

PRACE POGLĄDOWE

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Orbitofrontal cortex dysfunction and risk for antisocial behavior: An analytical review

Dysfunkcja kory czołowo-oczodołowej a ryzyko wystąpienia zaburzeń antyspołecznych

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STRESZCZENIE

Cel. Celem pracy jest ustalenie zależności pomiędzy dysfunkcją kory czołowo-oczodołowej (OFC) a występowaniem zaburzeń antyspołecznych na podstawie o przeglądu aktualnej literatury.

Metoda. Materiały odnoszące się do roli dysfunkcji w obrębie OFC w determinowaniu zaburzeń zachowania, w tym o charakterze antyspołecznym (dysocjalnym), zostały zgromadzone metodą systematycznej kwerendy takich źródeł, jak MEDLINE, Google Scholar, czasopisma i biblioteki akademickie.

Wyniki. Rezultaty wielu badań potwierdzają występowanie zaburzeń antyspołecznych u osób z uszkodzeniem płatów czołowych mózgu, szczególnie obejmującym struktury OFC. Przemawia to za występowaniem wyraźnej zależności pomiędzy uszkodzeniem w obrębie OFC a zwiększonym ryzykiem zachowań agresywnych i antyspołecznych.

Wniosek: Dane uzyskane w wyniku badań neuropsychologicznych i neuroobrazowania przeprowadzanych w obrębie różnych subdyscyplin neuronauki dostarczają dowodów potwierdzających ważną rolę dysfunkcji OFC jako predyktora zaburzeń antyspołecznych.

Słowa kluczowe: kora czołowo-oczodołowa, dysfunkcja, zaburzenia antyspołeczne, agresja

ABSTRACT

Objective: This article is aimed to establish the relation between orbitofrontal cortex (OFC) dysfunction and antisocial behavior, based on a review of relevant literature.

Method: Materials presenting the role of OFC dysfunction in human behavioral disorders, including antisocial behavior, were collected through systematic survey of various sources, including MEDLINE, Google Scholar, academic libraries.

Results: Many studies showed prevalence of violent and antisocial behaviors in persons with frontal lobes damage, especially involving the OFC structures. The results support the assumption about association between focal orbitofrontal damage and increased risk of violent and aggressive behavior.

Conclusion: Neuropsychological and neuroimaging data from various fields within neuroscience provide evidence about importance of the OFC dysfunction as a predictor of violent and antisocial behavior.

Keywords: orbitofrontal cortex, dysfunction, antisocial behavior, aggression

Udział współautorów / Participation of co-authors: A – przygotowanie projektu badawczego/ preparation of a research project; B – zbieranie danych / collection of data; C – analiza statystyczna / statistical analysis; D – interpretacja danych / interpretation of data; E – przygotowanie manuskryptu / preparation of a manuscript; F – opracowanie piśmiennictwa / working out the literature; G – pozyskanie funduszy / obtaining funds

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Introduction

The human prefrontal cortex receives and processes information from most of the cerebral cortex and from subcortical structures. Selecting relevant information is a complex process, and must be conducted in cognitive and emotional context. It also involves other neural regions connected with prefrontal cortex. For example, the posterior orbitofrontal cortex, the anterior temporal cortex and amygdala are interlinked in form of a triad pathway that may help to integrate information on the sensory features and the emotional significance of events and facts. Nowadays, the important role of OFC in behavioral regulation and cognition in humans is no longer a matter of scientific dispute. Ironically, not so long ago the OFC had a relatively low status because it was viewed as a “redundant and silent cortex” [1]. This view prevailed even up to the second half of the 20th century and was the underlying factor for accepting psychosurgical lobotomy in the treatment of psychiatric disorders. This dramatic form of treatment was used in psychiatry between 1940s and 1960s despite quite widespread skepticism in relation to its real effectiveness. The shame of the acceptance of such psychosurgery extends beyond the undoubted harms done to the ill persons and their families. It should be mentioned that at that time authorities, both political and scientific, tolerated this extreme procedure despite an obvious lack of scientific foundations.

