Personalized Psychiatry and Neurology

Case Report

Atypical Structure of Broca's Area in a Patient with Primary Progressive Atrophy Syndrome at the Onset of Alzheimer's Disease

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Abstract: This article presents a clinical case of Alzheimer's disease with a debut as primary progressive aphasia syndrome. Insufficient use of routine magnetic resonance imaging in this case in the diagnosis of neurodegenerative diseases and the advantage of such additional neuroimaging methods as positron emission tomography, functional magnetic resonance imaging with a scale assessment of atrophic changes. Additional neuroimaging techniques have been shown to significantly improve the early detection of pathological changes in brain structures and to reveal the location of functional areas involved in the neurodegenerative process.

Keywords: *Alzheimer's disease; neuroimaging diagnostics; positron emission tomography; functional magnetic resonance imaging.*

1. Introduction

There were about 1.061 million patients with dementia in the Russia Federation in 2006. This number is expected to increase to 1.354 million by 2020. This represents approximately 1% of the population [8]. Life expectancy is from 4 to 8 years since the manifestation of dementia, with average survival being higher than early debut of it [9-11]. Alzheimer's disease (AD) is the most common neurodegenerative disease. It causes dementia syndrome in 28-38 million people worldwide, which is about 60-80% of all cases of dementia [1-4]. In the next decades, the number of patients with Alzheimer's disease is expected to increase several times, and their possible number will be more than 110-130 million by 2050 [5-7].

At the present stage of development of diagnostics of AD open wide opportunities to study the pathological process, relying not only on the clinical picture of the disease, but also on neuroimaging methods with assessment of involvement of various brain structures. In typical cases of AD, the neurodegenerative process begins in the hippocampus and then progresses, gradually involving the temporal lobes, in the subsequent - frontal and parietal associative regions [12, 13]. Atrophy of the hippocampus, parahippocampal gyrus, amygdala and other anatomical structures of the temporal lobes is more common in AD and is considered the primary predictor of cognitive impairment progression [14-17]. A positive correlation of the degree of atrophy of target structures with the severity of cognitive impairment, in neuroimaging studies was confirmed [18]. For example, in patients with a subsequent AD, atrophy with a 10% [19] decrease in the medial temporal lobe was observed, and in some cases, a decrease in the posterior cingulate gyrus and frontal lobe was detected at the stage of mild cognitive impairment [20, 21]. Several clinical pathological studies have shown involvement in the neurodegenerative process of the posterior cingulate gyrus, parietal and temporoparietal cortex in patients with typical clinical AD. Atypical cases, without pronounced memory impairment, were more often associated with less involvement of the medial temporal lobe [17, 22, 23]. Atrophic changes in various structures occur in the early stages of the neurodegenerative process, so the routine use of neuroimaging techniques may be relevant for AD diagnosis [24, 25, 26]. The need to use specialized scales to assess the atrophy of target areas and voxel-based morphometry to estimate the total volume of brain structures becomes apparent [26, 27]. Due to the progression of the pathological process involving more areas of the brain, even the use of magnetic resonance imaging (MRI) with atrophy assessment scales is often insufficient. It is necessary to include in the diagnosis of more complex methods, such as MR-tractography, functional MRI (fMRT), positron emission tomography (PET) etc. In this article we will demonstrate a clinical case that shows the possibilities of application of neuroimaging in the framework of diagnosis of neurodegenerative process in AD with a complex clinical picture.

2. Clinical case

Patient I., 61 years old, was hospitalized at the Bekhterev National Medical Research Center for Psychiatry and Neurology in September 2022 with complaints of impaired speech and memory. The history of the disease is based on relatives. The disease began 5-6 years ago, when there were problems with memory (memorization of new information). Gradually began to show difficulties with spatial orientation, possession of household appliances and cutlery. Emotional background changed, "more sentimental". Patient applied to a neurologist in 2020, FAB (Frontal Assessment Battery) - 8 points were performed during the examination. The diagnosis was: «Primary progressive aphasia». Results of brain MRI 2020: hypertensive encephalopathy, benign enlargement of subarachnoid space and triventriculomegalium substitution type. Results of brain PET 2020: Decrease in glucose metabolism in the associative cortex of parietal lobes (mainly right), lateral sections of temporal and occipital lobes (also predominantly right), precuneus (right), and posterior cingulate gyrus cingularis on the right.

