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White Matter Dementia

Clinical Disorders and Implications

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Summary: Traditional concepts of dementia focus on diseases primarily affecting cortical gray matter, most notably Alzheimer's disease. Another group of diseases, termed "subcortical," is also believed to affect higher functions, but clinical distinction and neuropathological specificity of these syndromes have been problematic. We propose that the concept of white matter dementia may have a more specific meaning. A number of conditions demonstrate prominent white matter pathology—toluene-induced dementia, multiple sclerosis, Binswanger's disease, diffuse axonal injury, the AIDS dementia complex, alcoholic dementia, and normal pressure hydrocephalus—and even normal aging involves selective white matter loss. White matter dementias do not display characteristic cortical gray matter signs, such as prominent amnesia and aphasia, nor do they show the typical movement disorders of classical subcortical dementias. Attentional dysfunction may be the most salient neurobehavioral deficit in these diseases, although impaired learning, psychomotor function, and speed of information processing are commonly observed as well. **Key Words:** Dementia—White matter—Attention.
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Dementia is a neurobehavioral syndrome familiar to clinicians largely because of the urgent problem of Alzheimer's disease (AD) (Katzman, 1976). Neuropathologically, this devastating illness displays prominent cortical changes, and characteristic disorders of memory and other higher functions have been convinc-

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ingly linked with cortical pathology (Cummings and Benson, 1983). AD has provided abundant evidence that disturbances of intellect are critically dependent on damage to cortical regions (Katzman, 1986). Yet dementia may occur in many other diseases, most of which show their most significant pathology in noncortical areas. These dementias may be less obvious than in AD or may be somewhat obscured by other neurologic features, but they represent an opportunity to observe the contributions made to behavior by subcortical structures such as the basal ganglia, thalamus, and white matter.

An influential recent contribution to the investigation of dementia has been the proposal of a category known as "subcortical dementia" (Albert et al., 1974; McHugh and Folstein, 1975). Diseases such as progressive supranuclear palsy (PSP), Huntington's disease (HD), and Parkinson's disease (PD), each with prominent subcortical pathology, fall into this category, and dementia has been ascribed to subcortical nuclear involvement. A lively debate regarding the utility of the subcortical dementia concept has ensued, related to conflicting data and theoretical uncertainties (Whitehouse, 1986).

Relatively neglected in this controversy has been the group of dementias associated with white matter disease. Diseases such as multiple sclerosis (MS) are clearly subcortical, in that cortical regions mostly escape demyelination, but they differ from classical subcortical dementias in that deep gray matter structures are not primarily involved. It appears that damage to white matter alone can cause significant effects on higher functions.

It is our view that the distinction between cortical and subcortical dementias has merit, but that it is in need of clarification. Dementia syndromes are as diverse as the pathologies that produce them, and a simple division into cortical and subcortical types is only a beginning. We propose that a third category—white matter dementia—has meaning in that specific neurologic and neurobehavioral features appear to be associated with a specific neuropathology. This review will first summarize the evolution of the cortical–subcortical controversy and then present a consideration of selected white matter diseases that exhibit a dementia syndrome of clinical importance. A hypothesis regarding the pathogenesis of white matter dementia will be presented, and implications for possible treatment and further research will be explored.

CORTICAL AND SUBCORTICAL DEMENTIA

In 1974, a report appeared in which five patients with PSP had a distinctive dementia syndrome (Albert et al., 1974). The authors noted the presence of four characteristic features: forgetfulness, slowness of thought processes, emotional changes (including apathy, depression, and irritability), and an impaired ability to manipulate acquired knowledge. This profile was termed "subcortical dementia," and "cortical" signs, such as amnesia, aphasia, apraxia, and agnosia, were

TABLE 1. *Major causes of dementia classified according to most significant neuropathology*

