

**KOGNITIVNÍ DEZORGANIZACE A NÁHLED U
SCHIZOFRENIE**

**COGNITIVE DISORGANISATION AND INSIGHT
IN SCHIZOPHRENIA**

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Summary

Conscious awareness is related to brain activities represented as unitary, integrated and changeable processes reflecting binding of diverse modalities of basic neural informational processes and their subjective components. According to recent research disturbances of self-awareness and conscious experience have a critical role in pathophysiology of schizophrenia, which in early stages of the disease mainly include overactivation of the HPA axis. Together these studies suggest that the processes of disrupted awareness and conscious disintegration in schizophrenia likely might be related and represented by similar disruptions on the brain level, which in principle could be explained by various levels of disturbed connectivity and information disintegration that may negatively affect usual patterns of synchronous activity constituting adaptive integrative functions of consciousness. In this context, a purpose of the theoretical part of the dissertation is to describe basic neurobiological mechanisms underlying integrative processes in the brain with its complementarily related mental activities including self-awareness and insight reflecting interrelated processes between mind and brain that implicate direct effect of psychotherapy and other metacognitive activities on the brain.

The first part of empirical research included in this study was focused on cognitive disorganization and its critical role in the pathophysiology of schizophrenia. Recent findings indicate that first episode psychotic disorders are closely linked to stressful events which might be related to “kindling-like” sensitization and specific neuroendocrine changes. In this context, we have examined relationships between symptoms of disorganisation in adult young women with first episode psychosis, dissociative and somatoform symptoms and other stress related symptoms including hair cortisol.

Methods: In the clinical study 50 inpatients, adult young women with first episode psychosis, were assessed for disorganization symptoms and other positive and negative symptoms of schizophrenia (PANSS), stress symptoms and dissociation (TSC-40, DES, SDQ-20), complex partial

seizure-like symptoms (CPSI), depressive and anxiety symptoms (BDI-II, SAS) and hair cortisol.

Results: The data indicate that in the patients with first episode psychosis disorganization symptoms manifest significant negative correlation with anxiety, dissociation, complex partial seizure-like symptoms and hair cortisol levels.

Conclusion: These results suggest that the patients with the first episode psychosis might be according to their clinical symptoms divided into two subgroups, the first with high levels of disorganization symptoms and the second with high levels of dissociative and complex partial seizure-like symptoms which might have serious clinical implications for treatment of psychotic disorders.

In the second part of the empirical research we have followed and developed recent research studies that disturbances of self-awareness and conscious experience related to stressful experiences may have a critical role in pathophysiology of schizophrenia which in early stages of the disease mainly include overactivation of the HPA axis. We have assessed relationship of insight and hair cortisol levels in young women at the beginning of their first psychotic episode.

Methods: In the clinical study 45 inpatients, adult young women with first episode psychosis, were assessed for schizophrenia psychopathology symptoms (PANSS), experience of insight (BCIS), depressive and anxiety symptoms (BDI-II, SAS) and hair cortisol.

Results: Results show that positive symptoms measured by PANSS are negatively associated with insight composite index. The process of insight represented by self-reflection also manifests significant positive correlation to hair cortisol levels.

Conclusion: Results of this study report novel findings suggesting that hair increased cortisol levels are positively associated with self-reflective experiences in the first psychotic episodes. This result is in agreement with findings that the process of self-reflection may lead to anticipatory stress which may be reflected by increased cortisol. This finding is in agreement with evidence that positive coping (eustress) is related to anticipatory cortisol responses which suggest that manageable stress experiences may positively influence psychobiological resilience.

Shrnutí

Vědomí představuje projev aktivit mozku, které zahrnují jednotný, integrační a měnlivý proces, odrážející vazbu mezi rozdílnými modalitami základních informačních a subjektivních komponent. Podle současného výzkumu hrají změny vědomí a sebeuvědomění významnou roli v patofyziologii schizofrenie a často zahrnují zvýšenou aktivaci hypothalamo-hypofyzární osy. Studie poukazují na to, že proces poruchy uvědomění a dezintegrace vědomí u schizofrenie spolu pravděpodobně mohou souviset a být způsobeny obdobnými změnami na úrovni mozku, které pak mohou být vysvětleny různými stupni narušení konektivity a zpracování informací, což negativně ovlivňuje běžný vzorec synchronní aktivity tvořící adaptivní integrační funkce vědomí. S ohledem na tento kontext je účelem teoretické části disertační práce popsat základní neurobiologické mechanismy provázející integrační procesy v mozku spolu s komplementární duševní aktivitou zahrnující sebeuvědomění a náhled, které odrážejí návzájem propojené procesy psychiky a mozkové aktivity, což implikuje přímý efekt psychoterapie a dalších metakognitivních aktivit na funkci mozku.