Nevertheless, during the first half of 20th century there were some progressive scientists who appreciated the important role of OFC. For example, Alexander Luria opposed the notion that the frontal lobes have not defined function. Instead, he stressed that the majority of patients with lesions of the frontal lobe lose the ability to evaluate behavior and the adequacy of actions and that they present symptoms of personality disorders [2]. Similar view on the important role of OFC was presented by William D. Keane. He stated that “loss of frontal cortex as a major mediator of information exchange between cerebral cortex and the limbic system is followed not only by an impairment of strategic choice making, but also by a tendency of projected or current action systems to ‘fade out’ or become over-ridden by interfering influences” [3]. Finally, the studies performed by Antonio Damasio and colleagues definitively showed the important role of OFC in behavioral regulation. Basing on clinical observations they concluded that while damage of OFC may not impact intellectual functions measured by intelligence tests, it does impact subtle components of behavioral regulation. The most interesting observation was the dissociation between intact cognitive abilities and their poor utilization in everyday life [4].

The beginning of the 21st century is marked by a substantial shift in view regarding the role of the OFC that led to increasing interest in defining the behavioral functions of this cortical region. In the past, the domi-

nant approach to evaluating the structural and functional integrity of the prefrontal cortex was simply to examine the prefrontal cortex as a whole. However, in the past 20 years with the increasing knowledge based on brain imaging in healthy individuals, it is now recognized that this neural region, which was once considered a unitary structure, is a complex of anatomically and functionally distinct subsystems. Most of all, major differentiations have been made between the functional properties of the orbitofrontal and dorsolateral sectors [1,5]. The orbitofrontal regions, including the OFC and the ventromedial prefrontal cortex (vmPFC), are densely connected with many brain regions including the basal ganglia, the amygdala, and other neighboring prefrontal structures. Both the location and the anatomical connectivity allow these regions to receive and process the information concerning emotion and reward values, and output such information to the dorsolateral prefrontal cortex for final execution. Recent fMRI studies have shown that the orbitofrontal regions, the vmPFC in particular, are activated during ethical decision-making and moral reasoning [6,7]. As a consequence, the OFC is now a frequent subject of investigation for researchers representing a wide spectrum of scientific and practical fields such as, for example, neuropsychology or functional neuroimaging. Apart from diverse approaches, one common notion is that OFC is critical to the ability to assess the value of stimuli or situations that contribute to long-term behavioral guidance. In other words, value representation guides behavior by assessing whether options for action are likely to be connected with reward or punishment, both in the short-term and the long-term perspective [6,8,9,10]. Therefore, it is our assumption that the frontal cortex dysfunction found in antisocial individuals might be involved in antisocial features such as emotional deficits, wrong moral reasoning and decision-making, and also specific response perseveration, which result in life-long antisocial behavior despite repeated punishment and in poor planning and organizing ability, which leads to an occupationally and socially dysfunctional style of life.

Role of the OFC in socially adaptive behavior

The OFC has long been associated with adaptive behavior in the face of changing conditions, including social environment. In this regard, the OFC cooperates with amygdala and related neural structures in the appraisal and interpretation of socially relevant stimuli [5]. There is experimental evidence that OFC is involved in the mediation of at least three following constructs: 1. social knowledge networks that guide judgments and behavioral responses, 2. social emotional processing, including ability to recognize different affective conditions in other people, 3. theory of mind, defined as the ability to conceptualize what other people are feeling and thinking .

Ad 1. As it is widely known, the social environment is more complex, interactive and changeable than the material environment. Human beings have always needed to negotiate social relations in order to confirm their position in a group. This long-term process helped to develop an important capability, which psychologists now call “social intelligence”, defined as “the ability to interact with others in a complex and flexible manner” [11]. Furthermore, social intelligence (competence) must be distinguished from intellectual capability. This difference is clearly visible in adult patients with Asperger syndrome who can excel in solving difficult theoretical problems but their social functioning is significantly impaired. An opposite relationship is observed in patients with Williams syndrome who exhibit abnormally low intellectual abilities but, at the same time, relatively high level of social competence [12]. These differences lead to the conclusion that social cognition may be independent of general intelligence with different information processing. Contemporary research in neuroscience has suggested that social judgment processes are mediated by the frontal cortex including the amygdala [13]. For example, amygdala activation has been found when evaluating “trustworthiness” based on facial characteristics. In patients with amygdala damage such judgments were distorted [14]. The amygdala and medial frontal structures are also involved in activation of social stereotypes, for example, in situations when people view faces representing another race or gender. In cases of patients with damage of medial frontal lobes it was found that they are less regulated by gender stereotypes than in non-brain-injured controls [15,16]. These and other studies explicitly suggest that the frontal cortex structures in cooperation with amygdala are involved in social judgments based on other people’s personal characteristics. In other words, the prefrontal neural structures are a place where the social schema and social knowledge networks are stored. Damage of the frontal structures results in disorder of regulatory control over behaviors evoked by stimuli generated by social environment.