Psychic status. In consciousness. Contact is difficult due to speech disorders, often asks questions, does not perform complex commands. Speech is poor, confused. The mood is complacent, reduced, periodic anxiety against the background of episodes of disorientation in space. The conversation begins willingly, well-meaning. Expresses concern for his own condition, asks for help. Daily mood fluctuations are not determined. Mindset is concrete. Attention is drained. MMSE (Mini Mental State Examination) - 16 points; MoCA (Montreal Cognitive Assessment) - 7 points; FAB (Frontal Assessment Battery) - 4 points. There is no deception of perception in behavior. He does not express delusional ideas. Without dangerous and suicidal tendencies at the time of examination. Criticism to the condition is purely formal.

Neurological status. No symptoms.

Clinical psychological research. Contact is possible, but difficult due to cognitive and speech disorders. In conversation is well-meaning, smiling, emotionally labile. Eye contact supports. Speech is agrammatic, with literal and verbal paraphasia, lexically impoverished. The patient generally understands and responds to the question. Monological speech is possible, emotionally talks about his life, about his native region, about psychotraumatic events. Outwardly relatively neat. He serves himself rudely. In the self is oriented correctly, in the place - somewhat inaccurate, in time - only partially (can call the current year «21», month calls approximately - «March - April»), in the environment after adaptation is oriented quite well. Simple instructions are generally understood, but retain in memory; complex instructions are almost unavailable. Criticism is reduced.

Failure to perform most of the proposed tasks is explained by poor vision. A full-scale pathopsychological examination is not possible because of severe cognitive deficiency and speech disorders. Task «Exclusion superfluous» is not able to perform, does not understand what is required of him, irritated, referring to the fact that he does not see the image. Simple proverbs interpret concretely, indistinctly; the comparison of para-concepts produces by partial features. The patient can indicate only certain general details when describing the plot picture: «winter... landing...children...». Assistance, tips do not help. Schulte tables cannot be perform. Account (orally and in writing), understanding the number is not available. In general, he learns the numbers of the first ten. Automated enumeration of the numerical series from 1 to 20 and months of the year performs, disarming is not available. The demonstration of the specified finger of the hand is not always accurate. The reproduction of the position of the fingers, the positions of the hands is disturbed. The right-left difference. Independent drawing on the task (geometric shapes, face, house, clock dial), drawing from is not available. The placement of arrows on the painted dial, the determination of time on the layout and on the real clock is not possible. Folding a simple stick figure is not possible. The amount of auditory memory without repetition is 2. The mnemogram of memorization «10 words» has the form: 2-3-3-4-5-4-6 (6 words at the last presentation is possible with a hint). «Repeating of numbers»: in direct order - 2 units, in reverse order - is not possible. Repeating of complex sentences is possible only partially with paraphasia. Retelling of the short text is also possible partially. Naming objects from the surrounding environment and pictures is difficult, but possible. Reading individual letters, words is possible, but with the help of. Writing is not available. Severe impairment of all mental processes (attention, memory, thinking) are revealed in combination with confusion, acalculia, apraxia, aphasia. It indicates local-focal pattern of parietal and temporal brain disorders. The presence of a degenerative process with gross mnesic-intellectual disorders, with modal-specific disorders reflecting the deficiency of the parietal and temporal structures of the brain is revealed.

