


# Basic symptoms of schizophrenia are related to symptoms of traumatic stress: A pivotal role of sensitization. An observational study

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## Abstract

**Introduction:** Subjective cognitive deficits have been broadly reported in schizophrenia and described by Huber as basic symptoms. It remains unclear however to what extent they may be related to psychosocial stressors including trauma.

**Methods:** We assessed basic symptoms using the Frankfurt Complaint Questionnaire (FCQ) in a sample of 40 patients with schizophrenia. Trauma-related symptoms were assessed concurrently using the Trauma Symptom Checklist-40, symptoms of dissociation using the Dissociative Experiences Scale, and sensitization phenomena using the Complex Partial Seizure-like Symptoms Inventory and Limbic System Checklist-33. Psychotic symptoms were measured by Health of the Nation Outcome Scales. The dosage of antipsychotic medication was assessed in terms of equivalents of chlorpromazine, and antidepressant medication in terms of equivalents of fluoxetine. Spearman correlations were performed to explore the relationship between FCQ and other trauma-related measures. To determine the relative contributions of trauma-related symptoms to basic symptoms a linear regression analysis was performed.

**Results:** The results showed that higher levels of basic symptoms of schizophrenia were associated with greater levels of symptoms of dissociation, traumatic stress, and sensitization or kindling-like processes in schizophrenia. Among the trauma-related variables, sensitization phenomena assessed with Complex Partial Seizure-like Symptoms Inventory were closely associated with basic symptoms.

**Discussion:** These results indicate that basic symptoms measured by FCQ might be related to trauma. The potential of trauma to influence neurodevelopmental hypotheses of schizophrenia is discussed.

**Abbreviations:** CPSI = Complex Partial Seizure-like Symptoms Inventory, DES = Dissociative Experiences Scale, DSM = Diagnostic and Statistical Manual of Mental Disorders, FCQ = Frankfurt Complaint Questionnaire, HoNOS = Health of the Nation Outcome Scales, ICD 10 = International Classification of Diseases 10th Revision, PANSS = Positive and Negative Syndrome Scale, TSC-40 = Trauma Symptom Checklist-40

**Keywords:** basic symptoms, schizophrenia, sensitization, trauma

## 1. Introduction

To describe the fundamental disturbances which characterize schizophrenia, Huber and others<sup>[1-3]</sup> proposed what have since been referred to as basic symptoms. These include disturbances that are experienced by the person in their will, affect, thinking, speech, embodied perception, motor action, control of automatic cognitive processes, and stress tolerance. Like Bleuler's disturbances in association, affect, and volition, they are proposed to be a reflection of underlying disturbances in neurobiology and the cause of other symptoms in schizophrenia, such as positive symptoms.<sup>[4,5]</sup> They are also present in the earliest phases of the illness and persist thereafter.<sup>[6]</sup>

Unlike Bleuler's fundamental disturbances, basic symptoms are within the awareness of persons and experienced as burdensome.<sup>[7]</sup> Research has suggested that basic symptoms are associated with atypical patterns of neural activation in terms of reduced activity in discrete regions or atypical connections between neural networks, as well as aberrant brain activation, connectivity, and metabolism.<sup>[8]</sup> Basic symptoms are associated with positive and negative symptoms of schizophrenia.<sup>[9-11]</sup> However, research on their link to the onset of schizophrenia has been inconsistent.<sup>[12,13]</sup>

Most work has assumed that basic symptoms are the direct result of alterations in basic brain function. There has appeared little reason to look for the potential contribution of psychosocial

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events. At least one set of a psychosocial phenomenon, however, exists that theoretically might result in the disturbances noted by Huber. We refer here to childhood trauma. Childhood trauma has been broadly observed amongst persons diagnosed with schizophrenia and has been identified as having several things in common with basic symptoms.<sup>[14]</sup> These include being a risk factor for the onset of psychosis and particularly poor psychosocial outcomes,<sup>[15]</sup> as well as cognitive impairments.<sup>[16]</sup> At the level of phenomenology, trauma may also result in dissociation<sup>[17–19]</sup> and other disturbances in self-experience among persons with schizophrenia, which again could parallel what has been referred to as basic symptoms.<sup>[20–23]</sup>

Apart from dissociation, at the level of brain function, traumatization has been suggested to have the effect of sensitization or kindling-like processes in schizophrenia, which may play a role in the development of the condition and lead to seizure-like activity. Stress-related sensitization, in particular, has been suggested to effect changes in GABA postsynaptic receptors, which disrupts the function of the limbic system creating symptoms that resemble a subclinical form of temporal epilepsy.<sup>[24–27]</sup> Understanding whether childhood trauma may play a role in the development or expression of basic symptoms may have important implications for understanding emerging neurobiological models of schizophrenia, as well as for treatment approaches to these conditions.

