Published in final edited form as:

Psychiatry Res. 2008 July 15; 160(1): 38–46.

Patterns of stress in schizophrenia

Julia D. Betensky^a, Delbert G. Robinson^{a,b,c}, Handan Gunduz-Bruce^d, Serge Sevy^{a,b,c}, Todd Lencz^{a,b,c}, John M. Kane^{a,b,c}, Anil K. Malhotra^{a,b,c}, Rachel Miller^a, Joanne McCormack^a, Robert M. Bilder^e, and Philip R. Szeszko^{a,b,c,*}

^a*Department of Psychiatry Research, The Zucker Hillside Hospital, North-Shore - Long Island Jewish Health System, 75-59 263rd Street, Glen Oaks, NY, 11004, United*

^b*Feinstein Institute for Medical Research, Manhasset, NY, US*

^c*Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY, 10461, US*

^d*Yale University School of Medicine, VA Medical Center, Psychiatry Service 116A, 950 Campbell Avenue, West Haven, CT, 06516, United States*

^e*Jane and Terry Semel Institute for Neuroscience and Human Behavior, Lynda and Stewart Resnick Neuropsychiatric Hospital, David Geffen School of Medicine at UCLA, Room C8-849, 760 Westwood Plaza, Los Angeles, CA, 90095, United States*

Abstract

Although it is widely recognized that stress plays a key role in the pathophysiology of schizophrenia, little is known regarding the particular types of stress patients experience. Less is known about the interplay among stressful events, personality mediators, and emotional responses. In this study, we investigated 10 stress dimensions in 29 patients with schizophrenia and 36 healthy volunteers using the Derogatis Stress Profile, and the relationship between these dimensions and symptoms in patients. Overall, patients had an approximate .75 standard deviation increase in stress compared to healthy volunteers. Significant increases in stress among patients compared to healthy volunteers were observed specifically in areas related to domestic environment, driven behavior, and depression, but not in health, attitude posture, time pressure, relaxation potential, role definition, hostility, or anxiety. More DSP depression among patients correlated significantly with greater negative symptom severity. Patients with a shorter duration of antipsychotic drug exposure had significantly greater hostility compared to patients with a longer duration of exposure, but did not differ in any other dimension. Continued investigation of domestic environmental stressors, driven behavior, and depression may be useful in identifying high-risk groups, and understanding symptom exacerbation and precipitants of relapse in patients already diagnosed with schizophrenia.

Keywords

Personality; Emotion; Depression; Negative symptoms

*Corresponding author. Tel.: +1 718 470 8489; fax: +1 718 343 1659. *Email address:* szesko@lij.edu (P.R. Szeszko).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1. Introduction

Epidemiological studies suggest that environmental and psychosocial stressors may be risk factors for the development of schizophrenia. For example, prenatal exposure to maternal stress (Huttenen and Niskanen, 1978), and early postnatal psychosocial stress related to parental loss (Agid et al., 1999) have been linked to increased risk for and later development of schizophrenia (Corcoran et al., 2001). Patients with schizophrenia also demonstrate an impaired ability to adapt to stress, showing decreased norepinephrine and adrenocorticotropin responses to physical stress (Kudoh et al., 1999) and blunted cortisol responses to psychosocial stressors (Jansen et al., 1998) compared to healthy volunteers. Limited positron emission tomography data raise the possibility of differences in brain activity from cortisol infusions among patients with schizophrenia compared with healthy volunteers (Ganguli et al., 2002).

Several studies, which used paper and pencil measures, provide support for a multidimensional role of stress in the phenomenology of schizophrenia. Ponizovsky and colleagues (2004) reported that patients with schizophrenia had a higher level of emotional distress and utilization of emotion-oriented coping strategies, and a lesser availability of social support compared with healthy volunteers using the Talbich Brief Distress Inventory (Ritsner et al., 1995). The General Temperament Survey (Clark and Watson, 1990) has also differentiated between patients with schizophrenia and controls on trait negative affectivity, which refers to an increased likelihood to experience aversive emotional stress and distress (Watson and Clark, 1984; Horan and Blanchard, 2003). Norman and Malla (1994) demonstrated that amount of perceived stress correlated positively with symptom severity in patients with schizophrenia using a shortened version of the Daily Hassles Scale developed by Lazarus and colleagues (Kanner et al., 1981; Delongis et al., 1982). Taken together, these findings suggest that patients with schizophrenia differ from healthy volunteers in stress dimensions related to emotion and social support, and increased stress may be related to symptom severity in schizophrenia.

