Polygraphic investigation of the control of cerebral circulation

PhD Theses

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The energy demand of the brain tissue is covered in 85% by the oxidative phosphorilation of blood glucose. Under physiological circumstances, between 70-150 mmHg mean arterial blood pressure the global cerebral blood flow is constant. This is maintained by the autoregulation of cerebral blood flow. Despite of the constant global blood flow, increase of local neural activity might increase the regional cerebral blood flow (rCBF) by as much as 60-80%.

The global cerebral circulation is maintained by pressure dependent myogenic, partial CO_2 sensitive chemical processes and vasomotor mechanisms controlled by the brainstem. Dilatation of resistance vessels of the active neuronal tissue and the concomitant elevation of cerebral blood flow leads to increase of regional circulation. The physiological mechanism of local control is based on the neurone-astrocyte-endothel functional unit.

There is no ideal method of measuring cerebral circulation. Blood oxygen level dependent functional magnetic resonance imaging BOLD fMRI), which measures the tissue concentration ratio of oxy-deoxyhemoglobin provides high resolution images however it cannot be utilized for measuring the changes of activation within short time window. PET-CT imaging might be used for detecting both temporal and spatial changes of cerebral blood flow, however the high cost and the radiation danger limit its routine everyday use. The same can be applied for the Xenon-CT and the dynamic perfusion CT methods.

The non-invasive transcranial Doppler (TCD) technique, which was invented in 1982, has opened new avenues in the research of the control of cerebral circulation. It became possible to determine the cerebral blood flow velocity (BFV) in the main cerebral vessels. The alteration of BFV reflects the changes of the cerebral blood volume. The method can be used for long time follow up blood flow velocity changes and due to its good temporal resolution the fast alterations can also be detected. Under physiological circumstances, the diameter of the initial segments of the intracranial arteries of the brain is constant even in a wide range of blood pressure and partial CO_2 concentration. Therefore, the alteration of blood flow velocity is related to the alteration of cerebral perfusion in the supplied cerebral tissue. XeCT and fMRI investigations, which were carried out parallel with TCD, proved that the changes of BFV in the intracranial vessels are proportional to changes of cerebral perfusion.

Vasoreactivity is the capacity of cerebral arterioles to control their diameter. This can be evoked by vasoactive substances and/or alterations in cerebral perfusion pressure. Both intravenous acetazolamide and high CO_2 concentration lead to vasodilatation. Increased blood flow velocity in the large cerebral arteries suggests elevated cerebral perfusion caused by vasodilatation of arterioles (resistance vessels). The cerebral blood flow velocity and the perfusion pressure in steady-state conditions are linearly correlated: the $y = m*x + b$ equation describes the state of cerebral autoregulation. The cerebral perfusion pressure can be changed by rapidly tilting the body using a tilt table.

Functional TCD (fTCD) is a method for research the alteration of cerebral blood flow during cognitive processes. By the simultaneous use of bilateral TCD probes blood flow velocity changes can be detected and compared in symmetric brain regions evoked by psychophysiological tests. During verbal fluency test the arterioles in the dominant hemisphere dilate and the BFV significantly increases in the medial cerebral artery (ACM). Validity of hemispheric dominance determined by using cognitive test was confirmed by Wada-test and fRMI investigations.

However cognitive tests not only influence cerebral circulation but also provoke autonomic reactions (increase of blood pressure and heart rate, hyperventilation), which are known to influence cerebral blood flow. The above mentioned autonomic parameters have not been co-registered with fTCD and fMRI due to technical difficulties.

The EEG as indicator of cognitive processes

All neuropsychological events alter the EEG. The alterations might be quantified by spectral analysis. Magnetoencephalography proved significantly higher beta desynchronisation over the left frontal region during verbal fluency test (VF) compared to word repetition test. It has been suggested that special cognitive functions (apperception, memory) might be related to specific range in the high frequency beta bands. In the occipital region BOLD fMRI method proved inverse relation between regional blood flow and EEG alpha activity. In simple motor tasks (finger tapping) the BOLD signal was more pronounced over the contralateral motor cortex and the increase correlated well with the EEG power.

Verbal tests can be used to determine the speech-dominant hemisphere based on EEG power spectrum data, and the results were supported by Wada-test.

In our experiments we co-registered the EEG and the fTCD signals. The scalp EEG power spectra and frequency data were visualized using mapping methods.

