Neural correlates of ‘functional’ symptoms in neurology

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Summary

Functional symptoms are neurological deficits that are not explained by organic lesions in the nervous system, but usually associated with emotional “psychogenic” disturbances (1). These symptoms are common and can affect any aspect of elementary neurological function, presenting clinicians with difficulties in definition, diagnosis, and treatment. Although current concepts explain functional symptoms in the context of “psychogenic” stress, the exact nature of these symptoms remains largely unknown. Recent functional neuroimaging studies have shifted understanding of these deficits from a psychological and psychodynamic model to a neurobiological model. This review highlights the advances made using functional neuroimaging techniques in patients suffering from two conditions: unilateral loss of motor function and psychogenic parkinsonism. The evidence suggests that areas including the prefrontal and parietal cortices, anterior cingulate cortex, thalamus, and basal ganglia may be implicated. Future studies, assessing patients at different phases of their illness and using newer techniques such as functional MRI, are needed to extend current findings on functional symptoms.

KEY WORDS: functional neuroimaging, functional symptoms, hysteria, neural correlates, neuroimaging.

Introduction

The term “functional symptoms” refers to a loss or distortion of neurological function that cannot be fully explained by demonstrable structural or pathophysiologic abnormalities, but is usually associated with emotional “psychogenic” disturbances (1). Functional symptoms may be regarded as ‘negative’ or deficit symptoms, when a loss of a neurological function is apparent and examples include paralysis, anaesthesia or blindness, or as ‘positive’ symptoms when, rather than a loss of function, an active behaviour manifests itself against a background of normal neurology; examples may include dissociative convulsions and movement disorders (2).

Functional symptoms have been described since antiquity and have attracted many different terminologies, sometimes with derogatory connotations, reflecting the diverse concepts that have been used in the quest to understand the complexity of these symptoms (3). In the present classification systems (DSM-IV, ICD-10) functional symptoms can be classified as manifestations of somatoform disorders or dissociative disorders. However, the term “functional” is becoming more common in the medical literature, being less simplistic, more acceptable to patients (4), and more representative of scientific knowledge (1).

In clinical neurological practice functional symptoms are common, accounting for 1-3% of diagnoses in general hospitals (5), and up to 10-30% in some neurological settings (6). Functional symptoms can affect any aspect of elementary neurological function, presenting clinicians with several problems of management due to difficulties with definition, diagnosis, and therapeutic approaches (7). Patients with functional neurological symptoms are often diagnosed by neurologists, and treated by psychiatrists (up to two thirds have somatic psychiatric comorbidity); these patients, who may display significant distress and handicap (8), challenge the traditional division between neurology and psychiatry (9).

Although current concepts suggest that functional symptoms derive from auto-suggestion (10), innate coping styles (11), or disorders of volition (12) or attention (11), there is still debate over the neural and physiological mechanisms involved. Recent functional neuroimaging studies have shifted understanding of these disorders from a psychological and psychodynamic model to a neurobiological model. Demonstrating objective brain correlates of functional symptoms may therefore help to advance current understanding of the mechanisms that underlie the abnormal neurological function in these patients.

This article will highlight some of the advances that have been made using functional neuroimaging techniques in adult populations suffering from functional neurological symptoms. This review focuses explicitly on evidence from studies investigating two conditions: unilateral loss of motor function and psychogenic parkinsonism.
Method

Literature search

Literature searches were carried out in PubMed using the keywords: “conversion disorder”, “hysteria”, “somatization”, “functional symptoms”, “psychogenic symptoms”, “somatoform disorders”, “dissociation disorder”, “hysteria”, “neural correlates”, “functional neuroimaging”, “unilateral loss of motor function”, and “psychogenic parkinsonism”. Articles and book chapters in the first author’s personal collection were also utilized.

Results

Only a very few studies using functional neuroimaging have been performed in patients with functional neurological symptoms. Table I summarizes the findings of those assessing unilateral loss of motor function and psychogenic parkinsonism.

Table I - Functional imaging studies assessing unilateral loss of motor function and psychogenic parkinsonism.

