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Disorders of Diminished Motivation

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Disorders of diminished motivation occur frequently in individuals with traumatic brain injury. Motivation is an ever-present, essential determinant of behavior and adaptation. The major syndromes of diminished motivation are apathy, abulia, and akinetic mutism. Depending on their etiology, disorders of diminished motivation may be a primary clinical disturbance, a symptom of another disorder, or a coexisting second disorder. This article presents a biopsychosocial approach to the assessment and management of motivational impairments in patients with traumatic brain injury. The recognition and differential diagnosis of disorders of diminished motivation, as well as the mechanism and clinical pathogenesis, are discussed. **Key words:** *abulia, akinetic mutism, anterior cingulum, apathy, cholinesterase inhibitor, disorders of diminished motivation, dopamine agonist, methylphenidate, traumatic brain injury, ventral pallidum*

MOTIVATION is essential to adaptive functioning and quality of life. This is as true for individuals with traumatic brain injury (TBI) as it is for those with stroke, dementia, or any other neuropsychiatric illness. Clinicians understand intuitively the importance of motivation. Without motivation, individuals with TBI will fail to keep appointments, stay on their medications, devote themselves to friends and family, or return to their jobs. Motivational loss handicaps physical rehabilitation and coping skills,[1] and it is a major source of burden for families of individuals with TBI.[2]

Motivation is an ever-present, essential determinant of behavior and adaptation. Like attention, emotion, and other state variables, motivation is not a single function of the brain. Psychologically and biologically, motivation is a complex of capacities; the neural systems subserving it are themselves delimited and distributed, integrated and interdependent.

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This article presents an approach to the assessment and management of motivational impairments in patients with TBI. It introduces definitions of motivation and of the 3 major disorders of diminished motivation (DDM): akinetic mutism, abulia, and apathy. Diagnosis of DDM is further clarified in terms of behavior, thought content, and affective symptoms. Assessment and management of DDM are then described on the basis of a biopsychosocial approach to the causes of motivational loss.[3] Investigators from the fields of psychiatry,[4] neuropsychology,[5] rehabilitative medicine,[6] and occupational therapy[7] agree that DDM are a major source of disability for patients with TBI. Diminished motivation in patients with TBI contributes to loss of social autonomy,[6] financial and vocational loss, and family burden.[2] Given the frequency of diminished motivation in patients with TBI—estimates vary from 5% to 67%[4,8,9]—properly diagnosing and treating DDM has enormous potential to alleviate the resultant personal and social burden.

DISORDERS OF DIMINISHED MOTIVATION: RECOGNITION

Motivation refers to the characteristics and determinants of goal-directed behavior. Theories of motivation are intended to account

for the "direction, vigor, and persistence of an individual's actions,"[10] that is, for how behavior "gets started, is energized, is sustained, is directed, is stopped, and what kind of subjective reaction is present in the organism when all this is going on."[11]

Disorders of diminished motivation include akinetic mutism, abulia, and apathy. Recent literature[12-15] places DDM on a continuum of motivational loss, with apathy at the minor pole of severity and akinetic mutism at the major pole of severity. The 3 result from dysfunction of the neural machinery that mediates motivation.

Akinetic mutism is essentially characterized by a total absence of spontaneous behavior and speech occurring in the presence of preserved visual tracking.[12] Traumatic brain injury may cause akinetic mutism, although few cases have been reported in the TBI literature.[16]

Abulia, originally denoting a disorder of will (*bul* in Latin),[17,13,15] characterizes patients with symptoms less severe than but qualitatively identical to akinetic mutism: poverty of behavior and speech output, lack of initiative, loss of emotional responses, psychomotor slowing, and prolonged speech latency. Abulia evolves into akinetic mutism when it worsens and into apathy when it improves.

Apathy is a state of diminished motivation in the presence of normal consciousness, attention, cognitive capacity, and mood. Patients with apathy are generally able to initiate and sustain behavior, describe their plans, goals, and interests, and react emotionally to significant events and experiences. However, these features are less extensive, less common, less intense, and shorter in duration than they are in individuals who are not apathetic. In other words, apathy differs from normality quantitatively rather than qualitatively.

