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Relationships between information processing, depression, fatigue and cognition in multiple sclerosis

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Abstract

The neurobehavioral sequelae of multiple sclerosis (MS) consistently include fatigue, depression and cognitive dysfunction with slower processing figuring prominently. However, processing speed is often confounded with accuracy and the relative contributions of depressed mood and fatigue in influencing speed of processing are difficult to quantify. Therefore, there were three objectives in this study. First, compare processing speed in MS and healthy controls under conditions in which accuracy is not confounded with speed; second, determine the relationships between information processing speed and cognition; third, determine the contributions of clinical depression and fatigue in mediating these relationships. Forty-eight participants with confirmed MS participated. The findings suggested that slower processing was correlated with higher levels of depressed mood, fatigue, lower verbal fluency, fewer words and digits recalled and poorer recall of visual-spatial information. Depression and physical fatigue had the greatest influence on the association between processing speed and more effortful tasks (e.g., immediate word recall and word list learning). Current findings extend previous work by using a more sensitive measure of processing speed and by quantifying the relative contributions of depression and fatigue in mediating relationships between processing speed and cognition.

Keywords: Multiple sclerosis; Information processing speed; Depression; Fatigue; Prefrontal cortex

1. Introduction

The neurobehavioral sequelae of multiple sclerosis (MS) consistently include fatigue, clinical depression and cognitive dysfunction (DeLuca, Barbieri-Berger, & Johnson, 1994; DeLuca & Johnson, 1993; Diamond, DeLuca, Johnson, & Kelley, 1997; Krupp, Christodoulou, & Schombert, 2005; Rao, Huber, & Bornstein, 1992). Major depression occurs in MS at three times the prevalence rate reported for psychiatric comorbidity in community-based samples, and it also exceeds that for other disabling neurologic disorders (Schiffer & Babigian, 1984). Generally, the literature shows

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that depression is reported at a rate of 27–54% in MS (McGuigan & Hutchinson, 2006; Minden & Schiffer, 1990; Nocentini, 2006).

1.1. Mechanisms mediating depression in MS

Depression in MS has not been linked to a family (Sadovnick et al., 1996) or individual history of affective disorder pre-dating neurological symptoms (Minden, Orav, & Reich, 1987) or disease activity, duration, severity, or type of MS (Feinstein & Feinstein, 2001; Huber, Rammohan, Bornstein, & Christy, 1993; Minden et al., 1987; Rabins et al., 1986; Shnek, Foley, & LaRocca, 1997). Benedict, Carone, and Bakshi (2004) have reported that in MS cerebral atrophy and lesion burden are correlated with mood, cognitive dysfunction and personality disturbances and that both euphoria and disinhibition are predicted by atrophy (with executive dysfunction thought to mediate this relationship). However, there could be an alternative explanation. That is, cerebral atrophy is associated with greater cognitive and physical disability which would, therefore, cause more emotional distress and depression. Relatedly, in healthy participants, a reduction in perfusion of dorsolateral prefrontal cortex (DPC) appears to be related to the severity of depressive symptoms, psychomotor slowing, and cognitive impairment (Grady, 1999; Mayberg et al., 1999), in addition to structural changes in gray matter volume within the prefrontal cortex, the hippocampus, and the striatum (Fossati et al., 2004).

1.2. Cognition in MS

On recognition memory, incidental recall, verbal or visual recall (Arnett, Higginison, Voss, Wright, et al., 1999) and Digit Span (Wechsler Adult Intelligence Scale-Revised (WAIS-R): Wechsler, 1981) some studies have reported no differences in performance between MS and healthy controls (DeLuca & Johnson, 1993). However, some studies have shown differences (Beatty, Blanco, Wilbanks, Paul, & Hames, 1995). Diamond et al. (1997) using the California Verbal Learning Test (CVLT) reported that individuals with MS tended to use a less efficient serial versus semantic clustering encoding strategy compared to stroke patients and healthy controls.

Information processing speed is generally slower in individuals with MS versus healthy controls (DeLuca, Johnson, & Natelson, 1993; DeLuca & Johnson, 1993; Demaree, DeLuca, Gaudino, & Diamond, 1999; Diamond et al., 1997; Grossman, Robinson, & Onishi, 1995; Kail, 1998). Using the Paced Auditory Serial Addition Test (PASAT) (Gronwall, 1997) or a visually based computer version of the serial addition task, no disproportionate, modality-specific impairments in the MS group were reported (Johnson, DeLuca, & Natelson, 1996). Similar findings have been reported by Diamond et al. (1997), with slower processing thought to be particularly mediated by impairment in the operation of the central executive. Slower reaction and memory scanning times have been reported in both MS and healthy control groups using the Sternberg Memory Scanning Test. This task, however, eliminates the motor response component with the results suggesting that slower processing speed in MS is independent of slowed motor ability (Rao, Leo, Haughton, & St. Aubin-Faubert, 1989).

1.3. Fatigue and cognition in MS

Fatigue is a prominent symptom in MS and it has been differentiated on the basis of subjective versus objective or "cognitive fatigue" and described as a decline in cognitive performance during a task or across a testing session (Krupp & Elkins, 2000; Paul, Beatty, Schneider, Blanco, & Hames, 1998). Some researchers have reported cognitive fatigue in MS (Krupp & Elkins, 2000; Kujala, Portin, Revonsuo, & Ruutainen, 1995), while others have not (Beatty et al., 2004; Johnson, Lange, DeLuca, Korn, & Natelson, 1997; Paul et al., 1998). Moreover, studies examining short-term memory (Johnson, DeLuca, Diamond, & Natelson, 1998), attention and working memory (Bailey, Channon, & Beaumont, 2007), verbal fluency (Rao, Leo, Bernadin, & Unverzagt, 1991), and verbal memory (Paul et al., 1998; Schwartz, Coulthard-Morris, & Zeng, 1996) have failed to find a relationship between subjective fatigue and cognitive performance. While Krupp and Elkins (2000) found a decrement in MS cognitive performance compared to healthy controls over a 4-h testing session, self-reported fatigue was unrelated to the pattern of decline. In the Johnson et al. (1997) study, which induced fatigue, MS performance on the PASAT improved over repeated trials despite increased levels of self-reported fatigue. Speculation regarding the mechanisms mediating fatigue have included CNS and immune dysregulation (Krupp et al., 2005) and reduced glucose metabolism in the frontal cortex and basal ganglia (Roelke et al., 1997) with presumed impaired interaction between dorsolateral-prefrontal and motor circuits (Alexander, Crutcher, & DeLong, 1990).