Forgotten Frontal Lobe Syndrome or "Executive Dysfunction Syndrome"

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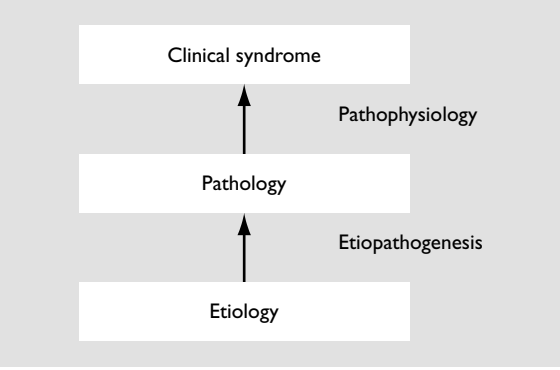
A syndrome is a constellation of clinical phenomena that tend to aggregate in the same patient[1] (Figure 1). A syndrome is the manifestation of a *disease* when it can be linked to a specific pathology, an abnormal structure, or a function of some bodily part, i.e., the brain in the case of psychiatric inquiry. The relationship between the pathology and the syndrome is the pathophysiology of the disturbance. The disease entity may be considered *validated* when the pathology can be linked to a cause, or etiology, which explains how the pathology came about, through an understanding of its pathogenesis. To illustrate this process further, the case of a patient with Huntington's disease and a complicated clinical course is presented.

Huntington's disease is a hereditary neurodegenerative disorder caused by an expanded CAG triplet repeat sequence in the huntingtin gene on chromosome 4. Huntington's disease is characterized by movement disorder, dementia, and psychiatric disturbances. The movement disorder includes chorea, usually an early symptom, and voluntary motor impairment, which generally becomes evident later and progresses for the duration of the illness, ending in rigidity and immobility.[2–4] Of all the psychiatric aspects of Huntington's disease, the executive dysfunction is perhaps the most difficult to define, characterize, and treat; yet it may be the most common psychiatric manifestation.[5]

FIGURE 1. The Disease Perspective



Case Report

Mr. A, a 52-year-old man with Huntington's disease, was admitted to our hospital's inpatient neuropsychiatry service for increasingly undirected motor activity, agitation, and disinhibited behavior.

History of the Present Illness

Mr. A's present illness began with a genetically confirmed diagnosis of Huntington's disease 3 years earlier. There may have been cognitive and personality changes for 1–2 years before that, with more rigid thinking and trouble solving problems. Around 6 months before admission, he developed "mood symptoms" and was given paroxetine, up to 20 mg/day, with initial improvement. A few months later, he became more agitated and was pacing, feeling energized, sleeping less. Because hypomania was considered the cause, the paroxetine was stopped, and he was administered risperidone, 0.5 mg b.i.d. He developed increased motor activity, which could not be redirected. His illness did not clinically resemble akathisia. He once hit his wife, something he had never done before and exhibited agitation, irritability, and combativeness. There was only oc-

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casionally apathy, and there was no confusion or clear cognitive change. The results of a neurological examination were normal, other than chorea.

Four weeks before admission, Mr. A woke up often at night, thrashed in his bed, had worsened sleep, was not showering, had worsened activities of daily living, looked sad, and was saying to his wife things like, "You and the girls would be better off without me." Two weeks before admission, he became more agitated, began hallucinating (seeing dogs or cats), became disoriented, and at various times reported that he was on a plane or a ship. Later that week, he went to work on a day when he was not scheduled to be there. He seemed unable to accept that he was there on the wrong day and would not go home. He grasped his manager's arm and would not let go. Eventually police were called to the scene. An altercation ensued, during which he struggled with the police, required multiple officers to get him to the ground, and was handcuffed. He was transported to a local hospital and admitted for 5 days. The risperidone dose was increased to 2 mg t.i.d. He was then transferred to our hospital.

Patient History

Mr. A had no psychiatric history. The medical history, other than for Huntington's disease, was negative. His mother died at age 55 of Huntington's disease, as did her sister. In addition, one brother has Huntington's disease, and two brothers were unaffected. He had graduated from high school and had attended college for 2 years. He had worked in law enforcement but had to stop working because of Huntington's disease. During the year before admission, he worked in the fast-food industry as a server. He lived with his wife and two children. He did not smoke, drink alcohol, or have other history of drug use.

