

Background

Neural hearing loss, characterised by poor auditory neural health, is associated with poor outcomes following cochlear implantation¹. Rincell-1 is a novel allogeneic cell-based therapy designed to regenerate spiral ganglion neurons (SGNs) and restore auditory neural health. However, standardised outcome measures for evaluating neural health—and the efficacy of regenerative therapies—are currently lacking.

Electrically-evoked compound action potentials (ECAPs) can be measured along the length of the cochlear implant (CI) array and have been shown to correlate with SGN survival² and speech outcomes³. More advanced ECAP-derived measures, comparing responses using different types of stimuli, are thought to provide even better estimates of neural health.

In this study we investigated three neural health tests: Panoramic ECAPs (PECAPs), interphase gap (IPG) effects, and polarity effects⁵⁻⁸.

	PECAPs	IPG Effects	Polarity Effects
What it measures	ECAPs for every masker and probe electrode combination.	Changes in ECAP characteristics when varying the stimulus IPG (0 vs 30 us); assessed at three electrode positions (base, mid and apex).	Changes in current corresponding to comfortable loudness level when varying the stimulus polarity; assessed at three electrode positions (base, mid and apex).
How it relates to neural health	Estimates SGN synchrony and underlying neural health; can identify regions of reduced responsiveness.	Effects depend on underlying condition of SGNs; potentially reflecting health of central axons.	Effects depend on underlying condition of SGNs; potentially reflecting health of peripheral processes.
What is expected with improved neural health	Increase in the neural health estimate.	Smaller IPG effect on amplitude at maximum current and larger on ECAP AGF slope.	Smaller polarity effect.

Study objectives

1. Assess test-retest reliability of the three neural health tests
2. Determine suitability for use in the FIH trial of Rincell-1

Methods

Six experienced (>1 year) adult users of Advanced Bionics cochlear implants from a single UK centre.

Assessments:

- Neural health tests (five testing sessions on different days)
- ECAP thresholds (once per session), electrode impedances (twice per session), speech perception (once)

Experiments were run using custom MATLAB scripts and the Advanced Bionics Bionic Ear Data Collection System (BEDCS) software. Average testing duration was 47 minutes for PECAPs, 29 for IPG effects, and 47 for polarity effects.

Table 1 - Participant characteristics

ID	Gender	Age (years)	Age at implantation (years)	Duration of implantation (years)	Side of cochlear implant	Re-implanted
PT 1	female	72.6	69.4	3.0	left	No
PT 2	male	25.3	23.1	2.2	right	No
PT 3	female	31.5	29.4	2.1	left	Yes
PT 4	male	52.2	41.9	10.2	right	No
PT 5	male	57.8	48.0	9.9	right	No
PT 6	female	68.9	64.3	4.6	right	Yes

Data analysis

Neural health test variables:

- PECAPs η value
- IPG amplitude
- IPG slope
- Polarity comfort

Test-retest reliability:

- Intraclass Correlation Coefficient (ICC): across groups variance / total variance (across and within groups).
- Coefficient of Variation (CV): (SD/mean)*100 (within groups).
- Repeatability Coefficient (RC): $1.96 \cdot \sqrt{2} \cdot \text{SD}$ (within groups).

All analyses run using MATLAB 2023b, Python 3.9 and R 4.4.1.

Discussion

Including all tests in the Rincell-1 FIH trial could increase sensitivity of the test battery for capturing changes in neural health.

Limitations

- Small sample size may not be representative of the population with neural hearing loss.
- Results depend on many testing and analysis parameters.
- PECAPs and IPG effects depend on current levels used.

Next steps

- Refine testing procedures to reduce testing burden and ensure applicability in clinical trial settings.
- Assess feasibility in a pilot study of newly implanted recipients.

Results

Table 2 - Descriptive statistics - all assessments

	Count	% missing	Mean	SD	Range	Min	Max
PECAPs η	480	13.13	0.14	0.17	0.78	0.002	0.79
IPG amplitude	90	20.00 ¹	0.39	0.15	0.66	0.15	0.82
IPG slope	90	20.00 ¹	0.36	0.22	0.83	-0.04	0.78
Polarity comfort	90	8.89	2.39	1.61	5.60	-0.20	5.40
ECAP threshold	90	0.00	165.95	69.84	279.62	20.38	300.00
BKB SNR ²	6	0.00	8.92	7.05	20.00	0.20	20.20
AB noise phonemes ²	6	0.00	43.53	10.98	28.90	30.00	58.90
Impedances ³	960	5.00	5.41	2.54	12.86	2.52	15.37

Counts for session*participant*electrode (if applicable).

