Interconnections of traumatic life events and schizophrenia spectrum disorders

PhD Theses

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1. INTRODUCTION

Dimensional view of psychiatric disorders has become more and more accepted in the last few decades. A dimensional view has become widely used in the field of schizophrenia research. There is a growing body of neurobiological and neuropsychological evidence for continuity between full blown schizophrenia and schizotypy as a personality trait. Our research has been built upon this theoretical base.

The interconnections of psychotic, especially schizophrenia spectrum disorders and childhood trauma have also been extensively studied. A dose-response relationship between the severity of traumas and symptoms of schizophrenia has been established by several cross-sectional and longitudinal studies. Some data gained in samples of ultra-high-risk young people suggest that subclinical psychotic symptoms can be reduced by stopping traumatisation. According to some results, not so much general traumas (e. g. accident, severe illness or natural disaster) but actions committed with a harming intention such as abuse are likely to be connected to later psychotic symptoms. The interconnectedness of psychotic symptoms with childhood physical, emotional and sexual abuse has been supported by various studies.

It can be well assumed that this connection may come about as a long-term consequence of the permanently elevated cortisol level due to constantly repeated traumatisation. It has been well established that permanently elevated levels of cortisol contribute to the hypersensitivity of glucocorticoid receptors of the hippocampus, which in turn may lead to an altered pattern of cortisol response and the volume reduction of hippocampus and amygdala. Volume reduction of these two cerebral structures and prefrontal areas, as well as a disturbed fronto-hippocampal connection has been documented in schizophrenia. Permanently elevated cortisol level contributes to the increased activity of the dopamine system which plays a pivotal role in schizophrenia.

Some similarities between posttraumatic stress and schizophrenia have been argued by several authors. Abnormal cortisol response and a dysfunction and volume reduction of the hippocampus has been documented in posttraumatic stress disorder too

It has been well established that dissociative symptoms or phenomena often show comorbidity with schizophrenia. On the one hand this can cause diagnostic problems; on the other hand dissociation may act as a mediator between traumatic life events and psychotic symptoms.

Trauma history seems to be relevant for the course of schizophrenia too. According to several studies, early traumas may be connected to earlier onset of the illness, more frequent psychotic episodes and hospitalisations, an increased suicide risk of people with schizophrenia and less confidence towards the therapist.

2. AIMS

General aims:

Aims of our studies were partly the psychometric analysis of measures assessing schizotypy and dissociation, the Hungarian version of which has previously been understudied.

It was our further intention to perform a detailed analysis of the interconnectedness of symptoms of schizophrenia and childhood traumatic events. Our aim was to test the role of posttraumatic stress symptoms and dissociation as possible mediating variables in the relationship of traumatic life events and psychotic symptoms. We also intended to investigate a possible relationship between early traumatic experiences and the course of illness in patients with schizophrenia.

Specific aims:

Study 1:

Our first study was designed to test the factor structure of Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE, Mason and Claridge, 1996) schizotypy questionnaire. Our further aim was to explore the factor structure of the internationally widely used Dissociative Experiences Scale (Carlson and Putnam, 1993) which has been translated into Hungarian recently and has been understudied in Hungarian samples.

Study 2:

Our second study was partly designed to test criterion validity of O-LIFE scale and also the continuity of symptoms of schizophrenia and dimensions of schizotypy.

Our further aim was to investigate the interdependence of different aspects of childhood traumatisation (general traumas, physical, emotional and sexual abuse) with present symptoms. It was our additional aim of research to analyse how much the specific circumstances of childhood abuse (frequency, age at onset, effect at onset, current effect) contribute to the understanding of the relationship between early traumas and psychotic symptoms.

We also intended to examine, whether such trauma-related phenomena as posttraumatic stress symptoms and dissociation possibly mediate the relationship between early traumatic events and psychotic symptoms.

Our intention was to get to understand how early traumas are connected to the duration of illness, the number of hospitalisations, suicide attempts and other measures of suicidality (such as depression, past and present suicidal thoughts).

