Does muscle fiber recruitment strategy during gait change in children with Fragile X syndrome?

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Summary

This study examined the muscle recruitment strategy during gait in children with Fragile X syndrome (FXS), and investigated the presence of differences not only with respect to healthy controls but also within different FXS phenotypes. Results revealed altered muscle activation patterns in both the investigated FXS phenotypes, including higher instantaneous mean frequency and energy distribution. These findings suggest that FXS is associated with a larger recruitment of fast twitch fibers which, being less fatigue resistant, might explain the fatigability typical of these children.

Introduction

FXS is a genetic condition arising from dysfunction of the FMRP-binding protein, essential for the proper development of the nervous system [1]. Mutations in the FMR1 gene lead to two primary forms: the premutation and full mutation (FXSFull), each associated with distinct clinical characteristics. Furthermore, somatic mosaicism (FXSMos) can significantly influence the severity of the FXS phenotype [1]. Among its diverse clinical features, musculoskeletal abnormalities are particularly prominent, often necessitating detailed gait assessments. Previous research has highlighted differences in lower-limb muscle activity between children with FXS and neurotypical controls, particularly in activation timing (e.g., onset, duration) and intensity (e.g., activation envelope) [3].This study investigated the relationship between these alterations and the motor fiber recruitment strategy in children with FXS.

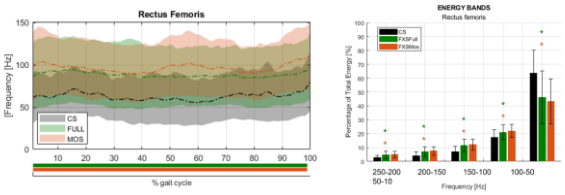
Methods

Participants included 35 children with FXSFull (BMI: 19.1 ± 6.2 kg/m²; age: 10.2 ± 3.6 years), 24 with FXSMos (BMI: 17.15 ± 7.6 kg/m²; age: 10.1 ± 2.9 years), and 14 typically developing children (healthy subjects, HS; BMI: 19 ± 3.19 kg/m²; age: 9.3 ± 2.4 years). Gait trials were recorded at a self-selected walking speed using four synchronized cameras (GoPro Hero7, 60 fps) and a surface electromyography (sEMG) system (Cometa, 2000 Hz). For each subject, three trials per limb were analyzed. Muscle activity from the Gastrocnemius Lateralis, Tibialis Anterior, Rectus Femoris, and Biceps Femoris was recorded. Key metrics such as peak activation envelope, timing within the gait cycle, onset/offset, and activity duration were extracted [3]. Additionally, continuous wavelet transform (CWT) was applied using the 'bump' mother wavelet to evaluate the percentage distribution of signal energy across nine frequency bands (50 Hz each) within a 450 Hz to 10 Hz spectrum. Instantaneous mean frequency (IMNF) distributions over time were also analyzed [4,5].

Results and Discussion

Results indicated that both FXSFull and FXSMos exhibit distinct fiber recruitment strategies compared to HS, along with higher IMNF values ($p<0.05$) (Figure 1, bottom). Overall, they demonstrated higher percentage values of total energy ($p<0.05$), with the exception of frequencies associated with slow-twitch fibers (50-10 Hz) across all analyzed muscles (Figure 1).

Figure 1. Group differences for Rectus Femoris in terms of Frequency of energy (on the top) and IMNF (on the bottom) for HS in black, FXSFull in green and FXSMos in orange



Conclusions

These findings emphasize the need for personalized interventions for children with FXS that takes into account their tendency to recruit less fatigue resistant fibers and more fast twitch fibers. Future research should further investigate the possible association of these results with mitochondrial dysfunction through muscle biopsies in adult FXS (for ethical reasons).

References

[1] Hagerman RJ, et al. (2018) Front Psychiatry ;9:564.
[2] Piatkowska WJ, et al.(2022) Appl Sci. ;12:1612.
[3] Sawacha Z, et al. (2021) Sensors (Basel) ;21(14):4746.
[4] Weiderpass HA, et al. (2013) Int J Numer Method Biomed Eng.;29(9):1000-1010.
[5] Sacco IC, et al. (2014) J Biomech.;47(10):2475-2482.

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