Stressful Life Events, Social Class and Symptoms of Schizophrenia

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Abstract

We test to see if severe stressful life events precede onset of specific symptoms of schizophrenia. Our analyses extend to possible variations in the effect by socioeconomic status (SES) of origin. The medical records of 431 schizophrenic patients were categorized into negative and positive subtypes by application of SANS, SAPS and PANSS scales. SES was bifurcated into low-SES and high-SES groups. Stressful life events were classified into four domains. The study variables were tested by the use of chi-square analysis. Our results show that there is an elevated rate of positive symptoms among low-SES patients who underwent a stressful life event before symptom onset. Significance is confirmed with an X^2 value of 5.418, p=.020. The finding does not hold true for high-SES patients and is not related to type of stressful life event. Thus, we conclude that environmental stressors frequently precede onset of positive symptoms of schizophrenia. This is only true for patients of low SES of origin. We hypothesize that low-SES patients have a heightened reactivity to stressors, a reactivity that is incubated by the human toll of impoverishment.

Key Words: Positive Symptoms, Schizophrenia, Life Stressors, Social Class

Introduction

The genesis of schizophrenia appears to be multifactorial and best explained by a holistic approach that accounts for the significance of interactions between biological underpinnings and psychosocial factors (1, 2). Both of these variables—biological and psychosocial factors—are thought to influence the onset and course of the psychosis (3, 4). This is the basic proposition of the diathesis-stress theory (5), a conceptual model that emphasizes the combined causal effects of a biological vulnerability to schizophrenia and environmental precipitants such as stressful life events (6-9). Life events are considered to "trigger" onset or exacerbation of the symptoms of schizophrenia (10-12).

The proposition that there is an excess of *major* life events preceding psychosis has been reported in a number of studies (13, 14, 6). Likewise, *minor* stressors and "daily hassles" may sometimes be a significant predictor of later psychotic symptoms (15-18). Additionally, research suggests that the typical timeframe for the initial episode of psychosis is during late adolescence or early adulthood (19). Adolescence has been recognized as a developmental period that places unique demands on social and psychological functioning (20-23) and is also correlated with biological changes including alteration in the structure and function of the brain (24-26). The impact of psychosocial stress during the developmental period marked by the maturation of neural networks may explain why schizophrenia typically presents

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Clinical Implications

We believe this study provides substantial evidence for a temporal association between low-socioeconomic status (SES) of origin, stressful life events, and onset of positive symptoms of schizophrenia. We also believe that low SES of origin at least partly explains a biological vulnerability to stress which is activated during late adolescence, the developmental period of elevated risk for the emergence of schizophrenia. This is not a "formula" which applies to all people born into poverty, but only to that subset who were exposed to serious life stressors.

In conclusion, there is a heightened likelihood of positive symptomatology among poor patients who experienced a stressful life event before symptoms onset. Our finding endorses the diathesis-stress theory, also known as the bio-psycho-social model (34). The stressful life event is considered to act as a trigger to a constitutional predisposition (diathesis) to schizophrenia. We hypothesize that a heightened reactivity to stressors is part of the core of the constitutional vulnerability of the diathesis-stress model. Consistent with other reports (40), we find that type of stressful event is not related to our central finding. The SES component of our finding connects with a number of possible risk factors, including diminished involvement of family members (84), fewer close and confiding relationships (6) and numerous stressful experiences in childhood and adulthood (58, 59).

during late adolescence. One research team characterizes the phenomenon as a process which moves "from childhood deviance to frank psychosis" (7, p. 132).

While some studies have established the *general* role of environmental factors in the onset of psychosis (6, 7, 27), other research has concentrated on the *type* of stressful events that elevate risk. Aside from childhood trauma, other stressful events include combat in war (28-30), sexual and physical assault (31-33) and extreme interpersonal conflict (34).

An overwhelming majority of studies that examine the connection between stressful life events and psychosis have concentrated specifically on schizophrenia. The early study by Brown and Birley (35) confirmed the connection between life crises and onset of schizophrenia. For decades, that study continued to be the primary source of evidence for the claimed connection. Many subsequent studies replicated the finding (8, 9, 36). On the other hand, a small number of studies failed to establish the consistency and validity of the original finding of Brown and Birley (37-39). However, a huge cross-national meta-analysis sponsored by WHO impressively concluded that socioenvironmental stressors often precipitate schizophrenic attacks (40). The role of stressful life events in the course of schizophrenia has many faces, including relapse (41, 42, 11, 43), as well as onset of initial symptomatology.

