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# The Relationship between Parkinson's Disease and Dementia

## A study using Proton NMR Imaging Parameters

J. A. O. BESSON, W. J. MUTCH, F. W. SMITH and F. M. CORRIGAN

The value of the spin lattice relaxation time ($T_1$) obtained during nuclear magnetic resonance imaging of the brain was studied in patients with idiopathic Parkinson's disease, with and without dementia. $T_1$ increases significantly in the basal ganglia and cerebral white matter of the demented and non-demented groups. $T_1$ of the cerebral white matter correlates with the severity of dementia.

Nuclear magnetic resonance (NMR) imaging of the brain involves the image reconstruction from proton density (PD) and spin lattice relaxation time ($T_1$) data from each pixel of the sample (Eastwood *et al*, 1985). Proton density measures are obtained by aligning the protons, using a static magnetic field, influencing them by the momentary application of a radio frequency pulse, and measuring the amplitude of the signal emitted. The measure is related (although not in absolute terms) to the concentration of protons in the tissue, but not all protons emit measureable signals. The signal is a measure predominantly of protons in water and free lipids. The spin lattice relaxation time is the time taken for the protons to relax back to their previously aligned position in the static magnetic field, having been influenced by the radio frequency pulse. Whereas there is little variation in proton density between grey and white matter, the $T_1$ differs quite markedly, being higher in the grey matter; this reflects the different fat/water ratio composition of the two tissues.

$T_1$ may be altered by a variety of pathological conditions. This varies from the very gross pathology of cerebral tumours (Bydder *et al*, 1982) and areas of demyelineation (Young *et al*, 1981) to the less morphologically disruptive pathologies of senile dementia of Alzheimer and multi-infarct dementia. In these last two conditions, there is a statistically significant increase in $T_1$, when compared with normal controls, while the more severe the dementia (as measured by MSQ), the greater the $T_1$. This correlation between MSQ score and $T_1$ is statistically significant (Besson *et al*, 1985).

In idiopathic Parkinson's disease, the primary lesion is thought to arise in the substantia nigra. Axons from the dopaminergic neurones ascend to the basal ganglia, putamen, and globus pallidus. Cellular degeneration affects the globus pallidus, putamen, and associated nuclei in addition to the substantia nigra (Greenfield, 1963). The NMR imaging techniques used in this study do not permit visualisation of the substantia nigra, but should future developments allow this, no doubt further light will be shed on the problem. Cognitive impairments have been variously reported to occur in 20% of an unselected series of patients with Parkinson's disease (Pollock & Hornabrook, 1966) and 33% of Parkinsonian patients admitted to a psychiatric hospital (Mindham, 1970). In this study, the occurrence was equally frequent among cases diagnosed as idiopathic or arterisoclerotic. Celesia & Wanamaker (1972) reported that cognitive impairment occurred in up to 40% of cases and that this correlated in frequency and severity with the duration of the disease.

### Method

Patients with a diagnosis of idiopathic Parkinson's disease were identified in a community and hospital survey, as part of a wider epidemiological study. Nine patients who were not demented (Mental Status Questionnaire (MSQ) score >7) and eight patients who were dementing (MSQ score >7) were selected for NMR brain imaging. The mean age of the patients was 71 years, the mean Webster score (Webster, 1968) of severity of Parkinson's disease was 14, and the mean Hoehn & Yahr score was 4 (Hoehn & Yahr, 1967).

The demented group had a mean age of 76 years, while that of the non-demented group was 68. The mean length of history of Parkinson's disease of the non-demented group (13 years) was twice that of the demented group (6.5 years). All the demented patients and all but one non-demented patient received Sinemet (L-dopa and carbidopa combination). There were 15 normal controls, of mean age 63 years. Imaging was carried out using the Aberdeen NMR Imager Mk II of magnetic field strength 0.08 Tesla and resonance frequency 3.4 MHz. The pixel size is 1.9 $mm^2 \times 12$ mm.

