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Stress precedes negative symptom exacerbations in clinical high risk and early psychosis: A time-lagged experience sampling study

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ABSTRACT

The experience sampling method (ESM) has revealed associations between fluctuations in stress and positive symptoms in psychosis. It is unknown, however, how negative symptoms including anhedonia respond to stress. Stress is divided according to its source: event-related stress stemming from negative events, and activity-related stress stemming from engaging in tasks beyond one's skill or control. Anhedonia is divided into consummatory and anticipatory anhedonia, reflecting a lack of pleasure in current and expected activities. This study uses ESM to determine whether each form of anhedonia increases in response to stress. Antipsychotic-naïve individuals with first episode psychosis ($n = 39$), clinical high-risk states for psychosis ($n = 44$), and healthy controls ($n = 34$) responded to daily prompts on a palmtop computer for up to ten days by indicating levels of stress and anhedonia. Time-lagged multilevel modelling was employed to explore increases in anhedonia following increases in stress while controlling for prior levels of anhedonia. Mean levels of anhedonia were also compared across groups. Only activity-related stress produced increases in anhedonia. This effect did not vary between groups. Clinical groups showed greater overall levels of anhedonia than healthy controls, but did not differ from each other. Anhedonia responds only to activity-related stressors, suggesting that this form of stress has a specific causal role in anhedonia. The results also provide further evidence for global increases in anhedonia in antipsychotic-naïve psychosis spectrum individuals.

1. Introduction

It is well established that individuals with schizophrenia-spectrum psychopathology (and familial risk) show increased stress sensitivity, both phenotypically and in terms of elevated dopamine response during stress-inducing tasks (Breier et al., 1993; Mizrahi et al., 2012; Myin-Germeys et al. 2005; Walker et al., 2008).Stress exposure further plays an etiological role in psychosis – affecting risk, onset and course of psychotic disorders (Zubin and Spring, 1977; Walker and Diforio, 1997). Stress exposure at many developmental junctures contributes to the development of these disorders, including prenatal stress (Van Os and Selten, 1998; Khashan et al., 2008) and early adverse experiences (Lardinois et al., 2011).

The specific role of ongoing, day-to-day stress however has received particular research attention, albeit this has focused almost exclusively on positive symptoms. Models of the physiological impact of momentary increases in stress primarily focus on mesocortical dopamine circuitry, and suggest that following stress, prefrontal cortex (PFC) receptors sensitive to glucocorticoids play a regulatory role in the release of subcortical (e.g., striatal) dopamine, which is thought to mediate the relationship between stress and positive symptoms (e.g., Moghaddam, 2002). Corcoran et al. (2003) have suggested that, in schizophrenia, hypofrontality (a hypothesized substrate for negative symptoms) leads to reduced down-regulation of midbrain dopamine. However, existing models do not predict or account for momentary changes in negative symptoms in response to stress. The existence of such changes is suggested however by animal models of anhedonia. Stanton et al. (2018) for example notes that different sources of stress may lead to anhedonia-like behaviours in rats, albeit through varying mechanisms involving either phasic increases or decreases in midbrain dopamine. The specific mechanisms underlying this stress-behaviour link are unknown (Stanton et al., 2018). In people with major depressive disorder, which is also characterized by anhedonia and reduced

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goal pursuit, stress is known to increase anhedonia via perceived uncontrollability, with long-term exposure to uncontrollable stress contributing to a blunting of midbrain dopamine responses (Pizzagalli, 2014). These observations suggest that stress may also contribute to momentary change in anhedonia in schizophrenia via as-yet unknown physiological mechanisms.