Although it is widely acknowledged that stress may play a key role in the pathophysiology of schizophrenia, little research has investigated the interactive roles of stress-inducing events, personality mediators, and emotional reactivity in patients. Such studies may clarify the mechanisms through which exposure to stress results in symptom exacerbation or relapse. In recent studies (Horan et al., 2005a; Moller-Leimkuhler, 2005), a transactional model of stress (Lazarus and Folkman, 1984; Lazarus, 1999) has been used as a framework for examining this stress process in schizophrenia. In this study, we administered the Derogatis Stress Profile (DSP; Derogatis, 1987) to target the multidimensional role of stress and examine its three purported domains, including environmental events, personality mediators, and emotional responses. The DSP is a widely used and reliable self-report questionnaire that has been used to measure stress levels in students (e.g. Helmers et al., 1997; Verlander et al., 1999; Gelberg and Gelberg, 2005), smokers (Kelley et al., 2003), cancer survivors (Greenberg et al., 1989), and cardiac patients (Duquette et al., 1994). There is evidence that this population is as competent as nonpatients in their ability to subjectively appraise stress severity (Grant et al., 1976) and describe their reactions to stress in a coherent manner (Horan and Blanchard, 2003; Horan et al., 2005a). We tested the hypothesis that patients would demonstrate the greatest magnitude of stress in areas related to the emotional sequelae of having schizophrenia as well as areas related to social support. We further predicted that among patients increased stress would be associated with greater symptom severity.

2. Methods and Materials

2.1. Participants

The 29 patients included in this study were recruited at the Zucker Hillside Hospital in Glen Oaks, NY and were participating in an NIMH-funded randomized clinical trial comparing the

efficacy of risperidone versus olanzapine. Further details regarding the overall sample are provided elsewhere (Robinson et al., 2006). The Structured Clinical Interview for Axis I DSM-IV Disorders (SCID-I/P; First et al., 1994) was administered to all patients and was supplemented with information from medical records and information from family members, when available. All patients met DSM-IV criteria for schizophrenia ($N = 24$), schizoaffective disorder ($N = 2$), or schizophreniform disorder ($N = 3$) and had less than 12 weeks exposure to antipsychotic medication prior to entry into the clinical trial. Mean duration of antipsychotic exposure from entry into the clinical trial until administration of the DSP was 102 weeks (range = 0 to 169 weeks). Mean (SD) age at first psychiatric symptoms was 18.5 (SD = 6.2). Mean age at first psychotic symptoms was 21.7 (SD = 5.1). Thirty-six healthy volunteers served as a comparison group. All healthy volunteers were recruited from newspaper advertisements or through word of mouth. They had no Axis I psychiatric disorder as determined by clinical interview and the Structured Clinical Interview for Diagnoses-Nonpatient Version (SCID-NP; Spitzer and Williams, 1988), no first-degree relative with a psychiatric disorder and were not taking any psychotropic medications.

2.2. Clinical Assessments

Stress was assessed using the DSP (Derogatis, 1987), a 77-item Likert scale paper-and-pencil self-report questionnaire that takes approximately 15 minutes to complete. Participants are asked to indicate the extent to which the statement is typically true of the way they behave or feel. The DSP targets 11 dimensions and 3 stress domains of stress. The 3 domains of stress include: (1) environmental events, comprising domestic (e.g. "I have a good relationship with my wife/husband or unmarried partner"), vocational (e.g. "I am frequently frustrated in my work"), and health (e.g. "I rarely exercise") environments, (2) personality mediators, comprising attitude posture (e.g. "I feel the most important thing in life that you achieve something with it"), driven behavior (e.g. "Every day I must get something tangible accomplished or I don't feel good about myself"), time pressure (e.g. "I feel there is never enough time to get things done"), relaxation potential (e.g. "I have trouble relaxing"), and role definition (e.g. "I believe you can get a lot of help from others in getting the job done in life"), and (3) emotional responses, comprising anxiety (e.g. "I am usually worried about something"), depression (e.g. "I sometimes have feelings of worthlessness"), and hostility (e.g. "I have no problems with control of my temper"). Each stress domain or dimension is scored as the sum of its corresponding items following reflection of individual items as required. Interscale correlations are relatively high between primary stress dimensions and their corresponding domains as compared to non-corresponding domains, which suggests an ideal multidimensional measurement (Derogatis, 1987). Internal consistency across the stress dimensions used in this analysis as determined using coefficient alpha was .75 for patients and .82 for healthy volunteers. We excluded vocational environment items from analyses given the potential confound that patients would not be working because they were ill.

We computed 2 symptom cluster scores based on items from the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1981) and Schedule for Affective Disorders and Schizophrenia-Change Version with psychosis and disorganization items (SADS-C + PD; Spitzer and Endicott, 1978). The negative symptom cluster score was computed as the average of the global ratings of affective flattening, alogia, avolition-apathy, and asociality from the SANS. The positive symptom cluster score was computed as the average of the severity of delusions and severity of hallucinations items from the SADS-C + PD. Median number of days between administration of the SANS and SADS-C + PD rating scales to the DSP was 5 and 2 days, respectively (range = -33 to 184 days for both scales).

