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Short report

The association between handedness and clinicodemographic characteristics in people with multiple sclerosis: a brief report

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Abstract

A relationship between handedness and clinicodemographic profiles of people with multiple sclerosis was sought using data from the Multiple Sclerosis Partners Advancing Technology Health Solutions network of 10 multiple sclerosis centers in the USA and Europe. Handedness data were available for 8888 multiple sclerosis patients, of which 917 (10.3%) were left-handed. Clinicodemographic profiles of right versus left-handed multiple sclerosis patients were similar except for a slightly increased proportion of men who were left-handed, and slightly reduced performance on the manual dexterity test using the non-dominant hand in left-handed patients. We found no evidence to suggest a prognostic implication of handedness in multiple sclerosis.

Keywords: Multiple sclerosis, handedness, epidemiology

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Introduction

The relationship between handedness and autoimmune diseases such as multiple sclerosis (MS) is debated.^{1–3} A previous study of female US nurses suggested a modest increase in the risk of MS among left-handed women.¹ It has also been proposed that HLA-alleles associated with an increased risk of MS and circulating autoantibodies may be more common among left-handed individuals.⁴

Approximately 11% of the general population is left-handed.⁵ Few population-based studies have examined the relationship between handedness and demographic or clinical characteristics of people with MS (PwMS). Multiple Sclerosis Partners Advancing Technology Health Solutions (MS PATHS)⁶ is a collaborative network including 10 MS centers in the USA and Europe and provides access to a large cohort of PwMS. In this study, we investigated the association between handedness and clinicodemographic profile of enrollees in MS PATHS.

Methods

This cross-sectional study utilized data from the MS PATHS network. MS PATHS is a collaborative network sponsored by Biogen which includes seven centers in the USA and three centers in Europe, and is based on the concept of a learning health system.⁶ During routine clinic visits, people with MS undergo the multiple sclerosis performance test (MSPT) which is an iPad-based assessment including structured patient history, electronic adaptations of the multiple sclerosis functional composite, and the neuro-quality of life (neuro-QoL) outcome instrument.⁷

We queried MS PATHS for PwMS recruited from the inception of the database (11/2015) through 3/2018. Requested variables included sex, age at MS onset and diagnosis, MS subtype, level of education, handedness, patient determined disease steps (PDDS) and relevant components of MSPT assessment including manual dexterity test (MDT), walking speed time (WST), contrast sensitivity test

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[#]Data used in preparation of
this article were obtained
from Multiple Sclerosis
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database. As such, the



investigators within MS PATHS contributed to the design and implementation of MS PATHS and/or provided data but did not participate in analysis or writing of this report.

(CST), processing speed time (PST), and the Neuro-QoL's upper extremity function and cognitive domains. Handedness data in MS PATHS is systematically collected by asking the patients which hand they learned to write with.

We compared right and left-handed patients for differences in demographic and clinical profiles using the chi-square test to examine the association between categorical variables, *t*-test for continuous variables, and Mann–Whitney U test for ordinal variables. *P* values less than 0.05 were considered statistically significant. The institutional review board at Washington University in St Louis approved the study.

Results

A total of 9618 PwMS were identified (73.2% women). Handedness data were available for 8888 patients, of which 917 (10.3%) were left-handed. Table 1 shows the demographic and clinical profiles of the patients. Among women with MS, 9.5% were left-handed whereas 12.4% of men with MS were left-handed. Women comprised a greater proportion of right-handed than of left-handed PwMS (74.0% vs. 67.8%, $P < 0.001$). Overall, right and left-handed patients had a similar age at MS diagnosis, PDDS, and MS subtype. Approximately 65% of PwMS had relapsing–remitting MS in both handedness groups. The mean time to complete MDT with the left hand was not associated with handedness. The mean time to complete MDT with the right hand was slightly longer in left-handed compared to right-handed PwMS (28.9 ± 8.3 vs. 27.6 ± 7.6 seconds, $P < 0.001$). Results for WST, CST, PST, and neuro-QoL upper extremity and cognitive domain scores were similar between right and left-handed PwMS. Stratification by sex did not change our findings.

To examine if any major underlying upper extremity dysfunction might have impacted our findings (by affecting patient-reported handedness), we performed a sensitivity analysis by including a subset of patients whose MDT performance values were in the best performance quartile (< 23 seconds) thus having minimal functional impairment of upper extremities. In this subset ($n = 1393$, 10.1% left-handed), the mean \pm SD time to complete MDT with the dominant hand was 20.0 ± 1.7 seconds for right-handed patients and 20.0 ± 1.8 in left-handed patients. Time to complete MDT with the non-dominant hand was 20.8 ± 1.6 in right-handed patients,

and 20.0 ± 1.8 in left-handed patients. These results did not change our interpretation of the findings.

We also investigated if right-handed and left-handed patients might have been differentially impacted when MDT performance is more severely impaired. To examine this, we performed another sensitivity analysis by including a subset of patients whose MDT performance values were in the worst performance quartile (> 32 seconds). In this subset ($n = 1184$, 10.1% left-handed), the mean \pm SD time to complete MDT with the dominant hand was 40.6 ± 6.4 seconds for right-handed patients and 40.3 ± 6.2 for left-handed patients. Time to complete MDT with the non-dominant hand was 38.9 ± 6.2 in right-handed patients, and 40.0 ± 6.8 in left-handed patients. These results did not change our interpretation of the findings, either.