Admission Examination

Mr. A was a tall, thin man who had psychomotor agitation and had trouble cooperating during an interview. His speech was rapid, and he would often interrupt the examiner. There was mildly accelerated speech but no flight of ideas. He would return to the same topic over and over, initially wanting to go home, and then asking if his family was "all right." His mood was reported to be normal, but he was labile and irritable. He reported no sadness or euphoria. He was anxious at times, mostly psychically, but was without somatic anxiety. There were no obsessions, compulsions, or phobias, but he repeatedly ruminated on the same topics. He did not report feeling energized or having excess energy. He had normal self-attitude, self-esteem, and level of confidence. He reported no suicidal or homicidal ideas. There were no delusions or hallucinations. Upon cognitive assessment, he was alert, with a normal level of consciousness. He scored 22 points on the Mini-Mental State Examination (MMSE), missing two questions on orientation to place, four on serial sevens, and two on recall. He could not learn the rules to the mental alternation test (the verbal test of Trail Making B), indicating very poor executive control.

Laboratory Studies and Hospital Course

At admission, the results of a CBC, a comprehensive metabolic screen, a thyroid-stimulating hormone test, liver tests, and a measurement of sedimentation rate were all normal. A computed tomography scan of his brain, completed later in the hospital stay because of initial uncooperativeness, was normal.

Mr. A's hospital stay was characterized by multiple episodes of disruptive behaviors. He had long periods of calm, during which he was isolative, withdrawn, and inactive, and he appeared apathetic. These were interspersed by a sudden change in his demeanor, when he would get an idea that he had to do something, like go home. He would approach staff and insist that they help him. If a response was not immediate, which was usually the case, he continued to be insistent, which rapidly escalated until he became combative. At other times, he paced incessantly, intruded into the rooms of other patients, or physically latched on to patients and staff and would not let go. During these times, his behavior seemed to be internally driven, as if he was stuck on having to do something and unable to shift his interest or attention to other activities. His drive to fulfill whatever his purpose was could not be shaken, and if others around him were not helpful, such as when they tried to stop him or tried to shift his attention, he would become violent toward them. The staff consensus was that these behaviors were neither reflective of delirium nor driven by delusions or hallucinations.

As Mr. A's hospitalization progressed, he would get stuck on ideas and behavior increasingly more often, and these escalations became more violent and aggressive. During efforts to redirect his attention, he injured several staff members and had to be restrained physically for hours at a time, during which he continued to verbalize the persistence of the ideas of what he "had to" do. Initial efforts at treatment were higher doses of neuroleptics, including

risperidone (up to 3 mg/day), olanzapine (up to 10 mg/day), quetiapine (up to 150 mg/day), haloperidol (up to 7.5 mg/day), and fluphenazine (up to 2 mg/day), in addition to lorazepam (up to 6 mg/day) and divalproex (up to 1500 mg/day), but he received no benefit.

Mr. A then developed a low-grade fever and confusion. During this time, his level of alertness became impaired and would fluctuate during the course of the day, becoming worse in the evening. He was often fearful and at times would cry or laugh without explanation. He was disoriented, and his speech became nonsensical. He also appeared to be seeing visions of people in his room late in the day. The MMSE score dropped to 9 points; he lost 8 points on orientation, 5 on serial sevens, 3 on recall, and 5 on language/praxis. A diagnosis of multifactorial delirium was made, but a laboratory workup, including a serum creatine phosphokinase level, a magnetic resonance imaging scan of his brain, and a lumbar puncture was unremarkable. It was concluded that the delirium was due to medications. All medications were stopped, and he was managed with restraint, supportive care, and limited use of intramuscular droperidol (used as needed when severe agitation was present; 1–1.5 mg/dose) until his delirium resolved after about 2 weeks. However, the "sticky" and perseverative behaviors that he had exhibited on initial admission returned and began to escalate steadily.

