Title

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Journal

The Journal of Clinical Psychiatry, 79(3)

ISSN

0160-6689

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Publication Date

2018-06-27

DOI

10.4088/jcp.17m11776

Peer reviewed

HHS Public Access

Author manuscript

J Clin Psychiatry. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

J Clin Psychiatry. 2018 ; 79(3): . doi:10.4088/JCP.17m11776.

Childhood Adversity and Schizophrenia: The Protective Role of Resilience in Mental and Physical Health, and Metabolic Markers

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Abstract

Objective: To determine the impact of childhood adversity and current (adulthood) resilience on mental and physical health and markers of metabolic function among adults with schizophrenia and non-psychiatric comparison participants (NCs).

Methods: We conducted a cross-sectional study of 114 participants with schizophrenia (DSM-*IV-TR* criteria) and 101 NCs aged 26–65 years during 2012–2017. Sociodemographic, clinical and laboratory measures were examined. Childhood Trauma Questionnaire (CTQ) was used to retrospectively assess emotional abuse/neglect, physical abuse/neglect and sexual abuse experienced during childhood. Connor-Davidson Resilience scale was employed to measure resilience.

Results: Persons with schizophrenia reported more severe childhood trauma, lower resilience, and worse mental and physical health; and had worse metabolic biomarker levels than NCs. Trauma severity correlated with worse depression in the NCs (r = 0.34), but not in the

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Contributors

Ellen E. Lee conducted literature reviews, data analyses, data interpretation, and manuscript preparation.
A'verria Sirkin Martin was involved in data collection and manuscript preparation.
Xin Tu was involved in data analyses and statistical modeling, data interpretation and manuscript preparation.
Barton W. Palmer was involved in data interpretation and manuscript preparation.
Dilip V. Jeste designed the study, obtained funding to support this work and was involved in data interpretation and manuscript preparation.

Conflicts of Interest

The authors declare no relevant conflicts of interest.

Potential conflicts of Interest:

The authors declare no financial or other relationship relevant to the subject of this article.

Previous presentations of this data: 2017 Childhood Adversity Symposium, University of California, San Diego

schizophrenia group (r = 0.02). In both groups, trauma severity was associated with worse physical well-being, higher fasting insulin levels and greater insulin resistance ($p \leq 0.02$). Notably, resilience appeared to counteract effects of trauma and diagnosis on mental and physical health. The schizophrenia subgroup with high resilience and severe trauma reported mental and physical well-being and had glycosylated hemoglobin levels and insulin resistance scores that were comparable to those of NCs with low resilience and severe trauma.

Conclusion: To our knowledge, this is the first study to quantitatively assess effects of both childhood trauma and resilience in schizophrenia on health, notably metabolic function. Interventions to bolster resilience in the general population and in people with schizophrenia may improve outcomes for those with a history of childhood adversity.

Keywords

Serious mental illness; childhood trauma; biomarkers; well-being; insulin resistance

Introduction

Childhood maltreatment has been linked to worse mental and physical health and premature mortality in the general population.[1–4] Afifi *et al.* reported that all types of childhood abuse were associated with physical illnesses, increased risk of obesity, and worse self-reported physical health in a nationwide Canadian study.[5] Even when accounting for sociodemographic variables, smoking and obesity, abuse was associated with a variety of physical illnesses including arthritis, cancer, stroke and back problems.

Several meta-analyses have shown that schizophrenia, a debilitating mental illness with prominent psychotic and negative symptoms, is strongly associated with childhood adversity, with a two to seven-fold higher prevalence of childhood abuse than in non-psychiatric comparison participants (NCs).[6–8] While there is no demonstrated causal link between trauma and psychosis,[8] childhood abuse appears to be associated with transition to psychosis[9] and is more prevalent among persons with psychotic disorders compared to those with mood or anxiety disorders.[10] Studies in people with schizophrenia and other serious mental illnesses consistently report that a history of childhood abuse is associated with poor outcomes, including: worse psychopathology,[11] worse social functioning,[12] treatment resistance,[13] and lower quality of life.[14] More specifically, childhood abuse is associated with positive symptoms[11, 15] while childhood neglect is associated with negative symptoms.[15]

Schizophrenia is also associated with increased physical morbidity and premature mortality, attributable to increased cardiovascular-related mortality, though the exact biological mechanisms are not clear.[16, 17] Metabolic dysfunction, a major risk factor for cardiovascular-related death, is more common in individuals with schizophrenia than in the general population: related in part to higher rates of smoking, sedentary behaviors, unhealthy diet, obesity, and long-term treatment with antipsychotic medications.[16, 18, 19] However, dysregulated glucose homeostasis,[20] an important component of metabolic dysfunction, has been observed even in antipsychotic-naïve, normal-weight, first-episode patients[21] and is more prevalent in individuals at elevated risk for schizophrenia.[19] This literature suggests

that while obesity and antipsychotic medications may contribute to metabolic dysfunction in persons with schizophrenia, there may be other contributing factors that are intrinsic to having schizophrenia that precede the cumulative metabolic burden of lifestyle behaviors.[22]

Childhood trauma itself may contribute to metabolic dysfunction in schizophrenia. One study in stable outpatients with schizophrenia (N = 62) found that overweight or obese participants had higher subscale scores of emotional abuse, emotional neglect, physical neglect and total Childhood Trauma Questionnaire (CTQ) scores.[23] Similarly, one study in non-obese first-episode schizophrenia participants with minimal antipsychotic exposure (N = 83) found that those with a history of childhood trauma (N = 33) had higher LDL cholesterol levels.[24] Another study in first-episode psychosis patients (N = 28) and NCs (N = 45) reported that patients with childhood maltreatment had higher body mass index (BMI) than NCs.[25] It has been reported that childhood adversity leads to neuroendocrine dysregulation and chronic inflammation, resulting in metabolic, endocrine and immune pathology.[26]