There are also some under researched variables that may connect with the influence of life stressors on onset of schizophrenia. One is type of symptomatology. Read et al. (34) report that childhood abuse is a causal factor for schizophrenia in general and, more specifically, for positive symptoms. Indeed, our own research in this area found that type of childhood stressor incubates the specific symptoms of schizophrenia (44). Others report that daily stressors and hassles later in life are independent predictors of positive symptoms (6, 45). Additionally, Tessner et al. (14) report that stressful life events during adolescence predict positive symptoms at onset.

Other studies on life stressors and symptomatology have produced mixed results. Although some report that higher levels of stress are associated with worse symptoms (8), assessments of symptom level in those studies are often ambiguous. The present study assesses severity according to *types* of symptoms: negative form and positive form. We employ standardized measures of both groups of symptoms. Negative symptomatology is a condition with poor prognosis and diminished responsiveness to medications (46-48). Some contend that negative symptoms have such poor outcome because they are linked with an abnormality in the physical structure of the brain (49, 50). This may explain why onset of illness is typically insidious for these patients (27). Positive symptoms are a domain of psychopathology within schizophrenia theoretically associated with a different etiology than negative symptoms. Indeed, since positive symptomatology is thought to be triggered by environmental stressors (51, 52), the division of symptoms into negative and positive categories provides a useful analytic framework for assessing the relative roles of diathesis and stress in the etiology of schizophrenia. Such is the case in the present study.

No discussion of the role of stress on mental health would be complete without including socioeconomic status (SES) of origin (53-56). Stress exposure and vulnerability to stress play a central role in sociological studies of SES differentials in mental health. An impressive amount of research has demonstrated that low SES of origin is a risk for a wide range of mental disorders in adults (12, 57). Researchers in this area theorize that the interconnections among SES, stress and mental health result from low-SES individuals shouldering a disproportionate number of stressful events in both

childhood and adulthood (58, 59).

Much of the research on SES and stress has concentrated on schizophrenia as the outcome variable (53). Those same studies report numerous stressful events experienced more frequently by impoverished people, including extreme negative exposures to violence, death of a close relative and parental substance abuse (60), among others. Parental neglect and lack of adequate supervision (56, 61) are also reported more frequently in low-SES families, as well as greater exposure to a range of environmental toxins (62). Other "mechanisms of harm" (63) connected to living in poverty are chaotic surroundings inside and outside the home, few material and psychosocial investments to stimulate development, overcrowding, noise, substandard housing conditions, persistent "daily hassles" (58) and diminished prenatal/overall healthcare (64). Although this is probably only a partial list, it clearly demonstrates an elevated risk for exposure to stressors (65) among impoverished individuals compared to their nonpoor counterparts. The sheer quantity and severity of these stressful life events supports an extensive empirical and theoretical literature on the "psychological costs of growing up poor" (63). For these reasons, SES is a key variable in the present study about the mental health effects of stress.

Numerous researchers are calling for studies that give greater detail to the interaction between socioenvironmental stressors and other causal agents of schizophrenia (9, 40). This can allow for a fuller understanding of the specific effects of stress on the development of the psychosis (14, 36, 57). John Read (59) makes an especially compelling case to include poverty in future studies because of the many disadvantages and adverse life events associated with being poor. Our study is a response to the call by others to examine some of these under researched needs. We test to see if stressful life events precede specific symptoms of schizophrenia. The analyses also extend to possible variation by SES of origin. Specifically, we hypothesize that there is an elevated risk for positive symptomatology among low-SES patients who experienced a stressful life event prior to symptom onset. *To date, no published report has tested for this particular association.*

Methods and Subjects

Patients

Data for this study are taken from the cumulative anonymous medical records of 431 schizophrenic patients discharged from Norristown State Hospital (NSH) in Pennsylvania, USA, between 1984 and 1990. Diagnostic procedures employed multidisciplinary evaluations with periodic review. Specific criteria for index diagnosis were based on the *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition* (66).

Upon admission, patients were evaluated by staff psychiatrists and other members of a multidisciplinary team within 48 hours for diagnosis and treatment plan purposes. Later diagnostic reviews were conducted for each patient every three months or as needed during hospitalization. Since some patients were discharged and readmitted over time, we employed a combination of three NSH operational measures to enhance longitudinal analysis of symptom stability. The measures include clinical assessments by NSH staff at intake and during last hospital stay, as well as *DSM* diagnosis at last discharge.

Clinical Assessments

In addition to diagnosis by *DSM* standards, NSH staff professionals further categorized patients into negative and positive subtypes as described above (67). Chart materials with detailed patient symptomatology enhanced subtyping in this study. A number of positive and negative scales have been retrospectively applied from chart materials in addition to subtyping drawn from patient files. They include the Scale for the Assessment of Negative Symptoms (SANS) (68), the Scale for the Assessment of Positive Symptoms (SAPS) (68), and the Positive and Negative Syndrome Scale (PANSS) (69).

