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From Hysteria to Functional Neurological Symptom Disorder: Developments in Clinical Diagnosis and Neurobiology

Histeriden Fonksiyonel Nörolojik Belirti Bozukluğuna: Klinik Tanı ve Nörobiyolojideki Gelişmeler

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ABSTRACT

Changes in the nomenclature of functional neurological symptom disorders (FND) from the past to the present represent historical changes in understanding etiology. Today, there is still difficulty in excluding potential underlying neurological disorders. In addition, there is no consensus on the psychological mechanism leading to the disorder. As a result, diagnostic problems continue to exist. While functional neuroimaging studies show that suppression and conversion mechanisms, which are the concepts of the psychoanalytical theory, may have neural counterparts, neurobiological data suggests that the conversion model cannot be explanatory for every patient. The dorsolateral prefrontal cortex (dlPFC), amygdala, temporoparietal junction (TPJ), insula, anterior cingulate structures, and their connections come to the fore. The fact that the connections between the dlPFC and the hippocampus can prevent the recall of an unwanted memory, as well as the changes detected in the amygdala in these disorders and the increased connectivity between the amygdala and the motor areas, suggest an abnormal connection between emotions and the motor system. It is addressed how changes in the TPJ are related to the loss of the sense of agency. However, it is unclear whether the findings of these studies suggest a "predisposition", "onset of disorder", or "compensatory changes secondary to disorder". Exploring FND to learn how the brain and mind react to psychosocial stressors can be a turning point in understanding the brain-mind connection. The goal of this review is to present the history of the changes in terminology and perspective on this disorder that followed the establishment of psychoanalysis, as well as what kind of evidence has been presented regarding hysteria in light of advances in neuroscience.

Keywords: Conversion disorder, functional neurological symptom disorder, functional neuroimaging

ÖZ

Fonksiyonel nörolojik belirti bozukluğunun (FNBB) isimlendirilmesinde geçmişten günümüze kadar yapılan değişiklikler tarihsel süreçte etiyolojiye ilişkin anlayışın değişimini yansıtmaktadır. Günümüzde halen altta yatan başka bir olası nörolojik hastalık tanısının dışlanmasında zorluklar yaşanmakta, bozukluğa yol açan psikolojik mekanizma konusunda bir fikir birliği bulunmamakta ve buna bağlı olarak tanı koyma ile ilgili sorunlar devam etmektedir. Fonksiyonel görüntüleme çalışmalarının sonuçları psikanalitik kuramın konversiyon modelinde yer alan bastırma ve döndürme (konversiyon) mekanizmalarının nöral karşılıklarının olabileceğini düşündürmekle beraber, bu modelin her hasta için açıklayıcı olamayacağına işaret etmektedir. Özellikle dorsolateral prefrontal korteks (dlPFK), amigdala, temporoparietal bileşke (TPB), insula, ön singulat yapıları ve aralarındaki bağlantılar ön plana çıkmaktadır. Bulgular istenmeyen bir anının hatırlanmasının dlPFK ve hipokampus arasındaki bağlantılar aracılığıyla engellenebileceğini düşündürmektedir. Ayrıca amigdalada saptanan değişiklikler ve amigdala ile motor alanlar arasında tespit edilen artmış bağlantısallık, duygu düzenlemenin bozulması ve duygular ile motor sistem arasında anormal bir bağlantı olması ihtimali ile ilişkilendirilmektedir. Temporoparietal bileşkede gösterilen değişikliklerin ise hareketin faili olma hissinin bozulması ile ilişkili olabileceği öne sürülmektedir. Ancak bu araştırmaların sonuçlarının 'hastalığa yatkınlığı' mı, 'hastalığın ortaya çıkışını' mı yoksa 'hastalığa ikincil telafi edici değişiklikleri' mi temsil ettiği henüz aydınlatılamamıştır. Psikososyal stresörlere beynin ve zihnin nasıl yanıt verdiğini anlamaya çalışmak için FNBB'yi araştırmak beyin-zihin ilişkisini anlamak adına önemli bir kavşak olabilir. Bu derlemede terminoloji ve bakış açısındaki değişimin tarihçesi, psikanalizin kuruluşuna eşlik eden bu bozukluğa psikanalizin bakış açısı ve nörobilimdeki gelişmeler ışığında histeriye dair ne gibi bulgular ortaya konduğunun sunulması amaçlanmaktadır.

