity-related stress measure was somewhat different. We used valence of the activity (unpleasantness) as a measure for stressor intensity, whereas other studies often used reports about whether someone felt skilled to do the activity and whether it required effort, sometimes combined with whether they rather did something else. These different conceptualizations may have yielded different results for activity-related stress. Finally, we conducted a relatively large number of statistical tests, which increased the chance of false positive findings. To deal with this issue, we only interpreted results that replicated at least once across sensitivity samples or daily life stressors.

Conclusions

The findings support the hypothesis that affective reactivity to unpleasant social interactions is a genuine vulnerability marker for depression, but they do not support this notion for psychosis. Potentially, increased affective reactivity in individuals with psychosis can be explained by an affective pathway, where increases in affective reactivity induce depressive

symptoms, which in turn incite psychotic symptoms. This hypothesized pathway needs further testing in a sample with increased levels of psychopathology, particularly with more severe or persistent psychotic symptoms.

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Tables

Table 1. Descriptive statistics of sociodemographic, psychopathological and diary variables.

Variable	**Total (n=411)**	**T>67 (n=190)**	**>80th percentile (n=123)**
	Mean (SD)		
Sociodemographic			
Sex (female, %)	79.1	76.3	82.1
Age (years)	43.0 (13.8)	43.6 (13.9)	42.2 (13.2)
Education level (1-8)	7.21 (0.99)	7.28 (0.94)	6.86 (1.24)
Partner status (yes, %)	72.3	70.0	62.6
Duration of relationship (years)	15.5 (12.6)	16.0 (12.4)	13.7 (12.1)
Psychopathology			
Depressive symptoms (0 – 42)	7.25 (8.13)	6.11 (6.98)	16.16 (9.12)
Positive psychotic experiences – frequency (0 – 60)	5.29 (4.14)	5.02 (3.84)	8.71 (5.30)
Positive psychotic experiences – distress (0 – 60)	2.85 (3.92)	2.64 (3.66)	6.04 (5.61)
Positive psychotic experiences – frequency & distress mean (0 – 60)	4.06 (3.78)	3.83 (3.53)	7.37 (5.08)
Diary measures (person-mean)			
Positive affect (0 – 100)	56.1 (12.7)	57.3 (11.3)	47.6 (13.6)
Negative affect (0 – 100)	27.0 (14.1)	25.5 (18.6)	37.5 (15.7)
Unpleasantness activity (0 – 100)	34.2 (10.8)	32.9 (9.3)	38.7 (10.5)
Unpleasantness social company	27.5 (11.1)	26.9 (9.4)	30.9 (12.0)

(0 – 100)			
Physical discomfort (0 – 100)	25.1 (19.7)	23.7 (18.6)	33.6 (24.1)

Note. T>67 refers to more than 67 diary assessments.

Table 2. Univariable models for affective reactivity to daily life stress (model 1).

Variable	Positive affect		Negative affect	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Activity-related stress	-0.38 (-0.40 – -0.35)	<0.001	0.28 (0.26 – 0.30)	<0.001
Social interaction-related stress	-0.33 (-0.35 – -0.30)	<0.001	0.23 (0.21 – 0.25)	<0.001
Physical discomfort	-0.19 (-0.21 – -0.18)	<0.001	0.18 (0.16 – 0.19)	<0.001

Note: CI = confidence interval.

Table 3. Association between affective reactivity to daily life stress and positive psychotic symptoms or depressive symptoms.

Model	Variable	Positive affect		Negative affect	
		Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Activity-related stress					
M2	Psych*stress	0.004 (-0.002 – 0.009)	0.19	0.002 (-0.003 – 0.006)	0.53
M3	*Dep*stress*	*0.003 (0.000 – 0.005)*	*0.04*	0.000 (-0.002 – 0.002)	0.97
M4	Psych*stress	0.002 (-0.004 – 0.007)	0.57	0.002 (-0.003 – 0.007)	0.50
	*Dep*stress*	*0.002 (-0.000 – 0.005)*	*0.08*	-0.000 (-0.003 – 0.002)	0.83
Social interaction-related stress					
M2	Psych*stress	-0.000 (-0.007 – 0.007)	0.99	0.003 (-0.003 – 0.010)	0.28
M3	Dep*stress	-0.001 (-0.004 – 0.003)	0.66	*0.003 (0.000 – 0.006)*	*0.04*
M4	Psych*stress	0.001 (-0.006 – 0.008)	0.75	0.001 (-0.006 – 0.008)	0.75
	Dep*stress	-0.001 (-0.004 – 0.003)	0.64	*0.003 (-0.000 – 0.006)*	*0.07*
Physical discomfort					
M2	Psych*stress	0.001 (-0.004 – 0.007)	0.65	*0.004 (-0.000 – 0.009)*	*0.06*
M3	Dep*stress	0.001 (-0.002 – 0.002)	0.93	0.002 (-0.000 – 0.004)	0.12
M4	Psych*stress	0.001 (-0.004 – 0.006)	0.65	0.003 (-0.001 – 0.008)	0.16
	Dep*stress	-0.000 (-0.003 – 0.002)	0.94	0.001 (-0.001 – 0.003)	0.33

Note: CI = confidence interval; Psych*stress= the interaction between positive psychotic symptoms and daily life stress; Dep*stress = the interaction between depressive symptoms and daily life stress. Model (M)2: Association between positive psychotic symptoms and affective reactivity to daily life stress; Model (M)3: Association between depressive symptoms and affective reactivity to daily life stress; Model (M)4: Association between

positive psychotic symptoms and affective reactivity to daily life stress, corrected for depressive symptoms, and vice versa.