In contrast to the negative effects of trauma, resilience may positively impact health.[27] Psychological resilience is a moderately heritable (30–50%) and relatively stable trait characterized by "positive adaptation, or the ability to maintain or regain mental health, despite experiencing adversity.[28–31]" In physically ill patients and the general population, resilience is associated with medically desirable behaviors (e.g., adherence to self-care routines, psychiatric treatment, and exercise), and better health outcomes (e.g., better emotional health, less depression, less pain, better social functioning, less alcohol and illicit substance use, and better physical health.)[32–37] In fact, resilience may even impact longevity. In a community-dwelling population aged 65 years or older, higher resilience was associated with 35.3% lower mortality risk.[38] Of these studies, one used the 25-item CDRS,[32] 3 used the 10-item CDRS,[34–36] and one chose 7 culturally relevant items from the CDRS.[38] The others used the Resilience Scale [39, 40] or a proxy of resilience based on factors such as self-efficacy, self-esteem, self-mastery and optimism.[33, 37] Despite differences between these measures of resilience, all studies showed how psychological resilience improved mental health, physical health, and mortality. Although resilience may have a moderating effect on the deleterious impact of childhood trauma on health in people in schizophrenia, to our knowledge there have been no prior published studies examining that possibility. In the present study, we focus specifically on the role of resilience in tempering the effects of childhood adversity on mental health outcomes (e.g., mental well-being and perceived stress) and physical health outcomes (e.g., physical well-being, medical comorbidity, BMI, and metabolic biomarkers.)

In this investigation of persons with schizophrenia and NCs, the relationships between sociodemographic, psychopathological, mental and physical health variables, as well as metabolic biomarkers were analyzed to assess the association of childhood adversity with subsequent (adulthood) mental and physical health outcomes. Based on the findings of high prevalence of childhood adversity in persons with psychotic disorders, we hypothesized that persons with schizophrenia would have histories of worse childhood adversity than demographically comparable NCs. Additionally given the association between childhood trauma and worse psychopathology, social functioning and obesity, we hypothesized that

greater childhood adversity would be associated with worse mental and physical health as well as worse levels of metabolic biomarkers among people with schizophrenia and NCs, and with worse psychopathology in the persons with schizophrenia. Lastly, in light of the link observed between resilience and better health behaviors and longevity, we hypothesized that resilience would neutralize the impact of childhood adversity on mental and physical health, including metabolic biomarkers in both subject groups.

Methods

Study participants

Participants included 114 persons with schizophrenia and 101 NCs. Data for the present report were collected between 2012–2017 as part of a larger ongoing study of aging in schizophrenia. Details of the parent protocol and recruitment are available in Joseph *et al.*[41] Briefly, non-institutionalized persons with DSM-IV-TR diagnoses of schizophrenia or schizoaffective disorder and NCs ages 26 to 65 years were recruited from the greater San Diego area. Most participants have provided data to prior published reports[41–45] and data on resilience on a subset of these participants has been presented previously;[46] however, this is our first examination of childhood trauma in these participants.

The Structured Clinical Interview for the DSM-IV-TR (SCID) was used to determine schizophrenia or schizoaffective disorder diagnosis.[47] The Mini-International Neuropsychiatric Interview (MINI)[48] was used to screen NCs, who were excluded if they were found to have a past or present diagnosis of a major neuropsychiatric illness. Other exclusion criteria were: 1) other current DSM-*IV-TR* Axis I diagnoses; 2) alcohol or other non-tobacco substance abuse or dependence within 3 prior months; 3) diagnosis of dementia, intellectual disability disorder, or a major neurological disorder; 4) medical disorder affecting a subject's ability to complete study procedures. The subjects were recruited in age-bins to yield comparable numbers across the full age range, and recruitment of NCs was stratified by gender, relative to the schizophrenia group, to yield comparable proportions of men and women within each study group. The study protocol was approved by the UC San Diego Human Research Protections Program, and each participant provided written informed consent prior to participation.

Sociodemographic characteristics and psychopathology:

Trained study staff interviewed the participants and administered standardized assessments for: psychotic symptoms (Scales for the Assessment of Positive and Negative Symptoms,) depression (Calgary Depression Rating Scale for depression,) and anxiety (Brief Symptom Inventory Anxiety Scale).[49–53]

Mental health measures:

Resilience was determined with the 10-item self-report Connor-Davidson Resilience scale (CDRS), which evaluated hardiness ("ability to cope with change and adversity") and persistence ("putting forth one's best effort despite adverse circumstances.[54, 55]") The 10-item CDRS was derived from the original 25-item scale and has been found to have good reliability (Cronbach's alpha 0.85). Each item response is scored on a 5-point likert scale

ranging from (no true at all, rarely true, sometimes true, often true, and true nearly all of the time.) Two such items include “I believe I can achieve my goals, even if there are obstacles” and “Under pressure, I stay focused and think clearly.” Individuals report on how they have felt over the past month. Total scores range from 0 to 40, with higher scores reflecting greater resilience.

