The First Positron Emission Tomography Study of the Brain of Patients with Glaucoma

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Abstract

Aim: To determine the location and pattern of changes in the rate of glucose metabolism in brain structures according to positron emission tomography (PET) in patients with primary open-angle glaucoma (POAG). **Methods:** Nine patients with initial, developed and advanced stages of glaucoma were examined. The control group consisted of patients of a similar age group without signs of glaucoma. The PET study was performed on an Optima 560 PET / CT scanner. 30-40 minutes before the start of the scan, the patient was given an intravenous radiopharmaceutical (RP) using 18F-fluorodeoxyglucose (18F-FDG). During the accumulation of the radiopharmaceutical, the patient was in a room with dim light, with a low noise level and minimal motor activity. **Results:** When conducting PET with 18F-FDG, a change in the rate of glucose metabolism (RGM) was recorded in the form of a decrease in RGM in the upper parietal lobe, lower parietal lobe and precuneus (the inner part of the parietal cortex), as well as an increase in RGM of the prefrontal cortex, sensorimotor cortex. Signs of a change in RGM in the posterior region of the lumbar cortex, in the nuclei of the caudate nuclei and in the optic thalamus were also revealed. Similar data on changes in the rate of glucose metabolism in brain neurons that we recorded in patients with POAG are usually recorded in patients with other neurodegenerative diseases. **Findings:** Undoubtedly, the revealed changes in the rate of glucose metabolism in the neurons of the brain of patients with POAG indicate the affinity of this nosology with other neurodegenerative diseases and reveal the basis of disorders (visual, cognitive, autonomic) associated with changes in the central nervous system in patients with POAG. Research in this direction needs to be continued.

Key Words: Positron Emission Tomography, PET, Glaucoma, Radiopharmaceutical, RFP, 18F-fluorodeoxyglucose, 18F-FDG, Parietal Cortex, Limbic System.

DOI Number: 10.14704/nq.2020.18.10.NQ20226 **NeuroQuantology 2020; 18(10):06-12**

Introduction

Currently, primary open-angle glaucoma (POAG) is considered a neurodegenerative disease characterized by structural damage to the optic nerve and slowly progressive death of retinal ganglion cells [Avdeev R. et al., 2014, Gazizova I. et al., 2016, Gazizova I. et al., 2016, 2019]. In this case, the damage extends to all structures of the conducting and central parts of the visual analyzer: the optic nerve, the optic cross, the optic tracts, the lateral cranked bodies with the lateral cranked nuclei, visual radiance and the cerebral cortex [Gupta N. et al. 2006, 2008, Bizrah M. 2011].

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 26 June 2020 **Accepted:** 17 September 2020

In 2016, in the United States, work was carried out to study the structure of the retina and activity of the visual cortex in glaucoma using optical coherence tomography and multimodal magnetic resonance imaging (MRI), in which it was shown that a decline in retinal thickness, optic atrophy and a decrease in activation of the visual cortex precede a narrowing of the visual fields (Bogorodzki P. et al., 2014, Murphy MC et al., 2016, Nuzzi R. et al., 2018). At the same time, there is a turning point between the activity of the visual cortex and the function of the field of view, indicating that the progression of glaucoma is already taking place in the eye and brain before significant loss of vision can be detected in patients using modern testing methods.

One of the modern methods of neuroimaging is positron emission tomography (PET). This technology uses appropriate radiopharmaceuticals (RFPs) and pharmacokinetic models describing the distribution and metabolism of the drug in the tissues, bloodstream and interstitial space. Method allows non-invasive and quantitative assessment of a number of physiological and biochemical processes. In clinical studies, the most common radiopharmaceutical is 18F-fluorodeoxyglucose (18F-FDG), which is used to evaluate energy metabolism.

The reason for the success of this drug is a high level of its accumulation in pathological active (increased rate of glucose metabolism (RGM)) and low - in atrophic (decreased RGM) focuses. 18F-FDG repeats the initial stage of glucose metabolism, the distribution of the drug in the brain reflects the different glycolysis rates in the normal and dysfunctional regions. The intensity of its accumulation is proportional to the activity of glycolysis, which reflects the rate of energy metabolism of cells.

The gray matter of the brain is characterized by a physiologically high level of glucose consumption, the white matter of the brain normally accumulates 18F-FDG significantly weaker than the cerebral cortex.