To further clarify the diagnosis of DDM, it is helpful to relate them to the changes in overt behavior, thought content, and emotion that contribute to the clinical recognition of diminished motivation. Motivation is the psychological domain concerned with *goal-directed* behavior. Thus, the recognition of diminished motivation requires examining *goal-related* aspects of overt behavior, thought content, and emotion. Disorders of diminished motivation are recognized by the *simultaneous* diminution in each of these 3 aspects of behavior:

Diminished overt behavior may range from a subtle attenuation in social or occupational functioning, for example, apathy, to profound deficits in the capacity to initiate any movement whatsoever, as with akinetic mutism. Symptoms of diminished overt behavior include diminished productivity, diminished effort, and diminished initiative.

Diminished goal-related thought content, if mild, is indicated by decreased interests, plans, or goals for the future. If severe, there is a virtual absence of goal-related thought content. The latter would characterize abulia and akinetic mutism.

Diminished emotional responses to goal-related events mean emotionally indifferent, shallow, or restricted responses to important life events. Clinically, this usually means flattened, labile, or shallow affect and emotional indifference.

To summarize, *diminished motivation is present if a patient with an intact level of consciousness, attention, language, and sensorimotor capacity presents with a simultaneous decrease in goal-related aspects of overt behavior, thought content, and emotion.* This operational definition of DDM leads to a clinical approach for differentiating between DDM and other disorders.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis of DDM depends on the acuity and severity of the TBI. For severe cases, differential diagnosis focuses on TBI complications that produce profound impairment in level of consciousness, attention, speech, or motor capacity, for example, vegetative states, delirium and stupor, locked-in syndrome, or quadriparesis. Patients who have chronic and less severe impairment must be evaluated for depression and dementia

as well as frontal-subcortical syndromes that affect personality and executive cognitive function.

Differential diagnosis requires awareness that if DDM are overdiagnosed, reversible or more readily treated causes of inactivity such as stupor or delirium are overlooked. Underdiagnosis leads to premature attempts at physical rehabilitation or other interventions whose success depends on strong motivation. Antidepressant treatment may also fail, not because a reversible mood disorder is absent but because it is overshadowed by a DDM that requires treatment first.

Patients with diminished motivation all show diminished activity. Inactivity, whether motor, cognitive, or emotional, may result from changes in virtually any domain of mental status. Therefore, differential diagnosis of DDM is simplified by considering these different aspects of mental status.

There are 2 groups of disorders to distinguish in differential diagnosis:

1. Those in which diminished activity is actually due to another impairment: In *stupor* and *coma*, diminished activity and the appearance of apathy are due to the diminished level of consciousness. Similarly, a person in a state of *delirium* may show diminished activity but it is primarily a disorder of attention (impaired ability to establish, shift, or maintain attention). *Aprosodia* is a disorder of emotional processing in which the ability to understand or express emotion is impaired.[18] Aprosodia may be mistaken for apathy because both may be associated with truncated emotional responses. Diminished motivation is not a feature of aprosodia, however.[3] *Catatonia* and *psychomotor retardation* resemble DDM because of reduced motor and speech activity. Executive cognitive impairments and waxy flexibility may be seen in catatonia. Slowing of thought and activity, the essential features of psychomotor retardation, occur in many disorders, including DDM. Therefore, psychomotor retardation should not be viewed as a pathognomonic feature of depression or any other diagnosis.[19,20] *Akinesia*, though it may be associated with apathy, is a disorder of movement, not motivation.
2. Those in which diminished activity is associated with diminished motivation but both are due to some other disorder: *Depression* is a disorder of mood. By definition, it is a dysphoric state. Negative thoughts about the self, the present, and the future (Beck's triad of depression) are characteristic. Consequently, one *suffers* from depression. By contrast, one does not suffer from apathy or other DDM as DDM are not dysphoric states. Although motivational symptoms are common in depression, it is dysphoria and negative thought content that distinguish depression. *Demoralization*, like depression, is a dysphoric state. Demoralization is distinguished by a sense of futility, resignation, or powerlessness to realize some goal that is still desired. *Dementia* is by definition a disorder of cognition, and cognitive impairments are essential to diagnosis. Apathy is a common and disabling aspect of dementia, although it is not the defining feature of the syndrome.

