Executive Functions in Frontal Lob Syndrome: A Case Report

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SUMMARY

Prefrontal cortex in the frontal lobe (FL) is the center of executive functions (EF). FL damage can lead to executive dysfunction by influencing frontal-subcortical circuits (dorsolateral, orbitofrontal, ventromedial). Damage to the dorsolateral prefrontal cortex (DLPFC) can lead to deterioration in EF, whereas damage to the orbitofrontal cortex (OFC) can lead to personality changes with characteristics of disinhibition and irritability. In addition, damage to the anterior cingulate cortex/medial prefrontal cortex (ACC/MPFC) can result in decreased spontaneity. Neuropsychological tests are important components in the assessment of EF including goal-directed behavior, decision-making, risk assessment, future plan management, prioritizing, and organization. Clinical conditions affecting frontal-subcortical connections outside of the FL can also lead to executive dysfunctions and frontal lobe syndrome (FLS). This case report is about an adolescent patient diagnosed with FLS. The clinical symptoms, assessment, and treatment processes of this case are discussed in this report. The case is a 15-year-old boy that was admitted to our clinic with behavioral problems that began after a car accident three years ago. A magnetic resonance imaging (MRI) study of the brain indicated hyper-intense signal increase in the periventricular deep white matter that was associated with traumatic brain damage. Neuropsychological test results (Stroop, Wisconsin Card Sorting Test, Serial Digit Learning Test, Judgement of Line Orientation Test, Verbal Memory Processes Scale) demonstrated impairment in the cognitive flexibility, verbal fluency, prioritizing, inappropriate response inhibition, sustained attention, planning, problem solving, organization, and subcortical memory functions. We thought that cognitive and behavioral symptoms of this case were associated with the dysfunctions of the frontal-subcortical circuits, independently from an obvious frontal lesion. FLS patients after head traumas, with sudden-onset behavioral and cognitive problems, should be kept in mind in differential diagnosis even in the absence of an obvious frontal lesion.

Keywords: Frontal lobe, executive function, neuropsychological tests.

INTRODUCTION

Originally defined by Harlow (1848), FLS involves cognitive, motor, personality, and behavioral changes due to the effect of factors such as trauma on the functions of the PFC part of the frontal lobe (Aydın 2009). The FL, which is the center of Executive Function (EF), plays an important role in the revision-reorganization of goal-oriented behavior, planning, problem-solving, demonstration of cognitive flexibility, the ability to inhibit inappropriate reactions, motivation, attention, time management, judgment, working memory, and meta-cognitive processes (Royall et al. 2002). The clinical manifestations of FLS may vary depending on the patient's age, sex, premorbid intelligence, level of education, location-severity of lesion, and function of other brain regions (Anderson and Catroppa 2005). The clinical conditions affecting the frontal-subcortical connections outside of the FL may also result in the clinical manifestations of FLS, thereby leading to impairment in EF (Levy and Dubois 2006). Behavioral and cognitive problems that may be commonly observed following a traumatic brain injury may become permanent (Kurowski et al. 2013). This paper will discuss the EF-related assessment

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and treatment processes of an adolescent patient diagnosed with FLS without any obvious frontal lesion.

CASE

A male adolescent aged 15 years and 6 months, who had dropped out of high school in first grade, was referred to our outpatient clinic with complaints of ideas of reference, suspiciousness, aggressive outbursts, harming goods and people, starting fights, profanity, interest in sharp-penetrating tools, skipping classes, decreased academic success, detachment from areas of interest, inappropriate emotional reactions, lack of attention, forgetfulness, sleep problems, smoking (1 pack/day), and alcohol (3-4 units/week) use. Based on his history, it was determined that the symptoms started following a traffic accident he had at the age of 12 and continued without any increase/decrease. The information shared by his school and mother revealed that he was a reserved, academically successful person with good adaptation and no peer problems. After the accident, his behaviors and acts started to change. He fought every day at school earning him the nickname 'psychopath' among his friends, his grades fell from four to two, and he slept during classes. The discharge report he received from the hospital after the accident revealed that he was unconscious when brought to the hospital (Glasgow Coma Score: 8); remained intubated for 10 days due to acute subdural hematoma and traumatic subarachnoid hemorrhage; and was monitored for 22 days in the intensive care unit. Inter-hemispheric fissure and diffuse, hyper-dense subarachnoid hemorrhage that was conspicuous in the cerebellum, acute subdural hematoma in the right fronto-parietal lobe, and effacement in both cortical sulci secondary to edema and edema-related pressure in all ventricles were identified as a result of the imaging studies performed after the accident.