Other mental health variables included mental well-being (Short Form Health Survey – Mental) and perceived stress (Perceived stress scale).[56, 57] While resilience (as measured by CDRS) is a stable trait of hardiness/persistence, mental well-being (as measured by Short Form Health Survey – Mental) is an outcome state that can fluctuate. The scales have no overlapping items. Cognitive measures included overall severity of cognitive deficits (Modified Telephone Interview for Cognitive Status), and an executive functioning composite score (derived from selected subtests from the Delis-Kaplan Executive Function System.)[58–60]

Physical health measures:

Physical health variables included physical well-being (Short Form Health Survey - Physical) and medical co-morbidity (Cumulative Illness Rating Scale).[56, 61] Height and weight was measured using a standard scale and wall-affixed height scale. BMI was calculated from the subject’s height and weight.

Childhood Trauma Assessment

Study participants completed the CTQ, a 25-item scale comprised of five subscales that retrospectively assess emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse.[62] The CTQ has high internal consistency (Cronbach’s alpha 0.79–0.94) and good test-retest reliability over 2–6 month interval (intraclass correlation = 0.88). The CTQ has been used in a number of published studies[10, 63, 64] and has specified cut-off classifications to describe severity of trauma in each of the five subscales.[62, 63]

Each CTQ subscale has four severity classifications (None/Minimal, Low/Moderate, Moderate/Severe, Severe/Extreme). Based on these classifications, the severe trauma group was defined as having one or more CTQ subscale severity that was classified as Moderate/Severe or Severe/Extreme while the low trauma group was defined as having all CTQ subscales rated as either None/Minimal or Low/Moderate in severity.

Biomarker Assays:

All assays were processed from a baseline fasting blood draw of roughly 65 mL of blood.

Fasting serum insulin levels were processed at the UC San Diego Core lab using serum samples that were frozen at −80° C and assayed using standard methods in duplicate (Quantitative Chemiluminescent Immunoassay).

Fasting blood glucose and glycosylated hemoglobin assays were completed at the UC San Diego Hospital lab using standard laboratory assays. Glycosylated hemoglobin assays are a stable measure of insulin resistance, reflecting glucose homeostasis over the past 120 days.

Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values were calculated from the fasting plasma insulin and fasting plasma glucose measures using the following formula:[65]

HOMA-IR = [Fasting plasma insulin (mIU/L) * Fasting plasma glucose (mmol/L)]/ 22.5.

Statistical Analyses:

Variables were assessed for violation of distribution assumptions for inferential statistics and were log-transformed as necessary. Significance of differences between schizophrenia and NC groups were assessed with independent sample t-tests for continuous variables, and Pearson's Chi-square for categorical variables. The association of total CTQ score with measures of psychopathological variables, mental and physical health variables, and metabolic biomarkers was assessed within each diagnostic group using Spearman's rho. The null of common Spearman's correlation between the schizophrenia and NC groups was tested by comparing two independent Spearman's correlations.

General linear models were used to analyze the effects of trauma severity, subject group and resilience on mental and physical health measures and metabolic biomarker levels. We limited the analyses to the outcome variables that were highlighted in the literature (mental well-being, physical well-being, BMI, glycosylated hemoglobin and HOMA-IR.) Model 1 included subject group (NC vs. schizophrenia), trauma severity (CTQ total score), and group x trauma severity interaction. Model 2 included subject group (NC vs. schizophrenia), trauma severity (CTQ total score), resilience (CDRS score), group x trauma severity interaction and group x resilience interaction. We also ran two additional models: Model 3 included the subject group, trauma, resilience, group x trauma, group x resilience, and trauma x resilience interactions; Model 4 included subject group, trauma, resilience, group x trauma, group x resilience, trauma x resilience, and group x trauma x resilience interactions. The additional interactions in Model 3 and 4 were not significant, so these interactions were not reported in the table. We used linear contrast tests and *post hoc* independent samples t-tests to compare multiple mental and physical health measures between subgroups with varying trauma severity and resilience levels. Resilience levels were described by tertiles, similar to several published studies on resilience and trauma.[34–36]

Statistical significance was defined as $p < 0.05$ (two-tailed). In addition, we calculated the effect sizes and interpreted those with medium or larger effect sizes (i.e., Cohen's $d \geq 0.5$ or $r \geq .30$) as clinically meaningful.

Results

Comparison of NC and schizophrenia group means and proportions:

The schizophrenia and NC groups were comparable on age, gender, and race/ethnicity (see Table 1.) The schizophrenia group had less education, more depression, worse self-reported mental well-being, worse cognition, worse physical well-being, higher BMI, and worse biomarkers of metabolic function (insulin, glucose, glycosylated hemoglobin, HOMA-IR). Additionally, the schizophrenia group had significantly higher rates of childhood trauma than NCs across all the CTQ subscales.

Bivariate correlations of childhood trauma with other characteristics:

The Spearman rho correlations between severity of childhood adversity (CTQ total score) with sociodemographic, psychopathological and mental health variables only differed significantly on depressive symptoms and overall cognitive dysfunction between the NC and schizophrenia groups (Table 2). While CTQ total score was significantly correlated with depressive symptoms, worse mental well-being and perceived stress in the NC group, such relationships were not seen in the schizophrenia group. In both groups, CTQ total scores were significantly associated with physical well-being, fasting insulin and HOMA-IR. Correlations with physical health and biomarkers did not differ between the participant groups.