The spin lattice relaxation time ($T_1$) was measured in the left and right putamen-globus pallidus, and in the cerebral white matter of right and left hemispheres in the frontal (RFW, LFW), parietal (RPW, LPW) and occipital (ROW,



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TABLE I

*$T_1$ (msec) values of Putamen-Globus Pallidus of patients with idiopathic Parkinson's disease and controls*

| | Non-demented Parkinson's ($n=9$) | Demented Parkinson's ($n=8$) | Mann Whitney U-Test P values | Total Parkinson's ($n=17$) | Controls ($n=15$) | Mann Whitney U-Test P values |
|---|---|---|---|---|---|---|
| $T_1$ R Basal ganglia | 348 (+/− 10) | 358 (+/− 16) | N.S. | 352 (+/− 19) | 316 (+/− 20) | 0.001 |
| $T_1$ L Basal ganglia | 348 (+/− 26) | 353 (+/− 19) | N.S. | 350 (+/− 23) | 322 (+/− 22) | 0.02 |
| MSQ | 9 (+/− 0.6) | 5 (+/− 2) | 0.001 | | | |
| Webster Score | 13.5 (+/− 5) | 14 (+/− 3) | N.S. | | | |

LOW) regions. These were taken from standard transaxial sections, commencing at the orbitomeatal line and moving cranially at 1 cm intervals. Areas of the putamen-globus pallidus and of the frontal, parietal, and occipital regions were mapped, using a graphic tablet, and 20 pixels counted in each basal ganglia region and in each cerebral white matter area.

## Results

The $T_1$ values (msecs) of the putamen-globus pallidus of patients with idiopathic Parkinson's disease and controls are shown in Table I. The $T_1$ values are significantly greater in patients with Parkinson's disease, suggesting a change within the basal ganglia of patients with Parkinson's disease, as distinct from those without. If we compare the $T_1$ values of the putamen-globus pallidus of patients with idiopathic Parkinson's disease with dementia and those without dementia, no significant difference is observed. It should be noted that the severity of Parkinson's disease did not differ in the two groups.

The MSQ score of the total group of patients with Parkinson's disease did not correlate with the Webster score or with the Hoehn & Yahr score, indicating that there is no correlation between severity of Parkinson's disease and severity of dementia.

We can now examine the relationship between cerebral white matter, $T_1$ values, and dementia in Parkinson's disease. Table II shows the correlations (Kendall's tau) between $T_1$ values of cerebral white matter areas (RFW, LFW, RPW, LPW, ROW, LOW) and severity of dementia, as measured by the MSQ.

These show a significant correlation between degree of dementia (i.e. lower MSQ score) and the length of the $T_1$ in four of the six areas. There is no correlation between severity of Parkinson's disease, as measured by the Webster scale, and $T_1$ value of cerebral white matter.

If the $T_1$ values of cerebral white matter areas of patients with Parkinson's disease are compared with normal controls, a significant difference between the two groups is noted (Table III) in four of the six areas measured.

The remaining two areas show a statistically non-significant increase in $T_1$ in the Parkinson's group. Comparing the demented with non-demented Parkinson's patients, increase in $T_1$ is observed in all cerebral white matter areas in the demented group, but this is statistically not significant.

TABLE II

*Correlations (Kendall's) between cerebral white matter $T_1$ values and (a) MSQ (b) Webster score*

| | | MSQ Score | Webster Score |
|---|---|---|---|
| $T_1$ (msecs) | RFW | −0.52, P=0.05 | +0.17, N.S. |
| | LFW | −0.31, N.S. | +0.08, N.S. |
| | RPW | −0.6, P=0.05 | +0.3, N.S. |
| | LPW | −0.46, P=0.05 | +0.02, N.S. |
| | ROW | −0.42, P=0.05 | +0.1, N.S. |
| | LOW | −0.15, N.S. | +0.1, N.S. |

## Discussion

The spin lattice ($T_1$) relaxation time obtained in NMR imaging is of some value in clarifying certain aspects of idiopathic Parkinson's disease. However, at the resolution of the imager used in this study, it is not possible to identify the substantia nigra—the nucleus thought to be the primary location of the affected dopaminergic neurones, though with future improvements in instrumentation, this might