Anahtar sözcükler: Konversiyon bozukluğu, fonksiyonel nörolojik belirti bozukluğu, fonksiyonel nörogörüntüleme

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Introduction

Functional neurological symptom disorders (FND) are neuropsychiatric conditions that may present with symptoms such as loss of motor functions, impairment of sensory functions, movement disorders, or non-epileptic seizures, and in which a neurological disease that would explain the symptoms cannot be structurally identified (Cretton et al. 2020). Around 30% of all patients who apply to the neurology clinics have symptoms that cannot be explained neurologically, and about half of these people are assumed to have FND (Stone et al. 2009). After headache, FND was found to be the second most frequent reason for admission to a neurological outpatient clinic. (Stone et al. 2010). Despite advances in topics such as the identification of clinical symptoms, accurate diagnosis, defining the predisposing characteristics, and the impact of psychiatric comorbidities, there are still many unanswered questions regarding the understanding of the etiology, recognition, prevention, and intervention of FND (Espay et al. 2018).

The terminology used in descriptive psychiatry has evolved, moving from the diagnosis of conversion disorder to that of FND, reflecting changes in both the view of the body-mind duality and the understanding of the pathophysiology of this condition (Cretton et al. 2020). The significance of an interdisciplinary approach to comprehending and managing this condition at the interface of psychiatry and neurology is highlighted by this change in terminology (McKee et al. 2018). The belief that conversion disorder incidence was declining toward the end of the 20th century caused a gradual decline in interest in this disorder among medical professionals, yet over the last 30 years it has become clear once more that the disorder is widespread and causes loss of function, and recent advancements in the neuroscience field have given rise to new hopes for understanding the neurobiological mechanisms underlying it (Keynejad et al. 2017). Functional imaging research has enhanced previous neurobiological studies, which were previously restricted to electrophysiology and structural imaging (Ejareh and Kanaan 2016, Begue et al. 2019). In this review, first of all, the historical shifts in clinical diagnosis from hysteria to FND and the challenges with diagnosis will be outlined. Next, contemporary research on "hysteria" will be presented in the context of developments in neuroscience.

Clinical Diagnosis from Hysteria to Functional Neurological Symptom Disorder

Hippocrates used the name "hysteria" for what the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) now refers to as "functional neurological symptom disorder" (APA 2013). Hysteria was first mentioned in papyri from the 20th and 17th centuries B.C. in Ancient Egypt. Although 'women behaving strangely' with difficulties swallowing or seizures were described in these papyri, the condition was not given a name. In the fifth century B.C., Hippocrates of Ancient Greece asserted that these symptoms, which he believed to be present only in women, were brought on by the uterus shifting inside the body (Simon 1978). He believed that the uterus needed to be replaced because the symptoms were molded by the organ in which it was housed. Hippocrates was the first to suggest a bodily issue based on the symptoms with his approach. In the Roman era A.D., Galen was known to have followed Hippocrates' lead and believed that this illness only affected women (Simon 1978). While Avicenna carried on Hippocrates' legacy by believing that hysteria was a disease that required medical treatment in the Middle Ages in the East, the predominate belief during the same period in Europe was that people with hysteria possessed supernatural powers, were sorcerers, and should have been punished (Simon 1978).

Hysteria started to be discussed in the field of medicine once more with the work of Sydenham, who asserted that it was one of the most prevalent diseases since the eighteenth century (Pearce 2016). Instead of the uterus, the brain was now the organ linked to the disease (Trimble and Reynolds 2016). According to Briquet's theory from the 1800s, hysteria symptoms were linked to the central nervous system and manifested in vulnerable individuals when stressful life events had an impact on the affective area of the brain (Chertok 1984). Following Briquet's studies, the French neurologist Charcot, one of the important figures of his period, thought that these patients had a neurological disorder to which there was an innate predisposition, and observed that the symptoms were also seen in men and that they could be induced or alleviated by hypnosis (Chertok 1984). Consequently, hysteria was no longer exclusively an illness of women. According to him, these "migraine-like neuroses," in which function is compromised but no neuropathology is found, may represent a "dynamic" lesion (Chertok 1984). Towards the end of the nineteenth century, Janet defined the inability to maintain the conscious synthesis of all aspects of the experience as 'dissociation', claiming that under some conditions, such as trauma, a part of the experience may be isolated from consciousness and the dominance over the symptom (for example, the strength of the limb) may be weakened (Jones 1980).

