Traumatic dissociation, epileptic-like phenomena, and schizophrenia

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Submitted: May 5, 2006 *Accepted: May 13, 2006*

Key words: **schizophrenia; dissociation; trauma; stress; epilepsy**

Neuroendocrinol Lett 2006; **27**(3):321–326 **PMID:** 16807521 NEL270306A06 ©Neuroendocrinology Letters **www.nel.edu**

Abstract

OBJECTIVES: According to recent evidence, trauma and stress are important etiological factors in pathogenesis of schizophrenia. However, the hypothetical influence of traumatic stress on epileptic-like (or kindling) phenomena in schizophrenia is at this time unclear.
METHODS: In order to discover the influence of trauma, 82 patients with a diagnosis of paranoid schizophrenia and 50 healthy controls were assessed for symptoms of dissociation, traumatic stress and psycho-sensory symptoms of epileptic origin.
RESULTS: We have found significant traumatization and dissociation in patients who met the cut-off score for psychosensory epileptic-like symptoms and also significant correlations among these measures have been found.
CONCLUSIONS: These data suggest a certain role of epileptic-like phenomena in dissociative states in schizophrenia and are in accordance with rare intracranial EEG findings which suggest a certain role of epileptiform events in schizophrenia.

ORIGINAL ARTICLE

Introduction

Several studies have proven that one influence of trauma in schizophrenia is that stress represents significant precipitating factors of schizophrenia [7, 12, 27, 38]. Pathological influence of traumatic stress closely relates to specific vulnerability of the nervous tissue (mainly in the hippocampus), genetic factors, and perinatal insults. Perinatal insults as well as later traumatic stress have lasting effect and play an important role in etiology of schizophrenia [5, 29, 30, 61]. Animal models show that minor birth complications may alter the way in which dopaminergic receptors are regulated by stress in the adult rat. These findings correspond to evidence that stress represents a precipitating factor of schizophrenia [7, 27, 38].

According to a neural diathesis-stress model, stressors can exacerbate symptoms but do not constitute causal factors. The model corresponds to evidence that specific vulnerability in schizophrenia patients is associated with heightened sensitivity to stressors [64]. According to neurodevelopmental research traumatic events such as childhood abuse or neglect in the first years of life often have long-term impact on emotional, behavioral, cognitive, social and physiological functions [12, 20, 23, 36, 43, 59]. Traumatic insults may induce a hyper-excitable state linked to a lowered seizure threshold and can lead to a latent epileptogenic process or may result in epilepsy. The kindling model of epilepsy has modeled these processes in animals. Kindling is actually the repetition of sub-convulsive electric stimuli that can induce lowered seizure threshold and may result in a progressive epileptic state. Although this model is quite elaborated in animals it is unclear whether

kindling really corresponds to human epileptogenesis [26, 63]. The kindling model has also been proposed as explanation for the "epileptic-like" phenomena in relationship to repeated trauma and stress, such as child abuse and neglect [41, 42, 59]. This is in accordance with evidence that in certain psychiatric patients, often without apparent EEG abnormalities, psycho-sensory symptoms of epileptogenic nature occur (the so-called complex partial seizure-like symptoms). These symptoms normally belong to characteristic manifestations of temporal lobe epilepsy but may also emerge without apparent seizures in the so-called Epilepsy Spectrum Disorders [21, 24, 44]. Symptoms which are characteristic in these cases are memory gaps, confusion spells, staring spells, episodic irritability, episodic rhinitis, episodic aphasia, jamais-vu, olfactory hallucinations, gustatory hallucinations, visual illusions (e.g., scintillations), paresthesia, anesthesia, auditory illusions (e.g., phone ringing). In addition, patients suffer from headache with nausea and/or photophobia, abrupt mood shifts, deja-vu, abdominal sensations, intrusive thoughts and parasomnias [21, 44, 46]. A great many of these symptoms are characteristic in the so-called Epilepsy Spectrum Disorder (ESD). Although the phenomenology of ESD and the positive clinical response to anticonvulsant seen in most ESD patients would suggest the presence of sub-clinical electrophysiological dysfunction, the lack of clear non-behavioral evidence of CNS dysfunction (i.e., EEG) may obscure the underlying neurological nature of ESD [21, 44]. On the other hand, these epileptic-like symptoms are also in close relationship to increased sensitivity to parental influence and dissociative tendency related to child abuse and other traumatic or aversive events [45].

