

Published Medication Findings with NPi® Pupillometry Figure 4

| Medication(s) | Medication Finding with NPi | Clinical Study |
|---|---|--|
| amphetamines, benzodiazepines, cocaine metabolites, ethanol, methadone, opiates (including oxycodone and fentanyl), phencyclidine, and tetrahydrocannabinol (THC) | ...NPi remains unaffected by clinical intoxication and can potentially be used for ED patient evaluation without risk of confounding by key intoxicants of abuse, such as opioids... | **Jolkovsky et al: Impact of acute intoxication on quantitative pupillometry assessment in the emergency department (JACEP Open, September 2022) |
| midazolam, remifentanyl, dexmedetomidine, propofol | ...NPi values were not significantly influenced by sedative drugs, consistent with previous studies... | Kim et al: Neurological Pupil Index as an Indicator of Neurologic Worsening in Large Hemispheric Strokes (Neurocritical Care, Feb 24, 2020) |
| midazolam, propofol, fentanyl | ...No significant correlation was found between NPi values and the average daily cumulative dose of sedatives... | Miroz et al: Neurological Pupil index for Early Prognostication After Venous Arterial Extracorporeal Membrane Oxygenation (CHEST, Feb 7, 2020) |
| sedatives, analgesics | ...In this setting, since it is not altered by sedatives/analgesics, NPi may confer a significant advantage over sPLR and provide accurate prognostic information, particularly in those patients with sedation or delayed awakening... | Oddo et al: Quantitative versus standard pupillary light reflex for early prognostication in comatose cardiac arrest patients: an international prospective multicenter double blinded study (Intensive Care Med, Nov 26, 2018) |
| neuromuscular blocking agent (NMBA) | ...PLR is generated by smooth muscle and is unaffected by neuromuscular blocking drugs... | Larson et al: Portable Infrared Pupillometry: A Review (Anesthesia-Analgesia, June 2015) |
| remifentanyl | ...Because our cases were titrated into the range of dangerous opioid toxicity and we observed no change in NPi, we conclude NPi changes cannot be attributed to opioid therapy... | **McKay et al: Detection of opioid effect with pupillometry (Autonomic Neuroscience: Basic & Clinical, Aug 2021) |
| epinephrine, atropine | ...Epinephrine and atropine do not abolish the PLR in patients who achieve ROSC after in-hospital cardiac arrest. Lack of pupillary response in the post-arrest patient should not be attributed to these drugs... | Achamalla et al: Pupillary Light Reflex is Not Abolished by Epinephrine and Atropine Given During Advanced Cardiac Life Support in Patients Who Achieve Return of Spontaneous Circulation (J of Intensive Care Medicine, April 2021) |

NPi has been validated in over 120 peer-reviewed clinical studies and scientific abstracts as the most important pupillary measurement parameter for assisting in detecting cerebral insult, guiding treatment, and informing prognosis.