To study the possibility that basic symptoms may be related to trauma among persons with schizophrenia, we gathered assessments of basic symptoms, trauma-related symptoms including dissociation, and assessments of complex partial seizure-like symptoms and temporo-limbic activity. We also included an assessment of general psychopathology as a potential covariate. We predicted that the report of basic symptoms would be related to trauma and dissociation, as well as partial seizure-like activity, after controlling for overall levels of psychopathology, psychiatric medication, and other demographic information.

## 2. Materials and Methods

### 2.1. Participants

The participants were recruited from regular daily treatment programs at the ESET Psychotherapeutic and Psychosomatic Clinic in Prague. All participants signed informed consent and the study was approved by Charles University Ethical Committee. The participants had diagnoses of schizophrenia which were based on DSM-IV criteria and which were reassessed using The Mini-International Neuropsychiatric Interview (M.I.N.I.).<sup>[28]</sup> Exclusion criteria were organic illnesses involving the central nervous system, substance, and/or alcohol abuse, and mental retardation (with a level of premorbid and current intellectual functioning lower than 90).<sup>[29]</sup> In addition to sociodemographic data, we calculated the actual day doses of antipsychotic medication in equivalents of chlorpromazine, and antidepressant medication in equivalents of fluoxetine for all participants.<sup>[30–32]</sup>

The sample included 40 patients with schizophrenia, i.e. 19 men and 21 women, mean age of 38.6 (SD = 10.7) with a mean period of psychiatric treatment of 16.2 (SD = 9.8) years and with an average of 6.0 hospitalizations (SD = 6.2). The mean daily dose of antipsychotic medication was 557.6 mg (SD = 525.6 mg) in equivalents of chlorpromazine, and the mean daily dose of antidepressant medication was 19.8 mg (SD = 38.3 mg) in equivalents of fluoxetine.

### 2.2. Psychometric measures

For the assessment of basic symptoms, we used The Frankfurt Complaint Questionnaire (FCQ).<sup>[33]</sup> It consists of 98 yes–no items, grouped in 10 phenomenological subscales (loss of control, simple perception, complex perception, language, thought, memory, motility, lack of automatism, anhedonia anxiety, and sensory overstimulation). The original German version of FCQ

was adapted to Czech cultural conditions (Cronbach's alpha 0.976, test–retest reliability 0.982).<sup>[34]</sup>

Trauma-related symptoms were measured using the Trauma Symptom Checklist-40 (TSC-40),<sup>[35]</sup> which is designed for measurement of posttraumatic symptomatology associated with childhood trauma. The TSC-40 is a self-reported scale containing 40 items with 6 subscales (dissociation, anxiety, depression, a sexual abuse trauma index, sexual problems, and sleep disturbances). The items are assessed on a 4-point Likert scale. The Czech version of the TSC-40 has high reliability and internal consistency (Cronbach's alpha 0.91, test–retest reliability after 1 week 0.88).<sup>[36]</sup>

Symptoms of dissociation were assessed by the Dissociative Experiences Scale (DES).<sup>[37]</sup> The DES evaluates the frequencies of various experiences of dissociative phenomena in the everyday life of the assessed person. It is constructed as a self-report questionnaire with 28 items. Each item ranges from 0 to 100. The mean of all item scores is calculated as the DES score. The Czech version of the DES was used in this study, which shows high reliability and internal consistency (Cronbach's alpha 0.92, test–retest reliability after one week 0.91).<sup>[38,39]</sup>

For the assessment of sensitization phenomena, we used the Complex Partial Seizure-like Symptoms Inventory – CPSI.<sup>[40]</sup> The CPSI originally served as an assessment tool for evaluation of sensory, somatic, behavioral, and memory symptoms associated with temporal lobe epilepsy (i.e., brief hallucinations, dissociative disturbances, paroxysmal somatic disturbances, and automatisms). It consists of 35 items using a 6-point Likert scale (Cronbach's alpha 0.95, test–retest reliability after week 0.87). A CPSI total score higher than 70 is suggested as a significant criterion for the so-called epilepsy spectrum disorder. Lower values may indicate an underlying electrophysiological dysfunction.<sup>[40]</sup> The resulting transient sensory, cognitive, and affective phenomena may be common in patients with affective disorders and other psychiatric diseases.<sup>[41,42]</sup>

