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Taste identification used as a potential discriminative test among depression and Alzheimer's disease in elderly: A pilot study

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ABSTRACT

Major Depression and Alzheimer's disease (AD) are two diseases in the elderly characterized by an overlap of early symptoms including memory and emotional disorders. The identification of specific markers would facilitate their diagnosis. The aim of this study was to identify such markers by investigating gustatory function in depressed and AD patients. We included 20 patients with unipolar major depressive episodes (MDE), 20 patients with mild to moderate AD and 24 healthy individuals. We investigated the cognitive profile (depression, global cognitive efficiency and social/physical anhedonia) and gustatory function (ability to identify four basic tastes and to judge their intensity and hedonic value) in all participants. We found that AD patients performed worse than healthy participants in the taste identification test (for the analysis of all tastants together); however, this was not the case for depressed patients. We found no significant differences among the three groups in their ability to evaluate the intensity and hedonic value of the four tastes. Overall, our findings suggest that a taste identification test may be useful to distinguish AD and healthy controls but further investigation is required to conclude whether such a test can differentiate AD and depressed patients.

1. Introduction

Alzheimer's disease (AD) and major depression (MD) are two common diseases in the elderly. The early stages of these diseases are closely related. For instance, AD patients often experience dysphoria, which is characterized by self-depreciation and sadness. This symptom is similar to apathy that is observed in depressed patients, which is defined as a lack of interests, emotions and motivation. In many cases, diagnosis is based on clinical observations. However, the identification of specific presymptomatic markers of each disease would facilitate the early diagnosis and the clinical care of patients.

Recently, it has been suggested that gustatory deficits may be an early marker of AD diagnosis (Steinbach et al., 2010). The impairment in gustatory function has been observed also in MD (Berlin et al., 1998; Swiecicki et al., 2009). Indeed, if a structured taste test can differentiate between AD and MD, it could be useful procedure in a clinical practice facilitating the diagnosis of these diseases. A sensory test permitting the differentiation between AD and MD has been already used by studying the olfactory identification capabilities (Solomon et al., 1998; Pentzek et al., 2007).

Comparing to other sensory modalities (olfaction and vision), few studies have examined taste deficits associated with these two diseases. A review of the literature reveals conflicting results about taste deficits in depression and thus underlines the need for more investigation. The taste detection threshold has been reported to be altered in MD (Berlin et al., 1998), whereas taste identification is preserved (Swiecicki et al., 2009). Hedonic responses have been extensively investigated in depression because of the anhedonia (lack of pleasure for stimuli previously considered as pleasant) which is a one of the major symptoms of depression (American Psychiatric Association, 1994). Previous studies found no differences in the ability of depressed patients and healthy controls to evaluate the hedonic value of tastes (Berlin et al., 1998; Swiecicki et al., 2009; Dichter et al., 2010). However, Amsterdam et al. (1987) suggested that hedonic ratings depend on the concentration of the taste compound. Indeed, high pleasantness ratings were observed only for high concentrations of sucrose solutions (Amsterdam et al.,

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1987). However, a study comparing unipolar and bipolar patients reported that bipolar patients tend to rate gustatory stimuli as less unpleasant compared to unipolar patients (Swiecicki et al., 2009). Thus, the heterogeneity of results prevents firm conclusions from being drawn. Moreover, most studies have analyzed all tastes together and not one by one, which does not take into account subtle differences. Therefore, the present study aims to avoid this drawback by studying several gustatory parameters of the usual basic tastes.

Regarding Alzheimer's disease, some studies suggest that taste deficits concern the tasks involving a more cognitive process (taste identification) and not the gustatory threshold (Broggio et al., 2001). A taste identification test has been used to differentiate AD and MCI (Mild Cognitive Impairment) patients from healthy controls, but this test could not distinguish between AD and MCI (Steinbach et al., 2010). More studies are necessary to investigate this issue given the lack of data.

Taken together, previous studies have shown that gustatory function is altered in AD and depressed patients, although the components involved differ between the two diseases. No study has directly compared gustatory function between AD and depressed patients. In the present pilot study we sought to investigate, whether taste can discriminate between these two diseases; therefore, we investigated the ability of AD and depressed patients to identify tastes, and evaluate their hedonicity and intensity. We hypothesized that, identification capacities, are preserved in depression and altered in AD.

2. Methods

2.1. Participants

We included 20 patients with mild to moderate AD (McKhann et al., 2011), 20 patients with unipolar major depression disorder (MDD) and 24 healthy volunteers. Patients with MDD were included according to DSM-IV criteria (Ansoleaga et al., 2013; Heath et al., 2006). A score of more than 20/60 on the MADRS scale (Montgomery–Asberg Depression Rating Scale, Montgomery and Asberg, 1979) was required for each depressed patients to be included in this study. The mean MADRS score of depressed patients was 29.2 ± 7.7. All MD patients included in this protocol were treated with antidepressant treatments (escitalopram, venlafaxine, paroxetine and seropram) which are the inhibitors of serotonin reuptake or the inhibitors of serotonin–norepinephrine reuptake. In addition, four patients had anxioloytic treatment, two had antihypertensive therapy, two had an antidiabetic treatment, and another had an antihistamine treatment. Half of patients have a commonly prescribed treatment in AD (memantine). Besides, five of MA patients were treated with antidepressant treatments (escitalopram and mianserine). These antidepressant treatments were prescribed to treat anxiety but none of the MA patients had a diagnosis of major depression episode.