¹3.33% if excluding missing due to no clear ECAPs. ²Measured once per participant. ³Measured twice per session.

Table 3 - Test-retest reliability and minimal clinically important difference (MCD)

Variable	Within participant/electrode groups				Across participant/electrode groups			ICC	CV	RC	MCD
	Mean	Variance	SD	Max Range	Variance	SD	Range				
PECAPs η	0.144	0.003	0.055	0.461	0.036	0.190	0.753	0.922	38.338	0.153	+0.2
IPG amplitude	0.391	0.003	0.055	0.305	0.021	0.145	0.663	0.874	14.08	0.152	-0.2
IPG slope	0.365	0.006	0.077	0.315	0.041	0.203	0.826	0.873	21.204	0.214	+0.3 uV/uA
Polarity comfort	2.420	0.2	0.447	2.4	2.377	1.542	5.6	0.922	18.47	1.238	-2dB

For PECAPs, including only data from e3, e8, and e13, corresponding to electrodes tested for IPG and polarity effects. For polarity effects for PT 6, including data from e12 (measured twice) and not e13 (measured once).

- All three tests had high test-retest reliability; despite some higher variability within specific participant and electrode groups.
- An expected MCD was defined for each assessed variable.

Figure 1 - PECAPs η

Inter-(coloured lines) and intra-session (shaded areas) variability. Results from all assessed electrodes.