In the same time frame, Freud and Breuer began to study hysteria cases and were influenced by Charcot's theories. In the book Studies on Hysteria (1895), they discussed the treatment of five patients in detail, with each heading including a theoretical part including Freud's presumptions. The clinical and theoretical underpinnings of psychoanalysis, which stems from a cathartic approach, were revealed in Freud's chapter 'Psychotherapy of Hysteria'. Freud initially took after Breuer, who employed hypnosis as a cathartic method of treating hysteria. The purpose of the therapy was catharsis, or giving misdirected emotions a safe outlet. In these patients, "the emotion remains coiled and the memory trace of the experience to which this emotion is tied is disconnected from consciousness." The emotional memory manifests itself as hysterical symptoms. Breuer and Freud postulated that psychological trauma is the root of hysterical symptoms and that reliving the initial emotion would help the patient recover from the condition. Later, as theory advanced, they argued—using the term "conversion" for this—that undesirable memories are repressed into the unconscious and turned into physical symptoms. This conversion lessens the anxiety, which Freud refers to as the primary gain. The symptom can sometimes lead to avoiding conflict or getting out of an undesirable situation, which he calls secondary gain. Freud later abandoned the trauma theory. He stated that the goal of treatment for hysteria should not be catharsis and that the veil covering the repression should be lifted during the development of psychoanalysis. He also termed the therapeutic approach he used as psychoanalytic rather than cathartic (Freud and Breuer 1895). Hysteria thus assumed its place in psychiatric research from a scientific perspective with the development of psychoanalysis in the twentieth century and played a key part in the development of modern psychiatry.

For a long time, Freud's description of conversion hysteria served as the basis for the name of this set of symptoms in descriptive psychiatry. The DSM diagnostic criteria have shown a comparable fluid alteration to nomenclature and historical assumptions regarding the causes and emergence of the condition. Starting with the first DSM (APA 1952), the term "conversion" was employed in descriptive psychiatry under the influence of psychoanalysis. From DSM-I to IV, the term "conversion" was still in use, and for the first time, DSM 5 underwent a significant nomenclature change (APA 1968, APA 1980, APA 1994, APA 2013). Table 1 displays the nomenclature and highlighted criteria used from the first DSM to its 5th version.

Table-1. Changes in the Diagnostic and Statistical Manual of Mental Disorders (DSM) in terms of the features emphasized for the nomenclature and diagnosis of hysteria in descriptive psychiatry

Version (Date)	Diagnostic category	Emphasized clinical features
DSM I (1952)	Psychoneurotic Disorders >>>> Conversion Reaction	Clinical signs are defined as functional signs in the body that are controlled voluntarily. These signs depend on the conversion of the impulses that cause anxiety.
DSM II (1968)	Hysterical Neurosis >>>> Conversion Type Hysterical Neurosis	The signs are defined as psychogenic involuntary loss or impairment of function. The concepts of secondary gain, symbolism, and *la belle indifference* are emphasized.
DSM III (1980)	Somatoform Disorders >>> Conversion Disorder	It is defined as a loss of function that is not explained by a known physical disease or pathophysiological mechanism. There is a psychosocial stressor associated with loss of function and there is a temporal relationship with this stressor.
DSM IV (1994)	Somatoform Disorders >>> Conversion Disorder	The criterion of the necessity of a psychosocial stressor was removed and impairment in functionality was emphasized.
DSM 5 (2013)	Somatic Symptom and Related Disorders >>> Functional Neurological Symptom Disorder	The symptom cluster of conversion disorder (with attacks and seizures) has expanded. It emphasizes that the symptoms cannot be explained even though the underlying physical conditions are investigated. Special emphasis was also placed on assessing predisposing factors.