MECHANISM AND CLINICAL PATHOGENESIS

The motivational deficits in patients with TBI result from complex mechanical and physiological processes affecting the neural systems that mediate motivation. These systems may be affected by gross pathology, such as contusion and hemorrhage, or by more subtle changes, such as diffuse axonal injury, hypoxia, and microvascular changes. Neurological dysfunction causing diminished motivation may be approached in anatomical, physiological, and chemical terms. Anatomically, the anterior cingulum (AC), nucleus accumbens (NA), ventral pallidum (VP), medial dorsal nucleus of the thalamus (MD), and the

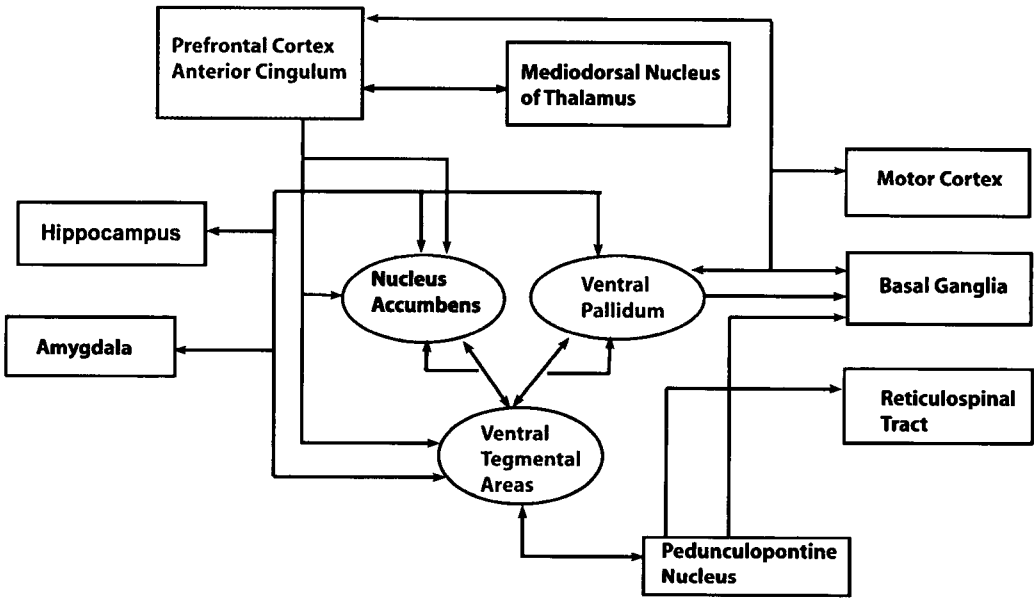

Figure 1. Motivational circuitry. The core circuit (shaded) consists of the anterior cingulum, the nucleus accumbens, the ventral pallidum, and the ventral tegmental area. Nucleus accumbens and the ventral pallidum are divided into (1) more medial portions that are associated with limbic input from the amygdala and the hippocampus and (2) more lateral portions associated with output circuits. Output is via the motor cortex, the basal ganglia, the reticulospinal tract, and the pedunculopontine nucleus. The amygdala and the hippocampus, as well as the prefrontal cortex, modulate information in the core circuit on the basis of the current environment and the drive state of the organism. The ventral pallidum output reaches the prefrontal cortex via the mediodorsal nucleus of the thalamus. The current motivational state is represented by the pattern of activity distributed within the core circuit. The flow of information within and through the core circuit permits the translation of motivation into action. Adapted with permission from Kalivas et al.[21]

