ORIGINAL ARTICLE

Correlation of depressive symptoms and olfactory dysfunction in patients on hemodialysis

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Abstract

Background and aim: A possible link between depression and olfactory dysfunction has been suggested in the literature, in research projects using the olfactory bulbectomy model. In human studies using a syndrome-oriented approach, such an association has not been reported consistently. The aim of the study was to test the association of olfactory dysfunction with depression using a symptom-oriented approach.

Paients and methods: Twenty eight end-stage renal failure patients took part in this project. The patients' olfactory identification ability was tested with the University of Pennsylvania Smell Identification Test (UPSIT). Immediately before olfactory testing, the subjects completed the Zung self-rating scale, which provides data on symptoms of depression in this group of patients.

Results: The mean value of the number of mistakes made in the olfactory identification ability (UPSIT test) by the total sample was 14.0±4.5, with a range 6-22. Half of the symptoms seem to bear an influence on the olfactory identification performance. Patients experiencing decreased libido and dissatisfaction exhibited significantly reduced olfactory function, as contrasted to those not experiencing these symptoms. The above results remain practically unaltered even after taking into account such probable confounding factors as age, sex, olfactory detection threshold and duration of illness.

Conclusion: These findings support previous evidence indicating that olfactory dysfunction may be related to specific depressive symptoms in humans. The present findings also suggest that the symptom-oriented approach is an effective research tool for the elucidation of such clinical issues. The need for further research in this field is pointed out. Hippokratia 2010; 14 (3): 189-192

Key words: depression, dissatisfaction, libido, olfactory dysfunction

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The association of olfactory dysfunction and depression has been convincingly shown in animal models. The olfactory bulbectomized animal has been proposed as a model of depression[1,2] and as a screen for antidepressant drugs[3,4]. In contrast to animal studies, there have been only few studies involving patient groups testing the association of depression and olfactory dysfunction, and these have produced inconsistent findings[5,6].

Methodological differences, such as differences in diagnostic subgroups and differences in the applied tests to assess the olfactory identification ability {(University of Pennsylvania Smell Identification Test (UPSIT), isoamylacetate}[7,8] may explain these discrepancies.

The current investigation seeks to address the possible association of olfactory dysfunction with symptoms of depression. The hypothesis was that olfactory dysfunction would be positively and significantly associated with some, but not all, symptoms of depression. Olfactory dysfunction would, therefore be more strongly associated with individual specific symptoms rather than with a collection of symptoms which characterize depression as a "syndrome" in the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) and International Classification of Diseases (ICD- 10). The primary hypothesis, was tested by identifying specific symptoms, or combinations of symptoms, which are more strongly associated with olfactory dysfunction. This was made possible by the employment of self-rating questionnaire. A second hypothesis was that patients characterized by specific affective symptoms as part of their illness, would perform significantly worse on the olfactory identification measure than patients without affective symptom. The above hypotheses were investigated in a sample of end-stage renal failure patients on hemodialysis

Patients and Methods

We studied 28 chronic renal failure patients undergoing hemodialysis, for periods longer than 3 months (average period of hemodialysis 53 ± 49 months).The sample included 13 male (48±10.9 years old) and 15 female (47± 11.1 years old) subjects. The primary illnesses, accounting for the renal failure, were interstitial nephritis and obstructive uropathy (25%) glomerulonehritis (35%), glomerusclerosis (20%) and other diseases such as diabetic nephropathy, amyloidosis and lupus nephritis(20%). Patients with other axis I psychiatric diagnoses, current

smokers and those with other medical illness were excluded. Patients were asked not to use cosmetics on the day of testing, not to eat or drink for at least two hours before testing, and to wash their hands with odorless soap immediately before start testing. Immediately before olfactory testing, the subjects were asked to complete the 20-item Zung Self-Rating Depression Scale (ZSDS), Greek version, that provided the severity of depressive symptoms[9,10]. The Zung Self-Rating Depression Scale (ZSDS) is a 20-item scale designed to measure the symptoms of depression. In this test, subjects rate each item according to how they felt during the preceding week. Item responses are ranked from 1 to 4 with higher numbers corresponding to more severe symptoms. Some items' scores are reverse.

Two different olfactory identification tests were used: The first one, in order to exclude the peripheral olfactory deficiency, was the Olfactory detection thresholds (give reference): For detection threshold acuity testing, the following procedure was applied. The odorant n-butyl alcohol was prepared in a series of 10 dilutions beginning with 4% v/v in deionized water. Each successive dilution was one-third the concentration of the preceding dilution. It has been suggested that n-butyl alcohol has been used in olfactory threshold testing because it is a potent stimulus for the olfactory nerve at concentrations which have no impact on the trigeminal nerve. The procedure of olfactory test consists of 10 steps. In each step the odorant (n-butyl alcohol) and a blank (distilled water) are presented to the subject. The subject sniffs each one approximately for 90 seconds and then chooses which one smelled stronger. Testing progresses from weaker to stronger concentrations of odorant. If the subject makes correct choices in the four first steps, as these described by Murphy et al[11] the last fourth step is repeated as verification. If the subject selects the following four steps correctly the 8th step is repeated and the procedure continues until the 10th step.

The second one was the Olfactory identification ability test: The University of Pennsylvania Smell Identification Test (UPSIT) was administered to subjects to assess olfactory identification ability. The test is in multiple-choice format, with four written response alternatives for each odor. The odors are released when the labels are scratched. The examiner scratched each target patch and instructed subjects to smell the patch and then select the name of the released odor from among four alternatives[11].

Statistical analysis

The primary outcome was the olfactory identification performance expressed through the number of mistakes made in the UPSIT test. The subjects' scores in each of the 20 symptoms, comprising the Zung test, served as the independent variables in the one-way ANOVA tests. Step-down procedures ensued to the purpose of elucidating the most important symptoms that account for the variability in the olfactory performance.