Mr. A's behaviors were then reformulated as manifestations of a "frontal lobe syndrome," and it was decided to try dopamine augmentation since all other approaches to manage his behaviors had failed. Amantadine, 50 mg b.i.d., was started and increased to 100 mg b.i.d. within a week. Within a few days, there was a rapid, almost total resolution of the problem behaviors. Mr. A was no longer "getting stuck" on ideas or behaving in an internally driven, "sticky," and intrusive fashion. He was cooperative and pleasant. He continued being apathetic and withdrawn most of the time, with little spontaneous interest in activities or people around him. However, he could be engaged in activities, including basic self-care, if they were offered to him as part of his daily structure. Given that his apathy might have reflected a mild degree of depression, fluvoxamine was added to his drug regimen and increased to 50 mg b.i.d., resulting in some increase in his level of interest. There were no further problematic behaviors over the ensuing week, and his family stated that he had returned to the behavioral baseline he had exhibited several months ago. He was able to go home on a pass, and that visit went very well. He was then discharged, with a score on the MMSE of 23 of 30. He was noted as doing well at his outpatient follow-up visits 6 and 12 months later, despite mild progression of the motor symptoms of Huntington's disease. He was able to return to his former job in the fast-food industry.

Discussion

We begin by discussing the elements in Figure 1, as applied to this case. What was the patient's syndrome? He exhibited a series of disinhibited, overactive, repetitive, and perseverative behaviors. These behaviors were internally driven and appeared to consist of a very intense "stickiness" in both his thoughts and actions—an example of stimulus-bound behavior. Once stuck on having to do something, his whole demeanor and behavior were consumed by following through in his actions to the point at which he would become violent and fight restraint for hours while attempting to execute what he felt he needed to do. During these times, he could not be distracted or shift his attention away, despite intensive efforts by an experienced staff with the help of a wide range of sedative medications. Of interest is that these behaviors were superimposed against a backdrop of notable apathy and a loss of interest in day-to-day activities. In addition, he exhibited a marked lability in mood and irritability. He exhibited a cognitive disturbance, with features of subcortical dementia, including mental rigidity (dysexecutive), slowness of thinking (delay), and forgetfulness (dysmnesia).[6]

As we pulled his clinical picture together, we saw that this patient exhibited a constellation of symptoms (disinhibition, stimulus-bound behavior, disorganization, social inappropriateness, overactivity, apathy, perseveration, and subcortical dementia) that are indicative of widespread dysfunction of *executive control* of both cognition and behavior. The syndrome in some ways resembled a mood disturbance mostly due to lability and disinhibition, but it was not fully consistent with a major depressive, mixed mood, or manic episode. Furthermore, anxiety was not a prominent feature of the presentation, and there were no clear obsessions or compulsions. Even though the patient was driven, at times, to repeat behaviors and actions, his behavior was not egodystonic, and he did not perceive it as trivial or attempt to resist the impulses. Other than when he was delirious, at no point was there evidence of delusions or hallucinations.

The pathology was presumably that of Huntington's disease, with degeneration of the caudate and other basal

ganglia nuclei. The pathophysiology is not well understood and will be discussed later. The etiology presumably is a genetic abnormality, i.e., expanded CAG triplet repeats in the huntingtin gene on chromosome 4. The resulting polyglutamine expansion in the huntingtin protein is thought to be toxic to neurons, especially the medium spiny neurons of the caudate and putamen.[7]

From the clinical point of view, this patient's behaviors caused problems for him, his family, and other persons in his care environment. The management of his condition was challenging. He worsened when he was treated with an atypical neuroleptic (a dopamine receptor blocker), but he appeared to improve substantially when he was treated with amantadine (a dopamine augmenter) and possibly after the addition of a selective serotonin reuptake inhibitor (SSRI).

A Common Encounter

This case illustrates a set of behaviors commonly encountered in neuropsychiatric patients, namely, disinhibition, stimulus-bound behavior, disorganization, social inappropriateness, overactivity, apathy, perseveration, and subcortical dementia. The clinical picture does not fit that of a classical psychiatric syndrome, such as mania, mood disorder, anxiety disorder, or psychosis. Here, the symptoms occurred in a patient with Huntington's disease, but similar presentations are seen at times in patients with traumatic brain injury, Parkinson's disease, stroke, AIDS, Alzheimer's disease, and frontotemporal dementia. Although patients with these behaviors present issues regarding problematic care, they have inconsistent or uneven responses to treatments considered standard in psychiatry, such as antipsychotic medication or behavioral therapy. In contrast, they sometimes respond to less frequently used agents, such as amantadine, SSRIs, and cholinesterase inhibitors. Often this presentation is referred to as a "frontal lobe syndrome." While this term has not been discussed much in textbooks or articles in recent years, it continues to be used in the clinical setting on a regular basis even though there is no widely accepted definition.

