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Autoreferát disertační práce



Štěpení a disociace u schizofrenie

Splitting and Dissociation in Schizophrenia

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Disertační práce bude nejméně pět pracovních dnů před konáním obhajoby zveřejněna k nahlížení veřejnosti v tištěné podobě na Oddělení pro vědeckou činnost a zahraniční styky Děkanátu 1. lékařské fakulty.

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Summary

The term splitting is defined as a process of formation of mental aggregates linked to incompatible experiences producing numerous divisions in mental apparatus. Current findings indicate that psychological splitting in schizophrenia is likely specifically presented on a neural level as disrupted organization in neural communication.

In this context, a purpose of the first part of the empirical research was to examine relationships between psychological process of splitting and disturbed cognitive and affective functions in schizophrenia. We assessed 30 patients with schizophrenia and 35 patients with borderline personality disorder (BPD) as a control group. The main results showed that the symptoms of splitting measured using self-reported Splitting Index (SI) were significantly higher in BPD group than in schizophrenia, and on the other hand, verbal fluency as a measure of semantic memory disorganization was significantly lower in schizophrenia group. The results suggest that processes of splitting are different in schizophrenia and BPD. In BPD patients splitting results to mental instability, whereas in schizophrenia the mental fragmentation may lead to splitting of associations observed as lower scores of verbal fluency.

The second empirical study assessed the occurrence of dissociative and other psychopathological symptoms in schizophrenia (31 patients) and compared the presence of these symptoms with BPD (36 patients) and beyond that it assessed the possible influence of antipsychotic medication on the dissociative symptoms. The results support an important role of dissociative processes in schizophrenia and BPD. The dissociative symptoms were significantly correlated with symptoms of traumatic stress and with psychopathological symptoms in the both disorders. Interestingly, we have found remarkably significant correlations between dissociative symptoms measured by the Dissociative Experiences Scale (DES) and levels of antipsychotic medication (measured by chlorpromazine equivalents). This finding suggests a significant relationship between manifestations of dissociative symptoms in BPD and antipsychotic medication.

Shrnutí

Pojem štěpení je definován jako proces, při kterém se tvoří agregované soubory psychických elementů, které není možné vzájemně propojit pro neslučitelnou psychickou zkušenost. Soubory pak vytvářejí mnohočetná dělení uvnitř psychického aparátu. Současné poznatky ukazují, že psychické štěpení u schizofrenie se pravděpodobně specificky projevuje na neurální úrovni jako narušení organizace v neurální komunikaci.

V této souvislosti bylo účelem první části empirického výzkumu ozřejmit vztahy mezi psychologickým procesem štěpení a narušenými kognitivními a afektivními funkcemi u schizofrenie. Vyšetřovali jsme 30 pacientů se schizofrenií a 35 pacientů s hraniční poruchou osobnosti (HPO) jako kontrolní skupinu. Hlavní výsledky ukázaly, že symptomy štěpení, měřené za použití sebemonitorovací škály index štěpení (Splitting Index - SI), byly signifikantně vyšší u HPO než u schizofrenie a na druhou stranu byla verbální fluence, použitá pro ohodnocení stupně dezorganizace sémantické paměti, signifikantně nižší ve skupině pacientů se schizofrenií. Výsledky naznačují, že proces štěpení je odlišný u schizofrenie a HPO. U pacientů s HPO štěpení ústí do psychické nestability, zatímco u schizofrenie psychická fragmentace může vést k asociačnímu štěpení, které lze sledovat v nízkých skórech verbální fluence.

Ve druhé výzkumné studii jsme vyšetřovali výskyt disociačních a dalších psychopatologických symptomů u schizofrenie (31 pacientů) a srovnávali přítomnost těchto symptomů s jejich výskytem u HPO (36 pacientů) a vedle toho jsme zjišťovali možný vliv medikace antipsychotiky na symptomy disociace. Výsledky podporují důležitou roli disociačních procesů u obou psychických poruch - schizofrenie a HPO. Disociační symptomy, měřené škálou disociačních zkušeností (Dissociative Experiences Scale - DES) byly signifikantně korelovány se symptomy traumatického stresu a s psychopatologickými symptomy. Zajímavým nálezem byly výrazně signifikantní korelace mezi disociačními symptomy (DES) a úrovní antipsychotické medikace (měřené v ekvivalentech chlorpromazinu). Nález naznačuje signifikantní vztah mezi projevy disociace u HPO a antipsychotickou medikací.