Degenerative neurological disorders with autonomic dysfunction

The common neuropathological characteristics of degenerative disorders causing autonomic dysfunction are the alpha synuclein or tau protein inclusion bodies in the neurons and/or in glia cells. The process is initiated by a pathological phosphorilation which triggers the alteration from the physiological alpha helical protein structure to beta sheet conformation. Parkinson's disease (PK) is the brainstem variant of Lewy-body disorders, and it is the most common neurodegenerative process. Lewy-body disorder is the pure autonomic failure syndrome (PAF), in which the neurons lof the lateral horn of the spinal cord are affected. In multisystem atrophy (MSA) besides the nerons the oligodendrocites are also involved. In MSA the dysfunction of the autonomic control can be explained by the deterioration of both the spinal and the supraspinal pathways. The disturbance of autonomic functions can be detected both in PK and in MSA, in the later usually prior to the appearance of motor symptoms. Collapses in PK patients might be due to orthostatic hypotension but also to dysfunction of cerebral circulation control.

The aim of our study was to investigate the control of cerebral circulation in PK-patients using tilt table and co-registering the autonomic variables and the BFV in the medial cerebral artery.

Aims

1. Analyzing the correlation between blood flow velocity in the ACM and the alteration of autonomic parameters during cognitive tests.
   a) How does blood flow velocity in the ACM change during verbal fluency and mental arithmetic tests?
   b) How does cognitive effort influence the autonomic parameters?
   c) Do alterations of autonomic parameters induced by cognitive effort influence cerebral blood flow control?
   d) Can we detect habituation of BFV and/or autonomic changes during cognitive tests?
2. Analyzing the changes of EEG and the BFV measured in the ACM
   a) Can we determine the localization and size of the activated brain tissue using EEG topography?
   b) Is there any correlation between the EEG changes and alterations of BFV measured in the ACM?
3. Polygraphic investigation of vasoregulation changes provoked by tilt-table method in Parkinson-patients.
   a) Investigation of regulation of cerebral circulation under physiological conditions in Parkinson's disease using tilt-table.
   b) Statistical analysis of Parkinson-patients' and controls' data.
   c) Determining the correlation between the clinical characteristics and circulatory data.

Methods

Investigation of blood flow velocity in the ACM and autonomic parameters during cognitive effort

Subjects

Sixteen healthy right-handed volunteers were investigated (6 male, mean age: 35.8±12.1 years). Handedness was determined by the Edinburgh Handedness Inventory (Oldfield 1971). The investigation was carried out in a quiet room, subjects were in supine position with closed eyes and were instructed not to speak and avoid soliloquizing. All signals and instructions were presented through loudspeaker.

Experimental paradigms

For testing the effect of **voluntary hyperventilation**, subjects were instructed to breathe deeply for 2 minutes.

Mental arithmetic (MA) paradigm: subjects were instructed to subtract sequentially the same number from a number close to 100 (i.e.: 102−8=94, 94−8=86, 86−8=78, etc). The trial started with a cueing tone at time 0 (*signal-a*) when the task was presented through the loudspeaker. Five seconds later (s*ignal-b*) the subject started the calculation. After 25 s (period-C) *signal-c* indicated the end of calculation, and 5 s later at *signal-d* the subject had to announce the result. A 60 s resting-period followed each trial. Data of 10 trials, each with a different subtraction task, were collected.

Verbal fluency test (VF): Subjects heard a consonant trough a loudspeaker at the first cuing signal, and they had to collect during 25 s as many Hungarian words beginning with the given consonant as they could. A signal marked the end of the task and the subjects had to announce the number of collected words. Data of 10 trials, each with a different consonant were collected, each trial was followed by a 60 s long rest period.

Blood flow velocity (BFV) was recorded using transcranial Doppler sonography. Signal of both middle cerebral arteries (MCA) was recorded at the depth of 45-55 mm. The software of the TCD equipment generated envelope curves derived from maximum frequency peaks of BFV after fast-Fourier transformation. The sampling rate was 57 Hz. ASCII files provided by the Multidop-T software were stored on hard disk for off-line analysis. Artifacts were rejected by linear interpolation after visual screening. Running averages of BFV were calculated using 5 s analysis intervals with 0.5 s stepping. To compute mean BFV the following equation was used: $(V_{sys}+2*V_{dia})/3$.