History: What Is Frontal Lobe Syndrome?

The earliest described case of "frontal lobe syndrome" dates back to 1835.[8] However, the best-known early case is that of Phineas Gage,[9] a man who suffered a frontal lobe injury for which the pathology and etiology were known. On Sept. 13, 1848, in New Hampshire, Phineas Gage suffered an accident while on the job as a railroad construction foreman. A tamping iron blasted through his left cheek, through his left frontal lobe, and his skull and landed far behind him.[10] He was knocked off his feet and may have briefly been unconscious but seems to have recovered rather quickly. He was unable to return to work as a foreman. Accounts of the time referred to him as a "changed person" who drifted down socially and could only briefly sustain work as a stable hand until his death in 1860.

While the origin of the term "frontal lobe syndrome" is unclear, the reader is referred to Mayer for a brief historical review.[11] Luria[12] popularized the term in 1969, derived from studies of patients who suffered lesions in the frontal lobes. Blumer and Benson[13] used the term "frontal lobe personality" when referring to much the same constellation of signs and symptoms. The literature contains multiple accounts of the clinical pictures of frontal lobe damage. Some use the term to describe specific neurological signs, such as frontal release or alien hand.[14] Others refer to cognitive features, such as difficulty in planning and sequencing.[12] Still others refer to the development of reduced initiative,[15] personality change,[13] disinhibition of behavior,[16,17] or the Greek term "moria," meaning acting like a baby.[18] There has been little consistency in the use of the term "frontal lobe syndrome."

One form of progressive neurodegeneration has been called "frontotemporal dementia."[19] The clinical description refers to progressive personality change and a breakdown in social contact. Some patients are said to be restless, distractible, or disinhibited, while others are apathetic, slowed, and amotivated. Many exhibit hypochondriasis, stereotyped behaviors, concrete thinking, echolalia, perseveration, and memory disturbances. It is of note that while most exhibit degeneration of the frontal lobes, many develop degeneration of the temporal lobes and/or subcortical structures.

The discussion so far has revolved around clinical presentations in patients with pathological lesions located in the frontal lobes.[12–14,19–24] However, some cases of so-called frontal lobe syndrome occur in patients who *do not* have obvious damage to the frontal lobes. Some examples include episodic dyscontrol after bilateral caudate nucleus lesions,[25] disinhibited behaviors after bilateral thalamic infarcts,[26] apathy and abulia with globus pallidus lesions,[27–28] or apathy and disinhibition in multiple sclerosis.[29,30] Similar cases have been described with CNS Sjogren's syndrome,[31] white matter subcortical stroke,[32] adrenal leukodystrophy,[33] Parkinson's disease,[34] Fahr's disease,[35] and, of course, Huntington's disease. Thus, fron-

tal lobe syndromes can occur in patients who have brain damage in subcortical structures, in both gray and white matter.

Some of these symptoms have been reported in more classical psychiatric disturbances. Some of these are major depression (apathy and mood lability), especially in old age,[36] which has been associated with disturbances in the anterior cingulum; schizophrenia[37] (apathy and executive disturbance), which has been associated with disruptions in the dorsolateral prefrontal cortex; attention deficit hyperactivity disorder[38] and obsessive-compulsive disorder[39] (repetitive, intrusive, and irresistible behaviors), which have been associated with overactivity in orbitofrontal lobe areas.