ventral tegmental area (VTA) are the most important structures for establishing and maintaining the current motivational state. The anterior cingulum, NA, VP, and MD comprise a cortico-striatal-pallidal-thalamic circuit[21,22] thought to mediate motivation (Fig 1). Disruption of this *core circuit* produces akinetic mutism, abulia, or apathy depending on the severity of the dysfunction.[3,15] Clinical effects of core circuit dysfunction correspond to animal research showing that the "initiation and maintenance of behavioral responses" depends on the circuit composed of NA, VP, and VTA.[23] Clinical arguments for including AC in the core circuit[3] are supported by experimental evidence[24,25] that AC has an essential role to play in motivational aspects of decision making.

A separate aspect of motivation is modifying the current motivational state on the basis of the reward value of the current environment. The reward significance of the environment is signaled by neurons in several forebrain regions, including VTA, striatum, ventral striatum, NA, dorsolateral and orbital prefrontal cortex, anterior cingulate cortex, and amygdala.[26] Modifying the current motivational state depends on the amygdala, the hippocampus, the prefrontal cortex,[21] and the greater limbic lobe.[27] This may explain why disease states affecting these structures present as apathy: if unable to register changes in the reward significance of the environment, the organism will be "apathetic" to these stimuli. This formulation may account for the apathy associated with

hippocampal dysfunction (amnestic disorder, Alzheimer's disease), the apathy and placidity seen with amygdala injury (Kluver-Bucy syndrome[28]), and the "background of apathy and abulia"[29] associated with orbitofrontal dysfunction. Similarly, inability to develop a motivational map of the external environment is postulated to account for the indifference associated with right hemisphere injury.[30]

Pathogenesis of TBI symptoms may also be understood in terms of the neurochemistry of the motivational circuitry, for example, dopaminergic or glutamatergic pathways. Dopaminergic activity is of particular importance for motivational deficits because of the central role that it plays in reward, novelty seeking, and response to unexpected events.[31,26] There is some evidence[32,33] that dopaminergic activity is affected in TBI.[34] Several other biochemical changes have been described in TBI, including changes in levels of glutamate, acetylcholine, neuropeptides, and oxygen-free radicals. Their direct and indirect participation in the motivational circuitry provides a rationale for the use of pharmacological therapies in DDM, including glutamatergic and cholinergic agents.[10]

ASSESSMENT

The assessment of patients with diminished motivation depends on the etiology of diminished motivation and the interaction of biological, psychosocial, and socioenvironmental factors that control motivated behavior. Table 1 lists conditions associated with apathy, abulia, and akinetic mutism.[3,35] The conditions that cause akinetic mutism may also cause abulia and apathy because all 3 may result from dysfunction of the AC-NA-VP-MD circuit mediating motivation. In other words, when less severe, the diseases that cause akinetic mutism cause abulia and apathy. In addition, there are many neurological and psychiatric disorders and psychosocial conditions that produce apathy but do not cause abulia and akinetic mutism because the core circuit structures are spared. The information given in Table 1 implies that assessment of patients with diminished motivation requires a comprehensive and systematic neuropsychiatric evaluation, including evaluation of the patient's social and physical environment.

The psychosocial history will indicate the patient's baseline level of motivation[3] and coping skills[1] that characterize adult personality. It is also important to keep in mind the enormous variability in individuals' accomplishments, interests, and goals and the way these are influenced by personal experience, education, social class, culture, and age cohort.

