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Estimation of cerebral perfusion among patients with eating disorders, anxiety and depressive disorders

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Summary

Aim. Assessment of the cerebral blood perfusion among patients with eating (ED), anxiety (AD) and depressive disorders (DD), diagnosed according to ICD-10.

Method. 57 female and 22 male, aged 17-50 were examined using the Single Photon Emission Computer Tomography (SPECT) and. the neuropsychological tests, Benton and Bender. We also used the Beck Depression Inventory, the Hospital Anxiety and Depression Scale and the Spielberger Self-Evaluation Questionnaire. Electroencephalography was also performed.

Results. In ED, hypoperfusion occurred in 84.21% and impairment of the central nervous system (CNS), was found in 27.77%, abnormalities in the electroencephalography - in 33.33% of the patients. In AD, hypoperfusion occurred in 72.72%, impairment of CNS - in 40%, abnormalities in EEG - in 48% of patients. In DD, hypoperfusion occurred in 81.48%, impairment of CNS - in 34.61%, abnormalities in EEG - in 38.46% of patients.

Conclusions. Hypoperfusion was observed mostly among patients with ED, mainly in the frontal, parietal areas and in the thalamus, on the left hand side, similar to the DD group. Among patients with AD, hypoperfusion at the left hand side occurred almost three times more frequently than among patients with DD (Chi^2=6.54, P<0.025). Anxiety as a trait was the highest in ED, but not significant. Among patients with AD, anxiety as a trait and as a state were almost at the same level.

SPECT / eating / anxiety and depressive disorders

INRODUCTION

Recent advancements in neuroimaging techniques (CT, MRI, fMRI, PET, MRS, SPECT) have brought about new, less invasive methods of examination and diagnostics. They allow a functional assessment of the brain's functioning, monitoring of therapy, assessment of receptors and recently also examination of genetic factors.

The radioisotopic diagnostic methods include Single Photon Emission Tomography (SPECT) and Positron Emission Tomography (PET). For the SPECT technique, one uses isotopes that emit gamma-radiation (technet-99, iod-131, iod-132, xenon-133, thal-201) and the emitted gamma radiation is registered and analysed by a computer.

The SPECT method allows examining cerebral blood perfusion, examination of the location of brain receptors and, using oncofilogical indicators, a diagnostic examination of cancer changes. As functional examination, the results of the SPECT examination change throughout the years and during the treatment process. This examination method is relatively safe for the patient. Its significant limitation is only the fact that this method does not always point specifically to the causes of the changes that are registered.

Machines that have both the functions of CT and SPECT, or MR and SPECT, offer new directions of development and new possibilities.

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The SPECT method is useful in diagnosing problems with cerebral blood circulation, systematic diseases of the connective tissue, after traumas, poisonings and in differentiating between retardation problems. It can also be used in depression, anxiety disorders and obsessive-compulsive disorders [1,2, 3, 4, 5, 6, 7, 8, 9, 10, 11].

In depression, one often finds hypoperfusion in the prefrontal or frontal lobe, bilaterally, or only at the left hand side. There may also be limited perfusion in the temporal lobe (bilateral or left-hand-side only), parietal lobe and the subcortical areas: thalamus, limbic system and the nucleus caudatus.

These findings are not always able to show convincingly the connection between depression and hypoperfusion. One may consider this probable, though, because the aforementioned areas are linked with mood regulation.

In eating disorders, hypoperfusion is observed in the temporal area, parietal area and in the occipital area and in anxiety disorders in the limbic system area [6, 7, 8].

AIM OF THE STUDY

The aim of this research was to assess cerebral blood perfusion among patients with eating, anxiety and depressive disorders, who were examined using the Single Photon Emission Computer Tomography (SPECT) and to establish a correlation between hypoperfusion, neuropsychological tests and more severe depressive and anxiety problems, as measured by psychological tests.

MATERIAL AND METHODS

The participants of this study were patients of the Psychiatry and Neurotic Disorders Department (57 female and 22 male), between 17 and 50 years old, who were treated at the Neurotic Ward between 2003 and 2005, diagnosed with eating disorders, anxiety, or depressive disorders. The diagnoses were made in accordance with ICD-10. In case of eating disorders, DSM-IV-R was also used.