Putting the Picture Together: Functional Anatomy

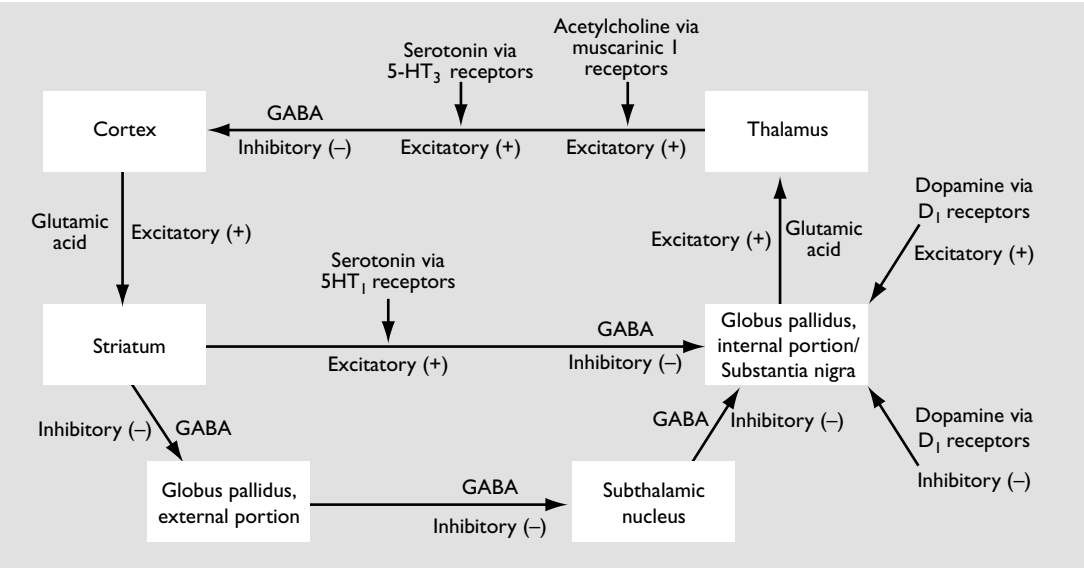
Understanding the functional anatomy of the frontal lobes and their linkages with key subcortical structures is critical to putting together this picture. The discussion here will summarize the work of others and put it into clinical context. For a more extensive discussion, refer to the work of Cummings and Houk and their collaborators.[40–42]

There is wide acceptance that there are five brain circuits originating in the frontal lobes and linking them as *functional units* to subcortical structures.[40–42] Two of these have primarily motor functions: one originates in the supplemental motor accessory area and is involved in the planning of movement; the other originates in the frontal eye fields and is involved in eye motion. The latter two circuits were originally described in association with Parkinson's disease to explain the motor dysfunction of that condition.[40] They appear to have little to do with the behaviors referred to as frontal lobe syndrome. Three other circuits originating in the frontal lobes appear to be the brain circuits whose dysfunction may underlie the syndromes in question. These include the dorsolateral prefrontal circuit, the lateral orbitofrontal circuit, and the anterior cingulum circuit (Figure 2).

These three circuits have several common features. First, they process and integrate information from disparate brain regions. Second, each one is anatomically discrete, even though they share the same brain structures: cortical origin in the frontal lobe, the striatum, the globus pallidus, the substantia nigra, and the thalamus. Third, their internal neurochemistry is similar (Figure 2). Fourth, they have progressively greater spatial constraint downward from cortex to subcortex. Fifth, they are functionally closed and parallel but communicate with other brain areas at each of the structural levels already mentioned, thus receiving external input at several points. Each circuit serves as the final step before the expression of both simple and complex behaviors.

The common internal neurochemical organization of each loop is illustrated in Figure 2.[40–42] Known external

FIGURE 2. Anatomical Organization, Internal Neurochemistry, and Known External Neurochemical Modulators of the Frontosubcortical Circuit



neurochemical modulators include dopamine, serotonin, and acetylcholine (Figure 2). The external modulators may explain the success of some of the medications used to treat these disturbances.

Functionally, these circuits serve some aspect of executive function, the set of "cognitive skills responsible for the planning, initiation, sequencing, and monitoring of complex goal-directed behavior."[43] Critically, executive function is associated with *both* the initiation and the modulation of behavior in that both lack of initiation (motivation) and dyscontrol of behavior might be concurrent features of executive dyscontrol. Executive function is also associated with working memory,[44] memory retrieval,[45] and meta-cognitive functions, such as the "theory of mind."[46] Given the anatomic segregation of function in their frontal lobe origins,[47] each circuit may serve different aspects of executive control. For example, the anterior cingulum circuit appears to be central to the motivation of behavior.[36–38] The dorsolateral prefrontal circuit serves organizational aspects of executive functioning by integrating information, focusing attention, and deciding on response.[40–42] The lateral orbitofrontal circuit is critical to the integration of limbic and emotional information into contextually appropriate behavioral responses.[40–42]

What Does This Mean for Psychiatry? A Hypothesis

The term "frontal lobe syndrome" is no longer useful because it implies damage to a specific region of the brain. The clinical presentations involved reflect dysfunction in several parts of the brain, some of which are in the frontal lobes and some of which are not. It is best not to use an anatomical term to describe a clinical syndrome. The common theme is not anatomy but behaviors that reflect dysfunction of the executive system.