Comparison of low, moderate, and high resilience groups:

Within the NC and schizophrenia groups, those in high resilience tertile had better mental well-being, regardless of trauma severity, compared to those with moderate or low resilience (see Figure 1a.) Significant differences in mental well-being were observed between the lowest and highest resilience tertiles in the NC group and between all tertiles in the Schizophrenia group. Results of a general linear model showed that resilience and subject group contributed significantly to mental well-being (R-squared = 0.45; Table 3.) The schizophrenia subgroup with high resilience and severe trauma had mental well-being scores that were comparable to or better than those of NCs with low resilience and severe trauma ($t(28) = 0.28$, $p = 0.8$, $d = 0.1$.)

Similarly, high resilience was associated with improved physical well-being and metabolic biomarkers, including glycosylated hemoglobin (see Figure 1b.) While significant differences in glycosylated hemoglobin levels were noted between the lowest and other resilience tertiles in the NC group ($p = 0.001$ and $p = 0.008$), no significant differences were seen among the schizophrenia subgroups ($p > 0.10$.) The general linear models showed the resilience contributed significantly to the outcomes of physical well-being (R-squared = 0.25), glycosylated hemoglobin (R-squared = 0.10) and HOMA-IR (R-squared = 0.20), but not BMI. Of note, unlike with mental well-being, subject group did not have a significant main effect on the physical health outcomes, which may reflect the importance of trauma history and resilience on physical health, regardless of serious mental illness. Persons with schizophrenia who had high resilience and severe trauma had comparable or better physical health as NCs with low resilience and severe trauma across a number of measures: physical well-being ($t(28) = 0.11$, $p = 0.91$, $d = 0.04$), glycosylated hemoglobin ($t(28) = 1.07$, $p = 0.29$, $d = 0.42$), and HOMA-IR ($t(27) = 0.77$, $p = 0.45$, $d = 0.32$.)

Discussion

Consistent with our *a priori* hypotheses, relative to NCs, people with schizophrenia reported significantly more childhood emotional abuse/neglect, physical abuse/neglect and sexual abuse. In the NC group, such childhood trauma was associated with worse mental and physical health; however in the schizophrenia group, childhood adversity was associated with worse physical, but not mental, health. Resilience was associated with significantly

better mental and physical health outcomes and metabolic biomarkers, regardless of trauma severity.

Overall, the higher prevalence and severity of childhood trauma among persons with schizophrenia compared to NCs was consistent with the literature.[6–8] The values of CTQ total and subscale scores in our study were comparable to those reported in investigations of schizophrenia and NC groups.[14, 63, 64]

In contrast to some published studies,[11, 14] trauma was not consistently associated with worse psychopathology or mental health across a variety of measures in the schizophrenia group. The lack of a significant association between childhood trauma and worse mental well-being in the schizophrenia group could be related to a longer average duration of illness in our participants relative to the Andrianarisoa *et al.*[14] and van Dam *et al.*[11] samples. Illness-related stigma and other stresses over a long period of time may contribute to current psychopathology and mental health, independently of childhood adversity. Other differences include the van Dam *et al.* sample's inclusion of in-patients and the use of different scales to assess psychopathology and quality of life, thus making direct comparisons not possible. It may be noted, however, that in retrospect the lack of such an association in the context of schizophrenia is not counterintuitive. People with schizophrenia have a neurodevelopmental disorder that strongly influences the expression of psychopathologic symptoms. Moreover, there is substantial heterogeneity among people with schizophrenia in terms of the severity and pattern of brain-based impairment. In that context, the negative effects of childhood trauma on psychopathology may be less salient in people with schizophrenia, given the many other competing factors (i.e. genetic factors, medication adherence).

Our study has several limitations. The cross-sectional design of our study limits the ability to make causal inferences between clinical variables, including resilience, assessed in the present with retrospective reports of childhood adversity. In this sample with average age 48 years, the childhood adversity may have occurred many years ago. Despite the absence of a significant effect of childhood adversity found in this study, childhood adversity has been consistently shown to have important effects on symptoms and functioning in persons with psychotic disorders and the general public. A prospective study is needed to assess whether resilience mitigates the damaging effects of childhood adversity. A recent review found no clear "gold standard" among the 14+ resilience scales.[66] Self-reported CDRS scores may be subject to social desirability bias among the participants. There may be drawbacks of the CTQ compared to clinical interviews or longer scales such as the Life Experiences Questionnaire that might collect more detailed information about the trauma history. This study used the CTQ as it was well-validated, well-studied, easy to administer, and correlated well with qualitative interview and corroborative data sources (i.e. interviews with family and other informants, child welfare records).[62, 67]

Strengths of our study include: a relatively large sample size of over 100 participants with schizophrenia and over 100 NCs, comprehensive and well-validated assessments of mental and physical health, and inclusion of clinically relevant biomarkers. Despite its limitations, the CDRS is easy and efficient to administer, well-studied in the literature, and has the best psychometric ratings.[66]

These current findings suggest that resilience has an important role in mental and metabolic health in people with schizophrenia and NCs. While individuals diagnosed with schizophrenia report higher prevalence of childhood trauma and have generally worse mental and physical health, including metabolic biomarkers, resilience is a potentially modifiable protective factor that could bolster mental and physical health. Along similar lines, our previous work on successful aging in a large community-dwelling cohort of NCs aged 50 to 99 years (N = 1,006) reported a strong association between resilience and successful aging, that was comparable to the relationship between the absence of physical disability and successful aging.[68] In fact, high levels of resilience seemed to enable persons with schizophrenia and severe trauma to have comparable or better mental and physical health outcomes as NCs with severe trauma and low levels of resilience. This finding suggests a promising opportunity to improve functioning in persons with schizophrenia as well as NCs with a history of childhood trauma.