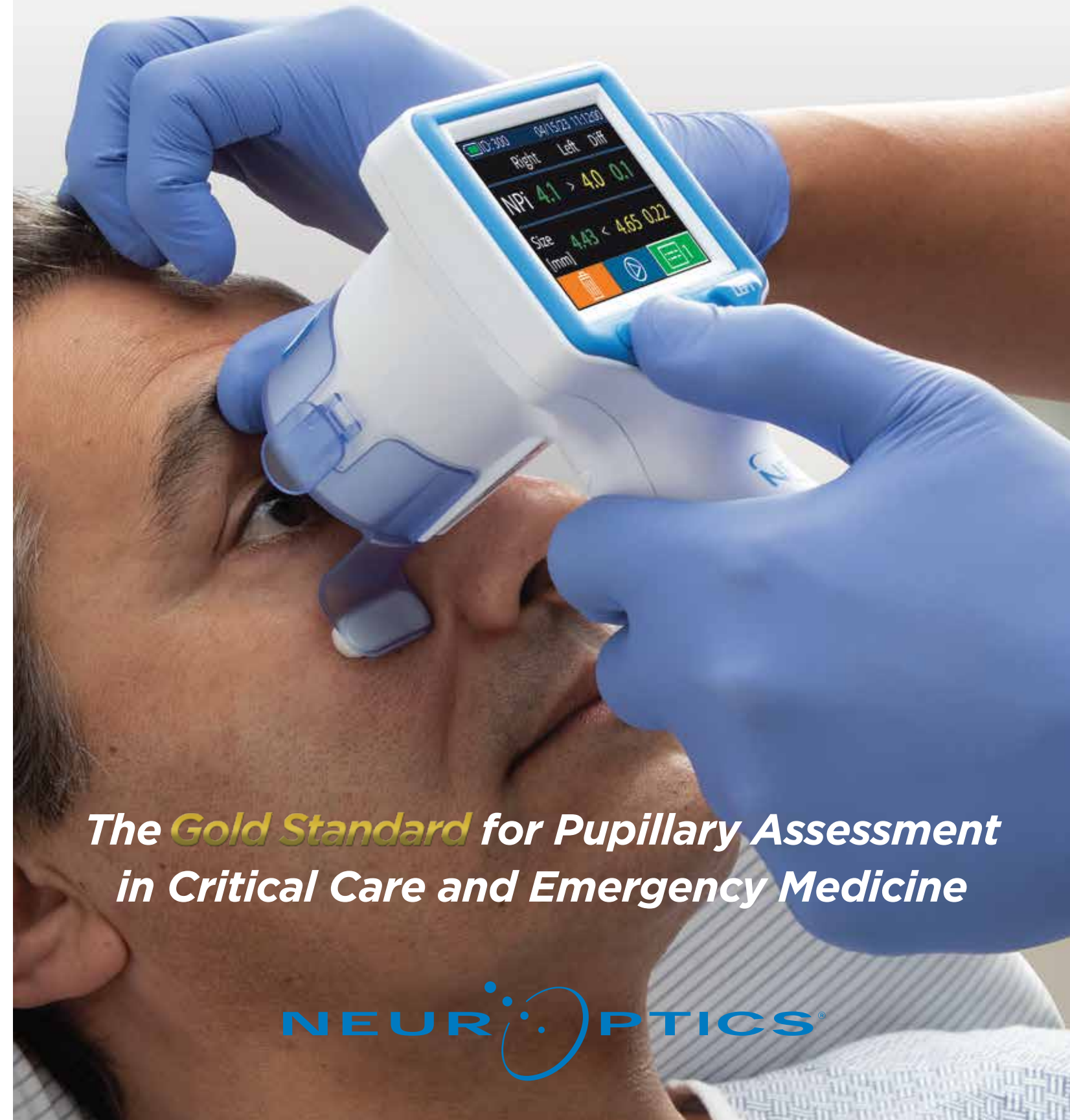
To access all NPi Pupillometry clinical publications and scientific abstracts, scan the QR code to the left or visit: <https://neuroptics.com/clinical-publications-critical-care/>



