

MODIFICATIONS OF OLFACTION IN EARLY STAGES OF ALZHEIMER DISEASE

Nicola-Antoniou Iuliana

Neurology Department, "Colentina" Clinical Hospital, Bucharest, Romania

ABSTRACT

The study aims at revealing the decrease in the olfactory sense, since early stages of the Alzheimer disease, by testing a battery of seven odorous substances on a group of 72 patients accusing memory loss signs and MMSE ranging between 20 and 30 and on a witnessing group not accusing any signs of memory loss and MMSE 30. The answers, classified in three categories: correct, partially correct or wrong, correlated with the corresponding number of patients and MMSE, show a decrease of sensitivity as well as of discrimination capacity of the olfactory sense, since the early stages of the disease.

Key words: Alzheimer Disease, hippocampal degeneration, decrease of the olfactory sense

Although the information processed by the brain: optical, auditory, tactile, olfactory represent only 1%, it is especially important because it is involved in processes which make the difference between the humans and the animals: memory and olfactory sense. Probably, olfaction is most closely related, from an anatomic point of view, to the cerebral zones responsible for emotion and respectively to the limbic system and the frontal zones involved in the emotional reactions. There are only two synapses separating the olfactory nerve from the amygdala involved in emotion experiencing and in emotional memory and only three synapses separating it from the hippocampus which is involved in memory, particularly in working and short term memory.

During the past 20 years, the scientific literature has evoked, on several occasions, the remark that smell disturbance may stand for an early indicator of subsequent memory and thinking problems.

Since the disease description until present, the decrease of the olfactory sense is commonly manifested by persons with Alzheimer disease. In Alzheimer disease, it is known that the most affected zones are located deeply in the brain, targeting the regions where the organization and integration of activities such as memory, attention and association

take place. The hippocampus is particularly vulnerable in the degenerative process, region CA1 being the most affected.

As well, the disease attacks preferentially the most vulnerable neurological place: the synapse, the place where the nervous cell connects with other cells.

The victims of Alzheimer disease become anosmic not by the massive loss of the neurons of the olfactory cortex or limbic system, but rather, by causing neurons to become "blind", giving them no reason to synapse or by eliminating enough neurons so that they synapse independently and non-synchronously. Their message is cancelled by the brain, being perceived as a background "noise" disturbing the messages processing activity communicated accurately through the integer neuronal networks. By preferentially affecting the temporal cortex, the Alzheimer disease not only affects the capacity to detect smells but rather hinders their identification.

OBJECTIVES

The study aims at revealing the existence of a significant disturbance of the olfactory sense at persons in early stages of Alzheimer disease, such

Author for correspondence:

Iuliana Nicola-Antoniou, MD, Neurology Department, Colentina Clinical Hospital, 19-21 Stefan cel Mare Blvd, District 2, Bucharest, Romania

email: iuliananicola@yahoo.com

disturbances targeting the global acuity as well as the capacity to discriminate various odorous substances and the correlation between the degree of cognitive affectation and that of olfactory deterioration.

MATERIAL AND METHOD

The study has been executed on two groups: the patients group and the witnessing group.

A batch of 72 persons out of a total number of 150 subjects present at the Memory Study Centre, with ages between 65 and 86, men and women equally, has been considered for the study, subject to meeting simultaneously the following criteria:

1. the main reason for their visit to the physician is represented by the decrease in memory
2. the objective neurological examination: no signs of focus, no extrapyramidal signs, no signs of peripheral neuropathy
3. normal or exclusive CT cerebral examination, with cortical atrophy (diffused or prevalent at the level of the Sylvian valley or the hippocampus)
4. MMSE between 20 and 30
5. the possibility of a peripheral neuropathy is eliminated by anamnesis, clinical examination and biochemistry data (the diabetes mellitus, uremia, alcoholism have been especially considered)
6. an ENT affection is excluded: acute rhinitis, nasal polypus, sinusitis, atrophic rhinitis
7. the cerebral vascular accident is excluded
8. the following have been excluded: mental retardation, major depressive disturbance, delirium, organic amnesic syndromes, other degenerative dementia (Pick, Hunghigton, in Parkinson disease, etc.), secondary dementias (toxic, etc.), cerebral neoplasm, thyroidal gland disturbance, vitamin deficiency, infections (pulmonary, renal, HIV, etc.), sedatives and hypnotic substances intake.
9. there are no prior cranial trauma