Patients were examined in the Nuclear Medicine Department using the Single Photon Emission Computer Tomography method (SPECT). A three-headed gamma camera Multispect-3 (Siemens, Erlangen, Germany) was used, after applying the gamma-emitting tracer Tc-99m-ECD (FAM, Łódź, Poland) with activity 370 μBq, in the patient's second week of stay in the Ward. As significant in the SPECT examination, we considered areas of asymmetrical gathering of the tracer over 6% for frontal lobes, 8% for temporal and parietal lobes, 10% in the basal ganglia and 12% in the thalamus. Hypoperfusion was analysed in comparison to perfusion in the cerebellum.

In the Neurotic Ward, patients were examined psychiatrically and using psychological methods. The tests used included Benton test (testing recollection of figures) and the L. Bender test (test of copying figures), examining sight and spatial functions. These tests do not burden the patient and allow for assessment of organic changes in the central nervous system [12, 13, 14].

Scales and questionnaires that assess depressive and anxiety symptoms were also used: the Beck Depression Inventory (BDI), the Hospital Anxiety and Depression Scale (HADS) and the Spielberger Self-Evaluation Questionnaire (STAI). Additionally, electroencephalography was performed in the Biological Psychiatry Department.

Patients were divided into three groups. In the first group (ED), comprising of patients with eating disorders, there were 19 women (six with anorexia nervosa of the bulimic type, one with anorexia nervosa of the restrictive type and twelve with bulimia nervosa of the purging type, according to the DSM-IV-R). We connected cases with anorexia nervosa of the restrictive type with bulimia nervosa of the bulimic type, because they have some common traits. The women's mean age was 24.34 years, with a standard deviation of 3.34 years.

In the second group (AD), we included patients with mostly anxiety disorders (panic attacks- 12, depressive-anxiety disorders- 10, social phobia- 7, agoraphobia- 4, obsessive-compulsive disorders- 3, other- 2). This group comprised of 33 patients (20 women and 13 men), with the mean age of 33.37 years (SD=10.98).

One patient suffered from comorbidity of more than one anxiety disorder.

In the third group (DD), we included patients with depressive disorders (first depressive episode), with comorbidity of panic attacks, agoraphobia and social phobia. This group comprised of 27 patients (18 women and 9 men), with the average age of 30.33 years (SD=14.02, (see Tab. 1, 2).

In the statistical analyses, we used the $\chi 2$ test.

Table. 1. Demographic data.

Group n=79	Female n=57	Male n=22	Age 17-50
I ED, 7AnN 12 BnN	19		24.34±3.34
II AN 33	20	13	33.37±10.98
III DD 27	18	9	30.33±14.02

ED - Eating Disorders, AN - Anxiety Disorders, DD - Depressive Disorders, AnN - Anorexia Nervosa, BnN - Bulimia Nervosa

Table 2. Abnormalities in: SPECT, Neuropsychological Tests, EEG.

Group n=79	Hypoperfusion in SPECT	Benton, Bender Tests	EEG
ED 19	84.21%	27.77%	33.33%
AD 33	72.72%	40.00%	48.00%
DD 27	81.48%	34.61%	38.46%

RESULTS

In the first group (Eating Disorders group, ED), hypoperfusion (as compared with perfusion in the cerebellum) occurred in 84.21% of the patients and a decline in the functioning of the central nervous system, as diagnosed using the Benton and Bender tests, was found in 27.77% of the patients. Abnormalities in the electroencephalography were found in 33.33% of them (see Tab. 2).

Hypoperfusion occurred more frequently at the left hand side, with the odds ratio of 1.2:1. In four cases (over 20% of this group), we found hypoperfusion up to 61% in both hemispheres. As far as exact localization is concerned, hypoperfusion occurred most frequently in parietal, frontal and pericentral areas.(see Tab. 3, 4, 5)

Table 3. Localization of cerebral hypoperfusion.

Diagnosis n	ZO 19	ZN 33	ZD 27
Right hemispher	19	17	41
Left hemisphere	23	46	45
L: P	1.21	2.70	1.09
Both hemispheres hypoperfusion (%)	n=4 65-76%	n=4 68-80%	n=1 77-80%

Table 4. Localization of cerebral hypoperfusion

Diagnosis Localization n	ED 19	AD 33	DD 27
Prefrontal	4 21%	5 15.5%	9 33.3%
Frontal	9 47.3%	17 51.5%	14 51.8%
Temporal	2 10.5%	4 12.12%	7 25.9%
Parietal	11 58%	15 45.4%	21 77.7%
Occipital	2 10.5%	5 15.15%	9 33.3%
Pericentral	8 42%	20 60.6%	13 48%
Roland' s Reg.			1
Thalamus	5 26.3%	3 9.0%	7 25.9%
Cerebellum	1		