3. METHODS

Subjects:

Study 1:

406 volunteers - students of Semmelweis University Budapest and Eötvös Loránd University Budapest (88.4% women) filled out our online questionnaires including shortened O-LIFE scale. The mean age (SD) of participants was: 26,84 years (sd=11,6). Potential participants received an e-mail informing them about the study and inviting them to participate.

Test-retest reliability of the questionnaire was checked on a subsample of 38 participants (76,3% women, mean age: 23,5 years, sd=2,62).

Participants produced informed consent before answering the questionnaire and they received no payment.

Study 2:

Our second study included 65 inpatients and 37 outpatients with the diagnosis of schizophrenia and schizoaffective disorder, medicated with atypical antipsychotics. There were no significant between-group differences regarding gender, age and education. 58,5% and 40,6% of the patient groups and 58,6% of the control group were women. Mean age for the groups were 45,74 (sd=11,87), 48,35 (sd=11,53) and 44,55 (sd=14,67) years respectively. Participants were recruited in seven different psychiatric institutions in Budapest and Szeged. Participants were contacted through their therapist and produced informed consent before answering the questionnaire and they received no payment

Participants were included in the patient groups or the control groups based on the results of their SCID-I interview and psychiatric documentation.

Measures

Study 1:

Oxford-Liverpool Inventory of Feelings and Experiences, short version (O-LIFE, Mason et al., 2005)

It contains 43 dichotomous items and has been designed to measure different dimensions of schizotypy. It contains 4 subscales: Unusual Experiences, Introvertive Anhedonia, Cognitive Disorganisation and Impulsive Nonconformity.

Dissociative Experiences Scale (Dissociative Experiences Scale, DES, Carlson & Putnam, 1993)

DES is a 28-item self-report questionnaire designed to measure specific disturbances of identity, thought and self-awareness. It measures dissociation as a trait on a 10-point Likert-types scale, it's not a diagnostic measure. According to the factor analysis of the authors it contains the following factors:1. amnesia, 2. fantasy-proneness. 3. derealisation and depersonalization.

Study 2

Additionally to the measures used in Study 1 the following further measures were included:

Scale for Assessment of Negative Symptoms (SANS, Andreasen, 1983)

The 24-item questionnaire measures negative symptoms of schizophrenia, containing 5 subscales: affective flattening (1-7), alogia (8-11), avolition (12-14), anhedonia (15-18) and attention deficit (19-24). Symptoms are scaled on a 6-point Likert-type scale. (0 = not present, 5 = present all the time).

Scale for Assessment of Positive Symptoms (SAPS, Andreasen, 1984)

The 30-item questionnaire measures positive symptoms of schizophrenia and contains 4 subscales: hallucinations (1-6), delusions (7-18), bizarre behaviour or disorganised symptoms (19-22) and thought disorders (23-30). Symptoms are scored on a 6-point Likert-type scale. (0 = not present, 5 = present all the time).

Early Trauma Inventory – Self Report, (ETI-SR, Bremner et al., 2007)

A 62-item self-report inventory aimed at measuring the following traumatic experiences: general childhood traumas (e. g. death of a family member, accident), general adulthood traumas, childhood physical, emotional and sexual abuse. Participants are asked to report the frequency of the abuse, the age of onset, effect at onset and current effect of the abusive even

Impact of Event Scale, (IES Horowitz et al., 1979)

It's a measure widely used to test the subjective stress, suffering and cognitive processes as consequences of adverse life events (Horowitz et al., 1979). It cannot be used to establish the diagnosis of posttraumatic stress disorder, it only measures certain symptoms of it. It contains 15 items scored on a 4-point Likert-type scale and consists of the avoidance and intrusions factors.

Beck Depression Inventory, short form (Beck & Beck, 1972, Kopp & Fórizs, 1993)

It has been designed to measure lack of joy, avoidance of social stimuli, inability of decision, insomnia, lack of energy, exaggerated anxiety concerning physical symptoms, pessimism and self-blame. It consists of 9 statements which are to be scored by participants on a 4-point Likert-type scale.