The SADS-C + PD scores were converted into Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) scores using an algorithm described by Endicott and colleagues (Endicott et

al., 1981). The HDRS is a widely-used and well-validated instrument for the clinical assessment of depressive symptoms. Higher scores were indicative of greater severity of depression.

2.3. Data Analysis

Data analyses were performed SPSS for Windows, v. 11.5 software (SPSS Inc., Chicago, Illinois). We tested for a difference in total DSP scores between patients and comparison subjects using an independent groups *t* test. In addition, we used separate multivariate analyses of variance (MANOVA) with Greenhouse-Geisser correction to determine whether patients differed from healthy volunteers on the 3 stress domains or the 10 individual stress dimensions and to assess the potential interaction of stress domain and dimension with group. Thus, the statistical model included group (patients vs. controls) and sex as between subjects factors with stress domain as the within subjects factor in one MANOVA and stress dimension as the within subjects factor in a separate MANOVA. Individual stress dimensions were expressed as *z* scores (with higher values indicative of more stress) based on data from our healthy volunteer group. This was done separately for males and females given the unequal distribution of sex between the groups. Thus, by definition healthy volunteers had a mean of 0 on the stress dimensions and a standard deviation of 1. Mean substitution was used to replace missing items for 7 patients and 4 healthy comparison subjects, affecting less than 1% of the total items.

We assessed univariate normality for each stress dimension to determine whether the assumption of multivariate normality would be met. Box's test was used to determine whether the assumption of equality of covariance matrices was met. Subsequent analyses investigated whether the pattern of stress would be comparable in recent-onset patients with a shorter duration of antipsychotic treatment ($N = 10$; mean duration = 7.67 weeks; range = 0 to 20) compared to patients with a longer duration of antipsychotic treatment ($N = 19$; mean duration = 152 weeks; range = 74 to 169).

In addition, HDRS scores for patients were computed. Group differences in demographic variables were examined using independent groups *t* tests. Chi-square tests were used to examine differences between categorical variables. Spearman correlations were used to examine the relationship between dimensions of stress and clinical scales. Alpha was set at .05 for all analyses.

3. Results

3.1. Sample

Sample characteristics are provided in Table 1. The groups did not differ significantly from each other in distributions of age, race, or parental social class (all $ps > .05$). The distribution of sex differed significantly between groups. As expected, education differed significantly between groups, with patients having less education compared to healthy volunteers.

3.2. Pattern of stress

Each of the individual dependent variables was normally distributed as determined from visual inspection of scatterplots and assessment of skewness and kurtosis. In addition, the assumption of equality of covariance matrices (as determined from Box's *M*) was met for MANOVA. As expected, an independent groups *t*-test revealed that patients had a greater total stress score compared to healthy volunteers ($t = 3.32$, $df = 1, 63$, $p = .002$). MANOVA using the 3 stress domains (e.g., environmental events, personality mediators, and emotional response) revealed a significant main effect of group ($F = 9.98$, $df = 1, 61$, $p = .002$) and a trend for a significant group-by-domain interaction ($F = 3.08$, $df = 1.83$, $p = .054$, with Greenhouse Geisser correction). The use of education as a statistical covariate did not alter any of these findings. Neither the main effect of sex nor interactions involving sex were statistically significant.

MANOVA for the individual stress dimensions revealed a significant main effect of group ($F = 3.88$, $df = 10, 52$, $p < .001$) such that patients had greater stress overall across the dimensions (corresponding to an increase of .75 standard deviations) compared to healthy volunteers. Also, the group-by-stress dimension interaction was statistically significant ($F = 4.02$, $df = 7.61$, $p < .001$, with Greenhouse Geisser correction). Follow up univariate tests revealed that patients had significantly greater stress on dimensions related to depression ($t = 4.97$, $df = 1, 63$, $p < .001$; partial eta squared = .28), domestic environment ($t = 3.52$, $df = 1, 63$, $p = .001$; partial eta-squared = .16), and driven behavior ($t = 3.28$, $df = 1, 63$, $p = .002$; partial eta-squared = .15) compared to healthy volunteers. The use of education as a covariate did not alter these significant findings. Patients did not differ from healthy volunteers in other stress dimensions related to health posture, attitude posture, relaxation potential, role definition, time pressure, anxiety, and hostility ($ps > .05$). Neither the main effect of sex nor interactions involving sex were statistically significant. Figure 1 illustrates the individual DSP stress dimensions for the patients relative to the healthy comparison group.

Subsequent analyses investigated the potential association between duration of antipsychotic drug exposure in the clinical trial and the individual stress dimensions. Both patients with a short ($n = 10$) and long ($n = 19$) duration of antipsychotic drug exposure had significantly ($p < .05$) greater stress compared to healthy volunteers on the depression, domestic environment and driven behavior dimensions. Patients with a short duration of antipsychotic drug exposure had significantly greater hostility ($t = 2.56$, $df = 1, 27$, $p = .016$) compared to patients with a long duration of exposure, but did not differ in any other dimension.

