Neuropsychological Support for the Concept of White Matter Dementia

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INTRODUCTION

Advances in the diagnosis and treatment of cognitive disability depend on an understanding of the neurologic basis of cognitive disorders. Our group has focused on dementia as a syndrome of cognitive dysfunction that can be used to examine the organization of cognition in the brain. In particular, we have chosen to focus on the cerebral white matter, which has heretofore been largely overlooked in the study of brain-behavior relationships.

Dementia resulting from cerebral white matter involvement has been termed white matter dementia (WMD). Among the proposed features of WMD is a profile of retrieval deficit in declarative memory, similar to subcortical dementia, and preservation of procedural memory, similar to cortical dementia. This study was conducted to investigate the concept of WMD by examining specific neuropsychological characteristics of subcortical diseases affecting primarily cerebral white or gray matter.

METHOD

Participants. Sixteen patients with multiple sclerosis (MS), 16 patients with Huntington's disease (HD) and 16 normal controls (NC) participated in this study. The MS patients all had the relapsing-remitting subtype and had either never used any immunomodulatory medications (e.g., Avonex, Betaseron, Copaxone) or used them for less than 1 year. The HD patients were all diagnosed on the basis of genetic testing and were demonstrating movement disorder, personality disorder, or cognitive decline. The MS and HD groups had been diagnosed for an average of 8.5 and 2.5 years, respectively. Participant characteristics are described in Table 1.

Table 1.
Characteristics of the MS, HD and NC Groups

Characteristic	MS M	MS SD	HD M	HD SD	NC M	NC SD
Age (yrs)	46.2	(4.9)	44.6	(8.0)	43.9	(8.2)
MMSE	29.3	(1.0)	28.4	(1.7)	29.9	(0.5)
Education (yrs)	15.6	(2.0)	14.6	(3.1)	16.2	(1.6)
Gender (M/F)	(3/13)		(9/7)		(1/15)	

Neuropsychological Tests.

Rotary Pursuit (RP): This is a test of procedural learning and memory and is shown in Figure 1. It involves the learning of repetitive motor sequences, which depends heavily on the basal ganglia.

Mirror Tracing (MT): This is a test of procedural learning and memory, and is shown in Figure 2. It involves the learning of new mappings between visual cues and motor responses, which depends on posterior parietal cortex and premotor cortex.

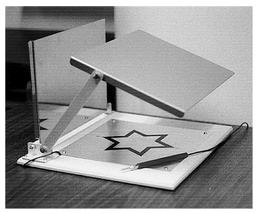
Nine-Hole Peg Test (NHPT): This is a test of manual dexterity. In this study, it was used as a global measure of upper extremity movement disorder.

Neuropsychological Tests. continued

California Verbal Learning Test (CVLT): This is a test of verbal memory. Performance is evaluated in terms of standard scores that are based on normative data stratified by age and gender.

Figure 1. Rotary Pursuit Task

Figure 2. Mirror Tracing Task



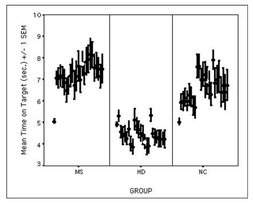
RESULTS

Rotary Pursuit

See Figure 3. The MS, HD, and NC groups were tested at mean rotations per minute of 22.7 s (SD = 6.8), 21.0 s (SD = 10.4), and 29.5 s (SD = 5.7). The groups differed significantly from each other, F (2, 43) = 5.1, p < .05, with post-hoc Tukey HSD tests revealing that the HD group was tested at a slower speed than the NC group, p < .05. All 3 groups were well matched on initial time-on-target performance, with the MS, HD, and NC groups scoring means of 5.1 s (SD = 0.4), 4.9 s (SD = 0.3), and 5.0 s (SD = 0.6), respectively; these differences were not significant.

Time-on-target scores were analyzed in a repeated measures analysis of covariance (ANCOVA) with variables of group (MS, HD, NC), block (Block 1, Block 2, Block 3), and trial (8 trials per block); trials were nested within blocks. NHPT score was the covariate, to control for the effects of movement disorder. Results revealed significant differences among the three groups, F (2, 42) = 9.8, p < .001. Follow-up tests revealed that the HD group demonstrated less skill learning than the MS group as evidenced by a significant effect of group, F (1, 27) = 26.3, p < .001, and a significant interaction between group and trial, F (2, 196) = 2.0, p < .05. The interaction between group and block approached significance, F (2, 56) = 2.4, p = .10.