První část empirického výzkumu zkoumá konceptuální dezorganizaci a její důležitou roli v patofyziologii schizofrenie. Podle současného výzkumu mohou být epizody první psychózy úzce spojeny se stresovými událostmi, které mohou souviset se senzitivací a specifickými neuroendokrinními změnami. V tomto kontextu jsme zkoumali souvislost mezi symptomy dezorganizace, disociativními a somatoformními symptomy a dalšími příznaky souvisejícími se stresem, které zahrnují hladiny kortizolu ve vlasech u dospělých mladých žen s první psychotickou epizodou.

Metodika: V rámci klinické studie jsme vyšetřili 50 hospitalizovaných pacientek, mladých žen s prvozáchytem psychózy. Hodnotili jsme příznaky dezorganizace a pozitivní a negativní symptomy schizofrenie (PANSS), stres a disociaci (TSC-40, DES, SDQ-20), symptomy podobné komplexním parciálním záchvatům (CPSI), příznaky deprese a úzkosti (BDI-II, SAS) a kortizol ve vlasech.

Výsledky: Data ukazují, že u pacientů s prvozáchytém psychózy příznaky dezorganizace signifikantně negativně korelují s úzkostí, disociací, symptomy podobnými komplexním parciálním záchvatům a hladinou kortizolu ve vlasech.

Závěr: Výsledky této studie poukazují na to, že pacienti s prvozáchytém psychózy mohou být rozděleni podle klinických příznaků do dvou podskupin. První, s vysokou hodnotou dezorganizace a druhá s vysokou hodnotou disociace a symptomů podobným komplexním parciálním záchvatům, což může mít významný klinický dopad pro léčbu pacientů s psychotickým onemocněním.

Ve druhé části empirického výzkumu jsme navázali na studie, které ukazují důležitou roli narušení sebeuvědomění a vědomého prožitku u patofyziologie schizofrenie, což také často zahrnuje zvýšenou aktivaci hypothalamo-hypofyzární osy. Hodnotili jsme vztah mezi náhledem a kortizolem ve vlasech u mladých žen na počátku první psychotické epizody.

Metodika: V rámci klinické studie jsme vyšetřili 45 mladých žen s první epizodou psychózy. Hodnotili jsme psychopatologii schizofrenie (PANSS), náhled (BCIS), depresi a úzkosti (BDI-II, SAS) a hladinu kortizolu ve vlasech.

Výsledky: Výsledky ukazují, že pozitivní symptomy měřené PANSS negativně korelují s kompozitním indexem náhledu. A dále, že náhled ve složce sebereflexe vykazuje signifikantní pozitivní vztah s hladinou kortizolu ve vlasech.

Závěr: Studie přináší nové výsledky poukazující na to, že zvýšená hladina kortizolu pozitivně koreluje s prožitkem sebereflexe u pacientů s první epizodou psychózy. Tyto výsledky jsou ve shodě s nálezy, že proces sebereflexe může vést k anticipačnímu stresu, který může být představen zvýšeným kortizolem. Tento nálezež je ve shodě s důkazy, že pozitivní coping (eustres) souvisí se zvýšenou odpovědí kortizolu na dobře zvládnutý stres, který může pozitivně ovlivnit psychobiologickou odolnost.

1. Introduction

According to recent research disturbances of self-awareness and conscious experience have a critical role in pathophysiology of schizophrenia, and in this context schizophrenia is currently understood as a disorder characterized by distortions of acts of awareness, self-consciousness and self-monitoring (Ford et al., 2007; Lou, 2012; Lysaker et al., 2010; Mishara, 2007; Mishara et al., 2014; Uhlhaas and Mishara, 2007). Together these studies suggest that the processes of disrupted awareness and conscious disintegration in schizophrenia likely might be related and represented by similar disruptions on the brain level, which in principle could be explained by various levels of disturbed connectivity and information disintegration that may negatively affect usual patterns of synchronous activity constituting adaptive integrative functions of consciousness (Bob and Mashour, 2011). On the other hand mental integration based on self-awareness and insight likely may significantly increase information integration and directly influence neural mechanisms underlying basic pathophysiological processes in schizophrenia (Touskova and Bob, 2015)

The concept of insight and its relationship to mental disorders is most frequently understood as a conscious recognition of one's own mental state or the degree of personal awareness or self-understanding (Amador et al., 1993; Lysaker et al., 2013). In recent reported studies, insight is most frequently studied in schizophrenia patients (Mintz et al., 2003). Furthermore, recent research suggest that deficits in self-awareness and disturbed conscious experience underly pathophysiological mechanisms of schizophrenia (Kircher and Leube, 2003; Mishara et al., 2014).