The patient was started on risperidone 0.5 mg/day and escitalopram 5 mg/day with the diagnosis of Conduct Disorder at an external center ten days before his presentation to our outpatient clinic. In his mental status assessment, the male adolescent patient was observed to look his age with some increase in his psychomotor activity, decreased self-care, irritable affect, and depressive-irritable mood. His calculation and abstract thinking skills were lower than expected for this age and he had a short attention span. His orientation was normal and his speed of thought had decreased. The contents of these thoughts were hypersensitive and focused on what his neighbors were saying about him, being teased by his friends, and beating up people for "fun". His past history did not include any characteristics suggesting a physical or emotional disorder. According to the family history, his mother had received treatment for three months due to a diagnosis of "depression". His neurological examination, laboratory (biochemistry, total blood cell count, VDRL, Anti-HIV), brain tomography, and electroencephalogram study results were normal. The brain MRI indicated a hyper-intense signal increase in the periventricular deep-white matter associated with trauma. He received a score of 47 on the Total Intelligence subscale of the Wechsler Intelligence Scale for Children. Stroop test (ST) revealed findings supporting the failure to resist distractors and impulsivity. It was observed that he had a reduced interest towards the end of the Wisconsin Card Sorting Test (WCST), and he cast the cards away while sorting them. We observed that the patient had a limited number of categories completed in WCST, an elevation in perseveration scores, a reduced ability to maintain the correct response pattern, and an inability to inhibit a perseverative response even though he noticed a change in the sorting principle, which suggested a problem in prefrontal processes. His failure to get any points at the Serial Digit Learning Test (SDLT) pointed to a problem in the processes that required the right FL functions, and were not based on simple learning. The lack of a significant increase in learning in spite of repetition during the Verbal Memory Process Test (VMPT) was interpreted in favor of a failure to compose a consistent learning plan, a learning skill devoid of organization, and an influence on memory of a slightly subcortical type. The Judgement of Line Orientation Test (JLO) result was normal. As a result of the neuropsychological tests, the moderate degree of deterioration in the frontal functions was interpreted in favor of FLS. The escitalopram treatment was lowered in dose and discontinued. In addition, risperidone treatment was started at 1 mg/day and titrated upwards. During the follow-up, the anger control of the case was partially better, but his mood swings persisted. Therefore, the mood stabilizer, valproic acid, was added to the risperidone treatment for augmentation purposes, and it was progressively increased to 2000 mg/day. With the addition of valproic acid, the mood swings of the case remitted. His follow-up could not be continued due to the physician moving to another city following the second month of his treatment.

DISCUSSION

This report includes the process of EF-related assessment and treatment of a case that sustained head trauma due to a traffic accident three years ago. The temporal relation between the onset of symptoms and trauma and the presence of trauma signs from the image in the right frontal region were taken after the accident. When interpreted in connection with the study findings, the observation of ongoing changes in personality pattern following the trauma support the view that the symptoms developed due to accident-related changes in the brain. The impairment in EFs that was present in the patient was indicated by behavioral problems and neuropsychological tests, which are considered to be consistent with FLS.

The mutual connections of FL with the basal ganglia and thalamus constitute the frontal-subcortical circuits (Lyketsos et al. 2004). These connections are thought to be

responsible for EF impairment in patients with lesions other than FL (Levy and Dubois 2006). The connections formed by DLPFC, OFC, and ASC/MPFC with subcortical structures are networks that are held responsible for FLS and EF (Lyketsos et al. 2004, Nishio et al. 2003, Mori 2002). Each and every network is associated with a different aspect of EF (Lyketsos et al. 2004). The DLPFC circuit is responsible for EFs such as verbal fluency, ability to maintain and change the response, planning, prevention of response, working memory, organization skills, inference, problem solving, and abstract thinking. Damage in the ASC/MPFC circuit, which has a central role in motivation, leads to decreased social interaction and psychomotor retardation. The OFC circuit is critical in creating a behavioral response appropriate for the situation with respect to the integration of emotional information in the limbic system. Its damage results in disinhibition and anti-social behaviors (Lyketsos et al. 2004, Nishio et al. 2003, Mori 2002, Alvarez and Emory 2006).

The affected anatomic region and scale of damage influence the clinical picture in FLS (Anderson and Catroppa 2005). The dysexecutive type (dorsal convexity), disinhibited type (orbitofrontal), and apathetic type (mesial frontal) are three clinical pictures defined per the anatomic sites (Hariri et al. 2004). In addition to the views that prioritize the neural network influenced by the resultant clinical picture, there are also views stating that the characteristics of all three circuits may be observed together (Lyketsos et al. 2004). Fronto-subcortical circuits are associated with shared subcortical structures. The situations where sub-cortical structures are affected lead to symptoms pertaining to all three circuits rather than symptoms specific to a single circuit (Nishio et al. 2003, Mori 2002). In a way consistent with this view, a trauma-related signal increase in the periventricular white matter indicated sub-cortical influence and was identified in the patient's MRI.