Challenges in Diagnosis

Two major diagnostic challenges for FND include challenges in ruling out neurological disease and a lack of agreement on the psychological process (Nicholson et al. 2011). Although psychological mechanisms such as the symbolic resolution of the unconscious conflict, the transformation of the stressor into a physical symptom, and the formation of the symptom by the partial or complete loss of normal integrity between past memories, and control of bodily movements and sensations are accepted, it is not always possible to identify a stressor or clarify a psychological mechanism in every patient (Aybek et al. 2014). Accordingly, some attempts have been made to first make a diagnosis based on the patient's clinical findings and to distinguish neurological examination findings. However, no finding serves as the gold standard in diagnosis, despite the fact that correct diagnosis rates have grown over time (Stone et al. 2005). The presence of positive signs that are not expected to be present

in the normal examination, as well as the loss of normal signs that should be present in the examination (negative neurological signs), such as loss of strength or loss of sensation, also support the diagnosis (Daum and Aybek 2013, McKee et al. 2018). The positive signs that offer crucial diagnostic hints are reported in Table 2.

Table 2. Positive signs that support the diagnosis of functional neurological symptom disorder when detected in addition to negative signs in examination

Negative sign	Positive signs
Lower limb paresis	Hoover's sign: The involuntary extension of the paretic lower limb, when the healthy leg is tried to flex against resistance.
Upper limb paresis	Fall without pronation: If the patient is asked to hold their arms in the air with their palms facing up, fingers in adduction, and eyes closed, the affected arm slides downwards without pronation.
Paresis	Inconsistency: While a movement made with one muscle cannot be performed, other movements made with the same muscle can be continued.
Movement disorder	Decrease in the intensity of movement due to distraction
Gait disorder	Uneconomical postures that waste muscle energy
Sensory loss	Sensory loss is not compatible with any radicular, truncal, or central sensory area
Vision loss	Tunnel vision

Neurobiological Findings from Past to Present

A Common Theory for Motor and Sensory Symptoms: Central Inhibition Theory and Related Brain Regions

The first neurobiological findings regarding conversion hysteria are based on case reports reporting electrophysiological findings made in the 1960s and 1970s. It has been shown that there is a decrease in somatosensory evoked potentials (SEP) when the leg with sensory loss is compared with the healthy leg of a patient with hysterical symptoms (Hernandez-Peon et al. 1963). It was found that in other patients with impaired evoked potentials, these potentials returned to normal patterns after their symptoms disappeared (Levy and Mushin 1973). These findings were repeated in two patients with sensory loss in the following years (Yazıcı et al. 2004). Similar results have been reported for vision; in a patient who had vision loss in two quadrants of the visual field, lower visual evoked potential (VEP) amplitudes were found in the blind quadrants in the evaluation made before psychotherapy, and it was found to improve after psychotherapy (Schoenfeld et al. 2011). The evoked potentials in other case reports, however, were discovered to be normal(Sierra and Berrios 1999). Ludwig (1972) proposed that conversion symptoms emerged as a result of corticofugal inhibition of afferent stimulation considering the limited data available during these years. For patients with motor and sensory complaints, this central inhibition theory represents a common first perspective.

Over the previous three decades, imaging studies have made contributions to the field. First, studies with a small number of samples and case reports showing structural imaging results were carried out in the 1990s to determine whether conversion symptoms were brought on by a lesion in any particular area of the brain. Functional imaging research became more significant in later years as imaging technology advanced. Single Photon Emission Computerized Tomography (SPECT) revealed hypoperfusion in the contralateral parietal region and hyperperfusion in the contralateral frontal region when electrical stimulation was delivered to the left side of a female patient with left-sided sensory loss (Tiihonen et al. 1995). Positron Emission Tomography (PET) findings of another patient with left hemiparesis showed that while there was increased activity in the right anterior cingulate and orbitofrontal cortex (OFC) with movement effort, there was no neural activation in the primary motor cortex (Marshall et al. 1997). These results imply that when the patient tries to move, the motor and premotor areas of the frontal region are suppressed. The central inhibition theory has evolved over time as new data about the roles of neuroanatomical structures has become available. Based on these findings, it was hypothesized in the 1990s that the anterior cingulate, along with the OFC, functionally blocked the connection between the premotor/prefrontal area and the primary motor cortex and that motor symptoms manifested when the anterior cingulate's activity interfered with the delivery of motor commands.