Cortical dementias
Alzheimer's disease
Pick's disease
White matter dementias
Toluene abuse
Multiple sclerosis
Binswanger's disease
Diffuse axonal injury
AIDS dementia complex
Alcohol abuse
Normal pressure hydrocephalus
Subcortical dementias
Huntington's disease
Parkinson's disease
Progressive supranuclear palsy
Wilson's disease
Mixed dementias
Multiinfarct dementia
General paresis
Creutzfeldt-Jakob disease
Neoplastic dementia
Subdural hematoma

absent. A year later, eight patients with HD were described as having a "subcortical dementia syndrome"; in these cases, there was a "dilapidation" of cognition, as well as apathy and inertia, and an absence of amnesia, aphasia, alexia, and agnosia (McHugh and Folstein, 1975). Subsequently, subcortical dementia has been described in PD (Albert, 1978), Wilson's disease (Cummings and Benson, 1983), the lacunar state (Cummings and Benson, 1983), other extrapyramidal syndromes (Cummings and Benson, 1983), and the dementia syndrome of depression (Caine, 1981). Others have suggested that tardive dyskinesia may be associated with dementia (Famuyiwa et al., 1979), and this combination may represent another subcortical dementia syndrome.

The cortical dementias are limited to two conditions: AD and Pick's disease. These diseases are characterized by well-known neuropathologic changes in the cortex and relative sparing of subcortical nuclear structures. Another category, known loosely as the "mixed" dementias, includes entities such as multiinfarct dementia, general paresis, and Creutzfeldt-Jakob disease, and the pathology involves both cortical and subcortical areas (Cummings and Benson, 1983) (Table 1).

An intriguing feature of the subcortical dementias is the close similarity to disorders related to bifrontal lobe pathology (Albert et al., 1974; Cummings and

Benson, 1984). Many of the features of subcortical dementias—forgetfulness, emotional changes, and impaired abstracting ability—find parallels in syndromes related to frontal lobe disease (Damasio, 1985). These similarities have prompted efforts to consider renaming subcortical dementia as "frontal system dementia" (Albert, 1978) or "frontosubcortical dementia" (Freedman and Albert, 1985); to date, the term "subcortical" remains most popular.

Criticism of the dichotomy between cortical and subcortical dementia has been spirited and frequent. First, clinicians are often uncertain in distinguishing clinical features; for example, the distinction between cortically-determined amnesia—difficulty learning new material—and subcortically-mediated memory impairment—characterized by more retrieval difficulty—may not be straightforward in all cases, particularly late in the disease process. Dementias of all sorts tend to resemble each other as advanced stages are reached. It has been argued that the only reliable clinical difference is the presence of a movement disorder in subcortical dementias, a feature not obviously related to mentation at all. Second, neuropathological distinctions may not be very clear. To illustrate this point, AD has been shown to involve subcortical degeneration in the nucleus basalis of Meynert (Whitehouse et al., 1981), and PD dementia may be explained by Alzheimer's changes in the cortex (Hakim and Mathieson, 1979).

Nevertheless, clinical experience does suggest that dementias differ clinically, particularly in their early stages, and the search for useful differentiating features continues. One of the difficulties with subcortical dementia is the problem with measuring and quantitating its neurobehavioral features. Standard mental status tests, and even comprehensive neuropsychological batteries, are heavily weighted toward memory and language tasks, and may overlook or underestimate deficits in less obvious areas such as attention, motivation, and mood. In part because of this difficulty, there is a paucity of systematic studies comparing cortical and subcortical dementias (Whitehouse, 1986).

Despite persistent questions about the validity of the subcortical dementia concept, some interesting speculations have been generated. An explanation for subcortical cognitive dysfunction has been that timing and activation of cortical processes are disturbed, and that by implication, the cortical apparatus for carrying out intellectual functions is intact but cannot be recruited properly (Albert et al., 1974). Later formulations of this idea have distinguished between the "fundamental" functions of arousal, attention, mood, and motivation, and the "instrumental" functions of memory, language, praxis, and perception (Albert, 1978: Cummings and Benson, 1984). If fundamental functions are disturbed, instrumental functions will also be impaired, but only because the underlying activation and timing abilities are deficient; clinicians recognize, for example, that memory is grossly disturbed in a patient with an acute confusional state. If instrumental functions are primarily impaired, on the other hand, fundamental abilities may be quite intact. Mesulam (1985) has described a similar distinction be-

tween state-dependent and channel-dependent functions; the former consist of diffusely-organized phenomena, such as arousal, mood, and motivation, whereas the latter involve more specific, cortically-related abilities, such as memory and language.