Recently, the experience sampling method (ESM; Csikszentmihalyi and Larson, 1992; Delespaul, 1995) has been applied to investigate stress-symptom relationships. ESM involves the collection of self-report data in real time, usually over the course of several days. It provides information that is more accurate than later-recalled data, is more ecologically valid (i.e., its findings generalize more accurately to participants' day-to-day lives), and can be examined at a high temporal resolution (Kimhy et al., 2006). Such studies have reliably demonstrated that momentary fluctuations in mood and positive symptoms correspond to concomitant fluctuations in stress (Klippel et al., 2017a; Myin-Germeys et al., 2001b, 2002, 2003, 2005a; Palmier-Claus et al., 2012). They have furthermore divided stress according to two primary sources; event-related stress, caused by occurrences in an individual's daily life; and activity-related stress, stemming from an individual's appraisal of their capability, control and enjoyment in whatever activity they are engaged in (Myin-Germeys et al., 2003, 2005a). Myin-Germeys et al. (2005a) found that both were associated with increases in positive symptoms in remitted psychosis. Stress has also been associated with increases in negative affect and decreases in positive affect in psychosis (Myin-Germeys et al., 2001b; Palmier-Claus et al., 2012).

Some researchers have extended this methodology to those at Clinical High Risk (CHR) for psychosis. The CHR state represents a putative precursor to a psychotic disorder, as approximately 29% of CHR individuals develop a psychotic disorder within two years (Fusar-Poli et al., 2012). Palmier-Claus et al. (2012) employed ESM with CHR individuals and found that they showed similar stress-related elevations in positive symptoms as did psychotic-disordered participants, suggesting that stress sensitivity precedes psychosis and may contribute to the early development of a first episode. Van der Steen et al. (2017) and Klippel et al. (2017a) found similar associations.

While many studies have converged on the observation that stress is associated with concomitant increases in positive symptoms, these studies have been critiqued for several reasons. Firstly, they cannot reveal the direction of this relationship. Some authors have suggested that it is likely that symptoms themselves produce increases in stress, as symptoms are distressing and can impact affect (e.g., van der Steen et al., 2017). Arguments have likewise been put forth favouring the opposite interpretation: one longitudinal study revealed that increased stress sensitivity in CHR individuals at baseline was predictive of both positive and negative symptom increases weeks later (deVylder et al., 2013). A second critique is that the research to date has focused almost exclusively on positive symptoms and psychotic-like experiences; few researchers have examined the parallel relationships between stress and negative symptoms. Finally, existing studies have employed individuals medicated with antipsychotics, making it unclear whether these findings are endogenous to disease processes themselves or secondary to medication effects.

One method that holds promise in resolving the ambiguity in causal direction is the introduction of *time-lagging* into ESM data sets. Using this technique, one may examine the impact of one variable on another measured later in time, supporting a causal interpretation. This approach has shown promise in revealing that psychotic-like experiences are preceded by stress (Klippel et al., 2017b), cannabis use (Verdoux et al., 2003), experiences of aberrant salience (So et al., 2017), and negative affect states (Myin-Germeys et al., 2001a; Ben-Zeev et al., 2010; Kramer et al., 2013; So et al., 2017).

Some negative symptoms are difficult to measure via self-report, as they may produce little subjective distress (Tek et al., 2001) and are best rated by expert observers. A notable exception to this is anhedonia, the focus of the current study. Anhedonia may be divided into two components, termed *consummatory* and *anticipatory* anhedonia (i.e., reductions in the experience of pleasure while performing hedonic activity and the expectation of such experiences, respectively: Gard et al., 2007). Consummatory anhedonia exemplifies “anhedonia” as defined in DSM-5 (“Lack of enjoyment from, engagement in, or energy for life's experiences…” APA, 2013, p. 817), while anticipatory anhedonia is believed to be a core component of avolition (e.g., Gold et al., 2013). Some prior research has found that anticipatory anhedonia is more elevated among those with schizophrenia than consummatory anhedonia (Chan et al., 2010; Favrod et al., 2009; Gard et al., 2007); however, Strauss et al. (2011) found elevations only in *consummatory* anhedonia in schizophrenia relative to healthy controls. Furthermore, Gard et al. (2014), using ESM, further found *lower* anticipatory anhedonia among those with schizophrenia, highlighting the need for clarifying research.