Statistics

Study 1:

Confirmatory factor analysis O-LIFEwith the use of Mplus 7.3 (Muthén & Muthén, 1998-2014) was applied to investigate the fit of the original four-factor structure (Mason et al, 2005). Measurement model with ordered categorical factor indicators was estimated using robust weighted least squares estimator (WLSMV). Model fit was evaluated using several indices. For acceptable model fit, root mean square error of approximation (RMSEA) was expected to be less than .05, comparative fit index (CFI) and Tucker-Lewis index (TLI) was expected to be higher than .90.

In order to explore the factor structure of DES, our sample was randomly split, explorative factor analysis was conducted on one half and confirmatory factor analysis was conducted with the use of Mplus 7.3 (described above) on the other half of the original sample in order to investigate the fit of the factor structure found in the exploratory analysis.

Factors resulted by the analyses were tested further with using IBM SPSS 21. Missing values were not substituted. Between-group comparisons were analysed with t test. When lacking homogeneity of variance, Welch test was chosen. Relationships of variables were tested with Pearson`s correlation coefficients. Level of significance was set at $\alpha = .05$.

Study 2:

In our second study again IBM SPSS 21 was applied used for data analysis. Missing values were not substituted. Normal distribution of our data was tested by Kolmogorov-Smirnov and Shapiro-Wilk test. Most of our variables were not normally distributed. In spite of this and because of the sample size our first choice was a parametrical test in each case. Chi square test was used to calculate between-group differences regarding gender. While testing possible between-group differences regarding education the conditions for chi square test were not fulfilled, so Fisher`s Exact Test was applied. Between-group differences as regards to age, duration of illness, number of hospitalisations, severity of symptoms and schizotypal traits were calculated with the use of t-test or one-way ANOVA. As a post hoc test Bonferroni test was chosen. When lacking homogeneity of variance, Welch test was used. In order to test the relationship between two variables, Pearson`s correlation coefficient was calculated. In order to control the relationship of two variables for a third variable, partial correlation was applied, after conducting z transformation in the case of scales with not normal distribution. For testing the relationship of ordinal scales, Spearman`s rank correlation was applied. In order to test one variable predicting another variable, linear regression enter method was chosen. Mediation was computed with the use of Hayes's PROCESS tool for SPSS. Level of significance was set at $\alpha = .05$.

4. RESULTS

Study 1:

1. In order to reach an acceptable fit of the model, seven items with the lowest factor loadings were excluded. Our final four-factor model with the remaining 36 items had acceptable model fit indices: $\chi^2(588)=688,589$, $p<0,05$; RMSEA=0,028, CFI=0,931, TLI=0,926 and stable factor loadings above 0,20 on each of the four factors. Standardized factor loadings ranged between 0,302 and 0,779 for Unusual Experiences, 0,372-0,710 for Cognitive Disorganisation, 0,265-0,829 for Introvertive Anhedonia and 0,206-0,766 for Impulsive Nonconformity. The four subscales were significantly correlated, correlation coeffeicients were between r=0,202 ($p<0,001$) and r=0,844 ($p<0,001$).

2. Confirmatory factor analysis to test one-factor structure of DES did not yield acceptable goodness-of-fit indices: $\chi^2(324)=802{,}473$, $p<0{,}001$; RMSEA=0,060, CFI=0,766, TLI=0,747. Our sample was randomly split and in one subsample exploratory factor analysis with Maximum Likelihood method was conducted, the number of possible factors was determined in three. The resulting three factors explained only 39,36% of the variance but model fit was acceptable $\chi^2(273)=872{,}738$, $p < 0{,}001$. In order to get a better picture of the factor structure, a confirmatory factor analysis of the three-factor structure on the other subsample was conducted. Our model was modified according to the modification indices. As a consequence of this, the final factor structure had acceptable model fit indices: $\chi^2(310)=403.882$, $p<0{,}001$; RMSEA=0,039, CFI=0,908, TLI=0,896. Our analysis resulted the following three stable factors: depersonalisation, derealisation (factor loadings: 0,348-1,610), phantasy proneness (factor loadings: 0,366-1,122), amnestic dissociation (factor loadings 0,319-0,650). The three factors were strongly correlated (r=0,777-0,781, p<0,001).