3.3. Clinical correlates

Investigation of the clinical correlates of the DSP depression, domestic environment and driven behavior stress dimensions in relationship to the symptom clusters revealed that greater DSP depression was significantly correlated with more negative symptoms ($r = .38$, $df = 28$, $p < .05$; see Figure 2), but not with positive symptoms. It is noteworthy that examination of the individual items comprising the DSP depression dimension and the SANS did not reveal any significant overlap in the individual items for these constructs. Neither the domestic environment nor driven behavior dimensions correlated significantly with any of the symptom clusters. Hamilton Depression scores did not correlate significantly with any of the stress dimensions or symptom clusters among patients. Duration in the clinical trial was not significantly correlated with the depression, domestic environment or driven behavior dimensions on the DSP.

4. Discussion

The purpose of this study was to characterize patterns of stress in patients with schizophrenia studied early in the course of illness. Consistent with prior work (e.g. Serban, 1975; Norman and Malla, 1994; Ponizovsky et al., 2004), we observed an overall increase in stress of .75 standard deviations in patients compared to healthy volunteers. More interestingly, however, the pattern of stress was not uniform across the dimensions examined. We observed increased stress in patients in dimensions tapping domestic environment, driven behavior, and depression without associated group differences in health environment, attitude posture, relaxation potential, role definition, time pressure, anxiety or hostility. There was also a significant trend towards non-uniformity across domains in patients. Additionally, more DSP depression correlated with greater negative symptom severity among patients.

A transactional model of stress (Lazarus and Folkman, 1984; Lazarus, 1999) is emerging as a preferred approach to assessing stress in patients with schizophrenia. One reason for this is that the way in which patients appraise the meaning and potential impact of stressful events is more likely to affect their health and functioning (DeLongis et al., 1982; Lazarus and Folkman,

1984; Folkman and Lazarus, 1985) than is the frequency of stressful events. The DSP paradigm treats stress as a process and enables the clinician to evaluate how patients subjectively appraise the influence of real-world stressors. Our findings suggest that there is an interplay between domestic environmental stressors, a need to act constructively, and resulting depressive symptoms in patients recently diagnosed with schizophrenia.

One major study finding is that patients with schizophrenia expressed increased stress relating to their domestic environment. This finding suggests that interpersonal conflicts between patients and their parents, children, neighbors or extended family result in high levels of stress. The domestic environment may be particularly stress-inducing early in the course of illness due to the recent shift in patient status and the resulting need to reconstruct interpersonal dynamics. Deficiencies in the use of effective interpersonal problem-solving strategies (Bellack et al., 1992) may also provoke distress. Epidemiological studies also indicate that schizophrenia is associated with lower marital and fertility rates (Eaton, 1975; Odegard, 1980; Saugstad, 1989). Patients with schizophrenia report receiving less social support than individuals without mental illness or with other non-psychotic disorders (Neeleman and Power, 1994). An insufficient social support network may contribute to an increased sensitivity to environmental stress in general (Phillips et al., 2007) or increased emotional reactivity towards stressors (DeLongis et al., 1988; Affleck et al., 1994). In other words, it may be that patients are more likely to appraise interpersonal relationships in a negative fashion or label them as stressful because they lack strong support networks.

Our study also suggests that patients reported increased driven behavior. High scores on the DSP driven behavior dimension suggest that patients with schizophrenia feel a compulsive need to be involved in constructive activities. It is purportedly this self-imposed, demanding criterion of tangible accomplishment that enables patients to achieve feelings of well-being and self-worth (Derogatis, 1987). Whereas most studies on personality characteristics in schizophrenia have focused on chronically ill patients (e.g., Horan et al., 2005b), our research concerns patients earlier in the course of their illness. The personality characteristic of driven behavior found in the present study is thus less influenced by prolonged exposure to antipsychotic medications, progression of illness, or acquired patterns of adaptation to a chronic mental illness (Horan et al., 2005b), and may be associated with vulnerability (Nuechterlein et al., 1992). Given that driven behavior did not differ between patients with short and long durations of antipsychotic exposure, it is possible that driven behavior is a stable personality trait that moderates stress reactivity. Furthermore, driven behavior may be directly related to the impact of domestic environment. A recent meta-analysis acknowledges that in schizophrenia, social-evaluative threat elicits cortisol changes only in the context of a motivated performance task that requires active cognitive responses (Dickerson and Kemeny, 2004). In other words, the impact of socially-relevant stress on physiological responses may be mediated by the need to motivate oneself. Patients may be motivated to engage in constructive behaviors to resolve interpersonal conflicts, but they may lack problem-focused coping strategies (van den Bosch et al., 1992).