The witnessing group is classified on age and sex classes, similarly to the batch under study. They have been recruited amongst the patients in the Neurology Clinic of Colentina Hospital, subject to the following criteria:

1. The absence of any memory disturbances
2. The absence of any smell disturbance, affirmative
3. MMSE: 30

4. normal objective neurological examination in the majority of cases (two cases of a frigate peripheral facial paresis)
5. Exclusion, based on the clinical examination, of peripheral neuropathy
6. Absence of diabetes mellitus, uremia, alcoholism
7. Absence from anamnesis of the cranial trauma notion, tabacosis
8. Normal cerebral CT examination
9. Exclusion of substance abuse, of any kind

The related diseases have been the following: HTA, dyslipidemia, cervical spondylosis, chronic atrial fibrillation.

The smell of the persons under study has been tested using a battery of seven substances.

The substances used in testing have been chosen based on the following criteria:

- A. non volatile, to represent a certain olfactory stimulus
- B. known substances, easy to recognize and name
- C. not to stimulate simultaneously the trigeminal receptors (chemical stimulation)

Thus, the substances used in testing have been the following: lemon peel, tobacco, vanilla, shaving soap, menthe, coffee and garlic.

The test has been performed in accordance with a standard procedure, within approximately 5 to 7 minutes. The answers of the patients have been classified as following:

- A. Integrally correct answers, for the case when all the odorous substances used in testing have been correctly designated
- B. Partially correct answers, for the case when all the odorous substances used in testing have been correctly designated
- C. Incorrect answers – the patient does not name any of the substances

OUTCOMES

Most of the patients subject to the study provided incorrect answers (51%), a small percent (9.7%) provided correct answers and the rest (39%) provided partially correct answers.

As opposed to the study batch, the majority of the witnessing batch members answered correctly (45%), the number of partially correct answers being slightly lower than the number of correct answers (40%) while only a small number of subjects answered incorrectly (15%).

For reduced MMSE scores, no correct answers have been registered, for MMSE inferior to 25, no

