EMG-driven biomarkers for Fragile X Syndrome: a feasibility study using Dynamic Time Warping as a summary score

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Summary

Fragile X Syndrome (FXS) is the most common inherited cause of intellectual disability and autism spectrum disorder. Variability in clinical presentation often leads to misdiagnosis. Gait analysis offers a promising approach to differentiate individuals with FXS from healthy subjects. This study introduces an innovative method for analysing surface electromyography (sEMG) envelopes using the dynamic time warping (DTW) algorithm. DTW effectively captures differences in shape and temporal shifts within time-series data. Statistical analysis confirmed that features extracted via DTW could distinguish FXS children from healthy peers. These findings highlight the potential of DTW-based features in identifying FXS. Future work will integrate these features into machine learning models, further enhancing their diagnostic utility and supporting early, accurate identification of the syndrome.

Introduction

Fragile X Syndrome (FXS) is a genetic disorder caused by CGG triplet expansion in the *FMR1* gene [1], leading to premutation or full mutation (FXSFull). Somatic mosaicism (FXSMos) can strongly modulate the FXS phenotype. FXS is the most common inherited cause of intellectual disability and autism spectrum disorder, however it is often misdiagnosed. It represents a rare disease, and its diagnosis is carried on through genetic screenings. Growing interest in non-invasive early screenings explores the possibility to introduce gait analysis (GA) [2] as a possible preliminary screening. With this respect Dynamic Time Warping (DTW) [3], by capturing shape and temporal shifts in time-series data relative to a control group, might provide a summary score.

Methods

A cohort of 14 typically developing children (healthy subjects, HS; BMI: 19 ± 3.19 kg/m²; age: 9.3 ± 2.4 years), 35 with FXSFull (BMI: 19.1 ± 6.2 kg/m²; age: 10.2 ± 3.6 years) and 24 with FXSMos (BMI: 17.15 ± 7.6 kg/m²; age: 10.1 ± 2.9 years) was analyzed. Markerless GA was performed through four synchronized cameras (GoPro Hero7, 60 fps) and a surface electromyography (sEMG) system (Cometa, 2000 Hz, 8 channels) to record the muscle activity of Gastrocnemius Lateralis (GL), Tibialis Anterior (TA), Rectus Femoris (RF) and Biceps Femoris (BF). Six trials per subject were assessed at self-selected speed, and muscle envelopes extracted [2]. The mean value extracted from HS served as a reference, and through DTW analysis two biomarkers were defined: DTW distance (DTWdist) and energy of the optimal DTW path (DTWpath). Wilcoxon test ($p<0.05$) was applied to assess significance across groups: HS vs. FXSFull, HS vs. FXSMos, FXSFull vs. FXSMos, and HS vs. FXS.

Results and Discussion

Significant differences were found for TA, GL, and BF ($1.52E\text{-}15<p<0.014$) in all comparisons except for FXSFull vs. FXSMos. This latter group showed significant differences for DTWdist in GL and BF and DTWpath in TA ($2.69E\text{-}05<pmax<0.031$). Figure 1 presents boxplots of DTWdist and DTWpath for TA, comparing HS (blue), FXSFull (green), and FXSMos (orange), and HS vs. FXS (yellow).

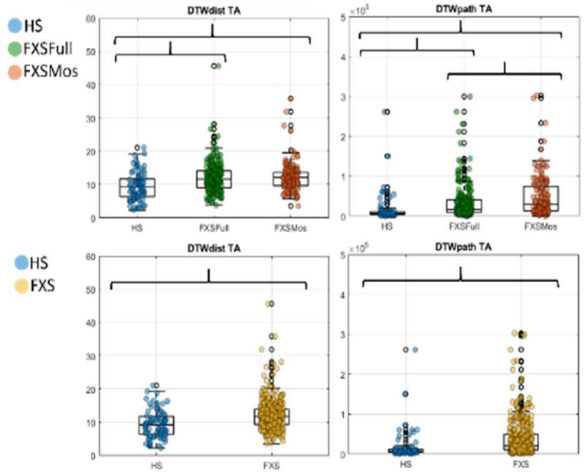

Figure 1: Boxplot with scatter plot of DTWdist (left) and DTWpath (right) for TA for the comparison between HS, FXSFull and FXSMos (top) and between HS and FXS (bottom).

Conclusions

The DTW algorithm seems promising in providing a summary score for classifying FXS subjects from HS, thus suggesting their adoption biomarker for FXS.

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References

[1] Hagerman RJ, et al. (2018) *Front Psychiatry*, **9**:564
[2] Sawacha Z, et al. (2021) *Sensors*, **21**:4746.
[3] Steinmetzer T. et al. (2018) *IWOBI*-IEEE conference,1-6