

**PERSEVERATIONS IN ALZHEIMER DISEASE:
ANALYSIS OF THE DISTURBANCE AND POSSIBLE CORRELATIONS**

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Summary

Perseverations are the involuntary repetition of a previous verbal or motorial answer, not appropriate to the current stimulus. Being attributed to frontal lobe dysfunction, they should be found in the late stage of Alzheimer's disease (AD).

We evaluated 25 patients with mild to moderate AD and correlated the presence of perseverations to the severity of both the cognitive damage and the frontal involvement.

We classified the perseverations according to Sandson and Albert (1) model in continuous, recurrent and stuck-in-set type and submitted patients to specific tests to identify them. All AD subjects showed one or more type of them, regardless to the severity of cognitive impairment. The stuck-in-set type was more frequent in those showing an impairment in the Stroop Test and / or Phonological Fluency Test, showing that this kind of perseveration are related to a frontal involvement.

Keyword: Perseverative phenomena, perseveration in Alzheimer disease.

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Introduction

Perseverative behaviors indicate verbal or motorial answers previously given and no longer appropriate to the current situation. Being a frequent behavior found inside different brain disorders, perseverative phenomena have been investigated both from a clinical and research perspectives. Their underlying mechanisms are, however, still debated. The three primary forms of perseveration have been described by Mc Namara and Albert and by Sandson and Albert. They have distinguished the stuck in set type, the recurrent type, and the continuous type. The first type, the Stuck in set perseverations, consist in the inability to perform the set shifting, leading to the persistence of the same set of answers even though a new task is introduced. The recurrent perseverations involve either the complete or partial repetition of a prior response to a new stimulus.

The continuous perseverations, mainly found in graphic tasks, are the abnormal prolongation of a current activity leading the subject to produce a number of stimuli greater than required. Perseverations may be found in normal subjects during fatigue and in the elderly, but in some conditions, as cerebrovascular diseases and dementia, they may be pervasive and significantly interfere with many tasks. Different mechanisms have been suggested to explain perseverations. The stuck in set type has been related to the impairment of the executive functions, (Sandson and Albert 1987) (2); the recurrent type to an involuntary retrieval of previous informations, possibly due to the lacking of left hemisphere inhibitory control. Finally, the continuous type has been associated to attentional and motorial control impairment (Heilman and Von Den Abell 1980, Mesulam 1981) (3). The diseases where perseverations have been more frequently found are those leading to lesions in the frontal lobe, the Lewy body dementia (Dubleday et al, 2002) (4), and the frontal variant of Alzheimer disease (Thomson J.C. et al, 2005) (5). In vascular dementia (VD) perseverations are also frequently found and they have been associated with frontal dysfunctions too (Desmod 2002) (6). Some findings however have casted doubt about the predominant role of the frontal lobes dysfunctions to produce perseverations, so that this topic is still debated in Alzheimer disease (AD) perseverations are mainly found in the advanced stage (Paulson G.W. 1971) (7), however mild to moderate AD subjects may already show them when they are submitted to tasks involving the working memory (Sebastian et al, 2001) (8).

Aims

The aim of our study is to contribute to the knowledge of the mechanisms of perseverative behaviors. We then evaluated it in a group of subjects affected by mild to moderate Alzheimer disease. Our purpose was to investigate if the perseverations found in patients might be associated with the impairment of executive functions.

Methods

Twenty-five patients (15 women) from a continuous series of subjects examined in our Unit were admitted to the study. Inclusion criteria were: mild to moderate Alzheimer's disease (MMSE 24-30), three years' education at minimum, and a good cooperation level. Patients' mean age was 73 and mean education level 7 years. The Mean MMSE was 19.

According to Sandson and Albert we distinguished perseverations in the following types :

- 1) continuous perseverations: the uncontrolled and uninterrupted repetition of a behavior (e.g., motor act) beyond its usefulness
- 2) recurrent perseverations: after giving one or more correct answers the patient repeats those previously given.
- 3) stuck-in-set perseverations: the whole set is repeated.

The tasks employed were graphic in all cases, as it is shown in **Table 1**. For the continuous perseverations two tasks were employed : the first consisting in asking the subjects to reproduce loops of three circles, the second in copying the letter m and n, the one after the other, without interruption between, and in cursive characters. For the recurrent perseverations we asked a) to name some pictures, b) to produce words beginning with the letter "a", "f", and "s" (one minute was given for each letter); c) to produce the names of colours, animals, fruits and towns (two minutes were given for each category, d) to draw simple objects (a daisy, a boat, a Christmas tree, a watch, a tree, a hand). For the stuck in set type the patients were asked a) to draw a

circle under a previously drawn circle and a square under a previously drawn square; b) to draw the inverse pattern, that is a circle under a previously drawn square and a square under a previously drawn circle; c) to draw a circle under the previously written word "circle" and a square under the previously written word "square"; d) to draw a square under the word circle and a circle under the word square e) to draw the sign + under the same sign (+) and the sign ÷ under the same sign (÷); f) to draw the opposite pattern that is the sign + under the sign ÷, and the sign ÷ under the sign +;

g) to draw + and ÷ under the words "plus" and "divided"; h) to draw the inverse pattern that is the sign + under the written word "divided" and the sign ÷ under the word "plus"; i) to draw alternatively the number "3" and the letter "e".