Common response to traumatic stress exists in two main forms. The first includes disturbances of self-regulatory systems such as hypothalamus-pituitary-adrenal axis (HPA) resulting in hyperarousal, tachycardia or other symptoms of autonomic nervous system instability. The second form of response to stress includes dissociative symptoms. A main characteristic feature of dissociation is "breaking" or "splitting" of "psychic unity" predominantly because of experienced traumatic stress [40, 43, 67, 68]. Dissociation represents a special form of consciousness in which events ordinarily connected are divided from one another [28]. According to the modern definition, dissociation represents a disturbance or alteration in the normally integrative functions of identity, memory, or consciousness and may lead to characteristic somatoform symptoms [1, 37, 52, 66].

History of the study of dissociation began in the second half of the nineteenth century mainly in the work of Pierre Janet, who elaborated the concept of dissociation in his work "Psychological Automatism" where he described psychopathological phenomena during hysteria, hypnosis, states of suggestion or possession [4, 17, 25, 69]. The same aspects of cognitive pathology were pointed out in Bleuler's notion of schizophrenia, who understood disturbed schizophrenic cognition because of "splitting", closely related to Janet's concept of dissociation [8, 9, 47, 48]. In his *Textbook of Psychiatry* [8], Bleuler wrote, *"It is not alone in hysteria that one finds an arrangement of different personalities one succeeding the other. Through similar mechanism schizophrenia produces different personalities existing side by side."* [p. 138]. The creation of personalities in multiple personality, according to Bleuler [8, 9, 48], is the similar to the process of splitting in schizophrenia due to dissociative mechanism most often because of abuse or traumatic experiences in childhood. Bleuler's introduction of a group of schizophrenias in 1911 replaced Kraepelin's term dementia praecox and defined new concepts for the understanding of the disease. A review of Index Medicus from 1903 to the revival of interest in multiple personality in 1978 shows a dramatic decline in the number of reports of multiple personality, which indicates that many patients with multiple personality had been diagnosed and treated as patients with a diagnosis of schizophrenia [47]. It corresponds to findings that a substantial number of patients with multiple personality disorder have previous diagnoses of schizophrenia [9, 48].

The close relationship of schizophrenia and dissociative disorders is clinically important due to the presence of the same positive symptoms of schizophrenia, both in patients diagnosed with multiple personality as well as in those diagnosed with schizophrenia. In many cases, those with multiple personality actually report more positive symptoms of schizophrenia than patients diagnosed with schizophrenia [13, 14].

These historical and recent findings suggest a hypothesis that traumatic stress and dissociation in schizophrenia are closely related. It implicates close relationship between important etiological factors in schizophrenia such as increased stress and trauma and increased dissociation. A second hypothesis states that trauma, stress, and dissociation in schizophrenia relate to epileptic-like phenomena that might arise from repeated trauma and lead to increased complex partial seizure-like symptoms. This hypothetical connection among traumatic stress, dissociation and epileptic-like phenomena is in accordance with evidence that in patients with dissociative disorders frequent and unusual EEG abnormalities without common epileptic seizures occur [2, 4, 6, 11, 23, 34, 49, 51, 58, 59]. This hypothesis may also contribute to the problem of indication of several schizophrenic patients to anticonvulsant therapy because of reported evidence that a clear majority of patients with epilepsy spectrum disorder respond well to anticonvulsant treatment.

Methods

Participants

The participants consisted of 82 adult schizophrenic outpatients from the university hospital and 50 healthy controls from general population. 47 males and 35 females with a mean age of 28.3 took part in the study. The 50 healthy controls were 20 males and 30 females with a mean age of 28.7. Patients had diagnosis of paranoid schizophrenia. Actual state of patients was relatively

stabilized in partial remission. All of the patients at the time of the recruitment were being treated with antipsychotic medications. Exclusion criteria were organic illnesses involving the central nervous system, substance and/or alcohol abuse, mental retardation and significant extra pyramidal symptomatology. Two of the authors of this article independently confirmed the given diagnoses according to DSM IV criteria [1].