Study 2:

3. Inpatients and outpatients did not differ from each other regarding symptom severity (differences in each symptom group were not significant: p>0,1), so the two patient samples were united for further analysis.

4. When comparing patients and controls along measures of positive symptoms, negative symptoms, and disorganisation, the patient group scored significantly higher along all variables than controls (in each case p<0,001)

5-6. In order to test the relationship of symptoms of schizophrenia and dimensions of schizotypy we tested the correlation of the 3 symptom scales (SAPS positive symptoms including hallucinations and delusions, SAPS thought disorders and the whole of SANS scale) with the 3 schizotypy dimensions (positive, negative and disorganised). As expected, we found that positive schizotypy measured by UE had a significant positive correlation with SAPS positive symptoms (hallucinations and delusions) (r= 0,338, p<0,001, n=93) and SAPS disorganised symptoms (r=0,343, p<0,001, N=93). Similarly, a positive correlation was found between negative symptoms measured by SANS and negative schizotypy measured by IA (r=0,232, p<0,05, n=87). Contrary to our expectations, no significant relationship was found between disorganised symptoms and disorganised schizotypy measured by CD.

7-8. Using Early Trauma Inventory we first examined how much new information the subscales of Early Trauma Inventory rating frequency, age of onset, the subjective effect of the event at onset and its current subjective effect add to simply summing up the occurrence events. In order to determine this we conducted correlation analyses to see how similar these scales are to simply summing up occurrence. All the scales correlating with a coefficient greater than 0,8 with the occurrence of childhood abuse were excluded from further analysis. Remaining scales were the following: general trauma, occurrence of physical abuse, subjective effect at onset of physical abuse, current subjective effect of physical abuse, emotional abuse, and current effect of emotional abuse. Patients and controls were compared along these five variables and general adult traumas. Patients reported significantly more general childhood traumas ($p<0,001$) childhood abuse in total ($p<0,05$) and childhood emotional abuse ($p<0,001$) than controls. Patients and controls did not differ regarding the subjective effect of childhood abuse.

9-10. There were no between-group differences found regarding posttraumatic stress symptoms but patients scored significantly higher than controls on Dissociative Experiences Scale ($p<0,01$).

11. According to our correlation analysis positive symptoms ($r=0,323$, $p<0,01$), hallucinations ($r=0,230$, $p<0,05$) and delusions ($r=0,279$, $p<0,05$) were significantly correlated with general childhood traumas, but negative symptoms did not correlate at all with traumatic life events. Childhood abuse was not correlated at all with either positive or negative symptoms. Posttraumatic stress symptoms were not correlated either with positive or negative symptoms. Dissociation was only significantly correlated with positive symptoms ($r=0,259$, $p<0,05$).

12. In order to test the predictive value of the different types of trauma for the symptoms of schizophrenia, linear regression analyses with enter method were run, where the sum of positive symptoms (SAPS total), hallucinations, delusions and thought disorder subscales of SAPS were chosen as dependent variables and general childhood trauma, childhood emotional and physical abuse were entered as independent variables.

Our regression analyses were in each case controlled for gender, age, education and family history of schizophrenia. In the whole sample of patients only general childhood traumas predicted the total of positive symptoms ($p<0,05$) and also hallucinations ($p<0,05$) but this latter effect was not independent of gender. General traumas also predicted delusions but this relationship was not independent of education. In order to get a better understanding of the possibly different connections of traumatic life events and psychotic symptoms in the two gender groups, regression analyses were run separately in the groups of men and women. In the two gender groups different aspects of childhood traumas were connected to different symptom groups: in the case of men general traumas were the only significant predictors of positive symptoms ($p<0,05$) and of delusions ($p<0,05$), although in the latter case not independently of education. Our regression model was only significant in the case of positive symptoms. In the group of women childhood physical abuse was the only predictor of thought disorder ($p<0,01$), independently of age and education, although our regression model was not significant. Results of our regression analyses are showing tendencies. Men and women did not differ significantly regarding their socio-demographic characteristics, their positive symptoms or the amount of reported traumas. The only difference between them was that men exhibited significantly stronger negative symptoms ($p<0,01$).

