Neurol Sci (2002) 23:S61–S62

Perfusion-weighted dynamic susceptibility (DSC) MRI: basal ganglia hemodynamic changes after apomorphine in Parkinson's disease

L. Brusa[1,2] · A. Bassi[1] · M. Pierantozzi[1,2] · F. Gaudiello S. Frasca[4] · R. Floris[3] · P. Stanzione[1,2] (✉)

[1] IRCCS Fondazione S. Lucia, Via Ardeatina 306, I-00179 Rome, Italy
[2] Neurology Clinic, Tor Vergata University of Rome, Rome, Italy
[3] Institute of Radiology, Tor Vergata University of Rome, Rome, Italy
[4] Department of Anesthesiology and Reanimation, Tor Vergata University of Rome, Rome, Italy

Abstract Relative regional blood flow of basal ganglia was studied by means of perfusion-weighted dynamic susceptibility (DSC) MRI. Parkinson's disease (PD) patients showed a significant inter-hemispheric asymmetry due to a higher perfusion in the more affected side, while normal subjects did not. PD exhibited an abnormal "asymmetry index" in the measured nuclei. A second DSC-MRI examination performed after subcutaneous apomorphine administration did not show any significant asymmetry in PD patients. DSC-MRI of basal ganglia confirms the asymmetry observed in PET studies of PD patients, suggesting that this method is a promising and low-cost technique in neurodegenerative diseases.

A pattern of increased perfusion in the basal ganglia (BG), related to a decreased perfusion in the cortical regions, was found by positron emission tomography (PET) [1]. PET is a very expensive imaging method, while magnetic resonance imaging (MRI) is a less expensive imaging technique available almost in every neurological centre. In the last years several researchers attempted to utilise dynamic susceptibility (DSC)-MRI to measure regional cerebral blood flow (rCBF) and in epilepsy [2].

Our target was to study whether DSC-MRI perfusion method may detect an altered pattern of rCBF in patients with Parkinson's disease (PD) in comparison to normal subjects and whether this altered pattern may be normalised by apomorphine.

Fifteen subjects affected by idiopathic PD were enrolled for this study. Twelve normal subjects were included as controls. Eight of them performed a retest procedure. All included subjects gave their informed consent.

PD patients, after at least 20 days of therapy withdrawal, were submitted to perfusion DSC-MRI. Ten of them were retested after apomorphine injection (2–4.5 mg subcutaneously, motor improvement of at least 50% on UPDRS section III [6]).

MRI was performed in the dark, utilising a 1.5 T MR scanner (Philips gyroscan ACS-NT) with gradient strength of 23mT/m, rise time of 0.2 ms with sinusoidal gradient profile and echo-planar capabilities; a circularly polarized head coil with quadrature was used. T2*-weighted echo-planar sequences were used to obtain DSC-MRI images along the anteroposterior commissural (AP-CP) plane. A dose of 0.4 mmol/kg gadolinium-DTPA was injected to the subject lying with closed eyes. The bolus perfusion data were processed and converted into parameter maps for relative rCBF.

Regions of interest (ROI) of 15 pixels were manually placed on the head of caudate nucleus (CN), on the putamen (PU), on the external and internal globus pallidus (GPe/GPi) separately and on the ventrolateral nucleus of thalamus (TH). CU, PU and GPe were localised on the slice placed 3 mm above the AC-PC line, while TH and GPi were localised on the slice placed 3 mm below the AP-CP line [3]. Moreover, perfusion was evaluated in a white parieto-occipital matter (WPOM), to perform normalisation of the data.

Row flow data, calculated as the mean of each ROI in the BG nuclei and in the WPOM of each side, were logarithmically transformed, and then normalised as percentage of the value obtained from the ipsilateral WPOM. For asymmetry determination ("contrast" effect), normalised data were expressed as a ratio of the contralateral corresponding nucleus, according to the formula: [(right nucleus - left nucleus)/(right nucleus + left nucleus)*100]. In PD patients, the contrast was expressed as [(best side - worst side)/(best side + worst side)*100] according to their clinical asymmetry. An individual "contrast index" was considered abnormal when exceeding the mean ± 2 SD of normal subjects.

Data analysis was performed with STATISTICA for Windows program. Normalised data were analysed with parametric ANOVAs utilising the following main factors: "group" (between factor: PD vs. control subjects); "treatment" (within factor: before-after drug administration or test-retest); "nuclei" (within factor: CU, PU, TH GPe and GPi); "side" (within factor: right side or best side vs. left side or worst side).

