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COGNITIVE STIMULATION OF PATIENTS WITH DEMENTIA: PRELIMINARY RESULTS

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SUMMARY

We present the first results of a cognitive stimulation programme for patients with dementia. Fifty-six subjects entered a study involving two parallel, randomized groups. Assessment was blind for the main criteria (neuropsychological tests). Twenty-nine patients were stimulated and were compared to 27 non-stimulated patients. The stimulated group attended 10 stimulation sessions over 5 weeks. Each group was assessed on the first and seventh week. Following stimulation, there was significant improvement of Mini-Mental State (MMS) scores ($p < 0.01$) and increased performance for the Word List Memory Test (one-tailed $p = 0.09$) in the Consortium to establish a Registry for Alzheimer's Disease (CERAD) battery. Verbal fluency remained unchanged. Stimulation tended to improve items of an additional battery (one-tailed $p < 0.01$). The composite sum of test scores showed a significant difference in favour of the stimulated group. These results were positively correlated with the initial MMS scores and negatively with education. The Activities of Daily Living (ADL) scale did not show a significant change. We concluded that global stimulation of cognitive functions improves certain parameters among demented outpatients.

KEY WORDS—Cerebral plasticity, dementia, Alzheimer's disease, cognitive stimulation.

It has been held that after initial development, the adult brain does not have the capability of regenerating or otherwise showing significant plasticity (Cajal, 1928). More recently, however, neurobiology research has shown that brain structures and networks have the potential to be modified under appropriate circumstances. In the late sixties and early seventies, the first evidence of regeneration within the central nervous system was demonstrated by Raisman (Raisman, 1969) and by Björklund and his colleagues (Björklund *et al.*, 1971; Katzman *et al.*, 1971). Animal (Brailowsky and Knight, 1987) and human (Bach-y-Rita, 1990; Péschanski, in press) studies have demonstrated that specific procedures may be induce functional recovery following lesions. On the basis of these data, several authors have proposed rehabilitation strategies aimed at improving the deficits associated with specific pathologies such as the physical deficits that follow strokes (Sunderland *et al.*, 1992) or head injuries (Cohadon *et al.*, 1988; Grimm and Bleiberg, 1986). Among the cognitive deficits that follow focal pathologies, aphasia has been studied most extensively (Basso, 1989; Holland, 1989; Holland, in press).

It appears legitimate to wonder to what extent similar strategies may be applied to dementia and to Alzheimer's disease (AD) (de Rotrou, 1992, in

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press). Even though AD affects certain cerebral areas more than others, the pathology tends to affect the entire central nervous system in a progressive fashion which seems to preclude significant prospects for rehabilitation. On the other hand, certain morphological alterations such as synaptic changes are shared by AD and by normal ageing (Cotman and Nieto-Sampedro, 1982; Cotman *et al.*, 1993; Bertoni-Freddari *et al.*, 1992) in which stimulation techniques have been shown to be effective (Yesavage, 1985). It is also known that certain aspects of cognition such as implicit learning are relatively spared in AD (Deweer *et al.*, 1991). In fact, some positive results have been shown in AD patients. The domains involved have been highly specific and therefore the number of subjects has been small (Van der Linden and Van der Kaa, 1989; Wilson, 1991).

From the point of neuropsychology, it has been observed that one of the characteristics of AD is that, even when several cognitive functions are compromised, patients are still able to elaborate strategies. Failures tend to occur at recall because these strategies are not properly applied. This has been the rationale for our method of global cerebral stimulation (de Rotrou, 1989). The programme relies strongly on mental imagery, which is used in its visual and semantic mode to stimulate encoding, consolidation and retrieval of information. This technique utilizes various perceptual modalities related to a diversity of daily life situations. Cognitive functions are not used in isolation but as a functional whole. This article presents the first results of our stimulation programme in demented out patients randomly distributed into two comparable groups. Assessment was blind for the main criterion (neuropsychological performance) and open for the accessory criterion (ADLs).