Arterial blood pressure (ABP) was recorded beat-to-beat over the left radial artery using a surface radial tonometry method (Colin-508T, Colin Corporation, Komaki City, Japan) Calibration to mmHg before and after the cognitive test was performed by the same equipment's sphygmomanometer.

End tidal partial pressure of CO2 (ETP$_{CO2}$) was recorded with the capnograph of the above described tonometer using a soft plastic mask, which was fixed on the face of the subject.

Heart rate (HR) was calculated from the ABP systolic peak-to-peak distance.

Respiratory rate (Rr) was calculated on the basis of peak intervals of ETPCO2 curves.

Cerebral vascular resistance index (CVR) is the ratio of the actual ABP and BFV values and it was calculated using the following equation: CVR=ABP/BFV.

Statistical analysis

Group average BFV and autonomic variable data were given as mean ± standard deviation (S.D.). Reference values were calculated from the period between -15 s to -3 s before the start of voluntary hyperventilation or before *signal-a* in the mental calculation test. In the cognitive trials, we calculated the average increase of BFV in the ± 2 s period around the first BFV peak that is between the 6.5- 10.5 s of the trial. The distribution of all examined values passed the Kolmogorov- Smirnov normality test. For statistical analysis, relative values of the parameters were calculated according to: Xrel [%] = (Xact − Xref)/X ref*100 + 100. We used repeated-measures of ANOVA test to find significant differences between the values of the reference and the cognitive period as well as MAX and MIN values of all parameters. The within subject factors for all parameters were the reaction (baseline, actual, MAX and MIN values of reactions), and in case of BFV and CVR the side (left and right) as well. In case of significant effect the Neumann-Keuls post hoc test was performed.

Reactions of the 2 minutes long voluntary hyperventilation were also evaluated by ANOVA method.

Cross correlation index was calculated for the corresponding 40 - 40 distinct values of CVR and ETPCO2 from the first 20 s of period-C. The level of significance of the correlation coefficient was determined according to the *t*-distribution threshold value (2.022); the degree of freedom (df) was 38.

We also analyzed the habituation of parameters using multivariance, repeated measure ANOVA. The group factors were:: RESPONSE, RANGE OF REACTION, LATERALITY.

We also investigated the correlation between CVR index and ETP_{CO2} during the first 20 s of cognitive tasks. The significance level of correlation coefficient was set at 2.022; the degree of freedom was 38. The level of significance was $p<0.05$ in all tests. All statistical analysis was performed using Statistica 7.1 software.

Investigation of blood flow velocity in the MCA and the EEG

Twelve healthy volunteers were investigated (7 male, mean age: 28.6±5.4 years). Eight subjects were right handed and four left-handed assessed by the Edinburgh Handedness Inventory.

EEG analysis

Sixteen channel EEG was recorded against average reference according to the 10–20 electrode placement system. The EEG was digitalized at a sample rate of 128 Hz. Absolute power values within the 1.0–30 Hz frequency range were calculated using a Fast Fourier Transform (FFT) for 1 s analysis intervals with 125 ms successive overlapping. Central frequency (CF) was calculated using the following equation:

$\mathbf{CF=\sum_f f*P(f)/ \sum_f P(f)}$, where f is a given frequency between 5 and 30 Hz, and P is the power at f frequency. Relative CF- and alpha power were calculated dividing the actual data by the reference value (-15 s to -3 s). Colour coded alpha power and CF topograms were constructed for every 0.5 s by the use of Overhauser interpolation.

Laterality index (Li) for BFV and CF

Right and left BFV values were compared using Wilcoxon statistics both in MA and VF tests. Around the first data point where the left(l)–right(r) BFV difference was significant -2 s and +2 s long segments (8 paired data points) were chosen and averaged (avBFVl and avBFVr). To get the LiBFV, the avBFVr value was subtracted from avBFVl. Samples of left- and right-handed subjects were evaluated separately. LiCF from the EEG was calculated similarly to the BFV in period-B. The mean values of right sided derivations were subtracted from the left (i.e., T5–T6; F7–F8, etc). Positive values indicated left hemispheric dominance.