1. Introduction

The term splitting can be defined as a forming of mental aggregates of incompatible experiences that cannot be synthesized (Freedman, 1980). Freud and Breuer (Breuer, 1893) defined splitting process as a division in mental apparatus and as a split of different psychic groupings or ego nuclei. Later authors defined “splitting of representations” and characterized it by disaggregation of mental images and semantic descriptions of objects, events and the self, for example splitting of one object into two images – ”good” one and ”bad” one (Freud, 1915a; Brook, 1992) or explained splitting as a consequence of a defense mechanism against destructive impulses within the self (Bychowski, 1956; Klein, 1946, Kernberg, 1975). In general, the psychological concept of splitting on its various levels leads to a separation of mental groupings that creates relatively autonomous psychic structures due to reduction of the synthetic and integrative capabilities in order to protect mind against conflicting processes within mental apparatus (Fairbairn, 1941; Glover, 1943; Bromberg, 2009; Stern, 2009; Hinshelwood, 2008).

In schizophrenia Bleuler suggested a systematic description of splitting—as a form of dissolution—based on psychodynamic approach (1911/1950) in his monograph ‘Dementia praecox or the group of schizophrenias’. Bleuler described basic forms of splitting in schizophrenia as a consequence of disturbed associations there. The first form of this process represents associative splitting or “loosening of associations”, when normal pathways of associations have decreased their ”cohesiveness”, which leads to displacements, condensations, confusions, generalizations, clang-associations, illogical thinking and incoherence. In this context Freud (1923) postulated that basic aspect of schizophrenia represents a conflict between the ego and external reality that leads to defense mechanisms (projection, disavowal with formation of delusions or hallucinations) related to preservation of the ego identity against mental fragmentation. Lately, splitting has been also described as a disturbance or disconnection between two (or more) mental states or thoughts preventing conscious awareness against unbearable negative emotions

(Klein, 1946; Bion, 1959). Moreover, a limited capacity to differentiate between inner and outer world, and between subject and object has been also considered to be closely linked to schizophrenic splitting (Lustman, 1977; Freedman, 1980; Lerner and Lerner, 1982; Blatt and Auerbach, 2001). Many theories supposed that the process leading to a loss of differentiation and distinctions that causes the undifferentiated state is rooted already in psychic development (Peciccia and Benedetti, 1996; Stern, 1985; Ogden, 1989).

Current findings indicate that psychological splitting in schizophrenia is likely specifically presented on a neural level as disrupted organization in neural communication. This disrupted neural communication likely underlies deficits in mental processing described by various neuroscientific concepts such as theories of disturbed connectivity, dynamic complexity and corollary discharges.

The relationship between mental disintegration and disturbed functional integration of the brain has been significantly developed in the theory of disconnection (Friston, 1996) or dysconnectivity (Stephan et al., 2009) of neural activities across different brain regions which likely may significantly influence perceptual, emotional and cognitive processes (Park and Thakkar, 2010). In this context, disconnection means a deficit of functional integration among functionally specialized systems of various neural populations represented in different cortical areas (Friston, 1996; Park and Thakkar, 2010). The neural disconnections may also be linked to various dysplastic changes and related to abnormal modulation of plasticity through dopamine and acetylcholine neurotransmitter systems (Friston, 2002). The disconnection processes also significantly influence regionally specialized neural activities responsible for emotional learning and memory such as prefrontal and temporal cortex, mainly mediated by NMDA glutamate transmissions (Friston, 1996, 1998; Stephan et al., 2006, 2009).

The theory of dynamic complexity deals with the process of disturbed neural integration leading to increased or decreased functional segregation among groups of neurons which might also be quantified using concepts from statistical information theory and in particular by defining a measure of neural complexity that could provide a possible explanation for a

failure of stability and self-regulatory processes related to disorganized cognition in schizophrenia (Bob, 2008; Breakspear, 2006; Sporns et al., 2000; Sporns et al., 2002; Bob et al., 2009; Tononi and Koch, 2008). An increase in complexity is often associated with symmetry breaking and the ability of a system to have different states, which is also associated with a decrease in coherence in space over the long range (Weng et al., 1999).