2.1. Results of Instrumental Methods

The brain MRI is performed on the MP scanner Atlas Exelart Vantage XGV (Toshiba, Japan) with induction of 1.5 Txl magnetic field using T1- and T2-weighted images (WI), FLAIR and T2* pulse sequences (PS), DWI. In addition, the mediobasal temporal lobe sections were subjected to targeted examination using T2 WI-oblique Cor and FLAIR PS-oblique Cor with 2.2 mm thickness perpendicular to the hippocampus long axis. At this stage, atrophic changes and localized brain lesions were assessed on visual scales. To carry out the MP-morphometry with the estimation of quantitative indicators of various brain structures, the PS T1 3D-MPRAGE with a slice thickness of 1mm and isotropic voxel was used with further post-processing handling using the software FreeSurfer 6.0. DTI (diffusion tensor imaging or MP tractography) was used to obtain information about the relationships between different parts of the brain and the integrity of the pathways. In order to map the functional zones, a functional MRI (fMRT) with post-processing in the CONN and SPM12 software packages has been performed. MRI of the brain revealed focal changes of the vascular character of the 2nd degree according to the classification Fazekas. Evaluation of atrophic changes on visual scales: Global cortical atrophy scale (GCA scale) - grade 2, Medial temporal lobe atrophy score (MTLA score) - grade 2, Posterior atrophy score of parietal atrophy (Koedam scale) - grade 2.

Pronounced asymmetrical expansion of lateral fissure on both sides (D>S) and parietooccipital fissure on both sides (D<S) has been identified. Interuncular - 36 mm (rate up to 30 mm). We present the differences ($p \leq 0.05$) of quantitative indicators of different structures of the brain of patient I. and a group of healthy volunteers of similar age from the database of the Department of Neuroimaging Studies (Table 1) [28].

Table 1. Morphometric indicators of brain structures of patient I. and control group.

Structure of the brain	Volumes (3 mm) of the right hemisphere		Volumes (3 mm) of the left hemisphere	
	Patient I.	Control (60-69 years old), M	Patient I.	Control (60-69 years old), M
Cortical gray matter	213736,2	224867,0	223635,9	234364,9
Hippocampus	3338,9	4099,4	3420,6	3836,7
Lateral ventricles	26898,8	11597,2	27068,1	11104,7
Grey matter of the upper temporal gyrus	1145	2126,9	972	1929,9
Grey matter of the fusiform gyrus	5732	9369,4	5287	9088,9
Gray matter of the lower parietal gyrus	6257	11476,9	7524	13606,9
Grey matter of the lateral occipital gyrus	8318	12274,3	7501	11659,9
Grey matter of postcentral gyrus	6347	9197,4	5685	8938,8
Grey matter of the precuneus	6019	8450,6	6088	9090,1
Grey matter of the upper parietal gyrus	7011	13276,7	6184	11896,9
Grey matter of the upper temporal gyrus	7607	11699,4	7235	10756,0
Grey matter of the supramarginal gyrus	6453	10828,0	5496	9701,3
Grey matter of the transverse temporal gyrus	680	1270,4	489	876,1

In patient I. was a marked decrease in the amount of gray matter in the temporal, parietal and occipital lobes of both hemispheres of the brain. It should be noted that the decrease in the cortex of the lower parietal gyrus and hippocampus was more pronounced on the right, the decrease in the volume of the cortex of precuneus was quite symmetric, and the decrease in the volume of the remaining structures was more pronounced on the left.

Functiomal MRI of the brain (Figure 1): to determine the lateralization and localization of the motor speech zone (Broca's area) 2 activating tasks were presented: 1) word generation on a certain letter, 2) the selection of verbs to nouns. The area has been visualized and is located in the right hemisphere in the area of the posterior third of the lower frontal gyrus during post-processing.