Statistics

EEG and BFV data were averaged in all subjects. Based on EEG power topograms maximal changes of absolute and relative power and CF were found at T5, T6, F7, F8 and F3, F4 derivations, therefore activity of these channels were statistically analyzed. Grand averages were calculated for the right- and left-handed groups separately. Laterality of BFV and EEG data were evaluated by paired Wilcoxon test. Significance level was determined at $P \leq 0.05$. Intra- and interhemispheric correlation between alpha power, CF and BFV, furthermore, between HR and BFV was also computed. The significance level of correlation coefficients (r) for EEG/TCD relations was determined according to the T values.

Investigation of cerebral circulatory control in Parkinson's disease

Eight control subjects (K, 4 male) and 17 patients with Parkinson's disease (PK, 10 male) were investigated. The diagnosis of Parkinson's disease was determined by using the UK Parkinson's Disease Society Brain Bank criteria (1992). The mean age of the two groups did not differ. Brain CT excluded any cerebral infarction and atrophy. Doppler ultrasonography did not find any cerebral hemodynamic alteration in either group. Based on the clinical picture 6 patients had equivalent type, 6 akinetic-rigid type and 5 tremor dominant Parkinson's disease. Eleven patients were in early stage (Hoehn-Yahr II) and 6 in advanced stage (Hoehn-Yahr III-IV) of the disease. Shellong-test did not prove orthostatic hypotension in any patient.

Methods

Subjects laid on a tilt table in a flat position. After obtaining the baseline values the table was tilted p to an angle of 10, 30, 70 degrees (for 5 min each), then table was returned to horizontal position. Arterial blood pressure

(ABP), blood pressure at the level of the Willis-circle (ABPw), BFV in both MCA, pulsatility of the MCA (PI), HR, CVR and the $ETCO_2$ were recorded at the 30., 60., 120., 180., 240. and 300. s. The ABP was monitored using photopletismography on the right III. finger.

Mathematical analysis of cerebral circulatory control

The ABP_W (perfusion pressure) values were distributed in three domains according to the tilt of 0, 30 and 70 degrees; among them the mean-values were significantly different. We calculate the equation of linear regression for the perfusion pressure referred to the altitude of Willis circuit and the actual bilateral BFV. We used the correlation coefficients of the left and right regression lines for the estimation of the cerebral autoregulation.

Treatment of data and statistical elaboration

Analogue values were digitized by the DWL Multidop T2 Monitoring Software MF 8.27 c program; packages were stored on computer's hard disc. After ASCII exportation the artifacts were removed by visual inspection, and running average elaboration was performed for 10 s intervals with 0.8 s overlapping.

For statistical evaluation we used a reference value (BL) from one minute period before the tilting experiments. If the reference value fell into the same domain we used the absolute values for statistical elaboration, in case of large individual differences we preferred the relative values. We used repeated measures of ANOVA.

Results

The change of BFV during mental arithmetic and verbal fluency tests

During 25 s MA and VF tests on the diagrams of average values of BFV three characteristic periods could be observed. The BFV increased immediately after the *signal-a,* and within some s reached the first maximum in both side approximately at the same time. During the cognitive period (5-25 s) the BFV slightly decreased but exceeded the level of the pre-test period. In this time epoch the curves diverged but the values according to the left MCA were significantly higher compared to the right one both in MA and VF tests. Second maximum of BFV developed after the end-signal when the subjects reported the results of the tests. Thereafter the average values of BVF returned to the baseline within 15-30 s.

Change of Rr and ETP_{CO2}

After the *signal*-a hyperventilation was observed in all subjects during both cognitive tests. Increased rate of respiration led to significant hypocapnia which lasted up to the end of cognitive effort.

Change of ABP and HR

ABP increased significantly within a few seconds in all subjects except during the MA test in one and during the VF test in two persons. After the initial increase ABP stayed stable in the cognitive period of the test. The HR increased continuously until the end of the task.

Change of CVR-index

After *signal*-a the CVR index transiently decreased in both sides during MA. Higher values were recorded during the cognitive effort. CVR-index calculated to the right MCA proved significantly higher than the left. After declaring the result the CVR index decreased significantly in both tests and in both MCA. During VF transient decrease of CVR index was followed by significant increase in the right MCA, no considerable change was seen on the left. Near to the end of cognitive period the CVR-index begun to sink and minimal values developed during the resolution period. Similarly to MA the CVR calculated for the left MCA was consequently lower than the right one.