All the patients were also submitted to the Raven PM 47 test, to investigate their logical and attentional abilities, and to the Stroop Test to investigate their frontal functions.

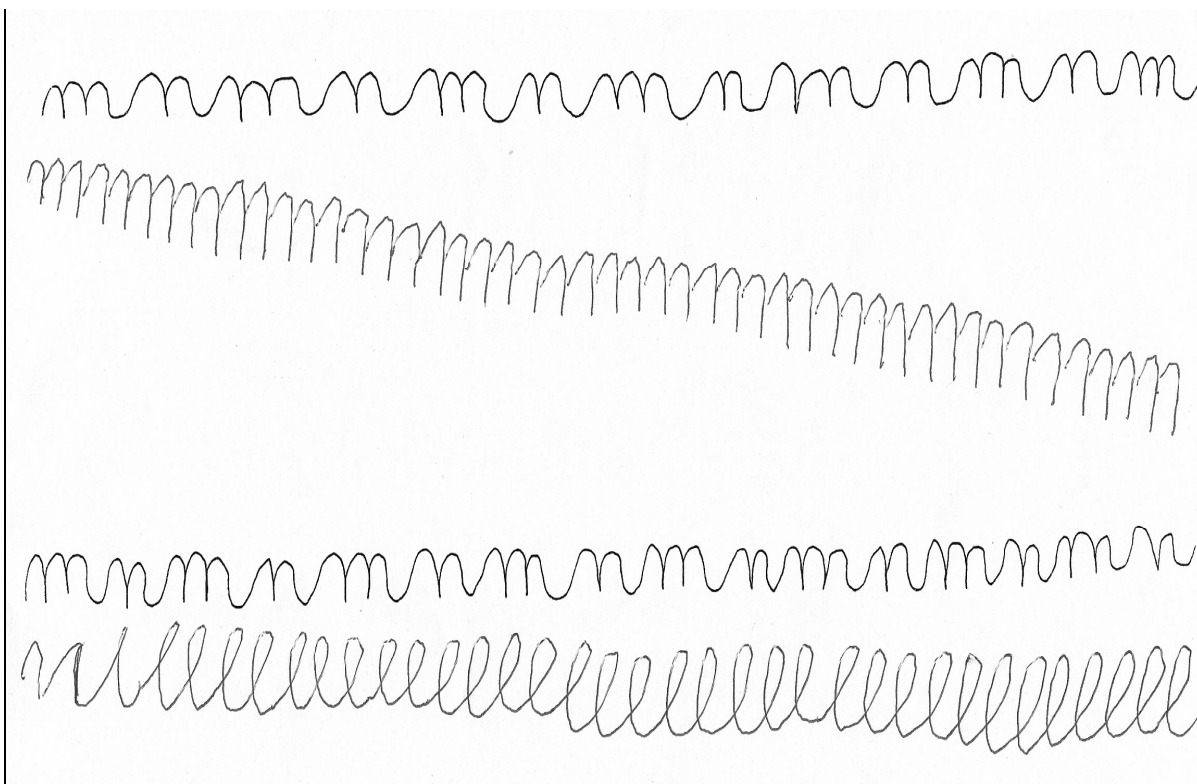
Table 1

The Tests employed:

For continuous perseverations:

- graphic production of multiple loops;
- graphic production of "m" and "n" in cursive characters (**Fig 1**)