The WCST, which ranks the first among EF tests, assesses characteristics such as executive attention, cognitive flexibility, prioritization, perseverance, working memory, conceptualization, problem-solving, abstract thinking, and maintaining response (Alvarez and Emory 2006, Karakaş and Doğutepe Dinçer 2011). WCST, which was used as a FL test, has a broad evaluating function that also includes the DLPFC in the right FL. Supporting this view association between persevering reaction and right DLPFC damage has been shown (Alvarez and Emory 2006, Lombardi et al. 1999, Karakaş and Doğutepe Dinçer 2011). The high scores for perseverance obtained by the case in WCST indicate the influence on DLPFC. SDLT, which also requires processes related to FL functionality, measures the memory and learning capability (Karakaş and Doğutepe Dinçer 2011). During the execution of SDLT in the patient, activation of the right hemisphere was demonstrated (Karakaş and Karakaş 2001, 2006). Inconsistency in VPMT indicates a difficulty in maintaining the learning strategy. In other words, it shows that one learning strategy was discontinued and another was taken up (Öktem Tanör 2011). The VPMT results of the case also pointed out to the fact that his planning and organization skills were influenced as part of EFs. Assessing the ability to change one's perceptive status in the face of a changing requirement, ST measures the performance in suppressing distractors and delaying response to inappropriate stimuli (Alvarez and Emory 2006, Stroop 1935). It was reported that ST was especially sensitive to damage in the lateral and superior medal regions of FL (Alvarez and Emory 2006). The observation of findings that supports failure to resist distractors and impulsiveness with ST supports the symptoms of attention and impulsiveness, which are related to the FL functions of the case. No pathologies in the cortical areas of the case were identified in the final imaging studies. The presence of personality changes accompanied by disinhibition and irritability in the clinical picture of the case, existence of problems with motivation, and spontaneity as well as the EF impairments demonstrated by the neuropsychological test results suggested that all three circuits were influenced at the level of sub-cortical connections.

In the case, the temporal stability of findings and maintenance of orientation ruled out the diagnosis of delirium, while the absence of episodic nature of behavioral problems ruled out the impulse control disorders. The lack of an episodic nature in the complaints and failure to meet diagnostic criteria in terms of mood disorders ruled out the diagnosis of mood disorders, while the absence of a history of seizure ruled out epilepsy. The personality disorder diagnosis in our case was ruled out because of the following: unnecessarily aggressive behaviors, personality pattern before the accident not suggesting pathology, and the etiological connection between the accident-related influence on FL and change in the personality pattern (American Psychiatric Association 1994, Hariri et al. 2004). One of the conditions to be considered in the differential diagnosis of FLS is the disruptive behavior disorder. Since no findings were identified that would lead us to think about disruptive behavior disorders in the pre-trauma period history of the case, these disorders was excluded. On the other hand, it is known that Attention Deficit Hyperactivity Disorder (ADHD) develops in 1/5 of children with trauma-related brain damage (Gerring et al. 1998, Sinopoli et al. 2011). The psychiatric history of the case before the accident does not exclude this clinical condition called ADHD, either.

It is reported that agents such as antipsychotics, mood stabilizers, propranolol, methylphenidate, buspirone, and trazodone may be used depending on the symptom patterns in FLS treatment. For this reason, the underlying pathology makes drug selection difficult and that treatment response is often low (Hariri et al. 2004). Four potential indications regarding the use of anti-psychotics were suggested as follows: agitation following traumatic brain damage, excessive aggressiveness and anger, mania, and Tourette syndrome (Burnett et al. 1999). In the limited number of case reports regarding

the use of risperidone for traumatic brain damage, risperidone treatment was shown to be effective in sleep problems, psychosis, jealousy paranoia, secondary motor restlessness and agitation (Schreiber et al. 1998, Zimnitzky et al. 1996, Silver et al. 2003, Mizoguchi et al. 2002, Elovic et al. 2003). Regarding mood stabilizers, their effects on reducing the risk for seizures in the acute period are most often dwelt upon (Chiaretti et al. 2000). It was reported in animal experiments that the chronic use of valproic acid prevented secondary metabolic disease (Basselin et al. 2008). In a case series, divalproex was shown to be an effective alternative to neuroleptics and benzodiazepines in alert, labile, impulsive, and disinhibited brain trauma patients (Chatham Showalter and Kimmel 2000). The better response could be received with dopaminergic agents such as stimulants since the use of neuroleptics could exacerbate the FLS picture in certain cases (Lyketsos et al. 2004). In addition to studies showing the positive effect of methylphenidate on cognitive functions after traumatic brain damage, there are also studies where no effects were identified (Moein et al. 2006). Even though methylphenidate was assessed as one of the treatment options, a stimulant was not preferred in this case due to the symptoms of irritability, ideas of reference, and suspiciousness. In conclusion, the treatment with antipsychotics and the added mood stabilizers proved to be useful in our case in spite of attention and EF problems.

Developing approaches to target symptoms are in the forefront of FLS treatment. It is important to perform a combined assessment of the age, affected brain area, level of influence, and factors that could predict the outcome in treatment management. The neuropsychological measurement results for EF and professional, academic, and social outcomes are closely related (Ryu et al. 2010). In our case, the significant influence on both academic and social functionality following a traumatic brain damage was mediated by the EF impairment. The case was reported since he received an FLS diagnosis. However, his final imaging results did not show any FL damage. When sudden onset behavioral and cognitive problems are encountered in adolescents with a history of trauma, FLS should be considered for differential diagnosis. Detailed multidisciplinary evaluations need to be conducted even in cases that lack open frontal lesions.

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