Resilience-enhancing interventions exist across a variety of settings, including military training[69, 70] as well as Stress Management and Resilience Training (SMART)[71] and Mindfulness-Based Stress Reduction.[72, 73] However, aside from one pilot study of positive psychotherapy[74] and individual resiliency training (e.g. using positive psychology exercise to improve self-esteem and self-efficacy for illness management) for persons with first episode psychosis,[75] specific resilience-focused interventions have not been tested in persons with schizophrenia and furthermore, the metabolic effects of such interventions have not been assessed. The latter is particularly important in the context of schizophrenia because of the high prevalence of metabolic disorders in schizophrenia, the association of the latter to early mortality, and tentative correlational findings suggestive that resilience may decrease the risk of metabolic disorders. Although causal relationships cannot be determined here, the potential benefits and relative low risk/cost of resilience interventions suggest strong reasons for prospective studies testing such interventions among people with schizophrenia (with or without a history of childhood trauma) on physical health outcomes, especially metabolic effects.[1, 2]

Acknowledgments:

The authors thank all of the study participants and staff. The authors also thank Rebecca Daly, AA (Department of Psychiatry and Sam and Rose Stein Institute for Research on Aging, University of California San Diego, La Jolla, CA, United States) for support with data management and analyses. Ms. Daly has no conflicts of interest to declare.

Funding Support:

This study was supported, in part, by National Institutes of Health [NIH R01MH094151–01 (PI: Dilip V. Jeste, MD)], the National Institute of Mental Health [NIMH T32 Geriatric Mental Health Program MH019934 (PI: Dilip V. Jeste, MD)], and by the Stein Institute for Research on Aging at the University of California, San Diego.

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Clinical Points:

- Both childhood adversity and psychological resilience affect mental and physical health, yet this relationship has not been studied in persons with schizophrenia.
- Persons with schizophrenia who have high levels of resilience and severe trauma have comparable or better mental and physical health as non-psychiatric comparison subjects with low levels of resilience and severe trauma.
- Resilience may counter the negative effects of childhood adversity on mental and physical health in both persons with schizophrenia and the general population.

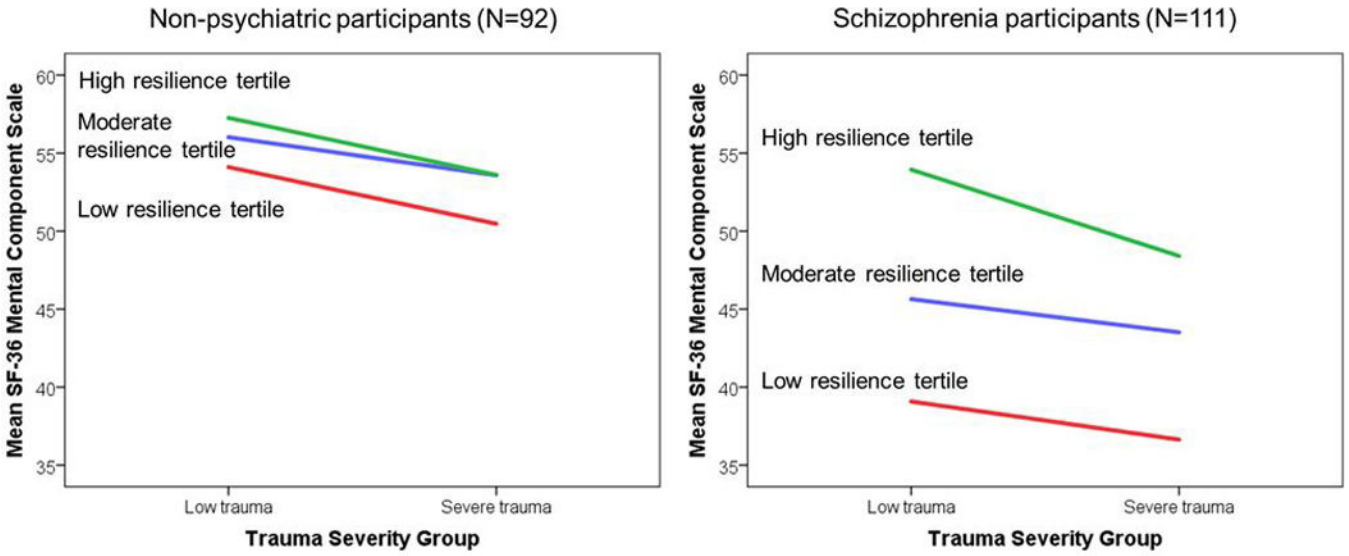

Figure 1a:
Resilience and mental health well-being scores in participants with and without schizophrenia