The concept of corollary discharges describes a specific form of mental disintegration in schizophrenia linked to loss of differentiation of the internal and external world that is likely related to deficits in communication between the frontal and temporal lobes (Ford et al., 2005). The loss of distinctions between internally generated psychic activity and external input might be a neural substrate for hallucinations leading to defective self-monitoring and self-integrity originating in motor brain structures (Feinberg, 1978; Feinberg and Guazzelli, 1999). The motor commands from the brain structures are associated with neural discharges that alter activity in both sensory and motor pathways. These neural discharges called corollary discharges (or efference copies) enable monitoring and modification of the commands themselves before an effector event is processed. In addition, they enable to inform sensory systems that the stimulation produced by movement is self-generated or produced by an environment, which is crucial for the distinction between self and non-self (Feinberg, 1978; Ford et al., 2001; Ford et al., 2005; Ford et al., 2007; Poulet and Hedwig, 2007). In addition, this loss of distinctions may cause auto-noetic agnosia as an inability to discriminate a self-generated mental activity from an externally generated one (Keefe et al., 2002).

In summary, the process of mental splitting likely might be related to some form of “neural splitting” in coordinated brain activity and information processing. Particular consequence of the splitting is also disturbed process of self-reference based on an ability to distinguish between the self and an external world.

2. Hypotheses and aims of the study

2.1. Several findings indicate that splitting as an alteration on mental level may be linked to great and abrupt changes in patterns of neural activity that may dissociate, or split off, certain external and internal stimuli and information out of awareness, which may lead to distinct states of divided consciousness (Hilgard, 1986; Crawford, 1994; Rainville et al., 2002; Vermetten and Douglas, 2004; Bob, 2008) and disorganization of semantic memory (Goldberg et al. 1998, Paulsen et al. 1996, Robert et al. 1998). A purpose of the study was to examine relationships between psychological process of splitting and disturbed cognitive and affective functions in schizophrenia. A sample of patients with borderline personality disorder (BPD) was used as a control group, because the process of splitting has been specifically described in schizophrenia as well as in BPD. We have tested relationship between splitting and verbal fluency as an indicator for semantic memory disorganization (Goldberg et al., 1998; Paulsen et al., 1996; Franceschi, 2013) in patients with schizophrenia and BPD. To test how the splitting process is typically represented in schizophrenia and BPD we have compared occurrence of these psychopathological manifestations in schizophrenia and BPD and their relationships to other symptoms.

2.2. Dissociation in principle describes fragmentation of conscious experience that is typically related to long-term or acute stress that significantly disturbs self-concept, identity, memory, and perception of the external world (Breuer and Freud, 1895; Stone, 1988; Bob, 2008; Ellenberger, 1970). Dissociation also reflects shifts of mind related to a consciously experienced conflict of opposing mental forces. In the similar context as Janet, also Bleuler coined the term splitting and described the process of mental fragmentation in schizophrenia as a basic step in the pathogenesis of the disease (Bob, 2012; Hilgard, 1986; Bleuler, 1911/1950). The term fragmentation of consciousness in the sense of splitting was also defined in borderline personality disorder (BPD) as a specific form of dissociation, and recent studies suggest that the relationship between dissociative symptoms and BPD per se is very close

(Korzekwa et al., 2009; Zanarini and Jager-Hyman, 2009; Zanarini et al., 2008).

With the aim to find specific relationships between dissociative symptoms, stress-related symptoms and other psychopathological symptoms in schizophrenia we assessed a group of schizophrenia patients and compared with a sample of patients with borderline personality disorder (BPD). We compared manifestation of dissociation between these groups and assessed relationships between dissociation and other symptoms. We also assessed the possible influence of antipsychotic medication using chlorpromazine equivalents (EC).

