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Verbal Memory Deficits in Multiple Sclerosis

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Abstract

The main objective of this work was to study memory impairments associated with multiple sclerosis (MS). A Spanish version of Rey Auditory-Verbal Learning Test (RAVLT), with a MS group (n=10 subjects) and a control group (n=10 subjects) was used. Different measures were obtained from the RAVLT: memory span, a learning curve, and curve of serial position of words. The results did not reveal differences between groups in memory span or learning curve, but significant differences were found in the curve of serial position. Absence of recency effect in the immediate form of RAVLT, and a effect of negative recency in the delayed form of RAVLT were seen in the MS group, but not in the control group. These results are discussed with reference to preservation of learning capacity and impairment of short term recall.

Multiple sclerosis (MS) is characterized by a wide range of clinical symptoms and neurological changes. Regarding the early clinical symptoms, large individual variability (Aranda, Martinez-Lage, Maravi, Gallego, De Castro, & Villanueva, 1991; Whitaker, 1984), the most frequent being paresis, paresthesia, visual impairment, and alterations in motor coordination. In more advanced stages, excretory, sexual, and psychological dysfunctions appear.

In neuropsychological studies the memory alterations are the most robust findings (Grant, McDonald, Trimble, Smith, & Reed, 1984; Rao, Hammeke, McQuillen, Khatri, & Lloyd, 1984; Rao, 1986). These results suggest that no problems in immediate memory capacity were found, but that there were systematic differences when learning and memory were combined in long-term tasks both with verbal and visual material. Finally, with respect to learning capacity, it was seen that MS patients learn more slowly.

In regard to the studies on memory in MS patients, the progression of these studies has followed two different lines. One of these has been to discover

a correlation between memory or neuropsychological damage and neurological variables measured by use of cerebral imaging techniques (Annzzola, Bevilacqua, Cappa, Faglia, Farina, Frisoni, Mariani, Pasolini, & Vignolo, 1990; Hubber, Paulson, Shuttleworth, Chakares, Clapp, Pakalnis, Weiss, & Rammohan, 1987; Pozzilli, Passafieme, Bernardi, Pantano, Incoccia, Bastianello, Bozzao, Lenzi, & Fieschhi, 1991, Rao, 1985; Rao, Leo, Haughton, Aubin-Faubert, & Bernardin, 1989). The second line of research has concentrated in describing the memory deficit and in studying the causes of the given deficit (Beatty, Goodkin, Monson, Beatty, & Hertsgaard, 1988; Caine, Bamford, Schiffer, Shoulson, & Levy, 1986; Litvan, Grafman, Vendrell, Martinez, Junque, Vendrell, & Barraquer-Bordas, 1988; Van der Burg, Van Zomeren, Minderhod, Prange, & Meijer, 1987).

Concerning the first line of investigation and the range of results extend from low or no correlation (Rao, 1985) to significant correlation between functional character of certain cerebral areas associated and neuropsychological deficits. Hubber et al. (1987) established a clear correlation between

level of dementia (intellectual deficit) associated with MS and atrophy of the corpus callosum. Ral et al. (1989), using NMR images looking at the total lesioned area (TLA), corpus callosum atrophy (SCC), and vestibular atrophy (VBR), found that TLA was the best predictor of memory or abstract/conceptual reasoning problems, while SCC best predicted the speed of processing. TLA and SCC, but not VBR, were independent of the age of the subject. Anzolla et al. (1990) classified their subjects according to whether a discrete or a diffuse demyelinized lesion was seen in the MRI, and encountered significant differences in concept formation, intelligence (as measured by the Raven), and verbal memory (texts) in favor of the discrete lesion group. Finally, Pozzilli et al. (1991), using SPET scanning in addition to NMRI, found a correlation between hypoactivity of the left temporal lobe and measures of word fluency and verbal memory [Rey Auditory-Verbal Learning Test (RAVLT)]. Additionally, while classifying the subjects into cognitively damaged and non-affected groups according to the neuropsychological test scores, Pozzilli et al.

found that the cognitively affected group showed lower frontal and temporal lobe activity than the cognitively intact and the control groups.