Design

In the clinical study, 82 adult patients with diagnosis of paranoid schizophrenia and 50 healthy controls were assessed. In the assessment, five measures for symptoms of dissociation, traumatic stress and complex partial seizure-like symptoms in the patients were used**.** Investigations took place in a quiet room and all the interviews were performed individually as a clinical interview with informed consent of all the participants.

Measures

Psychic dissociative symptoms were assessed by Dissociative Experiences Scale (DES) [3]. DES represents 28 items self-reported questionnaire examining main dissociative phenomena such as absorption, amnesia, depersonalization, derealization, reality distortion, and others. Subjects indicate a degree of their experience on the continuum from 0% to 100%. DES scores were separated into two sets. The first set contains the whole group of patients and the second characterizes patients who satisfy cut-off scores for dissociative disorders (DES≥25).

Somatoform dissociative symptoms were assessed using the 20-item self-reported somatoform dissociation questionnaire SDQ-20 [37]. Somatoform dissociative symptoms represent alterations in sensations of pain (analgesia, kinesthetic anesthesia), alterations of perception, inhibited or loss of motor control, gastrointestinal symptoms, etc. Subjects indicate the degree of their experience on 5-point likert scale. Again, the SDQ scores were also separated into two sets, the first set for the whole group of patients and the second that characterized patients who satisfy cut-off scores for somatoform dissociative disorders (SDQ≥40).

For investigation of childhood traumas, TSC-40 (Trauma Symptom Checklist) [10] was used. TSC-40 is a self-reported 40-item questionnaire done on a 4-point likert scale. Along with the main score it also contains subscales for assessment of dissociation, anxiety, depression, sexual abuse trauma index (SATI), sleep disturbances and sexual problems. Total scores on TSC-4 higher than 70 are associated with symptoms of significant childhood traumas.

Subjectively experienced stress was assessed by IES (Impact of Event Scale) [22]. IES is a 15-item self-reported questionnaire on a 4-point likert scale. This instrument reflects the intensity of posttraumatic phenomena based on subjectively experienced stress. IES consists of two main groups of questions that measure intrusion and avoidance. For IES, a score ≥ 35 is highest value of prediction (0.88) and subjective stress measured by IES is associated with the criteria for posttraumatic stress disorder [55].

The 35-item Structured Clinical Interview [the so-called Iowa interview] assessed complex partial seizure-like symptoms that reflect temporal lobe epileptic activity [44, 46]. Symptoms experienced by the patients are indicated on 6-point likert scale. These symptoms represent characteristic manifestations indicated in patients with complex partial epilepsy at first described by Hughlings Jackson in his classical studies about dreamy states and psychological dissolution, which are conceptually analogical to dissociation [45].

Analysis

Descriptive statistics in a statistical evaluation included medians, means, and standard deviations. For further statistical evaluation, Pearson product-moment correlations and t-test for independent samples for the whole group of patients and normal healthy controls were calculated.

Results

Results of descriptive statistics are in Table 1 and Table 2. This data suggests significant dissociation and traumatization in the schizophrenic patients (30.5%, N=25) who met the cut-off score for dissociative disorders [either psychic or somatoform]. Most significant traumatization has been found in patients who met the cut-off score of psycho-sensory epileptic-like symptoms which is characteristic for the epilepsy spectrum disorder (8.5%, N=7). Significant correlations (Table 3) between dissociative symptoms, characteristics of traumatic stress and complex partial seizure-like symptoms were found. These correlations suggest significant relationships among traumatic influence, subjectively experienced stress, dissociation, and epileptic-like phenomena. Results of t-tests between measures for the patients and for the control group (Table 1) suggest that both groups are significantly different.

