

Caffarra, P., Durante, D, Previdi, P, Ghidoni, E, Malvezzi, L, Salmaso, D. (1999). Serial memory in Parkinson's disease. *The Italian Journal of Neurological Sciences*, 20(S), 119-119.

Objective. One aspect of recall that appears to be related to frontal lobe function is memory for temporal order. Patients with frontal lesions exhibit difficulty in remembering the order of the items in a list but are not impaired in tests of recognition or recall. In Parkinson's disease (PD) the motor component is prevalent but usually not isolated symptomatology. Basal ganglia and frontal cortex participate in a partially closed feedback loop system ("complex loop") which could explain the occurrence in PD of neuropsychological deficits more closely related to frontal dysfunction. The present study was designed to ascertain whether PD patients show poor memory in a serial verbal recall paradigm aimed at exploring different organizational mnemonic processing. **Materials and methods.** 20 non demented PD subjects and 20 controls (C) matched for age and school level, underwent neuropsychological examination (MMSE, PM47, Snoop tests, WCST, Digit and Corsi span, Logical memory) and experimental serial memory test consisting of seven high frequency disyllabic words displayed for 200 msec on a videoscreen at a rate of one every two seconds. Subjects were invited to recall as many words as possible in the same order they appeared until the criterion or at the end of 12 trials. Analysis was performed on a global index of storage (A) and indexes of organization as items organization, and interval-distance between words (D).

Results. No significant differences emerged on standard neuropsychological measures between PD and C, with exception of perseverative errors on WCST ($t=2.240$; $DF=21$; $p=0.036$). On experimental memory test PD needed more trials to reach criterion than controls ($t(29)=5.006$; $p=0.000$) and had more intrusions ($F(1,29)=7.144$; $p=0.012$). They were also significantly impaired on ITR ($F(1,29)=15.84$; $p=.000$) and on different measures of memory organization versus global mnemonic capacity, where significant interaction appears for A vs ITR ($F=15.84$; $p=.000$) and A vs D ($F=15.42$; $p=.000$). Clinical stage is also significantly involved on global retention and organizational memory processes, but not on number of repetitions.

Conclusions. Quantitative retention of information to be retained is not a complete measure of the processes involved in memory. PD patients exhibited poor performance not only on measures of global memory, but particularly on the ability to retain the sequential order of information, which is attained after several attempts. The ability to organize the items in serial order is resulted to be an index of mnemonic efficacy which may prove useful in monitoring the disease progression or drug-induced cognitive changes. This pattern seems to be related to the disease severity.

tions of the integrated area under the curve of Expanded disability status scores normalized to entry baseline (Δ EDSS AUC), Gd+ MRI and the neutralizing antibodies (NABs) to rIFN β -1b production (MxA) in 36 RR MS. **Results.** During the first 12 months of treatment levels of sICAM-1 increased and MMP-9 decreased significantly (Friedman $p < 0.0001$). After 12 months levels returned toward baseline. Levels of sICAM-1 and MMP-9 were significantly negatively correlated (Spearman $p < 0.05$). MMP-2 levels did not change significantly during the same period. During the second semester of the study Δ EDSS AUC was significantly reduced (Friedman $p < 0.05$). The percentage of patients with Gd+MRI decreased significantly ($p < 0.05$) in the first (33%), second (29%), third (20%) and fourth (28%) semesters of treatment compared to baseline (62%). The NAB+ patients (14%) tended to have lower sICAM-1 levels at the 9th month ($p = 0.07$), a higher MMP-9 activity at the 6th, 12th and 18th months ($p < 0.05$) and a greater Δ EDSS AUC in the 3rd semester ($p = 0.07$) of treatment in comparison with the NAB-. **Conclusions.** These results suggest that the effect of rIFN β -1b on the BBB may be mediated by changes in sICAM-1 and MMP-9.