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NPi®

The Neurological Pupil index™



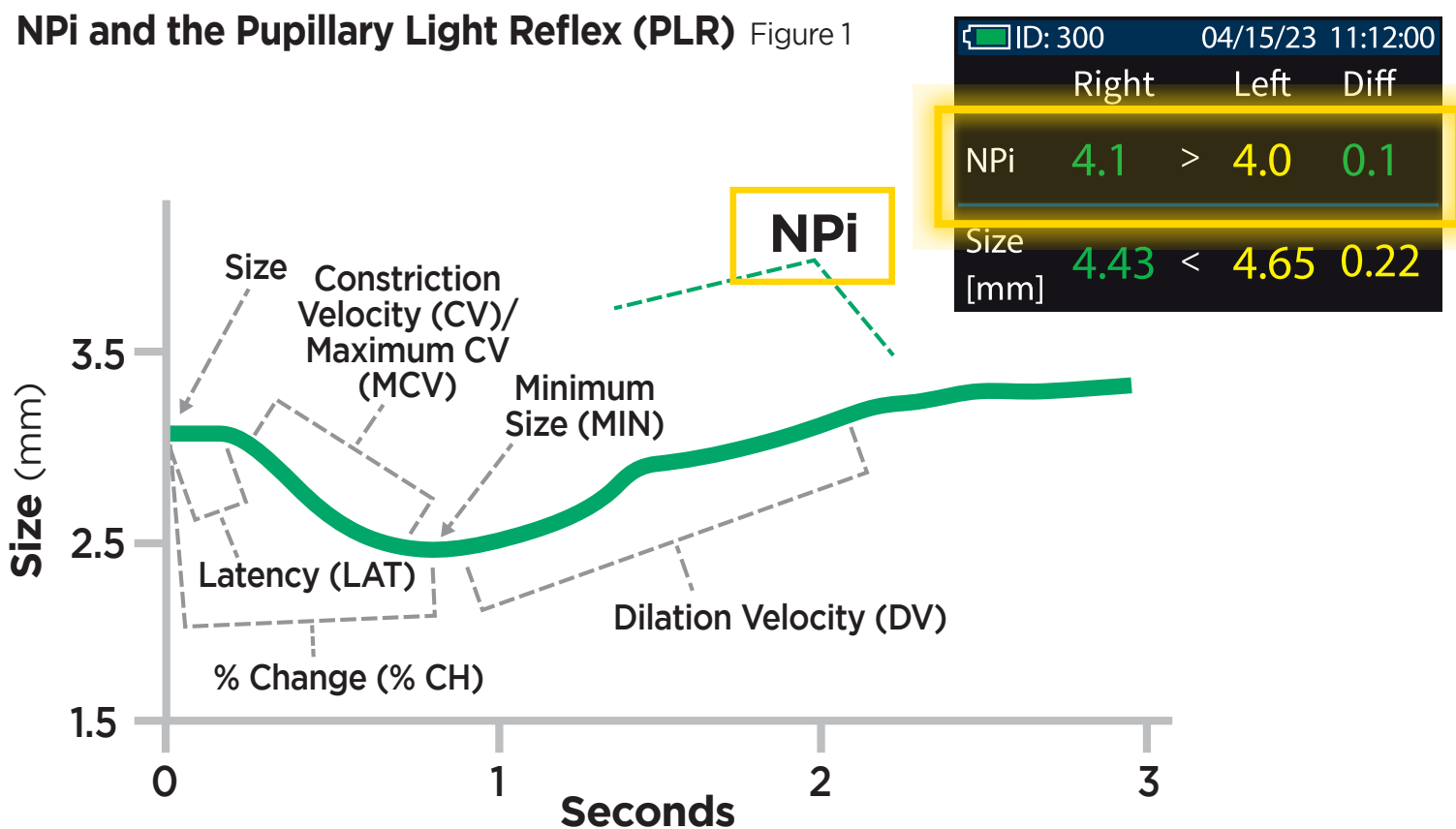
The Gold Standard for Pupillary Assessment in Critical Care and Emergency Medicine



NPi Measures the Entire Pupillary Light Reflex (PLR)

- The Neurological Pupil index™, NPi®, was developed as a quantitative measure of the entire PLR, because any one parameter alone is insufficient.
- NPi incorporates all 7 components of the PLR** using analysis of the waveform measured by the NPi Pupillometer (Figure 1).