MATERIAL AND METHODS

Subjects

Subjects were selected on the basis of a diagnosis of demential (established by DSM-III and other criteria as in previous research from our group (Forette *et al.*, 1989; de Rotrou *et al.*, 1991). We used in addition the CERAD (Morris *et al.*, 1989) exclusion criteria, including impaired hearing and vision severe enough to interfere with the tests; severe aphasia; behavioural disorder incompatible with integration within a group for an hour; dementia due to potentially treatable causes including depression; and inclusion in another research protocol. Five patients were excluded during the course of the protocol. Reasons included anosognosia and personality disorders in two patients (stimulated (S) group), stroke with aphasia, making reevaluation impossible for one patient (non-stimulated (NS) group), and in two other cases (one S, one NS) families' refusal.

Sixty-one patients were selected for the study. They were all outpatients selected on the basis of criteria that have been validated previously (Forette *et al.*, 1989); these criteria include a diagnosis of dementia (American Psychiatric Association, 1987) and are based on clinical history, general physical and neurological examination and a CT scan. All patients had a MMS (Folstein *et al.*, 1975) superior to 9, but with no upper limit. In all cases, informed consent was provided by the patients and by their family. All those who for any reason did not attend all evaluation and training sessions were eliminated (five subjects altogether). We therefore present our results on 56 patients, 29 stimulated, 27 non-stimulated.

The following therapeutic agents were authorized: drugs without obvious CNS effect including folic acid and vitamin B12; antidepressants, antiparkinsonian drugs, thyroid replacement, hypnotic and sedatives as long as their therapeutic effect was in a plateau phase and they did not produce an effect on cognitive functions during the study.

Methodology

During 5 weeks, the patients selected were divided into groups of approximately 10 patients. Each group received 10 sessions lasting about 1 hour. Each session was conducted by two therapists, one physician and one psychologist.

The following examples illustrate the method of cognitive stimulation used during each session:

1. Each subject in the group was shown the dotted outline of an umbrella and was asked to connect the dots in order to create an object (an umbrella). They were then asked to draw an umbrella closed and upside down, to evoke associated words (rain, raincoat, boots, etc), to talk about rainy months and about regions of France such as Brittany customarily associated with great rainfall. They were then asked to mention characteristic aspects of Brittany such as cities, foods and cultural events.

2. Subjects were shown an array of 16 pictures depicting easily identifiable objects. They were asked to name each object, to classify them into categories (fruit, vegetables, household items and working tools) and to mention other objects belonging to those categories. They were then asked to mention fruits from foreign countries, fruits from the present and other times of the year, vegetables used in cooking specialty dishes from France and other countries, the wines that could accompany them, etc.

Evaluation criteria. Each group was assessed at week 0 (W0) and week 6 (W6). If no more than two sessions were missed, these could be made up for.

Neuropsychological test. Each patient was administered the neuropsychological tests of the CERAD battery (Consortium to Establish a Registry for Alzheimer's Disease, Morris *et al.*, 1989; Welsh *et al.*, 1992), which assesses the main cognitive functions through eight items (verbal fluency, naming, MMS, word list memory, constructional praxis, word list recall, recognition or non-recognition). This battery, which has been validated in the USA in 1989, is easy to use and reproducible and is included in a number of research protocols, enabling assessment of the course of the disease.

In addition to the CERAD test, patients were administered an additional battery which included three subtests:

— Picture pair associate test: this test consists in showing 12 pairs of drawings with no obvious relationship and asking the patient to make up a sentence in order to memorize them. The experimenter then shows a picture and asks the patient to recall the missing one. A score is obtained for spontaneous recall, and a score for cued recall
— Immediate associate memory: a list of six words is read and is to be recalled. Then the experimenter reads the same words again and asks the patient to integrate them in a story. A score is obtained for immediate memory, and a score for associate memory
— Verbal fluency: the experimenter asks the patient to produce a maximum number of words starting with the stimulus letter P

The neuropsychological tests were administered by a neuropsychology technician who was unaware of whether the subject had received cognitive stimulation or not.

The ECA (*échelle comportementale adaptive*) (behaviour adaption scale) (Ritchie and Ledesert, 1991) is designed to assess the effects of cognitive stimulation on activities of daily living (ADL). It was carried out by open assessment with the patients' families.

Statistical analysis

Neuropsychological changes in each group were compared using Student's *t*-test. Linear regression was used to detect factors linked with improvement among stimulated patients.