We propose that these disturbances be referred to as "executive dysfunction syndrome." This term identifies a clinical syndrome—akin to "psychosis," "manic episode," or "affective/mood disturbance"—and avoids the use of a pseudoanatomical term ("frontal"). It also distinguishes the disturbance from a personality disorder. The DSM-IV diagnosis that best fits the disturbance is "personality change due to a general medical condition." However, the disturbance is no more a personality disturbance than would be a mood or psychotic syndrome. Furthermore, this syndrome is best not construed as a personality change since personality disorders are the extremes of dimensions.[1] In contrast, it is best construed as a syndrome caused by brain disease, and its name should emphasize the common theme, namely, executive dysfunction. Executive dysfunction has a series of *behavioral* manifestations in addition to the well-described *cognitive* manifestations. The behavioral aspects are the least well characterized and for which widely accepted measurement methods do not appear to exist.

Several proposals have been made to subgroup or subtype this syndrome based on the apparently distinct functions of each circuit.[23,40–42] However, in our experience, many of these features co-occur in the same patient. For example, the case study illustrates the co-occurrence of apathy with disinhibition and perseveration. There may be purer subtypes associated with damage to the frontal cortex and less pure subtypes associated with damage to subcortical structures. Since there is greater spatial constraint in the basal ganglia, a single lesion might more easily affect several circuits at the same time. In contrast, a single lesion in the frontal cortex might only affect a single circuit. Despite this, we do not believe that there is sufficient evidence to define three syndromes, and the existence of subtypes is an empirical question that requires further study.

The clinical features of executive dysfunction syndrome are listed in Appendix 1 and organized along three core areas.[23] These are presented as a starting point. In the future, it will be important to validate the syndrome as a whole, as well as possible subtypes, by standard methods that examine the co-occurrence of psychopathologic phenomena (cluster or factor analysis), predictive ability (course, response-to-treatment, or genetic studies), and clinicopathological correlation.

What is the pathogenesis associated with the executive dysfunction syndrome? It is hypothesized that damage to one or more of the three frontal-subcortical circuits produces characteristics of the syndrome. The specific clinical features depend on the location of dysfunction and whether one or more circuits are affected. Trauma or degeneration might result in underactivity within a circuit, while loss of external inhibitory input might lead to overactivity. The pathology might be located in the cortex, the subcortex, or both. Different diseases (Huntington's disease, trauma, or stroke) might lead to different clinical presentations, depending on the exact location of injury. Dysfunction brought on after injury might have different clinical characteristics than dysfunction due to degeneration because the brain's capability to compensate would differ. As a result, the longitudinal course might be different.

Treatment

Little is known about the treatment of executive dysfunction syndrome. While the relevant circuits involve the same neurotransmitter loops, they each may have different receptor subtypes and second messengers. A better understanding of the neurochemistry of each circuit and its interaction with outside brain areas will allow pharmacological manipulation to alleviate the disturbances.

In addition to pharmacological approaches to up- or down-regulation of circuit activity, surgical approaches in key areas might be used to affect circuit activity. The latter approaches are in use for the management of some of the motor symptoms of Parkinson's disease by manipulating the parallel motor circuits. External palidotomy might increase circuit activity, while cingulotomy might reduce circuit activity (see Figure 2). The latter has enjoyed some success for the management of obsessive-compulsive symptoms, likely because of its effects in the anterior cingulum circuit.