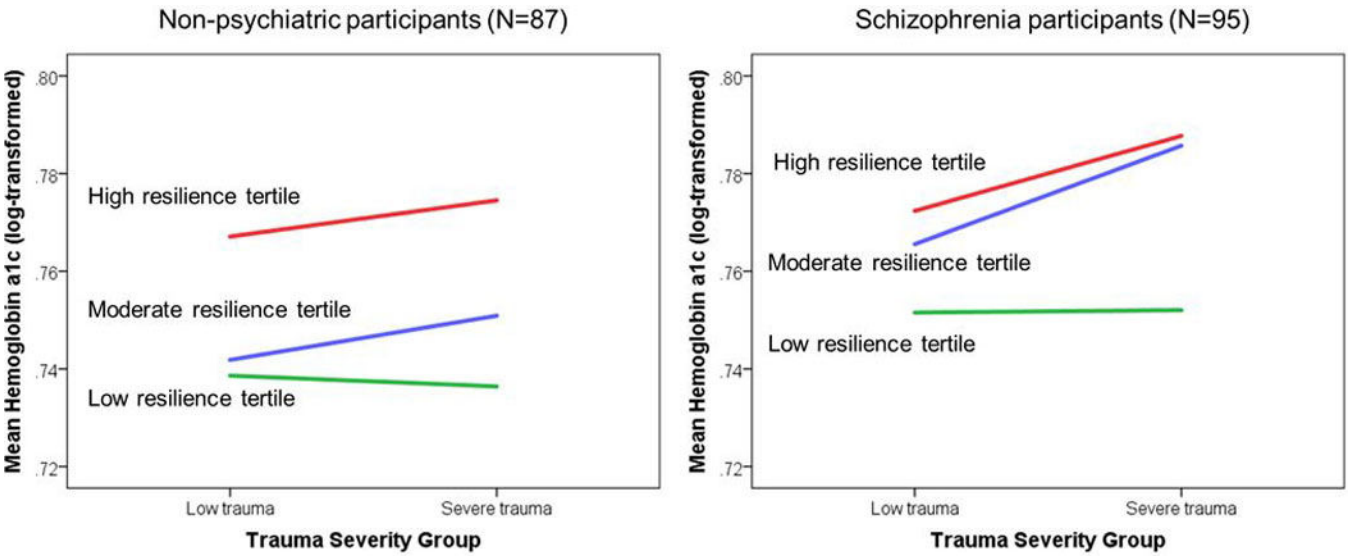

Figure 1b: Resilience and glycosylated hemoglobin in participants with and without schizophrenia

SF-36 = Short Form Health Survey, Hemoglobin A1c = glycosylated hemoglobin, CDRS = Connor-Davidson Resilience Scale

Definition of high resilience tertile: Non-psychiatric subjects with low trauma (CDRS score > 36.7), Non-psychiatric subjects with severe trauma (CDRS score > 36.0), schizophrenia subjects with low trauma (CDRS score > 30.0), schizophrenia subjects with severe trauma (CDRS score > 27.0)

Definition of moderate resilience tertile: Non-psychiatric subjects with low trauma (CDRS score between 31.3 and 36.7), Non-psychiatric subjects with severe trauma (CDRS score between 31.0 and 36.0), schizophrenia subjects with low trauma (CDRS score between 21.0 and 30.0), schizophrenia subjects with severe trauma (CDRS score between 18.0 and 27.0)

Definition of low resilience tertile: Non-psychiatric subjects with low trauma (CDRS score < 31.3), Non-psychiatric subjects with severe trauma (CDRS score < 31.0), schizophrenia subjects with low trauma (CDRS score < 21.0), schizophrenia subjects with severe trauma (CDRS score < 18.0)

Table 1:

Clinical characteristics of the schizophrenia and healthy comparison groups

Subject Group	Non-psychiatric participants			Schizophrenia			t or X^2	df	p-value (2-tailed)	*Cohen's d*
	N	Mean or Percent	Std. Deviation	N	Mean or percent	Std. Deviation				
Demographic Factors										
Age at visit (years)	101	49.4	11.3	114	48.3	10.1	0.74	213	0.5	0.1
Gender[a] (% female)		53.4			43.9		1.98	1	0.2	
Race[a] (% Caucasian)		60.3			50		2.34	1	0.1	
Education (years)	101	14.7	2.2	114	12.5	2.4	7.03	213	<0.001	0.96
Psychopathology										
Duration of Illness (years)				111	25.4	10.9				
Antipsychotic dose (mg)[b]				114	1.91	1.59				
Positive symptoms[c]				114	6.02	4.23				
Negative symptoms[d]				114	7	4.33				
Depressive symptoms[e]	100	0.54	1.3	114	3.54	3.92	−7.72	138.6	<0.001	−1.03
Anxiety symptoms[f]	92	1.3	2.1	111	7.2	6.4	−9.23	138.2	<0.001	−1.25
Mental Health										
Resilience[g]	92	33.1	5.7	110	23.4	8.2	9.95	193.6	<0.001	1.38
Mental well-being[h]	92	54.6	6.13	111	43.2	11.3	9.12	175.3	<0.001	1.25
Perceived stress[i]	91	10.6	6.14	111	18.5	6.41	−8.85	200	<0.001	−1.25
Overall cognitive dysfunction[j]	99	38	4.05	111	31.5	5.6	9.74	199.4	<0.001	1.33
Executive Functioning[k]	101	0.42	0.55	114	−0.46	0.72	10.2	208.2	<0.001	1.38
Physical health										
Physical well-being[l]	92	51.7	9.5	111	43.6	10.2	5.87	198.6	<0.001	0.83
Physical comorbidity[m]	101	2.83	3.12	114	6.4	4.32	−7	205	<0.001	−0.95
BMI	101	27	6.2	112	32.3	7.4	−5.7	210	<0.001	−0.78