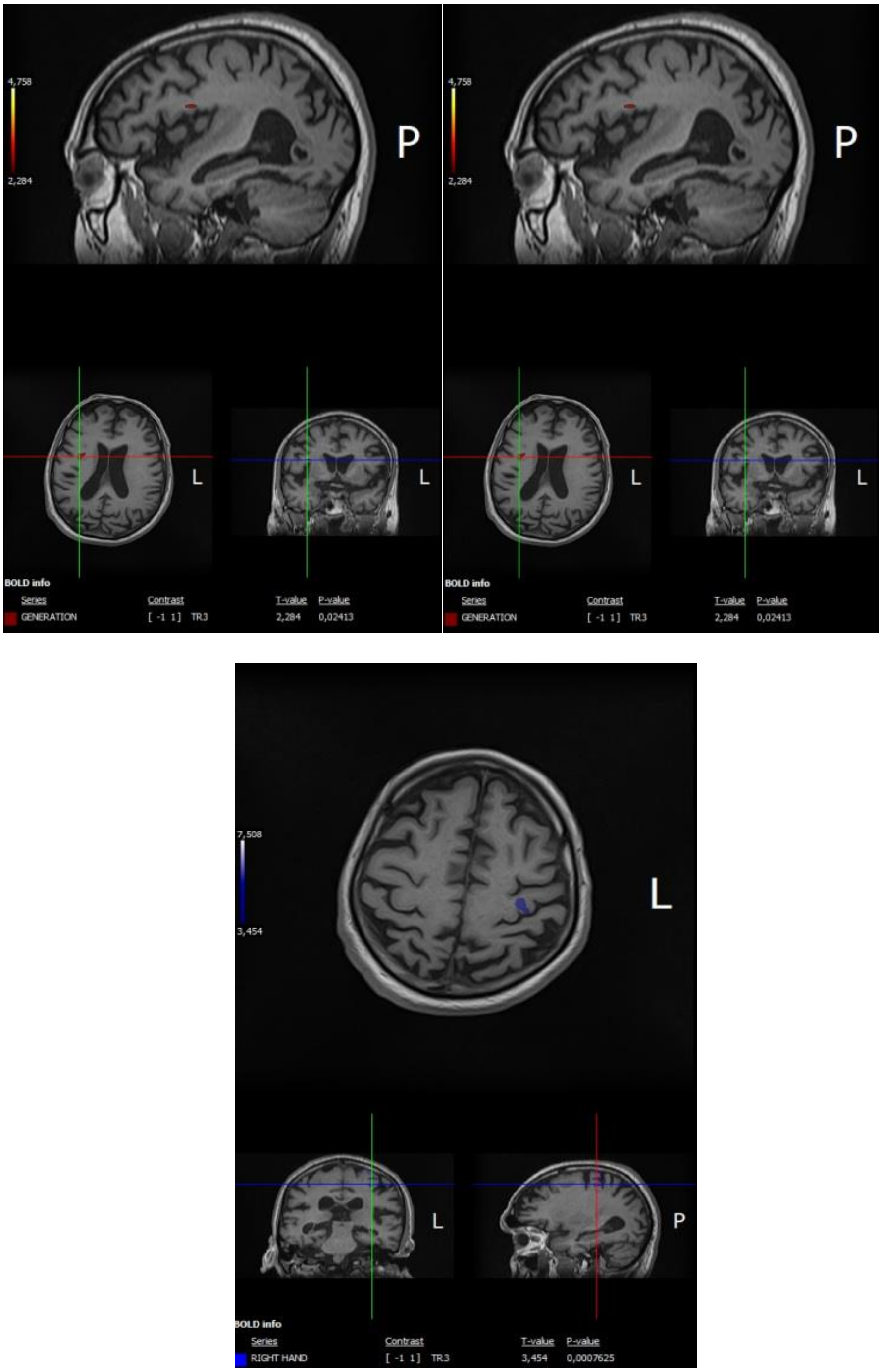

Figure 1. Visualization of the Broca's area with a functional MRI (on top), visualization of the motor representation of the right hand (at the bottom) on fMRT in the patient I.

In order to verify the data through the resulting activation zone, tracts have been developed according to the results of the MR-tractography. The front part of the arcuate fascicle and part of the pyramid tract pass through the activation area (Figure 2). Analysis of the data obtained during diffusion - tensor MRI allowed visualization of conductive paths of white matter - associative, comissural and projection. In qualitative analysis, no significant impoverishment and breakdowns were found.