As noted above, little is currently known about the impact of stress on negative symptoms. One study (deVylder et al., 2013) examined the relationship between stress sensitivity and both negative and positive symptoms, and found that increased stress sensitivity in CHR individuals was followed by increases in both symptom types; however, these authors did not employ ESM methodology and their measures were administered at three-month intervals. Myin-Germeys et al. (2001b) found associations between stress and reduced positive affect in their non-time lagged study including first degree relatives of those with psychotic disorders, supporting the possibility that anhedonia may be reactive to stress in those at genetic risk (however this study did not include CHR individuals). All of these findings converge on the possibility of negative symptom reactivity to stress among those at risk for psychosis, as well as those with psychotic disorders per se.

The purpose of the current research is three-fold. Firstly, it seeks to explore the temporal relationship between momentary stress and increases in negative symptoms among those at CHR for psychosis as well as those experiencing a first episode of psychosis. Given the evidence reviewed above, it is hypothesized that increases in stress will precede increases in symptoms in both groups, supporting a causal view. Both event- and activity-related stress will be examined in their impacts on both forms of anhedonia reviewed above. Secondly, the current study will compare overall levels of consummatory and anticipatory anhedonia collected via ESM among CHR and first episode psychosis individuals with a view toward clarifying which of these is most impacted in first episode psychosis and, for the first time, to examine these phenomena in a CHR sample while avoiding the pitfalls of retrospective self-report methodology. Finally, the CHR and FEP samples employed currently are antipsychotic-naïve, eliminating the possible confound of medication-induced anhedonia.

2. Methods

2.1. Participant selection

Samples of participants were selected within three groups: Healthy Controls, Clinical High Risk (CHR) individuals, and individuals experiencing First Episode Psychosis (FEP). CHR participants were recruited from the Focus on Youth Psychosis Prevention (FYPP) Clinic at the Centre for Addiction and Mental Health (CAMH). CHR status was confirmed using the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2003). FEP participants were recruited from the First Episode Psychosis Clinic at CAMH. FEP diagnoses with onset within the previous five years were confirmed via SCID-IV. All FEP participants underwent the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) to assess symptom levels. CHR and FEP participants were excluded if they had a lifetime history of antipsychotic use at therapeutic doses for ≥4 weeks. Healthy Control participants were recruited via postering and screened for axis I psychopathology using the SCID-IV and could not have any family history of psychotic disorder. Additional inclusion criteria for all groups included ability to consent, age 18–40, negative urine drug screen, and no history of substance dependence (except nicotine) within 6 months of participation.

2.2. ESM measures and procedures

The collection of ESM data was carried out using computerized ESM methodology (Barrett and Barrett, 2001) validated previously in schizophrenia-spectrum samples (Kimhy et al., 2006) and implemented on a PalmZ22 palmtop computer (Palm Inc.; Sunnyvale, CA). It consisted of an orientation session in which participants were instructed to respond to beeps emitted by the palmtop device at semi-random intervals throughout the day by answering a brief questionnaire. The day after the orientation, the data collection phase began, in which for between four and ten consecutive days the device beeped ten times between 9:00 am and 11:00 pm. Beeps were timed semi-randomly such that no two beeps would occur within a time period defined as one tenth of the 14-hour daily data collection window (i.e., within the same 84-minute period).

The questionnaires consisted of items rated on a 100-point slider scale, set by default to 50. Visual anchors were added to each item on a seven-point Likert-style scale and ranged from “not at all” to “very much.” Item content inquired about the participant's current experience of consummatory anhedonia (“How much enjoyment are you getting out of whatever it is you are doing?”); anticipatory anhedonia (“How much enjoyment do you think you will get out of [whatever you are looking forward to doing]?”); and event-related stress (“Since the last beep the most significant thing that happened to me has been very unpleasant”). Activity-related stress was measured as the mean of five questions using the same response scale (see Table 2 for item content). The activity-related stress scale had an alpha coefficient of 0.73 (as measured in the current sample), indicating adequate reliability. All items formed a subset of a larger battery including items related to affect, apathy, psychosis-like experiences, substance use and socialization (as per Kimhy et al., 2006 and Myin-Germeys et al., 2001b). While these items were developed to maximize face validity, such items for use in computerized ESM with psychosis-spectrum individuals have also been shown to possess construct and discriminant validity (Kimhy et al., 2006).