Although some may question the validity and reliability of chart-based assessments of negative and positive symptoms, we do not think these are serious problems in this study. It was standard procedure at NSH to require that interview observation of the patient be completely and directly recorded onto the charts. NSH staff professionals solely conducted the clinical assessments. We retrospectively applied the identical assessments to our sample. Both the original assessments at NSH and our replication of those assessments were conducted independently of patient history of stressful life event(s). It has been documented that the retrospective applications of the SANS, SAPS and PANSS can be completed based on chart materials if the latter are sufficiently detailed (69, 70). Such was the case in the present study.

One of the issues we faced was how to deal with diagnoses that changed over time. This proved to be a minor problem since this type of discrepancy rarely occurred and, when it did occur, we simply eliminated the case from the sample. Thus, as stated above, diagnosis was operationalized from three temporal sources: clinical assessment at first intake, during last hospital stay and *DSM* diagnosis at last discharge. The temporal points of these measurements not only permit the observation of symptom stability over time, but also reflect reports that schizophrenic patients who show *persistent* positive or negative symptoms are important subgroups within the overall schizophrenic population (71).

Negative/positive assessments were conducted by three independent raters who are experts in the field. Consensus was reached on the classification of all included cases. Thus, interrater reliability is one hundred percent because, in the rare instances where there was disagreement, the cases were dropped. The end result is that the sample only includes patients who clearly presented as negative or positive and were *known* to have/have not been exposed to a stressful life event before symptom onset. No evidence of extrapyramidal complications is present.

SES Classification

Epidemiological analyses of SES and risk of schizophrenia are often confounded by the "social stress" versus "social drift" controversy. This study is not compromised by that debate, since SES is only assessed at the time of patients' births. This provides a direct measure of a potential risk factor connected to SES of family of origin (72).

Information about the SES of the patients is contained in the "social history" section of their hospital records. The social history typically includes detailed accounts of the family into which the patient was born. The histories were compiled at intake by psychiatric social workers from personal interviews with first-degree relatives. These verbal accounts often provide specific information about SES, such as the occupation, income status and level of education of family head(s).

Researchers using occupational scales to rate SES frequently dichotomize social class into higher and lower class groups (73, 74). Consistently, our sample is bifurcated into low-SES and high-SES categories at the time of the patient's birth. SES classification was facilitated by the application of the Occupational Distributions of the U.S. Bureau of the Census (75). This classification scheme is comprehensive and also temporally matches the time span of our data set. Whenever nonoccupational information was available in the social histories (e.g., "the family was well-off financially"), it was used to facilitate the dichotomous classification. Low SES includes the indigent, the unemployed and unskilled laborers; high SES generally consists of skilled laborers and above. Thus, the final sample is comprised of 431 cases that have been carefully delineated by both schizophrenic subtype and SES as described above.

Assessments of Stressful Life Event

Consistent with the literature (6), we define stressful life events as stress-inducing changes that may occur outside the individual's control (such as death of a loved one), as well as those that may be influenced by the person's own actions (such as divorce). Our information bank did not definitively allow us to distinguish between those events that were out of the patients' control and those events that could be a consequence of patients' behavior. Some of the "content areas" of life-event classifications of other studies (14, 40, 76) were only roughly related to the stressful life events in our patient sample. Others utilized "event domains," which more closely paralleled our patients' life events (10, 36, 77). Relevant domains from other studies were combined with new domains found in our patient sample to create the classification system below.

We collapsed life-event stressors into four groups: social networks, health, military and other. The social networks domain includes such stressors as death of a loved one, marital disruption and social rejection. Health-related stressors include physical trauma, illness, drug abuse and surgery. The military domain includes adjustment problems and combat. No patients comorbid with posttraumatic stress disorder were included in the military domain. The "other" category includes (but is not limited to) incarceration and loss of job. In our total sample of 431 patients, 78 patients had experienced one or more life-event stressors. The specific breakdown of the frequency and type of life-event stressors is displayed in Table I. Note that social network events comprise the largest domain of stressors in our patient sample. Also note that we discovered it is not unusual for patients to have encountered more than one type of life-event stressor prior to the onset of schizophrenia. This occurred in 41% of our patients who had undergone life-event stressors.

Table 1 Type, Frequency and Percentage Breakdown of Life-Event Stressors

Type of Stressor	Frequency*	Percentage
Social networks	55	48.7%
Health	35	31.0%
Military	10	11.5%
Other	10	8.8%

*Note: frequency includes total number of life-event stressors. Almost half of the patient sample who had undergone life-event stressors experienced multiple stressors.