Discussion

The present data shows that a marked number of schizophrenic patients who satisfy cut-off scores for dissociative disorders (30.5%, N=25, DES≥25 or SDQ≥40) had significantly higher traumatization, subjectively experienced stress and complex partial seizure-like symptoms than the whole group of patients. Significant correlations of these symptoms support the hypothesis of a close relationship between traumatic stress and dissociation in schizophrenia, and confirm the findings that reported a marked level of dissociative symptoms in schizophrenic patients and schizotypal individuals [3, 33, 43, 53, 54,]. From the neurobiological point of view, influence of psychosocial stressors on schizophrenia confirms an important role of neurohormonal indicators of stress responsivity, mainly cortisol release resulting from

Table 1. Descriptive statistics for the whole group of schizophrenic patients and for the healthy controls.

	All schizophrenic patients N=82		Normal healthy controls N=50		All the patients and controls
Variable	Mean±SD	Median	Mean±SD	Median	t-test
Age, years	28.3±8.3	27.0	28.7±8.5	26.0	-0.26*
DES	15.7±13.1	13.0	8.5±9.0	5.4	3.43***
SDQ-20	29.2±9.9	26.0	21.8±3.5	20.0	5.08*****
TSC-40 Tot.	32.7±21.6	29.5	13.7±15.4	8.0	5.44*****
TSC-40 Diss.	5.15±4.0	4.5	3.3±4.0	2.0	2.49 **
TSC-40 Anx.	6.7±5.2	5.0	2.7±3.6	1.0	4.86*****
TSC-40 Dep.	7.2±5.1	7.0	2.2±3.2	0	6.28*****
TSC-40 SATI	5.4±4.2	4.5	1.5±2.5	0	5.94*****
TSC-40 Sleep	5.5±3.9	5.0	1.8±3.1	0	5.87*****
TSC-40 Sex.	5.9±5.0	5.0	2.8±4.3	0	3.7****
IES	25.2±16.9	25.0	9.0±11.9	3.5	5.93*****
Iowa	25.6±23.5	23.0	9.7±10.3	7.0	4.51*****

Note. DES= Dissociative Experiences Scale, SDQ-20= Somatoform Dissociation Questionnaire, TSC-40 Tot.= Trauma Symptom Checklist- total score, Diss.= dissociation, Anx.= anxiety, Dep.= depression, SATI= sexual abuse trauma index, Sleep= sleep disturbances, Sex.= sexual problems, IES= Impact of Event Scale, Iowa= Structured Clinical Interview for Complex Partial Seizure-like Symptoms, *p =0.80, **p =0.014, ***p= 0.002, ****p = 0.000337, *****p < 0.00001

activation of the hypothalamic-pituitary-adrenal axis. In this manner, stress worsens the schizophrenia symptoms. Stress takes effect simultaneously with abnormalities of dopaminergic receptors and hippocampal damage and at the same time influences the patient hypersensitivity to stress. The close relationship of dissociative symptomatology and traumatic stress suggests an important role of dissociative processes in schizophrenia as a typical manifestation of cognitive pathology. Neurobiological levels related to this cognitive disintegration are intuitively attributed to damaged neural connectivity because of a widely accepted fact that connectivity plays a fundamental role in brain functions [39, 60]. A more comprehensive explanation of neurobiological mechanisms of cognitive disintegration in schizophrenia might help in the neuroscientific search to find neural correlates of consciousness. Contemporary research of neural correlates of consciousness is confronted with the so-called binding problem that points to unresolved mechanisms that connect neural activities at the forming of mental representations and enables the unity of consciousness [60]. Disturbances in the binding process are hypothetically attributed to epileptiform activity as an antibinding mechanism [31, 32] and concomitant breaking of psychic unity thus might represent a fundamental process in the pathogenesis of schizophrenia and dissociative disorders. This data seems to be in accordance with Bleuler's concept of splitting [or dissociation] in schizophrenia with a possible role of epileptic-like phenomena related to dissociation.

