Electrophysiological Brainstem Biomarker of Early Parkinsonś Disease: A Pilot Study Using EMG and Sensory Data

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Today

Background Motivation

- Parkinsonś Disease (PD) is often diagnosed too late for neuroprotective interventions.
- Early pathology occurs in the olfactory bulb and medullary autonomic regions.
- Traditional biomarkers (olfactory, SPECT imaging) lack specificity and cost-effectiveness.
- We explore an electrophysiological brainstem response (nR1) combined with sensory testing as a novel, non-invasive early biomarker.

Study Overview

Cohorts:

- 30 Healthy Controls
- 30 Early-Stage PD Patients (Hoehn Yahr Stage 2 or less)
- 30 Alzheimerś Disease (AD) Patients

Design:

- Electromyographic (EMG) measurements of orbicularis oculi muscle (OOM)
- Electrical stimulation of trigeminal nerve branches: CN V1, V2, V3
- Smell and taste tests: UPSIT, OMT, PEA
- Pre/post visual deprivation (2 hrs) in PD group
- Time-series and clinical metadata integrated for analysis

The nR1 Response

- Novel oligosynaptic brainstem response from nasotrigeminal (CN V1) stimulation.
- Present in PD patients **only**, absent in AD and healthy controls.
- Latency 10ms, recorded via surface EMG.
- Highly reproducible and robust.

Feature Engineering Signal Processing

- EMG time series were denoised and segmented.
- Extracted features include:
  - Latency, amplitude, and area under curve
  - Paired-pulse response ratio
  - Fractal dimension using Higuchi and Box Counting algorithms
- Clinical and olfactory scores were integrated with EMG-based features for classification.

Experimental Findings

- nR1 detected in 100% of PD patients (n=20); 0% in AD, healthy, MG, PSP, DLB.
- Visual deprivation suppressed nR1 amplitude by **58-88%** in PD patients.
- Flumazenil (GABA-A antagonist) induced nR1 in healthy controls.
- High test-retest reliability (ICC = 0.65-0.92).

Machine Learning Approach

- Classification task: PD vs AD vs Healthy using time-series and sensory features.
- Models: Random Forest (RF), Logistic Regression (LR), Support Vector Machine (SVM)
- Feature set includes signal-based and clinical variables.
- Results: High accuracy, outperforming olfactory and SPECT-based diagnostics.

Biological Insight: GABAergic Mechanism

- nR1 response is modulated by brain GABA levels.
- Visual deprivation $\rightarrow$ $increasedGABA \rightarrow reducednR1.Flumazenil \rightarrow GABA - Aantagonism \rightarrow restorednR1$.

- Suggests early PD disrupts GABAergic inhibition in the brainstem.

Comparison with Traditional Biomarkers

- nR1 vs Olfactory testing:
  - Higher specificity and sensitivity.
  - Discriminates PD from AD.
- nR1 vs SPECT imaging:
  - Non-invasive, inexpensive, more accurate in early stages.

Future Directions

- Scale-up to multi-site studies with 100+ participants.
- Explore deep learning architectures: CNNs for time-series, GNNs for multimodal graphs.
- Apply Transformer-based models to capture long-range dependencies in EMG and clinical sequences.
- Use nR1 as a surrogate endpoint in early-phase drug trials.
- Support from Michael J. Fox Foundation for early detection initiatives.

Conclusion

- The nR1 response is a promising early, specific marker for PD.
- Combined EMG, olfactory, and time-series features enhance diagnostic power.
- Transformer-based modeling may further advance predictive accuracy.
- AI tools can revolutionize non-invasive screening for neurodegenerative diseases.

Thank You

Questions? Collaboration ideas?

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