Another major study finding is that patients reported increased depression. High scores on the depression dimension of the DSP indicate more mild-to-moderate symptoms, including fatigue, loss of interest, feelings of loneliness and lowered self-esteem. It has been demonstrated that depressive symptoms exist during the first episode (Johnson, 1981; Koreen et al., 1993; Addington et al., 1998) and after psychosis has remitted (Leff and Wing, 1971; Hirsch et al., 1973; Knights et al., 1979). While studies suggest that minor stressors are associated with increased depression and anxiety (Hardesty et al., 1985; Malla and Norman, 1992; Norman and Malla, 1994), it may be that heightened levels of depression lead to over-reporting of the occurrence of stressful events (Phillips et al., 2007). The DSP paradigm posits that the quality of the individual's emotional response to a stressor itself becomes an aspect of

the stimulus environment to result in the phenomenologic experience of stress (Derogatis, 1987). Our findings suggest a bidirectional relationship between stressful events and depression such that the domestic environment elicits depressive affective responses, which further magnify the burdens arising from the domestic environment. An association between elevated trait negative affectivity and emotional responses during social interactions in schizophrenia has been demonstrated before (Horan and Blanchard, 2003). Because HDRS scores did not correlate significantly with DSP depression scores or other stress dimensions, it is likely that mild-to-moderate depressive symptoms are associated with stressful events in schizophrenia, rather than more profound symptoms of clinical depression.

In our study, more DSP depression correlated with greater negative symptom severity. Our results converge with previous studies conducted in patients with schizophrenia that reported an association between depression and negative symptom severity as measured by the SANS (Kulhara et al., 1989; Kitamura and Suga, 1991; Aydemir et al., 2002). Although psychosocial stressors have consistently been associated with exacerbation of psychotic symptoms (e.g. Norman and Malla, 1993), the nature of this relationship is unclear. Horan and Blanchard (2003) note that one approach to identifying mechanisms by which stress contributes to symptom exacerbation in schizophrenia is to examine subjectively experienced emotional responses. It has been demonstrated that patients with schizophrenia experience elevations in negative mood prior to symptom exacerbations (Subotnik and Nuechterlein, 1988; Tarrier et al., 1991) and heightened emotional reactivity to naturally occurring stressors compared with controls (Myin-Germeys et al., 2000, 2001). Despite evidence that stress only worsens symptoms of schizophrenia when it is perceived as presenting an uncontrollable or social-evaluative threat to the self (Jones and Fernyhough, 2006), we found no association between symptom severity and driven behavior or domestic environmental stress. Our results suggest that depressive symptoms may mediate the impact of stress on negative symptom severity in schizophrenia.

There were several limitations to this study that preclude firm conclusions. One limitation is that patients with schizophrenia were not compared to psychiatric controls or unemployed healthy controls. Although the differences in stress dimensions between patients and controls may be found in other psychiatric disorders, the association between stress dimensions and negative symptom severity is likely to be specific to schizophrenia. Another potential limitation is that patients completed the DSP at different phases of their illness, although the pattern of stress appeared comparable in patients with both a short and long duration of antipsychotic drug exposure compared to healthy volunteers. Patients with a short duration of antipsychotic drug exposure had significantly greater levels of hostility compared to patients with a longer exposure. Given the number of statistical comparisons this should be interpreted with caution. It is noteworthy, however, that hostility in patients early in the course of illness may predict high expressed emotion in the domestic environment, which is a risk factor for relapse (Bachman et al., 2002). It might be of interest in future work to compare patients close to illness onset with chronic patients to clarify the stability or change of the stress process in schizophrenia.

In sum, our findings suggest that the pattern of stress in patients recently diagnosed with schizophrenia is not uniform, but related specifically to the domestic environment, driven behavior, and depression. Characterizing patterns of stress in patients early in the course of illness may be useful in identifying high-risk groups, and understanding symptom exacerbation and precipitants of relapse in patients already diagnosed with schizophrenia. Continued investigation may contribute to psychosocial interventions focused on the development of adaptive interpersonal skills, the prevention of compulsive behaviors, and the modification of depressed reactions.

Acknowledgements

This work was supported in part by grants from NARSAD (PRS) and the National Institute of Health to Dr. Szeszko (MH01990), Dr. Bilder (MH60374), Dr. Kane (MH60575) and Dr. Robinson (MH60004), Dr. Sevy (DA015541) and the NS-LIJ Feinstein Institute for Medical Research General Clinical Research Center (M01 RR018535).

