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Evaluating a Pupillometry App Considering Sedation's Impact: A Step Unexplored

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Dear Editor,

I have read the recent paper authored by Maxin et al [1] with great interest. The paper explores the use of a smartphone pupillometer to differentiate between healthy volunteers and patients with severe traumatic brain injury (TBI) based on pupillary variables.

However, the interpretation of the findings warrants careful consideration and could be misleading. Beyond the pupillary responses, a crucial confounding factor, namely sedation, distinguishes patients with TBI from healthy subjects.

Patients with severe TBI admitted to the intensive care unit receive sedation, a confounder absent in healthy, awake individuals. While the authors do acknowledge this limitation in their discussion, a more comprehensive analysis of the impact of sedation is imperative.

The literature demonstrates that sedation exerts multifaceted effects on pupillary variables, a point elucidated by Rollins[2] that observed that healthy volunteers receiving remifentanil experienced swift declines in pupil constriction and diameter, directly corresponding to the sedative's effects. Although the authors indicate that the pupillary light reflex (PLR) remains quantifiable despite analgesic administration, the diminished PLR variables demonstrates the effect of sedation. The broader body of research also underscores the influence of sedatives on PLR responses. This influence is well described by McKay and Larson[3], illustrating the severe impact on pupil size and constriction velocity.

Even the study's authors acknowledge the significance of sedation's effect on PLR. They note that sedative and pain medications commonly used in the patient population have been investigated for their influence on parameters such as maximum diameter and constriction velocity, which tend to decrease under the influence of continuous sedation and analgesia.

Evidently, medication-induced alterations stand as a pivotal confounding variable in pupillary assessments between the two subject groups.

It becomes apparent that the paper ultimately highlights this aspect. Relying solely on basic pupillary variables (size, constriction, latency, and velocities) without duly acknowledging the interdependence of these variables, and without considering the intricate biomechanics of the pupil under varying sedation conditions, all aspects that are, on the other

hand, implicitly reflected in the Neurological Pupil index (NPi), raises the risk of yielding an unreliable evaluation of intracranial functionality, neurological deterioration, or overall neurological outcomes. Notably, the NPi is minimally influenced by sedation than the other directly measured pupillometric variables, and it has therefore been more often reported in critical care studies.[4, 5]

A prospective, observational, multicenter cohort study on more than 500 patients demonstrated that NPi has a significant prognostic value for neurological outcome and mortality after acute brain injury, not influenced by sedation, and its assessment could describe the dynamics of outcome prediction at the bedside. [6]

In conclusion, I would like to highlight the importance of conducting a more comprehensive investigation into the impact of sedation on pupillary responses. Such an expanded exploration could contribute to strengthening the study's credibility and increasing its potential relevance in real-world clinical settings.

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