3. Material and Methods

3.1. The sample included 30 patients with schizophrenia, i.e. 15 men and 15 women, mean age 35.7 (SD = 9.2) with mean period of psychiatric treatment 12.89 (SD = 7.8 years) and with average of 4.1 hospitalizations. The sample of BPD patients included 35 participants, i.e. 10 men and 25 women, mean age 32.0 (SD = 7.9) years with mean period of psychiatric treatment 6.2 (SD = 3.97) years and with average of 2.28 hospitalizations. The symptoms of splitting were measured using self-reported Splitting index (SI) (Gould et al., 1996). Other psychopathological manifestations in both groups of patients were measured using Health of the Nation Outcome Scales (HoNOS) (Wing et al., 1996). As a measure of semantic memory disorganization we have used verbal fluency test (Preiss et al., 2002; Goldberg et al., 1998, Paulsen et al., 1996). Statistical evaluation of the results of SI and other psychometric measures included descriptive statistics, Mann-Whitney test for independent samples and Spearman correlation coefficients.

3.2. The schizophrenia sample comprised 31 patients (15 men and 16 women) of mean age 36.2 ± 9.5 years. The BPD sample comprised 36 patients (eleven men and 25 women) of mean age 31.0 ± 8.7 years. We used the Dissociative Experiences Scale (DES) to screen for dissociative

symptoms (Bernstein and Putnam, 1986). Symptoms related stress and traumatic experiences were measured using the Trauma Symptom Checklist-40 (TSC-40) (Elliot and Briere, 1992). Psychotic manifestations in both groups of patients were measured with Health of the Nation Outcome Scales (HoNOS) (Wing et al., 1996). As measurable equivalent characterizing their current medication we have used EC. Statistical evaluation of the results for the DES and other psychometric measures included descriptive statistics, the Mann–Whitney U test for independent samples, and Spearman correlation coefficients.

4. Results

4.1. Results show significant differences in scores of splitting, verbal fluency and psychopathological symptoms measured by HoNOS between schizophrenia and BPD groups that were compared using Man-Whitney test. Mean score of the Splitting Index (SI) was significantly higher in BPD group than in schizophrenia. On the other hand score of verbal fluency was significantly lower in schizophrenia group. Results also show significant Spearman correlation coefficients characterizing relationships between splitting, verbal fluency and psychopathological symptoms measured by HoNOS in both samples. Very significant relationship between verbal fluency and the SI “factor of others” in schizophrenia patients was found (Spearman $r = -0.52$, $p, 0.01$). Other significant correlations in schizophrenia patients were found between self-reported score of HoNOS (HoNOS(S)) and total score of splitting (SI) (Spearman $r = 0.42$, $p, 0.05$) and between HoNOS(S) and SI(S) [representing splitting of the self] (Spearman $r = 0.63$, $p, 0.01$). On the other hand significant correlations in borderline personality disorder were found between HoNOS(S) and SI(S) [representing splitting of the self] (Spearman $r = 0.45$, $p, 0.01$) and between HoNOS self-reported score and verbal fluency (Spearman $r=0.37$, $p, 0.01$).

4.2. Although the differences in DES scores between patients with schizophrenia and those with BPD were not statistically significant, scores

for symptoms of traumatic stress measured by the TSC-40 were significantly higher in the BPD group. The results also show that scores on the DES, TSC-40, and HoNOS were significantly correlated. Significant correlations were found in BPD patients between levels of EC and the DES score (Spearman's correlation $r=0.37$; refined Fisher's exact test $Z=0.14$) and between EC and depersonalization/derealization score on the DES (Spearman's correlation $r=0.37$; refined Fisher's exact test $Z=0.38$).

5. Discussion

5.1. Main results of this study indicate significant differences in splitting, verbal fluency and psychopathological symptoms between schizophrenia and BPD patients. These findings show significantly higher level of splitting measured by SI in BPD patients compared to schizophrenia. On the other hand schizophrenia patients show significantly lower scores of verbal fluency most likely as a consequence of cognitive disorganization that in principle is in agreement with Bleuler's historical concept of splitting in schizophrenia (Bleuler, 1911). In this context, the correlation between verbal fluency and splitting (factor of others) in schizophrenia suggests that stronger levels of splitting into opposite aspects related to external objects and persons is related to disassociation of memory patterns that is manifested as disturbed verbal fluency.

