In-vivo detection of dopamine in the substantia nigra using 3D MRSI

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Introduction

Parkinson's disease (PD) is a frequently occurring, age-related, neurodegenerative disorder and is caused by progressive loss of dopamine-secreting neurons in the substantia nigra (SN) pars compacta. Metabolic alterations in this region found in post mortem studies [1], [2] and in vivo could be used to differentiate patients with idiopathic PD and atypical Parkinsonian syndromes [3]. This study reanalyzed these data [3] to investigate metabolic alterations in the SN regions in order to identify the known dopamine loss in PD patients in vivo.

Material and Methods

3D MRSI data, acquired using a PRESS sequence (TE/TR = 30/1350 ms, nominal voxel volume = 0.25 cm^3) with water saturation at 3 T [4] from 21 PD patients [3], 24 neurologically healthy controls in the same age range and 39 younger controls were processed using LCModel with an optimized and region-specific basis data set. The volume of interest (VOI) was exactly localized in all subjects so that two enclosed voxels (rostral and caudal) defined the SN regions (Fig. 1). All model spectra were generated based on reported chemical shifts and coupling constants. Macromolecule spectra were acquired from the same VOI using an inversion recovery sequence (TI = 410 ms) and included in basis data set. Metabolite quantifications were corrected for possible differences in the T_2* values (iron deposition) by estimating the line width during LCModel analysis. To overcome inaccuracies due to insufficient signal-to-noise ratios (SNR), group-averaged spectra were evaluated.

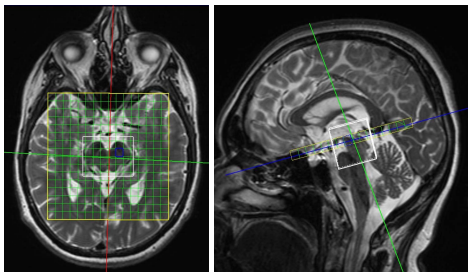

Fig. 1: *3D MRSI voxel localization in SN region for rostral slice.*

Tab. 1: *Metabolite concentrations [arbitrary units] with Cramer-Rao lower bounds [%] of young controls, age-matched controls, and PD patients*

	Young controls (n = 39)		Age-matched controls (n = 24)		PD patients (n = 21)	
	rostral	caudal	rostral	caudal	rostral	caudal
SNR	64	58	46	41	41	38
FWHM (ppm)	0.095	0.079	0.107	0.095	0.119	0.095
NAA+NAAG	52.9 3%	51.7 %	50.2 4%	40.7 4%	41.0 4%	31.9 3%
GPC+PCh	5.9 2%	6.9 2%	5.4 2%	6.3 2%	5.2 3%	5.6 2%
Cr+PCr	29.7 3%	28.7 3%	28.0 3%	27.2 3%	25.0 4%	21.8 3%
Ins+Gly	21.4 7%	26.3 5%	27.2 6%	21.8 8%	21.9 8%	19.1 9%
Glu+Gln	11.5 26%	3.8 101%	10.1 37%	5.0 72%	14.1 27%	13.9 23%
GABA	9.8 34%	26.4 14%	21.1 18%	8.4 18%	31.8 15%	21.7 15%
GSH	13.7 8%	14.3 7%	20.7 6%	20.2 6%	14.0 14%	11.9 11%
Taurine	2.7 65%	6.7 24%	14.8 15%	10.5 20%	24.4 12%	13.4 16%
Dopamine	**14.0 13%**	**8.1 20%**	**12.5 17%**	**12.1 17%**	**7.8 37%**	**2.8 78%**
HVA	2.7 58%	2.0 77%	7.2 23%	9.2 17%	11.8 20%	11.2 17%

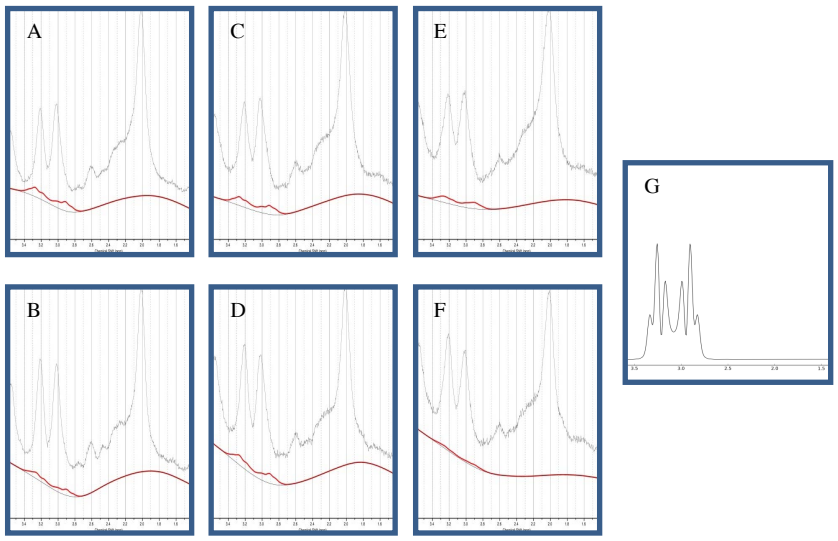

Fig. 2: *Dopamine fitting results in young controls (A rostral, B caudal), age-matched controls (C rostral, D caudal) and PD patients (E rostral, F caudal) and simulated dopamine signal with FWHM = 7 Hz (G).*

Results

In addition to the main metabolites NAA, choline (Cho), and creatine (Cr), lower-concentration metabolites such as glutamate+ glutamine (Glx), GABA, glutathione (GSH), myo-inositol (Ins), taurine, homovanillic acid (HVA) and dopamine were estimated with Cramer-Rao lower bounds (CRLB) less than 20% (Tab. 1). Levels of NAA, Cho, Cr, Ins, GSH and dopamine were lower in PD patients compared to age-matched controls, whereas Glx, GABA, taurine and HVA were higher. In particular, the dopamine concentration was clearly reduced in the caudal SN voxels of PD patients. All dopamine fittings are shown in Fig. 2 with a clear disappearance in Fig. 2F from these voxels.

Discussion

Differences between rostral (dominated by the SN pars reticulata) and caudal voxels (dominated by the SN pars compacta) are in accordance with anatomical features. Additionally, the pathological alterations in PD are in good agreement with post-mortem results [1], [2]. Progressive degeneration of dopamine-producing neurons within the SN pars compacta may be caused by mitochondrial dysfunction and oxidative stress which can also explain our findings of reduced NAA (putative marker of viable neurons), Cr (marker for impaired energy metabolism due to mitochondrial dysfunction), GSH (marker for oxidative stress) and dopamine as well as elevated taurine (modulates the action of neurotransmitters and protects against glutamate excitotoxicity), GABA and glutamate (neurotransmitter from inhibitory and excitatory systems and therefore coupled with dopaminergic pathway). Slight elevation of HVA might be explained by the fact that dopamine, given as a drug in PD, finally degrades to HVA by the action of the enzymes monoamine oxidase and catechol-O-methyl transferase.

References

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