The central idea in these discussions leads to an expansion of thinking about dementias: intellectual and emotional disturbances may relate to pathology in areas outside the traditional region that is assumed to govern conscious behavior—the cerebral cortex. Perhaps the major impact of the subcortical dementia concept lies in the suggestion that "higher cortical functions" should be reconsidered as "higher cerebral functions."

WHITE MATTER DEMENTIA

It is not a new observation that cognitive impairment can be associated with disease of cerebral white matter, nor should such an association be surprising. This section will summarize data from investigations of a number of dementing diseases that primarily affect white matter. We have been particularly impressed with the patterns of neurobehavioral impairment that are emerging from studies of toluene abuse and MS. Table 1 presents a classification of major dementias based on the location of the most significant neuropathology.

Dementia Associated with Toluene Abuse

The first case of persistent encephalopathy from toluene inhalation was reported in a patient who had ataxia, tremor, and emotional lability (Knox and Nelson, 1966). Neuropsychological impairment has also been noted (Fornazzari et al., 1983), and multifocal CNS damage has been observed (Lazar et al., 1983; Hormes et al., 1986). We have studied a large number of individuals who have abused toluene for many years. This solvent is inhaled as an intoxicant and is usually abused in the form of spray paint; it is the most commonly abused organic solvent. Toluene is highly lipophilic and rapidly enters the CNS; this phenomenon undoubtedly explains the rapid "high" obtained by toluene abusers.

Among 20 chronic toluene abusers, whose abuse was for 2 or more years, 13 had neurobehavioral impairment detected by standardized evaluation; this was the most frequent and disabling neurologic feature (Hormes et al., 1986). The dementia was uniformly characterized by apathy, inattention, poor memory, impaired complex cognition, and the absence of aphasia (Hormes et al., 1986). Computerized tomographic (CT) scans showed diffuse brain atrophy and enlarged lateral ventricles (Hormes et al., 1986). Magnetic resonance imaging (MRI) in other toluene abusers has demonstrated diffuse white matter changes, with loss of gray–white differentiation and increased periventricular white matter signal intensity on T2-weighted images (Rosenberg et al., 1988) (see Fig. 1). One individual who died suddenly after 20 years of toluene abuse was found to have

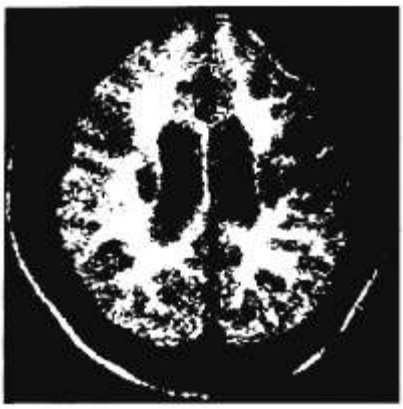

FIG. 1. T_2-weighted cerebral magnetic resonance imaging scan of a chronic toluene abuser (TE, 2.0 s; TR, 60 ms). Note the diffuse hyperintensity of subcortical white matter.

analogous diffuse white matter change pathologically; there was no evidence of cortical or subcortical neuronal damage, nor was there any axonal injury, suggesting that the white matter changes were not secondary to neuronal or axonal loss (Rosenberg et al., 1988).

Our studies suggest that toluene may be a primary white matter toxin and that the most prominent clinical effect is on neurobehavioral function. The dementia syndrome resembles previously described subcortical syndromes, with the notable exception that a movement disorder is absent. The inattention and apathy are particularly noteworthy and signify a disruption of the fundamental functions of arousal, attention, and motivation.