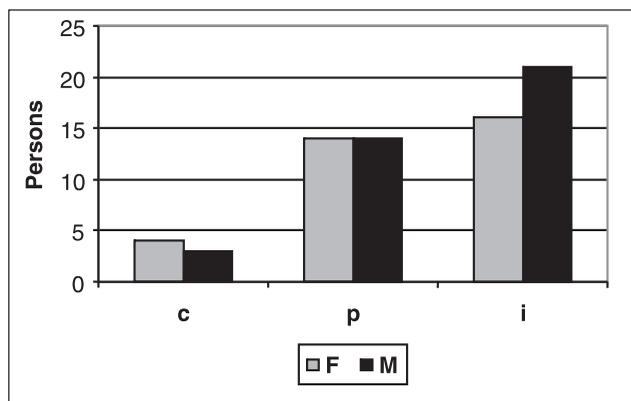


Figure 1. The number of persons, subject to the type of answer and sex

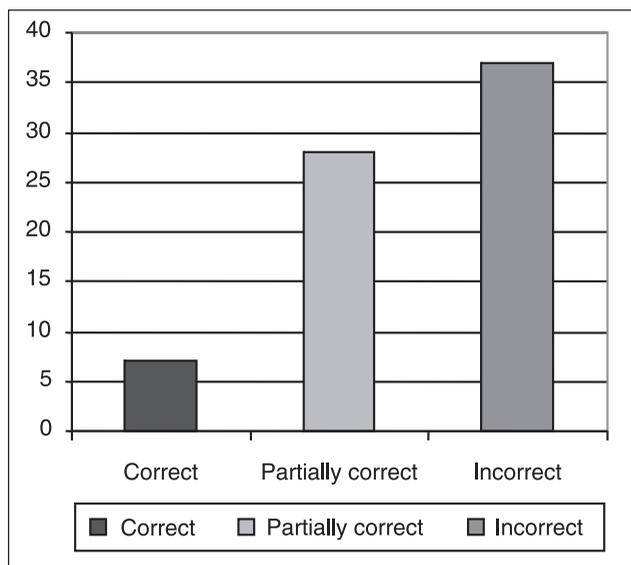


Figure 2. Distribution of answers types of the studied batch

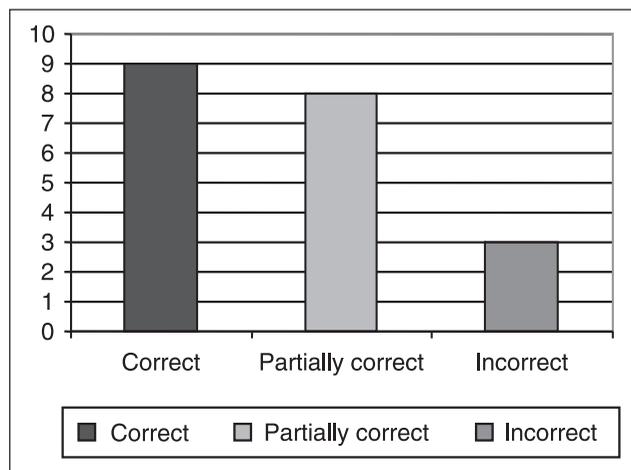


Figure 3. Distribution of the answers types of the witnessing batch

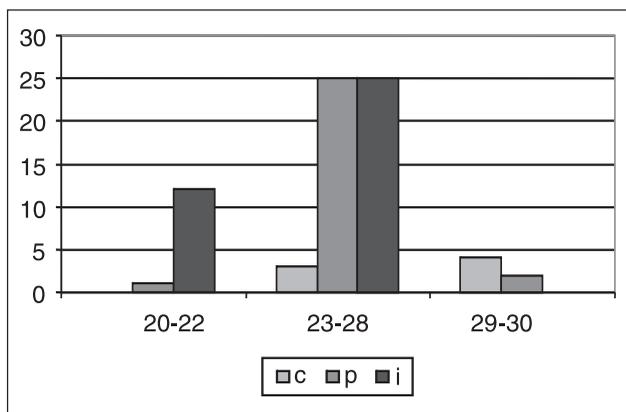


Figure 4. Distribution of the answers types subject to MMSE

correct answers have been obtained while for MMSE 29-30, all the answers have been correct or partially correct.

The low values of MMSE are correlated to incorrect answers while high MMSE scores are correlated to correct answers. For the middle MMSE range 23-38, the numbers of incorrect and partially correct answers are equal.

The number of partially correct answers is slightly different from the incorrect answers as opposed to the correct ones.

CONCLUSIONS

In Alzheimer disease, the olfactory sense is significantly decreased, beginning from MMSE values comprised between 23 and 28, corresponding to the stage of the initial cognitive disturbances. Olfactory disturbance targets the olfactory sensibility (the incorrect answers) as well as the olfactory discrimination capacity (the partially correct answers).

The selective vulnerability towards the neurodegenerative process in Alzheimer disease is manifested by neuronal loss and synaptic disorganization of the structures involved in the olfactory sense, ever since the initial stages of the disease, so much that determination of the olfactory acuity may represent a valuable method for the early diagnose of Alzheimer disease.

It is necessary that olfaction testing constitutes a mandatory stage of any routine neurological examination, being a simple and inexpensive method, within easy reach of any clinician.

BIBLIOGRAPHY

- Doty RL, P Shaman, SL Applebaum, R Giberson, L Sikorsky & L Rosenberg. – 1984 Smell identification ability: changes with age. *Science* 226:1441-1443
- Corwin J, M Serby, Pconrad & J Rotrosen. – 1985. Olfactory recognition deficit in Alzheimer’s and Parkinsonian dementias. *IRCS Med. Sci.* 13:260

- Axel, Richard. – (1995). The Molecular Logic of Smell. *Scientific American*. Oct. Pgs. 154-159
- Peabody C A & J R Tinklenberg – 1985. Olfactory deficits and primary degenerative dementia. *Am J Psychiatry* 142: 524-525
- Reyes PF, PL Flage & GT Golden – 1986. Olfactory cortex in Alzheimer’s disease: Neuropathological studies with clinical correlation. *J Neopathol. Exp. Neurol.* 45: 341