Prior to analysis, all reports given >15 min after a given beep were excluded due to prior evidence of unreliability of such reports (Delespaul, 1995). Participants who failed to respond to at least 1/3 of the beeps were also removed from analysis, in keeping with the method recommended in prior studies (Delespaul, 1995; Myin-Germeys et al., 2001a; Kimhy et al., 2006). Two additional subjects were removed as they only complied with the ESM collection for two days despite meeting the 1/3 response rate criterion, and three participants whose initial responses were inconsistent (e.g., only providing one response set per day) were allowed to keep their Palm Pilots until up to ten consecutive days of data were collected, and their initial data were discarded. This study was conducted under approval from the CAMH Research Ethics Board.

2.3. Data analysis

Prior to analysis, any responses given after the ten-day window were discarded. The first report within each participant's regimen was also excluded as these could not be time-lagged (i.e., there were no preceding responses). In all, 90% of data from retained participants were included in the analyses.

Given the hierarchical structure of our data and the likelihood of autocorrelation across beeps (Schwartz and Stone, 1998), all analyses were performed using multilevel modelling (MLM) implemented in the Linear Mixed Models function in the Statistical Package for Social Sciences version 24.0 (SPSS: Aramonk, NY: IBM Corp.). Individual observations were entered within subjects to account for non-independence of these observations. A first-order autoregressive covariance structure was specified to model within-subject effects, given that observations made closer in time were more strongly correlated (this was confirmed via correlational analysis). Group was entered as a factor. Four models were specified; one for each crossing of the two dependent variables (consummatory and anticipatory anhedonia) and two independent variables (event-related and activity-related stress); i.e., each model specified a pairing of one anhedonia variable and one stress variable. In each model, anhedonia at a given timepoint (T_n) was predicted by stress at the timepoint immediately prior to it (T_{n-1}), and by anhedonia at the timepoint immediately prior (T_{n-1}) to ensure that the unique contribution of variance made by preceding stress was modelled; this was critical given the possibility that responses to stress-related items at T_{n-1} were influenced by anhedonia at T_{n-1} due to similarities in the wordings of the related items (leaving only the unique variability of stress per se at T_{n-1} to impact anhedonia at T_n). These predictors were entered as fixed effects along with an interaction term (group by stress at T_{n-1}) to determine whether the association between stress and anhedonia varied according to group. A random intercept was included in each model, and a random time slope was fitted given an observed decrease (improvement) in the Akaike Information Criterion (AIC) when doing so. Random effects were modelled using variance components. Restricted Maximum Likelihood Estimation was employed in all models. The four models were tested for significant fixed effects using the Holm-Bonferroni method (Holm, 1979) to maintain a family-wise alpha of 0.05.

To determine any group-wise differences in levels of consummatory and anticipatory anhedonia, one additional multilevel model was built for each type of anhedonia using the same parameters as the models above but without fixed terms for stress, interaction terms or any predictors at T_{n-1} (i.e., only the group variable constituted a fixed effect). Univariate effects of the grouping variable within each of the models were then examined using the Holm-Bonferroni method (Holm, 1979) to control family-wise error. Significant effects were followed by pairwise contrasts, corrected for family-wise error via a least significant difference (LSD) procedure, to determine where the source of group differences lay.

3. Results

3.1. Sample characteristics

A total of 169 participants were enrolled across the three groups – 57 in the CHR group, 68 in the FEP group and 44 healthy controls. After excluding participants according to the criteria set out in the Methods section, 117 (44 CHR, 39 FEP, 34 HC) remained. This rate (70%) is comparable to that observed in prior work using similar methods and populations (e.g., Myin-Germeys et al., 2001a). See Table 1 for the demographic and clinical characteristics of each group, including mean symptom severity. CHR, FEP and HC participants completed the ESM measurement for an average of 7.1, 5.2 and 6.0 days, respectively.

Table 1
Sample characteristics.