Aim

To determine the location and pattern of changes in the rate of glucose metabolism in brain structures according to positron emission tomography in patients with primary open-angle glaucoma.

Materials and Methods

Nine patients with initial, developed and advanced stages of glaucoma were examined. The control group consisted of patients of a similar age group without signs of glaucoma. The exclusion criterion for this group of patients were also expressed morphological changes according to MRI and PET. The complex of ophthalmological examination included standard methods: tonometry, biomicroscopy, gonioscopy, ophthalmoscopy, computer static perimetry, optical coherence tomography. The diagnosis of POAG was verified using functional and morphometric research methods. Patient characteristics are presented in Table 1.

The PET study was performed on an Optima 560 PET / CT scanner. The duration of the study was 15 minutes. 30–40 minutes before the start of the scan, patients were given an intravenous radiopharmaceutical, 18F-fluorodeoxyglucose (18F-FDG) was used. During the accumulation of the radiopharmaceutical, the patient was in a room with dim light, with a low noise level and minimal motor activity.

As noted above, 18F-FDG is the most common metabolic tracer in clinical practice. Semi-quantitative analysis of PET consisted in assessing changes in the radiopharmaceutical metabolism in various zones of interest. PET images were transformed into a standard anatomical space adapted to the atlas of Talairach and Tournoux (1988). The spatial normalization of images of each patient and persons from the control group was carried out by creating a standard image (template) using affine rigid and nonlinear transformation (deformation or distortion of images for 3D processing).

Rigid affinity transformation was used to align images by standardizing their size and position. The affinity transformation was carried out according to 12 parameters (3 image displacements, 3 spatial displacements, 3 rotations along the x, y, z axes and 3 image resizes). Changes in each voxel were evaluated in accordance with the general linear model. In POAG, comparisons were also made between groups of patients and groups of control. The effect of total metabolism was offset by normalizing the count in each voxel to the total count in the brain using a proportional scale. In addition, PET and MRI data were combined in three projections.

Table 1. Localization of the area of increase or decrease of RGM in the cerebral cortex in patients with POAG

Age (Years)	Factor MD OD/OS (db)	Factor RIM area OD/OS (mm2)	Factor Average thickness RNFL OD/OS (μm)	Index of interhemispheric asymmetry of the optic thalamus	Localization of the area of increase or decrease of RGM in the cerebral cortex	Z score quantitative measure of the degree of decrease in RGM (-) or an increase in RGM (+)
71	-4,5/-4,8	0,98/1,07	60/75	1,8 (S>D)	Right hemisphere precuneus	-2,06
					The upper divisions of the right parietal lobe	-2,82
					The upper parts of the left parietal lobe	-3
57	-1.1/-3,5	0,91/0,94	81/79	1,58 (D>S)	Lower parietal lobe of the left hemisphere	-2,01
75	-0,31/-3,0	1,26/0,91	117/74	2,85 (S>D)	Areas of increase or decrease in RGM have not been established	
67	-11,2/-0,2	0,82/1,17	63/92	6,22 (D>S)	Left hemisphere precuneus	- 2,14
					The upper divisions of the right parietal lobe	- 2
					The upper parts of the left parietal lobe	- 3,32
63	-0,2/-18,0	1,11/0,74	73/58	3,98 (D>S)	Primary visual cortex of the right hemisphere	3,64
					Primary visual cortex of the left hemisphere	3,28
71	-5,6/-3,6	0,99/0,89	71/89	3,54 (D>S)	Right hemisphere precuneus	-2,44
					Left hemisphere precuneus	- 2,04
					The upper divisions of the right parietal lobe	- 2,36
					The upper parts of the left parietal lobe	- 2,14
					Lower parietal lobe of the left hemisphere	- 2,09
69	-3,3/-2,6	0,76/0,87	78/75	6,96 (D>S)	Areas of increase or decrease in RGM have not been established.	
68	-0,45/-3,44	1,01/1,2	71/95	12,1 (D>S)	Primary visual cortex of the right hemisphere	3,42
					Primary visual cortex of the left hemisphere	2,89
72	-7,6/-1,1	0,7/1,13	61/73	0,29 (D>S)	Right Frontal Cortex	2,01
					Sensomotor cortex of the left hemisphere	2,28
					Occipital lobe of the right hemisphere	2,31
					Occipital lobe of the left hemisphere	2,28

Results

On a series of PET tomograms of the brain of patients, combined with computed tomograms, all parts of the brain are visualized. According to the results of the visual analysis of PET in the control group, a diffuse heterogeneous decrease in the lateral and medial cortex of the cerebral hemispheres was determined, which corresponds to normal age-related changes.