The whole group of PD patients exhibited a significantly ($F(1/25)= 7.98$; $p<0.05$) different mean rCBF in the best (BS) vs. worst side (WS), in comparison to control subjects (interaction "group" x "side"). This was due to a significantly (post hoc $p<0.001$) higher mean basal rCBF in the WS (117.6) in comparison to the mean in the BS (107.3) in PD patients, not observed in control subjects (110.9 vs. 111.2). This was confirmed by "contrast" analysis showing a significant difference ($F(1/25)= 9.44$; $p<0.01$) of the mean contrast in the two groups (-4.39 vs. -0.064; PD vs. controls). The difference was similar in all the studied nuclei so that no significant interaction "group" x "nuclei" was found. Eleven out of the fifteen PD patients showed abnormal "contrast index" in the putamen and nine showed the same abnormality in the thalamus. Only three control subjects showed abnormal values in the putamen and none in the thalamus.

A significant ($F(1/16)= 5.65$; $p<0.05$) difference was found between the two groups due to a mean rCBF higher in PD patients in comparison to control subjects (116.8 vs. 112.3). More importantly, the interactions "group" x "treatment" ($F(1/16)=6.15$; $p<0.05$) and "group" x "side" ($F(1/16)= 4.53$; $p<0.05$) were also significant. The first interaction was due to a significant (post hoc $p<0.001$) difference between the mean rCBF before (111.6) and after (122.0) apomorphine in PD, while the test-retest procedure did not produce significant changes in controls. The second interaction was due to a significant (post hoc $p<0.01$) difference between the BS (114.5) and the WS (119.1) in PD which was not true in normal subjects. Finally, a significant ($F(1/16)= 4.34$; $p<0.05$) interaction among "groups" x "treatment" x "side" was found. This was related to a significant (post hoc $p<0.001$) difference of rCBF between the BS (107.4) and the WS (115.7) present in PD patients before apomorphine but not after drug administration (121.6 vs. 122.5); normal subjects never showed significant differences between the two sides (Table 1).

Contrast data (Table 1) confirmed what was observed in normalised data. There was a significant ($F(1/16)= 4.82$; $p<0.05$) effect of the factor "group" and of the factor "treatment" ($F(1/16)=4.32$; $p<0.05$). Moreover a significant ($F(1/16)= 4.57$; $p<0.05$) "group" x "treatment" interaction was found, due to a significant (post hoc $p<0.05$) decrease of asymmetry after treatment in PD patients (from -3.75 to -0.38) while normal subjects never showed a significant asymmetry (from -0.60 to -0.16).

Discussion

Our data show that rCBF in the BG of untreated PD patients is strongly asymmetric between the WS and the BS, and that this asymmetry is normalised by apomorphine. No asymmetry was present in controls in the test-retest procedure. Our study confirm previous PET findings of a relatively increased and asymmetric rCBF in the BG in unilateral or bilateral PD patients [1]. Interestingly, PET studies did not show the asymmetry between homologous BG regions but only if the rCBF of BG nuclei were compared to those of several cortical areas. On the contrary, the less expensive DSC-MRI technique seems to be able to reveal the asymmetry by examining homologous subregions of BG. This was allowed by the higher resolution of MRI in comparison to PET.

Apomorphine treatment was able to normalise the asymmetry of rCBF, probably related to a dopamine depletion-dependent mechanism. The post-apomorphine recovery was due to an increased rCBF in the BS, while the WS did not change. Dopamine receptor stimulation in the BG may selectively change the rCBF in these regions, thus accounting for this finding. However apomorphine also produces relevant vasodilatation, possibly accounting for part of the increase in rCBF observed in the BS. The larger loss of dopamine in the WS might have produced a maximal increase of rCBF already in basal conditions. Thus, apomorphine may not be able to induce further increase of rCBF in that side.

