Commentary

Dementia in Multiple Sclerosis: Why Is It Rarely Discussed?

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Abstract

Cognitive deficits in multiple sclerosis (MS) have been well studied in decades of MS research. Severe deficits are acknowledged, but the frequency is minimized in the literature, and there is a striking lack of discussion of the presence of a dementia state in MS. Possible reasons for this omission are discussed, along with an argument to define the dementia state and to provide terminology that will be palatable to patients.

Keywords: Multiple sclerosis; Dementia; Professional issues

Cognitive deficits were among the earliest symptoms described in patients with multiple sclerosis (MS). Dr Friedrich von Frerichs first cited MS-related cognitive impairment in 1849, 25 years after the disease’s initial clinical description. Charcot (1877) wrote that among MS patients there is “marked enfeeblement of the memory, conceptions are formed slowly and intellectual and emotional faculties are blunted in their totality.” Despite multiple early accounts of MS as a disease commonly affecting cognition, reports of the prevalence of cognitive impairment in patients with MS were mixed over the following century. The waning appreciation of the cognitive impact of MS is often attributed to a report by Cottrell and Wilson (1926) indicating that “after careful observation,” only 2 of 100 patients with “disseminating sclerosis” showed “any signs of actual intellectual deterioration” (p. 24). This perception of impaired cognition as a rarity in MS persisted through much of the 20th century, and was reiterated by Kurtzke (1970) in his paper describing the observed frequency of various neurologic symptoms in MS using the Disability Status Scale. In this work, Kurtzke reported that approximately 5% of patients with MS had cognitive deficits. These claims were likely fueled by the identification of MS as a white matter disease, and lack of appreciation of both the gray matter damage in MS and the role of white matter in cognition.

In the 1980s and 1990s, the presence, nature, and prevalence of cognitive deficits in MS became a burgeoning area of systematic scientific investigation. Studies demonstrated that cognitive deficits are apparent in at least 43% of individuals with MS within the community (Rao, Leo, Bernardin, & Unverzagt, 1991), with notably higher prevalence in clinic samples. Following decades of research, the typical nature of MS-related cognitive deficits has been elucidated, though researchers often comment on the variability in the extent and nature of these impairments. There is general agreement in the literature that the cognitive deficits in MS most commonly involve slowed processing, memory impairment, difficulties with complex attention/working memory, impairments in aspects of executive functioning and, at times, deficits in aspects of visuospatial skills. It is also generally agreed that the duration of MS is a poor indicator of the presence of cognitive deficits, the severity of deficits is often minimally related to the degree of physical involvement, and cognitive deficits are minimally related to common imaging findings such as white matter burden. Secondary progressive MS is typically associated with more significant cognitive impairment than other forms of MS, and once present, unless developed during an exacerbation, the cognitive deficits tend not to remit and may slowly progress over time. Rarely discussed in the literature, however, is patients who would meet generic criteria for dementia (e.g., DSM-IV, ICD-9 and -10, or “major neurocognitive disorder” in DSM-V) due to their MS-related cognitive impairments. When mentioned, statements that severe cognitive deficits or dementia in MS are “rare” or “uncommon” tend to be unreferenced, and the prevalence of dementia in MS is uncertain.
I am aware of only one paper which examined the prevalence of dementia (retrospectively) in a previously described sample. In describing these findings, Benedict and Bobholz (2007) indicate that 22% of the patients in their 2006 study (Benedict et al., 2006) met their criteria for dementia (i.e., impairment > 2 SD below the mean on at least one memory test, impairment > 2 SD below the mean on at least one neuropsychological test in another domain, and impairment in vocational status). They describe the cognitive deficits in these patients as virtually always including memory impairment (though part of the criteria) and cognitive slowing. Especially given the surprising lack of studies on this topic, this paper is valuable in providing some description of the prevalence and nature of dementia in MS, though it is limited, particularly in regard to the definition of functional impairment (i.e., limiting this to “vocational impairment”).

