Clinical Utility of the P300 Wave as a Biomarker for Methylphenidate Response in Adult Patients with ADHD: first phase report.

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Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) in adults is marked by executive dysfunction and underlying neurophysiological alterations [1]. The P300 component—an event-related potential (ERP) associated with attentional allocation and working memory updating [2,3]—has demonstrated biomarker potential in pediatric populations[4,5]. However, its clinical applicability in adults remains underexplored. This study investigates the feasibility and potential utility of P300 assessment in adults using a three-stimulus visual ERP paradigm.

Objectives

To evaluate the characteristics of the P300 wave in adults with ADHD prior to treatment, to estimate its predictive value for methylphenidate response, and to assess the technical feasibility of obtaining it in a clinical context.

Methods

A three-stimulus visual oddball paradigm (Figure 1, Table 1) was administered to 40 consecutive adults referred for evaluation of suspected ADHD. ERP recordings were obtained, re-referenced to average montage, with primary analysis focused on the Fz-Pz electrodes, and processed using Python 3.11. Principal metrics included mean amplitude, peak latency, and area under the curve (AUC) within the 280–450 ms window. Manual artifact rejection and systematic visual inspection of waveform morphology were performed to ensure data integrity [6].

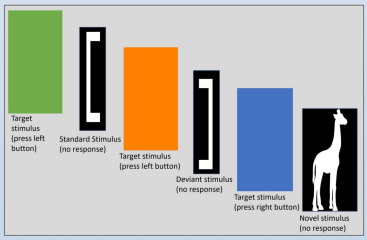


Figure 1. Diagram of 3-Stimulus Visual Oddball Paradigm including deviant stimulus.

Stimulus Type	Description	Percentage (%)	Response Required
Standard	Frequent non-target stimulus used to establish a baseline expectation. **Repetitive figure** (e.g., blue circle, left button press).	80%	Yes
Target	Infrequent stimulus requiring a motor response. **Target figure** (e.g., red star, right button press).	10%	Yes
Novel	Infrequent and novel stimulus, not requiring a response, designed to elicit an orienting response. **Novel figure** (e.g., elephant).	5%	No
Deviant	Visually distinct variant of the standard stimulus, used to assess perceptual discrimination. **Altered figure** (e.g., mirrored symbol).	5%	No

Table 1. Stimulus Distribution – Visual Three-Stimulus Oddball Paradigm including deviant stimulus.

Results

87.5% of patients exhibited a poorly developed P300 waveform (Figure 2). The mean age was 38.2 years (16–68), with 47.5% female (Table 2). A low trial rejection rate (<15%) was achieved. A concordance rate of 96.5% (Table 5) was observed between P300 waveform development and available neuropsychological evaluations.

Individual illustrative examples of two poorly developed cases are depicted (Figure 3 and 4), with amplitude distribution comparison (Figure 5 and 6) and metrics (Table 4).

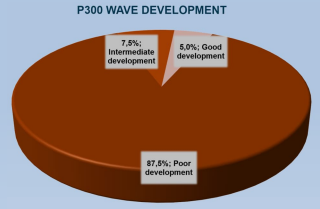


Figure 2. Baseline P300 waveform development in untreated patients with ADHD.

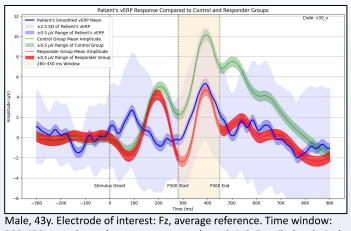
Demographic Characteristics (n=40)	
Variable	**Value**
Mean age (range), years	38.1 (16–68)
Male sex, n (%)	21 (52.5%)
Education level	
Secondary education, n (%)	9 (22.5%)
Undergraduate degree, n (%)	25 (62.5%)
Postgraduate degree, n (%)	6 (15%)

Table 2. Demographic characteristics.

Neuropsychological Assessment (n = 29)	
Neuropsychological assessment outcome vs. P300 waveform development*	**n(%)**
Concordant	28 (96,5 %)
Discordant	1 (3,5 %)
Total	29 (100 %)

* Based on the conclusion of the formal neuropsychological assessment. Poor P300 waveform development was considered a criterion for probable good responder status.

Table 3. Neuropsychological assessment and P300 development concordance.



Male, 43y. Electrode of interest: Fz, average reference. Time window: 280-450ms. Independent components selected: 1-6. Detailed technical steps applied available in Supplementary Material (Table 2).

Figure 3. Amplitude vs Time vERP P300 plot for illustrative patient V30.

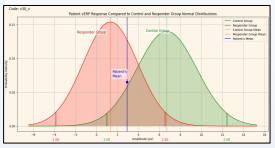
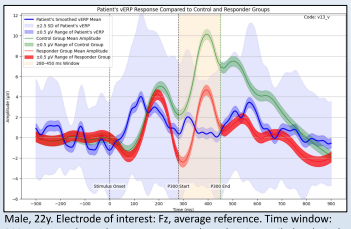


Figure 5. Amplitude Distribution Comparison for patient V30.



Male, 22y. Electrode of interest: Fz, average reference. Time window: 280-450ms. Independent components selected: 1-6. Detailed technical steps applied available in Supplementary Material (Table 2).

Figure 4. Amplitude vs Time vERP P300 plot for illustrative patient V13.

Figure 6. Amplitude Distribution Comparison for patient V13.

Condition (280–450 ms window)	Mean Amplitude (µV)	Peak Latency (ms) from 0 ms	Area Under the Curve (AUC) (uV-ms)	n
Pretreatment Patient V30	2.914	396.10	504.40	42
Pretreatment Patient V13	0.777	321.46	135.66	42

Technical note: Electrode of interest: Fz, average reference. Time window: 280–450 ms. Selected independent components: 1–6. Detailed technical procedures applied are available in the Supplementary Material (Table 2).

Table 4. Extracted vERP Parameters for Illustrative Patients (280–450 ms window).

Conclusion

Visual ERP-based recording of the P300 wave is technically feasible in adults with ADHD. A poorly developed baseline P300 may represent a promising predictor of clinical response to methylphenidate. Limitations of this initial phase include a small internal normative sample and incomplete neuropsychological data. Clinical validation will require intraindividual comparisons and ROC curve analysis in the ongoing second phase.

References

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Conflict of interest Disclosure - Data Management and Availability - Acknowledgments

The authors declare no conflicts of interest. The data were anonymized and are part of an ongoing study; they are available upon reasonable request. We thank the patients, assistants, and institutions.

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