Further Development of Photoplethysmography-based Narcolepsy Type-1 Detection for Home Sleep Tests

Chris Fernandez, MSc*, Tom Vanasse, PhD*, Yoav Nygate, MSc*, Sam Rusk, BSc*, Matt Sprague, MSc*, Jan Wodnicki, BSc*, Fred Turkington, BSc*, Nick Glattard, MSc*, Nathaniel F. Watson, MD, MSc**

* EnsoData Research, EnsoData, Madison, WI, USA, ** Department of Neurology, University of Washington School of Medicine, Seattle, WA

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Introduction

Narcolepsy Type-1 (NT1) is a neurological disorder characterized by a "pentad" of symptoms: **severe excessive daytime sleepiness (EDS), cataplexy, sleep paralysis, hypnagogic hallucinations, and disrupted nocturnal sleep architecture** (Bassetti et al., 2019). NT1 remains significantly underdiagnosed in part to the high cost and patient burden associated with standard in-lab Polysomnography (PSG) and Multiple Sleep Latency Tests (MSLT) (Acquavella et al., 2020). Resolving this diagnostic bottleneck will become increasingly critical given likely FDA approval of novel orexin receptor agonists (Dauvilliers et al., 2023).

Preliminary research indicates that photoplethysmography (PPG)—a low-cost, non-invasive technology routinely used in Home Sleep Apnea Tests (HSATs)—can identify NT1 signatures with reasonable diagnostic accuracy (Nygate et al., 2023; Fernandez et al., 2025).

- **Prior Work:** Utilized a two-step pipeline that extracted macro-architectural features via automated sleep staging, followed by a Random Forest classifier.
- **Current Architecture:** Leverages end-to-end deep learning trained directly on raw EEG and PPG signals.
- **Advantages:** Deep learning enables the model to identify subtle, underlying physiological indicators within raw PPG waveforms.

Objective: This work evaluates the performance of deep learning models across two primary clinical dimensions:

1. **Signal Modality**: Contrasting PSG metrics (EEG) against peripheral autonomic waveforms (PPG).
2. **Recording Environment**: Comparing controlled, gold-standard In-Lab testing against real-world At-Home screening.

Materials & Methodology

- **Signal Processing:** Raw data inputs—either cortical metrics (EEG) or peripheral autonomic waveforms (raw PPG)—were provided as time-series input.
- **Architecture Design:** The core pipelines utilize deep convolutional neural networks.
- **Evaluation Framework:** Performance was contrasted across two primary dimensions: signal modality (EEG vs. PPG) and environmental setting (controlled, in-lab PSG vs. home multi-night testing).

Datasets

Simultaneous PSG & PPG (MNC Data)
The Mignot Nature Communications Dataset (Stephansen et al., 2018) contains a sub-cohort of simultaneous PSG and PPG data on both NT1 patients and controls. All MNC subjects were verified using the gold-standard diagnostic methodology of hypocretin-1 extraction via cerebrospinal fluid (CSF).

A critical characteristic of this cohort is the high proportion of **non-narcoleptic hypersomnia** patients (**n = 38**, representing 42.7% of the total sample), alongside **n = 37 confirmed NT1** patients and **n = 14 clinical controls**. Incorporating a heavy concentration of confounding hypersomnolence disorders presents a difficult clinical screening scenario, as these patients exhibit overlapping phenotypes (such as severe daytime sleepiness) with NT1.

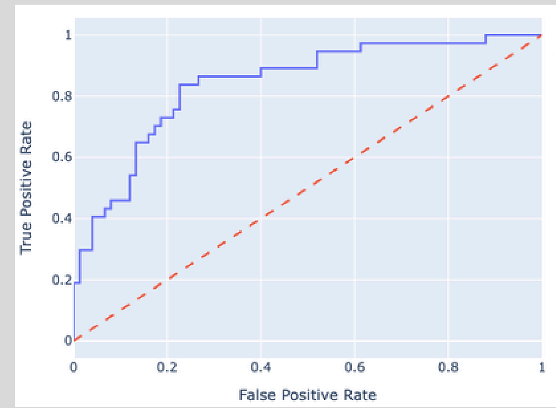
Real World PPG Sample (EnsoData)
EnsoData, Inc. deploys an FDA-approved (K231355) software-as-a-medical device (SaMD) PPG solution, EnsoHST, to monitor both sleep and disordered breathing events across multiple nights. Using International Criteria for Sleep Disorders (ICSD) guidelines, we applied narcolepsy criteria to identify labels from an internal dataset of >74k individual nights, which comprised:

- 105 NT1 Suspected Positive Patients
- 18,962 NT1 Suspected Negative Patients

Results

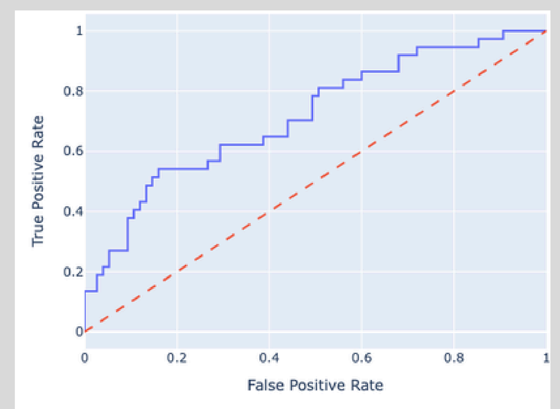
PSG Model (MNC Data, N=89) **AUC: 0.841**

Spec Target	Spec ROC	Sens ROC
0.75	0.733	0.837
0.85	0.84	0.648
0.95	0.96	0.297



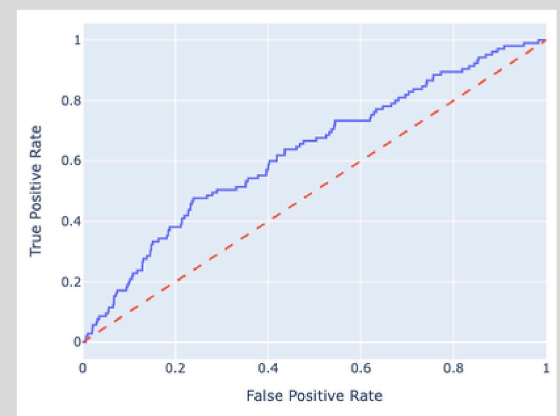
PPG Model (MNC Data, N=89) **AUC: 0.717**

Spec Target	Spec ROC	Sens ROC
Spec Target	0.733	0.545
Spec Target	0.853	0.486
Spec Target	0.946	0.216



PPG Model (EnsoHST Multi-Night, N=19k) **AUC: 0.629**

Spec Target	Spec ROC	Sens ROC
0.75	0.761	0.46
0.85	0.848	0.323
0.95	0.95	0.085



The PSG Model achieved the highest diagnostic accuracy (AUC = 0.841), leveraging direct cortical metrics (EEG). Transitioning to a single-night PPG Model demonstrated a modest performance trade-off (AUC= 0.717). In real-world conditions (EnsoHST Multi-Night), the model showed alignment with a screening fraemwork (AUC = 0.629), highlighting the challenges of artifact and environmental variability in home testing while confirming the scalability of PPG-based screening.

Conclusions & Future Work

- While transitioning from in-lab PSG to PPG results in an approximate 12% reduction in AUC, PPG-based deep learning models represent a highly scalable, low-cost screening alternative for Narcolepsy Type-1.
- The performance shift in home setting (EnsoHST multi-night: AUC 0.629) highlights real-world challenges in model deployment. This drop also reflects the transition to imperfect, surrogate clinical labels (ICSD-suspected criteria) in the large-scale dataset, compared to the CSF-verified labels of the in-lab MNC cohort.
- Given underdiagnosis of NT1 due to the high burden of PSG/MSLT testing, deploying these models via HSATs could drastically shorten the time to treatment.
- Our next steps will focus on advanced transfer learning techniques to close the performance gap and improve generalizability across diverse home-testing hardware.

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