In regard to the nature and causes of memory deficits in MS, Caine et al. (1986), among others, have investigated the hypothesis on whether the memory problem is caused by using inadequate strategies to code and store information or possibly a problem of limited learning and information retrieval. Caine et al. results found that patients were using the same strategies as the controls to retain information but less effectively. In addition, they observed that MS subjects did not show recognition problems but did show recall deficits. This seems to indicate that the problem is one of retrieval more than of storage capacity. Van der Burg et al. (1987) found that the memory alterations of MS subjects were due to problems in acquisition of new information and that these results can not be explained by an attentional problem or by fatigue. In an attempt to relate the deficits of memory to a theory of memory such as that of working memory (Baddley, 1986), Litvan et al. (1988a, 1988b)

found that MS had a slower speed of processing and that this was due to a lower capacity of the temporary coding buffer, and this suggests that the MS patients had a damaged articulatory buffer. Beatty et al. (1988), in a different line of thought, conducted a study in which the different aspects of memory were evaluated in a sample of MS subjects classified as organic [Mini-Mental State Examination (MMSE) less or equal to 28] or not organic (MMSE, 28 to 30). They found differences in word fluency, speed of processing (measured with digits-symbols), visuo-spatial anterograde memory, verbal memory, and anterograde memory of images and events. In all cases, the performance of the <28 MMSE group was worse.

The main objective of the present study was to investigate possible alterations in memory associated with MS using a widely accepted test of memory combined with a more robust experimental design than previously used.

Method

Subjects

The experimental group (EG) was composed of 10

patients from both sexes, diagnosed with MS of different types and developments. Patients were able to complete a screening battery comprised of intellectual and emotional measures. There were no serious emotional alterations present (Godoy, Muela, & Perez, 1993; Muela, Perez, Garcia, Anguiano, Mendoze, & Godoy, 1992; Muela, Perez, & Godoy, 1992).

The control group consisted of 10 non-clinical subjects with similar demographic and sociocultural characteristics of the experimental subjects (EG). These demographic and sociocultural characteristics with the respective means, standard deviations, and ranges are found in table 1.

Insert Table 1 about here

Measures

A Spanish version of the Rey Auditory Verbal-Learning Test (RAVLT) (Rey, 1964) was used to measure memory. This test consists of a list of 15 common spanish words (cafe, luna, jardin, etc.) which were presented verbally to the subjects at a rate of one

word every two seconds. At the conclusion of the 15 word presentation subjects were asked to indicate the words they remembered, regardless of presentation order. This sequence was repeated five times. In a delayed condition, the subjects were asked to recite works remembered from the same list, which had been presented 15 minutes earlier.

Procedure

Each subject went through the above-described protocol, either in the Spanish Association of Multiple Sclerosis building or in his/her private residence in those cases where mobility was a problem. First, the RAVLT was given in its immediate form. Right after this, the subjects were given an automatized task of word superiority (as a distractor) and a test of visuo-graphic attention, in a counterbalanced order. Finally, the delayed form of the memory test was administered.

The list of works was presented by a Sony auditory tape recorder, model TCM-5000EV, while the experimenter noted the number and order of the words recalled by each subject. Scores were calculated from

the number of remembered words in each trial, the position each word had held in the list, and the difference between the total number of remembered words in the first and the delayed conditions.

Results

Two one-way analysis of variance (ANOVA) across the experimental and control groups, with the factors of age and cultural level were conducted. No significant differences were found.

For the memory task data, three ANOVAS were conducted with a mixed factorial design (experimental and control groups, within subjects repeated measures). Data in the first analysis were the scores from both groups in the first trial of RAVLT and the delayed form. Significant differences were observed in the within subject factor (immediate recall, delayed recall) [$F(1,18)=46.19$; $p<.01$], but in no other, which indicates that no difference in memory span exists with short term recall. (See Table 2)

Insert Table 2 about here

A second analysis was conducted to study the learning curve obtained across the five test trials. Significant differences were seen in the within subjects factor [$F(4,72)=45.6$; $p<.01$] but in no other. The posteriori comparisons, using the Newman-Keuls test, showed significant ($p < 0.05$) differences between all the trials, except between the third and the fourth. Data presented in table 2 shows that the progression in acquisition across the trials was similar in both groups, with a tendency to remember more in each subsequent trial.

A third analysis was conducted to investigate the effect of word position in the list, across the five trials in the immediate condition. A significant interaction effect was found [$F(2,36)=3.47$; $p<.05$], and significance differences in the within subject factor [$F(2,36)=3.98$; $p<.02$]. An analysis of the interaction showed significant differences in the control group between the different levels of the within subject variables [$F(2,36)=4.8$; $p<.05$]. Also in this group, the a posteriori comparisons analysis (Newman-Keuls test) showed significant differences between the

initial and the middle positions, and between the center and the final positions, but no significant difference between the initial and the last positions. In the experimental group, no significant differences were found in position. Table 3 present the different sources obtained in both groups in each of the positions. The data supports that while the effects of primacy and of recency appear in the control group, this effect is not seen in the experimental group.