References

- Addington D, Addington J, Patten S. Depression in people with first-episode schizophrenia. *British Journal of Psychiatry Supplement* 1998;172:90–92. [PubMed: 9764133]
- Affleck G, Tennen H, Urrows S, Higgins P. Person and contextual features of daily stress reactivity: Individual differences in relations of undesirable daily events with mood disturbance and chronic pain intensity. *Journal of Personality and Social Psychology* 1994;66:329–340. [PubMed: 8195989]
- Agid O, Shapira B, Zislin J, Ritsner M, Hanin B, Murad H, Troudart T, Bloch M, Heresco-Levy U, Lerer B. Environment and vulnerability to major psychiatric illness: a case control study of early parental loss in major depression, bipolar disorder and schizophrenia. *Molecular Psychiatry* 1999;4:163–172. [PubMed: 10208448]
- Andreasen, N. The Scale for Assessment of Negative Symptoms (SANS). Iowa City, Iowa: 1981.
- Aydemir O, Esen, Danaci A, Pirildar S. Distinguishing depressive from nondepressive patients in schizophrenia in terms of symptomatology. *Turkish Journal of Psychiatry* 2002;13:173–8. [PubMed: 12794651]
- Bachman S, Bottmer C, Jacob S, Kronmüller K, Backenstrass M, Mundt C, Renneberg B, Fielder P, Schröder J. Expressed emotion in relatives of first-episode and chronic patient with schizophrenia and major depressive disorder: A comparison. *Psychiatry Research* 2002;112:239–250. [PubMed: 12450633]
- Bellack AS, Sayers M, Mueser KT, Bennett M. Evaluation of social problem solving in schizophrenia. *Journal of Abnormal Psychology* 1994;103:371–8.
- Corcoran C, Gallitano A, Leitman D, Malaspina D. The neurobiology of the stress cascade and its potential relevance for schizophrenia. *Journal of Psychiatric Practice* 2001;7:3–14. [PubMed: 15990497]
- DeLongis A, Coyne JC, Dakof G, Folkman S, Lazarus RS. Relationship of daily hassles, uplifts, and major life events to health status. *Health Psychology* 1982;1:119–136.
- DeLongis A, Folkman S, Lazarus RS. The impact of daily stress on health and mood: Psychological and social resources as mediators. *Journal of Personality and Social Psychology* 1988;54:486–495. [PubMed: 3361420]
- Derogatis LR. The Derogatis Stress Profile (DSP): quantification of psychological stress. *Advances in Psychosomatic Medicine* 1987;17:30–54. [PubMed: 3591564]
- Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychological Bulletin* 2004;150:355–391. [PubMed: 15122924]
- Duquette RL, Dupuis G, Perrault J. A new approach for quality of life assessment in cardiac patients: rationale and validation of the Quality of Life Systemic Inventory. *Canadian Journal of Cardiology* 1994;10:106–112. [PubMed: 8111664]
- Eaton WW. Marital status and schizophrenia. *Acta Psychiatrica Scandinavica* 1975;52:320–329. [PubMed: 1199771]
- Endicott J, Cohen J, Nee J, Fleiss J, Sarantakos S. Hamilton Depression Rating Scale: Extracted from regular and change versions of the schedule for affective disorders and schizophrenia. *Archives of General Psychiatry* 1981;38:98–103. [PubMed: 7458574]
- Folkman S, Lazarus RS. If it changes, it must be a process: Study of emotions and coping during three stages of a college examination. *Journal of Personality and Social Psychology* 1985;48:150–170. [PubMed: 2980281]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for Axis I DSM-IV Disorders-Patient Edition (SCID-I/P). Biometrics Research Department, New York State Psychiatric Institute; New York: 1994.
- Ganguli R, Singh A, Brar J, Carter C, Mintun M. Hydrocortisone induced regional cerebral activity changes in schizophrenia: a PET scan study. *Schizophrenia Research* 2002;56:241–247. [PubMed: 12072173]

