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$T1$ and $T2$ Relaxation Times from Substantia Nigra in Parkinson's Disease and Control

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The diagnosis of Parkinson's disease, and also other neurodegenerative disorders, is based on clinical examination. Many attempts are undertaken to find a test that could confirm this clinical diagnosis. Many hopes were attributed to magnetic resonance imaging but its importance remains obscure. The aim of this study was to compare $T1$ and $T2$ relaxation times from *substantia nigra* of patients with clinical diagnosis of Parkinson's disease and age-matched controls. A decrease of $T2$ (54.5 ± 1.4 ms vs. 58.0 ± 1.5 ms) in Parkinson's disease vs. control was found with confidence level of 5%. $T1$ did not differ significantly between Parkinson's disease and control (624 ± 17 ms vs. 614 ± 21 ms).

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1. Background

Parkinson's disease (PD) is one of the neurodegenerative disorders. Motor symptoms of the disease (slowness of movements, rigidity, and tremor) are a consequence of the death of nervous cells in brain structure named *substantia nigra* (SN). This structure is located in mesencephalon as shown in Fig. 1 (top right). There is currently no cure for the disease and the primary cause of the nervous cells death has not yet been determined. Nevertheless there are several hypotheses trying to explain this process; one of which is iron induced oxidative stress [1].

The diagnosis of PD, and also other neurodegenerative disorders, is based on clinical examination. Many attempts are undertaken to find a test that could confirm this clinical diagnosis. Many hopes were attributed to magnetic resonance imaging (MRI) but its importance remains obscure. Unfortunately, until now conventional $T1$-weighted and $T2$-weighted imaging did not show significant differences between PD and control [2]. It seems, however, that measurements of longitudinal ($T1$) and transverse ($T2$) relaxation times (RT) could have some importance. The absolute values of $T1$ and $T2$ RT depend on number of factors (such as: viscosity, water content, ions concentration) one of them being for sure the concentration of iron. According to some authors, $T2$ RT is decreased in parkinsonian SN compared to control as a result of an increase in the iron concentration [3, 4]. Longitudinal RT was much less studied.

The aim of this study was to compare $T1$ and $T2$ RT from SN of patients with clinical diagnosis of PD and age-matched controls.

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2. Materials and methods

15 patients (5 females and 10 males) and 10 controls (3 females and 7 males) were assessed with 1.5 T MRI. The clinical diagnosis was made according to generally accepted criteria [5]. All patients had a moderate severity of the disease (stage 2 according to Hoehn and Yahr scale [6]).

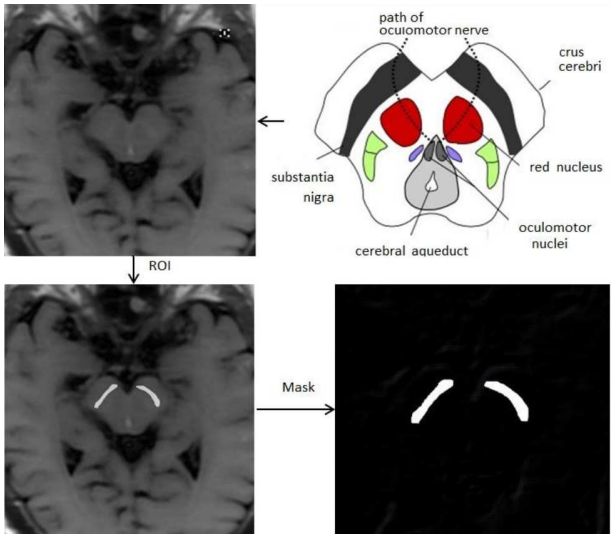

Fig. 1. Individual steps of $T2$ image segmentation. Schema of brain stem (top right) is rescaled to fit brain stem in $T2$ image (top left). From the obtained result (bottom left) the *substantia nigra* mask (bottom right) is created.

The measurements of $T1$ and $T2$ were performed with the use of General Electric 1.5 T Sigma Exite MRI with a head coil using pulse methods. Inversion recovery (IR) pulse sequence was used to measure T1 (TI = 100, 200, 500, 800, 1600, 2400 ms; TR = 10000 ms) and fast spin echo (FSE) pulse sequence was used to measure $T2$

(TE = 15, 30, 45, 60 ms; TR = 3000 ms), echo times (TE) were constant. The signal-to-noise ratios based on the TE (15, 30, 45, 60 ms) were 31, 28, 24, 21.