We also used an alternative tool that evaluates symptoms similar to temporal lobe epilepsy – the Limbic System Checklist (LSCL-33).<sup>[43]</sup> The LSCL-33 measures temporo-limbic activity in the form of somatic, sensory, behavioral, and memory symptoms. These symptoms are associated with phenomena similar to temporal lobe epilepsy and may be generally described as brief hallucinations, paroxysmal somatic disturbances, automatisms, and dissociative disturbances. The Czech version of LSCL-33, as well as the original English version,<sup>[43]</sup> show good psychometric properties and internal consistency (Cronbach's alpha 0.90, test–retest reliability  $r = .91$ ).

For assessment of psychotic manifestations, we used the Health of the Nation Outcome Scales (HoNOS).<sup>[44]</sup> The HoNOS includes 12 items (overactive, aggressive, disruptive, or agitated behavior; nonaccidental self-injury; problem drinking or drug-taking; cognitive problems; physical illness or disability problems; problems with hallucinations or delusions; problems with depressed mood; other mental and behavioral problems; problems with relationships; problems with activities of daily living; problems with living conditions; problems with occupation and activities). There are two versions available, that is the version for external evaluators and the self-rating version for patients. Both versions were translated into the Czech language (Cronbach's alpha 0.797, test–retest reliability after one week 0.85).<sup>[45]</sup>

### 2.3. Data analysis

Statistical evaluation of the results for psychometric measures included descriptive statistics and Spearman correlation coefficients. Nonparametric analyses were preferred because the data of psychometric assessments were not normally distributed. All the methods used for statistical evaluation were performed using Statistica version 6 software (StatSoft Inc., Tulsa, OK, USA). To

prevent type II error, which would not be able to reject the null hypothesis that symptoms of traumatic stress, dissociation, and sensitization are not linked to basic symptoms of schizophrenia, we performed a power analysis and assessed the effect sizes by characterizing differences between means or correlation coefficients of the samples.

To further explore the associations and to find what is the relative importance of symptoms of traumatic stress, dissociation, and sensitization as independent variables toward basic symptoms as a dependent variable, a multiply linear regression analysis was executed. We normalized the data into the range 0-1 and conducted the enter method of the analysis.

### 3. Results

The results show significant correlations between FCQ and measures of symptoms of dissociation (DES,  $P < .001$ ), traumatic stress (TSC-40,  $P < .001$ ), and sensitization (LSCL-33,  $P < .001$  and CPSI,  $P < .001$ ). Significant correlations were also found between DES, LSCL-33, and CPSI mutually. Psychotic manifestations (HoNOS) were significantly correlated to daily doses of antipsychotic medication (EC,  $P = .005$ ), symptoms of traumatic stress (TSC-40,  $P = .038$ ), and temporo-limbic activity (LSCL-33,  $P = .042$ ). In addition to HoNOS, doses of antipsychotic medication were significantly correlated to symptoms of dissociation (DES,  $P = .029$ ) and symptoms of traumatic stress (TSC-40,  $P = .029$ ) (see Table 1).

The power analysis of correlations between FCQ and other measures (DES, TSC-40, LSCL-33, CPSI) revealed Fisher Z scores higher than 0.6 (see Table 2).

The regression analysis with FCQ as a dependent variable showed explained variance of 63 % in the model ( $R = .82$ ,  $R^2 = .67$ , adjusted  $R^2 = .63$ ,  $F(4,35) = 17.45$ ,  $P = .001$ ). Table 3 indicates the results of the regression analysis. When controlling for DES, TSC-40 and LSCL-33, the indicator of

sensitization CPSI had the strongest association with the dependent variable. No other independent variable explained any further variance.

### 4. Discussion and Conclusions

In this paper, we examined the association of basic symptoms with trauma-related phenomena among adults with schizophrenia. As expected, higher levels of basic symptoms of schizophrenia were associated with higher levels of symptoms of dissociation, traumatic stress, and sensitization or kindling-like processes. These relationships persisted after controlling for the severity of psychotic symptoms and dosages of antipsychotic and antidepressant medication. Regression analysis revealed that sensitization has the strongest unique link with basic symptoms.

