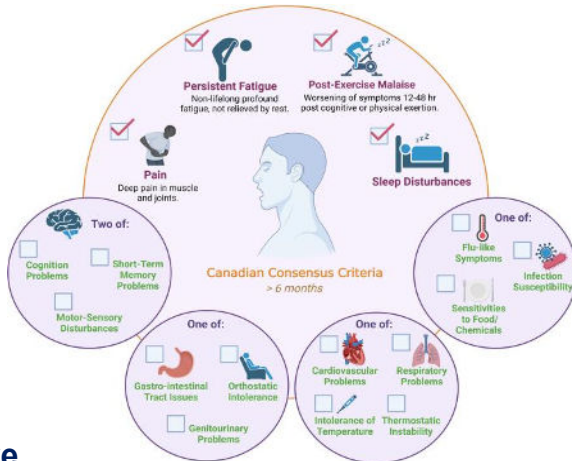




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Background

- Myalgic Encephalomyelitis (ME) is a heterogeneous and multisystem disease with uncertain etiology.
- Fibroblast Growth Factor-21 (FGF-21) is a key regulator playing a role in the homeostasis of energetic metabolism and many other biological processes.



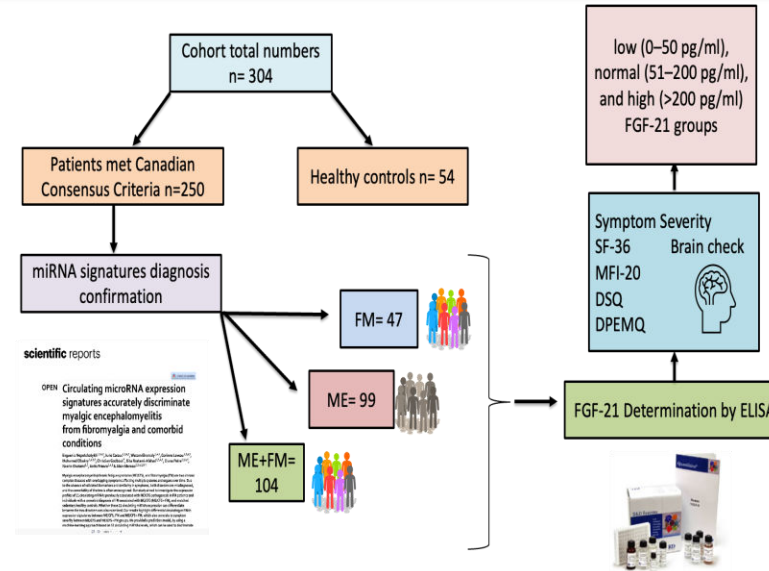
Objective

To investigate how stratification by plasma FGF-21 levels reveals clinical and cognitive heterogeneity in ME and FM.

Methods

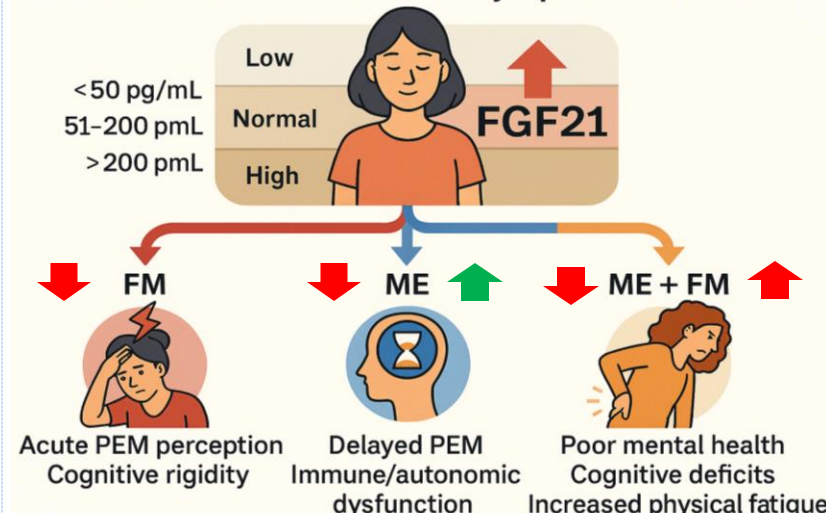
Table 1. Demographic and clinical data of the participants

	FM	ME	ME+FM	HC
n	47	99	104	54
Female/Males	38/9	83/16	94/10	25/29
Age (year)	48 ± 1.7	47 ± 1.4	48 ± 1.3	47 ± 1.5
BMI (kg/m ²)	26 ± 0.8	26 ± 0.7	26 ± 0.8	25 ± 0.6
Illness duration (years)	11 ± 1.6	12 ± 1.1	14 ± 1.3	n/a



Results

FGF21 Stratification and Symptom Profiles



Discussion

- Low FGF-21 levels were linked to worsened PEM perception in FM, increased PEM severity and immune/autonomic symptoms in ME, and poorer mental health in ME + FM.
- Conversely, high FGF-21 levels correlated with better cognition in ME but greater fatigue in ME + FM.
- These findings support the development of new treatments strategies based on precision medicine principles.

Treatment Strategies by FGF21 Stratification

Low FGF21 (<50 pg/mL)	High FGF21 (>200 pgnl)
<ul style="list-style-type: none"> Metformin Enhances FGF21 signaling via FAP inhibition FGF21 analogs Efruxifermin, Pegzofermin SGLT2 inhibitors Boost hepatic FGF21 Glucosamine Activates Akt/mtOR → boosts FGF21 	<ul style="list-style-type: none"> PPARγ agonists Restore β-Klotho expression FGF21 mimetics Direct receptor activation Senolytics Reduce inflammation restore receptor sensitivity Anti-inflammatory agents IL-1β inhibitors, NF-κB modulators

Low-carb, high-protein diet
 Reduces compensatory FGF21 overproduction ✓

Acknowledgements