	HC $n = 34$	CHR $n = 44$	FEP $n = 39$
Mean age in years (SD)	23.6 (4.3)	20.5 (3.0)	30.5 (10.6)
Mean years of education (SD)	15.4 (1.4)	13.9 (1.9)	13.7 (2.0)
Male %	47.1	53.3	64.1
GAF score, mean (SD)	87.6 (4.9)	52.8 (7.5)	49.6 (10.1)
SOPS, mean (SD)			
Positive symptoms	N/A	11.2 (3.3)	N/A
Negative symptoms	N/A	11.2 (6.1)	N/A
Disorganized symptoms	N/A	4.3 (2.6)	N/A
General symptoms	N/A	8.0 (3.9)	N/A
PANSS, mean (SD)			
Positive symptoms	N/A	N/A	18.5 (4.1)
Negative symptoms	N/A	N/A	16.0 (5.6)
General symptoms	N/A	N/A	32.1 (7.4)
Mean illness duration in months	N/A	N/A	24.4

Table 2
Items included in the activity-related stress scale.

1. Since the last beep, my activities have been a challenge.
2. Since the last beep, I cannot control my activities.
3. Since the last beep, I am skilled to do my activities.
4. Since the last beep, I'd rather do something else.
5. Since the last beep, my activities cost a lot of energy.

3.2. Examination of univariate group effects

The three groups showed differences in estimated marginal mean levels of consummatory anhedonia (HC mean = 63.81, SE = 2.55; CHR mean = 54.99, SE = 2.25; FEP mean = 58.87, SE = 2.33). These differences were significant, $F(2, 109.81) = 3.36$, $p = .038$. They also showed differences in estimated marginal mean levels of anticipatory anhedonia (HC mean = 74.89, SE = 2.46; CHR mean = 66.01, SE = 2.17; FEP mean = 66.52, SE = 2.25), which were significant, $F(2, 110.31) = 4.38$, $p = .015$. Both findings survived the Holm-Bonferroni correction. Pairwise comparisons of estimated marginal means of consummatory anhedonia revealed significant differences between the HC and CHR groups (LSD-corrected $p = .01$), but not between the HC and FEP groups (LSD-corrected $p = .16$) or between the CHR and FEP groups (LSD-corrected $p = .23$). Pairwise comparisons of estimated marginal means of anticipatory anhedonia revealed significant differences between the HC and CHR groups (LSD-corrected $p = .01$) and between the HC and FEP groups (LSD-corrected $p = .01$), but not between the CHR and FEP groups (LSD-corrected $p = .87$). See Fig. 1 for a representation of group differences.

3.3. Impact of event-related stress on anhedonia

The impact of event-related stress at T_{n-1} on consummatory anhedonia at T_n was non-significant; $F(1, 3340.09) = 0.47$, $p = .49$. The interaction term between the group variable and event-related stress at T_{n-1} was likewise non-significant; $F(2, 3277.77) = 0.31$, $p = .73$. The impact of consummatory anhedonia at T_{n-1} on consummatory anhedonia at T_n was, as expected, significant; $F(1, 3437.50) = 64.77$, $p < .001$.

The impact of event-related stress at T_{n-1} on anticipatory anhedonia at T_n was non-significant; $F(1, 3337.55) = 3.13$, $p = .07$ (the Holm-Bonferroni adjusted alpha value for this effect was 0.025). The interaction term between the group variable and event-related stress at T_{n-1} was likewise non-significant; $F(2, 3313.81) = 0.54$, $p = .58$. The impact of anticipatory anhedonia at T_{n-1} on anticipatory anhedonia at T_n was, as expected, significant; $F(1, 3439.22) = 55.58$, $p < .001$.

3.4. Impact of activity-related stress on anhedonia

The impact of activity-related stress at T_{n-1} on consummatory anhedonia at T_n was significant; $F(1, 2684.84) = 15.17$, $p < .001$. The unstandardized fixed effect size estimate for this effect was −0.14, corresponding to a reduction in consummatory pleasure of 0.14 points for every unit increase in activity-related stress at T_{n-1}. The interaction term between the group variable and activity-related stress at T_{n-1} was non-significant; $F(2, 2491.71) = 2.51$, $p = .08$. The impact of consummatory anhedonia at T_{n-1} on consummatory anhedonia at T_n was, as expected, significant; $F(1, 3450.00) = 40.12$, $p < .001$.