<table>
<thead>
<tr>
<th>Authors (ref. no.)</th>
<th>Subjects</th>
<th>Diagnosis</th>
<th>Imaging technique</th>
<th>Resting state/ neuroactivation</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Tiihonen et al., 1995 (13)</td>
<td>1 P</td>
<td>Unilateral loss of motor function</td>
<td>$^{99m}$Tc-MPAO SPECT</td>
<td>Electrical stimulation medial nerve</td>
<td>Increased activation of right frontal, and decreased activation of right parietal cortex</td>
</tr>
<tr>
<td>Marshall et al., 1997 (14)</td>
<td>1 P</td>
<td>Unilateral loss of motor function</td>
<td>PET</td>
<td>Movement task with affected limb</td>
<td>No activation of right sensorimotor cortex, and increased activation of right orbital and cingulate cortex</td>
</tr>
<tr>
<td>Spence et al., 2000 (15)</td>
<td>2 P 6 C</td>
<td>Unilateral loss of motor function</td>
<td>PET</td>
<td>Movement task with affected limb</td>
<td>Decreased activation of left DLPFC</td>
</tr>
<tr>
<td>Vuilleumier et al., 2001(16)</td>
<td>7 P</td>
<td>Unilateral loss of motor function</td>
<td>$^{99m}$Tc-ECD SPECT</td>
<td>Passive vibration (proprioception)</td>
<td>Decreased activation of contralateral thalamus and basal ganglia</td>
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<td>Lang et al., 1995 (17)</td>
<td>4 P</td>
<td>Psychogenic parkinsonism</td>
<td>PET</td>
<td>Resting</td>
<td>Decreased fluorodopa uptake in left putamen (in one patient)</td>
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<tr>
<td>Factor et al., 1998 (18)</td>
<td>2 P</td>
<td>Psychogenic parkinsonism</td>
<td>$^{123}$I β-CIT SPECT</td>
<td>Resting</td>
<td>Normal DTA density</td>
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<tr>
<td>Booij et al., 2001 (19)</td>
<td>4 P</td>
<td>Psychogenic parkinsonism</td>
<td>$^{123}$I FP-CIT SPECT</td>
<td>Resting</td>
<td>Normal DTA density</td>
</tr>
<tr>
<td>O’Sullivan et al., 1999 (20)</td>
<td>3 P</td>
<td>Psychogenic parkinsonism (suspected initially)</td>
<td>$^{123}$I FP-CIT SPECT</td>
<td>Resting</td>
<td>Reduced $^{123}$I FP-CIT SPECT uptake in putamen and caudate</td>
</tr>
</tbody>
</table>

Abbreviations: P=patients; C= controls; SPECT=single photon emission computed tomography; PET=positron emission tomography; DLPFC=dorsolateral prefrontal cortex; DTA=dopamine transporter.

Unilateral loss of motor function

Studies have found altered patterns of regional cerebral blood flow (rCBF) in response to sensory stimulation and during attempts to move the affected area, and differences have been found during the acute presentation of symptoms when compared to recovery. In 1995, in what was one of the first functional neuroimaging studies performed in patients with functional symptoms, Tiikhonen et al. (13) reported a single patient with left side hysterical paralysis and comorbid major depressive disorder who was examined using single photon emission computed tomography (SPECT) while undergoing electrical stimulation of the median nerve. Median nerve stimulation is expected to increase contralateral parietal lobe rCBF, and the authors indeed detected increased activation of the right frontal area and decreased activation of the right parietal area. These results were interpreted as an inhibitory effect exerted by the frontal cortex on the somatosensory cortex during the paralysis episode.
Altered rCBF patterns have also been found during attempted movement of the affected limb (as compared to movement of the normal limb) in patients with chronic functional symptoms. A positron emission tomography (PET) study, conducted in 1997 (14) and also performed in a single patient with a long-lasting history of hysterical left paralysis, reported no activation of the primary motor cortex when the patient prepared and attempted to move the affected leg (as was expected, given the lack of movement), together with an increased activity in the right orbitofrontal and cingulate cortex. Given that both these areas seem to be important for suppression of inappropriate motor responses, the activity in them was interpreted as the source of active inhibition exerted on the primary motor cortex.

In another study, in 2000, Spence et al. (15) used PET to elucidate the distinction between hysterical and feigned paralysis. They studied two patients with hysterical weakness of the left limbs and two healthy individuals who simulated paralysis by feigning difficulty moving a limb (feigners). The patients exhibited reduced activation of the left frontal regions, specifically in the dorsolateral prefrontal cortex (DLPFC). This pattern of activation differentiated the hysterical patients from the feigners, who exhibited reduced activation of the right anterior prefrontal cortex.

Metabolic deficits associated with functional symptoms may not be limited to the cerebral cortex. Using 99mTc-ECD SPECT, Vuilleumier and colleagues (16) detected a consistent decrease of rCBF in the thalamus and basal ganglia in the side contralateral to the perceived deficit in seven patients with unilateral hysterical sensorimotor loss. Importantly, the decreased activation in the contralateral basal ganglia and thalamus resolved after clinical recovery.

**Psychogenic parkinsonism**

In a 1995 PET study performed in four patients with functional symptoms of psychogenic parkinsonism, Lang and coworkers (17) reported decreased fluorodopa uptake in the left putamen in one patient who also presented symptoms of depression, suggesting that this condition may coexist with organic parkinsonism. The PET scans were reported as normal in the other three patients.

Factor and colleagues, in 1995 (18), reported the results of β-CIT SPECT imaging in two patients with a diagnosis of psychogenic parkinsonism. In both patients, the SPECT scans were reported as normal, with dopamine transporter (DAT) density in normal range for their age.

