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ORIGINAL ARTICLE

Neuropsychiatric symptoms in patients with Alzheimer's disease with a vascular component

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Abstract

Objective. Vascular changes are observed in most cases of Alzheimer's disease (AD). Observations of AD and vascular disease (VD) allow us to surmise that vascular changes may not only affect cognitive impairment in AD but may also have a negative influence on the neuropsychiatric symptoms which often occur in the course of the disease. The aim of the study was to evaluate the impact of vascular factors on the neuropsychiatric symptoms in Alzheimer's Disease.

Material and methods. The study included 48 people with a preliminary diagnosis of Alzheimer's Disease on the basis of NINCDS/ADRDA criteria. The evaluation of impairments in cognitive functioning was carried out by means of the Alzheimer Disease Assessment Scale – the cognitive part (ADAS – cog), whereas the behavioural and psychological symptoms were evaluated by means of the Neuropsychiatric Inventory – the version adapted for residents of nursing homes for the elderly (Neuropsychiatric Inventory – Nursing Home Version) (NPI – NH). The score on the Hachinski scale was the basis for dividing the study participants into two groups – those with a mild vascular component (0–1 points on the Hachinski scale) and those with a severe vascular component (2–4 points).

Results. The analyzed groups did not differ with respect to the intensity of cognitive impairments (ADAS-cog) or age of the participants. Scores obtained on the NPI – NH scale as well as some of its elements (depression/dysphoria and anxiety) had a discriminating value.

Studies show that vascular factors are a serious risk factor for neuropsychiatric symptoms in AD.

Conclusions. Vascular factors in Alzheimer's Disease influence the presence of neuropsychiatric symptoms. In the course of angiogenic dementia a greater frequency in depressive disorders was shown. The most visible differences between individuals with a greater and lesser burden of vascular factors was in the realm of depressive and dysphoric disorders.

Key words

nursing homes, psychosocial isolation, AIDS dementia complex, sleep disorders, depression

INTRODUCTION

Typical changes within Alzheimer's as a disease involve the degeneration of nerve cells, this most often occurring in the structures of the hippocampus and olfactory cortex, and subsequently spreading to the frontal, temporal, and parietal associative cortex [1]. There also simultaneously occurs in Alzheimer's varied vascular changes which have been noted in around a third of patients with Alzheimer's [2]. Additionallyy, some of the vascular changes (amyloid angiopathy, pericellular leucoencephalopy) are seen in almost all tested cases of Alzheimer's [3].

Between the dementias of Alzheimer's and angiogenic dementias there exist certain differences within the clinical picture. Patients with angiogenic dementias often display greater difficulties in the course of function evaluation connected with localised mechanisms in the frontal lobes and the subcortical areas. However, patients with Alzheimer's usually present a more intensified disturbance in the course of undertaking tests for the evaluation of memory and linguistic functions [4].

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Besides the distinctness in relation to disturbances to the cognitive symptoms, there is equally observed a difference within the neuropsychiatric symptoms. Under this notion, after Cummings, there should be understood a series of psychopathological symptoms not directly connected with the cognitive sphere, such as mood disturbance, anxiety, stimulation (arousal) psychotic symptoms, sleep disturbance, and a series of others [5]. Data exist showing the varied intensification of such symptoms depending on the presence of a vascular substratum [6].

In tests carried out earlier based on a patient population of outpatients, the influence of vascular factors on the psychopathological image of Alzheimer's was noted [7]. The presented research was conducted upon a more uniform patient population, as well as being based, in comparison to earlier tests conducted, on widely accepted and more appropriate methods for the measurement of neuropsychiatric symptoms.

OBJECTIVE

The aim of the research was evaluation of the influence of vascular factors present within Alzheimer's on the frequency in the appearance and intensification of neuropsychiatric symptoms.

MATERIALS AND METHOD

The initial population were individuals residing at a Social Care Home in Gdynia (n = 188). Patients with diagnosed Alzheimer's were qualified for the research. The initial procedure for inclusion in the research was the obtainment of permission for participation in the tests, as well as an evaluation of the criteria excluding testing i.e., the presence at the moment of testing or during the course of the questionnaire of one of the following diseases: affective disease, schizophrenia, alcoholism, addiction to medications or intoxicants, epilepsy, Parkinson's disease, mental handicaps; the presence at the moment of testing of disturbances in consciousness, lower limb, eye or hearing conditions noticeably hampering the carrying out instructions and procedures contained within the applied clinical scales, and serious somatic ailments. The initial selection also incorporated the use of the MMSE scale [8]. Verification in the diagnosis of AD was carried out for all of those tested who in the test using the MMSE scale obtained 24 or fewer points. The diagnostic approach in the confirmation or exclusion of probable Alzheimer's was based on NINCDS/ADRDA criteria [9]. In all of those tested, the Hachinski scale was applied. [10]. As a criterion for exclusion was the adoption of a Hachinski Scale score of more than 4 points.