In the following years, the number of functional imaging studies gradually increased. According to a review of the literature, 13 functional magnetic resonance imaging (fMRI) studies with sample sizes ranging from one to 16 were published between 2000 and 2015. Four focused on sensory symptoms and nine on motor symptoms. There were four PET and three SPECT studies. These investigations have started to raise the possibility that subcortical structures may also be crucial in the effect of central inhibition, which was previously assumed to be

mediated by cortical structures. For instance, it was discovered that blood flow reduced in the contralateral thalamus, putamen, and caudate when SPECT was performed by delivering vibration to the affected limbs of seven individuals with unilateral sensory or motor type conversion disorders while they had symptoms (Vuilleumier et al. 2001). It has been discovered that following healing, the reduced blood flow returns to normal. Another study examining sensory-type conversion disorders revealed relatively consistent findings in terms of decreased activity in primary sensory areas and increased activity in another brain region and drew attention to subcortical structures (Burke et al. 2014). In a series of ten cases, the regions where increased activity was detected with vibrotactile stimulation included the right paralimbic areas (insula and anterior cingulate), right temporoparietal junction (TPJ), bilateral dorsolateral prefrontal cortex (dlPFC), right OFC, right caudate, right ventral anterior thalamus and left angular gyrus. Another study that examined five individuals with vision loss reported that patients who received visual stimulation showed suppression in the visual cortex and increased activity in the left inferior frontal cortex, insula, limbic regions, and bilateral striatum (Werring et al. 2004).

Trauma/Abuse/Stressful Life Events

According to studies on patients with conversion disorder, a history of physical abuse was reported at rates of 28–44%, sexual abuse at rates of 24-26%, childhood abuse at a rate of 3% in cases with motor symptoms, and a history of physical/sexual abuse at rates of up to 67% in cases with seizures (Mökleby et al. 2002, Roelofs et al. 2002, Binzer and Eisemann 1998, Stone et al. 2004, Bowman and Markand 1996, Roelofs et al. 2002). In a relatively recent meta-analysis by Ludwig et al. (2018), it was reported that in a total of 1405 conversion disorder cases in 34 case-control studies, emotional neglect was experienced 5.6 times more frequently, physical abuse 3.9 times more frequently, and sexual abuse 3.3 times more frequently than controls. Stressful life events were found to be 2.8 times more likely before symptoms in the same study. In contrast to these results, no recent event or early stressor was discovered to be significantly associated with conversion disorder in 13 studies.

The results show that it is crucial to look into the neurological correlates of how trauma and recent life experiences affect symptoms. In this regard, it is noted that there is a case report demonstrating the association between recalling a traumatic experience and conversion disorder symptoms when studies in the literature are examined. When the traumatic event that caused the symptoms was remembered, task-dependent fMRI in a female patient with right hemiparesis revealed an increase in activity in the right medial temporal lobe (including the amygdala) and a simultaneous decrease in activity in the contralateral primary motor cortex (Kanaan et al. 2007). In another study that assessed autobiographical memory, 13 healthy controls and 12 patients with motor symptoms were examined (Aybek et al. 2014). Stressful life events that might be connected to the loss of function were questioned, and the specific event that was thought to have caused each participant's symptom development was determined, then fMRI was conducted by asking them to recall these events. First, it was observed that when autobiographical memory was recalled, the activity in the relevant regions was altered in the group with conversion disorder compared to healthy controls. Right supplementary motor area (SMA) and TPJ activity increased, left dlPFC activity increased while left hippocampal activity decreased when the events assumed to have caused the symptoms were recalled. It was demonstrated that when all negative life events were recalled, including those that were supposed to cause conversion or not, the right inferior frontal cortex was less likely to be activated than in controls, and the connectivity between the amygdala and motor regions (SMA, cerebellum) was higher. This study is significant since it is the first to present life events and imaging results together. It was suggested that a top-down regulation (dlPFC) could prevent the hippocampus from remembering an undesirable memory. The traumatic memory may "short-circuit" and interfere with regular motor and sensory function.