Correlation between CVR and ETP_{CO2} during MA and VF

During the first 20 s of cognitive effort significant negative correlation was found between CVR-index and ETP_{CO2} in 11 subjects in the left and 12 subjects in the right MCA during MA, and in 7 subjects in the left and 10 in the right MCA during VF.

Habituation

During the successive execution of 10 MA subtests the reference, the maximum values and the left-right differences of BFV did not change; that is no habituation of these parameters was observed. Despite of this during VF tests the reference values of BFV decreased significantly from the 4^{th} subtest in the right and from the 5^{th} subtest in the left MCA. Similar diminution of the maximum values of BFV was found bilaterally. Notwithstanding no habituation was found in the left-right BFV differences during the VF trials. Similar decrease of CRV-index maximums was proved in the right MCA from the second subtests. During VF the mean values of ABP maximums significantly decreased from the 4^{th} subtest. No habituation was found during subtests of MA and VF in the averages of Rr and ETP_{CO2}.

Estimation of handedness based on BFV laterality index

Positive values of Li_{BFV} during MA and VF indicate a dominance of the left hemisphere. In 10 subjects out of 12 the significant correlation of Li_{BFV} (r^2_{BFV}=0.51) corresponded to the result of the Edinburgh-handedness test.

According to the correlation analysis one right handed subject was ranked to the negative (left hand) field.

Correlation between EEG spectral data and BFV

Alpha power and BFV

Relative (%) change of alpha power was compared to the pre-test reference values. The alpha power recorded on the T5-, T6- electrodes decreased significantly after the signal-a within 0.5 s during MA and VF tests. Power reduction preceded the first BFV maximum. In right handed subjects diminution of alpha power was significant at T5 and P3 electrode positions compared to the right. In left-handed subjects the power asymmetry was not significant.

Central frequency (CF) topograms

On the CF maps maximum power was localized on the temporal and centro-parietal regions in the 14-15 Hz frequency domain. During mental arithmetic tests in 12 subjects out of 14 the CF maximums migrated towards the fronto-temporal and parietal regions. During the firs period of VF investigation in 6 persons out of 8 the CF maximums developed over the left temporal lobe.

Correlation between BFV and EEG parameters

In the reference period there was no significant lateralization of the CF and resting alpha power between the hemispheres. During mental arithmetic in 4 out of 8 subjects significant intrahemispheric correlation was found between BFV and EEG parameters [($T5_{CF}/BFV_{left}$ ($r_{mean} \geq 0.39$) and $T6_{CF}/ BFV_{right}$ ($r \geq 0.301$)]. In contrast of this during verbal fluency test in 7 out of 8 subjects significant correlation was calculated between CF over the left temporal region and the left BFV (CF_{left}/BFV_{left} - $r_{mean} \geq 0.44$). Non-significant negative correlation was found between relative alpha power and the simultaneously recorded BFV in most of the subtests. During MA the correlation of relative alpha power at T5 and left BFV r=0.218 (non-significant), the same was found between T6 relative alpha and right BFV (r=0,115). During the VF trials in 7 subjects out of 8 significant negative correlation (r≥0.42) was calculated between T5 relative alpha power and the BFV in the left MCA. Regarding the right hemisphere between T6 relative alpha power and ipsilateral BFV changes there was no significant correlation except two subjects. (r_{mean}≥0.107).

Intrahemispheric correlation of LiBFV és LiCF

One person out of 4 left-handed subjects proved to have left hemispheric dominance based upon Li_{CF} and this result correlated well with the Li_{BFV} values. Two other left-handed subjects right hemispheric dominance was supported by both Li_{BFV}, and $Li_{CF.}$. The CF_J/BFV_J correlation was negative in the fourth subject, but the Li_{BFV} result correlated well with the Edinburgh-handedness inventory data. In the right handed group one person had Li_{BFV} suggestive of left hemispheric dominance; however Li_{CF} correlations showed right dominance. In one subject hemispheric dominance was difficult to assess, the correlation data suggested left hemispheric dominance.

Regulation of cerebral circulation in Parkinson's disease

Arterial mean pressure (ABP)

The ABP of healthy controls and Parkinson-patients was similar in the baseline period. At 70 degrees tilt the blood pressure increased significantly in both groups. When subjects were returned to flat position the decrease of blood pressure was significantly more pronounced in the healthy group compared to Parkinson-patients (p_{K-PK} <0,05).