Ad 2. Neurological and neuroimaging studies, performed both on humans and animals, univocally evidenced that dysfunction within fronto-limbic circuit, including OFC, the amygdala and anterior cingulate, is responsible for impaired emotion recognition [17]. Normally, the ability to identify emotional states in other people, also called empathy, is a valuable element of social cognition. Patients with impairment of frontal cortex are unable to correctly evaluate emotional aspects of behavior in their conversational partners and, as result, they cannot modify their own social reactions accordingly. Developmental psychology provides us with data showing that there is a close relationship between recognition of emotional states and socio-emotional experience. For example, even small children use their mother’s facial

expression of emotions as a cue helping them to respond adequately to ambiguous situations [18]. The emotional experience is later used by adults who tend to mirror the facial expressions of those with whom they interact. This kind of emotional exchange play a significant role in all social interactions. Results of some studies indicate that an emphatic response can be elicited even before conscious awareness [19]. Frontal lobe pathology caused by, e.g. traumatic brain injury, fronto-temporal dementia and focal lesions, occurring in adult patients can significantly reduce their responsiveness to emotional materials. Such findings, as mentioned above, give us strong arguments that frontal neural systems mediate both recognition of emotional stimuli occurring in social milieu and affective response to those stimuli.

Ad 3. Another aspect of social information processing related to the role of the OFC is theory of mind, i.e. individual’s ability to make judgments regarding the mental states of other people. Because of this ability it is possible to predict how others will behave and interpret their actions. Patients with frontal cortex damages, both focal and diffuse, demonstrate serious difficulties while making judgments related to theory of mind [20,21]. Empirical data based on the studies using neuroimaging and magnetic resonance techniques have provided significant evidence for involvement of the OFC in reasoning related to theory of mind [11,22]. It is also interesting that judgments about subtle mental states in others, e.g. “feeling guilty”, “bored”, or “thoughtful”, were often incorrectly made by patients with frontal lobe injuries [23,24]. Analogically, adult patients with damage done solely to amygdala made poor judgments concerning theory of mind issues. This applies mostly to impaired ability to interpret unemotional mental states [25]. It should be emphasized that research on the role of the OFC and other frontal regions in mediation of affective responses and decisions is still in its infancy. Continuation of such studies increases our understanding of significance of dysfunctions that arise from frontal cortex impairment. Furthermore, we must expect that importance of these studies will be heightened because of the complex and changing world of social relationships.

Impairment of the OFC and psychiatric disorders

The OFC, like the whole frontal lobe, is involved in a variety of psychiatric disorders (PD) such as, anxiety, depression, psychopathy, or psychotic conditions. Structural and functional neuroimaging techniques report reduced OFC volume or impairment of its structure in patients with different disorders such as schizophrenia, panic disorder, antisocial personality, PTSD, drug addiction and affective disorders. In this group, schizophrenia belongs to the most persistent and disabling mental disorders. It affects approximately 0.5-1.5% of the adult

population [26]. Dysfunctions observed in patients related to basic cognitive processes including thinking, memory, attention and also emotions and personality. Structural and functional magnetic resonance imaging (MRI) studies performed in patients with schizophrenia reported considerable volume reductions in medial and lateral OFC [27]. Functional MRI studies have also showed impaired activation of medial OFC and the amygdala in schizophrenic patients during social-decision making [28, 29].

Significant reductions of OFC volume have also been observed also in patients who suffered from major depression. For example, analysis of results of structural imaging studies have found smaller gray matter volumes in right medial and left lateral OFC among patients with major depressive disorder [30]. According to Drevets [31], a reduction of 5-HT_{1A} receptor binding in OFC is observed in depressive patients. Furthermore, an evident reduction of OFC volume was also found in adolescent and adult patients with bipolar disorder which resulted in reduced activation of OFC subregions, especially during manic episodes [32].

Functional neuroimaging studies have been conducted in order to investigate the nature of neurocircuitry involved in the symptoms of emotional disorders, such as post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), and panic disorder. Although the number of such studies is relatively small, some results are encouraging. For example, studies using the MRI among patients with panic disorder displayed reduction in posterior-medial OFC [33]. In case of patients with OCD, neuroimaging studies discovered the OFC hyperactivity that can be traced back to impairments of thalamic regions [34]. There are some important reasons for supposition that the OFC is involved in development of substance use disorders (SUD). Neuroimaging studies related to the SUD often use PET and SPECT techniques which allow for an assessment of changes in dopamine. The PET study performed in a group of cocaine, marijuana and alcohol abusers has found a significant reduction in OFC activity of D₂DA receptors in striatum region [35,36]. Such observations have an important clinical significance because they help to understand the role of OFC in development and course of common PDs. Nevertheless, it should be remembered that in each specific PD this role may be moderated by other factors. Although neuroimaging studies have proved an important OFC involvement in many PDs, future research is needed to characterize the specific role in psychopathological behavior [37].