Insert Table 3 about here

Additionally, for the delayed condition, two ANOVAS using a within subject design (serial position of word) were conducted for each group revealing significant differences were seen [$F(2,18)=3.81$; $p<.05$]. The a posteriori analysis (Newman-Keuls test, $p<.05$) revealed significant differences between level 2 and level 3 (central position > final position), which indicates a negative effect of recency (See table 3). The analysis of the control group data did not show any significant differences, which indicates that

the effects of primacy and of recency, which appeared in the immediate memory test, disappear after a delay with interference.

Discussion

Although other aspects of memory have also been reported to be affected (Beatty et al., 1988) this investigation has concentrated on verbal memory because, according to Rao (1986) this is variable of memory most deteriorated in MS patients.

No significant differences were observed between the experimental and control groups in memory span during short term recall, using the first trial of the RAVLT as a measure of span. Previous studies in this same line of research also found no differences, using either the digit subtest of the Wechsler Memory Scale (Litman et al., 1988), of the Wechsler Adult Intelligence Scale (Pozzilli et al., 1991), or the first test of the RAVLT (Litvan et al., 1988). (See also Rao's review, 1986.) In contrast, some researchers have found differences in this area (Van den Burg et al., 1987), the clearest differences being those seen in delayed recall of the list (Caine et al.,

1986; Litvan et al., 1988; Van den Burg et al., 1987).

Neither were there significant differences seen in the learning curves, nor as such, in the pattern of acquisition. These data are supportive of those obtained by Caine et al. (1986). The small differences found between MS and control subjects in the present study might have been due to fatigue, a very common symptom in MS. However, differences in learning curve data, but not in pattern of acquisition, have been reported (Litvan et al., 1988; Van den Burg, et al., 1987) and these were used to explain the memory deficit in MS. The absence of difference between our subjects indicates that those affected by MS and the controls benefit from.

Other important results were seen from the serial word position effect in the immediate test form. The controls clearly showed the serial position curve, just as is typically described in the literature. However, in the MS group, just as in the control group, the effect of primacy was demonstrated, although the effect of recency was not. These results indicate a problem in short term recall that could be explained by an

attentional deficit, as reported in the study by Callanan, Logsdail, Ron, and Warrington (1989) with subjects having lesions similar to those present in MS patients, or by Mari-Beffa et al. (1992), and Perez et al. (1992) with definitively diagnosed MS patients. In this last case, it is necessary to discard the possible influence of emotional alterations (depression or anxiety), which was the case in the present study (Godoy et al., 1993; Muela et al., 1992a, 1992b).

In the delayed test condition, a negative recency effect was found in the MS subjects. This effect can be explained by the absence of a recency effect in the immediate test. This can be explained as resulting from a low level of learning the last words, and this effect would have been produced by the period of delay with interference, which impeded reviewing of the material.

To summarize the principal alterations that appeared in the MS group relate to the serial position effect with words. However, it is important to note that the present study's results are limited by the small number of subjects and the heterogeneity of the

sample. Future research with larger, homogenous samples will help to understand and assess these phenomena.

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Table 1. Demographic and Sociocultural Characteristics of the Sample.

	EXPERIMENTAL GROUP N=10	CONTROL GROUP N=10
Age	X=36.2 SD=9.62 R=18-49	X=36.7 SD=12.80 R=18-52
Gender	2 M / 8 F	2 M / 8 F
Education Level*	X=1.8	X=1.8

* Primary = 1
Secondary = 2
Junior = 3
Sophmore = 4
Graduate = 5

Table 2

Total Number of Words Remembered in the Immediate and Delayed Trials.

	TRIALS					
	1º	2º	3º	4º	5º	DELAYED
MS	58	83	94	94	103	87
CONTROL	59	88	102	112	124	102

Table 3

Total Number of Words Remembered in Each Serial Position in Both Immediate and Delayed Trials.

	IMMEDIATE			DELAY		
	INITIAL	MIDDLE	FINAL	INITIAL	MIDDLE	FINAL
MS	162	148	123	29	38	21
CONTROL	183	133	174	39	34	31