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Stress exposure and sensitivity in the clinical high-risk syndrome: Initial findings from the North American Prodrome Longitudinal Study (NAPLS)☆

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ABSTRACT

There is inconsistent evidence for increased stress exposure among individuals at clinical high risk (CHR) for psychosis. Yet similar to patients with a diagnosed psychotic illness, the preponderance of evidence suggests that CHR individuals tend to experience stressful life events (LE) and daily hassles (DH) as more subjectively stressful than healthy individuals. The present study utilizes data from the North American Prodrome Longitudinal Study Phase 2 (NAPLS-2) to test the hypotheses that (1) CHR individuals manifest higher self-reported stress in response to both LE and DH when compared to healthy controls (HC), (2) group differences in self-reported stress increase with age, (3) baseline self-reported stress is associated with follow-up clinical status, and (4) there is a sensitization effect of LE on the response to DH. In contrast to some previous research, the present findings indicate that the CHR group ($N = 314$) reported exposure to more LE when compared to the HC group ($N = 162$). As predicted, CHR participants rated events as more stressful, and those who progressed to psychosis reported a greater frequency of LE and greater stress from events compared to those whose prodromal symptoms remitted. There was also some evidence of stress-sensitization; those who experienced more stress from LE rated current DH as more stressful. The results indicate that the "prodromal" phase is a period of heightened stress and stress sensitivity, and elevated cumulative lifetime exposure to stressful events may increase reactions to current stressors.

1. Introduction

Etiological theories have posited that patients with psychotic disorders are vulnerable to psychosocial stress due to a congenital diathesis. Despite the theoretical assumption of a causal role for general life stress in the course of psychosis, Norman and Malla (1993) noted that exposure to life stress would not necessarily be expected to differ between diagnosed patients and controls, as patients are assumed to have an elevated vulnerability to psychosis and, hence, require lower levels of stress to precipitate a psychotic episode. Further, among patients, prolonged hospitalizations and reduced social and occupational activities would be expected to decrease exposure to some life events (LE) (Heila et al., 1999).

Indeed, contemporary reviews suggest no consistent cross-sectional evidence that individuals with psychosis experience more recent LE

Abbreviations: LE, life events; DH, daily hassles.

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(past 3 months to 1 year) than those without psychosis (Norman and Malla, 1993; Phillips et al., 2007; Holtzman et al., 2012). Yet several retrospective and prospective studies have revealed elevations in psychosocial stressors preceding psychosis (Canton and Fraccon, 1985; Bebbington et al., 1993; Castine et al., 1998; van Winkel et al., 2008), although others do not (Horan et al., 2005). Thus, the results generally suggest that patients with psychosis are not necessarily exposed to more stressful LE (e.g., moving to a worse neighborhood, social exclusion), but may be more sensitive to them when they occur (Holtzman et al., 2012). Further, in the domain of severe negative life events (NLE) or "trauma," there is evidence that risk for psychosis is heightened among individuals who have experienced childhood trauma, such as abuse, with cumulative trauma exposure increasing risk (Shevlin et al., 2008; Galletly et al., 2011; Holtzman et al., 2013).

The evidence to date for increased exposure to stressful LE and daily hassles (DH) in clinical high risk (CHR) samples is also inconsistent (Aiello et al., 2012; Holtzman et al., 2013). Yet similar to the findings with diagnosed patients, the preponderance of findings indicate that CHR individuals tend to experience stressful LE and DH as more subjectively stressful than healthy samples. In a review, Aiello et al. (2012) concluded that CHR groups manifest greater stress sensitivity than controls, as indexed by multiple measures (e.g., Experience Sampling Methods, metabolic stressor, and cortisol). Further, like diagnosed patients, research on CHR samples has shown a higher rate of self-reported childhood trauma exposure (Holtzman et al., 2013).

The present study utilizes data from the North American Prodrome Longitudinal Study, Phase 2 (NAPLS-2), to investigate stressful events and the subjective stress response in CHR participants. NAPLS-2 is a multi-site prospective longitudinal study of prodromal syndromes aimed at enhancing psychosis prediction and uncovering neural mechanisms of conversion (Addington et al., 2012). A recent study using this sample revealed significantly elevated cortisol levels in CHR individuals relative to healthy control (HC) participants (Walker et al., 2013). Baseline cortisol levels were also found to be associated with interim clinical status; CHR participants in NAPLS-2 who progressed to psychosis had significantly higher baseline cortisol than those whose prodromal symptoms remitted.