Patients with AD were included according to the McKhann criteria (McKhann et al., 2011), including clinical findings, neuropsychological evaluations and brain imaging. AD patients also suffering from MDD were excluded. AD patients were required to have a Mini Mental State Examination score (Folstein et al., 1975) of at least 15/30 (mean MMSE score: 19.4 ± 3.1). Patients were recruited at the university hospital of Tours (the CMRR "Centre Mémoire de Resources et de Recherche" unit and the psychiatric department).

Healthy volunteers were matched for age, educational level and smoking status with both clinical groups. The exclusion criteria for all individuals included head injury, current substance abuse, alimentary allergy, current cold or any alteration to their sense of taste.

The characteristics of the three groups are presented in Table 1.

2.2. Procedure and experimental design

This was a prospective and observational pilot study conducted in accordance with good clinical practice and the Declaration of Helsinki. Each participant provided written informed consent prior to their participation. The experimental procedure was clearly explained and participants were informed that they were free to discontinue testing at any time.

All gustatory tests were carried out first. After tasting each solution, the participant was asked to assess first the hedonic aspect, then the intensity and finally, the participant had to identify each taste. The participant was then invited to complete scales for the physical and social anhedonia scales. The different tasks were presented in the same order for all participants.

2.2.1. Clinical measures

The state of anhedonia of all participants was evaluated according to the French version of the Physical and Social Anhedonia scales (PAS and SAS; Chapman et al., 1976; Assouly-Besse et al., 1995).

2.2.2. Taste identification test

For the identification task, four taste solutions preconized by the French association of normalization (AFNOR, 2007) were used: saccharose (1.8 g/100 ml, sweet), sodium chloride (0.3 g/100 ml, salty), caffeine (0.05 g/100 ml, bitter) and citric acid (0.05 g/100 ml, sour). The tastants were supplied by Fisher Scientific (France). Water was used as a control. To avoid a possible influence of taste intensity on hedonic response and to assure a better gustatory perception, the concentrations of the four tastants were chosen such that the solutions were approximately iso-intense and at surpathreshold level that is to say neither too strong nor too weak (to be above the recognition threshold). They were selected after a preliminary experiment undertaken with 16 subjects who did not participated in this study.

Each solution was prepared daily with water and presented in a disposable goblet of 33 ml. A three-digit random number coded each goblet. The five solutions were presented one after the other in a random order. Thus, acid, salty, bitter, sweet solutions and water were presented to each participant. The same presentation order was kept for all participants. Participants were asked to taste each solution and to choose one of five answers including: "sour", "salty", "bitter", "sweet" or "water". One point was given for the correct answer and none for the incorrect answer.

Participants were allowed to taste the same tastant several times. Participants were asked to rinse their mouth with water and to wait one minute between tastings to avoid interference between tastes.

2.2.3. Taste hedonicity and intensity

A 10 point linear scale labeled at each end (highly unpleasant/highly pleasant; very low intensity/very high intensity) was used to evaluate the pleasantness and the intensity of the perceived tastes. The resulting response was expressed with a score ranging from 0 to 10. Because of the difference of the hedonic valence of the four used tastes (for example, the hedonic valence of sugar is usually positive and that the hedonic valence of bitter is usually negative) and in order to take into account the subtle difference between tastants, the results of the hedonic and intensity evaluations were treated for each taste separately.

2.3. Statistical analysis

All statistical analyses were performed with XLSTAT®-Pro, release 5.2.

Statistical analyses were carried out with non-parametric tests due to the heterogeneous variance of most variables (Levene tests) and lack of normal distribution (Kolmogorov-Smirnov test).

The Kruskal–Wallis test (unpaired test) was used to compare the scores of the three groups (depressed patients, AD patients and healthy controls) for the clinical scales (PAS and SAS), for the hedonicity and intensity measures of each taste, and for the identification of all taste stimuli. The post-hoc Dunn multiple comparison test was performed for two-by-two comparisons of the different groups. These tests were performed with Bonferroni correction ($\alpha* = \alpha/k$, where $\alpha = 0.05$ and k is the number of the comparisons performed; i.e., $\alpha* = 0.0167$).

The Chi-square test with the Marascuilo procedure (significance level Bonferroni corrected) was used to compare the number of correct responses for the identification of each taste between the three groups.

Table 1
Demographic and clinical characteristics of the three groups of individuals.

	Depressed patients ($n=20$)	AD patients ($n=20$)	Healthy controls ($n=24$)
Female/male ratio	15/5	14/6	17/9
Mean age, years (S.D.)	64.9 (11.2)	73.0 (11.2)	67.4 (12.9)
Age range, years	50–98	53–87	51–98
Non smokers/smokers ratio	16/4	18/2	22/2
MMSE, mean score (S.D.)	24.9 (3.0)	19.4 (3.1)	28.5 (1.0)
MADRS, mean score (S.D.)	29.2 (7.7)	8.6 (6.3)	3.3 (2.9)
Socioeducational level, mean score[a]	2 (0.7)[A]	1.75 (0.8)[A]	1.83 (0.8)[A]

Values with the same letters are not significantly different at $\alpha = 0.0167$ (significance level Bonferroni corrected) according to the Dunn post-hoc procedure.

[a] Socioeducational level was calculated on a three-point scale (1, 2 and 3, corresponding to primary, middle and high school education, respectively).