Neural Structures Associated with Conversion Disorder/Functional Neurological Symptom Disorder

Recent research suggests that FND and somatic symptom disorders may have issues with similar circuits. To investigate structural alterations in these disorders, various volumetric measuring studies have been conducted (Begue et al. 2019). Imaging studies have shown that there is a structural change concurrent with the change in the circuits, highlighting the integrity of structure and function even though neurobiological findings suggest that functional symptoms occur with a change in brain circuits rather than a structural change in a single region of the brain.

The amygdala, anterior cingulate, insula, SMA, and TPJ stand out among the areas where these structural and functional alterations take place. Regions involved in emotion regulation and the stress response include the amygdala and anterior cingulate. It is observed that the impairment in perigenual anterior cingulate cortex

inhibition on the amygdala output is a corticolimbic change defined in mood and trauma-related disorders, whereas the amygdala, insula, and periaqueductal gray matter (PAG) connections of the perigenual anterior cingulate cortex are associated with emotion regulation. As a result, structural and functional changes in the perigenual anterior cingulate cortex are thought to be not specific to functional symptoms and are associated with mood dysregulation and accompanying trauma symptoms (Ospina et al. 2019). The insula is another significant structure that the study findings highlight. Cinguloinsular functional and structural alterations may be caused by a failure to integrate affect, cognition, and bodily information, as well as a loss of awareness (Perez et al. 2012; Perez et al. 2015). The posterior part of the brain is linked to internal representations of the physiological state of the body, the SMA is linked to spontaneous movement or the sensation of control over movement, and the insula is linked to self- and emotional awareness (Begue et al. 2019). The TPJ is the area of the brain that receives sensory data, compares experiences from the inside and outside of the body, and is linked to a sense of agency or subjective control (Voon et al. 2010). TPJ is a region linked to autoscopy, out-of-body experiences, vestibular illusions, and sensory illusions (like the sensation of flying or shortening limbs), and it has been found that increased activity of this region in both schizophrenia patients and healthy people is linked to the perception of involuntary movement (Blanke et al. 2004).

Possible Predisposition to Conversion Disorder/Functional Neurological Symptom Disorder: Emotional Processing and Stress Response

Connections between the amygdala and motor areas indicate an impairment of emotion regulation and an aberrant connection between emotions and the motor system (Hassa et al. 2021). This increased connectivity in FND is regarded to suggest a potential susceptibility. When faces representing various emotions were shown to 16 patients with functional movement disorders and 16 healthy controls, it was found that the healthy controls' amygdalas were clearly activated by angry faces, whereas the FND group's amygdalas were clearly activated by both angry and happy faces. This finding may reflect a risk factor for the formation of functional symptoms. Social cues may be interpreted as dangerous in the patient group, or there may be a general hypersensitivity related to emotional response (Voon et al. 2010). When 11 patients with tremor, dystonia, and gait disorder type FND and 11 matched controls were given a two-choice task that was either externally or self-directed, the left SMA, which is responsible for motor preparation and inhibition, was found to have less activity in the patient group (Voon et al. 2011). In addition, it was found that activity was increased in the right amygdala, left anterior insula, and bilateral posterior cingulate, which are regions associated with emotional processing, and there was a reduced connectivity between SMA and bilateral dlPFC when initiating movement spontaneously.

There are conflicting findings in studies examining the processing of facial expression recognition that might or might not detect differences between patients and controls in terms of recognizing emotions. In another investigation, it was discovered that increased attention to happy faces was linked to fewer seizures and that increased attention to angry faces was linked to both basal cortisol levels and childhood sexual trauma (Pick et al. 2018). A more pronounced rise in left amygdala activity was found in the patient group when exposed to faces expressing negative emotions when it was investigated whether there may be abnormal excitation or inhibition difficulty against a familiar stimulus in functional disorders (Aybek et al. 2015). Additionally, it was observed that after a period of fear expression, the amygdala activity decreased in the control group, but not in the patient group, indicating the presence of a "hypersensitization" state for patients (Aybek et al. 2015).