- Gelberg S, Gelberg H. Stress management interventions for veterinary students. *Journal of Veterinary Medical Education* 2005;32:173–181. [PubMed: 16078169]
- Grant I, Gerst M, Yager J. Scaling of life events by psychiatric patients and normals. *Journal of Psychosomatic Research* 1976;20:141–149. [PubMed: 1271314]
- Greenberg HS, Kazak AE, Meadows AT. Psychologic functioning in 8- to 16-year-old cancer survivors and their parents. *Journal of Pediatrics* 1989;114:488–493. [PubMed: 2921697]
- Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry* 1960;23:56–62.
- Hardesty, J.; Falloon, IRH.; Shirin, K. The impact of life events, stress and coping on the morbidity of schizophrenia. In: Falloon, IRH., editor. *Family management of schizophrenia*. Johns Hopkins University Press; Baltimore: 1985. p. 137-152.
- Helmers KF, Danoff D, Steinert Y, Leyton M, Young SN. Stress and depressed mood in medical students, law students, and graduate students at McGill University. *Academic Medicine* 1997;72:708–714. [PubMed: 9282148]
- Hirsch SR, Gaiend R, Rohde PD, Stevens BC, Wing JK. Outpatient maintenance of chronic schizophrenic patients with long-acting fluphenazine: double-blind placebo trial. Report to the Medical Research Council Committee on Clinical Trials in Psychiatry. *British Medical Journal* 1973;17:633–637. [PubMed: 4571196]
- Horan WP, Blanchard JJ. Emotional responses to psychosocial stress in schizophrenia: the role of individual differences in affective traits and coping. *Schizophrenia Research* 2003;60:271–283. [PubMed: 12591589]
- Horan WP, Ventura J, Nuechterlein KH, Subotnik KL, Hwang SS, Mintz J. Stressful life events in recent-onset schizophrenia: reduced frequencies and altered subjective appraisals. *Schizophrenia Research* 2005a;75:363–374. [PubMed: 15885527]
- Horan WP, Subotnik KL, Reise SP, Ventura J, Nuechterlein KH. Stability and clinical correlates of personality characteristics in recent-onset schizophrenia. *Psychological Medicine* 2005b;35:995–1005. [PubMed: 16045066]
- Huttenen MO, Niskanen P. Prenatal loss of father and psychiatric disorders. *Archives of General Psychiatry* 1978;35:429–431. [PubMed: 727894]
- Jansen LM, Gispens-de Wied CC, Gademan PJ, De Jonge RC, van der Linden JA, Kahn RS. Blunted cortisol response to a psychosocial stressor in schizophrenia. *Schizophrenia Research* 1998;33:87–94. [PubMed: 9783348]
- Johnson DA. Studies of depressive symptoms in schizophrenia. *British Journal of Psychiatry* 1981;139:89–101. [PubMed: 7030447]
- Jones SR, Fernyhough C. A new look at the neural diathesis-stress model of schizophrenia: The primacy of social-evaluative and uncontrollable situations. 2006
- Kanner AD, Coyne JC, Schaefer C, Lazarus RS. Comparison of two modes of stress measurements: Daily hassles and uplifts versus major life events. *Journal of Behavioral Medicine* 1981;4:1–39. [PubMed: 7288876]
- Kelley FJ, Thomas SA, Friedmann E. Health risk behaviors in smoking and non-smoking young women. *Journal of the American Academy of Nurse Practitioners* 2003;15:179–184. [PubMed: 12715598]
- Kitamura T, Suga R. Depressive and negative symptoms in major psychiatric disorders. *Comprehensive Psychiatry* 1991;32:88–94. [PubMed: 2001626]
- Knights A, Okasha MS, Salih MA, Hirsch SR. Depressive and extrapyramidal symptoms and clinical effects: a trial of fluphenazine versus flupenthixol in maintenance of schizophrenic out-patients. *British Journal of Psychiatry* 1979;135:515–523. [PubMed: 394794]
- Koreen AR, Siris SG, Chakos M, Alvir J, Mayerhoff D, Lieberman J. Depression in first-episode schizophrenia. *American Journal of Psychiatry* 1993;150:1643–1648. [PubMed: 8105706]
- Kudoh A, Ishihara H, Matsuki A. Pituitary-adrenal and parasympathetic function in chronic schizophrenic patients with postoperative ileus or hypotension. *Neuropsychobiology* 1999;39:125–130. [PubMed: 10087456]
- Kulhara P, Avasthi A, Chadda R, Chandiramani K, Mattoo SK, Kota SK, Joseph S. Negative and depressive symptoms in schizophrenia. *British Journal of Psychiatry* 1989;154:207–11. [PubMed: 2775947]