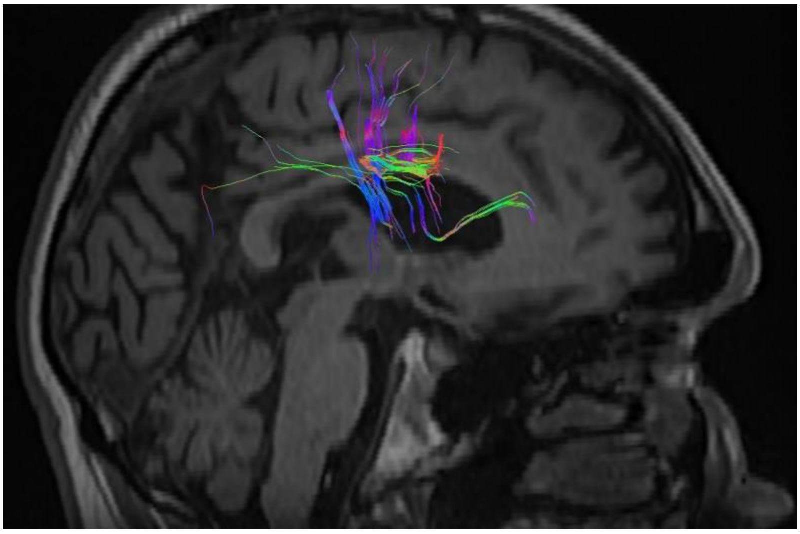

Figure 2. MR-tractography of patient I.

According to the results of the functional scanning, an area of the motor representation of the right hand, located in the precentral gyrus of the left hemisphere, is visualized.

According to the results of clinical, neuropsychological and neuroimaging examination the diagnosis is as follows: Alzheimer's disease with mild dementia syndrome with a debut as primary progressive aphasia nonfluent form (ICD code: G30).

3. Discussion

In this clinical case, we observe a pattern of AD debuting as primary progressive aphasia syndrome followed by gradual progression and involvement of other cognitive spheres. Although no pronounced atrophic changes in the cortex were detected in the routine brain MRI in 2020, PET scans have already shown a decrease in glucose metabolism in the associative cortex of the parietal lobe (greater right), lateral temporal and occipital lobes (also more to the right), precuneus (on the right), as well as the posterior sections of the cingulate gyrus on the right. This indicates the prevalence of neurodegenerative process in the clinical picture were presented only by speech disorders. According to the MR - morphometry from 2022, irregular atrophic changes in the cerebral cortex, mainly the temporal and parietal lobes, as well as the lateral regions of the occipital lobes, are detected. It should be noted that, according to several authors, in the case of clinical manifestations of PPA, a typical neuroimaging sign is asymmetric left temporoparietal atrophy, with a pronounced extension of the left lateral cleft [29,30]. However, according to our study, atrophic changes in the crust of the lower parietal gyrus and hippocampus were more pronounced on the right, and the decline in the cortex percuneus was symmetric. There was also a more pronounced extension of the right lateral slot.

We drew attention to the discrepancy between the clinical picture and the neuroimaging data (patient I. - right-handed) because the disease debuted speech impairment in motor aphasia with relative safety of other cognitive functions. In order to find the cause of this phenomenon, an additional MRI was conducted on the special programme and fMRT. The purpose of the study is mapping of functional-significant zones, in particular - localization of the Broca's area. The functional scan visualized an area in the right hemisphere at the posterior third of the inferior frontal gyrus. In order to verify the data through the resulting activation zone, tracts have been developed according to the results of the MP-tractography. The front of the arcuate fascicle and part of the pyramid path pass through the activation area. Thus, the atypical location of the Broca's area was discovered.