5.2. Results show that dissociative symptoms and symptoms of traumatic stress are significantly correlated in patients with BPD and in those with schizophrenia. The data also show that symptoms of traumatic stress are higher in BPD than in schizophrenia, which is in agreement with the findings of other (Kingdon et al., 2010; Putnam et al., 1996; Brunner et al., 2004). On the other hand, DES and TSC-40 scores were significantly correlated with symptoms of psychosis in both disorders and, as in other studies of patients with schizophrenia, symptoms of traumatic stress were associated with psychotic symptoms (Read et al., 2005; Ross et al., 1994). In agreement with other studies, we also found that dissociation in

schizophrenia is closely related to symptoms of trauma (Sar et al., 2010; Schafer et al., 2012; Ross 2009; Spitzer et al, 1997; Vogel et al., 2009,). Similar relationships between stress and dissociation have also been found in patients with BPD (Korzekwa et al., 2009; Howel and Blizard, 2009). An interesting finding of this study was the correlation between doses of antipsychotics measured in EC and dissociative symptoms in patients with BPD. This result suggests a specific psychotropic effect of antipsychotic medication in these patients. The possible influence of medication on dissociative symptoms might reflect the extremely important role of stress in BPD.

6. Conclusions

In the presented experimental studies we aimed at finding relationships between psychological splitting and dissociation in schizophrenia on one side and other cognitive dysfunctions like semantic memory disorganization or symptoms on the other side. Mental fragmentation in schizophrenic patients may be related to deficits in contextual processing that may be primarily based on brain's ability to integrate information that may be linked to various etiological conditions reflecting pathological processes on molecular, physiological and psychological levels. This brain potentiality to integrate information is on cognitive level specifically linked to ability to create integrated self-concept and synthetic capabilities related to various forms of metacognitive deficits that is typical impaired in schizophrenia (Lysaker et al., 2013; Dimaggio et al., 2008). Metacognition as a psychological process is defined as a spectrum of mental activities that involves thinking about thinking and integration of mental events into larger complex representations of self and others including also a reflection about that larger representation (Lysaker et al., 2013). Synthetic metacognition is assessed by analyzing discourse. The concept of synthetic metacognition links also splitting in schizophrenia with novel trends in psychotherapy of schizophrenia. Psychotherapeutic approaches directed to integration of splitted parts of mental content or to fostering of stabile mental representation in schizophrenia has been

applied in the last decades, e.g. complex forms of cognitive remediation (Roder et al., 2011), supportive psychodynamic approaches (Rosenbaum et al., 2012), psychoanalytic psychodrama (Corcos et al., 2012), self-complexity (Martens, 2009). Considering the possible close relationship between defective synthetic metacognition and splitting we can expect further progress from recent forms of therapy related to improvement of synthetic metacognition (Hasson-Ohayon, 2012; Brent, 2009). The aim of this novel treatment is to help persons to form more complex and integrated representations about themselves and others and use this knowledge to respond to psychological problems.

Continuous research that would further clarify mutual relatedness between brain functions, splitting and metacognition might enable to follow a progress in psychotherapy not only by means of assessment on psychological level, but also to apply more measurements on neural level, e.g., EEG, to track neural binding processes interconnected with better integration on a psychological level.

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List of original publications

1. publications *in extenso* with relationship to the subject of dissertation
a) with IF

1. Pec, O., Bob, P., Raboch, J. Dissociation in schizophrenia and borderline personality disorder (2014) *Neuropsychiatric Disease and Treatment*, Mar 17, 10, pp.487-91. doi: 10.2147/NDT.S57627. IF=2.154

2. Pec, O., Bob, P., Raboch, J. Splitting in schizophrenia and borderline personality disorder (2014) *PLoS One*. Mar 6;9(3):e91228. doi: 10.1371/journal.pone.0091228. IF=3.534

3. Lysaker, P.H., Bob, P., Pec, O., Hamm, J., Kukula, M., Vohs, J., Popolo, R., Salvatore, G., Dimaggio, G. Synthetic metacognition as a link between brain and behavior in schizophrenia (2013) *Translational Neuroscience*, 4 (3), pp. 368-377. IF=0,716

b) without IF

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2. publications *in extenso* without relationship to the subject of dissertation.

a) with impact factor --

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Total cumulative IF = 7,807

b) without impact factor –

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