Table 5. Cerebral hypoperfusion in %

Diagnosis n	ED 19	AN 33	DD 27
Up to 15%	4 (21.0%)	8 (24.2%)	12 (44.4%)
16-25%	7 (36.8%)	12 (36.3%)	6 (22.2%)
over 26%	5 (26.3%)	4 (12.1%)	4 (14.8%)

In five cases (over 25% of the group), hypoperfusion occurred in the thalamus and in one case also in the cerebellum. A percentage assessment of the hypoperfusion gave the following results. Four patients suffered from a mild hypoperfusion (up to 15%), seven patients suffered from a moderate hypoperfusion (16-25%) and five pa-

tients (over 25% of the group) suffered from severe hypoperfusion (over 25%). Thus, moderate and severe hypoperfusion occurred in 63.1% of the patients in the eating disorders group.

Analysis of the severity of depressive and anxiety symptoms using the aforementioned questionnaires and scales gave the following results. In the Beck Depression Inventory we found a mean of 19.42 points (SD=10.42) and in the Hospital Anxiety and Depression Scale the patients had a mean of 7.75 points (SD=4.08) for depression and 13.38 points (SD=6.25) for anxiety. In the Spielberg Self-Evaluation Questionnaire (STAI), anxiety as a state had a mean of 47.07 points (SD=3.86) and the highest indicator of anxiety as a trait had a mean of 53.26 points (SD=6.65, see Table 6.). However, the difference between this group and the other two groups was not significant ($\chi 2$=3.15, P<0.20).

In the second group (Anxiety Disorders patients), hypoperfusion occurred in 72.72% of the patients, decline in the functioning of the central nervous system (as measured with the Benton and Bender tests) occurred in 40% of the patients and abnormalities in EEG occurred in 48% of the patients (see Table 2). Hypoperfusion in this group occurred almost three times more frequently on the left hand side than on the right hand side (ratio 2.7:1). Hypoperfusion was localized in the pericentral areas and in the frontal and parietal lobes. In four cases (12%) we observed hypoperfusion in both hemispheres. The percentage assessment of hypoperfusion was the following. Perfusion decrease up to 15% occurred in 8 cases (24% of the group), decrease between 15-25% occurred in 12 cases (36% of the group) and a decrease over 25% occurred in 4 cases (12% of the group). Thus, moderate or severe hypoperfusion occurred in 48.3% of patients from the anxiety disorders group.

Assessment of the severity of the depressive and anxiety symptoms using the aforementioned methods was the following. Assessment of depression (using Beck's BID) gave on average 18.45 points (SD=13.85), the level of depression in the HADS depression scale was on average 5.05 points (SD=4.92) and the level of anxiety was on average 14.06 points (SD=5.92). Anxiety as a state (STAI) had on average 47.31 points (SD=4.92) and anxiety as a trait had 48.37 points (SD=4.74 (see Table 6.).

Table 6. Characteristic anxiety and depressive symptoms

Group N 79	Beck	HADS depression	HADS anxiety	STAI anxiety -state	STAI anxiety -trait
ED 19	19.42± 10.42	7.75± 4.08	13.38± 6.25	47.07± 3.86	53.26± 6.65
AD 33	18.45± 13.85	5.05± 4.92	14.06± 5.92	47.31± 4.92	48.37± 4.74
DD 27	16.00± 8.51	9.29± 5.55	17.42± 4.95	45.28± 3.92	52.31± 4.67

In the third group (Depressive Disorders) hypoperfusion occurred in 81.48% of patients, decline in the central nervous system functioning (as assessed with the Benton and Bender tests) occurred in 34.61% of patients and abnormalities in EEG occurred in 38.46% of the patients (see Table 2).

Hypoperfusion occurred somewhat more frequently on the left hand side (ration 1.09:1). It was localized in the parietal, frontal and pericentral areas. In one case we observed hypoperfusion in both hemispheres.

The percentage assessment of hypoperfusion gave the following results. A decrease in perfusion up to 15% occurred in 12 patients (44% of the group), a decrease between 15-25% occurred in 6 patients (22% of the group) and a decrease over 25% occurred in 4 patients (14.8% of the group). Thus, moderate or severe hypoperfusion occurred in 36.8% of the patients with depressive disorders.