Personal loss, psychological trauma, and phase-of-life events may alter motivation. Occasionally, apathy is the primary symptom of an adjustment disorder, for example, the empty nest syndrome or a retirement reaction. Apathy can also be a defense mechanism when it is the primary means for dealing with anxiety. The social withdrawal or emotional distance seen in Cluster A personality disorders may mistakenly be interpreted as neurogenic motivational loss. Conversely, one can err by attributing subtle motivation loss to Cluster A personality disorder when, in fact, one has encountered the first symptoms of neurogenic apathy.[3]

Interactions of medical, psychological, and neurological variables are particularly relevant in elderly patients because they often have multiple clinical problems. Many drugs may alter motivation. Dopaminergic agents, agonists or antagonists, are most familiar as mediators of motivational change. But equally important are serotinergic, cholinergic, and adrenergic agents because of their interaction with dopamine systems. Pharmacokinetic variables have an independent influence on motivation. For example, there are case reports suggesting that selective serotonin reuptake inhibitors (SSRIs) may dispose to apathy.[36] Furthermore, SSRIs, particularly fluoxetine and paroxetine, are potent 2D6 inhibitors. If an irritable patient with TBI is treated with haloperidol and then, because apathy is misdiagnosed as depression, treated with one of these SSRIs, motivation

Table 1. Conditions associated with apathy, abulia, and akinetic mutism

*Neurological disorders**	*Medical disorders*
Frontal lobe	Apathetic hyperthyroidism
Frontotemporal dementia	Hypothyroidism
Anterior cerebral artery infarction	Pseudohypoparathyroidism
Tumor	Lyme disease
Hydrocephalus	Chronic fatigue syndrome
Trauma	Testosterone deficiency
Right hemisphere	Debilitating medical conditions, for example, malignancy, congestive heart failure, renal or heart failure
Right middle cerebral artery infarction	*Drug induced*
Cerebral white matter	Neuroleptics, especially "typical" neuroleptics
Ischemic white matter disease	Selective serotonin reuptake inhibitors
Multiple sclerosis	Marijuana dependence
Binswanger's encephalopathy	Amphetamine or cocaine withdrawal
HIV	*Socioenvironmental (lack of reward, loss of incentive, lack of perceived control)*
Basal ganglia	Role change
Parkinson's disease	Institutionalism
Huntington's disease	
Progressive supranuclear palsy	
Carbon monoxide poisoning	
Diencephalon	
Degeneration or infarction of thalamus	
Wernicke-Korsakoff disease	
Amygdala	
Kluver-Bucy syndrome	
Multifocal disease	
Alzheimer's disease (apathy may be mediated by damage to the prefrontal cortex, the parietal cortex, and the amygdala)	

*Akinetic mutism results from bilateral dysfunction of the cortico-striatal-pallidal-thalamic circuit, which consists of anterior cingulum, nucleus accumbens, ventral pallidum, and mediodorsal nucleus of thalamus. When improving or less severe, such cases present as abulia or apathy. Etiology may be vascular, trauma, tumor, degeneration, or toxin (eg, carbon monoxide poisoning).

may worsen for 2 reasons. The SSRI may induce apathy directly and haloperidol-induced motor apathy may worsen because the SSRI increases levels of haloperidol.

Neurological disorders affecting motivation and its neural machinery should direct the clinician's attention to several aspects of the neurological examination. Since frontal and diencephalic diseases figure prominently in differential diagnosis of DDM, it is important to know whether olfactory function, visual acuity, and visual fields are intact. Frontal release signs and paratonic rigidity (gegenhalten) are relevant for the same reason.

Extrapyramidal motor signs clarify the evaluation of motor subtypes of DDM. For example, chorea, micrographia, loss of associated movements, or conjugate eye movement abnormalities suggest that diminished motivation may be due to Huntington's disease, Parkinson's disease, or progressive supranuclear palsy.

Neuropsychological assessment clarifies the cognitive context of motivational loss. Executive cognitive assessment may suggest that lack of activity in one patient reflects impairment in sequencing while in another it reflects loss of verbal fluency and initiation. Each will benefit from a different type of "psychological prosthesis."