Results

The mean value of the number of mistakes made in the olfactory identification ability (UPSIT test) by the total sample was 14.0±4.5, with a range 6-22.

Table 1 show the number of mistakes made in the ol-

Table 1: Mean values (±SD) of the number of mistakes made in the olfactory identification ability (UPSIT test) in relation to the subject's score in the symptoms.

	Score				
Symptom	**1**	**2**	**3**	**4**	**p (ANOVA test)**
Depressed affect	11.1±3.8	16.8±2.2	15.9±2.7	20±1.7	0.001
Crying spells	16.4±3.9	14.8±3.7	12.1±4.8	11.0±0	0.172
Diurnal variation	10.3±2.7	16.2±3.4	18.0±2.8	-	0.001
Sleep disturbance	11.4±4.1	14.9±4.5	16.6±3.3	-	0.022
Decreased appetite	20.5±0.7	15.0±3.3	14.9±4.5	11.3±3.8	0.024
Decreased libido	18.2±4.4	15.4±1.5	15.5±3.6	10.4±3.0	0.001
Weight loss	12.8±4.4	15.4±4.6	15.0±4.2	-	0.339
Constipation	14.4±3.3	15.1±3.4	11.0±3.9	10.0±0	0.350
Tachycardia	13.9±5.5	15.9±3.5	10.7±2.8	-	0.037
Fatigue	15.1±4.9	12.9±5.3	13.6±2.7	17.0±7.1	0.583
Psychomotor retardation	12.0±4.1	16.0±5.2	16.1±3.0	-	0.047
Psychomotor agitation	12.8±4.1	15.4±1.1	19.5±1.6	11.3±3.8	0.001
Confusion	14.7±5.2	12.6±4.6	14.0±2.9	16.3±3.8	0.553
Hopelessness	13.9±6.1	13.5±4.8	15.7±4.2	14.0±3.0	0.928
Irritability	11.1±3.8	15.9±3.3	18.2±2.0	18.0±1.4	0.001
Indecisiveness	12.6±4.8	14.3±4.6	15.7±3.6	15.5±4.9	0.566
Personal devaluation	13.7±5.3	13.8±4.8	15.0±3.2	13.5±3.5	0.938
Emptiness	14.2±4.9	12.5±4.5	15.2±3.6	11.0±0	0.741
Suicidal rumination	13.6±4.5	-	16.8±2.9	-	0.193
Dissatisfaction	20.3±0.6	17.1±2.6	14.8±2.7	10.1±2.6	0.001

factory identification ability (UPSIT test) in relation to the subject's score in the symptoms, as well as the results of the ANOVA tests, where, in each case the number of mistakes in the UPSIT test was the dependent variable and the score for the specific symptom was the independent variable. Half of the symptoms seem to bear an influence on the olfactory identification performance, in the sense that an increase in the intensity of the symptom is coupled with an increase in the number of mistakes made in the olfactory identification ability test. However there was an interesting exception: In the symptom of psychomotor agitation the maximum number of olfactory mistakes has been observed at the score 3 of the Zung scale, while the minimum number of olfactory mistakes has been associated significantly at either side of this psychometric score (Table 1).

Step-down procedures proved that the most important symptoms accounting for most of the variability in the olfactory identification performance were dissatisfaction and decreased libido. The above results remain practically unaltered even after taking into account such probable confounding factors as age, sex, olfactory detection threshold and duration of illness.

Discussion

The present study investigated the relationship between olfactory performance and depressive symptoms in end-stage renal failure patients. This was accomplished by using the Zung self-rating scale (for depressive symptoms appraisal) and the UPSIT test for the assessment of the patients' olfactory identification ability. The obtained results indicate that reduced olfactory performance is associated with decreased libido and dissatisfaction**.** The relevance of the present study is best appreciated by taking into account behavioral and neurochemical evidence from animal studies using the olfactory bulbectomy (OB) model. This model, includes several behavioral, neurochemical, neuroendocrine, and neuroimmune parallels between the olfactory bulbectomized animal and the patients with depression[2,13]. In this context, there are reports on sexual dysfunction of OB in which the antidepressant treatment reverses these deficits following an OB[4,14]. Likewise, the insensitivity to positive and negative 'reinforcement' as is used to describe, a well-known characteristic of depressive patients, is comparable to deficits in learning tasks involving positive and negative reinforcement in the olfactory bulbectomy model[15,16]. The significance of the present findings may also be appreciated in view of the fact that specific brain regions such as amygdala and hippocampus involved in processing of olfactory information in human subjects[17], have been implicated in the pathophysiology of depressive symptoms[18]. These brain regions have been proposed as a site for the behavioral alterations and antidepressant action in the OB model[19,20]. Finally, the current findings are in accordance with earlier studies reporting abnormal olfactory identification ability in depressive patients[5] while they disagree with other earlier reports suggesting that depressive patients have normal olfactory performance[6]. As mentioned earlier, methodological differences, such as differences in diagnostic subgroups as well as differences in odorant testing (monorhinal/birhinal administration of UPSIT) or the employment of a different odorant test e.g. isoamylacetate[7,8] may account for the discrepancies of the results of these earlier studies.

In conclusion these results strengthen the possibility that there exists a relationship between olfactory dysfunction and specific depressive symptoms. However, given the rather small sample studied, the results must be interpreted with caution. In order to obtain definitive conclusions this study should be applied to a larger population. The observed association between decreased odor identification ability and symptoms of decreased libido and dissatisfaction in the patients, suggests that smell disturbances deserve greater attention from diagnosticians and health professionals

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