In conversion disorder, increased PAG and frontal region (bilateral premotor, SMA, left dlPFC, and left cingulate cortex) activity and increased amygdala-SMA connectivity were detected against negative emotions (Aybek et al. 2015). PAG activity is known to be associated with the freeze response to threat and the fear-bradycardia response in animals. Increased frontal activity corresponds to areas involved in motor planning, while amygdala-SMA connectivity may reflect abnormal emotion-motor area connection. In another study, functional imaging was used to assess 24 individuals with FND and 24 healthy controls and it was found that the patients displayed a particular arousal and emotional rating profile toward negative emotional stimuli, and the increased activation seen in the right amygdala reflected a change in emotional processing, supporting previous research (Hassa et al. 2021). In this study, it was shown that when cognitive restructuring strategies were used, the activity in the right amygdala did not decrease in patients compared to controls. Some of the cognitive restructuring strategies were thinking that the image watched was a movie scene rather than a real war, or that the blood seen was an artificial substance on the movie set. However, right amygdala activity could have decreased in situations where attention was distracted, such as when solving a mathematical problem.

Another factor that contributes to susceptibility to conversion disorder may be differences in stress responses. When the patients' salivary cortisol levels, heart rates, skin conductance levels, and responses were examined, it

was found that their autonomic arousal increased both when they were at rest and when processing emotions. Additionally, it was discovered that pituitary volume decreased inversely with the duration of the disorder; it has been suggested that this data may point to a problem with the stress-related neuroendocrine system (Atmaca et al. 2016). Oxytocin receptor genotypes were shown to be associated with higher amygdala activity during the processing of unpleasant emotions when gene-environment interactions were investigated, and elevated methylation was found in the oxytocin receptor gene of the patients (Dannlowski et al. 2016, Apazoglou et al. 2017, Begue et al. 2019).

Models that include both neurobiological and psychosocial components are required for functional disorders where psychosocial risk factors have been demonstrated. Stressors and the appearance of symptoms may be connected by changes in how emotions are processed and variations in how the body reacts to stress. The increase in implicit/preconscious processing of emotional stimuli may be connected to increased limbic reactivity (amygdala) and may lead to initiating defensive reactions through brainstem pathways such as the hypothalamus and PAG (Pick et al. 2018).

Differences with Malingering – The Neurobiology of Volition

Whether the patient is purposefully fabricating symptoms in order to obtain some advantage is one of the crucial diagnostic uncertainties when examining conversion symptoms. The central inhibition hypothesis fails to indicate whether the inhibition is intentional or involuntary from a neurobiological standpoint. There are a few research in the literature that focuses on the neurobiological results of individuals with conversion disorder and symptom mimicking in an effort to differentiate between voluntary and non-volitional disorders. Regardless of the lateralization of the condition, hypoactivation in the left dlPFC was found in three patients with motor conversion disorder when PET was performed during motor tasks (Spence et al. 2000). The absence of this finding in six controls and four symptom mimickers led researchers to hypothesize that the decline in left dlPFC activity may be related to the loss of volition. In another study, while imagining and trying to perform a movement, 13 controls mimicked the symptom, and 21 healthy controls were imaged (van Beilen et al. 2011). While the controls who mimicked the movement showed dlPFC activity similar to healthy controls, decreased activity in the prefrontal region was found in the patients, supporting the findings of the earlier study. Furthermore, compared to symptom mimickers, the patient group displayed decreased activity in the right TPJ and dlPFC, as well as higher activity in the contralateral primary motor cortex and left cingulate cortex. In another study, brain imaging was performed in eight patients with functional tremor while simulating tremor, during functional tremor and at rest. TPJ hypoactivity was detected during functional tremor, and the connectivity between the sensorimotor regions and limbic regions (ventral anterior cingulate and ventral striatum) and TPJ was also found to be reduced (Voon et al. 2010). Another group of researchers observed that connectivity between the right TPJ, sensorimotor cortex, cerebellar vermis, bilateral SMA, and right insula decreased in FND patients (Maurer et al. 2016). This observation has been interpreted as supporting an impairment in the sense of agency and perceived control over movement. As a result, it is thought that changes in TPJ are connected to the subjective sense of control over movement, while the reduction in dlPFC activity detected in patients but not in imitators is explained by the lack of volition.

Different Perspectives on Functional Neurological Symptom Disorder, Other Common Theories for Motor and Sensory Symptoms: Dimensional and Bayesian Approaches

Another current approach to understanding functional disorders is the dimensional perspective, which suggests that the categorical approach will be limited in making sense of neurobiological data (Spagnolo et al. 2021). The etiology and pathophysiology of this condition may be better understood by looking at its different dimensions, where symptoms of such a wide variety might manifest. Examining the neurobiology of FND from this perspective reveals that there are some dimensions in which significant changes can be seen. These dimensions include the responses to negative stimuli or threats, attention changes, stress response and regulation, planning and execution of motor movement, and the sense of agency (Spagnolo et al. 2021).