13. Patients having suffered childhood physical or emotional abuse from their mothers or close family members did not suffer from more severe symptoms than patients abused by others or even patients with no abuse history.

14-15. Neither posttraumatic stress symptoms, nor dissociation was proved to be a mediator between early traumatic experiences and symptoms of schizophrenia.

16. Neither patients reporting childhood physical, nor the ones reporting childhood emotional abuse were more likely to commit suicide than patients with no trauma history.

17. Our analysis revealed, that present suicidal ideation was significantly correlated with history of emotional abuse ($rS=0,281$, $p<0,05$) and past suicidal ideation was correlated with history ($rS=0,268$, $p<0,05$) and subjective effect of emotional abuse ($rS=0,272$, $p<0,05$). According to our partial correlation analyses, these latter correlations were independent of depression, whereas the correlation between present suicidal ideation and emotional abuse was influenced by it.

18. According to our results, total childhood abuse (r=-0,265*, p<0,05) and a more negative subjective effect of emotional abuse (rS=-0,389** p<0,01) were significantly correlated with an earlier onset of the illness.

19. Early traumatic experiences were not connected to the number of hospitalisations.

5. CONCLUSIONS

Study 1:

The four-factor structure of O-LIFE (Unusual Experiences, Cognitive Disorganisation, Introvertive Anhedona and Impulsive Nonconformity) and the three-factor structure of DES (amnesia, fantasy proneness and depersonalisation) was supported by our results. Our analyses yielded stable factors in both cases, although in the case of O-LIFE this was achieved by excluding 7 items with the lowest factor loadings.

Study 2:

Based on our results concerning O-LIFE scores in patients with schizophrenia, we can conclude that this measure is applicable to model the symptoms of schizophrenia on the level of personality traits, especially in the positive and negative symptom dimensions. At the same time, the continuity of schizophrenia and schizotypy has been established in our sample.

Childhood traumas have been proved to be definately important predictors of positive symptoms of schizophrenia, but in further analyses of the interconnections of different traumatic events and symptom groups gender differences must be considered. In our study general childhood traumas in men and physical abuse in women predicted different positive symptom groups. Our analysis revealed an unmediated relationship in both sexes, independent of the mediating role of posttraumatic stress or dissociation.

We can conclude that dissociation is more likely to be connected to psychotic symptoms or to the predisposition to develop psychotic symptoms as well as to certain personality disorders (such as borderline personality disorder) than to trauma history. So, it`s mediating role between traumatic life events and psychopathology cannot be generalised. Our results did not support that the person of the perpetrator commiting childhood abuse could have an effect on later symptom severity.

Our results undoubtedly support the connections of childhood abuse and a less favourable course of illness. Patients with abuse history – independently of having members with schizophrenia in the family or not – have an earlier onset of illness. Also, patients with history of childhood emotional abuse are characterised by a higher suicide risk – partly independently of their comorbid depressive symptoms.

6. LIST OF PUBLICATIONS

Publications related to the dissertation:

Kocsis-Bogár K, Nemes Zs, Perczel Forintos D. (2016) Factorial structure of the Hungarian version of Oxford-Liverpool Inventory of Feelings and Experiences and its applicability on the schizophrenia-schizotypy continuum. Pers Individ Dif, 90: 130-136.

Kocsis-Bogár K, Perczel Forintos D. (2014) The relevance of traumatic life events in schizophrenia spectrum disorders. Ideggyogy Sz, 67(9-10): 301-308.

Kocsis-Bogár K, Miklósi M, Perczel Forintos D. (2013) Impact of adverse life events on individuals with low and high schizotypy in a nonpatient sample. J Nerv Ment Dis, 201(3): 208-215.

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Kocsis-Bogár K, Kiss Zs. (2010) Különös élmények – különös logika. A pszichotikus zavarok kognitív-viselkedésterápiás szemlélete, Magyar Pszichológiai Szemle, 66(1): 169-183.

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Miklósi M, Martos T, Szabó M, **Kocsis-Bogár K**, Perczel Forintos D. (2014) Cognitive emotion regulation and stress: a multiple mediation approach. Transl Neurosci, 5(1): 64-71.

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