The OFC damage and antisocial behavior

It should be mentioned that systematic studies on the relation between frontal cortex injury and antisocial behavior have a long history. There is a growing interest in understanding the role of dysfunctions of medial

and lateral OFC in the development of psychopathic traits involved in antisocial behavior [38]. Symptoms of emotional dysfunction include lack of empathy, reduced guilt and disordered attachment to significant others. The antisocial dimension of psychopathy includes a predisposition for dissocial behavior from an early age. Contemporary research confirmed the continuity of psychopathic traits from childhood into adulthood [39]. What is interesting, psychopathy is not equivalent to dissocial personality (ICD-10) or antisocial personality (DSM-5), even if they seem similar. Additionally, psychopathy contains an increased risk for aggressive and violent behavior [40]. Some recently performed studies have suggested a genetic contribution to development of psychopathy. In a large-scale study involving about 3500 twin pairs it was found that psychopathic traits are strongly heritable at the age of 7 (67% heritability) [41]. It seems that genetic polymorphism influences the functioning of important brain structures such as medial OFC and the amygdala in individuals with behavioral disorders [42,43]. One possible explanation is that there is a set of genes whose polymorphism negatively influences the functional integrity of medial frontal cortex and the amygdala. This results in development of predisposition for reduced emotional responsiveness of the psychopathic individual. The amygdala plays an important role in stimulus-reinforcement learning and responding to emotional expressions, especially fearful ones. Those expressions are important factors of stimulus-reinforcement learning. In this context, psychopaths exhibit impairment in stimulus-reinforcement learning based both on reward and punishment. This kind of learning impacts their process of socialization. As a result, they are more inclined to learn antisocial strategies directed to achieving personal goals [44]. Additionally, dysfunction of the OFC, which is associated with the anticipation of negative responses, could logically result in failure to experience fear. Thus, OFC dysfunction is often associated with increased reactive aggression which common characteristic of psychopathic individuals [45].

Attention of some researchers is given to understanding sex differences in psychopathology, in order to understand better the etiology of antisocial behaviors. Such study usually test hypothesis that sex differences in ventral and middle frontal gray volume contribute to sex differences in antisocial personality disorder (APD) and criminal activity. For example, Raine et al. [46] have found reduced OFC volume in males with APD symptoms when compared with females. Such findings implicate structural differences in the ventral and middle frontal gray matter as both a risk factor for APD and a partial explanation for sex differences in development of APD [47].

As noted above, damage in prefrontal cortex leads to impaired decision making in individuals with psychopathy. This must be considered as an important factor

contributing to their antisocial style of life. It is a crucial issue because prefrontal cortex is responsible for successful decision making, and its dysfunction will increase chances of wrong decision making in achieving personal goals, e.g. use of violence. Additionally, individuals with psychopathy are at greater risk for frustration and aggression. The suggestion that in psychopaths OFC and the amygdala are impaired is based on considerable neuroimaging studies. Thus we know that it disrupts the integrated functions of those structures in individuals with psychopathic traits. As a result, this limits their ability for successful socialization and decision making. Numerous neuropsychological studies provide data supporting the link between prefrontal executive dysfunction, as measured by neuropsychological tests, and increased aggressive and antisocial behavior. It should be noted that maturation delay in the development of the prefrontal cortex and insufficient socialization may also account for deficits occurred in neuropsychological test performance [48,49]. Previous research on behavioral disorders in adolescents suggested that structural and functional abnormalities within the amygdala and OFC contribute to the pathophysiology of conduct disorder (CD). Passamonti et al. [50] investigated whether the integrity of the white-matter pathways connecting these regions is abnormal and may be regarded as a neurobiological marker for CD. They used diffusion tensor imaging (DTI) in order to investigate white-matter microstructural integrity in male adolescents with CD, compared with normal controls. The results provided evidence that CD is associated with white-matter microstructural abnormalities in the anatomical tract that connects the amygdala and OFC, the uncinate fascicle. Also these results implicate abnormal maturation of white-matter pathways which are fundamental in the regulation of emotions in patients with CD [50].

