Validation of the NeuroKit™ Platform for CNS Pharmacodynamic Assessment in Healthy Volunteers

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INTRODUCTION

- Quantifying pharmacodynamic (PD) effects of CNS-active compounds in early-phase development requires sensitive, reproducible neurophysiological and neuropsychological assessments.
- The NeuroCart test battery quantifies CNS drug effects across multiple functional domains but relies on specialized infrastructure that limits broader deployment.
- NeuroKit™ is a portable adaptation of NeuroCart that uses a virtual reality headset, a touchscreen tablet, and an accelerometer in place of fixed laboratory hardware, while preserving sensitivity to CNS drug effects.
- This second-part validation (Protocol ERG-NK-2025-001) evaluates reliability and external validity of NeuroKit™ when deployed at CPMI, a clinical research site in the US, benchmarked against contemporaneous reference data from a pharmacological validation study (poster W126) conducted at CHDR, a separate research site in the Netherlands.

OBJECTIVE

To establish the reproducibility and external validity of the NeuroKit™ platform outside its development site by demonstrating equivalence of CNS pharmacodynamic responses between CPMI and CHDR.

METHODS

- **Design:** Randomized, double-blind, placebo-controlled, three-period Williams crossover trial in healthy adults (18–45 y) at CPMI; participants matched 1:1 by age (±5 y) and sex to CHDR2442 reference participants.
- **Treatments:** 16 participants received single oral doses of lorazepam 2 mg, modafinil 200 mg, and placebo across three periods separated by 7–10 day washouts.
- **NeuroKit™ assessments:** 21-day training phase before first dose to minimize learning effects. Two baseline pre-dose assessments and post-dose assessments at 1.75, 3.75, 6.25, 10.25 and 24.25 h — timepoints harmonized with CHDR2442 and informed by the established PK trajectories of lorazepam and modafinil. Battery covers:
  - saccadic eye movements,
  - smooth pursuit,
  - adaptive tracking,
  - body sway,
  - N-back,
  - finger tapping,
  - VAS Bond & Lader,
  - VAS Bowdle.
- **Analysis:** Mixed-effects modeling (REML, Kenward-Roger DOF) on log-transformed parameters; treatment, time, site (CPMI/CHDR) and their interactions as fixed factors; participant terms as random; per-period baseline as covariate. Between-site effects reported as ratios with 90% CI. Sample size n=16, 80% power at two-sided α=0.05.

DISCLOSURES

1. Sponsored by Lotus / ERG.
2. Sponsored by CHDR.

RESULTS

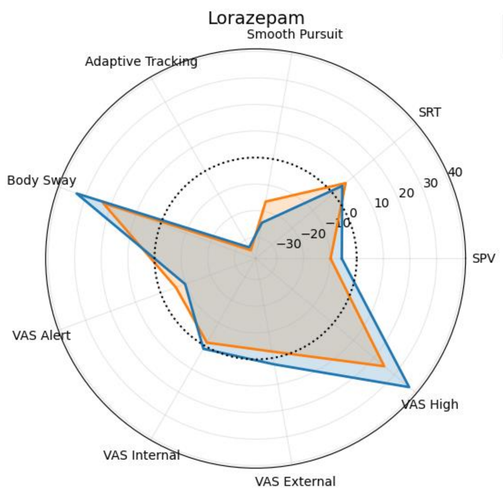

Figure 1. Drug profiling - Lorazepam. Radar plot comparing the CNS pharmacodynamic profile of lorazepam 2 mg at CPMI (orange) vs CHDR (blue) across nine NeuroKit™ endpoints. Values are placebo-corrected change. The overlap demonstrates reproducibility of the expected sedative signature off-site.

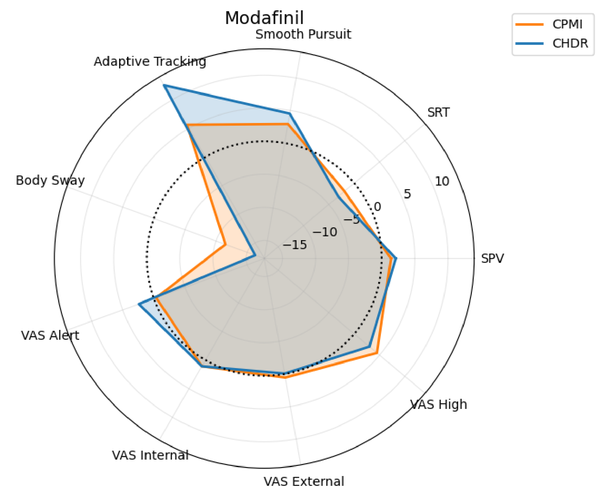

Figure 2. Drug profiling - Modafinil. Radar plot comparing the CNS PD profile of modafinil 200 mg at CPMI vs CHDR. Effects are small as expected, with a consistent trend toward improved adaptive tracking at both sites.