- Lazarus, RS.; Folkman, S. Stress, Appraisal, and Coping. Springer-Verlag; New York: 1984.
- Lazarus, RS. Stress and Emotion: A New Synthesis. Springer Publishing; New York, NY: 1999.
- Leff JP, Wing JK. Trial of maintenance therapy in schizophrenia. *British Medical Journal* 1971;3:599–604. [PubMed: 4936538]
- Malla AK, Norman RMG. Relationship of life events and daily stressors to symptomatology in schizophrenia. *Journal of Nervous and Mental Disease* 1992;180:664–667. [PubMed: 1402848]
- Moller-Leimkuhler AM. Burden of relatives and predictors of burden. Baseline results from the Munich 5-year-follow-up study on relatives of first hospitalized patients with schizophrenia or depression. *European Archives of Psychiatry and Clinical Neuroscience* 2005;255:223–31. [PubMed: 15549342]
- Myin-Germeys I, Delespaul PAEG, deVries MW. Schizophrenic patients are more emotionally active than is assumed based on their behavior. *Schizophrenia Bulletin* 2000;26:847–854. [PubMed: 11087017]
- Myin-Germeys I, van Os J, Schwartz JE, Stone AA, Delespaul PA. Emotional reactivity to daily life stress in psychosis. *Archives of General Psychiatry* 2001;58:1137–1144. [PubMed: 11735842]
- Neeleman J, Power MJ. Social support and depression in three groups of psychiatric patients and a group of medical controls. *Social Psychiatry and Psychiatric Epidemiology* 1994;29:46–51. [PubMed: 8178222]
- Norman RM, Malla AK. Stressful life events and schizophrenia: I. a review of the research. *British Journal of Psychiatry* 1993;162:166–174. [PubMed: 8435686]
- Norman RM, Malla AK. A prospective study of daily stressors and symptomatology in schizophrenic patients. *Social Psychiatry and Psychiatric Epidemiology* 1994;29:244–249.
- Nuechterlein KH, Dawson ME, Gitlin M, Ventura J, Goldstein MJ, Snyder KS, Yee CM, Mintz J. Developmental Processes in Schizophrenic Disorders: longitudinal studies of vulnerability and stress. *Schizophrenia Bulletin* 1992;18:387–425. [PubMed: 1411329]
- Odegard O. Fertility of psychiatric first admissions in Norway 1936-1975. *Acta Psychiatrica Scandinavica* 1980;62:212–220. [PubMed: 7457168]
- Phillips LJ, Francey SM, Edwards J, McMurray N. Stress and psychosis: Towards the development of new models of investigation. *Clinical Psychology Review* 2007;27:307–17.
- Ponizovsky A, Grinshpoon A, Sasson R, Levav I. Stress in adult students with schizophrenia in a supported education program. *Comprehensive Psychiatry* 2004;45:401–407. [PubMed: 15332204]
- Robinson DG, Woerner MG, Napolitano B, Patel RC, Sevy SM, Gunduz-Bruce H, Soto-Perello JM, Mendelowitz A, Khadivi A, Miller R, McCormack J, Lorell BS, Lesser ML, Schooler NR, Kane JM. Randomized comparison of olanzapine versus risperidone for the treatment of first-episode schizophrenia: 4-month outcomes. *American Journal of Psychiatry* 2006;163:2096–102. [PubMed: 17151160]
- Ritsner M, Rabinowitz J, Slyuzberg M. The Talbieh Brief Distress Inventory: a brief instrument to measure psychological distress among immigrants. *Comprehensive Psychiatry* 1995;36:448–453. [PubMed: 8565450]
- Saugstad LF. Social class, marriage, and fertility in schizophrenia. *Schizophrenia Bulletin* 1989;15:9–43. [PubMed: 2655069]
- Serban G. Stress in schizophrenics and normals. *British Journal of Psychiatry* 1975;126:397–407. [PubMed: 1125516]
- Spitzer, R.; Endicott, J. The schedule for affective disorders and schizophrenia, change version. 3. New York State Psychiatric Institute; New York: 1978.
- Spitzer, RL.; Williams, D. Structured Clinical Interview for Diagnoses-Nonpatient Version. New York State Psychiatric Institute; New York: 1988.
- Subotnik KL, Nuechterlein KH. Prodromal signs and symptoms of schizophrenic relapse. *Journal of Abnormal Psychology* 1988;97:405–412. [PubMed: 3204226]
- Tarrier N, Barrowclough C, Bamrah JS. Prodromal signs of relapse in schizophrenia. *Social Psychiatry and Psychiatric Epidemiology* 1991;26:157–161. [PubMed: 1948295]
- van den Bosch RJ, van Asma MJ, Rombouts R, Louwerens JW. Coping style and cognitive dysfunction in schizophrenic patients. *British Journal of Psychiatry* 1992;18S:123–8.

- Verlander LA, Benedict JO, Hanson DP. Stress and sleep patterns of college students. *Perception and Motor Skill* 1999;88:893–898.
- Watson D, Clark LA. Negative affectivity: the disposition to experience aversive emotional states. *Psychological Bulletin* 1984;96:465–490. [PubMed: 6393179]

Figure 1.

Individual stress dimensions in patients with new onset schizophrenia compared to healthy volunteers.

Patient scores are relative to scores for healthy comparison subjects; by definition, the healthy comparison group had a mean score of zero on each scale, and a standard deviation of 1. *** $p < .001$; ** $p = .001$; * $p < .005$. ^a partial eta-squared.

Figure 2.
Scatterplot of DSP depression and negative symptoms in patients.

Table 1

Sample Characteristics^a

Sample Characteristic	Patients with First-Episode Schizophrenia (N = 29)	Healthy Comparison Subjects (N = 36)	Statistical Analyses	
			Test statistic	p value
Sex (M, F)	22, 7	17, 19	$\chi^2 = 5.49$	0.02
Parental social class ^{a, b}	3, 4, 13, 3, 6	4, 7, 17, 3, 2	$\chi^2 = 2.32$	0.31
Race ^c	9, 16, 1, 3, 0	18, 12, 1, 3, 2	$\chi^2 = 3.20$	0.20
Age (years)	27.2 (7.1)	28.4 (7.3)	$t = -0.66$	0.51
Education (years)	12.5 (1.6)	14.8 (1.5)	$t = -5.97$	<0.001

^aThere were missing data from 3 healthy volunteers.

^bHollingshead Redlich Score coded from 1 (highest) to 5 (lowest). Due to the low number of expected frequencies in group 1 and group 5, groups 1 and 2 were combined, and groups 4 and 5 were combined for analysis.

^cRace coded as Caucasian, African-American, Hispanic, Asian, Other. Due to the low number of expected frequencies in the latter three groups, they were combined for analysis.