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A Novel Digital Biomarker on the Impact of Glucose Fluctuations on Nerve Conduction Velocity in Pediatric T1D

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Background / Purpose
Diabetic peripheral neuropathies (DPN) are significant complications of type 1 diabetes (T1D), marked by reduced nerve conduction velocity (NCV). Previous studies have linked glucose variability, measured by CGM standard deviation (SD), to NCV deviations from expected height-adjusted values (dNCV). However, high dNCV in patients with low SD suggest that cumulative glucose fluctuations also contribute. This study proposes a novel digital biomarker, the Glucose Fluctuation Moments Index (GFMI), that quantifies these fluctuations.
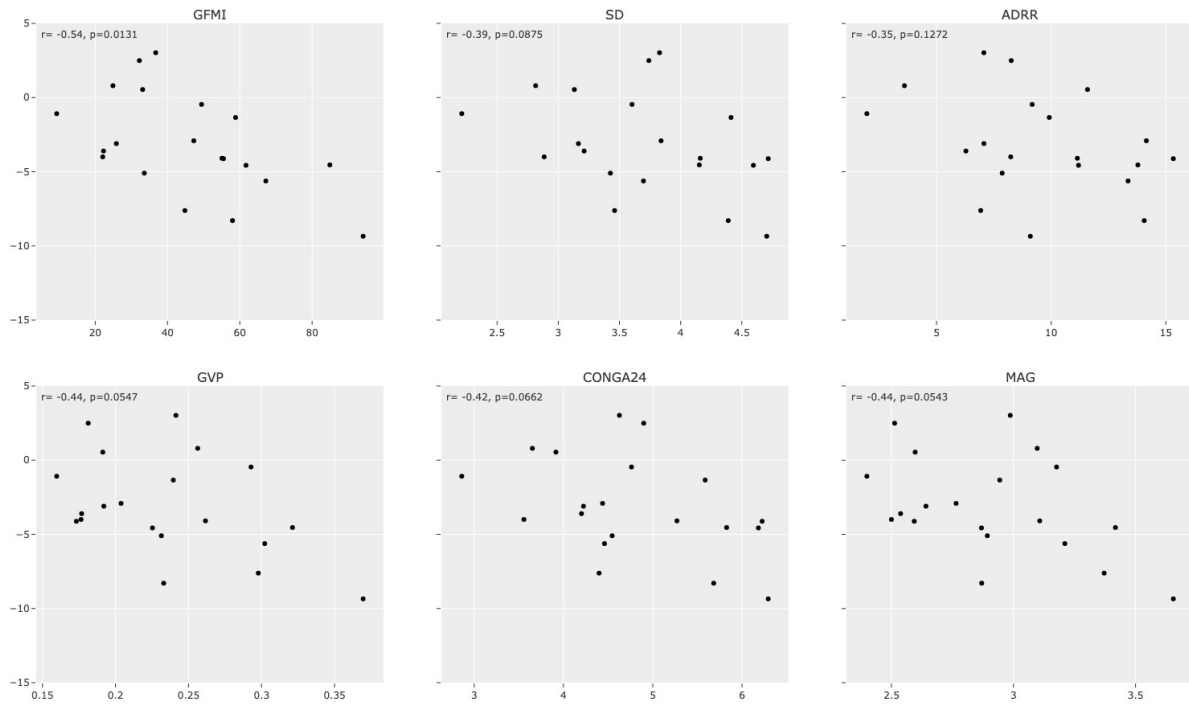
Methods
We conducted a prospective study with participants from the Children's Hospital of Eastern Switzerland, including children and young adults with T1D using CGM for at least six months (>80% data availability), excluding those with other chronic conditions, premature birth, or a family neurological disease history. We collected CGM data for 90 days prior to the annual nerve conduction study (NCS). The GFMI was developed and compared with existing digital biomarkers (SD, Average Daily Risk Range ADRR, Glycemic Variability Percentage GVP, Continuous Overall Net Glycemic Action CONGA, Mean Absolute Glucose MAG). Preprocessing included resampling CGM measurements and excluding out-of-range values.

Results
Including 17 T1D patients, GFMI exhibited a stronger negative correlation with dNCV ($r=-0.54$, $p=0.01$) in the peroneal nerve than existing (SD: $r=-0.39$, $p=0.09$; ADRR: $r=-0.35$, $p=0.13$; GVP: $r=-0.44$, $p=0.05$; CONGA24: $r=-0.42$, $p=0.07$; MAG: $r=-0.44$, $p=0.05$), evidenced by higher correlation coefficients at significant levels.

Correlation of dNCV with GFMI and five CGM-based Glucose Variability Digital Biomarkers

Conclusion

The novel GFMI provides a precise assessment of glucose fluctuations' impact on dNCV in pediatric T1D patients. This metric could enhance early detection and highlights the importance of minimizing glucose variability. Ongoing research will incorporate lifestyle factors to further refine intervention strategies aimed at slowing DPN progression.

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