MS Dementia

Although cognitive disturbance has long been noted in MS (Charcot, 1877), neurobehavioral impairment has only recently been evaluated in a systematic manner (Rao, 1986). Even today, authoritative general reviews of MS have paid relatively little attention to this problem (McFarlin and McFarland, 1982; McKhann, 1982). Recent studies, however, have documented neuropsychological impairment in significant numbers of patients with MS, especially in association with a chronic progressive disease course (Heaton et al., 1985). The degree of impairment may be slight in many cases, but deficits typically occur in attention, concept formation, and complex problem solving (Rao, 1986). Affective disorder is also common in MS, occurring as depression, mania, bipolar affective disorder, or late euphoria (Trimble and Grant, 1982). Memory and language are less affected than in AD (Filley et al., in press), a fact that helps to explain the subtlety of this dementia; instrumental functions, such as memory and language, are more easily assessed, and disorders in these areas are more readily detected.

MRI has proven to be very useful in MS (Young et al., 1981), and we have found that the extent of white matter involvement on MRI can be correlated with

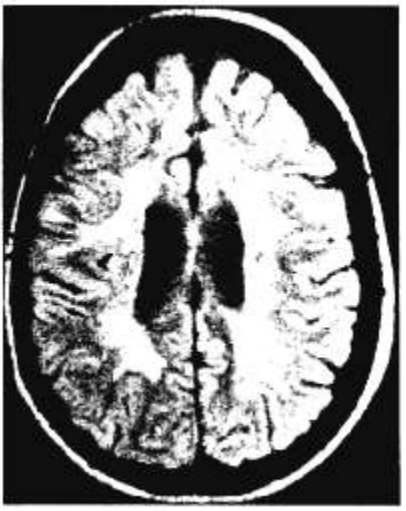

FIG. 2. T_2-weighted cerebral magnetic resonance imaging scan of a multiple sclerosis patient with dementia (TE, 2.0 s; TR, 40 ms). Here there is patchy multifocal white matter demyelination.

cognitive impairment as determined by neuropsychological testing (Franklin et al., 1988). In contrast to the diffuse white matter change seen in toluene abuse, MS is characterized by patchy, multifocal demyelination (see Fig. 2). The burden of white matter involvement appears to fall most heavily on frontal lobe white matter, a feature demonstrated by pathologic studies (Brownell and Hughes, 1962) and by the presence of lower extremity frontal release signs and gait disturbance in many patients with MS dementia (Franklin et al., in press). Movement disorders that are frequent in the subcortical dementias—resting tremor, chorea, athetosis, dystonia—are distinctly uncommon in MS.

Binswanger's Disease

This often-mentioned but poorly understood disease represents a vascular form of white matter dementia. In a recent review of 47 pathologically verified cases, the dementia of Binswanger's disease (BD) was described as an insidiously progressive constellation of mild memory loss, apathy, and alterations in mood and behavior appearing as euphoria, elation, or aggressiveness (Babikian and Ropper, 1987). Aphasia and apraxia were uncommon, as were movement disorders. Neuropathologically, the disease showed some evidence of deep gray matter ischemia, but the prominent feature was white matter ischemic change, often with lacunar infarctions (Babikian and Ropper, 1987).

CT scans often reveal areas of white matter low density in older persons (Kinkel et al., 1985), and MRI scans show similarly located hyperintensities (Kertesz et al., 1988). These changes have been speculated to represent BD (Kinkel et al., 1985), but as many normal elderly have white matter changes (Filley et al., 1987*b*), the diagnosis of BD should be made primarily on clinical grounds. White

matter changes in the elderly, sometimes referred to as leukoaraiosis, may have many etiologies and may indeed be a normal age-related phenomenon (Hachinski et al., 1987). Cerebral ischemia, however, also appears to contribute to leukoaraiosis (Kertesz et al., 1988), and it is of interest that healthy hypertensive men show selective deficits in vigilance and attention on neuropsychological testing (Boller et al., 1977). We speculate that an intermediate condition between health and BD may exist, and that ischemic white matter changes may have neurobehavioral effects that range from mild inattention to frank dementia.

