

Which Biomarker-Based Diagnostic Algorithm for Functional Motor Disorders? Investigating Motor, Exteroceptive, and Interoceptive Signatures Through Artificial Intelligence Analysis

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Objectives: Functional Motor Disorders (FMD) are common yet poorly understood neurological conditions marked by inconsistent limb weakness, tremor, dystonia, and gait disturbances [1]. This study is part of a broader research project aimed at developing a biomarker-based diagnostic algorithm for diagnosis of FMD, using behavioral, neurophysiological, and MRI biomarkers across motor, exteroceptive, and interoceptive domains (Fig.1). We present preliminary results based on the identification of gait analysis and postural stability parameters that can be used as biomarkers. The study was funded by the European Union - Next Generation EU - NRRP M6C2 - Investment 2.1 Enhancement and strengthening of biomedical research in the NHS (PNRR-MAD-2022-12376826).

Materials: Seventy-five people with FMD (pwFMD) were enrolled between the Department of Medicine, Surgery and Dentistry at the University of Salerno and the Integrated University Hospital of Verona, Verona, Italy, and matched with 75 healthy control subjects (HC). Inclusion/exclusion criteria were assessed at each center by a specialist neurologist in movement disorders.

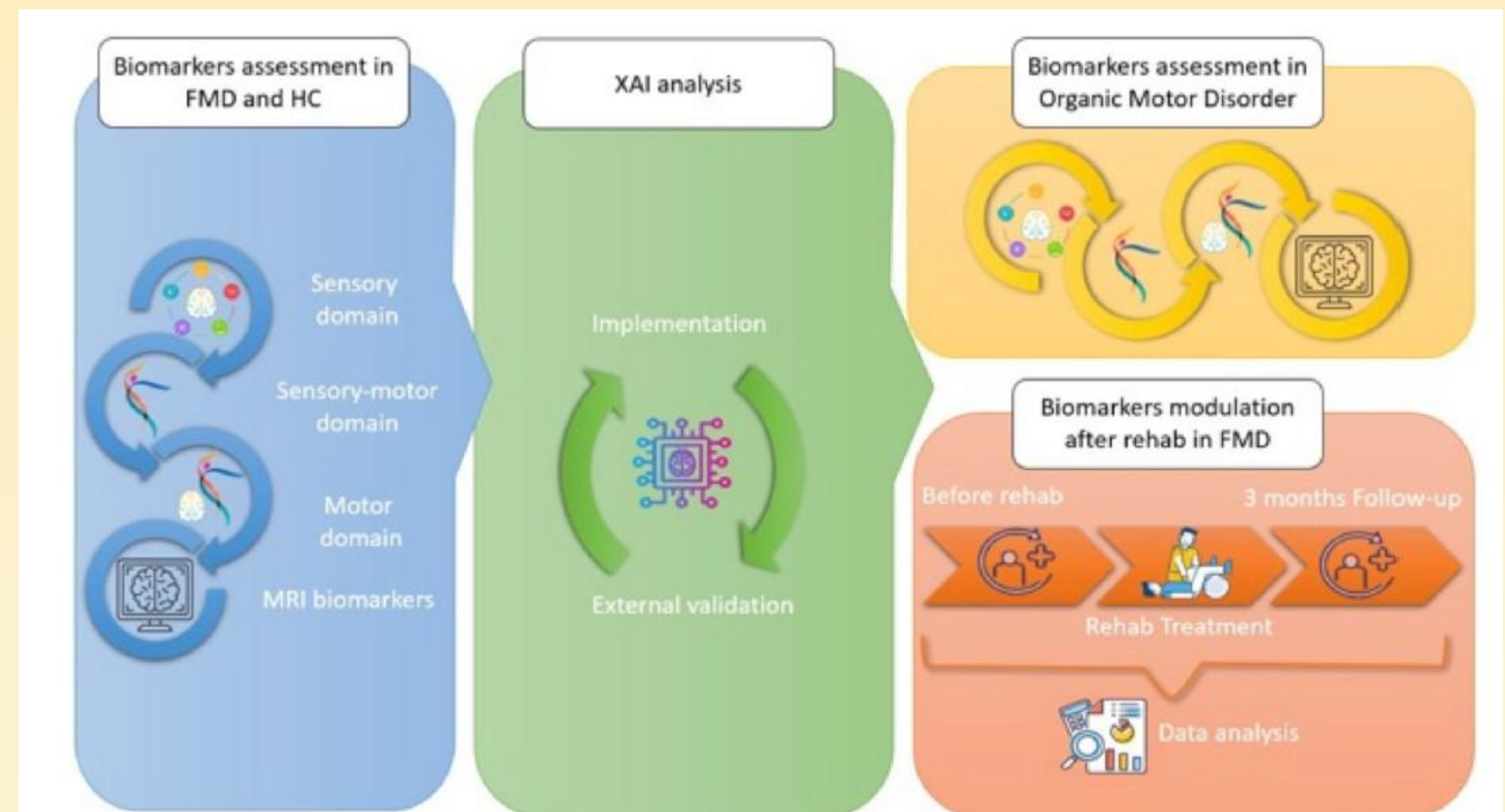
Methods: All participant underwent a motor and clinical assessment. Motor outcomes were measured using the objective-rated Simplified Functional Movement Disorders Rating Scale; fatigue, pain, anxiety, depression, alexithymia, and quality of life are assessed through the Multidimensional Fatigue Inventory Scale, Beck Anxiety Inventory, Beck Depression Inventory, Toronto Alexithymia Scale, and 12-item Short-Form Health Survey. Moreover, all participants underwent quantitative movement analysis and postural assessment under both single-task and dual-task conditions. Dual tasks included motor, cognitive, and visual components to comprehensively assess gait and postural stability under increased attentional load.