The impact of activity-related stress at T_{n-1} on anticipatory anhedonia at T_n was significant; $F(1, 2892.87) = 5.90$, $p = .015$. The unstandardized fixed effect size estimate for this effect was −0.01, corresponding to a reduction in anticipatory pleasure of 0.01 points for every unit increase in activity-related stress at T_{n-1}. The interaction term between the group variable and activity-related stress at T_{n-1} was non-significant; $F(2, 2748.78) = 0.99$, $p = .37$. The impact of anticipatory anhedonia at T_{n-1} on anticipatory anhedonia at T_n was, as expected, significant; $F(1, 3433.82) = 53.29$, $p < .001$.

4. Discussion

4.1. Stress and negative symptom exacerbations

As noted in the introduction, stress and negative symptoms have been associated in other studies (Myin-Germeys et al., 2001b;

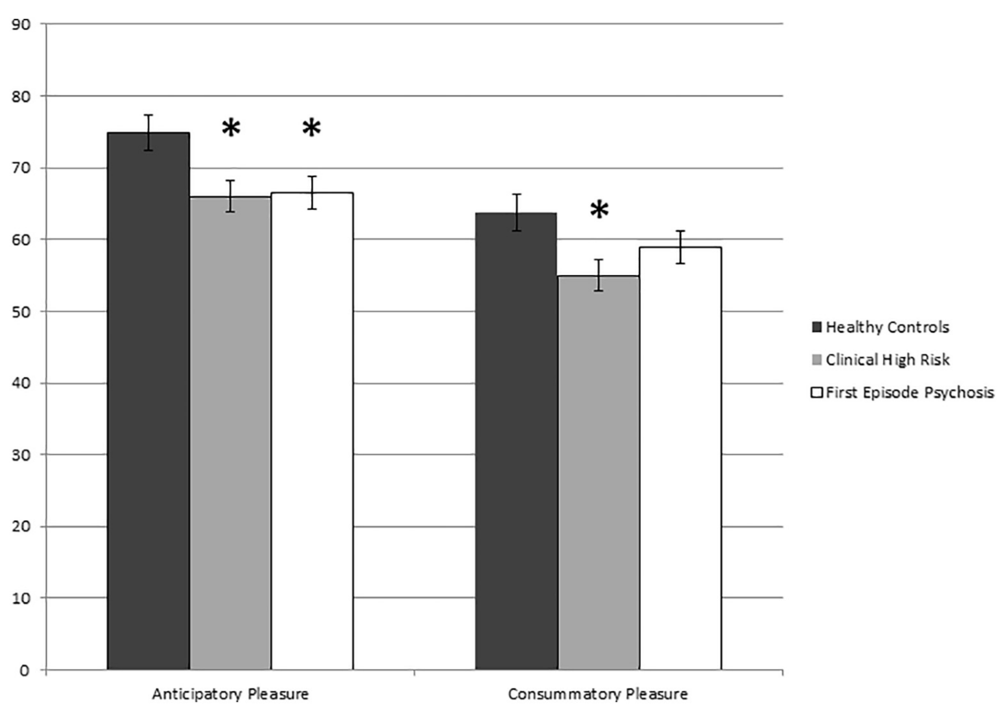

Fig. 1. Estimated marginal means of anticipatory and consummatory pleasure within each group (lower values indicate greater anhedonia). Error bars indicate standard error. *Significantly different from healthy controls, $p < .05$ (Bonferroni-Holm corrected).

deVylder et al., 2013). However, these have not employed time-lagging and do not therefore support a causal relationship. The current findings support such a relationship between experiences of day-to-day activity-related stress and both forms of anhedonia. To the best of our knowledge, this is the first demonstration of a unidirectional relationship, in which momentary fluctuations in negative symptoms follow episodes of activity-related stress. It is also to the best of our knowledge the first demonstration of such an association in antipsychotic-naïve FEP and CHR individuals, supporting the interpretation that this is not attributable to medication effects.