Clinicians, especially those unfamiliar with DDM, may find it helpful to rate the severity of motivational loss with formal rating scales. The rating process can familiarize one

with the clinical signs of motivation and its loss as well as aid differential diagnosis. For example, if a clinician is unsure whether a psychomotor-retarded patient is apathetic or depressed, it may be helpful for the clinician to discover that the apathy rating is high whereas the depression score is unexpectedly low. This would suggest that the psychomotor retardation is better characterized as bradykinesia and akinesia. If so, the next clinical step may be to perform a neurological examination and obtain a magnetic resonance image of the head rather than to have the patient start taking an antidepressant.

Several rating methods are available for quantifying loss of motivation. Construct validity is strongest for the Apathy Evaluation Scale (AES),[37] an 18-item scale that can be administered as a self-rated scale, a caregiver pencil-and-paper test, or a clinician-rated semistructured inventory (Table 2).[38,39] Several articles document the feasibility of rating apathy with the Apathy Scale,[40,41] which is derived from a preliminary version of the AES. The Children's Motivation Scale,[42] also derived from the AES, uses developmentally appropriate behavioral anchors to permit rating of apathy in children and adolescents. The

Table 2. Apathy Evaluation Scale (clinician version)

Name: _____ Date: __/__/____

Rater: _____

Rate each item on an interview at the subject. The interview should begin with a description of the subject's interests, activities, and daily routine. Base your ratings on both verbal and nonverbal information. Rating should be based on the past 4 weeks. For each item, ratings should be judged:

Not at All Characteristic (1)	**Slightly Characteristic (2)**	**Somewhat Characteristic (3)**	**A Lot Characteristic (4)**

___	1.	She/he is interested in things.
___	2.	She/he gets things done during the day.
___	3.	Getting things started on his/her own is important to him/her.
___	4.	She/he is interested in having new experiences.
___	5.	She/he is interested in learning new things.
___	6.	She/he puts little effort into anything.
___	7.	She/he approaches life with intensity.
___	8.	Seeing a job through to the end is important to her/him.
___	9.	She/he spends time doing things that interest her/him.
___	10.	Someone has to tell her/him what to do each day.
___	11.	She/he is less concerned about her/his problems than she/he should be.
___	12.	She/he has friends.
___	13.	Getting together with friends is important to him/her.
___	14.	When something good happens, she/he gets excited.
___	15.	She/he has an accurate understanding of her/his problems.
___	16.	Getting things done during the day is important to her/him.
___	17.	She/he has initiative.
___	18.	She/he has motivation.

The Apathy Evaluation Scale was developed by Robert S. Marin, MD. Development and validation studies are described in Marin et al.[38] Scoring instructions and administrations guidelines are available from Robert S. Martin, MD, Western Psychiatric Institute and Clinic, 3811 O'Hara St, Pittsburgh, PA 15213.

Neuropsychiatric Inventory[43] is a multidimensional instrument administered to caregivers. It is widely used to assess noncognitive symptoms of dementia and devotes 1 of 10 item domains to apathy.

TREATMENT

The growing interest in DDM is leading to novel approaches to understand the coping impairments[1] or neuropsychological losses[5] of patients with TBI. These and other new approaches are likely to lead to new therapies for DDM. Psychological and socioenvironmental approaches to DDM apply primarily to apathy and abulia. Their relevance to akinetic mutism arises once patients begin to respond to pharmacological therapies.

Some of the psychological treatments are also appropriate for patients with depression, often because patients with depression are suffering in part from diminished motivation. The applicability of such psychological approaches to depression and to DDM leads some to wonder if it is necessary to consider them for DDM. Actually, these interventions have a specific role for DDM. Once a clinician diagnoses a patient as apathetic and not depressed, the question becomes what kind of psychological therapies are indicated. If these treatments are viewed as treatments for depression, the clinician may fail to offer them to the patient with apathy. Clearly, this would be inappropriate.

Treatment of akinetic mutism and abulia is primarily pharmacological. Patients with apathy may require pharmacological interventions, but the preservation of cognitive and communicative capacity calls increasingly for psychological and social interventions. Such interventions are based on careful characterization of the patient's motivational and neuropsychological status. The general principle is to define the patient's losses and residual capacities and then design a "psychological prosthesis" that compensates for the deficits and makes the best possible use of residual abilities. Regardless of severity, treatment must consider the physical and psychosocial environment. Modifying the overall environment and attending to family and professional caregivers is an elementary but crucial dimension of treatment for DDM.