4. Conclusions

Based on the results of this study, we can see that additional methods of neuroimaging are clearly useful in diagnosing AD (atypical manifestations/forms of AD?). When performing a routine MRI, special visual scales should be used to assess in more detail atrophic changes in the cerebral cortex, in particular the Global cortical atrophy scale (GCA scale), Medial temporal lobe atrophy score (MTLA score) and Posterior atrophy score of parietal atrophy (Koedam scale). The use of MR-morphometry makes it possible to estimate the quantitative changes of various brain structures, which cannot be accurately determined by routine MRI research. Functional MRI allows you to refine the localization of the motor and speech zones, which is important when there is a mismatch of clinical manifestations and atrophic process of the brain.

5. Implications

Additional neuroimaging techniques show us the potential for early detection of pathological changes in brain structures in Alzheimer's disease, which will potentially expand the «window of possibilities», better predict treatment and plan therapy more effectively.

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References

1. Katsnelson, A.; De Strooper, B.; Zoghbi, H.Y. Neurodegeneration: From cellular concepts to clinical applications. *Sci Transl Med.* **2016**;8(364):364ps18. DOI:10.1126/scitranslmed. aal2074
2. Preobrazhenskaya I.S. Dementia: epidemiology, clinical picture, diagnosis, approaches to therapy. *Neurology, Neuropsychiatry, Psychosomatics.* **2013**; 5(4):71-77. (In Russ.) DOI: 10.14412/2074-2711-2013-2459
3. Yauzina, N.A.; Komleva, Yu.K.; Salmina, A.B.; Petrova, M.M.; Morozova, G.A.; Malinovskaya, N.A. Epidemiology of Alzheimer's disease in the world. *Neurological Journal.* **2012**; 17(5): 32-37. (In Russ.)
4. Yakhno N.N., Preobrazhenskaya I.S., Zakharov V.V., Stepkina D.A., Lokshina A.B., Mkhitaryan E.A., Koberskaya N.N., Savushkina I.Yu. Prevalence of cognitive impairments in neurological diseases: Analysis of the activities of a specialized outpatient reception office. *Neurology, Neuropsychiatry, Psychosomatics.* **2012**;4(2):30-35. (In Russ.) DOI: 10.14412/2074-2711-2012-378
5. Vasenina, E.E.; Levin, O.S.; Sonin, A.G. Modern trends in epidemiology of dementia and management of patients with cognitive impairment. *Zhurnal Nevrologii I Psikhiatrii imeni S.S. Korsakova.* **2017**;117(6-2):87-95. (In Russ.) DOI:10.17116/jnevro20171176287-95
6. Zakharov, V.V.; Lokshina, A.V.; Vakhnina, N.V. Combined therapy for Alzheimer's disease. *Neurology, Neuropsychiatry, Psychosomatics.* **2022**;14(3):74-80. (In Russ.) DOI:10.14412/2074-2711-2022-3-74-80