Discussion

The studies discussed in this review demonstrate that clinically significant impairment of frontal lobe, especially the OFC, is associated with antisocial behavior. Individuals with injuries, primarily involving the prefrontal cortex, exhibit increased tendency to antisocial and aggressive behavior when compared to people who have no such conditions. This tendency was confirmed by studies employing different methodological approaches, such as neurological examination, EEG, neuroimaging and neuropsychological testing. Impairment of prefrontal structures is strongly associated with impulsive and long-lasting aggressive behavior that may contribute to antisocial actions. It suggests that the results in neuropsychological tests may be used in prediction of possible future aggression, especially in young population of neurological patients. However, there have so far been no studies proving that dysfunction of prefrontal cortex may directly predict crime of the

violent type [51]. Nevertheless, there is a relatively big number of case studies reporting psychiatric disorders among death row prisoners and forensic psychiatric patients with history of violent crimes. In most cases the frontal lobe dysfunctions are responsible for the actions of those persons convicted of violent crimes because they failed to control impulsive and aggressive behavior [52,53].

Studies of individuals with acquired frontal lobe impairment, especially involving the OFC structures, support the assumption that there is an association between increased tendency to aggressiveness and antisociality and this kind of dysfunction. However, it should be noted that persons with clinically significant neuropsychiatric disorders involving focal injuries to particular components of the frontal cortex comprise a substantially heterogeneous group. For example, case studies suggest that the OFC focal injuries specifically impair capacities for empathy, risk avoidance and social judgment that control inappropriate behaviors [36, 54].

Advances in the neuroscientific exploration of criminal behavior, especially brain imaging, are likely to stimulate debate over the use of such evidence in courts. Currently, in many countries the law treats human beings as intentional, reasonable and practical individuals, not as purely mechanistic robots. Nevertheless, it seems possible that neuroscientists may uncover some of the causal mechanisms that objectively influence our antisocial behavior. Such discoveries could possibly revolutionize our concept of ourselves to the extent that we no longer treat ourselves as rational, intentional individuals with ultimate control over our behavior. Nevertheless, some researchers argue that only if we are able to achieve a very high level of biological understanding of ourselves, such that we have essentially explained away humanity, would legal determination of responsibility be reliant on neuroscience. An alternative perspective is that taking into account documented risk factors for antisocial and violent behavior in some specific cases does not mean that we have to completely abandon our general concepts of rationality, personhood, and responsibility for our own actions [55]. Finally, it should be emphasized that a close cooperation between neuroscientists, psychologists, philosophers, and lawyers is necessary in order to determine how new and potentially important findings from brain imaging research should or should not influence the way legal system views, and deals with antisocial behavior. Furthermore, results of such cooperation could review current policy of the state legal system which supports criminal sanctions aimed at antisocial persons. The current advances in brain imaging and other brain research have already provided the basis for a new approach to public policy within the criminal justice system. Failing to take advantage of advances in neuroscientific knowledge assures that the state policy

toward criminal justice will continue to follow practices that are criticized in light of new scientific achievements.

Conclusion

The studies reviewed in this paper illustrate a crucial role of damage to the prefrontal cortex in impairment of the complex psychological processes such as decision making, preference judgment, reversal learning, giving subjective value of potential choices, etc. Damage of the OFC in particular, disrupts self-monitoring processes that underlie the generation of emotions useful for controlling of individual's behavior. As a result, individuals with acquired damage of the OFC exhibit reduced ability to compare their behavior to social norms and the expectations of others. In normal persons such comparison evokes social emotions of shame, guilt or embarrassment that positively influence their behavior. In sum, the OFC damage significantly disrupts individual's capacity for effective socialization and makes it more likely to engage in antisocial activity.

We suggest that future investigations should also examine the relationship between the OFC deficits and performance on neuropsychological tests assessing its functions and should probe this structure while applying different neuroimaging paradigms to assess its activation patterns to different cognitive activities, such as emotional recognition or motivational response. Finally, it should be noted that our understanding of consequences that arise from the OFC injury is growing very fast. The beginning of 21st century is marked by an increase of sophisticated, sensitive and methodologically valid measures that enable us to assess deficits following the OFC damages in association with other neural structures as part of a complex and dynamic network. In order to develop the understanding of patients with the OFC damage, future studies, involving larger numbers of patients, would need to facilitate and integrate three different types of investigation; i.e., quantitative behavioral assessments of emotional, behavior and personality changes, development and application of more sophisticated and targeted neuropsychological tests, and high-resolution imaging techniques.

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