Blood pressure at the level of Willis-circle (BPw)

At 30 and 70 degrees BP_W decreased significantly in all subjects. The minimal (57±10Hgmm) and maximal BPw (85±9Hgmm) was not significantly different in the control and the Parkinson-group.

Heart rate (HR)

The HR of controls and Parkinson-patients was similar in the reference period. Similarly the HR was no significantly different between the control and patient group regarding the various body positions (p_{K-PK} =0.115). The duration of the disease and the severity of symptoms did not affect the results.

Changes of BFV in the ACM

The average BFV on the left and right side was similar (p_{L-R}=0.39). The BFV in the ACM in the control group during the reference period was significantly higher compared to the patient-group ($p<0.05$). The BFV decreased significantly on both sides at 70 degrees in the Parkinson-group ($p<0.001$). In controls the BFV dropped only minimally ($p = 0.66$). The difference between the control and Parkinosn-group was significant (p_{K-PK}=0.037).

Cerebrovascular resistance (CVR)

The CVR of the control group in the reference period was significantly smaller compared to the Parkinson-group ($p<0.05$), without any side difference (p_{L-R}=0.69). The CVR in the 70-degree position was significantly smaller compared to the flat position. The difference between the control and Parkinson-group was significant (p_{K-PK}=0.0051). The disease duration and the symptomatology did not affect the results.

End-tidal CO_2

The ETP_{CO2} of the control and Parkinson-group was similar. Changes of body position did not affect this parameter.

Autoregulation index (AR)

This parameter did not differ significantly in the two groups ($p_{K\text{-}PP}$= 0.012).

Analysis of clinical subgroups

The decrease of BFV at 70-degree position was the most pronounced in the tremor-dominant clinical subgroup (-17.2±15.9%), while AR was the highest (AR_{TREM}=0.55±0.34%cms^{-1}/Hgmm) however the difference compared to akinetic-rigid and equivalent subgroups was not significant.

Conclusions

1. We applied poligraphic methods to measure BFV in the MCA as well as ABP, HR, Rr and ETP_{CO2} parallel with the recording of 16-channel EEG.

2. We proved that fTCD can be used to detect changes of BFV induced by cognitive processes. We suggested that the regulation of cerebral circulation can only be assessed by parallel measuring various autonomous parameters.

3. We programmed two neuropsychological test (verbal fluency, mental arithmetic) which induced mental activation in an artifact-free manner.

4. Both tests activate the dominant hemisphere; therefore they can be used to identify the speech dominant hemisphere based upon the significantly asymmetric changes of cerebral blood flow velocity.

5. We interpreted the characteristic changes of cerebral blood flow induced by cognitive processes. We found that the involuntary hyperventilation during cognitive effort causes constriction of the resistance vessels leading to a relative decrease of the BFV. This observation was supported by the high correlation of cerebrovascular resistance and ETP_{CO2} values.

6. Based upon the reaction-time of cerebral circulatory changes and the close correlation between the EEG central frequency and BFV we suggested that there is a fast neurogenic regional control of cerebral circulation during cognitive effort. Our data show that the effects of autonomic reactions (most importantly the hypocapnia) are surpassed by this local neurogenic regulation.

7. We showed that there is no habituation of autonomic reactions during mental arithmetic, while during the verbal tests habituation of BFV, ABP and HR could be observed.

8. The EEG power and central frequency data proved to be an important indicator of cognitive effort. The central frequency topograms in most right

handed subjects showed frequency increase over the left posterior temporo-parietal region.

9. Using the BFV and the EEG data we constructed laterality index values. These could be used to identify the dominant hemisphere based upon the results of the cognitive tests.

10. EEG mapping data show that the central frequency distribution during verbal and arithmetic tasks is individual, and there is no clear correlation with the handedness data.

11. The intrahemispheric correlation between EEG changes and TCD data was better in the verbal task that in the mental arithmetic test.

12. We set up a poligraphic method involving a tilting-table which can be used in the clinical practice to investigate autonomic circulatory disturbances in degenerative neurologic disorders..

13. The autoregulation index in Parkinson-patients is significantly higher compared to controls. The symptomatology and/or the severity of the disease do not influence the results. The changes of blood pressure in the Parkinson-group proved the involvement of the sympathetic cardiovascular system. In Parkinson's disease BFV in the MCA is influenced by the perfusion pressure, which suggests the dysfunction of cerebral autoregulation.

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