Discussion

In this large cross-sectional study using data from MS PATHS, 10.3% of PwMS were left-handed, close to the estimated 11% prevalence of left-handedness or mixed-handedness in the US general population.⁵ The higher prevalence of left-handedness among male PwMS compared to women (12.4% vs. 9.5%) in our study is consistent with the general population. A meta-analysis found a higher prevalence of left-handedness in men in the general population, with an estimated male to female odds ratio of 1.23 (95% confidence interval (CI) 1.19–1.27).⁸

A previous cohort study using data from the Nurses' Health Study reported a 62% increased risk of MS among women who were naturally left-handed as compared to those who were right-handed (relative risk = 1.62, 95% CI 1.04–2.53)¹ and suggested that prenatal exposure to sex hormones may possibly play a role in MS risk.^{9,10} That study included only women, and was not designed to examine the clinical characteristics of incident MS cases. We compared the clinical profiles of right versus left-handed PwMS to seek any evidence to support that left-handed MS patients may have an earlier MS onset or altered clinical severity. No strong evidence to suggest this was found. However, we found a slightly longer mean time to complete MDT with the non-dominant hand (right hand) in left-handed PwMS. The mean time to complete MDT with the left hand was similar between right-handed and left-handed MS patients. The mean age at MS onset in left-handed PwMS was minimally higher than right-handed

Table 1. Demographic and clinical profile of right-handed versus left-handed patients with MS ($n = 8888$).

Characteristics	Right-handed ($n = 7971$)	Left-handed ($n = 917$)	<i>P</i> value
Sex, ^a n (%)			
Women	5898 (74.0)	622 (67.8)	<0.001 ^b
Men	2068 (25.9)	294 (32.1)	
Age at MS symptom onset, ^c years, mean \pm SD	32.3 \pm 11.2	32.6 \pm 11.8	0.008 ^d
Age at MS diagnosis, years, mean \pm SD	35.2 \pm 11.0	35.6 \pm 11.5	0.066 ^d
Education, ^f years, median (IQR)	14 (12–16)	14 (12–16)	0.068 ^g
Disease subtype, ^h n (%)			
Relapsing–remitting	4764 (64.3)	549 (65.5)	0.20 ^b
Secondary progressive	1381 (18.6)	164 (19.6)	
Primary progressive	595 (8.0)	50 (6.0)	
Progressive relapsing	665 (9.0)	75 (8.9)	
Patient determined disease steps, ⁱ median (IQR)	1 (0–3)	1 (0–3)	0.279 ^g
Manual dexterity test for right hand, ^j seconds, mean \pm SD	27.6 \pm 7.6	28.9 \pm 8.3	<0.001 ^d
Manual dexterity test for left hand, ^k seconds, mean \pm SD	29.0 \pm 7.7	28.7 \pm 8.0	0.333 ^d
Neuro-QoL ^l upper extremity function <i>t</i> -score, ^m mean \pm SD	45.5 \pm 9.5	45.1 \pm 9.5	0.95 ^d
Walking speed time, ⁿ seconds, mean \pm SD	7.4 \pm 4.9	7.7 \pm 5.2	0.187 ^d
Contrast sensitivity test ^o at high (100%) contrast, ^p mean \pm SD	57.0 \pm 6.3	56.6 \pm 6.1	0.248 ^d
Contrast sensitivity test ^o at low (2.5%) contrast, ^p mean \pm SD	33.7 \pm 13.0	32.9 \pm 13.5	0.174 ^d
Processing speed test, ^q seconds, mean \pm SD	46.9 \pm 12.9	46.6 \pm 12.9	0.613 ^d
Neuro-QoL ^l cognitive function <i>t</i> -score, ^m mean \pm SD	46.2 \pm 9.1	45.6 \pm 8.9	0.91 ^d

^aData for sex were missing for six patients.

^bChi-square test

^cData for age at MS symptoms onset were missing for 414 patients.

^dStudent's *t*-test

^eDate for age at MS diagnosis were missing for 538 patients.

^fData for education were missing for 310 patients.

^gMann–Whitney U test.

^hData for MS disease subtype were missing for 645 patients.

ⁱData for patient determined disease steps were missing for 75 patients.

^jData for manual dexterity test for the right hand were missing for 890 patients.

^kData for manual dexterity test for the left hand were missing for 922 patients.

^lScores for neuro-quality of life (Neuro-QoL) are reported using a *t* distribution, with the mean of the reference population set to 50 and the standard deviation set to 10 units. Lower *t* scores indicate less of the concept being measured. For instance, a *t* score of 45 for upper extremity function, is 0.5 standard deviation worse than the average.

^mData for Neuro-QoL were missing for 2083 patients.

ⁿData for walking speed time were missing for 1068 patients.

^oThe contrast sensitivity testing is based on the Sloan low contrast letter acuity test and evaluates binocular acuity with a maximum number correct of 60 at high (100%) and low (2.5%) contrast.

^pData for contrast sensitivity test were missing for 3814 patients.

^qData for processing speed test were missing for 625 patients.

PwMS. The implications of these subtle differences are unclear.

We were unable to examine the relationship between handedness and MS onset symptom laterality because MS PATHS does not capture the details of onset symptoms. Future studies should examine this potential relationship, given that the brain networks responsible for controlling the less dexterous

non-dominant hand may have a lower reserve capacity, and therefore impairments of the fine motor control of the non-dominant hand may be discernable at an earlier stage of MS.

Overall, we found no evidence to suggest a prognostic implication of handedness in MS. Our study also encourages using MS PATHS for conducting clinical research in MS.

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Conflict of Interests

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