These findings may suggest a way to understand basic symptoms from a different perspective. Originally, Huber supposed that basic symptoms are the most proximal emanation of neurobiological changes in schizophrenia. The study results here may be related to and potentially influenced by trauma. This possibility is consistent with the neural diathesis-stress model in schizophrenia<sup>[46]</sup> or the traumagenic neurodevelopmental model,<sup>[47]</sup> which supposed that diathesis is influenced by trauma and attachment patterns, and it is associated with a heightened response to stressors which may have the augmenting effect of the HPA axis on dopamine synthesis. Similarly, Barker et al. suggest that a pathway from childhood maltreatment to psychosis leads via HPA axis hyperactivation, reduced hippocampal BDNF and oxytocin levels, and NMDA hypoactivation by glutamate, leading to neurocognitive changes which create a background for the onset of schizophrenia.<sup>[48]</sup>

The finding that sensitization had the strongest association with basic symptoms may also point to several other possibilities. To clarify this finding, it is necessary to take into account that sensitization, as a form of kindling phenomena, assessed by CPSI, is a complex variable. Sensitization as reflected by heightened dopaminergic neurotransmission in the mesolimbic system responding to otherwise latent or non-salient stimuli is supposed to have multifactorial origins.<sup>[49]</sup> In addition to childhood trauma, there are other factors, such as genetic predisposition or adverse social and environmental conditions (urban birth, noise pollution, virus infection, cannabis use, etc).<sup>[27]</sup> However, there are more ways of detecting sensitization. In addition to measuring the level of kindling phenomena,<sup>[24]</sup> other researchers assessed the increased rate of persistence of normally transient developmental expressions of subclinical psychotic experiences which have the potential to move to clinically diagnosable psychosis.<sup>[25,50]</sup> It is a task of further research to determine whether both modes of detection resemble the construct of basic symptoms.

The proximity between basic symptoms and sensitization assessed with CPSI might have a further practical aspect.

**Table 1**  
Spearman correlation coefficients between day doses of psychotropic medication, HoNOS, FCQ, DES, TSC-40, LSCL-33, and CPSI.

	EC	EF	HoNOS	FCQ	DES	TSC-40	LSCL-33
EF	-0.057						
HoNOS	0.439	0.063					
FCQ	0.277	0.211	0.245				
DES	0.345	0.149	0.185	0.636			
TSC-40	0.346	0.159	0.330	0.556	0.580		
LSCL-33	0.248	0.299	0.323	0.539	0.571	0.699	
CPSI	0.281	0.254	0.191	0.766	0.608	0.630	0.749

Note: Values at  $P < .05$  are in bold, Fisher Z higher than 0.05.  
CPSI = Complex Partial Seizure-like Symptoms Inventory, DES = Dissociative Experiences Scale, EC = day dosages of antipsychotic medication in equivalents of chlorpromazine (mean in mg), EF = day dosages of antidepressant medication in equivalents of fluoxetine (mean in mg), FCQ = Frankfurt Complaint Questionnaire, HoNOS = version for external evaluation of HoNOS (mean), LSCL-33 = Limbic System Checklist, TSC-40 = Trauma Symptom Checklist-40.

**Table 2**  
Spearman correlation coefficients between FCQ and symptoms of dissociation, traumatic stress, and assessments of sensitization with refined Fisher Z

	R	Refined Fisher Z
DES	0.636	0.99
TSC-40	0.556	0.97
LSCL-33	0.539	0.96
CPSI	0.766	1

CPSI = Complex Partial Seizure-like Symptoms Inventory, DES = Dissociative Experiences Scale, LSCL-33 = Limbic System Checklist, TSC-40 = Trauma Symptom Checklist-40.

**Table 3**  
Results of the regression analysis with FCQ as a dependent variable

	Beta (SD)	B (SD)	T	P
Intercept		0.14 (0.05)	2.88	.007
DES	0.19 (0.13)	0.17 (0.11)	1.49	.144
TSC-40	0.18 (0.15)	0.16 (0.14)	1.17	.249
LSCL	-0.09 (0.17)	-0.08(0.15)	-0.52	.608
CPSI	0.61 (0.17)	0.60 (0.16)	3.66	<.001

Note: Values at  $P < .05$  are in bold.  
B = nonstandardized regression coefficient, Beta = standardized regression coefficient, CPSI = Complex Partial Seizure-like Symptoms Inventory, DES = Dissociative Experiences Scale, LSCL-33 = Limbic System Checklist, T = t-test, TSC-40 = Trauma Symptom Checklist-40.

Although basic symptoms measured by the FCQ self-reported tool showed inconsistent results for the prediction of the onset of the disease,<sup>[12,13]</sup> the assessment of sensitization through kindling-like processes might be promising in the early detection of schizophrenia. It would strengthen alternative access to early detection, supposing that they could provide more consistent results than basic symptoms assessed with FCQ.