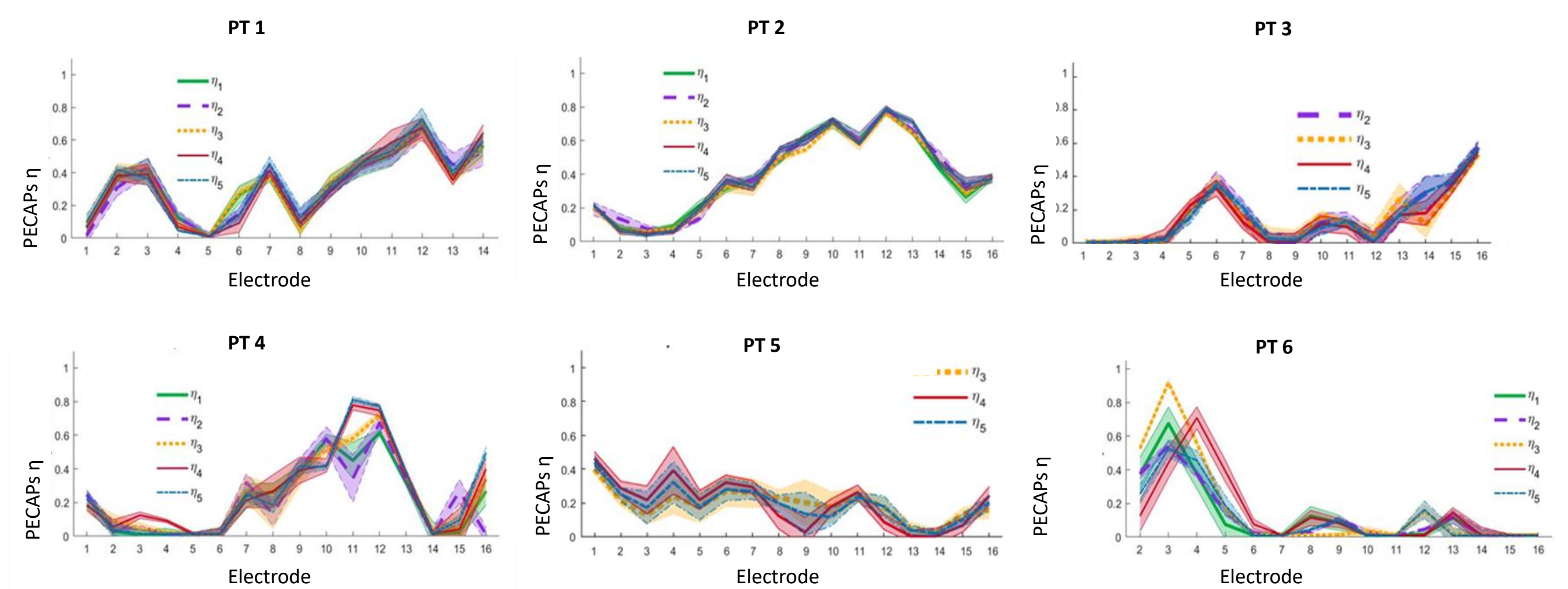
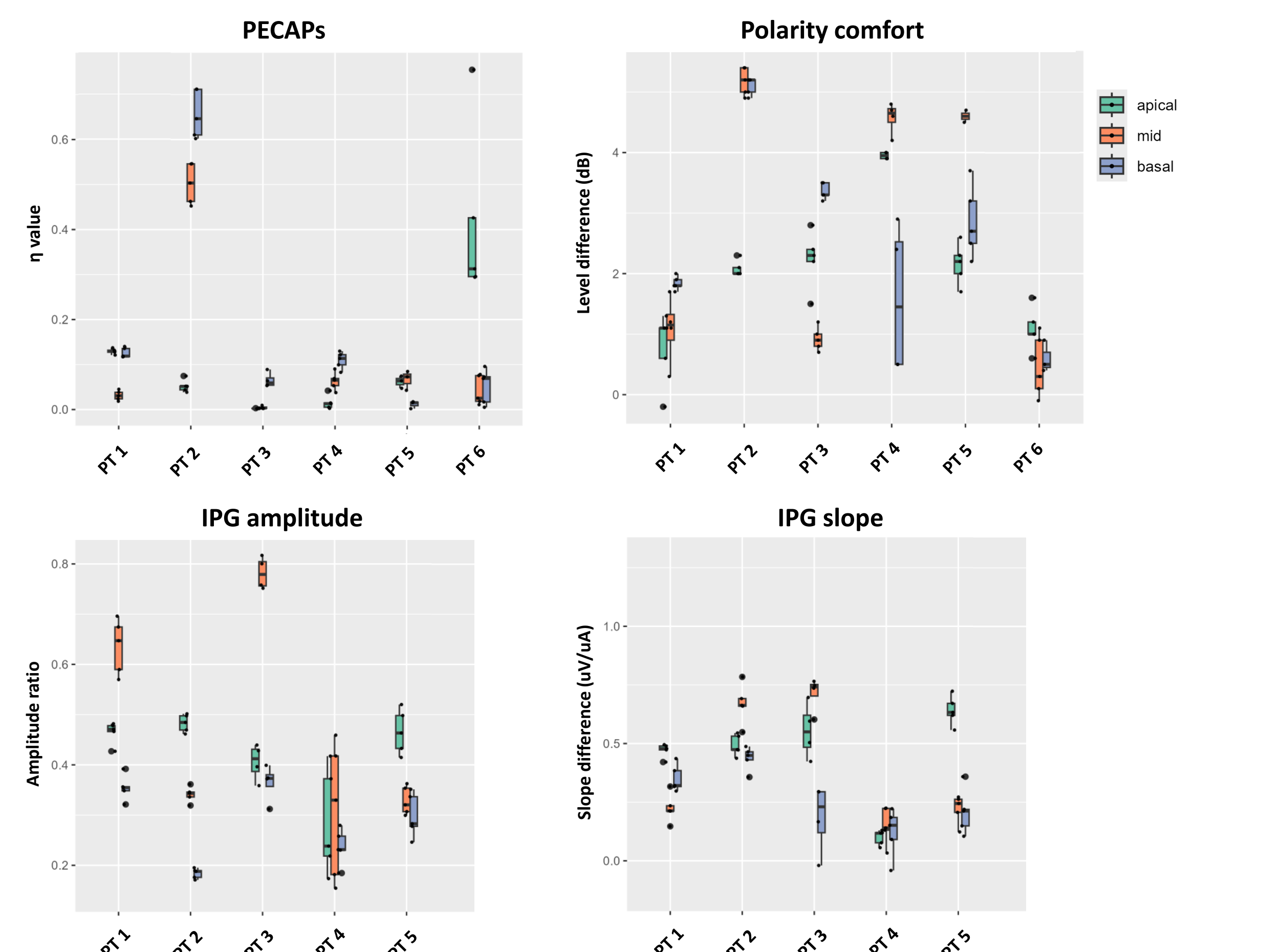


Figure 2 - Repeated measurements by participant and electrode group



The tests did not always yield consistent estimates of neural function, potentially indicating that each is **sensitive to different aspects of neural health.**

References

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