Advantages and Limitations of Study Measures

Many analyses of risk for schizophrenia fail to specify diagnoses. Some simply refer to schizophrenia as a general condition. Others clump all of the forms of schizophrenia spectrum disorders into one category. A significant (and unique) strength of the present study is that it measures

schizophrenia by subtype and examines for changing symptomatology over time. Another strength of our study is consistent with similar studies of life events since all interviews were undertaken with key informants and checked whenever feasible against the patients' recollections. Prior studies indicate that key informants are valuable sources of supplementary data, adding substantially to the information in the patients' own life-event reports (40).

The data set employed in this study has shortcomings. Detailed information was available to separate patients into negative/positive categories and to eliminate cases with mixed symptomatology. However, sample size attrition (approximately 10%) occurred by excluding cases with insufficient specifications for valid SES classification. Further limitations include the lack of precise time between life stressor and symptom onset (6), the usual problems of recall bias associated with retrospective research (9) and measuring "stress" solely through the "life-events" approach (6). We also could not definitively distinguish between those events that were out of the patients' control and those events that could result from patients' behavior. Additionally, our data set only includes patients from a single state mental hospital in the northeastern United States. Consequently, the cross-cultural and national representativeness of the sample (n=431) cannot be exhaustively tested.

Statistical Analyses

The analytical model built to test the hypothesis is straight forward: the presence/absence of a stressful life event (SLE) is cross tabulated by positive/negative symptomatology. The only complication involves SES, which is readily addressed by creating separate tables for low-SES and high-SES patients. The chi-square statistic serves as the direct test of significance for each cross tabulation.

Results

Table 2 examines the relationship between SLE and symptomatology for low-SES patients. As the literature would suggest, there is an overall preponderance of positive symptoms, but the distribution is not uniform. Note that 63.6% of patients in the "No evidence of SLE" row exhibit positive symptoms; this swells to 81.8% in the bottom row for those who had experienced such an event. Consistently, there is a decrease in negative symptoms for those who had experienced an SLE. The elevated presence of positive symptomatology among low-SES SLE patients tests out as statistically significant with an X^2 value of 5.418, p=.020.

In Table 3, this effect literally disappears. The top and bottom rows are virtually identical in distribution, with a net change of only 2.9%. Consistently, the chi-square value for the high-SES table is 0.123, p=n.s.

Table 2 Cross Tabulation of Evidence/No Evidence of SLE by Positive/Negative Symptoms for Low-SES Patients

	Symptoms	
	Positive	Negative
No Evidence of SLE	133 (63.6%)	76 (36.4%)
Evidence of SLE	36 (81.8%)	8 (18.2%)

n=253

Table 3 Cross Tabulation of Evidence/No Evidence of SLE by Positive/Negative Symptoms for High-SES Patients

	Symptoms	
	Positive	Negative
No Evidence of SLE	110 (76.4%)	34 (23.6%)
Evidence of SLE	25 (73.5%)	9 (26.5%)

n=178

This SES-specified result is as straightforward as the analytical model: for patients from low-SES families of origin, the incidence of an SLE significantly elevates the likelihood of positive symptoms; for high-SES patients, it simply does not. Additionally, chi-square tests (not shown) indicate that type of SLE is not significantly related to the central finding.

Discussion and Conclusion

The central finding of our study is that positive symptoms of schizophrenia are preceeded by a stressful life event, and this connection is concentrated among those from low SES of origin. This is consistent with the diathesis-stress theory of schizophrenia in *general*, as well as the *specific* theory that positive symptoms are triggered by a life stressor. There are numerous explanations for our finding, including the proposition that individuals with schizophrenia have stress-prone lifestyles with limited social support networks, diminished coping abilities, and SES deprivation. All of these may lead to a heightened responsivity to stress (10, 78).

Where does the heightened responsivity to stress originate? Our recent research indicates that it starts in childhood through exposure to a host of harmful experiences such as abuse and neglect (44). Others agree that it begins quite far back in time (13) and, consistent with our findings (44), the "active" forms of child abuse (physical, sexual, emotional

and/or verbal) are causal factors for positive symptoms of schizophrenia (34). Thus, subsequent stressful life events may reactivate a hypervigilance to threats experienced in childhood. Some studies suggest that the resultant increased sensitivity to stress may be a vulnerability marker for schizophrenia through psychological *and* biological pathways (52, 79).