NPi and the Pupillary Light Reflex (PLR) Figure 1

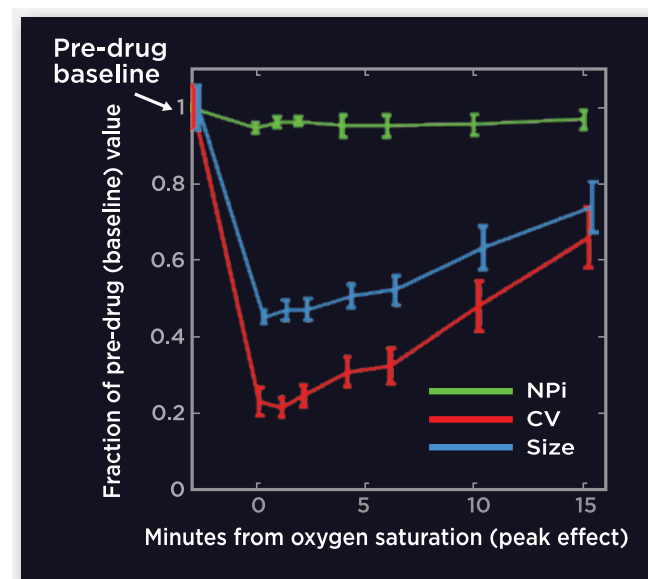


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NPi is the Only Accurate Measurement of Pupil Reactivity in the Presence of Many ICU Medications

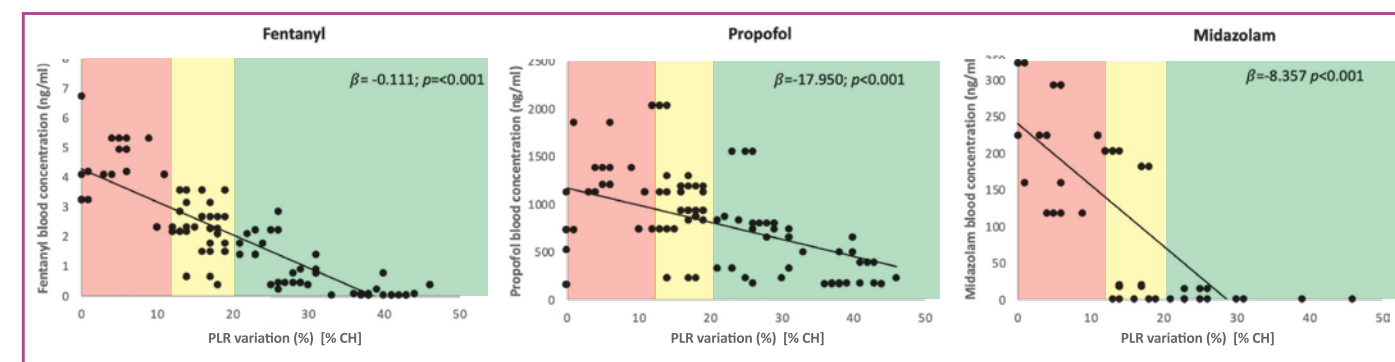
- NPi® is the ONLY pupillary measurement parameter that remains unaffected by many ICU medications and intoxicants**—including opioids (Figure 2), neuromuscular blocking agents (NMBA's), and sedatives—as demonstrated by numerous peer-reviewed clinical studies (see back page, Figure 4).
- Constriction velocity (CV), % change of pupil size (% CH), and **all other singular measurement parameters are subject to significant influence by common medications** and may lead to inaccurate conclusion of neurological changes (Figures 2, 3 and 4**).

Effects of High-Dose Opioids on NPi, CV, and Size Figure 2



Rollins MD, Feiner JR, Lee JM, Shah S, Larson M: Pupillary effects of high-dose opioid quantified with infrared pupillometry. Anesthesiology: The Journal of the American Society of Anesthesiologists, 121(5): 1037-1044, 2014.

Effects of Analgesics and Sedatives on % Change of Pupil Size Figure 3



Martineau-Lessard C, Arbour C, Germéus NE, Williamson D, De Beaumont L, Bernard F: Pupil Light Reflex for the Assessment of Analgesia in Critically Ill Sedated Patients With Traumatic Brain Injury: A Preliminary Study. Journal of Neuroscience Nursing, 54(1): 6-12, 2021.

The Neurological Pupil index™ (NPi®) Pupil Reactivity Assessment Scale

| Measured Value* | Assessment |
|-----------------|--|
| 3.0 – 4.9 | Normal |
| < 3.0 | Abnormal |
| 0 | Non-Reactive, Immeasurable, or Atypical Response |

*A difference in NPi between Right and Left pupils of ≥ 0.7 may also be considered an abnormal pupil reading

*Per the Neurological Pupil index (NPi) algorithm