The depression level in this group was on average 16.00 points (SD=8.51) on Beck's scale. On the HADS, the average score on the depression scale was 9.29 points (SD=5.55) and on the anxiety scale 17.42 points (SD=4.95). Anxiety as a state (STAI) was on average 45.28 points (SD=3.92) and anxiety as a trait, on average 52.31 points (SD=4.67, see Table 6).

To summarize the data, the greatest degree of hypoperfusion occurred in the Eating Disorders group. It occurred in 84% of the patients in this group and in 63% we found moderate or severe hypoperfusion. The differences between groups were not statistically significant, however if one takes into account the fact that patients in the eating disorders group had smaller central nervous system decline (measured with the Benton and Bender tests) and fewer EEG abnormalities, as compared with the other two groups, it seems that these abnormalities could have to do with

the patients' restrictive eating and could be reversible.

In the Eating Disorders group, hypoperfusion occurred in the parietal, frontal, pericentral areas and in the thalamus.

In his examination of patients with eating disorders (anorexia nervosa of the restrictive type and of the binge-purging type), Van den Eynde [15] found hypoperfusion in the thalamus and in the basal ganglia, in the left temporal lobe and in the superior temporal gyri and superior frontal gyri, but no abnormalities in computer tomography. Based on these findings, he suggested that the abnormalities in the cortical-subcortical pathway may be included both in the pathogenesis and pathophysiology of anorexia nervosa. According to him, this issue requires further research.

On the other hand, PET scans (Delvenne et al., 1999) [16] of patients with anorexia nervosa and bulimia nervosa suggested hypometabolism of glucose in the temporal lobe in both disorders, which would suggest a particular sensitivity of this area in eating disorders. However, this finding does not explain whether it is a consequence of the disorders, or a general dysfunction.

Temporal areas are linked to sensory and visual-spatial connections and might influence changes in perception.

Similar to the Depressive Disorders group, in the Eating Disorders group hypoperfusion also occurred in the frontal and pericentral areas. These similarities may be related to the fact that eating disorders are often accompanied by depressive symptoms or get ahead depression. These findings are consistent with some other published findings [5, 17].

In the Anxiety Disorders group, on the other hand, hypoperfusion was located in the pericentral areas, supposedly the ones that are most sensitive to fluctuations in cerebral perfusion. The other locations of hypoperfusion were the frontal and parietal areas. Hypoperfusion in the frontal lobe was most pronounced in the Depressive Disorders group and, together with the prefrontal areas hypoperfusion, it occurred in 85% of that group.

The frontal area plays a particularly important integrative role, because it participates in a number of higher nervous functions and it integrates impulses from the lower parts of the brain, the brainstem and hypothalamus. It is important for cognitive processes, for the selection of somatosensory impulses, for mood regulation and for consciousness. In the three discussed groups, hypoperfusion in the frontal area was observed, regardless of the group, as the second most frequent.

In the Depressive Disorders group, hypoperfusion in the prefrontal area occurred most frequently (in 33% of the group), as compared to the other groups and it could have been related to the clinical symptoms of depression. This findings are consistent with other published findings [5, 17]. The prefrontal area is responsible for executive functions (abstract thinking, creativity, accommodation of external impulses and impulses from the environment and comparison of the impulses in order to achieve particular goals).

Among patients with depressive and eating disorders, in 25% of the cases we observed hypoperfusion in the thalamus- area of vital importance to the filtering of information. Hypoperfusion may have an influence on disruptions in this important process and in attaining deformed or incomplete information and disruptions in information processing.

It is important to indicate that the differences are rather small and not generally statistically significant. Further, we have acknowledgement of the relatively high degree of comorbidity, both lifetime and concurrently, across the three disorders.

The fact that hypoperfusion was observed more frequently on the left hand side among anxiety disorders patients ($\chi 2=6.54$, $P<0.025$) requires further research, especially that this side is important for terming of emotions.

The analysis of correlations between hypoperfusion and the severity of depressive and anxiety symptoms will be elaborated upon in a next paper.

CONCLUSIONS

In this group, hypoperfusion was observed most frequently among patients with eating disorders.

Among patients with eating disorders, hypoperfusion was observed mostly in the pari-

etal and frontal areas and in the thalamus, on the left hand side, similar to the depressive disorders group.

Among patients with anxiety disorders, hypoperfusion at the left hand side occurred almost three times more frequently than among patients with depressive disorders (Chi2=6.54, P<0.025).

Anxiety as a trait was the highest in the eating disorders group, but the difference between groups was not significant (Chi^2=3.15, P<0.20).

Among patients with anxiety disorders, anxiety as a trait and anxiety as a state were almost at the same level.

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