The specific pathways through which early exposure to psychosocial stressors may ultimately result in greater biological vulnerability to stress are not fully understood (10). It is known, however, that abnormalities are found in the brains of children traumatized early in life (59). Specifically, chronic stress exposure during childhood is reported to lead to long-term dysfunction in neurological stress responses, resulting in exceptional risk for the development of serious mental illness (63). While a disturbed neural circuitry determines how an individual reacts to stress, the instrumental brain systems of this circuitry are not clearly identified. McEwen and Gianoros (80) report that the hippocampus, amygdale and areas of the prefrontal cortex are involved. Others report that the "stress cascade" connects with biochemical abnormalities such as glucocorticoid elevation (81). Hopefully, future research in neuropsychiatry will lead to a specific model of interaction between early stress and biological vulnerability to later stressful life events (9).

The low-SES component of our finding logically fits with the concept of "greater biological vulnerability to stress" discussed above. Given the extensive literature on the psychological costs of growing up poor, there is undoubtedly more stress imposed on children born into impoverished households. One research team (57) reports that chronic experience of discrimination biologically facilitates a paranoid (positive symptom) attributional style. Consistently, others find that persons of low SES are more strongly affected emotionally by undesirable life events than their higher status counterparts (82), and that this connects with impairments in the functionality of stress regulatory systems in the brain (80). Indeed, persistent poverty is reported by The Institute for Research on Poverty to affect the neurobiological circuits in children that are activated in response to stress and adversity (83).

To summarize briefly, we believe that this study provides substantial evidence for a temporal association between low SES of origin, stressful life events, and onset of positive symptoms of schizophrenia. We also believe that low SES of origin at least partly explains a biological vulnerability to stress which is activated during late adolescence, the developmental period of elevated risk for the emergence of schizophrenia. This is not a "formula" which applies to all people born into poverty, but only to that subset who were exposed to serious life stressors.

In conclusion, there is a heightened likelihood of positive symptomatology among poor patients who experienced a stressful life event before symptoms onset. Our finding endorses the diathesis-stress theory, also known as the bio-psycho-social model (34). The stressful life event is considered to act as a trigger to a constitutional predisposition (diathesis) to schizophrenia. We hypothesize that a heightened reactivity to stressors is part of the core of the constitutional vulnerability of the diathesis-stress model. Consistent with other reports (40), we find that type of stressful event is not related to our central finding. The SES component of our finding connects with a number of possible risk factors, including diminished involvement of family members (84), fewer close and confiding relationships (6) and numerous stressful experiences in childhood and adulthood (58, 59).

Our study has a number of limitations, including sample size attrition and recall bias. We also lack information on exact time between life stressors and symptom onset, making it difficult to discern whether the stressful life event was possibly a result of increasing symptoms. On a related note, other studies report that recent stressful events play a precipitating role rather than a formative one (85). Our finding would be further informed by future research examining the interaction between the timing of life stressors, symptom onset, and relapse, as well as analyses that test for cross-cultural differences.

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References

1. Andreasen NC. Understanding the causes of schizophrenia. N Engl J Med 1999;340(8):645-647.
2. Keltner NL, James CA, Darling RJ, Findley LS, Oliver K. Nature vs. nurture: two brothers with schizophrenia. Perspect Psychiatr Care 2001;37(3):86-94.
3. Bentall RP, Corcoran R, Howard R, Blackwood N, Kinderman P. Persecutory delusions: a review and theoretical integration. Clin Psychol Rev 2001;21(8):1143-1192.
4. Kinderman P. A psychological model of mental disorder. Harv Rev Psychiatry 2005;13(4):206-217.
5. Gottesman II, Shields J. A critical review of recent adoption, twin and family studies of schizophrenia: behavioral genetics perspectives. Schizophr Bull 1976;2(3):360-401.
6. Phillips LJ, Francey SM, Edwards J, McMurray N. Stress and psychosis: to-

wards the development of new models of investigation. Clin Psychol Rev 2007;27(3):307-317.

