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A case of spatial neglect dysgraphia in Wilson's Disease

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Abstract

We report here on a single neuropsychological case study of a young girl, KH, who presented with Wilson's Disease (WD) associated with a peripheral spatial neglect dysgraphia without major problems in the standard clinical tests of spatial neglect. Few studies have demonstrated a visuospatial deficit in WD and to date there has been no report of neglect syndrome arising from WD. However, recent studies have demonstrated that neglect is frequently associated with brain damage including the primary site of WD, the basal ganglia. KHs writing abilities were evaluated just after her admission to the rehabilitation department and 6 months later. The baseline evaluation demonstrated that KH had neglect dysgraphia with verbal stimuli (e.g., words or sentences) although her deficit was less evident in drawing multiple geometric shapes. Six months after the initial evaluation, KH showed evidence of neglect dysgraphia only when writing was associated with a secondary memory task. KHs writing performance is discussed with reference to previous cases of spatial neglect dysgraphia and in the context of spatial neglect. We suggest that the asymmetry between verbal writing and nonverbal drawing disturbances was caused by different attentional loads.

Keywords: Wilson's Disease; Hepatolenticular degeneration; Spatial dysgraphia; Unilateral neglect; Attentional load

1. Introduction

Wilson's Disease (WD), also known as progressive hepatolenticular degeneration (Wilson, 1912), is an autosomal-recessive disorder of copper metabolism characterized by copper accumulation in different tissues, especially in the liver and the brain. The clinical manifestations of WD are highly variable and patients usually present hepatic, neurological and/or psychiatric disturbances (Ala, Walker, Ashkan, Dooley, & Schilsky, 2007). The mean age of onset of the neurological features of the disease is usually in the second to third decade of life. In Europe, the prevalence rate of WD is evaluated at 12–29 cases per million (Chu & Hung, 1993), but this rate is probably underestimated as a consequence of the varied clinical manifestations of the disease (Gitlin, 2003; Prashanth, Taly, Sinha, Arunodaya, & Swamy, 2004). With the use of copper chelator agents, to promote copper excretion from the body, a reduction in the clinical symptoms is expected; however, the degree of recovery depends on the subtype of WD, the severity of the disease, the elapsed time since onset, and appropriate management of the disease (Brewer, 2000; Brewer & Askari,

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2005; Gitlin, 2003; Roberts & Schilsky, 2003). Sometimes, treated patients may have permanent neurological deficit because of irreversible neuronal cell loss. Nevertheless, even patients with a severe form of WD may have a good outcome (Prashanth et al., 2005).

Copper accumulation in the brain causes several abnormalities. Structural brain magnetic resonance imaging (MRI) studies show frequent bilateral involvement of the basal ganglia (particularly the putamen, the caudate head, the ventral thalamus and the dentate nucleus), the brainstem, and the cerebellum, as well as atrophy of the cortex and of the cerebral white matter (Alanen, Komu, Penttinen, & Leino, 1999; King et al., 1996; Page et al., 2004; Sinha et al., 2006; Walter et al., 2005). Supporting the notion that the basal ganglia are involved, the neurological features of the disease include movement disorders such as motor coordination deficit, slowness of voluntary limb movements, tremor, dystonia, dysarthria, writing tremor (Oder et al., 1991) and fine-motor disturbances (Hermann, Villmann, Grahmann, Kuhn, & Wagner, 2003). Signs of cortical impairment in WD, in contrast, have been reported more rarely. However, some MRI studies have shown signal abnormalities in the left and/or right frontal and parietal regions (Carlson, Al-Mateen, & Brewer, 2004; Hedera, Brewer, & Finck, 2002; Sener, 1997; Turk-Boru, Kocer, Alp, Gumus, & Gumus, 2003). For example, Hedera et al. (2002) described a 13-year-old male with WD who exhibited leukoencephalopathy early in the course of the disease. MRI showed increased signal intensities in the basal ganglia and throughout the cortical/subcortical white matter in the frontal lobes, which later extended to the parietal and occipital lobes. More recently, Carlson et al. (2004) reported on atypical childhood WD in a young child, with a frontal lobe syndrome associated with parietal and bifrontal T2-weighted signal abnormalities. Unfortunately, these studies did not report any neuropsychological details on the patients.

Cognitive dysfunction has been reported in WD (Collie, 2005; Tarter & Van Thiel, 2001), which is considered as a subtype of subcortical dementia because neurological deterioration is progressive without treatment and there is often an associated cognitive decline (Cummings, 1986). However, there is no consensus about the frequency and severity of the cognitive deterioration (Rathbun, 1996; Seniow, Bak, Gajda, Poniatowska, & Czlonkowska, 2002). Moreover, no significant correlation has been found between the level of copper toxicity and the neuropsychological deficits (Rathbun, 1996; Seniow et al., 2002). Nevertheless, different cognitive impairments have been reported in patients with the neurological form of WD. Of these deficits, slowed-down motor activity (e.g., as tested with the Purdue pegboard or finger tapping) appears to be the most sensitive to the pathophysiology of WD even before the onset of overt symptoms (Portala, Levander, Westermark, Ekeselius, & Knorring, 2001; Rathbun, 1996). Deficits may affect other cognitive domains, including visuospatial abilities, memory and abstract reasoning. Similar impairments have been described following strokes in the basal ganglia (Hochstenbach, van Spaendonck, Cools, Horstink, & Mulder, 1998) or corticobasal degeneration (Graham, Bak, & Hodges, 2003).

Patients presenting the neurological form of the disease perform worse on Benton's visuospatial test than control participants (Dening & Berrios, 1989; Seniow et al., 2002) and have problems with visuospatial analysis and construction (picture completion, block design). Memory deficits observed in WD are similar to those in other frontal dysfunctions: patients are able to store new information but have difficulties searching and retrieving information in their memory. Finally, some studies have also reported executive deficits such as short-term memory deficits (forward and backward digit span) and impulsivity (Portala et al., 2001). WD patients also find the alternate condition of the Trail Making Test difficult, suggesting that they have problems allocating attentional resources to simultaneous tasks (Medalia, Isaacs-Glaberman, & Scheinberg, 1988; Tarter, Switala, Carra, Edwards, & Van Thiel, 1987). Moreover, it has been shown that most neuropsychological impairments may be present well before the occurrence of the classic neurological symptoms of the disease (Tarter et al., 1987).

Copper-chelating therapy may also reduce the functional and cognitive impairments in advanced WD patients (Prashanth et al., 2005; Rosselli, Lorenzana, Rosselli, & Vergara, 1987). Rosselli et al. (1987) reported a case of WD associated with cognitive deterioration (memory deficit, visuospatial construction) whose performance on neuropsychological tests improved after 7 months of D-Penicillamine treatment. However, few studies deal with the functional and cognitive functional outcome of WD patients.

Here we report on a single neuropsychological case study of a WD patient, KH, who showed a variety of different cognitive deficits including neglect dysgraphia without major problems on the typical clinical tests of spatial neglect (e.g., canceling, line bisection, copy task). Visuospatial deficits have previously been reported in patients suffering from WD (Seniow et al., 2002; Wang, Hoosain, Yang, Meng, & Wang, 2003): line orientation judgment, visual form discrimination and unfamiliar face recognition were found to be impaired in WD patients in comparison with normal