Evaluation of the cognitive functions of patients included into the research was conducted on the basis of the Alzheimer's Disease Assessment Scale (ADAS) [11]. An 11-element subscale (ADAS – cog) for the evaluation of cognitive functions was used in the tests (speech quality, understanding of spoken language, remembering test instructions, difficulty with finding the right words during spontaneous speech, understanding instructions, naming of objects and fingers of the hand, copying figures/diagrams, ideomotor activities, orientation, remembering words, word recognition). The result of the cognitive part is placed within the range 0–70 points, where 0 means an absence of any difficulty whatsoever, while 70 means deep-rooted dementia.

The frequency of the appearance and intensification of neuropsychiatric symptoms was evaluated on the basis of the Neuropsychiatric Inventory, the version for nursing homes (NPI) developed by Cummings et al. [12, 13]. The Neuropsychiatric Inventory in the version employed in the presented research contains an evaluation of 12 categories (Tab. 3). For each of the categories, an evaluation is taken in relation to the frequency on a four-point scale (1 – sporadic, 4 – very often) and the depth (intensity) of the disturbances on a three-point scale (1 – mild, 3 – deep). Some versions of the scale also contain an evaluation of the influence of the ascertained disturbances upon the surroundings (annoyance factor), which was not analysed in the presented tests. In the evaluation of reliability and accuracy NPI obtained high scores [13]. A Polish-language version of the NPI-NH scale was used in the research. In the evaluation of the reliability of the Polish-language version the following results were obtained: evaluation of internal conformity: 0.92; evaluation of retesting reliability (test retest reliability): 0.69; evaluation of comparability (interrater reliability): 0.85 [14]. In addition the Montgomery-Asberg Depression Rating Scale (MADRS) was introduced [15].

The testing by means of the MADRS and NPI -NH scales was conducted exclusively by a specialist psychiatrist. The ADAS-cog scale was applied also by a specialist psychiatrist or clinical psychologist. However, social workers and nursing staff independently applied the MMSE, as well as constituting the source of information in conducting the NPI-NH scale.

In the presented study, 48 persons with diagnosed Alzheimer's were tested who had an average age of 70. The Hachinski scale result constituted the basis for differentiating the two test groups. The result that fitted the 0–1 point band resulted in the patients being placed in the group with an insignificant burdening with vascular factors – this condition was fulfilled by 22 people, while those with a result of 2–4 points were qualified as being burdened with a significant vascular factor, which applied to 26 individuals.

Analysis of the statistics was based on a test conducted for two mean independents, for which the average values of the applied clinical scales between the analysed groups were compared. The adopted level of significance (p) was 0.05. The results of the tests for which the level of significance was equal or lower than 0.05 ($p<0.05$ or $p=0.05$) was considered significant, while the remaining ($p>0.05$) as non-significant in the adoption of a two-sided division.

RESULTS

Table 1 are presented the mean values for age as well as the results of tests using the ADAS-cog, the MADRS scale and the NIP – NH scale.

Table 1. Mean results of age and values obtained in scales applied for the tested population (n = 48).

Variable	mean	Min	Max	SD
age	70.00	52.00	85.00	8.02
MMSE	15.96	0.00	24.00	4.91
Hachinski	1.77	0.00	5.00	1.37
ADAS – cog	32.14	14.66	69.00	12.45
MADRS	11.23	0.00	35.00	7.97
NPI	28.83	3.00	56.00	12.18

In Table 2 are compared the mean values of age as well as the applied scales obtained for individuals with a low value on the Hachinski scale (0–1 points) and a high value (2–4 points). Neither group differentiated in terms of age nor intensification of disturbances to the cognitive functions (ADAS-cog), while individuals with a high Hachinski Scale result also obtained a higher score on the MADRS scale; however, this dependence did not obtain statistical confirmation. Depressive and dysphoric disorders according to the NPI –NH scale, as well as an intensification in anxiety, were different in both groups. Equally, the differences in the total evaluation of disinhibition were close to statistical significance. In each of the discussed variables, a greater intensification in psychopathological phenomena occurred in individuals with a greater degree of burdening by potential vascular factors. Also in this group, a higher combined result of the NIP-NH scale was characteristic.

