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

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Introduction: Functional Motor Disorders (FMD) is yet poorly understood, with inconsistent limb weakness, tremors, dystonia, and gait disturbances. Delayed diagnosis and inadequate treatment lead to severe disability. Predictive coding theories suggest symptoms stem from disrupted neural circuits integrating interoception, exteroception, and motor control, distorting bodily perceptions.

Objective: To develop a biomarker-based diagnostic algorithm by modeling behavioral, neurophysiological, and MRI biomarkers.

Methods: A cross-sectional study was conducted in a preliminary sample of 50 FMD patients and 50 matched healthy controls (HC). Biomarkers were assessed in motor, exteroceptive, interoceptive domains. The diagnostic algorithm was developed by explainable artificial intelligence (XAI) methods. European Union funded the study (PNRR-MAD-2022-12376826).

Results: FMD exhibited higher levels of depression, anxiety, alexithymia, pain, fatigue, and lower quality of life (all $p<0.05$). Univariate analysis revealed a more negative cognitive dual-task effect on sway area ($p=0.003$) and gait speed ($p=0.033$) in FMD, indicating postural stability improvement but not in gait performance during a cognitive dual-task. Lower R2 blink-reflex magnitude ($p=0.036$) and increased ratio of HNCS to basal for N2/P2 laser-evoked potential amplitude in the lower limb ($p=0.029$) suggest impaired sensorimotor integration and descending pain modulation. Higher proprioceptive error ($p=0.037$) indicates an overestimating limb position in FMD. MRI findings showed increased left pallidal volume ($p=0.034$), functional connectivity within Basal Ganglia ($p=0.004$), and ventral Default Mode ($p=0.001$) networks in FMD. The diagnostic algorithm achieved 86.6% accuracy.

Conclusions: Motor and exteroceptive biomarkers might refine FMD diagnosis and therapeutic strategies, along with abnormal interactions between motor control circuits and emotional processing networks.

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