Results also support the hypothesis that epileptogenic phenomena are related to traumatic stress in pathogenesis of dissociative states in schizophrenia because of significant correlations of traumatic stress, dissociation, and complex partial seizure-like symptoms. This is in accord with recent findings that schizophrenia as well as epilepsy is related to a loss of physiological balance between excitation and inhibition. Epilepsy is linked to over-excitation while on the other hand schizophrenia is connected to over-inhibition in the nuclei of the limbic system, hypothalamus and their projection sites [57]. In epilepsy the normal equilibrium between excitation and inhibition is permanently altered by repeated focal excitation or kindling, resulting in a permanent state of excessive focal excitability and spontaneous seizures [15, 57]. Similar "kindling" or sensitization may be induced in inhibitory systems in response to focal physiological pulsed discharges of limbic and hypothalamic neurons and this excess of inhibitory factors may then be manifested as a psychosis [56, 57]. This might correspond to intracranial (stereo-tactic) EEG studies in schizophrenia patients which reported epileptic discharges in limbic structures [16, 18, 19, 35, 50, 65,]. This suggests the hypothesis that schizophrenia may represent a compensatory error, which is physiologically reciprocal to epilepsy [57]. Data reported in this study supports the kindling hypothesis of dissociation in schizophrenia and are in accord with rare intracranial EEG findings. A practical purpose of this assessed relationship between traumatization, dissociation and epileptic-like phenomena in the patients who met cut-off score for epilepsy spectrum disorder may be contribution to the problem of indication of several schizophrenic patients to anticonvulsant therapy because of reported evidence that a clear majority of patients with epilepsy spectrum disorder respond well to anticonvulsant treatment. Careful assessment of this test battery may be useful also for anticonvulsant treatment strategy.

Table 2. Descriptive statistics for the patients with DES≥25, for the patients with SDQ≥40 and for the patients with Iowa≥70.

	Schizophrenic patients with DES≥25, N=18		Schizophrenic patients with SDQ≥40, N=12		Schizophrenic patients with Iowa≥70, N=7	
Variable	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median
Age, years	25.9±6.4	25.0	27.7±9.5	25.0	24.3±9.2	19.0
DES	36.5±9.5	34.5	22.5±17.0	21.0	35.7±12.7	35.0
SDQ-20	34.8±12.7	34.0	48.5±8.8	46.0	43.3±15.8	40.0
TSC-40 Tot.	50.3±21.3	54.5	53.2±21.5	55.0	61.0±15.2	67.0
TSC-40 Diss.	8.7±3.9	9.0	8.8±4.1	8.0	10.1±2.7	8.0
TSC-40 Anx.	10.5±5.7	10.0	13.0±5.7	13.5	13.7±4.9	14.0
TSC-40 Dep.	10.0±4.6	11.0	11.9±5.3	12.0	12.1±3.6	12.0
TSC-40 SATI	8.7±4.3	10.0	8.7±3.8	8.5	9.6±3.6	11.0
TSC-40 Sleep	7.7±4.1	7.5	9.7±4.3	10.0	9.0±5.0	9.0
TSC-40 Sex.	9.2±5.7	10.0	7.3±4.8	7.0	11.0±3.5	12.0
IES	34.2±15.3	36.5	43.1±8.7	42.5	37.1±12.0	42
Iowa	49.5±30	44.5	43.7±33.2	38.5	82.6±6.3	85.0

Table 3. Correlation among measures for 82 schizophrenic patients

Variable	DES	SDQ-20	TSC-40 Tot.	IES	Iowa
DES	1.0	0.34*	0.56**	0.38**	0.57**
SDQ-20	0.34*	1.0	0.58**	0.6**	0.47**
TSC-40 Tot.	0.56**	0.58**	1.0	0.7**	0.69**
TSC-40 Diss.	0.61**	0.47**	0.9**	0.61**	0.59**
TSC-40 Anx.	0.49**	0.62**	0.88**	0.65**	0.54**
TSC-40 Dep.	0.43**	0.55**	0.87**	0.64**	0.64**
TSC-40 SATI	0.54**	0.47**	0.89**	0.59**	0.57**
TSC-40 Sleep	0.47**	0.53**	0.78**	0.56**	0.58**
TSC-40 Sex.	0.43**	0.37**	0.82**	0.55**	0.41**
IES	0.38**	0.6**	0.7**	1.0	0.48 **
Iowa	0.57**	0.47**	0.69**	0.48**	1.0**

Note. Marked correlations are significant at: *p < 0.01; **p < 0.001

Acknowledgements

Authors thank for support by research project 1M06039 (Center for Neuropsychiatric Research of Traumatic Stress).

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