Table 2. Mean results for age, ADAS cog scale, MADRS and NPI - NH (individual categories of disorder are presented) in individuals with a lower (Hachinski Scale result 0 -1 pts) and higher (Hachinski Scale result 2 – 4 pts) burdened by vascular factors.

Variable	Hachinski 0–1 n = 22		Hachinski 2–4 pkt n = 26		Significance
	average/ mean	SD	average/ mean	SD	
Age	69.48	8.10	70.42	8.11	NS
ADAS – cog	32.38	14.32	31.94	10.90	NS
MADRS	9.36	7.27	12.81	8.33	NS
A. DELUSION					
frequency:	0.32	0.65	0.46	0.58	NS
intensification:	0.32	0.65	0.42	0.70	NS
frequency x intensification	0.32	0.65	0.42	0.70	NS
B. HALLUCINATION					
frequency:	0.23	0.43	0.12	0.33	NS
intensification:	0.27	0.55	0.12	0.33	NS
frequency x intensification	0.27	0.55	0.12	0.33	NS
C. AROUSAL / AGGESSION					
frequency:	0.73	0.83	0.92	0.93	NS
intensification:	0.73	0.94	1.12	1.14	NS
frequency x intensification	1.18	1.76	2.00	2.55	NS
D. DEPRESSION / DYSPHORIA					
Frequency:	0.14	0.35	1.27	0.87	p< 0.05
Intensification:	0.14	0.35	1.23	0.95	p< 0.05
Frequency x intensification	0.14	0.35	2.15	2.20	p< 0.05
E. ANXIETY					
Frequency:	1.05	0.79	1.42	0.86	p< 0.05
Intensification:	1.05	0.84	1.73	1.15	
Frequency x intensification	1.68	1.70	3.04	2.66	p< 0.05
F. MOOD UPLIFTING / EUPHORIA					
Frequency:	0.50	0.67	0.35	0.56	NS
Intensification:	0.50	0.67	0.35	0.69	NS
Frequency x intensification	0.59	0.80	0.42	0.95	NS
G. APATHY/INDIFFERENCE					
Frequency:	0.68	0.89	1.00	0.75	NS
Intensification:	0.73	0.98	0.92	0.69	NS
Frequency x intensification	1.27	1.88	1.38	1.42	NS
H. DISINHIBITION					
Frequency:	0.27	0.46	0.62	0.85	NS
Intensification:	0.41	0.73	0.81	1.13	NS
Frequency x intensification	0.41	0.73	1.35	2.10	p = 0.052
IRRITABILITY/EMOTIONAL INSTABILITY					
Frequency:	1.00	0.93	1.04	0.82	NS
Intensification:	1.18	1.10	1.31	1.09	NS
Frequency x intensification	2.05	2.48	2.08	2.06	NS
J. ABNORMAL MOTOR FUNCTIONING					
Frequency:	0.27	0.46	0.12	0.33	NS
Intensification:	0.41	0.73	0.15	0.46	NS
Frequency x intensification	0.41	0.73	0.15	0.46	NS
K. SLEEP AND NOCTURAL ACTIVITY DISORDERS					
Frequency:	0.68	0.84	1.08	1.06	NS
Intensification:	0.82	1.05	1.27	1.28	NS
Frequency x intensification	1.32	1.89	2.58	2.98	NS
L. APPETITE AND EATING DISORDERS					
Frequency:	0.09	0.29	0.23	0.43	NS
Intensification:	0.14	0.47	0.27	0.53	NS
Frequency x intensification	0.14	0.47	0.27	0.53	NS
NPI –sum	**22.41**	**12.92**	**34.27**	**8.45**	**NS**