Preliminary evaluation requires optimizing the patient's general medical condition. This may mean controlling seizures or headaches, arranging physical or cognitive rehabilitation for cognitive and sensorimotor loss, or ensuring optimal hearing, vision, and speech. These elementary steps also increase motivation because improved physical status may enhance functional capacity, drive, and energy and thereby increase the patient's expectation that initiative and effort will be successful.

The aim of environmental interventions is to increase the reward potential of the environment. Adaptive devices, such as motorized wheel chairs or voice-activated computers, compensate directly for the sensorimotor and neurological impairments that deny the patient full benefit of the environment. In impoverished environments, either at home or institutions, it is important to introduce new sources of pleasure, interest, and stimulation. Increasing opportunities for socialization is also helpful. For many, returning to the familiar personal and physical circumstances of their homes may be the fastest way to a healthier physical or social environment.

General psychological status contributes to motivation in the same way that general medical condition does. Goal-directed behavior depends not only on motivation but also on other state variables: arousal, attention, mood, and cognition. Psychological treatments may include a variety of behavioral techniques[7,16,44] or specialized cognitive rehabilitative approaches, for example, enhancing attention or performance speed.[45] Psycho-education, vocational counseling, and psychotherapy should not be overlooked. Psychotherapy may focus on injury-related loss, interpersonal problems, or family stressors.

Behavioral interventions should be introduced methodically, making clear the tasks and skills required of the patient. Goals should be defined collaboratively to strengthen

engagement and enhance the patient's sense of control and expectation of success. Once goals are defined, staff should be careful to follow through with the treatment plan.

Finally, there is the integration of neuropsychological assessment with the treatment of motivational loss. Accurate assessment provides the template for developing an individualized plan for psychological treatment. The treatment can be thought of as a "psychological prosthesis" because it is precisely molded to the pattern of abilities lost and retained as a result of injury. Thus, for deficits in initiation and perseveration, the psychological prosthesis requires the caregiver to prompt the patient when to begin or end a particular task. If patients are able to initiate behavior but fail to act because they are unable to sequence, plan, and monitor behavior, their motivational prosthesis requires the caregiver to tell the patient, "go into the kitchen . . . now open the refrigerator door . . . now take out the sour cream on the top shelf . . . bring the sour cream into the dining room . . . thank you very much." Here the motivational prosthesis is a specific substitute for the impairments in planning and sequencing.

Similar psychological prostheses aid DDM patients with other neurobehavioral impairments. Of particular importance is the association of diminished motivation with environmental dependency or stimulus-bound behavior. A bland or unfamiliar environment will aggravate this condition because there is nothing to trigger the "old" behaviors. Families complain, "All he does is sit around here and do nothing." Professional caregivers may have the same complaint. A variety of neuropsychological impairments contribute to environmental dependency. For example, the patient may be unable to generate an idea or a goal for behavior. The psychological prosthesis in this instance uses the pathology itself to treat the problem. Instead of trying to create new habits, the caregiver returns the person to an environment that habitually elicits the desired behavior. In most cases, this means returning the patient home or at least creating an environment that looks like home, for example, by bringing in family photographs or favorite books.

There are 5 steps to pharmacological treatment: (1) Optimize medical status. (2) Diagnose and treat other conditions more specifically associated with diminished motivation (eg, apathetic hyperthyroidism, Parkinson's disease). (3) Eliminate or reduce doses of psychotropics and other agents that aggravate motivational loss (eg, SSRIs, dopamine antagonists). (4) Treat depression efficaciously when both DDM and depression are present. When depression is associated with apathy, consider using more activating antidepressants (eg, sertraline, bupropion, venlafaxine). (5) Increase motivation through use of stimulants, dopamine agonists, or other agents such as cholinesterase inhibitors (Table 3). These agents have been used for treating a variety of behavioral and cognitive impairments in patients with TBI.[32-34] Cholinesterase inhibitors (donepezil, galantamine, rivastigmine) may also benefit apathy in TBI. [46,47]

With stimulants and dopamine agonists, treatment is initiated with minimal doses and slowly titrated upward once improvement begins. Some patients respond to small doses, but when impairment is significant and risk factors few, higher doses should be considered.