There may be specific pharmacotherapy that should be *avoided* in some cases. For example, the patient in the case study became worse while taking neuroleptics (dopamine receptor antagonists) but improved when treated with amantadine, a dopamine augmenter. The use of dopamine augmentation merits further discussion. Dopamine neurotransmission may stimulate the functioning of one or more of the frontosubcortical loops (Figure 2), which might improve clinical signs and symptoms. Imamura and collaborators[48] treated eight patients with dementia who exhibited perseveration and "stuck-in" behaviors by using bromocriptine, up to 10 mg/day. Several exhibited marked reduction or remission of the behavior problem. Kraus and Maki[49] treated seven patients with moderate to severe traumatic brain injury and executive dysfunction by using amantadine, 300 to 400 mg/day, leading to improvements on select neuropsychological test measures. In this issue, we report a chart review of 30 patients with executive dysfunction and dementia, about half of whom benefited from treatment with amantadine.[50] Other means of dopamine augmentation that merit mention are treatment with buproprion and psychostimulants, both of which appear to inhibit the synaptic reuptake of dopamine.

Findings on the use of cholinesterase inhibitors in treating neuropsychiatric disturbances in patients with dementia suggest a role for cholinergic modulation of executive dysfunction, especially apathy.[51] However, these findings were secondary analyses and did not randomly assign patients with executive dysfunction syndrome. Similarly, a case study of two patients with traumatic brain injury who were treated with donepezil found improvement in executive dysfunction, especially apathy.[52]

Case studies also suggest that patients with executive dysfunction syndrome may improve when treated with SSRIs,[22,53] anticonvulsants,[54] psychostimulants,[5] or specific behavior-modification interventions.[55] All of these outcomes make sense in light of the neurochemistry already discussed.

In day-to-day practice, the following treatment recommendations can be summarized. When patients with a brain disease—broadly speaking—present with disturbances similar to the ones described here (Appendix 1), the first step is for the clinician to carefully describe the disturbance. If a classical psychiatric syndrome, such as major depression, mania, or a schizophrenia-like psychosis, is evident, then treatment for the syndrome should be instituted. The clinician should also be mindful that traditional therapies, neuroleptics in particular, might unexpectedly lead to a worsening of the patient's condition, as illustrated in the case study. If this occurs, the presentation should be reassessed[6] to determine if an incorrect syndromic diagnosis was made and a different syndrome, e.g., executive dysfunction syndrome, was present. If the disturbance is not a classical psychiatric syndrome, consideration should be given as to whether it fits the pattern of an executive dysfunction syndrome, either a mixed or a pure subtype. If that is the case, then the clinician might consider the use of less traditional therapies, such as a dopamine augmenter, a cholinesterase inhibitor, an SSRI, a psychostimulant, or a combination of these.

Conclusions

Executive dysfunction syndrome is commonly encountered in psychosomatic medicine. It likely reflects dysfunction anywhere along the multiple circuits connecting the frontal lobes with subcortical matter. It is clear that these circuits are important functional units that underlie many disorders in psychiatry. Therefore, it is important that specific clinical criteria to define the syndrome be established, both for clinical and research purposes. Data are needed to determine if executive dysfunction syndrome is best construed as a single syndrome or three syndromes. Scales with good reliability are needed to quantify different aspects of this syndrome, especially the behavioral aspects. Such measures might be used to quantify severity and to assess response in targeted treatments. The pathogenetic

APPENDIX 1. Key Features of Executive Dysfunction Syndrome

Disorganization
- Impaired memory search
- Impaired planning and organization
- Impaired set shifting
- Stimulus-bound behaviors
- Verbal manual dissociation

Disinhibition
- Tactlessness
- Undue familiarity
- Nonconformity with social norms
- Overactivity
- Repetitive behaviors
- Perseveration
- Mood lability
- Environmental dependency

Apathy
- Impaired motivation
- Underactivity
- Disinterest
- Limited spontaneous speech
- Slowness

relationship of executive dysfunction syndrome with the frontal-subcortical loops will require delineation, as this ultimately will lead to more targeted therapy. Finally, little can be said at present about treatment. There is some suggestion that executive dysfunction syndrome responds poorly in some cases to traditional psychiatric therapies, which at times lead to a worsening of the patient's condition. Several alternative therapies might be considered in this context, including dopamine augmenters, SSRIs, and cholinesterase inhibitors.

Presented in part at a psychiatry grand rounds at Johns Hopkins Hospital, Baltimore, April 23, 2001, and May 3, 2003.

The authors thank Patrick Carroll, M.D., for the case preparation and David Blass, M.D., for his critical review of the manuscript.

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