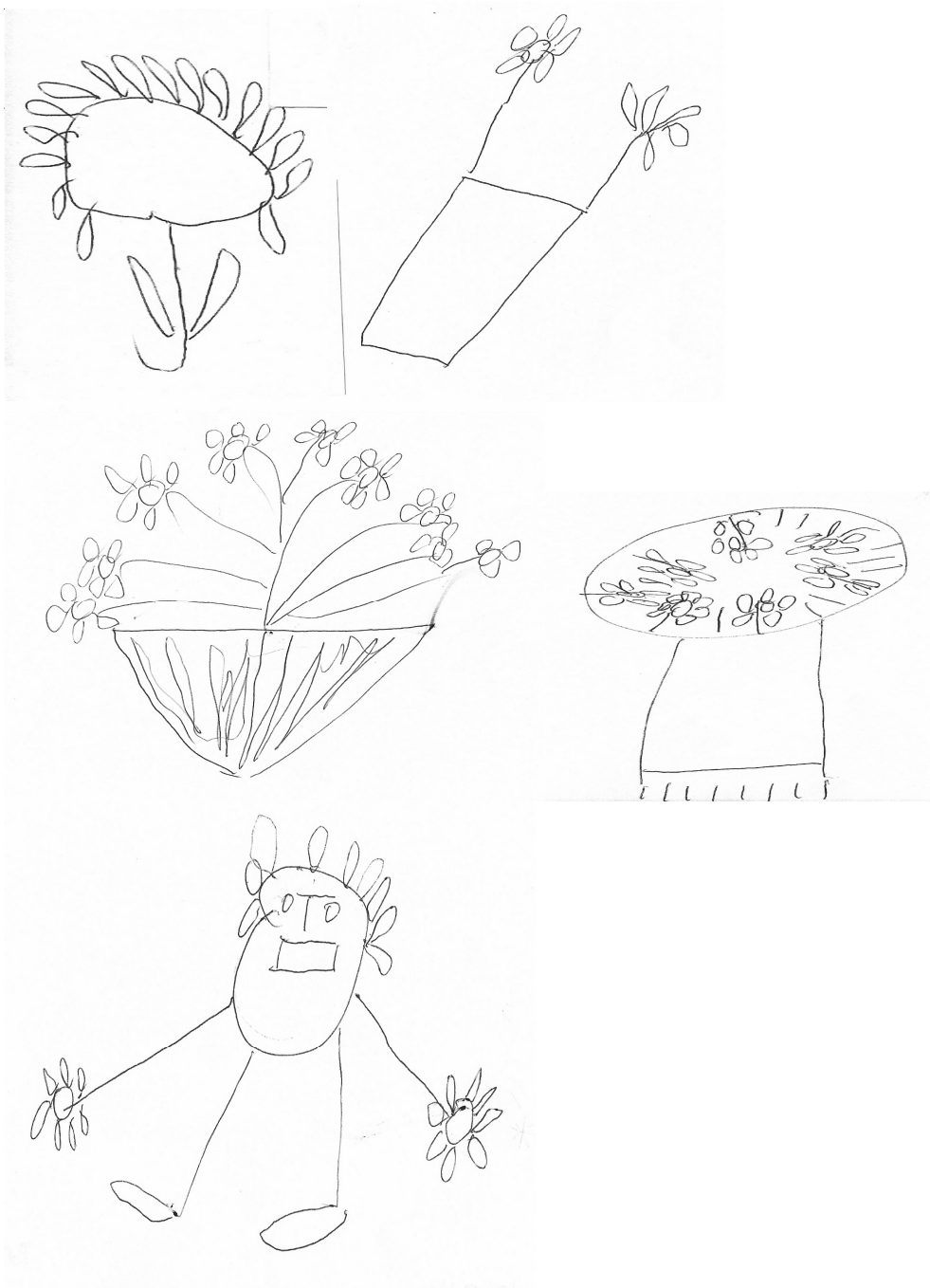
Fig 1



For recurrent perseverations:

- naming single figures;
- phonological fluency ("a", "f", "s");
- semantic fluency (colors, animals, fruits, towns);
- drawings of objects on a verbal order (**Fig 2**)

Fig 2



For stuck-in-set perseverations:

- alternative drawing of a circle and a square;
- drawing a circle when a square is requested and the contrary;
- copying a circle under a square and the contrary;
- drawing + and ÷ under the words plus and divided;
- drawing + under the word divided and ÷ under the word plus (**Fig 3**);
- drawing + under the sign + and ÷ under the sign ÷;
- drawing + under ÷ and ÷ under +;
- drawing alternatively 3 and e.

Fig 3

plus divided plus divided plus divided plus divided plus divide
 : + : + : + : + : +

plus divided plus divided plus divided plus divided plus divided
 + : + : + : + : + :

plus divided plus divided plus divided plus divided plus divided
 + : + : + : + : + :

Results

All Alzheimer patients showed recurrent perseverations and 76% of them also showed the continuous and stuck-in-set types. In 44% of the patients “particular “ phenomena were found, that is some perseverative phenomena not classifiable in any of the previous indicated categories. When the relationship among the different perseveration types and the Stroop and Fluency Tests were investigated, we found a positive correlation among the scores obtained in these tests and the stuck in set perseveration type.