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**Figure 1** - A) PET study showing increased activity in the right orbitofrontal and cingulate cortex associated with attempted movement of the left (affected) leg in a patient with hysterical paralysis (14). B) fMRI study showing reduced activation of left frontal regions (DLPFC, darker areas on the right) in patients with hysterical motor symptoms relative to controls (15). C) SPECT study showing decreased activation in the thalamus and basal ganglia in the side contralateral to the perceived deficit in patients with hysterical sensorimotor loss (16).
Similar results were reported in another SPECT study conducted in 2001 by Booij and colleagues (19), who studied a group of patients with inconclusive forms of parkinsonism. Among 19 cases, four patients were diagnosed as having psychogenic parkinsonism and their \(^{123}\text{I}\)FP-CIT SPECT scans were also considered normal. Finally, in a 1999 study by O’Sullivan and coworkers (20), it was seen that SPECT imaging could effectively exclude psychogenic parkinsonism. These authors reported the results of \(^{123}\text{I}\)FP-CIT SPECT imaging of three patients initially suspected of having psychogenic parkinsonism. \(^{123}\text{I}\)FP-CIT SPECT uptake in the putamen and to a lesser extent in the caudate was reduced significantly in all the patients. The results of this study demonstrated the importance of SPECT imaging in cases where there is diagnostic uncertainty.

**Discussion**

Neuroimaging studies of functional symptoms are, to date, few in number and consist only of case reports or small series of cases. All the studies described in this review are therefore limited by small population size, and by heterogeneous patient populations, duration of deficits, presence of comorbid disorders, and use of functional imaging modalities, making their results difficult to interpret. Overall, they suggest variable alterations in the activity of specific cortical and subcortical areas, particularly the prefrontal and parietal cortices, anterior cingulate cortex, thalamus, and basal ganglia, which may underlie these disorders with functional symptoms. In the case of symptoms characterized by loss of motor function, the results of the studies reviewed revealed selective decreases in the activity of frontal and subcortical circuits involved in motor control and increased activation in limbic regions, such as the cingulate or orbitofrontal cortex during conversion symptoms affecting different sensory or motor modalities. These findings may indicate a malfunction between the regions of the brain controlling intention and execution (21). On the basis of models from cognitive neuroscience of action, the completion of a successful motor action depends upon three stages — the formulation of an intention to move, motor command preparation, and the execution of the intended movement (22). The imaging studies described above suggest two mechanisms that may explain functional symptoms of loss of motor function. In the first one, the intention to move would be intact and the failure would lie in the preparation to move (14), while in the second, by contrast, the failure would concern areas that are thought to be responsible for volition and for the experiencing of movements as volitional (15,16).

For example, the orbitofrontal cortex and anterior cingulate cortex may have an inhibitory effect on prefrontal regions (DLPFC) involved in willed action (14). The basal ganglia and thalamus, on the other hand, and their reciprocal connections with the amygdala and orbitofrontal cortex, participate in fronto-subcortical loops that mediate motor intention and sensory awareness (23). Taken together, these findings generally do not support previous suggestions that “disconnection of intention from awareness may take place at the level of attention, producing a psychic blindness for sensation and movement analogous to anosognosia” (24). Instead, they seem to suggest a modulation of sensorimotor representations by stress-related or primary affective factors, perhaps involving primitive reflexive mechanisms of protection and alertness that are partly independent of conscious control, and mediated by dynamic modulatory interactions between limbic and sensorimotor networks (25).

In the case of symptoms characterized by abnormal motor function, such as psychogenic parkinsonism, the information available is more limited. Parkinson’s syndrome is frequently associated with prominent degeneration of the nigrostriatal pathway affecting motor circuits interconnecting the cortex, the basal ganglia, the cerebellum and the brainstem (26). Results from this review are in agreement with current concepts suggesting that psychogenic parkinsonism occurs without degeneration of the nigrostriatal pathway or other dopaminergic neuronal system (27). The few studies determining the integrity of the nigrostriatal pathway, using PET or SPECT techniques, suggest that DAT imaging is normal in psychogenic parkinsonism and underline its importance in confirming organic parkinsonism in cases where there is diagnostic uncertainty. The only abnormality reported was a decreased fluorodopa uptake in left putamen in one patient with symptoms of depression. This observation supports the idea that a dysfunction of the basal ganglia and its projections to the frontal cortex may presumably be involved in some cases of psychogenic parkinsonism. Given the role of the basal ganglia, thalamus and their connections with frontal areas in affective disorders (28), and the clinical observation that motor symptoms in psychogenic motor disorders respond to antidepressants irrespective of an underlying depression or anxiety (29), there arises the suggestion of an underlying and common neurobiological aetiology. The results of these studies support the hypothesis that conversion disorder is the result of dynamic reorganization of neural circuits which link volition, movement, and perception, and that disruption in these neural circuits may have a role in the pathogenesis of functional symptoms.

**Concluding remarks**

In summary, functional symptoms are common, chronic and disabling, and imaging findings suggest that volition may or may not be impaired, whereas areas such as the prefrontal and parietal cortices, anterior cingulate cortex, thalamus, and basal ganglia have been implicated. Although the findings of the studies reviewed are more intriguing than conclusive, and the neurobiological substrate of functional symptoms remains elusive, recent research has started to uncover some aspects of the pathophysiology of functional symptoms, reinforcing the view of functional symptoms as neurophysiological disturbances with functional and behavioural manifestations. Future studies, assessing patients at different phases of their illness and using newer techniques, such as functional MRI, are needed to extend current findings and explore other modalities of functional symptoms.
References