Diffuse Axonal Injury

Severe traumatic brain injury can have profound effects on cortical areas damaged by focal contusions, but diffuse axonal injury (DAI) may be the more common neuropathologic lesion. Injury to white matter has long been known to follow head trauma (Strich, 1956), and recent studies have reemphasized the importance of cerebral DAI and associated white matter damage in head injury (Adams et al., 1982). Although not routinely listed among the dementias, head trauma can result in severe and chronic neurobehavioral impairment. In a retrospective study of children and adolescents with severe traumatic brain injury, dementia due to DAI was marked by disorders of arousal, cognitive disturbance, rare aphasia, no movement disorder, and extremely disabling problems with emotional control and personality (Filley et al., 1987*a*). Damage to frontal–limbic and frontal–reticular systems was the likely explanation in these cases (Filley et al., 1987*a*).

DAI has broader implications than the dementia it can cause. A continuum probably exists between the mildest sequela of head trauma, the concussion (Oppenheimer, 1968), and the most severe residual syndrome, the persistent vegetative state (Jennett and Plum, 1972). In all of these entities, varying degrees of white matter damage are evident, and there is relative sparing of cortex and subcortical nuclear structures.

AIDS Dementia Complex

A new and alarming addition to the list of dementias, AIDS Dementia Complex (ADC) has been recognized as a disease that primarily affects white matter (Navia, 1986*a*). The dementia syndrome involves poor concentration, impaired memory, psychomotor slowing, and behavioral disturbances (apathy or withdrawal), and the term subcortical dementia has been applied to this entity (Navia, 1986*b*). Although basal ganglia and thalamic structures may be involved (Navia, 1986*a*), and myoclonus can occasionally be seen (Navia, 1986*b*), we prefer to include ADC dementia in the white matter group, noting that aphasia and movement disorders are both uncommon.

The pathogenesis of white matter damage in ADC is unclear. No evidence for neuronal or oligodendroglial infection with human immunodeficiency virus type 1 (HIV) has been detected, although macrophages and multinucleated cells appear to harbor the virus (Price et al., 1988). ADC may therefore be due to an indirect effect of the HIV brain infection (Ho et al., 1987). It is possible that HIV-infected macrophages secrete monokines that are toxic to brain tissue or that induce inflammation. Another possible indirect effect may be provided by the HIV envelope glycoprotein (gp 120) inhibiting the action of neuroleukin, a CNS trophic factor and lymphokine (Gurney et al., 1986).

Alcoholic Dementia

After considerable debate, the entity of alcoholic dementia seems to have been established as a clinical syndrome that is distinct from the amnesic state of Korsakoff's psychosis (Lishman, 1981). Initial neuropathologic studies indicated prominent cerebral cortical cell loss (Courville, 1955), but others have questioned these findings (Victor and Adams, 1985). A more plausible explanation for dementia in non-thiamine-deficient disorders may be white matter damage; a recent report noted significant loss of white matter in 22 postmortem alcoholic brains (Harper et al., 1985). The dementia syndrome is again familiar: inattention, forgetfulness, psychomotor slowing, and no aphasia or movement disorder (Lee et al., 1979). Of interest is that both neuropsychological deficits (Ron, 1977) and measures of brain atrophy (Ron et al., 1982) can show improvement in patients who become abstinent. Although further studies on the neuropathology of alcoholic dementia are necessary, this recovery pattern is evidence in favor of reversible white matter damage and against the idea of cortical cell loss (Harper et al., 1985).

Normal Pressure Hydrocephalus

This syndrome has a controversial history, but most authorities accept the triad of dementia, urinary incontinence, and gait disturbance as a legitimate entity (Adams et al., 1965). The dementia clearly mimics other white matter diseases—with apathy, forgetfulness, and intellectual slowing, all without aphasia or movement disorder (Ojemann et al., 1969)—and periventricular demyelination and spongiosis are present at autopsy (DiRocco et al., 1977). The gait disturbance is quite similar to the abnormal gait we have seen in many MS patients with prominent periventricular demyelination (Franklin et al., in press). Similar to the findings with alcoholic dementia, recovery in some patients with ventricular shunting procedures suggests that cell bodies are not primarily damaged in this condition.