Results: PwFMD showed significantly higher levels of depression, anxiety, alexithymia, pain, and fatigue, along with a lower quality of life compared to controls (all $p < 0.05$). Repeated measures ANOVA revealed impairments in walking and balance in the FMD-group, characterized by reduced speed and stride length, and increased stride time (all $p < 0.05$). However, both groups exhibited similar patterns when performing different tasks: walking worsened during combined motor and cognitive tasks but improved during visual tasks (Table 1). Regarding postural control, the Romberg index differed significantly between pwFMD and HC during the single task ($p = 0.04$), indicating poorer postural stability in the FMD-group. In contrast, no significant difference was observed during the dual task (Table 2).

Discussion: The study highlights potential diagnostic biomarkers in both the motor and exteroceptive domains. Furthermore, the use of complex tasks are reliable tools that helps to identify FMD.

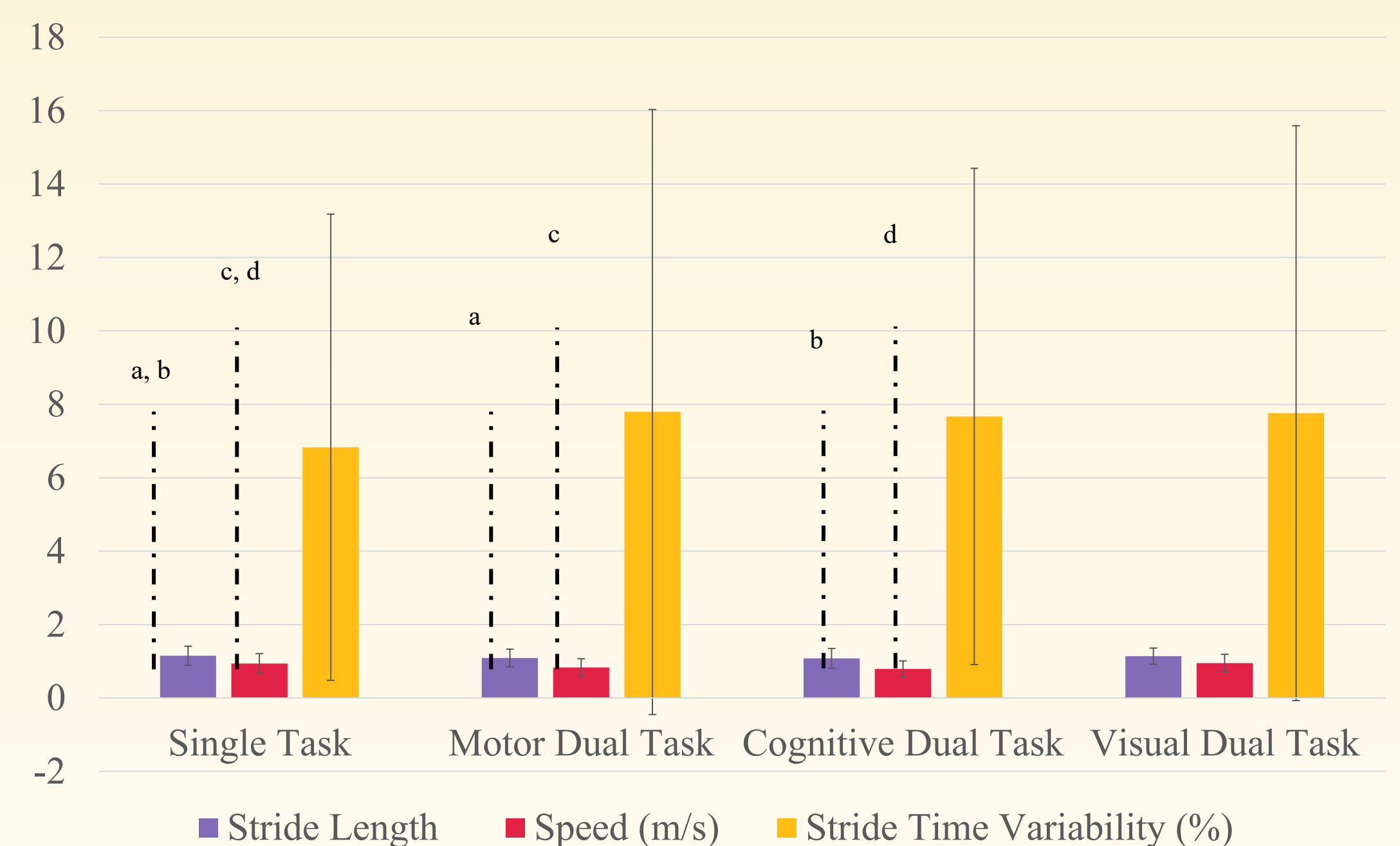
Conclusion: These findings could help refine FMD diagnosis and guide more effective treatment approaches.

Fig 1: An overview of the organization of the study program.



Abbreviation: FMD, Functional Motor Disorder; HC, Healthy Control; MRI, Magnetic Resonance Imaging; XIA, eXplainable Artificial Intelligence

Table 1: Comparison within FMD group at gait analysis conditions



Post hoc analysis ($p < 0.05$): ^a Stride Length Single Task vs Motor Duale Task; ^b Stride Length Single Task vs Cognition Dual Task; ^c Speed Single Task vs Motor Duale Task; ^d Speed Single Task vs Cognition Dual Task. **Abbreviation:** FMD, Functional Motor Disorder.

Table 2: Comparison between FMD and HC on Romberg Index

Stabilometric Index	HC MEAN ± SD	FMD MEAN ± SD	P
Romberg Single Task	257.76 ± 167.18	364.76 ± 189.23	0.004
Romberg Motor Dual Task	209.07 ± 98.26	253.17 ± 130.12	0.352
Romberg Cognitive Dual Task	178.62 ± 112.15	146.80 ± 66.65	0.408

Abbreviation: FMD, Functional Motor Disorder; HC, Healthy Control