Subject Group	Non-psychiatric participants			Schizophrenia						
	N	Mean or Percent	Std. Deviation	N	Mean or percent	Std. Deviation	t or X^2	df	p-value (2-tailed)	*Cohen's d*
Metabolic biomarkers										
Fasting insulin (mIU/L)	96	7	5.61	106	13	12	−4.71	196.5	<0.001	−0.66
Fasting glucose (mg/dL)	101	89.5	17	113	105.5	50.9	−2.97	165	0.003	−0.4
Hemoglobin A1c (%)	87	5.7	0.63	95	6.1	1.25	−2.54	152.6	0.012	−0.37
HOMA-IR	96	1.6	1.53	106	3.8	5.13	−5.23	194.4	<0.001	−0.73
Childhood adversity measures[n]										
Emotional Abuse subscale score	101	8.31	3.94	114	10.66	4.81	−3.89	213	<0.001	−0.53
Physical Abuse subscale score	101	7	3.04	114	8.81	4.55	−3.46	198.4	0.001	−0.47
Sexual Abuse subscale score	99	6.71	3.86	114	9.1	5.81	−3.58	198	<0.001	−0.48
Emotional Neglect subscale score	101	9.48	4.64	114	12.03	4.78	−3.96	213	<0.001	−0.54
Physical Neglect subscale score	101	6.77	2.98	114	9.08	3.47	−5.24	212.8	<0.001	−0.71
Total score	99	38.3	14	114	49.7	17.1	−5.27	211	<0.001	−0.73

[a] Chi-square test

[b] Antipsychotic medication daily dosages were converted to WHO average daily doses based on published standards [WHO: Guidelines for ATC classification and DDD assignment, 2010 and WHO: Introduction to Drug Utilization Research, 2009]

[c] As assessed with the Scale for the Assessment of Positive Symptoms (SAPS) total summary score of the four global domain scores (ranging from 0 to 20, higher scores indicating more positive symptoms)

[d] As assessed with the Scale for the Assessment of Negative Symptoms (SANS) total summary score of the five global domain scores (ranging from 0 to 25, higher scores indicating more negative symptoms)

[e] As assessed with the Calgary Depression Scale total score (ranging from 0 to 27, higher scores indicating more depressive symptoms)

[f] As assessed with the Brief Symptom Inventory Anxiety Scale total score (ranging from 0 to 24, higher scores indicating more anxiety symptoms)

[g] As assessed with the Connor Davidson Resilience 10-item Scale (ranging from 0 to 40, higher scores indicating greater overall resilience)

[h] As assessed with the Short Form Health Survey (SF-36) Mental Composite score (computable range from −1.3 to 62.1, higher scores indicating better mental health)

[i] As assessed with the Perceived Stress Scale (ranging from 0 to 40, higher scores indicating greater perceived stress)

[j] As assessed with the Modified Telephone Interview for Cognitive Status (TICS-M) (ranging from 0 to 50, higher scores indicating better cognitive status)

[k] As assessed with the Delis-Kaplan Executive Function System (reported as a standardized z-score, with higher values indicating better executive functioning)

[l] As assessed with the Short Form Health Survey (SF-36) Physical Composite score (computable range from 1.7 to 76.3 from 0 to 100, higher scores indicating better physical health)

[m] As assessed with the Cumulative Illness Rating Scale total score (ranging from 0 to 56, higher scores indicating a higher number or greater severity of physical comorbidities)

[n] As assessed with the Childhood Trauma Questionnaire (CTQ). Subscale scores range from 5 to 25 (higher scores indicating greater childhood adversity)

Abbreviations:
Hemoglobin A1c = glycosylated hemoglobin, HOMA-IR = Homeostatic Model Assessment for Insulin Resistance

Table 2:

Spearman correlations between trauma severity and key sociodemographic, mental, and physical health variables in the study participants with and without schizophrenia

	Non-psychiatric participants Total CTQ score			Schizophrenia Total CTQ score			Test for equal correlations	
	r	*p*	N	*r*	*p*	N	*z*	*p*
Sociodemographic								
Age at visit	0.071	0.48	99	−0.039	0.68	114	0.79	0.21
Education (years)	−0.187	0.06	99	−0.101	0.29	114	−0.63	0.27
Psychopathology								
Duration of Illness				0.13	0.18	111		
Antipsychotic dose (mg)[a]				−0.077	0.41	114		
Positive symptoms[b]				0.131	0.17	114		
Negative symptoms[c]				0.015	0.87	114		
Depressive symptoms[d]	**0.341**	0.001	98	0.024	0.8	114	2.35	**0.009**
Anxiety symptoms[e]	0.202	0.06	90	0.089	0.35	111	0.8	0.21
Mental Health								
Resilience[f]	−0.074	0.49	90	**−0.204**	0.03	110	0.92	0.18
Mental well-being[g]	**−0.209**	0.05	90	−0.1	0.3	111	−0.77	0.22
Perceived Stress[h]	**0.21**	0.05	89	0.119	0.21	111	0.64	0.26
Overall cognitive dysfunction[i]	−0.15	0.14	97	0.105	0.28	111	−1.83	**0.03**
Executive Functioning[j]	−0.096	0.35	99	−0.06	0.53	114	−0.26	0.4
Physical Health								
Physical well-being[k]	**−0.292**	0.005	90	**−0.251**	0.008	111	−0.3	0.38
Physical comorbidity[l]	**0.275**	0.006	99	0.062	0.52	114	1.57	0.06
BMI	0.144	0.16	99	**0.29**	0.002	112	−1.08	0.14
Biomarkers								
Fasting glucose (mg/dL)	0.064	0.53	99	0.094	0.32	113	−0.22	0.41
Fasting insulin (mIU/L)	**0.266**	0.009	95	**0.231**	0.02	106	0.25	0.4
Hemoglobin A1C (%)	0.13	0.23	85	0.13	0.21	95	0	0.5
HOMA-IR	**0.26**	0.01	95	**0.227**	0.02	106	0.24	0.4

[a]Antipsychotic medication daily dosages were converted to WHO average daily doses based on published standards [WHO: Guidelines for ATC classification and DDD assignment, 2010 and WHO: Introduction to Drug Utilization Research, 2009]