RESULTS

At W0 both populations were comparable in terms of age, gender and level of education (Table 1), drug therapy, CERAD scores and scores for the additional battery.

Table 1. Summary data of patients initially included in the stimulation protocol

	S	NS
Number	32	29
Sex ratio (M/F)	10/22	14/15
Age	76.1 (61–87) SD = 7.1	78.3 (55–93) SD = 7
Education (1/2/3)	9/7/16	6/13/10
Diagnosis	AD: 31 Parkinson's: 1	AD: 25 M.I.D.: 1 Combined: 2 Other: 1
Excluded	3	2

S, stimulated group; NS, non-stimulated group; MID multi-infarct dementia; SD, standard deviation.
Education: 1, junior school (6 year or less); 2, high school (12 years); 3, college (> 12 years).

CERAD test results at W6

— Four items could not be used because of a ceiling effect; these included the naming procedure, constructional praxis, word list recognition (positive and negative), with a score range of

0–15, 0–11, 0–10 and 0–10, respectively; at W0, 21% of patients from the NS group and 39% of the S group reached a ceiling for these four items in spite of a very similar total CERAD distribution in both groups; at W6, in both groups, approximately 35% of the values of these four items had reached maximum scores.

— One item, word list recall (scored from 0 to 10), had to be left aside because of a floor effect. Approximately 45% scored 0 at W0 and W6, similarly in both groups.

Having discarded five items, results were studied among the three remaining items only: MMS, word list memory and verbal fluency, with a score range of 0–30, 0–30 and 0 to infinity, respectively. Gross values are given in Table 2.

It was noted that although no change in verbal fluency occurred through stimulation, there was significant improvement in MMS ($p < 0.01$) and increasing performance in word list memory (one-tail $p = 0.09$).

Table 2. Variations (W6 − W0) of useable CERAD items through a 5-week stimulation compared with a control group of demented patients

Test	Group	Mean	Standard deviation	One-tail p
MMS	NS	−0.7	3.1	
	S	1.4	2.7	<0.005
Word list	NS	0.1	2.2	
memory	S	1.1	3.1	0.09
Verbal	NS	−0.1	2.9	
fluency	S	0.0	3.1	0.46

There was no regression towards the mean of the MMS score in the S group. MMS change and MMS initial score were independent ($r = -0.07$). We therefor did not make further attempts to match the patients for initial MMS score.

When the non-AD patients were excluded, we found similar results in terms of MMS change: -0.9 ± 3.1 in the NS group ($N = 24$) compared to 1.4 ± 2.8 in the S group ($N = 28$), one-Tail $p < 0.005$.

Additional battery results

An increasing performance appears with the association test under the effect of global stimulation (one-tail $p < 0.10$).

A global score was constructed by adding the results of the MMS, of the two usable CERAD subjects (word fluency and word list memory) and those of the additional battery. Table 3 shows that there was a marked improvement (5.8 score points) for the stimulated patients, but a much smaller one for the non-stimulated group. The difference was significant.

Table 3. Change in global scores between week 0 and week 6 for the stimulated and the non-stimulated groups

	Non-stimulated	Stimulated	One-tail p
Mean	1.0	5.8	<0.01
Standard deviation	7.8	7.3	
Range	−12–13	−9–26	

Further analyses were carried out to determine possible factors affecting results, ie the difference W6−W0 of the total five association scores + MMS + WLM + VF in the stimulated group. Linear regression showed that sex ($p = 0.55$), age ($p = 0.25$) and listed drug intake ($p = 0.89$) had no effect on the results. Hence, despite a different sex distribution, a slightly different age mean in the two groups and a somewhat more frequent drug intake among the non-stimulated group, results of both groups could be compared.

Starting with equal scores at the initial MMS, the lower the educational standard (ES), the higher the gain after stimulation ($p < 0.05$). For an average global gain equal to 5.8 (S.D. 7.3), global gain on all test increased by three points when educational standard decreased by one degree. Going from ES 1 to ES 2 had the same effect on the course as that of going from ES 2 to ES 3; thus, even if ES distribution was different in the two groups, these remained quite comparable, since the mean ES was strictly identical (2.2).