Taken together, sensitization is a very promising concept for further study, that may shed light on Huber's original concept of basic symptoms. Sensitization need not be entirely specific for schizophrenia. Complex partial seizure-like symptoms were found in depressed patients,<sup>[36]</sup> in persons with borderline personality disorder,<sup>[51]</sup> in persons following closed head injuries,<sup>[52]</sup> or in smokers with higher levels of distress.<sup>[53]</sup> Similarly, basic symptoms are also found in affective disorders.<sup>[54]</sup> Therefore, sensitization may represent a risk state common to more psychopathological conditions characterized by hypersensitivity to stress, accompanied by heightened dopaminergic transmission in the mesolimbic system and temporolimbic dysfunction which was brought about by the interplay of several etiological factors, where psychic trauma can play an important role. How a specific disorder can develop from this risk state thus emerges as a significant question for further research.

Of note, this study also found the trauma-related measures that were significantly related to one another. This finding was intuitively assumed because all these measures assess trauma- or stress-induced phenomena. On the other hand, it has also been found that these measures do not significantly (CPSI, DES), or only weakly (TSC-40, LSCL-33), correlate to psychotic manifestations (HoNOS). This finding may be seen as consistent with Huber's original hypothesis that there are two levels of symptoms in schizophrenia: basic symptoms resulting from basic disorders and, on the other hand, observable psychotic symptoms which develop from basic disorders after amalgamation with the anthropomorphic matrix, which includes psycho-reactive mediation and adaptive reactions of the mind.<sup>[55]</sup> This dichotomy in the manifestations of the disease may also imply different therapeutic strategies focused on each of these levels. Specific strategies might be developed for the first level of basic disorders and basic symptoms with respect to its stress-induced component.

Interestingly, we have also found significant correlations of day dosages of antipsychotic medication to symptoms of dissociation (DES) and trauma symptoms (TSC-40). A similar finding was also found earlier in the group of patients with borderline personality disorder, but not in the schizophrenia group. It was hypothesized that antipsychotic treatment might decrease activation of the anterior cingulate cortex linked to the detection of cognitive conflict, while a resulting decrease of conscious awareness of conflicting stressful experiences may produce dissociative symptoms measured by DES.<sup>[56]</sup> Data of this study show that this hypothesis may also apply to patients with schizophrenia.

Finally, there are limitations. Our sample size was moderate and included only persons willing to consent to treatment. We used a convenience sample. Replication is needed with larger samples including those who refuse treatment and using probability sampling methods. While we also measured trauma-related phenomena we did not include a fine-grained assessment of the nature of trauma itself. Further work is needed with detailed accounts of the forms and severity of a person's history of trauma. Finally, we employed a cross-section design and thus firm conclusions regarding causality cannot be drawn. While we have largely interpreted results in terms of the effects of trauma on basic symptoms, the reciprocal influence of basic symptoms on trauma symptoms cannot be ruled out nor can the possibility that trauma-related symptoms and basic symptoms are themselves related as the result of variables not measured here. Longitudinal research is needed with multiple assessments of trauma-related and basic symptoms in order to more carefully detangle their causal influences upon one another. Another limitation of our research is the sample of patients with a relatively

long period of previous treatment (the mean period of psychiatric treatment is 16.2 years). A sample of patients at risk for psychosis or with first-episode psychosis would also need to be used in further research to verify the relevance of the findings of this study to the risk of developing the disease. In this regard, it would be appropriate to supplement the assessment of basic symptoms with interview-based instruments to make the predictive validity of basic symptoms assessment more plausible.<sup>[57]</sup> Limitations also did not escape our assessment methods. Taking into account the sample of patients with long-term treatment and reduced social competence, we used the HoNOS scale to measure symptoms, although due to more frequent use in research and better comparability of results, it would be more appropriate to use other tools such as the Positive and Negative Syndrome Scale (PANSS).<sup>[58,59]</sup>

The study found significant correlations of subjective cognitive deficits in schizophrenia, referred to as basic symptoms, to other trauma-related measures. Among these measures, sensitization in the form of kindling phenomena assessed by CPSI showed the major impact. The results may have important relationships to developmental hypotheses of diathesis in schizophrenia and to future research in early detection studies.

### Author contributions

OP - conception and design of the work, data collection, data analysis and interpretation.  
 drafting the article; PL - data analysis and interpretation, drafting the article.  
 critical revision of the article; PB - critical revision of the article, final approval of the version to be published.

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