7. McDonald C, Murray RM. Early and late environmental risk factors for schizophrenia. Brain Res Brain Res Rev 2000;31(2-3):130-137.
8. Norman RM, Malla AK. Stressful life events and schizophrenia. I: A review of the research. Br J Psychiatry 1993;162:161-166.
9. Norman RM, Malla AK. Stressful life events and schizophrenia. II: Conceptual and methodological issues. Br J Psychiatry 1993;162:166-174.
10. 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. Schizophr Res 2005;75(2-3):363-374.
11. Hultman CM, Wieselgren IM, Ohman A. Relationships between social support, social coping and life events in the relapse of schizophrenic patients. Scand J Psychol 1997;38(1):3-13.
12. Cohen P, Chen H, Gordon K, Johnson J, Brook J, Kasen S. Socioeconomic background and the developmental course of schizotypal and borderline personality disorder symptoms. Dev Psychopathol 2008;20(2):633-650.
13. Bebbington P, Wilkins S, Jones P, Foerster A, Murray R, Toone B, et al. Life events and psychosis. Initial results from the Camberwell Collaborative Psychosis Study. Br J Psychiatry 1993;162:72-79.
14. Tessner KD, Mittal V, Walker EF. Longitudinal study of stressful life events and daily stressors among adolescents at high risk for psychotic disorders. Schizophr Bull 2011;37(2):432-441.
15. Brown GW, Birley JL. Crises and life changes and the onset of schizophrenia. J Health Soc Behav 1968;9(3):203-214.
16. Malla AK, Norman RM. Relationship of major life events and daily stressors to symptomatology in schizophrenia. J Nerv Ment Dis 1992;180(10):664-667.
17. Monroe SM, Bellack AS, Hersen M, Himmelhoch J. Life events, symptom course, and treatment outcome in unipolar depressed women. J Consult Clin Psychol 1983;51(4):604-615.
18. Monroe SM, Imhoff DF, Wise BD, Harris JE. Prediction of psychological symptoms under high-risk psychosocial circumstances: life events, social support, and symptom specificity. J Abnorm Psychol 1983;92(3):338-350.
19. Jablensky A. Prevalence and incidence of schizophrenia spectrum disorders: implications for prevention. Aust N Z J Psychiatry 2000;34 Suppl:S26-S34.
20. Compas BE. Stress and life events during childhood and adolescence. Clin Psychol Rev 1987;7:275-302.
21. Goodyer IM. The depressed child and adolescent. 2nd ed. New York: Cambridge University Press; 2001.
22. Goodyer IM, Herbert J, Tamplin A, Altham PM. Recent life events, cortisol, dehydroepiandrosterone and the onset of major depression in high-risk adolescents. Br J Psychiatry 2000;177:499-504.
23. Goodyer IM, Herbert J, Tamplin A, Altham PM. First-episode major depression in adolescents. Affective, cognitive and endocrine characteristics of risk status and predictors of onset. Br J Psychiatry 2000;176:142-149.
24. Ebling FJ. The neuroendocrine timing of puberty. Reproduction 2005;129(6):675-683.
25. Giedd JN, Blumenthal J, Jeffries NO, Castellanos FX, Liu H, Zijdenbos A, et al. Brain development during childhood and adolescence: a longitudinal MRI study. Nat Neurosci 1999;2(10):861-863.
26. Sowell ER, Thompson PM, Tessner KD, Toga AW. Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: inverse relationships during postadolescent brain maturation. J Neurosci 2001;21(22):8819-8829.
27. Van Os J, Jones P, Sham P, Bebbington P, Murray RM. Risk factors for onset and persistence of psychosis. Soc Psychiatry Psychiatr Epidemiol 1998;33(12):596-605.
28. Butler RW, Mueser KT, Sprock J, Braff DL. Positive symptoms of psychosis in posttraumatic stress disorder. Biol Psychiatry 1996;39(10):839-844.
