

Left-Right Differences in $^1\text{H}_2\text{O}$ T_1 Values of Multiple Sclerosis Normal Appearing Brain Tissue

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Introduction

There is accumulating evidence supporting the concept of innate hemispheric asymmetries in normal human brain structure and physiology.¹⁻¹⁷ Furthermore, these interhemispheric inequalities for healthy adults are likely different between the sexes.^{2,4,7-9} Therefore, it is conceivable that pathological changes in the normal-appearing (NA) brain tissue of subjects with multiple sclerosis (MS) may be different between hemispheres, and between sexes. Of many MS studies, only a few have investigated possible hemispheric differences in disease expression.^{18,19} A recent quantitative MR study²⁰ found significant increases in the mean NA white matter (NAWM) and NA gray matter (NAGM) T_1 values of MS subjects compared with healthy control (HC) subjects. The data suggested that the mean NAGM T_1 value increase was due to the women (no significant differences were observed for men), whereas that for MS NAWM T_1 values was similar between the sexes. In this report, we delve further into sex-related NAGM T_1 changes by examining possible hemispheric differences in increased mean NAWM and NAGM T_1 values in a substantially larger group of MS and HC subjects.

Methods

46 HC subjects [18 W, mean age 33 (± 10) y, and 28 M, mean age 39 (± 12) y] and 33 MS subjects [23 W, mean age 36 (± 8) y, and 10 M, mean age 42 (± 7) y] provided informed consent before participating in this study. All MR data were obtained using a 4 T Varian INOVA instrument, and employing a head birdcage RF transceiver coil. Experimental details pertaining to data collection and quantitative T_1 mapping are similar to the literature.²⁰ Bilateral regions of interest (ROIs) were carefully selected from three interior NAGM areas [putamen, thalamus, and the head of caudate nucleus] and five NAWM structures [centrum semiovale, genu of corpus callosum, splenium of corpus callosum, forceps major, and forceps minor]. All T_1 values and standard deviations (SD) are given in msec units. Hemispheric and group comparisons were performed, respectively, using two-tailed t-tests for paired and unpaired data. All P values were corrected for multiple comparisons.

Results

We find significantly ($P < 0.05$) increased mean T_1 values of $\sim 5\%$ in MS NAWM compared to HC, with similar increases for both men and women (Figure 1A). The overall average T_1 values were increased by $\sim 2\%$ in MS NAGM, but were observed only in the women, for whom the increase was $\sim 3\%$, Fig. 1B. No significant hemispheric differences in mean NAWM T_1 values were observed in male and female HC and MS groups, Fig. 1A, but significant hemispheric differences (right > left) in mean NAGM T_1 values were found in the HC ($\sim 2\%$) and MS ($\sim 3\%$) men, and in the MS ($\sim 1\%$) women, Fig. 1B.

Discussion

The findings of significant sex-independent and sex-dependent increases, respectively, in the mean MS NAWM and MS NAGM $^1\text{H}_2\text{O}$ T_1 values, is similar to findings from a study of fewer subjects.²⁰ Increased T_1 values likely reflect diffuse inflammation and edema in MS. Regarding hemispheric inequality, no significant differences in NAWM T_1 values were observed for either sex in the MS and HC groups (Fig. 1A), whereas significant right > left hemispheric differences were found in the NAGM T_1 values of the male HC and MS subjects, and female MS subjects (Fig. 1B). The finding of hemispheric differences in NAGM, but not NAWM, suggests that the differences are real, and not an experimental artifact. Our hemispheric results are consistent with a 1.5 T T_1 study,¹⁷ which found no hemispherical differences in white matter T_1 values but significant (right > left) inequalities in the internal gray matter T_1 values of healthy adults. However, the mean white matter T_1 values did reveal a right > left trend in the male MS and HC groups, and female MS group, which suggests that asymmetry does exist, but to a lesser degree than that of gray matter. In fact, a quantitative 1.5 T MR study reported significant asymmetry in the white matter MTR values of healthy adults.¹⁵ Though sex-related differences in internal gray matter T_1 values were not examined in the 1.5 T study,¹⁷ our 4 T results indicate that the hemispheric asymmetry in mean HC NAGM T_1 values is due to the men. The hemispheric asymmetry in the male HC NAGM T_1 values may be associated with the significantly higher right hemisphere glucose metabolism reported for healthy men.⁹ Furthermore, our lack of significant laterality of T_1 values in HC women is consistent with no hemispheric difference in glucose metabolism.⁹ The same rationale may be applied to the observed hemispheric differences in the female MS NAGM T_1 values, as a PET study of primarily MS women reported a significant decrease in left hemisphere glucose metabolism.¹⁸ These findings suggest possible hemispheric differences in MS disease expression between the sexes.

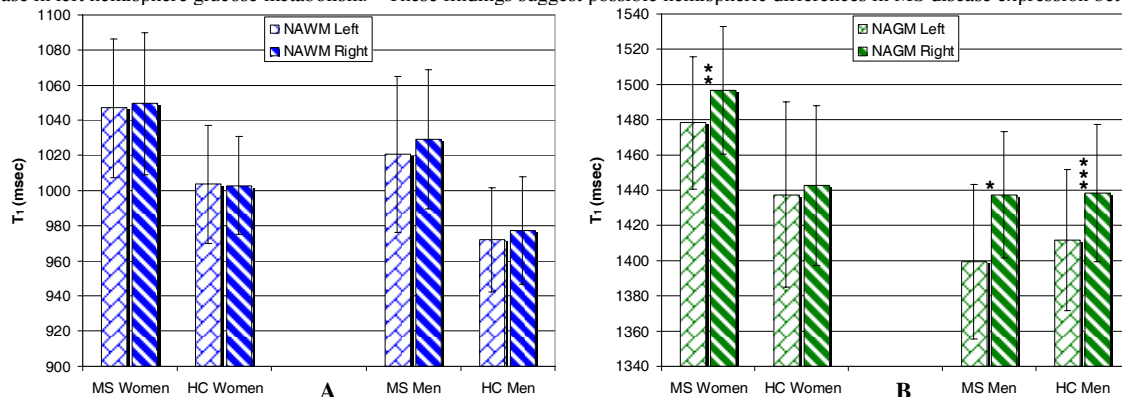


Figure 1. Bar graphs representing left vs. right comparisons of mean NAWM (A) and NAGM (B) T_1 values (\pm SD). * $P < 0.05$; ** $P < 0.005$; *** $P < 0.0005$.

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