In this report, we test the following hypotheses. First, based on the past literature, it is predicted that CHR individuals will manifest higher self-reported stress than HC in response to both LE and DH. Second, it is predicted that group differences in self-reported stress will increase with age through adolescence and young adulthood. Age-related increases in stress exposure (particularly trauma exposure) have been demonstrated in clinical and healthy samples (Finkelhor et al., 2009), likely due to increased opportunity to experience stressors as development progresses and role responsibilities broaden (Aldwin, 2011). Third, it is predicted that higher baseline stress will be associated with poorer clinical status at follow-up. Finally, the current research examines the potential sensitization effect of LE on subjective stress from DH (van Winkel et al., 2008).

2. Methods

2.1. Sample

Participants were recruited as part of NAPLS-2 (Addington et al., 2012), which at the halfway mark included 540 individuals. This study presented here included those subjects with baseline self-report ratings of LE and DH. These data were available for 476 participants; 314 CHR participants (58.6% male) who met prodromal syndrome criteria and 162 HC participants (48.3% male). The age range of participants at baseline was 12 to 35 years, with a mean age of 18.99 years (SD 4.18) for the CHR group and 19.54 years (SD 4.77) for the HC group. The protocol was approved by Institutional Review Boards at all NAPLS sites (Addington et al., 2012). All participants provided informed consent or assent.

As of this writing, 296 individuals in the present CHR group were either followed at least 24-months without conversion to psychosis or were documented to have developed psychosis within the follow-up period or subsequent to it. Thus, the outcome classification is based on the most recently available data on conversion for the present sample. CHR participants were classified as manifesting prodromal stabilization or progression (i.e., exhibiting symptoms in the prodromal range [scores from 3–5 in severity] on the SOPS), psychotic (i.e., currently meeting criteria for a psychotic disorder or evidencing scores of 6 on one or more SOPS positive symptoms), or in remission (i.e., scores of 2 or less on the five SOPS positive symptoms scales). Clinical status data yielded the following groups: remission = 91; prodromal stabilization or progression = 160; and psychotic = 45.

2.2. Assessment procedures and measures

Participants were interviewed using the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 2003). Interview responses were then quantified by trained interviewers on the Scale of Prodromal Symptoms (SOPS, Miller et al., 2003). The SOPS provides an index of symptom severity that ranges from 0 (absent) to 6 (severe, psychotic).

A detailed description of the study measures and procedures is presented elsewhere (Addington et al., 2012). In brief, general exclusions included an Axis I psychotic disorder, substance dependence, neurological disorder or full scale IQ <70. HC were excluded if they had a first-degree relative with a current or past psychotic disorder, or met prodromal criteria.

Study participants completed a modified version of the Psychiatric Epidemiology Research Interview Life Events Scale (LES) (Dohrenwend et al., 1978) and the Daily Stress Inventory (DSI) (Brantley et al., 1987) at baseline. The LES was modified to exclude items that would be of unlikely relevance to the adolescent/young adult age range included in this study (e.g., getting a divorce, encountering serious financial loss). The modified version of the LES included 59-items pertaining to significant events or life changes that could conceivably be experienced at any of the ages included in the study sample. Events on the LES have been designated as "independent" of or "dependent" on an individual's characteristics. Items are also classified as positive or negative (Dohrenwend et al., 1978). Participants indicated whether the LE occurred at any point in their lives. Interviewers queried participants about their level of subjective stress for each LE endorsed on a 7-point Likert scale ranging from "occurred, but was not very stressful" to "caused me to panic."

The Daily Stress Inventory (DSI) is a 58-item measure of minor, common DH occurring within the past 24 hours. Examples of such items include "was interrupted during task/activity," "was criticized or verbally attacked," and "had your sleep disturbed." Participants indicated if the event occurred and rated each endorsed DH on the same 7-point Likert scale as described above.

2.3. Data analyses

Statistical analyses were conducted with PASW statistics 18 statistical software (SPSS Inc., Chicago, Illinois). Independent-sample *t* tests or chi-square tests were used to compare the CHR and HC groups on demographic characteristics. Analyses of covariance (ANCOVA) were used to test group differences in the frequency of stressful LE, DH, and the self-reported stress ratings. Stress data were normalized using a logarithmic transformation. All ANCOVAs included sex as a covariate. Further, the statistical analyses of subjective stress included the frequency of LE or DH as covariates, in order to test for group differences in sensitivity to stressful events/hassles, independent of the frequency of events. For follow-up clinical status, comparisons were tested for (1) remission vs. stabilization/progression, (2) remission vs. psychotic, and (3) stabilization/progression vs. psychotic for stress

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