29. Sautter FJ, Brailey K, Unno MM, Hamilton MF, Beard MG, Borges AH. PTSD and comorbid psychotic disorder: comparison with veterans diagnosed with PTSD or psychotic disorder. J Trauma Stress 1999;12(1):73-88.
30. Steinberg HR, Durrell J. A stressful social situation as a precipitant of schizophrenic symptoms: an epidemiological study. Br J Psychiatry 1968;114(514):1097-1105.
31. Cascardi M, Mueser KT, DeGiralomo J, Murrin M. Physical aggression against psychiatric inpatients by family members and partners. Psychiatr Serv 1996;47(5):531-533.
32. Davidson J, McNamara L. Systems that silence. In: Breckenridge J, Laing L, editors. Challenging silence: innovative responses to sexual and domestic violence. Sydney: Allen and Unwin; 1999. p. 35-48.
33. Ritsher JE, Coursey RD, Farrell EW. A survey on issues in the lives of women with severe mental illness. Psychiatr Serv 1997;48(10):1273-1282.
34. Read J, van Os J, Morrison AP, Ross CA. Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. Acta Psychiatr Scand 2005;112(5):330-350.
35. Brown GW, Birley JL. Crises and life changes and the onset of schizophrenia. J Health Soc Behav 1968;9(3):203-214.
36. Castine MR, Meador-Woodruff JH, Dalack GW. The role of life events in onset and recurrent episodes of schizophrenia and schizoaffective disorder. J Psychiatr Res 1998;32(5):283-288.
37. Chung RK, Langeluddecke P, Tennant C. Threatening life events in the onset of schizophrenia, schizophreniform psychosis and hypomania. Br J Psychiatry 1986;148:680-685.
38. Gruen R, Baron M. Stressful life events and schizophrenia. Relation to illness onset and family history. Neuropsychobiology 1984;12(4):206-208.
39. Malzacher M, Mertz J, Ebonther D. [Einscheidende lebenssereignisse im vorfeld akuter schizophrener episoden.] German. Arch Psychiatr Nervenkrankh 1981;230:227-242.
40. Day R, Nielsen JA, Korten A, Ernberg G, Dube KC, Gebhart J, et al. Stressful life events preceding the acute onset of schizophrenia: a cross-national study from the World Health Organization. Cult Med Psychiatry 1987;11(2):123-205.
41. Malla AK, Cortese L, Shaw TS, Ginsberg B. Life events and relapse in schizophrenia. A one year prospective study. Soc Psychiatry Psychiatr Epidemiol 1990;25(4):221-224.
42. Ventura J, Nuechterlein KH, Lukoff D, Hardesty JP. A prospective study of stressful life events and schizophrenic relapse. J Abnorm Psychol 1989;98(4):407-411.
42. Nuechterlein KH, Dawson ME, Ventura J, Gitlin M, Subotnik KL, Snyder KS, et al. The vulnerability/stress model of schizophrenic relapse: a longitudinal study. Acta Psychiatr Scand Suppl 1994;382:58-64.
44. Gallagher BJ 3rd, Jones BJ. Childhood stressors and symptoms of schizophrenia. Clin Schizophr Relat Psychoses 2013;7(3):124-130.
45. Norman RM, Malla AK. A prospective study of daily stressors and symptomatology in schizophrenic patients. Soc Psychiatry Psychiatr Epidemiol 1994;29(6):244-249.
46. Gallagher BJ 3rd, Jones BJ, McFalls JA Jr, Pisa AM. Schizophrenic subtype, seasonality of birth and social class: a preliminary analysis. Eur Psychiatry 2007;22(2):123-128.
47. Edwards J, McGorry PD, Waddell FM, Harrigan SM. Enduring negative symptom in first-episode psychosis: comparison of six methods using follow-up data. Schizophr Res 1999;40(2):147-158.
48. Malla AK, Norman RM, Takhar J, Manchanda R, Townsend L, Scholten D, et al. Can patients at risk for persistent negative symptoms be identified during their first episode of psychosis? J Nerv Ment Dis 2004;192(7):455-463.
49. Nasrallah HA, Weinberger DR. Neurology of schizophrenia. In: Nasrallah