In the main group of patients with POAG, a change in RGM was recorded in the form of a decrease in RGM in the upper parietal lobe, lower parietal lobe and peruneus (the inner part of the parietal cortex), as well as an increase in RGM of the prefrontal cortex, sensorimotor cortex:

1. The decrease in RGM in the projection of the precuneus on the right (Z score = 2.06) and the upper divisions of the parietal lobe of both hemispheres (Z score = 2.82 on the right and 3.0 on the left).
2. The decrease in RGM in the projection of the inferior parietal lobe on the left (Z score = 2.01).
3. The decrease in RGM in the projection of the precuneus on the left (Z score = 2.14) and the upper divisions of the parietal lobe of both hemispheres (Z score = 2.0 on the right and 3.32 on the left).
4. Increased RGM in the projection of the primary visual cortex of both hemispheres (Z score = 3.64 on the right and 3.28 on the left).
5. The decrease in RGM in the projection of the precuneus of both hemispheres (Z score = 2.44 on the right and 2.04 on the left), the upper parts of the parietal lobe of both hemispheres (Z score = 2.36 on the right and 3.14 on the left) and the lower parietal lobe on the left (Z score = 2.09).
6. Increased RGM in the projection of the primary visual cortex of both hemispheres (Z score = 3.42 on the right and 2.89 on the left).
7. Increased RGM in the projection of the prefrontal cortex on the right (Z score = 2.01), the sensorimotor cortex on the left (Z score = 2.28) and the occipital lobe of both hemispheres (Z score = 2.31 on the right and 2.28 on the left).

In 2 patients, areas of decrease and increase in RGM were not established (Table 1).

Table 2 shows the characteristic changes in the structures of the limbic and striatal systems of the brain in patients with POAG according to PET with 18F-FDG.

Table 2. Changes in glucose metabolism in the structures of the limbic and striatal systems in 9 patients with POAG

Brain structure	Metabolic changes	Number of patients	
		Absolute	%
Orbitofrontal cortex	RGM increase	1	0,09
Posterior cingulate gyrus	RGM decrease	7	77,8
Anterior cingulate gyrus	RGM increase	2	22,2
The heads of the caudate nuclei	RGM decrease	7	77,8
Optic thalamus	RGM decrease	8	88,9
Lenticular nuclei	RGM increase	1	0,09

Discussion

When conducting PET with 18F-FDG, a change in RGM was recorded in the form of a decrease in RGM in the upper parts of the parietal lobe, lower parietal lobe and precuneus (the inner part of the parietal cortex), as well as an increase in RGM of the prefrontal cortex, sensorimotor cortex. There were also signs of changes in RGM in the posterior region of the lumbar cortex, in the nuclei of the caudate nuclei and in the optic thalamus (Fig. 1, 2). Similar data on changes in the rate of glucose metabolism in brain neurons that we recorded in patients with POAG are usually recorded in patients with other neurodegenerative diseases. We can also assume that the obtained PET / CT characteristics of the brain in patients with glaucoma indicate an affinity of this nosology with other neurodegenerative diseases. On the other hand, the localization of the areas of lowering of RGM in patients with glaucoma reveals the basis of disorders (cognitive, autonomic) associated with changes in the central nervous system in patients with POAG.

From the point of view of continuing research in the study of the pathogenesis of POAG of the brain, PET / CT is a unique non-invasive method for intravital determination of brain cell metabolism. As an additional diagnostic criterion for the differential diagnosis of neurodegenerative diseases and POAG, it is possible to use the data of PET / CT of the brain obtained and described by us.