There is significant and sometimes dramatic benefit of bromocriptine in abulia and akinetic mutism.[16] Presumably, other and less toxic dopamine agonists have comparable potential. Pramipexole may have some advantage for DDM because it has selectivity for D3 dopamine receptors that are preferentially distributed in the limbic forebrain. All of the dopaminergic drugs dispose to behavioral toxicity, including psychosis, motor activation and restlessness, sleep disturbance, and delirium. Caution should be taken with the stimulants to monitor pulse and blood pressure, although serious problems are unusual. Amantadine alters both dopaminergic and glutamatergic receptors, which may actually be a clinical advantage[48] since DDM are not due only to lack of dopaminergic activity. In older patients, amantadine dosage must

Table 3. Drugs used in the treatment of apathy, abulia, and akinetic mutism

Agent	Usual total daily dosage, mg*
Stimulants	
Dextroamphetamine	20 (5-60)
Methylphenidate	20 (10-60)
Activating antidepressants	
Bupropion	200 (100-400)
Parnate	45 (30-90)
Protriptyline	40 (20-60)
Venlafaxine	150 (100-450)
Dopamine agonists (selective and mixed)	
Amantadine	200 (100-300)
Bromocriptine	10 (5-90)
Selegiline	10 (5-40)†
L-DOPA/carbidopa	25/100 TID -25/250 QID
Pergolide	2 (1-5)
Pramipexole	5 TID (0.375-4.5)
Other psychotropics	
Modafinil (Provigil)	200 (100-400)
Donepezil (Aricept)	5 (5-10)
Galantamine (Reminyl)	8 BID (4-8)
Rivastigmine (Exelon)	3 BID (1.5-6)

*Values in parentheses represent range.
†Requires diet low in tyramine, especially at doses above 10 mg; lower doses may produce serotonin syndrome if administered with agents that slow selegiline metabolism.

be adjusted to account for decreased creatinine clearance.

Disorders of diminished motivation associated with extrapyramidal motor symptoms are treated with the same agents, including amantadine. The goal of treatment is to manipulate dopaminergic function for the sake of motivation, not just to improve motor ability. Overlooking this may compromise outcome in the end because the benefit of improved mobility will be undercut by lack of motivation.

Newer psychotropic medications may be helpful for treating DDM. Modafinil, introduced recently for the treatment of narcolepsy, has stimulating or arousing effects that may prove useful in some patients. Modafinil may cause headache and gastrointestinal symptoms, but it is relatively free of major toxicity. The growing knowledge of glutamate systems raises the possibility that glutamatergic agents may prove useful as well.[49]

CONCLUSION

Motivation is fundamental for adaptive behavior. The major DDM are apathy, abulia, and akinetic mutism. Depending on their etiology, DDM may be the primary clinical disturbance, a symptom of some other disorder, or a coexisting second disorder requiring independent diagnosis and management. Differential diagnosis usually focuses on delirium, dementia, depression, demoralization, akinesia, catatonia, and aprosodia. In recent years, the neurological model for DDM has been based on the cortico-subcortical circuit involving AC-NA-VP-MD and the modification of current motivational state by the prefrontal cortex, the amygdala, the hippocampus, and the greater limbic lobe. Current knowledge permits

us to approach assessment and treatment of DDM on the basis of our understanding of these systems. Treatment of DDM includes the full range of biomedical, psychological, and socioenvironmental approaches available in neuropsychiatry. By treating DDM, we offer individuals with TBI a way to improve their functional abilities and quality of life.

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