The region of interest (ROI) of SN was determined basing on the anatomical atlas and the picture obtained from IR of each subject studied as shown in Fig. 1. Mask created from schematic brain stem cross-section was rescaled to fit $T2$ MRI image of proper brain section. The ROI defined this way was used as the mask for determination of the boundary of SN in the following measurements series of the subject.

$T1$ and $T2$ relaxation times were calculated from the best fit to experimental points of Eqs. (1) and (2), respectively

$$M_z(t) = M_z(0)\left(1 - 2\mathrm{e}^{-\frac{t}{T_1}}\right), \tag{1}$$

$$M_{xy}(t) = M_{xy}(0)\mathrm{e}^{-\frac{t}{T_2}}, \tag{2}$$

where M_z — longitudinal component of the magnetization, M_{xy} — transverse component of the magnetization.

3. Results and discussion

RT's of control and PD group were calculated as means of single RTs in both groups. Experimental errors were estimated as standard error of the mean. Results are presented in Table. Typical $T2$ MRI images obtained from both groups are shown in Fig. 2.

TABLE

Transverse and longitudinal relaxation times of control and Parkinsonian groups obtained as a mean of relaxation times of individual subjects. Experimental errors were estimated as standard error of the mean.

Relaxation time [ms]	Group	
	Control	PD
$T1$	614 ± 21	624 ± 18
$T2$	58.0 ± 1.4	54.5 ± 1.5

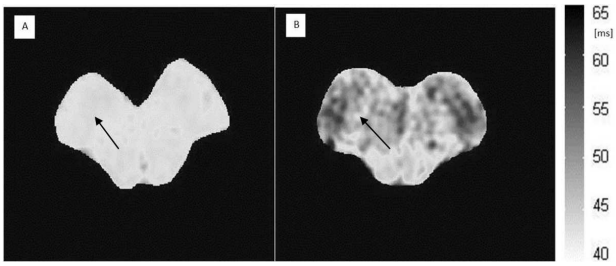

Fig. 2. Transverse relaxation times maps of Parkinsonian (A) and control (B) mesencephalon. Substantia nigra is marked with an arrow. For more details refer to Fig. 1.

As can be seen in Fig. 2, in PD there is a decrease of $T2$ in whole mesencephalon not only in *substantia nigra*. The reason for that remains obscure. This finding may be due to a change in the water content in the tissue, changes in the structure with proliferation of glia and many other reasons. As the pathological process in PD affects mostly SN all our measurements concern this structure only.

A decrease of $T2$ (54.5 ± 1.4 ms vs. 58.0 ± 1.5 ms) in PD vs. control was found with confidence level 5%. Similar slight decrease of $T2$ in parkinsonian SN compared to control was found also by others [7]. These authors did not report $T1$ relaxation time. In our experiment $T1$ did not differ significantly between PD and control (624 ± 17 ms vs. 614 ± 21 ms). As both $T1$ and $T2$ relaxation times depend in the same way on iron concentration (an increase of the concentration of iron causes a decrease of $T1$ and $T2$ relaxation time), the change of $T2$ relaxation time only in parkinsonian SN without any change in $T1$ speaks against the increase of the concentration of iron as the reason of this finding.

In order to assess possible decrease in $T1$, that might be due to iron content change, we performed estimation based on data obtained for a real tissue [8]. Simple mathematical assessment shows that $T1$ should drop to about 400 ms. However, in our experiment we see only a slight, statistically non-significant, increase of $T1$ (from 614 ± 21 ms to 624 ± 18 ms).

The results of our study with a decrease of the $T2$ relaxation time in PD compared to control without a change in $T1$ relaxation time, suggest that the change of $T2$ cannot be due to an increase of the total iron concentration in the tissue. Such an increase would certainly shorten also $T1$ relaxation time, as it was recently shown in our experimental study [9]. On the other hand, the results of the Mössbauer spectroscopy show that there is no increase of the total iron concentration in parkinsonian SN, only labile iron rises slightly [10].

It is important to note that MRI studies produced controversial results as it was summarized in a recent review [11]. Possible causes of these discrepancies were discussed by Deoni [12].

4. Conclusions

MRI study demonstrated that in parkinsonian SN there is a statistically significant decrease of $T2$ relaxation time compared to control, which is not paralleled by a similar change in $T1$ relaxation time. This change of $T2$ relaxation time cannot be explained by a change in the concentration of iron in parkinsonian SN.

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