96

VARIABILITY OF IL-1 RECEPTOR ANTAGONIST INDUCTION BY INTERFERON-BETA $_{1b}$: IMPLICATIONS FOR THE THERAPY OF MULTIPLE SCLEROSIS

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Objective. Several inflammatory cytokines contribute to the acute and chronic inflammatory phases of MS. The serum levels of the anti-inflammatory interleukin (IL) -1 receptor antagonist (IL-1ra) are normal in serum of relapsing remitting (RR) MS patients during remission phases but are increased during exacerbations or in response to IFN β treatment. We longitudinally measured the IL-1ra serum levels in MS patients receiving subcutaneous alternate day IFN β_{1b} treatment or no treatment at all. **Methods.** We studied 23 patients from Milan and Bari affected by definite RR MS. Sixteen of these patients were treated with IFN β_{1b} ; 7 untreated patients formed our control group. Plasma was obtained from all treated patients from Milan just before IFN β_{1b} treatment (time 0) and thereafter at 1, 3, 6 and 18 months and, in untreated patients at 0, 1, 3 and 6 months. Serum was obtained from all patients from Bari at time 0 and after 3, 6, 9 and 12 months. The levels of sIL-1ra were measured by a commercial double antibody ELISA. **Results.** Marked variability of IL-1ra levels was observed in serum of IFN β_{1b} -treated MS patients longitudinally evaluated. IL-1ra levels tended to increase after the beginning of treatment and correlated with the clinical response to the therapy. In untreated MS patients, IL-1ra serum levels randomly fluctuated over time. **Conclusions.** The induction of IL-1ra may contribute to the reduction of exacerbation rate shown in most IFN β_{1b} -treated MS patients. We are currently evaluating whether intersubject differences of this anti-inflammatory response induction results from the genetic background of patients and accounts for the variability of the IFN β_{1b} therapeutic action.

PP10

Movement Disorders II

97

CUTANEOUS ELECTROMYOGRAPHIC SILENT PERIOD IN PARKINSON DISEASE (PD)

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Objective. To evaluate if the duration of CSP may be a useful tool to follow the functional changes after L-dopa treatment in patients with idiopathic PD, vascular parkinsonism, and MSA. The effect of L-dopa therapy on this electrophysiological parameter and the relationship between the CSP and clinical symptoms were studied as well. **Patients.** We studied 30 patients assigned to three different groups. The group 1 consisted of 10 patients with a newly diagnosis of idiopathic PD; group 2 was composed of 10 PD patients with long time levodopa treatment; group 3 was composed of 10 patients affected by secondary parkinsonism. **Results.** Our data reveal that there is a direct relationship between the amelioration of symptoms due to levodopa treatment and the decrease of the duration of the CSP in patients with a new diagnosis of Parkinson's disease. The

same relationship was inconsistent in group 3. In group 2 the duration of CSP was reduced as well. **Discussion.** Because dopaminergic drugs modulate the duration of the cutaneous silent period through mechanisms acting mainly at basal ganglia, the changes seen in PD may reflect an indirect action at the spinal level decreasing excitation (or increasing inhibition) of spinal interneurons relaying these impulses to motor neurons; the final effect is a shortening of the cutaneous silent period. **Conclusion.** The cutaneous silent period changes after L-DOPA could be used as an adjunctive, safe and effective diagnostic tool to assess dopamine responsiveness of parkinsonian syndrome.

98

SERIAL MEMORY IN PARKINSON'S DISEASE

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Objective. One aspect of recall that appears to be related to frontal lobe function is memory for temporal order. Patients with frontal lesions exhibit difficulty in remembering the order of the items in a list, but are not impaired in tests of recognition or recall. In Parkinson's disease (PD) the motor component is prevalent but usually not isolated symptomatology. Basal ganglia and frontal cortex participate in a partially closed feedback loop system ("complex loop") which could explain the occurrence in PD of neuropsychological deficits more closely related to frontal dysfunction. The present study was designed to ascertain whether PD patients show poor memory in a serial verbal recall paradigm aimed at exploring different organizational mnemonic processing.

Materials and methods. 20 non demented PD subjects and 11 controls (C) matched for age and school level, underwent neuropsychological examination (MMSE, PM47, Stroop tests, WCST, Digit and Corsi span, Logical memory) and experimental serial memory test, consisting of seven high frequency disyllabic words displayed for 200 msec on a videorecorder at a rate of one every two seconds. Subjects were invited to recall as many words as possible in the same order they appeared until the criterion or at the end of 12 trials. Analysis was performed on a global index of storage (A) and indexes of organization as items organization (ITR) and interval-distance between words (D).