MMS at W0 was positively correlated with the results even though the correlation fell short of statistical significance ($p < 0.12$). ES remaining equal, global gains on all tests increased by three points when initial MMS increased by seven. It is worth pointing out that initial MMS was slightly lower in the stimulated group (21 vs 22), consequently the S group was not favoured.

The two factors ES and initial MMS accounted for 19% of the variance of the results. On the other hand, initial VF value and total exploitable test

score had no effect on the results ($p = 0.53$ and $p = 0.23$, respectively).

Results of ADL scale

The 32 items on this scale registered about 76% maximum scores at W0 (ranging from 32% to 100% as at W6 (38% to 100% maximum scores; mean = 78%). This scale was obviously not suited for this study.

DISCUSSION

This study, which was performed on two blindly assessed, parallel, randomized groups, indicates that global cognitive function stimulation, over a period of only 5 weeks, entails significant improvement of the MMS ($p < 0.01$) in patients with degenerative dementia. It also appears to induce increased memory performance by a word list and by association tests.

It is unlikely that the changes in MMS scores were due to practice effects. The control group was administered the same instrument the same number of times. Other studies have confirmed that MMS learning effects are small ((Katz *et al.*, 1991).

The sessions required a great deal of organization (transportation, availability of a relative, etc) on the part of the families that could only be feasible over a limited period. We therefore chose standard duration for memory training methods (Yesavage, 1985): 4–12 weeks, with sessions of 1–1.5 hours. In this study, overall acceptability was good since only five patients were excluded. It can be safely stated that the method in itself is not responsible for dropouts. Of course, such limited action in a disease that has been evolving over a period of several years cannot results in a dramatic improvement of the clinical condition of these patients; however, it is likely that patients would have refused such interference over a long period.

Results were analysed in parallel as both groups were comparable. Indeed, age, sex, education and authorized drug intake had no effect on the results, and one can assume that motivation was equal since in each group patients committed themselves to attend the 12 planned sessions. Global CERAD scores at W0 were comparable in both groups.

Simple blind assessment was done through objective tests which are easily reproducible. The patient knew that he/she had been stimulated; this may have improved performance through the placebo effect of receiving care, or altered the results through examination stress after sessions intended to improve it.

Although our population did not consist exclusively of AD patients, these made up 90% of our sample. We thus felt this legitimized the use of CERAD, which is a new recognized and validated international tool for studies concerning AD and which has the advantage of standardizing results obtained in therapeutic trails in AD, as these can be subjected to confrontation. Five of the eight CERAD tests had to be dismissed; this may be explained by the fact that CERAD is validated for a MMS score of 10–24, and although the mean MMS in our population was 21.5, values ranged from 9 to 29. Discarding five out of eight items may have concealed certain effects of stimulation; under the circumstances, the fact that it elicited an improvement through stimulation with only three items is in itself encouraging. Furthermore, increasing performance in WLM might be confirmed with a larger sample size. For further studies, we suggest using the new, recently perfected CERAD, which addresses early stages of the disease (1992 protocol), on a larger sample size.

The behaviour adaption scale did not enable assessment of the benefits of stimulation in daily life. Indeed, this scale is intended for severely impaired (institutionalized) patients, but there is presently no scale adapted to the early stages of dementia, in which alterations in activities of daily living do exist but remain minimal, allowing maintenance of the patient at home.

The present study did not allow us to establish a typical profile for respondents. MMS and ES explain only 19% of the variance of the results. This can be accounted for by the variability of the impairment at different times in the same patient, and by the heterogeneity of AD deficits, which differ both in quality and in quantity and have various symptomatic expressions, probably in relation to varying types of dysfunction (Friedland, 1988; Boller *et al.*, 1992).

AT the present stage of the research, we are unable to determine the precise mechanisms by which the beneficial effect was achieved. New functional imaging techniques such as single photon emission tomography and position emission tomography (Rapoport *et al.*, 1990) could allow better assessment and understanding of the neurobiological effects of stimulation.

In conclusion, at a time when no pharmacological treatment has been proved efficient in degenera-

tive dementias, cognitive stimulation techniques, which present no toxic effects, must be considered both for their palliative therapeutic value and in view of a better understanding of the physiopathology of these conditions. Cognitive stimulation appears to improve certain cognitive performances in outpatients suffering from degenerative dementia. These first results await confirmation and clarification in the course of further studies.

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