7. Koberskaya, N.N. Alzheimer's disease: new diagnostic criteria and therapeutic aspects depending on the stage of the disease. *Medical Council.* **2017**;(10):18-24. (In Russ.) DOI:10.21518/2079-701X-2017-10-18-24
8. Belousov, Yu.B.; Zy`ryanov, S.K.; Belousov, D.Yu.; Beketov, A.S. Clinical and economic aspects of therapy for Alzheimer's disease in Russia. *Quality clinical practice.* **2009**; S1:3-28.
9. Prince, M.; Ali, G.; Guerchet, M.; Prina, A. Matthew; Albanese, E.; Wu, Yu-Tzu. Recent global trends in the prevalence and incidence of dementia, and survival with dementia. *Alzheimer's Research & Therapy.* **2016**;8(1):23. DOI:10.1186/s13195-016-0188-8
10. Rhodius-Meester, H.F.M.; Tijms, B.M.; Lemstra, A.W.; Prins, N.D.; Pijnenburg, Y.A.L.; Bouwman, F.; Scheltens, P.; van der Flier, W.M. Survival in memory clinic cohort is short, even in young-onset dementia. *Journal of Neurology, Neurosurgery & Psychiatry*. **2018**; jnnp-2018-318820. DOI:10.1136/jnnp-2018-318820
11. Villain, N.; Dubois, B. Alzheimer's Disease Including Focal Presentations. *Semin Neurol.* **2019**;39(2):213-226. DOI:10.1055/s-0039-1681041.
12. Braak, H.; Braak, E. Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathol.* **1991**;82(4):239-59. DOI:10.1007/BF00308809
13. Marquié, M.; Siao Tick Chong, M.; Antón-Fernández, A.; Verwer, E.E.; Sáez-Calveras, N.; Meltzer, A.C.; Ramanan, P.; Amaral, A.C.; Gonzalez, J.; Normandin, M.D.; Frosch, M.P.; Gómez-Isla, T. [F-18]-AV-1451 binding correlates with postmortem neurofibrillary tangle Braak staging. *Acta Neuropathologica.* **2017**;134(4):619-628. DOI:10.1007/s00401-017-1740-8.
14. De Carli, C.; Frisoni, G.B.; Clark, C.M., Harvey, D.; Grundman, M.; Petersen, V.; Thal, L. J.; Jin, S.; Jack, C. R.; Scheltens, P. Alzheimer's Disease Cooperative Study Group. Qualitative estimates of medial temporal atrophy as a predictor of progression from mild cognitive impairment to dementia. *Arch Neurol*. **2007**;64(1):108-15. DOI:10.1001/archneur.64.1.108.
15. Du, A.T.; Schuff, N.; Kramer, J.H.; Rosen, H.J.; Gorno-Tempini, M.L.; Rankin, K.; Miller, B. L.; Weiner, M. W. Different regional patterns of cortical thinning in Alzheimer's disease and frontotemporal dementia. *Brain.* **2007**;130 (Pt 4):1159-66. DOI:10.1093/brain/awm016.
16. Pyun, J.M.; Park, Y.H.; Kim, H.R.; Suh, J.; Min, Ju Kang, 1.; Beom Joon Kim, 1.; Youn, Y.C.; Jang, J.W.; Kim, S.Y. Posterior atrophy predicts time to dementia in patients with amyloid-positive mild cognitive impairment. *Alzheimers Res Ther.* **2017**;9(1):99. DOI: 10.1186/s13195-017-0326-y.
17. Shi, F.; Liu, B.; Zhou, Y.; Yu, C.; Jiang, T. Hippocampal Volume and Asymmetry in Mild Cognitive Impairment and Alzheimer's Disease: Meta Analyses of MRI *Studies. Hippocampus.* **2009**;19(11):1055-64. DOI:10.1002/hipo.20573.
18. Burke, S.L.; Rodriguez, M. J.; Barker, W.; Greig-Custo, M.T.; Rosselli, M.: Loewenstein, D.A.; Duara, R. Relationship between Cognitive Performance and Measures of Neurodegeneration among Hispanic and White Non-Hispanic Individuals with Normal Cognition, Mild Cognitive Impairment, and Dementia. *J Int Neuropsychol Soc*. **2018**;24(2):176-187. DOI:10.1017/S1355617717000820.
19. Frisoni, G.B.; Prestia, A.; Zanetti, O.; Galluzzi, S.; Romano, M.; Cotelli, M.; Gennarelli, M.; Binetti, G.; Bocchio, L.; Paghera, B.; Amicucci, G.; Bonetti, M.; Benussi, L.; Ghidoni, R.; Geroldi, C. Markers of Alzheimer's disease in a population attending a memory clinic. *Alzheimers Dement*. **2009**;5(4):307-17. DOI:10.1016/j.jalz.2009.04.1235
20. Karas, G.B.; Scheltens, P.; Rombouts, S.A.; Visser, P.J.; van Schijndel, W.; Fox, N C.; Barkhof, F. Global and local gray matter loss in mild cognitive impairment and Alzheimer's disease. *Neuroimaging.* **2004**;23: 708–716. DOI:10.1016/j.neuroimage.2004.07.006
21. Trivedi M.A., Wichmann A.K., Torgerson B.M., Ward M.A.; Schmitz, V.; Ries, Michele L.; Koscik, Rebecca L.; Asthana, S.; Sterling, C. Structural MRI discriminates individuals with Mild Cognitive Impairment from age-matched controls:

A combined neuropsychological and voxel-based morphometry study. *Alzheimers Dement.* **2006**;2(4):296-302. DOI: 10.1016/j.jalz.2006.06.001

22. Lehmann, M.; Rohrer, J.D.; Clarkson, M.J.; Ridgway, G.R.; Scahill, R.I.; Modat, M.; Warren, J.D.; Ourselin, S.; Barnes, J.; Rossor, M.N.; Fox, N. C. Reduced cortical thickness in the posterior cingulate gyrus is characteristic of both typical and atypical Alzheimer's disease. *J Alzheimers Dis.* **2010**;20(2):587-98. DOI:10.3233/JAD-2010-1401.
23. Whitwell, J.L.; Jack, C.R.; Przybelski, S.A.; Parisi, J.E.; Senjem, M.L.; Boeve, B.F.; Knopman, D.S.; Petersen, R.C.; Dickson, D.W.; Josephs, K. A. Temporoparietal atrophy: a marker of AD pathology independent of clinical diagnosis. *Neurobiol Aging.* **2011**;32(9):1531-41. DOI: 10.1016/j.neurobiolaging.2009.10.012.
24. Emelin, A. Yu.; Odinak, M. M.; Trufanov, G. E.; Boykov, I. V.; Vorobiev, S.V.; Kashin, A.V.; Lobzin, V.Yu.; Kiselev, V.N.; Rezvantsev, M.V. Possibilities of positron emission tomography in the differential diagnosis of dementia. *Bulletin of the Russian Military Medical Academy*. **2010**;4(32):46-51. (In Russ.)
25. Illarioshkin, S. N.; Vlasenko, A. G.; Fedotova, E. Yu. Modern opportunities for identifying the latent stage of the neurodegenerative process. *Annals of Clinical and Experimental Neurology.* **2013**;7(2): 39-50. (In Russ.)
26. Litvinenko, I.V.; Emelin, A.Yu.; Lobzin, V.Yu.; Kolmakova K.A. Neuroimaging techniques for diagnosing Alzheimer's disease and cerebrovascular diseases with cognitive impairment. *Neurology, Neuropsychiatry, Psychosomatics.* **2019**;11(3S):18-25. (In Russ.) DOI:10.14412/2074-2711-2019-3S-18-25
27. Lobzin, V.Yu.; Kiselev, V.N.; Fokin, V.A.; Emelin, A.Yu.; Vorobyov, S.V.; Lupanov, I.A.; Sokolov, A.V.; Efimtsev, A.Yu. Application of magnetic resonance morphometry in the diagnosis of Alzheimer's disease and vascular cognitive impairment. *Bulletin of the Russian Military Medical Academy.* **2013**;3(43):48-54. (In Russ.)
28. Anan'eva, N.I.; Lukina, L. V.; Andreev, E. V.; Tikhonov P. M. Gender features of normal age-related aging of the central nervous system. Database registration certificate 2021621983 dated 09/17/2021.
29. Madhavan, A.; Whitwell, J.L.; Weigand, S.D.; Duffy, J. R.; Strand, E. A.; Machulda, M. M.; Tosakulwong, N.; Senjem, M. L.; Gunter, J. L.; Lowe, V. J.; Petersen, R. C.; Jack Jr, C.R.; Josephs, K. A. FDG PET and MRI in logopenic primary progressive aphasia versus dementia of the Alzheimer's type. *PLoS One.* **2013**;8(4):e62471. DOI: 10.1371/journal.pone.0062471.
30. Mikhailov V.A.; Kotsiubinskaya Yu.V.; Safonova N.Yu.; Ananieva N.I.; Stulov I.K. Primary progressive aphasia. *Neurology, Neuropsychiatry, Psychosomatics*. **2019**;11(1):4-11. DOI:10.14412/2074-2711-2019-1-4-11