Attention-related dysregulation, symptom-related beliefs, and expectations are key concepts in comprehending functional symptoms (Edwards et al. 2012). Functional symptoms may be caused by the attention being focused on the symptom and a process that is directed by prior beliefs and expectations from the past (Edwards et al. 2012). This hypothesis states that the hierarchically determined centers that allow for the perception of the sensation or the execution of the motor action combine two data to produce an expectation (prediction). The first set of information is based on prior experiences and beliefs; this information includes cognitive biases, physical and emotional experiences (such as trauma, depression, anxiety, etc.), as well as personal and cultural

assumptions about the illness. Based on the fact that sensory stimuli are received via the proprioceptive mechanisms in the motor system, it is reasonable to presume that sensory input is available for all symptom clusters including motor function. These facts are combined to produce a prediction or expectation. Every prediction introduces the chance of a prediction error. For instance, if people anticipate a strong electrical stimulation, they could perceive it as stronger than it actually is, even if a weak electrical stimulus is delivered. This is an example of a prediction error. Attention is the most essential function for correcting this prediction error. This approach proposes that by focusing attention on the functional symptom, the earlier aberrant beliefs that contribute to the disorder become certain. It is known that people with functional symptoms have attentional biases that are body-focused, therefore these patients may also have a tendency to have difficulties with attention. This theory appears to be supported by instances like Hoover's sign or the change in the frequency of functional tremor when attention is diverted.

Questions/Issues

Other reviews have gone into greater detail about the limitations of the neurobiological findings found in FND (Pick et al. 2018, Begue et al. 2019, Cretton et al. 2020). In conclusion, there are basically two different sets of issues with these investigations. First, the studies have clear methodological problems. Nearly all of these studies had small and largely heterogeneous sample sizes, did not exclude comorbid psychiatric disorders, did not account for some confounding variables including the use of psychotropic medications, and did not perform any cognitive tests. Another issue arises when interpreting the results. Structural and functional changes in sensory and motor regions may differ even in patient groups presenting similar symptoms. It is unclear whether these results occur as a product of the disorder, are compensatory alterations, or are simply indicators of predisposition. The impact of gender differences, disease duration, and age on symptoms, the meaning of neural circuits that intersect with depression and anxiety disorders, the neurobiology of patients with a single symptom versus those with multiple symptoms, culture-specific prevalence and various clinical presentations, the influence of culture on different clinical presentations are all matters that need to be considered.

Conclusion

Although neurobiological studies have not yet provided a coherent model to explain FND, evidence of attention-related dysregulation, self-evaluation deficit, loss of the sense of agency, loss of volition, and changes in emotion regulation mechanisms have been found. Relatively consistent findings are inhibition of normal networks manifested by increased activity in the prefrontal region and decreased activity in sensorimotor areas, a motor planning deficit detected by changes in SMA activity, a deficit in self-evaluation, volition, and sense of control reflected by changes in the TPJ and dlPFC regions and the interaction of these areas with the limbic system indicating the relationship between attention and autobiographical processing, with the bodily stimuli. Additionally, abnormalities detected in emotion regulation, abnormal connections between the emotional areas and the motor areas, and the absence of a normal habituation process to negative emotions in the amygdala may indicate predisposing factors. The explanations of psychological models for how the human mind and body react to psychosocial stressors appear to be increasingly confirmed by contemporary neuroscientific results, which is an important conclusion on the path taken. A psychoanalytic conversion model by itself, however, falls short in its ability to fully explain the mechanism in all individuals. It is a multifactorial disorder in which separate factors that predispose, trigger, and worsen can be identified rather than a single explanation. In order to understand the individuals diagnosed with "hysteria," who have historically been perceived as trauma victims, who are acting out or feigning their symptoms, it is crucial to have a better understanding of neurobiological mechanisms. This will also help to advance the treatment of this disorder, which causes as much disability as organic neurological disorders, and even reduce stigma

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