At times the cognitive deficits in MS have been referred to as a “subcortical dementia” (e.g., Rao, Leo, Bernadin, & Unverzagt, 1991) or “white matter dementia” (e.g., Filley, 2012), though the application of these labels has been mostly for the purpose of characterizing the nature of the deficits, rather than describing the impact of the deficits on one’s functional capacity. At other times, the term “dementia” has been used interchangeably with “cognitive impairment,” or to identify patients who had more notable deficits, though again, without consideration of the functional impact. For example, Mahler and Benson (1990) elaborate on appropriate use of the term “dementia” in MS: “the term cognitive dysfunction may be used when deficits involve only one or two areas; more extensive dysfunction deserves the term dementia” (p. 96). This selective yet loose use of the term is in very striking contrast to how the term is used in the best characterized dementia syndromes such as Alzheimer’s disease (AD). In AD, very specific and evolving criteria have been proposed to distinguish those patients who have cognitive deficits that do not meaningfully impact their daily functioning (i.e., mild cognitive impairment, MCI) from those who have become functionally impaired due to their cognitive deficits (i.e., dementia). Given that the concept of dementia is nearly absent from the MS literature, it is not surprising that the concept of MCI in MS is also largely missing (Devere, 2011). However, the distinction can be important in regard to recommendations for daily support for the patient and appropriate treatments, in addition to providing criteria for selection into early intervention studies and research outcomes/endpoints.

There are likely numerous reasons why the term “dementia” is so strikingly scarce and avoided in MS. First, “dementia” is often thought of as being associated with aging or the aged and is often used among lay people as being synonymous for AD (Longley, 2007). This alone may make the term unpalatable for many middle-aged people who may have recently had active careers and are paying off mortgages, raising young children, and still trying to run a household. It is a killer of hope for the patients and caregivers for whom management of these issues is an endeavor that potentially lasts for decades, and in patients who may also be contending with notable physical limitations in a very dynamic and unpredictable disease.

Reluctance in assigning the term dementia to younger adults is not exclusive to MS. For example, in HIV, the term is used (i.e., HIV-Associated Dementia), yet still in a much more conservative and restricted way than with Alzheimer’s disease. Evidence for this comes from some of the literature examining the impact of cognitive deficits on various functional tasks in HIV. For example, several studies report on the relationship between impaired driving skills or unemployment status and cognitive dysfunction in in “nondemented” patients with HIV (e.g., Heaton et al., 1994; Marcotte et al., 1999). In Alzheimer’s disease, if a patient’s employment status and driving abilities have been affected by their cognitive deficits, they would likely be considered to have a dementia. In the MS literature, the impact of cognitive deficits on driving and work has also been studied. In fact, cognitive impairment has been identified as one of the leading predictors of occupational disability (Larocca, Kalb, Scheinberg, & Kendall, 1985; Strober et al., 2012) and driving impairment (Akinwuntan et al., 2013; Badenes et al., 2014). With the exception of the Benedict and Bobholz (2007) paper, these patients are not identified as either “demented” or “nondemented;” rather, the possibility of dementia is not considered at all.

Another factor which likely contributes to the lack of identification of a dementia state in MS is the growing and intense distaste for the term itself. The term “dementia” is first attributed to Aulus Cornelius Celsus in the first century CE. Although the Latin root of the word means “madness” or “without mind,” from its earliest recognition, the label was not necessarily intended as derogatory, but was associated with an appreciation of the need to protect the affected individual. Over time, however, the pejorative connotation has taken hold, and for our patients, likely overshadows the intended medical meaning. Indeed, the current lay perception of the term “dementia” is that the patient is exhibiting erratic and disturbing behaviors. As has been pointed out by others arguing against perpetuating the use of the term (Jellinger, 2010), the online Merriam Webster dictionary provides the following definition of dementia: “having or showing a very abnormal or sick state of mind,” and offers the following synonyms: batty, bonkers, brain-sick, certifiable, crackbrained, crackpot, crazed, deranged, loony, kooky, lunatic, maniacal, psycho, unbalanced, and unhinged, among others.