Results. No significant differences emerged on standard neuropsychological measures between PD and C, with exception of perseverative errors on WCST ($t = 2.240$; $DF = 21$; $p = 0.036$). On experimental memory test PD needed more trials to reach criterion than controls [$t(29) = 5.006$; $p = 0.000$] and had more intrusions [$F(1,29) = 7.144$; $p = 0.012$]. They were also significantly impaired on ITR [$F(1,29) = 15.84$; $p = .000$] and on different measures of memory organization versus global mnemonic capacity, where significant interaction appears for A vs ITR ($F = 15.84$; $p = .000$) and A vs D ($F = 15.42$; $p = .000$). Clinical stage is also significantly involved on global retention and organizational memory processes, but not on number of repetitions.

Conclusion. Quantitative retention of information to be retained is not a complete measure of the processes involved in memory. PD patients exhibited poor performance not only on measures of global memory, but particularly on the ability to retain the sequential order of information, which is attained after several attempts. The ability to organize the items in serial order is resulted to be an index of mnemonic efficacy which may prove useful in monitoring the disease progression or drug-induced cognitive changes. This pattern seems to be related to the disease severity.

99

THE MANAGEMENT OF THE LONG-DURATION RESPONSE TO LEVODOPA IN THE TREATMENT OF EARLY PARKINSON'S DISEASE

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Objective. The long-duration response (LDR) is a sustained antiparkinsonian benefit deriving from the prolonged administration of levodopa in Parkinson's disease (PD). However, the clinical relevance of this response has been often underestimated, since levodopa is usually scheduled without considering its long-duration effect. The aim of the present study was to investigate whether different regimens with levodopa may achieve a LDR to the drug.

Methods. Twenty-four patients (age 60.8 ± 11.1 years) with mild or moderate PD were investigated. The study was a crossover trial, comparing three different 15-day treatment periods with levodopa defined as treatments A, B and C. In treatment A, 250 mg of levodopa were administered with an inter-dose interval (IDI) of 24 hours; in treatment B, 250 mg of levodopa were administered with an IDI of 8 hours; in treatment C, 125 mg of levodopa were administered with an IDI of 8 hours. The LDR was calculated as the percentage of the maximal improvement

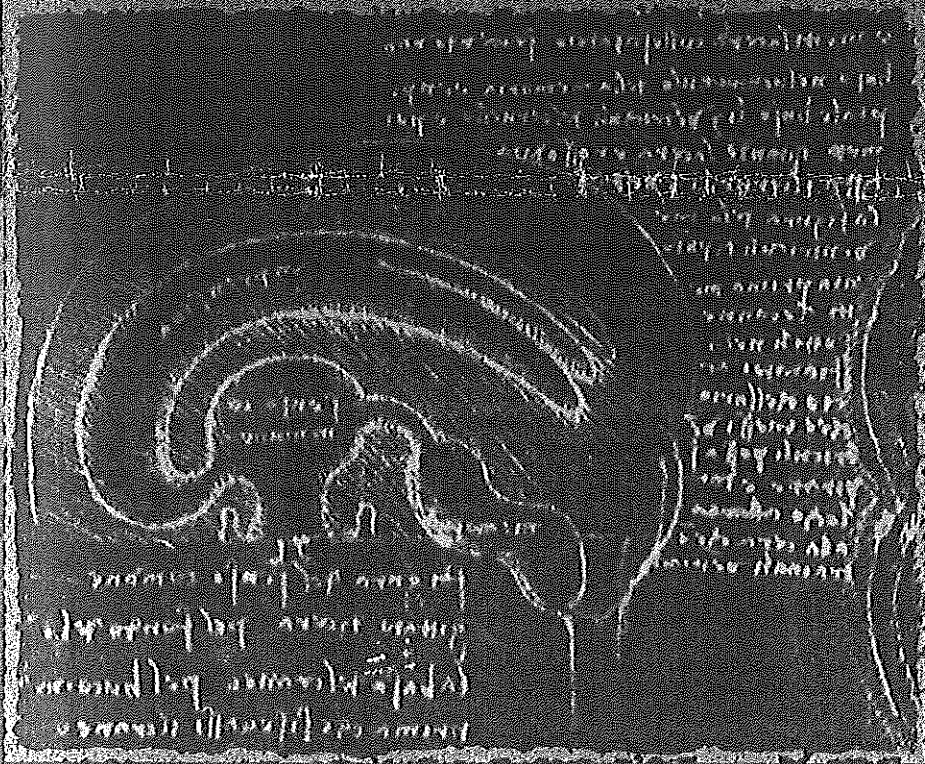
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