TABLE III

*$T_1$ (msecs) values (mean +/− SE) for cerebral white matter areas of patients and controls*

| | Non-demented Parkinson's ($n=9$) | Demented Parkinson's ($n=8$) | Mann Whitney U-Test P values | Total Parkinson's ($n=17$) | Controls ($n=15$) | Mann Whitney U-Test P values |
|---|---|---|---|---|---|---|
| $T_1$ RFW | 282 (+/− 22) | 301 (+/− 23) | N.S. | 289 (+/− 20) | 267 (+/− 10) | 0.01 |
| $T_1$ LFW | 288 (+/− 27) | 302 (+/− 24) | N.S. | 295 (+/− 23) | 274 (+/− 13) | N.S. |
| $T_1$ RPW | 291 (+/− 18) | 308 (+/− 19) | N.S. | 305 (+/− 24) | 269 (+/− 13) | 0.007 |
| $T_1$ LPW | 294 (+/− 20) | 315 (+/− 16) | N.S. | 310 (+/− 28) | 271 (+/− 16) | 0.002 |
| $T_1$ ROW | 298 (+/− 29) | 308 (+/− 19) | N.S. | 292 (+/− 20) | 280 (+/− 11) | N.S. |
| $T_1$ LOW | 303 (+/− 22) | 308 (+/− 19) | N.S. | 305 (+/− 20) | 283 (+/− 13) | 0.01 |

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be possible and might throw further light on the problem. The putamen-globus pallidus of the basal ganglia, however, provides a large enough volume of tissue for $T_1$ measures to be accurately calculated, and, as the recipient of the substantia nigra neurones and the site of pathological changes in Parkinson's disease, is also relevant. A significant increase in $T_1$ values occurs in the putamen-globus pallidus of patients with Parkinson's disease. The presence of dementia in one sub-group is not associated with alteration of the $T_1$ in putamen-globus pallidus, even taking into account the fact that the severity of Parkinson's disease is not different in the demented and non-demented group respectively. Both groups had similar drug treatments, which are therefore unlikely to explain the varying results. The fact that the two groups had similar clinical severity scores and that the demented group in fact had a shorter history of Parkinson's disease than the non-demented group would suggest that the dementia is not simply a reflection of more severe Parkinson's disease.

Perhaps of even greater interest are the changes in cerebral white matter $T_1$ values in patients with Parkinson's disease, with and without dementia. Firstly, cerebral white matter pathology, as reflected by increased $T_1$, is present in idiopathic Parkinson's disease, particularly when dementia is present. Secondly, the correlation between increased cerebral white matter $T_1$ and severity of dementia, observed in this study, is similar to the relationship also observed in patients with both Alzheimer's and multi-infarct dementia (Besson *et al*, 1985). Furthermore, it appears that altered $T_1$ in the cerebral white matter occurs in patients with idiopathic Parkinson's disease, even in the absence of dementia. This implies that patients with that disease who are demented are probably not a pathologically separate group, in terms of morphology, from the non-demented. This would tend to oppose the view of Marsden (1982) that the presence of dementia reflects co-existing Alzheimer's disease, and would tend to support the view that those with dementia merely have a more profound pathological white matter change than those without. If this were the case, then the findings of Perry *et al* (1983) that distinct Alzheimer change was not a necessary accompaniment of the dementia of Parkinson's disease may well be more accurate.

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*J. A. O. Besson, BSc, MB, ChB, MRCPsych, *Wellcome Senior Lecturer, Department of Mental Health, University of Aberdeen, Clinical Research Centre, Royal Cornhill Hospital, Aberdeen AB9 2ZH*

W. J. Mutch, BMedBiol, MB, ChB, MRCP, *Senior Registrar in Geriatrics, Aberdeen Royal Infirmary*

F. W. Smith, MB, ChB, DMRD, FFR, *Consultant Radiologist and Specialist in Nuclear Medicine, Aberdeen Royal Infirmary*

F. M. Corrigan, MB, ChB, MRCPsych, *Lecturer, Department of Mental Health, University of Aberdeen*

*Correspondence

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