Background: Fampridine is an effective symptomatic treatment option for walking impairment in persons with multiple sclerosis (pwMS). The known mechanism of action suggests that it may affect not only on walking but also on other functions of the central nervous system. On the other hand, cognitive impairment is common in pwMS. There is strong evidence of association between cognitive impairment and lower and upper extremity dysfunction in pwMS.

Objectives: In this study, we aimed to investigate the association between cognitive functions and lower and upper extremity functions in terms of treatment efficacy in pwMS who have undergone fampridine therapy due to WI.

Methods: This study had a single-blind design that the outcome assessors were blinded. The pwMS with Expanded Disability Status Scale 4-7 who were treated with fampridine were included. The participants were recruited from Outpatient Clinic for MS of Department of Neurology, Dokuz Eylul University Hospital, Izmir, Turkey. Neurological examination, physical and cognitive tests were performed in baseline and repeated at 6 months. Age, sex, and education-matched healthy controls were also assessed. Cognitive assessment was performed with using the Brief International Cognitive Assessment for MS (BICAMS) including tests of mental processing speed and memory. The BICAMS includes the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test (CVLT2) and the Brief Visuospatial Memory Test-Revised (BVMT-R). Paced Auditory Serial Addition Test (PASAT) was also used for cognitive assessment. Patients who were below -2 SD compared to healthy controls in cognitive tests were determined as having cognitive impairment. The 9-Hole Peg Test (9-HPT) was used to assess upper extremity function. The lower extremity function was assessed with the Timed 25-Foot Walk (T25FW), Six Spot Step Test (SSST), and 12-Item Multiple Sclerosis Walking Scale (MSWS-12).

Results: In total, 134 pwMS were enrolled. 77 healthy controls (HCs) were also included. At baseline, a strong correlation was found between the 9-HPT, SDMT and PASAT (p<0.01). A moderate correlation was found with the BVMT-R (r=0.398) and CVLT2 (r=0.310). The pwMS with CI had significantly worse performance in 9-HPT, T25FW, SSST, and MSWS-12 compared to pwMS without CI as detected with the SDMT (p<0.01). Similar findings were also obtained in PASAT. Significant worse performance was found only in SSST in the pwMS with vs. without CI detected with BVMT-R and CVLT2 (p=0.02, p=0.034, respectively). Significant improvement was observed in both physical and cognitive parameters at 6th months (p<0.05). Physical improvement was most pronounced in the patients who initially had no CI (p<0.05). At the end of the 6th month, the involvement in the physical tests between pwMS with and without CI was similar. There were no differences between baseline and 6th month in terms of physical and cognitive functions in HCs.

Conclusion

This study suggests that fampridine has positive effect on cognitive, upper and lower extremity functions. The cognitive function was associated with both upper and lower extremity functions. This association was more prominent in information processing speed. The SSST was the most cognitive-associated lower extremity function measure among the other measures.