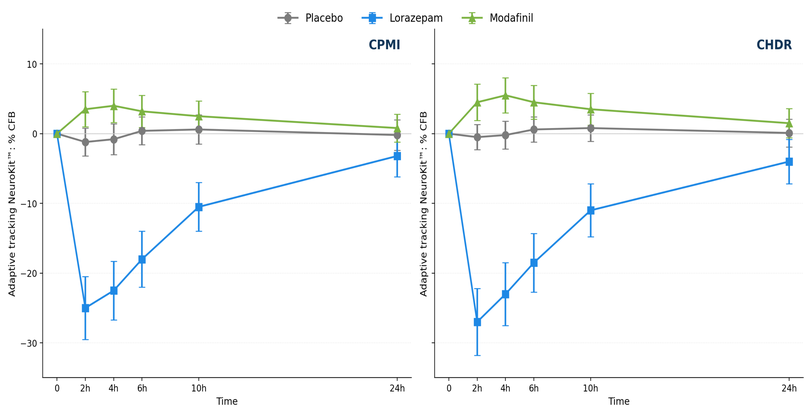

Figure 3. Adaptive Tracking time course. Placebo-corrected change from baseline (%CFB) in adaptive tracking performance over 24 h post-dose at CPMI (left) and CHDR (right). Lorazepam impairs tracking with peak effect at 2 h, recovering toward baseline by 24 h; modafinil produces a small sustained improvement. Profiles are visually superimposable across sites.

Test	Endpoint	CPMI		CHDR	
		Value	%	Value	%
Saccadic Eye Movement	Saccadic Peak Velocity (deg/sec)	11.649	2.70%	22.968	4.40%
	Saccadic Reaction Time (sec)	13.124	6.50%	14.233	6.80%
Smooth Pursuit	Smooth Pursuit (%)	12.33	6.60%	14.07	7.70%
Adaptive Tracking	Average Performance (%)	2.235	10.20%	3.023	12.60%
	Standard Deviation in Performance (%)	0.398	10.00%	0.585	13.20%
N-Back	Average Reaction Time – Zero Back (ms)	21.522	5.30%	32.131	4.70%
	Average Reaction Time – One Back (ms)	29.376	4.50%	33.456	4.70%
	Average Reaction Time – Two Back (ms)	39.503	5.30%	46.745	5.80%
	Performance – Zero Back	0.037	3.80%	0.067	7.40%
	Performance – One Back	0.041	4.30%	0.065	7.20%
	Performance – Two Back	0.086	12.10%	0.076	9.50%
Finger Tapping	Mean number of taps	7.397	11.70%	3.055	4.80%
	Standard Deviation of taps	4.448	58.60%	1.596	35.30%
VAS – Bond & Lader	Alertness (mm)	3.199	6.00%	2.768	5.70%
	Calmness (mm)	4.064	7.10%	2.547	4.90%
	Mood (mm)	2.214	4.00%	1.321	2.60%
VAS – Bowdle	External Perception (log(2+mm))	0.03	9.50%	0.015	4.90%
	Internal Perception log(2+mm))	0.023	7.50%	0.014	4.50%
	Feeling high log(2+mm))	0.096	27.50%	0.095	27.90%
Body Sway	log(Anteroposterior RMS (mm/s2))	N/A	22.90%	N/A	21.20%

Figure 4. Minimum Detectable Effects (MDE) by endpoint and site. Smallest effect detectable at each site (Value and percentage of mean).

SUMMARY

- NeuroKit™ deployed at CPMI reproduced the expected sedative profile of lorazepam, with significant decreases in saccadic peak velocity, smooth pursuit, adaptive tracking, and N-back reaction time, and increases in body sway and VAS High.
- Modafinil produced the expected smaller, mostly non-significant stimulant pattern at both sites, including a trend toward improved adaptive tracking.
- For the great majority of endpoints, the CPMI–CHDR comparison was not statistically significantly ($p > 0.05$), indicating equivalent drug-induced PD responses across sites.
- Minimum detectable effects at CPMI were comparable to those at CHDR for most endpoints, demonstrating preserved assay sensitivity off-site.

CONCLUSION

NeuroKit™ shows reproducible CNS pharmacodynamic profiles outside its development site, supporting its use as a scalable tool for PD profiling of CNS-active compounds.

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