A much larger effect of stress was observed on consummatory than anticipatory anhedonia. This conforms to prior, transdiagnostic findings, in which enjoyment of activities is reduced following stressors (Pizzagalli, 2014). A differential impact on anticipatory anhedonia is consistent with models suggesting distinct brain mechanisms between the two forms of anhedonia (e.g., Berridge, 2007).

Interestingly, a parallel finding was not observed in the relationship between event-related stress and either form of anhedonia. This supports an important dissociation between event- and activity-related stress. The reason for this is unclear, however it appears that stress alone is not responsible for increases in anhedonia, and that the crucial element driving these fluctuations has to do with engaging in activity that one finds stressful due to challenge, lack of control, or lack of skill. One possible mechanism for this relationship may be one's sense of self-efficacy (Bandura, 1977), which is one's appraisal of one's own ability to act effectively and agentically. It is strongly correlated with negative symptoms in schizophrenia (Hill and Startup, 2013). Self-efficacy is also known to be responsive to experiences of activity-related stress and the appraisals that subjects make of themselves based upon such experiences (Bandura, 1982). More recent work regarding stress-anhedonia relationships in other areas, such as depression, reports similar mediators including lack of perceived control (Pizzagalli, 2014); for example, Haeffel et al. (2008) found that a negative inferential style influences the impact of stressors on reduced goal pursuit. Negative inferences about action have also been shown to be connected to negative symptoms in schizophrenia (Rector, 2004; Beck et al., 2009).

These possible mechanisms of mediation require further investigation, as do physiological mechanisms for this relationship. As noted in the introduction, stress-anhedonia links have been made in animal models, however opposing or uncertain physiological mechanisms have been observed and further study is required (Stanton, 2019).

4.2. Diagnostic specificity

Another interesting finding is the lack of any significant interaction between the above observations and diagnostic group, suggesting that unlike positive symptoms, negative symptom increases are *not* uniquely impacted by momentary stress in the schizophrenia spectrum but are similar across both clinical groups (CHR and FEP) and healthy controls. While it is clear that overall levels of anhedonia vary between groups (Fig. 1), of the impact of stress on anhedonia is similar. This may speak to the differential underlying psychopathology of positive and negative symptoms. Stress-induced increases in positive symptoms are typically viewed as a result of increased dopaminergic activity in the dorsal striatum, specifically increased in CHR and first-episode psychosis populations (Mizrahi et al., 2012, 2014; Soliman et al., 2008). While increases in striatal dopamine reactivity moderate the stress-positive symptom relationship in first-degree relatives of those with psychotic disorders (Myin-Germeys et al., 2005b), anhedonia may have a relationship with stress that is mediated differently. Given that those with schizophrenia-spectrum psychopathology tend to experience increased negative symptoms (including anhedonia) relative to controls, the lack of an interaction does not support a picture in which day-to-day stress is a sole or ultimate cause of these symptoms; but rather that day-to-day stress can exacerbate them in illness via similar mechanisms that exist in healthy individuals. Again, momentary reduction in self-efficacy or feelings of loss of control stands out as potential processes. In terms of physiology, the common mechanism remains unknown, as reviewed above.

4.3. Anhedonia level comparison

In terms of overall levels of anhedonia among the three groups, the current findings are in contrast with those of Gard et al. (2014), who found *lower* anticipatory anhedonia/greater anticipated pleasure among those with schizophrenia, using similar ESM methodology. The source of this discrepancy is unclear. However, one possibility arises from differences between the two samples. Interestingly, Gard et al. found that in their schizophrenia sample, individuals were more likely than controls to report goals that are pleasure-based to begin with; and less likely than controls to make goals that are effortful, long-term or social. Their sample was also older (mean age = 39.55 versus the current 21.44). In the current, younger and antipsychotic-naïve FEP sample, the relative frequency of work-related or effortful anticipated tasks was comparable to that of controls. These crucial differences may account for the current finding, with older and more chronic individuals with schizophrenia having adapted their lifestyle to the illness, and younger, pre-treatment FEP individuals continuing to struggle with daily demands in keeping with their peers.