DISCUSSION

The vascular factors that widely occur in Alzheimer's are treated as an increase in the risk of the disease. The observations of patients with angiogenic dementia and Alzheimer's show a certain changeability in the area of neuropsychiatric symptom manifestation. Also, the presence of vascular factors within the conducted tests significantly influences the psychopathological image of individuals with diagnosed Alzheimer's disease. However, no noticeable differences were noted with regard to the very intensification of the dementia process evaluated by the ADAS-cog scale; differences concerned first and foremost extra-cognitive symptoms appearing during the course of dementia. The clearest differences between those with a higher and lower burdening by vascular factors concerned depressive and dysphoric disorders. The results obtained show concurrence with those tests in which a greater frequency in depressive disorders during the course of angiogenic dementia was displayed [16]. Here, it is worth drawing attention to a range of publications pointing to a certain specific type of depression, referred to as vascular depression which is connected with advanced years and the presence in the MRI image of hyper-intensive zones of an ischaemic character, particularly in white matter and in the pericellular regions [17]. Regardless of the numerous controversies connected with the notion of vascular depression, it follows that the postulated connection of a lowered mood (state of mind) with the presence of vascular factors should be pointed out [18].

Almost all the participants in the tests conducted underwent neuroimaging tests; however, in the majority of those tested only a computer tomography was carried out. Unfortunately, with regard to this, it was therefore impossible to conduct an appropriate evaluation of the appearance of ischaemic focuses in the patients. Indirectly, however, one may, via the result obtained on the Hachinski Scale, refer to an intensification in vascular factors.

Other elements evaluated by the NPI-NH Scale which differed within the two groups were anxiety (in relation to intensification) and disinhibition; however, statistical confirmation was not obtained for the latter. The remaining elements of evaluation by means of the NPI–NH Scale also appear to show a greater tendency for manifestation in individuals with a greater intensification of vascular factors. This was confirmed by a statistically documented increased intensification in the joint NPI-NH evaluation.

The connection between the vascular factors and the often appearance of neuropsychiatric symptoms presumably has complex circumstances, and the confirmed differences may be explained on the basis of structural tests of the brain. An example of this are the above-mentioned changes in the MRI tests for individuals with depressive mood disorders.

The neurotransmitter systems of the brain are another area contributing important information useful in explaining the observed dependences. Certain aspects of research show a connection between disturbances in brain transmission and the appearance of certain neuropsychiatric symptoms [19]. It cannot be excluded that the presence of vascular factors additionally hamper the cholinergic transmission, as well as the functioning of other systems. [20]. The presence of vascular factors in Alzheimer's is treated by many authors as a widespread phenomenon, and they even show the vascular process as initiating the very process of the degeneration

of a nerve cell [21]. As a mechanism starting the process is indicated by the damage to the blood-brain barrier caused by a dysfunctioning of the endothelium of the brain's vessels [21, 22]. An increase in the permeability of the brain's blood vessels, resulting in the penetration of proteins, may cause activation of immunological processes initiating the process of neuron destruction [23, 24].

The presented research was conducted on residents of an old people's home, thanks to which there was a reduction in the number of uncontrolled variables, those which are most varied when tests are conducted on out-patient populations. Evaluation of the frequency that occurred and intensification in neuropsychiatric symptoms was based upon the NPI Scale, for which the version designated for the testing of individuals residing in care institutions was used. This is very important, not only for the results obtained, but also for the comfort of the patient according to the modern health care principles [25, 26]. On the basis of the presented research, it may be state that the application of an instrument of sufficient sensitivity and specificity enabled obtaining reliable data from the research. In tests that were conducted based on a different methodology than that applied previously, conformation was obtained of the previous observations showing an increase in the frequency of neuropsychiatric symptom manifestation and intensity in individuals with a greater burden of vascular factors.

Evaluation of the appearance of vascular factors was based on the result obtained through the Hachinski Scale which, however, constitutes a notable limitation in that it allows for wide-ranging conclusions to be drawn. Verification of the clinical evaluation for the appearance of vascular factors with radiological imaging is essential. Admittedly, in some of those tested (n = 16) nuclear magnetic resonance was conducted; however, the number in this group made it impossible to conduct a reliable evaluation. All the more so, that in radiological imaging there needs to be taken into consideration not only the quantity and scope of the ascertained vascular changes but first and foremost their location.

In summing up, it follows that it may be stated that the results obtained confirm earlier observations concerning the link between vascular changes and the manifestation of neuropsychiatric symptoms; however, to allow for a better understanding of the matter it is essential that radiological verification of the clinical data evaluated by means of the Hachinski ischaemic scale should be conducted.

CONCLUSIONS

Vascular factors in Alsheimer's disease influence the presence of neuropsychiatric symptoms. In the course of angiogenic dementia a greater frequency in depressive disorders was shown. The most visible differences between individuals with a greater and lesser burden of vascular factors was in the realm of depressive and dysphoric disorders.

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