[b]As assessed with the Scale for the Assessment of Positive Symptoms (SAPS) total summary score of the four global domain scores (ranging from 0 to 20, higher scores indicating more positive symptoms)

[c]As assessed with the Scale for the Assessment of Negative Symptoms (SANS) total summary score of the five global domain scores (ranging from 0 to 25, higher scores indicating more negative symptoms)

[d]As assessed with the Calgary Depression Scale total score (ranging from 0 to 27, higher scores indicating more depressive symptoms)

[e] As assessed with the Brief Symptom Inventory Anxiety Scale total score (ranging from 0 to 24, higher scores indicating more anxiety symptoms)

[f] As assessed with the Connor Davidson Resilience 10-item Scale (ranging from 0 to 40, higher scores indicating greater overall resilience)

[g] As assessed with the Short Form Health Survey (SF-36) Mental Composite score (computable range from −1.3 to 62.1, higher scores indicating better mental well-being)

[h] As assessed with the Perceived Stress Scale (ranging from 0 to 40, higher scores indicating greater perceived stress)

[i] As assessed with the Modified Telephone Interview for Cognitive Status (TICS-M) (ranging from 0 to 50, higher scores indicating better cognitive status)

[j] As assessed with the Delis-Kaplan Executive Function System (reported as a standardized z-score, with higher values indicating better executive functioning)

[k] As assessed with the Short Form Health Survey (SF-36) Physical Composite score (computable range from 1.7 to 76.3 from 0 to 100, higher scores indicating better physical well-being)

[l] As assessed with the Cumulative Illness Rating Scale total score (ranging from 0 to 56, higher scores indicating a higher number or greater severity of physical comorbidities)

Abbreviations: CTQ = Childhood Trauma Questionnaire, Hemoglobin A1c = glycosylated hemoglobin, HOMA-IR = Homeostatic Model Assessment for Insulin Resistance

J Clin Psychiatry. Author manuscript; available in PMC 2019 May 01.

Table 3:

General linear models examining the relationships of subject group, trauma severity, and resilience.

Outcome	Model 1				Model 2			
	Main effects & Interactions	**Parameter estimates(SE)**	***P* value**	**Cohen's *d***	**Main effects & Interactions**	**Parameter estimates (SE)**	***P* value**	**Cohen's *d***
Mental well-being	**Subject group**	12.7 (4.0)	**0.002**	0.47	**Subject group**	16.7 (6.9)	**0.017**	0.35
	Trauma severity	−0.037 (0.052)	0.18	0.19	Trauma severity	0.035 (0.046)	0.69	0.06
	Group x severity	−0.045 (0.088)	0.61	0.07	**Resilience**	0.70 (0.097)	**<0.001**	1
					Group x severity	−0.1 (0.08)	0.2	0.19
					Group x resilience	−0.23 (0.18)	0.2	0.19
Physical well-being	Subject group	5.2 (4.1)	0.21	0.18	Subject group	−2.2 (8.0)	0.08	0.04
	Trauma severity	−0.16 (0.05)	**0.002**	0.46	**Trauma severity**	−0.13 (0.05)	**0.008**	0.39
	Group x severity	0.028 (0.092)	0.76	0.04	**Resilience**	0.31 (0.11)	**<0.001**	0.55
					Group x severity	0.016 (0.09)	0.86	0.03
					Group x resilience	0.15 (0.21)	0.46	0.11
BMI	Subject group	−1.7 (2.8)	0.54	0.09	Subject group	7.4 (5.8)	0.2	0.19
	Trauma severity	0.089 (0.038)	0.07	0.25	Trauma severity	0.095 (0.039)	0.12	0.23
	Group x severity	−0.067 (0.062)	0.28	0.15	Resilience	0.032 (0.081)	0.21	0.18
					Group x severity	−0.09 (0.07)	0.17	0.2
					Group x resilience	−0.25 (0.15)	0.1	0.24
Hemoglobin A1c	Subject group	−0.019 (0.027)	0.49	0.11	Subject group	0.06 (0.05)	0.24	0.19
	Trauma severity	<0.001 (<0.001)	0.56	0.08	Trauma severity	<0.001 (<0.001)	1	0.007
	Group x severity	−4.8E-5 (0.001)	0.94	0.01	**Resilience**	−0.001 (0.001)	**0.002**	0.5
					Group x severity	<0.001 (0.001)	0.76	<0.09
					Group x resilience	−0.002 (0.001)	0.15	0.23
HOMA-IR	Subject group	−0.26 (0.16)	0.1	0.24	Subject group	−0.15 (0.32)	0.64	0.07
	Trauma severity	0.005 (0.002)	**0.002**	0.45	**Trauma severity**	0.003 (0.002)	**0.009**	0.4
	Group x severity	0.001 (0.004)	0.77	0.04	**Resilience**	−0.01 (0.005)	**0.01**	0.39
					Group x severity	0.003 (0.004)	0.45	0.11

Outcome	Model 1				Model 2			
	Main effects & Interactions	Parameter estimates(SE)	*P* value	Cohen's *d*	Main effects & Interactions	Parameter estimates (SE)	*P* value	Cohen's *d*
					Group x resilience	−0.003 (0.008)	0.74	0.05

Model 1: subject group, trauma severity, subject group x trauma severity

Model 2: subject group, trauma severity, resilience, subject group x trauma severity, subject group x resilience

Abbreviations: BMI = body mass index, Hemoglobin A1c = glycosylated hemoglobin, HOMA-IR = Homeostatic Model Assessment for Insulin Resistance