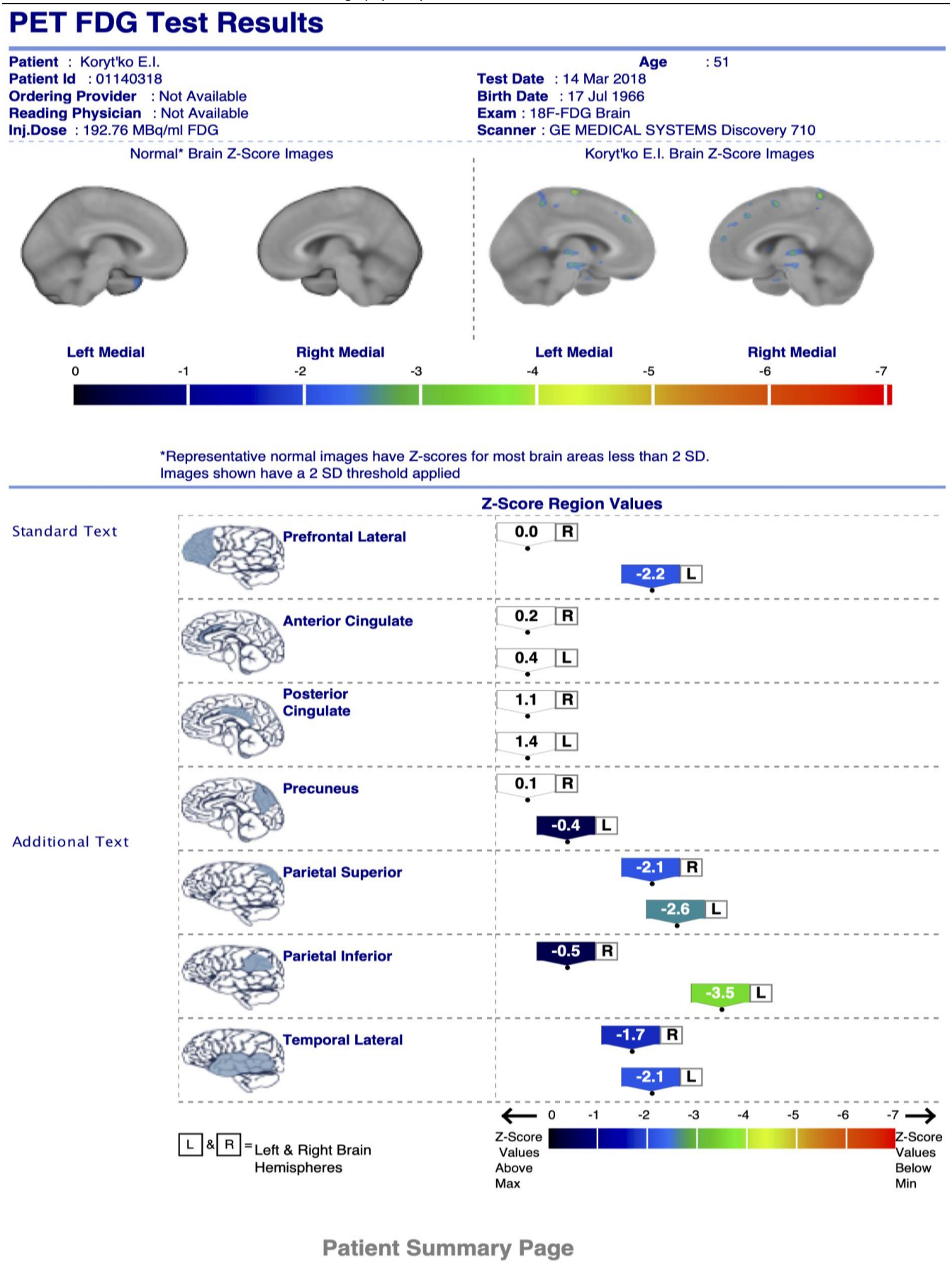

Fig. 1. PET FDG test Results

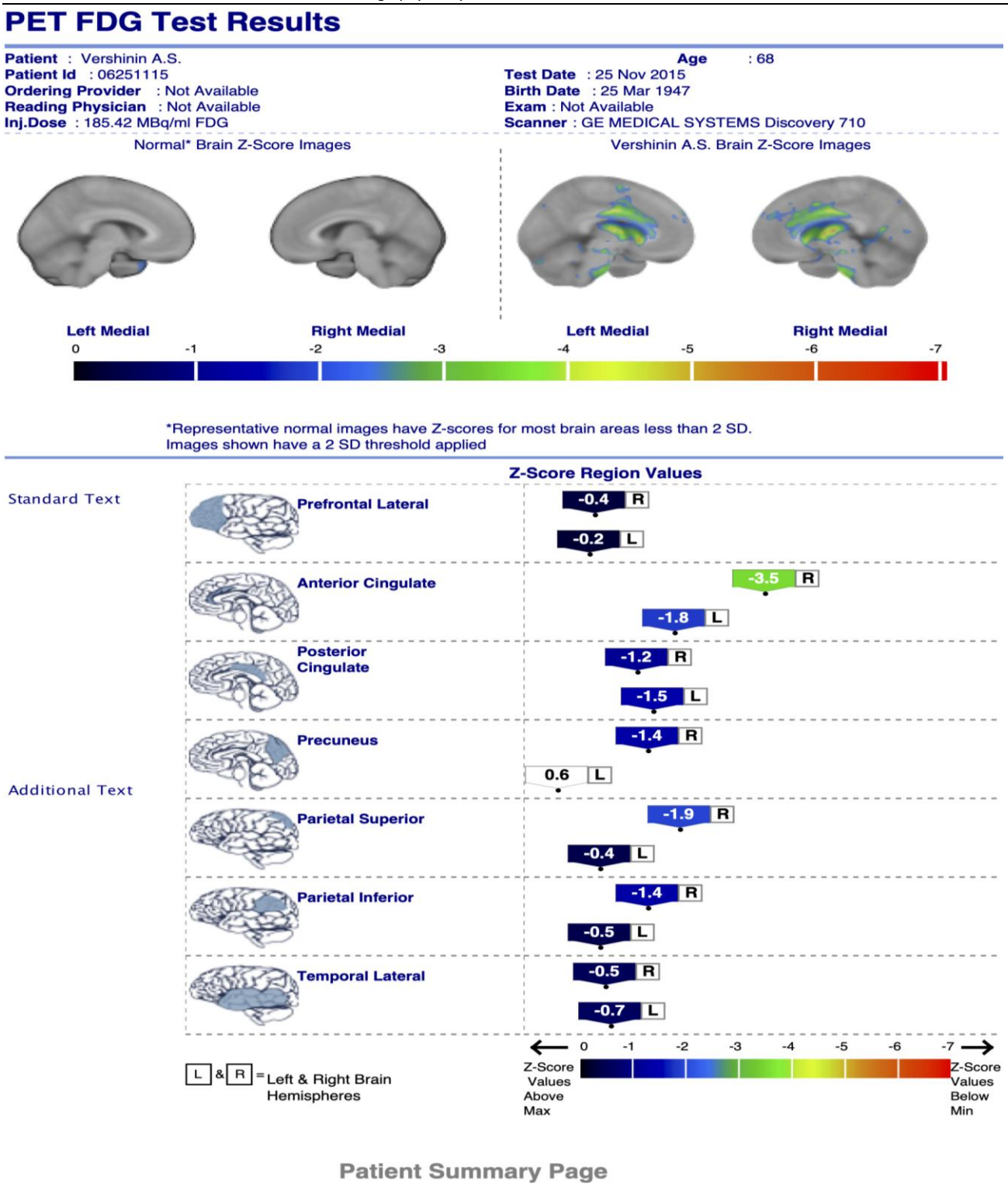

Fig. 2. PET FDG Test Results

The results obtained allow us to clarify the participation of various regions of the limbic and striatal systems (system of emotions) in patients with POAG. In addition, our data indicated that PET with 18F-FDG makes it possible to objectify the choice of target structures for targeted effects, possibly together with specialists from related specialties (neurologists, psychotherapists) for an integrated approach to the treatment of patients with POAG, as well as the ability to evaluate the effectiveness of the treatment.

Conclusion

Patients with POAG during brain PET with 18F-FDG showed signs of decreased RMG in the upper parietal lobe, lower parietal lobe and precuneus,

posterior lumbar cortex, in the heads of the caudate nuclei and optic thalamus. Undoubtedly, the revealed changes in the metabolism of the brain neurons in patients with POAG indicate the affinity of this nosology with other neurodegenerative diseases and reveal the basis of disorders (visual, cognitive, autonomic) associated with changes in the central nervous system in patients with POAG. Research in this direction needs to be continued.

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