ARE KINEMATICS AND MUSCULAR FUNCTION ASSOCIATED WITH MOSAICISM TYPE IN MALES WITH FRAGILE X SYNDROME?

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Introduction

Fragile X Syndrome (FXS) is the leading form of inherited intellectual disability and autism spectrum disorder, caused the transcriptional silencing of the gene Fragile X Messenger Ribonucleoprotein 1 (FMR1), which encodes an RNA binding protein that is implicated in a multitude of crucial neurodevelopmental processes, including early embryonic motor circuits [1]. There are two main categories of FMR1 mutations, "premutation" and "full mutation", that are associated with different clinical phenotypes, and somatic mosaicism can represent a strong FXS phenotype modulator [2]. Mosaicism in FXS refers to two different FMR1 allele variations: size mosaicism (i.e. different numbers of CGG repeats between the two alleles), methylation mosaicism (i.e. full-mutation allele is fully or partially methylated) [3]. The present study explored the association between full mutation and/or mosaicism types, and musculoskeletal alterations in terms of gait analysis in a group of FXS children.

Methods

After appropriate informed consent by the parents, the gait of 36 FXS children ((FX) mean(±SD) age of 10 (±3.6) years, BMI of 19.4(±3.6) Kg/m2) and 10 controls ((CS), mean(±SD) age of 10 (±3.07) years, BMI of 20.4 (±4.5) Kg/m2) was assessed at the BiomovLab (CS) and at the Paediatric Department of the University of Padua. Within the FXS group 28 children with full mutation ((FX-FM), 3 children with methylation mosaicism (FX-MET) and 5 with size mosaicism (FX-DYM) were evaluated. Kinematics in terms of joint angles and surface electromyographic data (sEMG) were simultaneously acquired through four synchronized cameras (GoPro Hero3, 30fps) and an sEMG system (FreeEmg, BTS, 1000Hz) that collected the activity of Tibialis Anterior, Gastrocnemius Lateralis, Rectus Femoris and Biceps Femoris. At least three left and right gait trials per subject were processed. From sEMG parameters, envelope peak and its occurrence within the gait cycle were computed, sagittal plane kinematics was assessed from video recordings [2].

Results

In terms of sEMG, FX-FM and FX-DYM showed alterations on the sEMG signals in all muscles analysed with respect to CS during loading response, midstance, and midswing, FX-DYM also during push off. Even though FX-MET didn't show any statistically significant differences neither with CS nor with FX-FM, their pattern differs from all the considered populations. In terms of joint angles FX-DYM and FX-MET showed significant reductions at the level of all the analysed joints when compared both with CS and FX-FM. An examples of the results is reported in Figure 1.

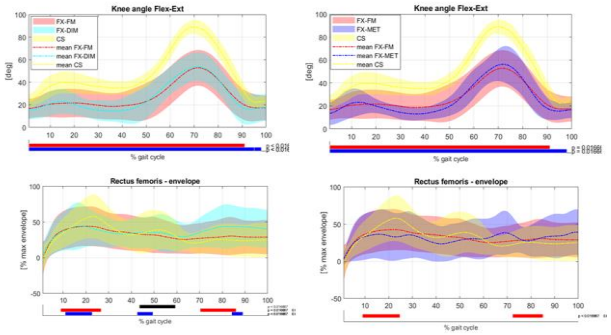

Figure 1 On the top knee flexion-extension angle, on the bottom Rectus femoris envelope shape. Mean and standard deviations are represented as bands according to the color reported in the legend.

Discussion

Results, even though preliminary, seem to suggest that FX-DYM and FX-FM presented the same differences in the pattern in terms of sEMG when compared with CS, while FX-MET displayed a pattern more similar to CS, meanwhile in terms of kinematics the data showed similar alterations in FX-MET and FX-DYM .

References

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2. Piatkowska W et al Appl. Sci. 12(3), 1612, 2022
3. Meng et al. Am J Med Genet.188A:858–866, 202