When used judiciously, a diagnosis of dementia in MS can be valuable in clinical practice. It may help family members appreciate the severity of a patient’s deficits and need for support, especially when the patient may not be particularly physically compromised, appears well, and on brief and casual interactions may seem cognitively more intact than s/he actually is. Services can often be more readily obtained with such a diagnosis, and deserving patients may more easily obtain disability services. Use of the term may also result in the treating physician to pause when considering treatment options. In MS, this is particularly relevant, as
treatment options have greatly expanded in MS in the past several years, including some highly effective treatments with potentially devastating adverse effects. Patients with MS-related dementias may be asked to consent to treatments when their ability to reason through the decision independently is potentially compromised, and a diagnosis of dementia may lead to more thoughtful consideration about when a proxy decision maker should be involved. This is not to say that a patient meeting criteria for dementia is categorically unable to consent to treatment, but would suggest that capacity to consent should be considered along with thoughtful determination of any additional steps that may need to be taken to ensure reasonable participation in the decision-making process (Basso et al., 2010).

In regard to research, well-defined criteria for neurocognitive disorders have equal importance, though they thus far has been lacking in MS research. Such criteria are critical for a fuller understanding of the study groups in any investigation of cognition in MS, and lack of such criteria may provide one explanation for discrepant study findings. Diagnostic criteria can also be important for identifying appropriate target groups for interventions, providing potential study outcomes/endpoints, and, more simply, for ease of communication. Given the significant lack of research in this area, the influence of important demographic and disease factors on the development of a dementia state of MS is unknown, including age of MS onset, duration of disease, MS subtype, degree of physical involvement, imaging data and other biomarkers of MS, genetic factors, family history, medical comorbidity, lifestyle factors such as smoking, and treatment history, among other factors. Measures to best assess functional abilities in patients with MS also need to be identified, potentially adapted for MS, or developed.

Because of the value of the theoretical construct of dementia for clinical and research purposes, the dementia state in MS should be defined and distinguished from less impairing cognitive deficits in MS. Although there are benefits to continuing the term “dementia,” the growing incongruence of the term and concept cannot be ignored. In reviewing arguments for abandonment of the term altogether (Jellinger, 2010; Kurz & Lautenschlager, 2010; Lau, 2011), it appears necessary for us to appreciate how the term is perceived by our patients, and accept that we must develop a new shorthand for communication. Given the nearly complete lack of research in this area, MS is well poised to adopt new terminology without any concern of discrepancy between existing literature and that which may follow as a result of new terms.

It is appreciated that replacing the term “dementia” may ultimately be a short-lived prospect. Terminology for conditions affecting intellect, cognitive capacity, psychological well-being, or behavioral control seems ultimately doomed for pejorative misuse in the vernacular. Consider that terms such as “imbecile,” “idiot,” and “moron” were once medical terms that became corrupted over time. It would be unthinkable in this day to refer to a patient as a “moron” or “imbecile.” More recent examples include referring to one with an intellectual disability as “retarded.” The word “retarded” should be relatively benign, were it not for the socially demeaning connotation which has been conferred upon it. For any term replacing that of “dementia” to retain its medically intended meaning would likely require a shift in social values and sensitivities, which does not appear forthcoming in the immediate future. Because of this, one could argue that descriptive terms that can be shortened to non-catchy acronyms may fare best in regard to avoiding lay corruption (e.g., varying degrees of MS-Associated Neurocognitive Disorder).

In sum, the presence, prevalence, and nature of dementia in MS has been ignored for far too long. The one prevalence study of which I am aware that suggests that 22% of clinic patients with MS may have a dementia. This certainly suggests that a dementia state in MS is not “rare” enough to be dismissed. MS-relevant criteria that can capture the varying degrees of cognitive and functional impairment need to be developed using terminology that is appropriately descriptive and palatable, and as a starting point, for example, could include the DSM-V criteria for neurocognitive disorders appropriately adapted for use in MS. These efforts will be essential to facilitate research in this area, and to provide patients with diagnoses that can be helpful in providing necessary services.

References