In addition, recent research indicates that cognitive disorganization has a critical role in pathophysiology of schizophrenia and suggests that first episode psychotic disorders are closely linked to stressful events (Reininghaus et al., 2016; Varese et al., 2012). The cognitive disorganization may be influenced by traumatic events that affect developing brain and may cause neurobiological abnormalities that frequently occur in patients with schizophrenia and mainly include overactivation of the HPA axis (Bremner, 1999; Read et al., 2001; Teicher

et al., 2003; Teicher et al., 2006). Furthermore, recent findings suggest that repeated stressful events may lead to an increased responsiveness to these stress stimuli and vulnerability to stressors which may determine sensitization process with lasting consequences with kindling-like progression (Kraus, 2000; Popovic et al., 2016; Post et al., 1997).

With respect to recent findings our first empirical study was focused on relationships of disorganization symptoms and their links to insight, dissociation, limbic irritability, and other stress related psychopathological symptoms, and long-term cortisol response in hair samples in young women with the first psychotic episode. In the second part of this empirical research we have tested a relationship of insight and various stress manifestations in drug naïve young women at the beginning of their first psychotic episode

2. Hypotheses and aims of the study

2.1. Recent research of cognitive disorganization indicates its critical role in pathophysiology of schizophrenia and suggests that first episode psychotic disorders are closely linked to stressful events that may be related to “kindling-like” sensitization and specific neuroendocrine changes. With respect to recent findings a purpose of this study is to examine a hypothesis whether there is a relationship between disorganization symptoms and dissociation, limbic irritability, other stress related psychopathological symptoms, insight and long-term cortisol response in hair samples in young women with the first psychotic episode

2.2. Recent research suggests that disturbances of self-awareness and conscious experience have a critical role in pathophysiology of schizophrenia (Frith, 1987; Gallagher, 2000; Kircher and Leube, 2003; Lou, 2012; Mishara et al., 2014) and first episode psychotic disorders are closely linked to stressful events (Reininghaus et al., 2016; Varese et al., 2012). With respect to recent findings we have tested a hypothesis

whether there is a relationship between insight and hair cortisol levels in drug naïve young women at the beginning of their first psychotic episode.

3. Material and Methods

3.1. In order to examine the hypothesis 50 inpatients, adult young women with first episode psychosis, were assessed for disorganization symptoms and other positive and negative symptoms of schizophrenia (PANSS), stress symptoms (Trauma Symptoms Checklist- TSC-40) and dissociation (Dissociative Experiences Scale- DES; Somatoform Dissociation Questionnaire- SDQ-20), complex partial seizure-like symptoms inventory (CPSI) and depressive and anxiety symptoms (Beck Depression Inventory- BDI-II, Zung's Self-reported Anxiety Scale- SAS). Cortisol from the hair samples was analyzed using photometric analysis ELISA (SPECTRA SLT).

3.2. With the purpose to examine the hypothesis 45 adult young women with first episode psychosis were assessed for experience of insight (Beck Cognitive Insight Scale- BCIS), schizophrenia psychopathology (Positive and Negative Symptoms Scale (PANSS), depression (BDI-II) and anxiety (SAS). Cortisol in the hair samples was analyzed using photometric analysis ELISA (SPECTRA SLT).

4. Results

4.1. Results indicate that disorganization symptoms measured by PANSS conceptual disorganization symptoms (P2) manifest significant negative correlation with anxiety ($r=-0.44$, $p<0.01$), symptoms of dissociation ($r=-0.35$, $p<0.01$) and somatoform dissociative symptoms ($r=-0.39$, $p<0.01$) and complex partial seizure-like symptoms ($r=-0.31$, $p<0.01$), but no significant correlation with symptoms of traumatic stress and depression. The symptoms of conceptual disorganization also manifest significant relationship to hair cortisol levels ($r=-0.38$, $p<0.01$). In addition the results

indicate that PANSS conceptual disorganization symptoms manifest significant positive correlation with lack of insight measured by PANSS (G12) ($r= 0.55, p<0.01$).