This account may additionally explain some of the inconsistencies in prior literature regarding anticipatory anhedonia in psychosis; in a context wherein individuals have fewer effortful tasks to perform, the relative frequency of pleasure-based goals itself may account for greater anticipated pleasure, whereas in samples who are still engaged in more effortful tasks, anticipatory anhedonia may be specifically elevated in response to these tasks. Such contextual factors have a clear importance in the evaluation of anticipatory anhedonia and avolition in psychosis; rather than being impaired in their anticipation of pleasure per se, these individuals may anticipate less pleasure specifically for effortful tasks, in accordance their observed tendency to assume greater effort expenditure in such tasks (Fervaha et al., 2013).

The current findings further suggest that difficulties with anhedonia precede the onset of a first episode of psychosis, as they are present in the CHR sample to the same degree as in the FEP sample.

4.4. Implications and limitations

In terms of clinical implications, the current findings suggest a specific target for behavioural interventions for consummatory anhedonia, anticipatory anhedonia and potentially its close cognate, avolition. If activity-related stress and any appraisals and attributions that underlie it are reduced, individuals across the schizophrenia spectrum may show improvements in hedonic capacity. This suggests two targets for psychosocial interventions, such as cognitive behavioural therapy (CBT). The identification of cognitive mediators, such as reduced belief in self-efficacy or other negative control- and outcome-related appraisals proposed above, would provide targets for cognitive restructuring. For example, clients may be taught to identify thoughts in response to stress that in turn lead to reductions in enjoyment and effort expenditure. Specifying these hypothetical mediators represent a valuable avenue for future research. Secondly, behavioural interventions may target activity-related stress by teaching clients to identify activities that reduce their sense of control and balance these with mastery-building activities (Beck et al., 2009). Finally, from a clinical and research standpoint, the finding of equivalent levels of anhedonia between CHR and FEP individuals suggests that these symptoms warrant additional attention in CHR populations, in parallel with the recent increase in focus on negative symptoms in psychosis and given the well-established impact of such symptoms on functioning (Barch et al., 2014; Kiang et al., 2003).

Some limitations exist in the current study. Although the number of participants removed due to partial compliance, and the number of observations removed for various reasons, were comparable to those in other similar studies, it is possible that these missing data represent a non-random sample of responses – especially in light of the plausible relationship between negative symptoms and survey non-completion (which could, itself, be viewed as an indication of avolition). This issue is endemic to ESM methodology and is likely unavoidable in longitudinal research with unmedicated FEP individuals but warrants the use of caution in generalizing these findings. A similar limit on generalizability stems from the exclusion of those with substance use disorders; while this ensured that substance-related sources of anhedonia were controlled for, it would be informative to examine how these effects generalize to heavy substance-users. Another issue that is endemic to the ESM method is the brevity of assessments and reliance upon face validity; although the current procedure used the best-validated ESM methods available, items assessing stress and anhedonia may benefit from further studies of discriminant and convergent validity. This is a limitation of the method as it currently exists. Additionally, baseline stress was not measured, therefore interactions between overall stress level and its momentary impact on anhedonia could not be ascertained. Lastly, while it is assumed that symptom levels were minimal in the HC group and increased stepwise in the CHR and FEP samples, the same severity measures were not administered across all groups and they cannot therefore be directly compared.

Contributors

Cory Gerritsen led the development of the research questions, methods and design, performed data analysis and wrote the initial draft. R. Michael Bagby and Michael Kiang provided consultation regarding methods and data collection, and edited the manuscript. Marcos Sanches contributed to the development of the statistical methods and preparation of the Methods and Results sections, and performed data cleaning. Margaret Maheandiran coordinated subject recruitment and provided editorial comments. Ivana Prce coordinated subject recruitment and data collection, performed study monitoring and provided editorial comments. Romina Mizrahi oversaw all aspects of protocol development, recruitment, variable selection, and data collection, contributed to study design and edited the manuscript. *All authors contributed to and have approved the final manuscript.*

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Declaration of Competing Interest

The authors declare no conflict of interest.

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