HA, Weinberger DR, editors. Handbook of schizophrenia: I. Amsterdam: Elsevier; 1990.

50. Andreasen NC, Arndt A, Alliger R, Miller D, Flaum M. Symptoms of schizophrenia. Methods, meaning and mechanisms. Arch Gen Psychiatry 1995;52(5):341-351.
51. Fenton WS, McGlashan TH. Antecedents, symptom progression, and long-term outcome of the deficit syndrome in schizophrenia. Am J Psychiatry 1994;151(3):351-356.
52. Pallanti S, Quercioli L, Pazzagli A. Relapse in young paranoid schizophrenic patients: a prospective study of stressful life events, P300 measures, and coping. Am J Psychiatry 1997;154(6):792-798.
53. Gallagher BJ 3rd, Jones BJ, McFalls JA Jr, Pisa AM. Social class and type of schizophrenia. Eur Psychiatry 2006;21(4):233-237.
54. Brown AS, Susser ES, Jandorf L, Bromet EJ. Social class of origin and cardinal symptoms of schizophrenic disorders over the early illness course. Soc Psychiatry Psychiatr Epidemiol 2000;35(2):53-60.
55. Werner S, Malaspina D, Rabinowitz J. Socioeconomic status at birth is associated with risk of schizophrenia: population-based multilevel study. Schizophr Bull 2007;33(6):1373-1378.
56. Harrison G, Gunnell D, Glazebrook C, Page K, Kwiecinski R. Association between schizophrenia and social inequality at birth: case-control study. Br J Psychiatry 2001;179:346-350.
57. van Os J, Krabbendam L, Myin-Germeys I, Delespaul P. The schizophrenia envirome. Curr Opin Psychiatry 2005;18(2):141-145.
58. Grzywacz JG, Almeida DM, Neupert SD, Ettner SL. Socioeconomic status and health: a micro-level analysis of exposure and vulnerability to daily stressors. J Health Soc Behav 2004;45(1):1-16.
59. Read J. Can poverty drive you mad? 'Schizophrenia,' socio-economic status and the case for primary prevention. New Zealand Journal of Psychology 2010;39(2):7-19
60. Parke RS, Clarke Stewart KA. Effects of parental incarceration on children: perspectives, promises and policies. In: Travis J, Waul M, Solomon A, editors. From prison to home. Washington, DC: Urban Institute Press; 2003. p. 189-232.
61. Serbin LA, Karp J. The intergenerational transfer of psychosocial risk: mediators of vulnerability and resilience. Annu Rev Psychol 2004;55:333-363.
62. Schell LM. Culture as stressor: a revised model of bicultural intersection. Am J Phys Anthropol 1997;102(1):67-77.
63. Dearing E. Psychological costs of growing up poor. Ann N Y Acad Sci 2008;1136:324-332.
64. Gallagher BJ 3rd, Jones BJ, McFalls JA Jr, Pisa AM. Schizophrenic subtype, seasonality of birth and social class: a preliminary analysis. Eur Psychiatry 2007;22(2):123-128.
65. Evans GW, English K. The environment of poverty: multiple stressor exposure, psychophysiological stress, and socioemotional adjustment. Child Dev 2002;73(4):1238-1248.
66. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Third Edition. Washington, DC: American Psychiatric Association; 1987.
67. Carpenter WT Jr. The deficit syndrome. Am J Psychiatry 1994;151(3):327-329.
68. Andreasen NC, Olsen S. Negative vs. positive schizophrenia. Definition and validation. Arch Gen Psychiatry 1982;29(7):789-794.
69. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13(2):261-276.
70. Fenton WS, McGlashan TH, Victor BJ, Blyer CR. Symptoms, subtype, and suicidality in patients with schizophrenia spectrum disorders. Am J Psychiatry 1997;154(2):199-204.
71. Malla AK, Norman RM, Takhar J, Manchanda R, Townsend L, Scholten D, et al. Can patients at risk for persistent negative symptoms be identified during their first episode of psychosis? J Nerv Ment Dis 2004;192(7):455-463.
72. Bresnahan M, Susser E. Investigating socioenvironmental influences in schizophrenia: conceptual and design issues. In: Murray RM, Jones PB, Susser E, van Os J, Cannon M, editors. The epidemiology of schizophrenia. New York: Cambridge University Press; 2003. p. 5-17.
73. Brown AS, Susser ES, Jandorf L, Bromet EJ. Social class of origin and cardinal symptoms of schizophrenic disorders over the early illness course. Soc Psychiatry Psychiatr Epidemiol 2000;35(2):53-60.
74. Hollingshead AB. Four factor index of social position. New Haven: Yale University Press; 1975.
75. Census of Population. Classified index of industries and occupations. Washington, DC: U.S. Government Printing Office; 1971.
76. Phillips LJ, Edwards J, McMurray N, Francey S. Comparison of experiences of stress and coping between young people at risk of psychosis and a non-clinical cohort. Behav Cogn Psychother 2011;40(1):69-88.
77. Paykel ES, Prusoff BA, Uhlenhuth EH. Scaling of life events. Arch Gen Psychiatry 1971;25(4):340-347.
78. Myin-Germeys I, van Os J, Schwartz JE, Stone AA, Delespaul PA. Emotional reactivity to daily life stress in psychosis. Arch Gen Psychiatry 2001;58(12):1137-1144.
79. Myin-Germeys I, van Os J. Stress-reactivity in psychosis: evidence for an affective pathway to psychosis. Clin Psychol Rev 2007;27(4):409-424.
80. McEwen BS, Gianaros PJ. Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. Ann N Y Acad Sci 2010;1186:190-222.
81. Corcoran C, Walker E, Huot R, Mittal V, Tessner K, Kestler L, et al. The stress cascade and schizophrenia: etiology and onset. Schizophr Bull 2003;29(4):671-692.
82. McLeod JD, Kessler RC. Socioeconomic status differences in vulnerability to undesirable life events. J Health Soc Behav 1990;31(2):162-172.
83. Boyce WT. Focus. Institute for Research on Poverty University of Wisconsin-Madison. 2012;29(1):1-6.
84. Erickson DH, Beiser M, Iacono WG, Fleming JA, Lin TY. The role of social relationships in the course of first-episode schizophrenia and affective psychosis. Am J Psychiatry 1989;146(11):1456-1461.
85. Jacobs S, Myers J. Recent life events and acute schizophrenic psychosis: a controlled study. J Nerv Ment Dis 1976;162(2):75-87.