References

1. Eidelberg D, Moeller JR, Dhawan V et al (1994) The metabolic topography of Parkinsonism. J Cereb Blood Flow Metab 14(5):783–801
2. Liu HL, Kochunov P, Hou J et al (2001) Perfusion weighted imaging of interictal hypoperfusion in temporal lobe epilepsy using FAIR-HASTE: comparison with H(2)(15)O PET measurements. Magn Reson Med 45(3):431–436
3. Talairach J, Tournoux P (1988) Co-planar stereotaxic atlas of the human brain. George Thieme, Stuttgart New York

Table 1 Basal ganglia mean rCBF and mean rCBF "contrast"

	Basal ganglia mean rCBF				Basal ganglia mean rCBF "contrast"	
	CU mean rCBF ± SD				CU mean rCBF "contrast" ± SD	
	PRE apomorphine/test		POST apomorphine/retest			
	R/B	L/W	R/B	L/W	PRE apo/test	POST apo/retest
PD n=15	111.6±7.32	121.2±1258	–	–	-3.45±5.82	–
Control n=12	115.1±6.53	116.2±6.12	–	–	-0.79±241	–
PD n=10	112.2±7.35	118.0±5.2	126.3±11.8	126.6±11.0	-2.97±3.75	-0.13±4.27
Control n=8	117.3±7.1	117.3±6.9	117.5±764	119.5±6.44	-0.34±2.554	-0.46±2.60
	PU mean rCBF ± SD				PU mean rCBF "contrast" ± SD	
	PRE apomorphine/test		POST apomorphine/retest			
	R/B	L/W	R/B	L/W	PRE apo/test	POST apo/retest
PD n=15	112.1±6.4	122.5 ± 13.4	–	–	-4.23±5.74	–
Control n=12	117.2±6.1	117.2 ± 7.62	–	–	-0.04±2.21	–
PD n=10	112.1±.25	121.2±6.2	126.6±11.1	128.2±11.4	-3.76±4.16	-0.52±3.93
Control n=8	117.3±6.08	118.7±5.1	119.1±6.11	119.7±6.26	-0.31±1.92	-0 44±1.31
	TH mean rCBF ± SD				TH mean rCBF "contrast" ± SD	
	PRE apomorphine/test		POST apomorphine/retest			
	R/B	L/W	R/B	L/W	PRE apo/test	POST apo/retest
PD n=15	111.4 ± 7.27	122.8 ± 13.0	–	–	-4.32 ± 5.51	–
Control n=12	115.2 ± 7.12	115.3 ± 7.4	–	–	0.22 ± 2.06	–
PD n=10	112.7 ± 7.73	120.0 ± 5.79	126.6 ± 12.1	128.1 ± 12.3	-3.22 ± 3.03	-0.51 ± 4.25
Control n=8	116.5 ± 6.88	116.1 ± 6.33	119.4 ± 6.23	118.1 ± 9.26	-0.023 ± 2.08	0.67 ± 4.33
	GPe mean rCBF ± SD				GPe mean rCBF "contrast" ± SD	
	PRE apomorphine/test		POST apomorphine/retest			
	R/B	L/W	R/B	L/W	PRE apo/test	POST apo/retest
PD n=15	101.2 ± 4.1	112.1 ± 12.2	–	–	-4.	–
Control n=12	106.1 ± 4.6	106.2 ± 7.6	–	–	-0.04 ± 3.14	–
PD n=10	101.6 ± 4.41	110.8 ± 5.74	114.6 ± 12.3	114.2 ± 10.4	-4.23 ± 4.44	0.066 ± 3.99
Control n=8	105.1 ± 4.04	107.2 ± 4.73	105.4 ± 3.20	106.1 ± 7.83	-0.94 ± 2.10	-0.16 ± 3.43
	GPi mean rCBF ± SD				GPi mean rCBF "contrast" ± SD	
	PRE apomorphine/test		POST apomorphine/retest			
	R/B	L/W	R/B	L/W	PRE apo/test	POST apo/retest
PD n=15	99.15 ± 12.5	109.5 ± 4.93	–	–	-4.72 ± 6.62	–
Control n=12	100.3 ± 7.4	101.1 ± 5.53	–	–	-0.14 ± 3.53	–
PD n=10	98.6 ± 5.16	107.6 ± 7.11	113.1 ± 13.32	114.5 ± 11.6	-4.53 ± 5.32	-0.78 ± 4.64
Control n=8	99.67 ± 4.71	102.1 ± 5.11	100.1 ± 2.79	102.2 ± 9.03	-1.44 ± 2.56	-0.72 ± 4.82

RCBF, regional cerebral blood flow; *CU*, caudate nucleus; *TH*, ventro lateral thalamus; *PU*, putamen; *Gpe*, external globus pallidus; *Gpi*, internal globus pallidus; *R*, right; *L*, left; *B*, best; *W*, worst. "contrast", [(right nucleus- left nucleus)/(right nucleus + left nucleus)*100] in normal subjects; "contrast", [(best side - worst side)/(best side + worst side)*100] in PD (see methods)