The syndromes reviewed above do not comprise a complete listing of white matter diseases causing dementia, but they do serve to illustrate a relatively uniform profile of neurologic and neurobehavioral impairment. It may be argued that, in neurobehavioral terms, the white matter dementias are indistinguishable

TABLE 2. *Differential clinical characteristics of cortical, white matter, and subcortical dementias*

Characteristic	Cortical	White matter	Subcortical
Inattention	−	+	+
Forgetfulness	−	+	+
Emotional changes	−	+	+
Amnesia	+	−	−
Aphasia	+	−	−
Movement disorder	−	−	+

from the subcortical dementias. Indeed, it is premature to attempt a differentiation using mental status examination alone. There are, however, cogent reasons for considering a category of white matter dementias. First, calling attention to a significant source of neurobehavioral disability in a wide variety of diseases can serve to increase awareness of the morbidity that these diseases can cause. Second, the typical absence of movement disorders in these diseases provides a simple and easily tested guideline for diagnostic purposes. Third, the advent of MRI offers an excellent means for assessing the presence and degree of white matter involvement. Fourth, the scope of neuropsychologic evaluation can be expanded by awareness of white matter dementia syndromes. Fifth, the neuropathologic specificity of white matter disease offers a useful common feature with which to conduct detailed and systematic neurobehavioral investigations. Finally, we have been impressed with the prominence of attentional disturbance in these conditions and regard it as sufficiently important to pursue as a specific hypothesis (see below).

It is not our claim that cortical, white matter, and subcortical dementias always present as discrete syndromes. Pick's disease, for example, can manifest emotional changes (Cummings and Benson, 1983) suggesting subcortical or white matter involvement, and MS has neuropsychologic features in common with PD, HD, and other subcortical diseases (Rao, 1986). Some overlap of dementia syndromes can indeed be expected in view of the multitude of connections between cerebral areas subserving higher functions. However, recognition of the white matter category can have heuristic value in the elucidation of differential brain–behavior relationships in the dementias.

Table 2 presents a brief and highly theoretical summary of selected features of the dementia syndromes discussed here. The list is not exhaustive, but represents a distillation of common signs that are relatively easy to detect. We propose these distinctions in an effort to simplify a confusing area and to stimulate further research.

NORMAL AGING AND WHITE MATTER

Any discussion of dementia naturally leads to a consideration of aging. Many observers have noted that some of the changes of "normal" aging appear to be

quite similar to the problems encountered in subcortical dementia syndromes—slowness, forgetfulness, poor concentration, irritability (Albert, 1978; Cummings and Benson, 1983). The changes of aging, of course, do not impair the functional status of individuals to the degree that dementia does (Kral, 1962), but the qualitative similarities are intriguing. It is not unreasonable to speculate that loss of or change in subcortical gray or white matter might underlie some of the mental status changes of senescence.

The nature of senescent brain alterations is not entirely clear, and much literature focuses on age-related cortical cell loss as a normal phenomenon (Anderson et al., 1983). However, some have pointed out that white matter shows more age-related degeneration than does gray matter (Creasey and Rapoport, 1985). This attrition may be a result of changes in the chemical composition of myelin (Malone and Szoke, 1985) or may be attributed to subtle ischemic changes that often appear on MRI scans (Kertesz et al., 1988).

We speculate that some of the mental status changes of normal aging may be due to alterations in white matter. Evidence from laboratory animals suggests that aging produces a slowing of conduction time between nucleus basalis and cortex, a decrement most easily explained by a deficiency of subcortical myelin (Aston-Jones et al., 1985). A similar process may occur in human aging.

