Identifying Neuromechanical Biomarkers of Multiple Sclerosis to Aid in Earlier Diagnosis

Annette Hahn[1], Brent J. Raiteri[1,2], Anke Salmen[3], Daniel Hahn[1,2]
[1]Human Movement Science, Faculty of Sports Science, Ruhr University Bochum, Bochum, Germany
[2]School of Human Movement & Nutrition Sciences, The University of Queensland, Brisbane, Australia
[3]Department of Neurology, St. Josef-Hospital Bochum, Ruhr University Bochum, Bochum, Germany
Email: annette.hahn@rub.de

Summary

The aim of this research was to provide insights into potential changes in motor unit (MU) behavior and joint torque output in people with multiple sclerosis (MS), which could serve as a basis for early MS diagnosis. As MUs represent the final common pathway of the central nervous system (CNS), we expected that any MS-related pathological CNS change would cause alterations in MU behavior and the resulting joint torque output during contraction. Therefore, we compared torque and high-density surface electromyography (HDsEMG) data between individuals with relapsing-remitting MS (RRMS) and healthy age- and strength-matched controls (HCs) during submaximal fixed-end ramp contractions of two lower limb muscles (tibialis anterior, TA; vastus lateralis, VL). Preliminary results show a higher variability in TA MU discharge rates and reduced knee extension torque steadiness in one individual with RRMS compared with one HC.

Introduction

Despite the high global burden of MS, early diagnosis remains challenging. This is due to the wide range of early MS symptoms, and their similarity to other neurological conditions [1]. Given that MS is caused by pathological changes within the CNS, changes should manifest in the final common pathway of the CNS: the MUs and their resulting neuromechanical output [2, 3]. Therefore, our goal was to obtain initial insights into potential changes in MU behavior and joint torque output, which could serve as a basis for early MS diagnosis.

Methods

Two participants have been tested so far in this ongoing study: one patient with RRMS (female, 21 yr, 1.73 m, 60 kg) and one HC (female, 21 yr, 1.65 m, 59 kg), both matched in age, sex and maximum torque output of the knee extensors (<10%). TA and VL of each participant's preferred leg were tested in a randomized order, during torque-matched, fixed-end ramp contractions on an isokinetic dynamometer (IsoMed2000, Ferstl GmbH, GER). To ensure torque matching between participants, visual torque feedback was displayed on a screen in front of them. Simultaneously, HDsEMG (MEACS, ReC Bioengineering Laboratories, ITA) with a 32-channel grid (M8X4D10) was used to record muscle activity. Torque and HDsEMG Data were collected at 2048 Hz with Spike 2.0 and Bp software, respectively, and synchronized via a 16-bit analog-digital converter (Power3 1401, CED, UK).

After a standardized warm-up, participants performed at least two maximum voluntary contractions (MVCs) until peak-to-peak torque differed <5%. The highest peak-to-peak torque was then used as a reference for three different contraction conditions. In a randomized order, participants were then asked to match their measured joint torque within ±5% until they completed three valid trials for each condition. Two conditions included a ramp up (5% MVC/s) and a hold phase at 20% and 40% MVC for 10 s, before a ramp down (5% MVC/s) to 0% MVC. The third condition started with a ramp up (20% MVC/s) to a hold phase at 70% MVC for 2 s, before a ramp down (20% MVC/s) and hold phase at 20% MVC for 10 s, and then a ramp down (20% MVC/s) to 0% MVC. Lastly, participants were asked to perform a fatiguing contraction at an intensity of 40% MVC until their torque dropped permanently below 30% MVC, despite verbal encouragement. After a 30-min break, the other muscle was tested, using the same protocol. So far, TA MU behavior at 40% MVC was decomposed using MUedit [4]. Further, torque steadiness at 20% and 40% MVC during knee extension contractions was assessed using the coefficient of variation (CoV).

Results and Discussion

For both participants, we identified 12 TA MUs. The identified MUs had similar discharge rates (median ± SD) of 15.8±1.7 Hz and 16.6±1.4 Hz for the RRMS patient and the HC, respectively. However, the CoV in discharge rate was higher for the RRMS patient (47.4±19.3%) compared with the HC (22.2±1.7%). Torque steadiness was reduced during knee extension contractions of the RRMS patient compared with the HC, with respective CoVs of 3.4% versus 2.6% at 20% MVC and 2.6% versus 1.3% at 40% MVC.

Conclusions

Our preliminary results suggest differences in neuromuscular control between one RRMS patient and one HC. As the changes in MU behavior and torque steadiness indicate impaired motor control, which might be linked with MS pathology, this neuromechanical approach might be promising for earlier MS diagnosis.

References

[1] Solomon et al. (2023). *Lancet Neurol.*, **22**: 750-768.
[2] Baloyannis (2020). *Multiple Sclerosis*; IntechOpen.
[3] Sherrington (1906). *The Integrative Action of the Nervous System*; Yale University Press.
[4] Avrillon, et al. (2024). *J. Electromyogr. Kinesiol.*, **77**: 102886.