4.2. Results indicate that insight manifestations in the patients with first episode psychosis measured by insight composite index are closely related to positive symptoms assessed by PANSS ($r= - 0.37, p<0.05$). The process of insight represented by self-reflection subscale also manifests significant relationship to hair cortisol levels ($r= 0.43, p<0.01$). The results did not show statistically significant relationships of insight manifestations as well as the hair cortisol levels with symptoms of depression and anxiety.

5. Discussion

5.1. In agreement with recent research (Aiello et al., 2012; Reininghaus et al., 2016; Varese et al., 2012) the results show that in the patients with first episode psychosis disorganization symptoms are significantly negatively associated with anxiety, dissociative and somatoform symptoms, and complex partial seizure-like symptoms but not with symptoms of traumatic stress and depression. The conceptual disorganization is also related to hair decreased cortisol levels and decreased insight. These results indicate reciprocal relationships of disorganization symptoms with dissociation and somatoform psychopathology, anxiety, seizure-like processes, cortisol levels and insight.

5.2. The results show that levels of positive symptoms are related to insight deficits that is usually linked to disturbances of self-consciousness and self-monitoring. These data are in accordance with findings about critical role of insight deficits in pathophysiology of schizophrenia (Mintz et al., 2003). The results also show that the process of insight represented by self-reflection manifests significant relationship to hair cortisol levels. These results represent novel findings suggesting that increased hair cortisol levels are positively associated with self-reflective experiences.

This inverse relationship of self-reflection and hair cortisol may reflect a protective process against stress disturbances during the first psychotic episodes. This result is in agreement with findings and conceptualization of “eustress” related to anticipatory cortisol reactivity which suggests that manageable stress experiences may increase psychobiological resilience (Aschbacher et al., 2013)

6. Conclusions

6.1. The first part of empirical research included in this study shows that dissociation in schizophrenia may play an important role (Lysaker and Larocco, 2008; Perona-Garcelan et al., 2008; Renard et al., 2016; Ross, 2004) and in addition these data suggest that dissociative processes are opposite to disorganization. In this context, “mental fragmentation” related to disorganization seems to play an opposite compensatory role as a defense mechanism against increased dissociative symptoms and other processes related to anxiety, decreased insight and somatoform (or somatization) processes linked to somatoform dissociation, complex partial seizure-like symptoms and neuroendocrine processes. In context of Ross’ conceptualization of the “dissociative schizophrenia” (Laferriere-Simard et al., 2014; Ross, 2004; Vogel et al., 2013) results of this study suggest that the patients with the first episode psychosis might be according to their clinical symptoms divided into two subgroups, the first with high levels of disorganization symptoms and the second with high levels of dissociative and complex partial seizure-like symptoms which might have serious clinical implications for using anticonvulsant treatment in the second group.

6.2. According to recent research patient with schizophrenia have significant lack of insight about their personal situation and life perspectives (Amador and Gorman, 1998; Mintz et al., 2003; Sevy et al., 2004), which is closely linked to manifestation of defense mechanisms (Donohoe et al., 2004; Lysaker et al., 2003). In this context, results of this study report novel findings suggesting that hair increased cortisol levels

are positively associated with self-reflective experiences in the first psychotic episodes. This result is in agreement with findings that the process of self-reflection may lead to anticipatory stress which may be reflected by increased cortisol. This finding is in agreement with evidence that positive coping (eustress) is related to anticipatory cortisol responses which suggest that manageable stress experiences may positively influence psychobiological resilience.

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List of original publications

Publication in journals with IF related to dissertation

Touskova T, Bob P, Consciousness, awareness of insight and neural mechanisms of schizophrenia. *Reviews in the Neurosciences*. 2015;26:295-304; IF (2015)= 3.198

Bob P, Pec O, Mishara AL, Touskova T, Lysaker PH, Conscious brain, metacognition and schizophrenia. *International Journal of Psychophysiology*. 2016;105:1-8; IF (2015)= 2.596

Articles under review

Tereza Petraskova Touskova, Petr Bob, Conceptual disorganization and stress related pathology in women with first episode psychosis.

Tereza Petraskova Touskova, Petr Bob, Zdislava Vanickova, Jiri Raboch, Insight and cortisol responses in first episode psychosis.

Cumulative IF=5.794