WHITE MATTER DEMENTIA AND ATTENTION: A HYPOTHESIS

Attentional disorders have been described as a "frontier in neuropsychology" (Geschwind, 1982). As a fundamental function of the human brain, attention—the ability to screen out irrelevant stimuli and concentrate on significant material—is critical to the performance of all of the instrumental functions that make possible effective human existence. Attentional dysfunction may be the most prominent neurobehavioral deficit in the white matter dementias. Other important deficits may also be a direct result of white matter disease, but we believe that attentional disorders merit particular consideration.

Attention is a function of the integrity of a variety of brain areas. The reticular activating system (RAS) is a key component in this network of structures, arising from the brainstem and ascending to thalamus, limbic system, basal ganglia, and cerebral cortex. Convincingly linked with the maintenance of arousal, the RAS also plays a role in attentional function (Mesulam, 1985). Another important structure in this network is the prefrontal cortex, an area known to be involved with maintenance of attentional tone in posterior cortical areas (Mesulam, 1985). The phenomenon of *selective* attention, a more specific function reflecting cerebral dominance for unilateral attention in the right hemisphere (Heilman and Van Den Abell, 1980), is another portion of this system, but is less relevant for our purposes, as white matter dementias involve diffuse, not focal, damage.

White matter diseases, which are typically diffuse or multifocal, could disrupt the global attentional system at several points. White matter pathways in the

rostral brainstem, medial forebrain bundle, and other subcortical regions could be damaged, or alternatively, frontal lobe efferents projecting to posterior cortical regions could be disrupted, by any of the diseases discussed above. Such a "disconnection" need not be irreversible, but loss of or damage to myelin might substantially reduce conduction velocity in the white matter pathways and might provide a pathophysiologic explanation for the slowness so often described in the clinical literature. Although the broad outlines of the neuropsychology of attention can be constructed in this way, details are largely missing; white matter diseases might provide a useful clinical model for exploring this important function.

TREATMENT POTENTIAL

From the time of its inception, the concept of subcortical dementia has engendered theories about possible pharmacotherapy (Albert et al., 1974). It does appear plausible that diseases in which timing and activation are impaired—but cortical functions are intact—would be amenable to activating agents such as dopamine agonists, amphetamines, and cholinergic agents. White matter dementia seems to involve such a defect in activation. Any therapeutic regimen that activates cortical regions would be reasonable and might indeed have a greater chance for success than in a subcortical dementia with nuclear cell loss.

Another aspect of white matter dementia appears to be promising. Myelin is critical for normal neuronal function, but loss of myelin may not be as significant as cell loss; diseases in which myelin is solely or preferentially damaged may be amenable to interventions that restore the integrity of the myelin sheath. We are currently following our toluene abusers to assess whether any reversibility is possible in that syndrome after abstinence is achieved. It has been noted above that alcoholic dementia can be improved after abstinence, perhaps because of remyelination in the absence of alcohol's toxic effect. Spontaneous improvement in MS, which is often seen clinically, may lead to research on agents that can enhance remyelination. Other intriguing reports describe reversal of white matter ischemic changes following treatment of hypertensive encephalopathy (Fisher et al., 1985), improvement in ADC with azidothymidine (Yarchoan et al., 1988), and clinical recovery after ventriculoperitoneal shunting in NPH (Adams et al., 1965). Presumably, a pure myelin disease should not permanently damage neurons if the pathologic process can be reversed or arrested.

SUMMARY

Dementia is a diverse neurobehavioral problem with many manifestations; the expression of each patient's clinical profile depends on the various areas of damage and preservation. White matter dementia appears to represent a rather consistent syndrome of impairment that is distinct from both the cortical and

subcortical dementias. Given the relatively specific neuropathology of white matter diseases, it would appear that useful studies exploring the link between myelin damage and dementia could be conducted. MRI offers a sensitive and useful means of pursuing clinical studies in these patients. A particularly important aspect of these diseases may be the opportunity to delineate the role of attentional disturbances in neurobehavioral disorders.

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