	MMSE	P. Cont	P. Ric.	P. S.S.	P. Part.	N° Par. Cor. Fl. Fon.	Stroop
MMSE	-	,112 ,595	,091 ,664	-,178 ,395	-,598** ,002	,274 ,185	,143 ,549
Cont. P.	,112 ,595	-	-,075 ,722	,041 ,845	-,096 ,649	-,040 ,849	,139 ,558
Rec. P.	-,091 ,664	-,075 ,722	-	-,058 ,785	,129 ,539	,091 ,664	,458* ,042
S.S. P.	-,178 ,395	,041 ,845	-,058 ,785	-	,166 ,429	-,407* ,044	-,585** ,007
Part. P.	-,598** ,002	-,096 ,649	,129 ,539	,166 ,429	-	-,196 ,348	,680** ,001
Corr W Phon. Fl.	,274 ,185	-,040 ,849	,091 ,664	-,407* ,044	-,196 ,348	-	,543* ,013
Stroop Test	,143 ,549	,139 ,558	,458* ,042	-,585** ,007	,680** ,001	543* ,013	-

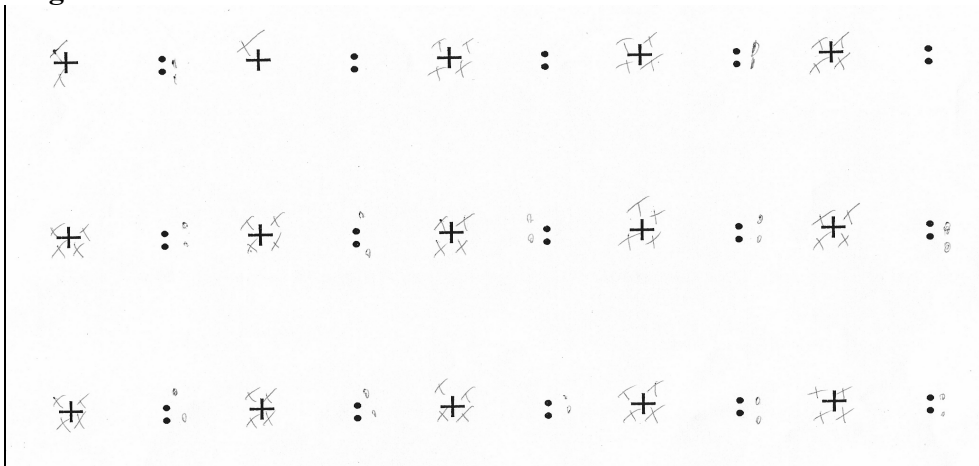
Table 1 Top : Correlation Index ; Bottom : Probability Level. The correlation is significant at 0,05 level. The correlation is significant at 0,01 level . MMSE: Mini Mental State Examination ; Cont. P : Continuous Perseverations ; Rec. P: Recurrent Perseverations ; S.S. P: Stuck-in-set Perseverations ; Part. P : Particular Perseverations; Corr. Phon Fl. : number of correct words at phonological fluency test ; Stroop: Stroop Test

Conclusions

In our sample of 25 mild to moderate AD subjects the global number of perseverative behaviors was related to a) the severity of the cognitive damage and b) the frontal lobe involvement. From a qualitative perspective instead, that is when the perseverations were distinguished in the continuous, recurrent and stuck-in-set types, we found different correlations. The “recurrent” perseverations in fact, (that is those where the patient involuntarily repeated a previous item or part of it) were found in all the examined subjects, independently from the disease severity. These perseverations have been attributed to the lacking of inhibitory control leading to the inclusion of some previous element in a subsequent tasks. One example is shown in figure 2. The patient was asked to draw a daisy, and then a boat, a house, a boat and a man. She correctly did the first drawing, the daisy, but in the following she continued to draw the daisy putting it inside the drawings of the boat and of the man with which it was completely incongruous.

The Stuck in Set perseverations were not found in all the subjects and their appearance was related with a lower score in the Stroop and Fluency test. We also found “particular” perseverations. With this term we indicate some perseverative behaviours whose features are not indicated by Sandson and Albert classification. These perseverations, that are showed in **Fig 4.**, have a less recognizable pattern, and were found in patients with lower MMSE score.

Fig 4



These results, globally taken, indicate, as we hypothesized, that perseverations are showed in all AD stages . Their global number , in fact, was unrelated to the severity of the disease, measured through the MMSE score, in our sample. Some specific perseverations however , that is those we called “particular” are found in more damaged subjects .

The different perseveration types seem furthermore to be related with the impairment of specific neuropsychological test. This is the case of the Stuck in Set perseverations that were significantly associated with a poor score in the Stroop Test. This is a finding suggesting that the impairment of the attentional capacity and of the ability to manage interference, are connected with the stuck in set behaviour and then to an executive impairment.

In summary these data are in agreement with those reported by Pekkala S, and colleagues ,2008, (9) who describe the appearance of recurrent and continuous perseverations even in the early phase of AD, and who claim that the different types of perseverations might reflect the deterioration of the frontal systems during AD.

Perseverations are then a possible behaviour found even in AD early stages. The Stuck in Set type is furthermore associated with a prefrontal impairment , that may be already found at the beginning of Alzheimer Disease.

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