Figure 3. Rotary Pursuit Results



Mirror Tracing

See Figures 4 and 5. On MT Trial 1, completion time did not differ significantly between the 3 groups, with the MS, HD, and NC groups scoring means of 71.6 s (SD = 42.8), 98.6 s (SD = 59.7), and 65.25 s (SD = 21.8), respectively. However, the 3 groups differed significantly on mean errors made on Trial 1, F (2, 44) = 5.2, p < .01, MS = 29.9 (SD = 24.5), HD = 62.5 (SD = 50.2), NC = 26.3 (SD = 21.8), with post-hoc Tukey HSD tests revealing that HD group made significantly more errors than both the MS and NC groups, p < .05, the latter two of which did not differ significantly from each other.

Completion time scores and error scores were analyzed in separate repeated measures ANCOVAs with variables group (MS, HD, NC), block (Block 1, Block 2), and trial (5 trials per block; trials were nested within blocks. NHPT was the covariate, to control for the effects of movement disorder. There was a main effect of group on errors, F (2, 43) =5.1, p < .01, but not completion time.

Follow-up tests revealed that both the MS and HD groups demonstrated skill learning by tracing the star pattern progressively faster across blocks, F (1, 29) = 37.1, p < .001, and trials, F (4, 116) = 13.0, p < .001, and by making fewer errors across blocks, F (1, 29) = 46.0, p < .001, and trials, F (4, 116) = 7.7, p < .001. For both skill-learning measures, there were block x trial interactions, indicating that within-block improvement across trials decreased across blocks: for completion time, F(4, 116) = 8.8, p < .001; for errors, F (4, 116) = 8.4, p < .001.

There was no effect of group on completion time, but a main effect of group on errors revealed that the HD group made more errors than the MS group, F (1, 28) = 5.5, p < .05. Overall, the MS and HD groups improved similarly on Mirror Drawing as reflected by the lack of group x trial interactions for either completion time or errors and the lack of a group x block interaction for completion time. There was a significant group x block interaction for errors, F (1, 29) = 4.1, p < .05, indicating that the HD group improved more rapidly than the MS group from Block 1 to Block 2.

Figure 4. Mirror Tracing—Completion Time Results

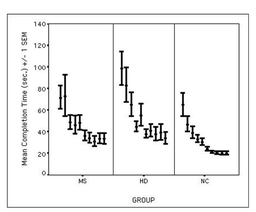
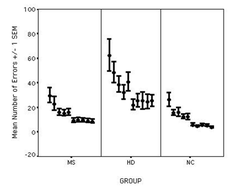


Figure 5. Mirror Tracing—Error Results



CVLT

See Table 2. Analysis of variance (ANOVA) on the CVLT indices demonstrated a significant difference among the 3 groups on LDFR, F (2, 45) = 8.0, p < .01, and discriminability, F (2, 45) = 9.1, p < .001. Post-hoc Tukey HSD tests revealed that the HD group scored significantly lower than the MS and NC groups on both variables. Both patient groups performed better on discriminability than on recall, indicating more difficulty with retrieval. This difficulty with retrieval is further reflected in the contrast between discriminability and LDFR standard scores.

Table 2.
Comparison of the MS, HD and NC Groups on the CVLT Standard Scores

CVLT Variable	MS M	MS (SD)	HD M	HD (SD)	NC M	NC (SD)
LDFR	-0.63	(1.26)	-1.69	(1.54)	-0.06	(0.85)
Discriminability	0.00	(0.63)	-0.88	(1.02)	0.13	(0.34)
Contrast (Discriminability – LDFR)	0.63		0.81		0.19	

CONCLUSIONS

- Compared to normal individuals, both MS and HD patients demonstrate a retrieval deficit in declarative memory.
- Only HD patients demonstrate a procedural memory deficit on a task that taps basal ganglia functioning.
- These data suggest that involvement of subcortical white and gray matter can be differentiated neuropsychologically.
- These results support the concept of white matter dementia as a distinct neurobehavioral syndrome.
- Implications for the care of individuals with cognitive disorders:
  - (a) Understanding the specific effects of neuropathologic patterns improves diagnosis, leading to earlier treatment.
  - (b) More effective rehabilitation of cognitive disorders and development of assistive devices.