Neurocrit Care
https://doi.org/10.1007/s12028-024-02023-0

NEUROCRITICAL CARE SOCIETY

LETTERS TO THE EDITOR

Letter to the Editor for: "Covert Consciousness in Acute Brain Injury Revealed by Automated Pupillometry and Cognitive Paradigms"

Charikleia S. Vrettou[1*] and Iannis K. Kominis[2]

To the Editor,

In their study, Othman et al. [1] explore the potential of using automated pupillometry alongside various passive and active cognitive paradigms to discern residual consciousness among intensive care unit patients with acute brain injury and disorders of consciousness. A quantitative pupillometry protocol is employed, incorporating responses to active cognitive paradigms. The authors show that these responses may detect covert consciousness and perform best in distinguishing between patients with clinical signs of residual consciousness (minimally conscious state or better) and those without (unresponsive wakefulness or worse) [1]. The authors have devised a version of a command-following test to identify covert command-following, as indicated by brain activity. This approach takes into account pupillary reaction when patients and controls are directed to engage in a cognitive task rather than solely relying on overt motor responses [2]. The authors acknowledge the inherent challenge of defining consciousness. To evaluate consciousness in their patients, they rely on assessments using the Glasgow Coma Scale and the Full Outline of Unresponsiveness score, which also have their limitations [3].

The pupil size measurement to explore cognitive processes, also known as cognitive pupillometry, lacks a universally agreed-on experimental methodology [4]. As a result, the study is subject to various methodological and technical equipment-related limitations, which have also been documented in the field of cognitive neuroscience. When considering study populations, it is probable that patients with acute brain injuries and focal lesions impacting pupillary size, such as those in the thalamus, the locus coeruleus, or the caudate, may exhibit different response patterns compared to patients with global lesions, such as postanoxic encephalopathy (notably, most positive results in the study were from patients with anoxic brain injury post cardiac arrest) [1]. The selection of pupillometry variables included in studies (such as pupillary size, speed of constriction or dilatation, and amplitude of elicited responses) should ideally be decided on physiological data from previous studies in patients with disorders of consciousness and normal controls. Maintaining consistent environmental conditions, including ambient light, which primarily determines pupil size, and controlling tactile and auditory stimuli between and during examinations is challenging but crucial to ensure that variations in the participant's cognitive state are accurately captured. Ideally, eye position should remain constant or be monitored, as eye movements can influence pupil size in various ways, such as introducing pupil-fore-shortening error, causing pupil constriction during movement, or triggering the near vision reflex. Although consensus suggests the need for prolonged time intervals for baseline and poststimulus pupil size monitoring, specific appropriate durations have yet to be

*Correspondence: vrettou@hotmail.com
[1] First Department of Critical Care Medicine, Evangelismos Hospital, Medical School, National & Kapodistrian University of Athens, 10676 Athens, Greece
Full list of author information is available at the end of the article

This article is related to the original article available at https://link.springer.com/article/10.1007/s12028-024-01983-7. The author's response is available at https://link.springer.com/article/10.1007/s12028-024-02024-z.

Springer

defined [4]. The promising findings shown by Othman et al. underline the need for standardized protocols in the application of pupillometry to detect covert consciousness in critical illness.

Portable automated pupillometers, intended for measuring the pupillary light response in intensive care unit settings, play an increasingly vital role in clinical examinations and neuroprognostication [5]. However, these devices monitor the direct pupillary response, lacking the ability to capture the congruent one. Additionally, they often come with preset and fixed observation times, and their effectiveness can be compromised by user technique and ambient light interference, as most lack protective covers to establish scotopic or near-scotopic conditions for each measurement. Even the NPi 3000, which has been designed as a research tool and was used in this study, is subject to many of these limitations. Nevertheless, advancements in technology may lead to the development of more precise and versatile instruments [6]. Coupled with ongoing refinement of protocols, pupillometry holds promise as a noninvasive clinical and research technique.

Author details
[1] First Department of Critical Care Medicine, Evangelismos Hospital, Medical School, National & Kapodistrian University of Athens, 10676 Athens, Greece.
[2] Department of Physics, University of Crete, 70013 Heraklion, Greece.

Author contributions
Drs Vrettou and Kominis contributed equally to the preparation of the manuscript.

Source of Support
N/A.

Conflicts of Interest
The authors report no competing interests.

Publisher's Note

Received: 2 May 2024 Accepted: 23 May 2024
Published online: 11 June 2024

References

1. Othman MH, Olsen MH, Hansen KIT, Amiri M, Jensen HR, Nyholm B, et al. Covert consciousness in acute brain injury revealed by automated pupillometry and cognitive paradigms. Neurocrit Care. 2024. https://doi.org/10.1007/s12028-024-01983-7.
2. Bayne T, Seth AK, Massimini M, Shepherd J, Cleeremans A, Fleming SM, et al. Tests for consciousness in humans and beyond. Trends Cogn Sci. 2024;28(5):454–66.
3. Wijdicks EFM, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. Ann Neurol. 2005;58(4):585–93.
4. Mathôt S, Vilotijević A. Methods in cognitive pupillometry: design, preprocessing, and statistical analysis. Behav Res Methods. 2023;55(6):3055–77.
5. Oddo M, Taccone FS, Petrosino M, Badenes R, Blandino-Ortiz A, Bouzat P, et al. ORANGE study investigators. The Neurological Pupil Index for outcome prognostication in people with acute brain injury (ORANGE): a prospective, observational, multicentre cohort study. Lancet Neurol. 2023;22(10):925–33.
6. Margaritakis A, Anyfantaki G, Mouloudakis K, Gratsea A, Kominis IK. Spatially selective and quantum-statistics-limited light stimulus for retina biometrics and pupillometry. Appl Phys B. 2020;126:99.