



The Possibilities of Pupillometry as a Novel Biomarker

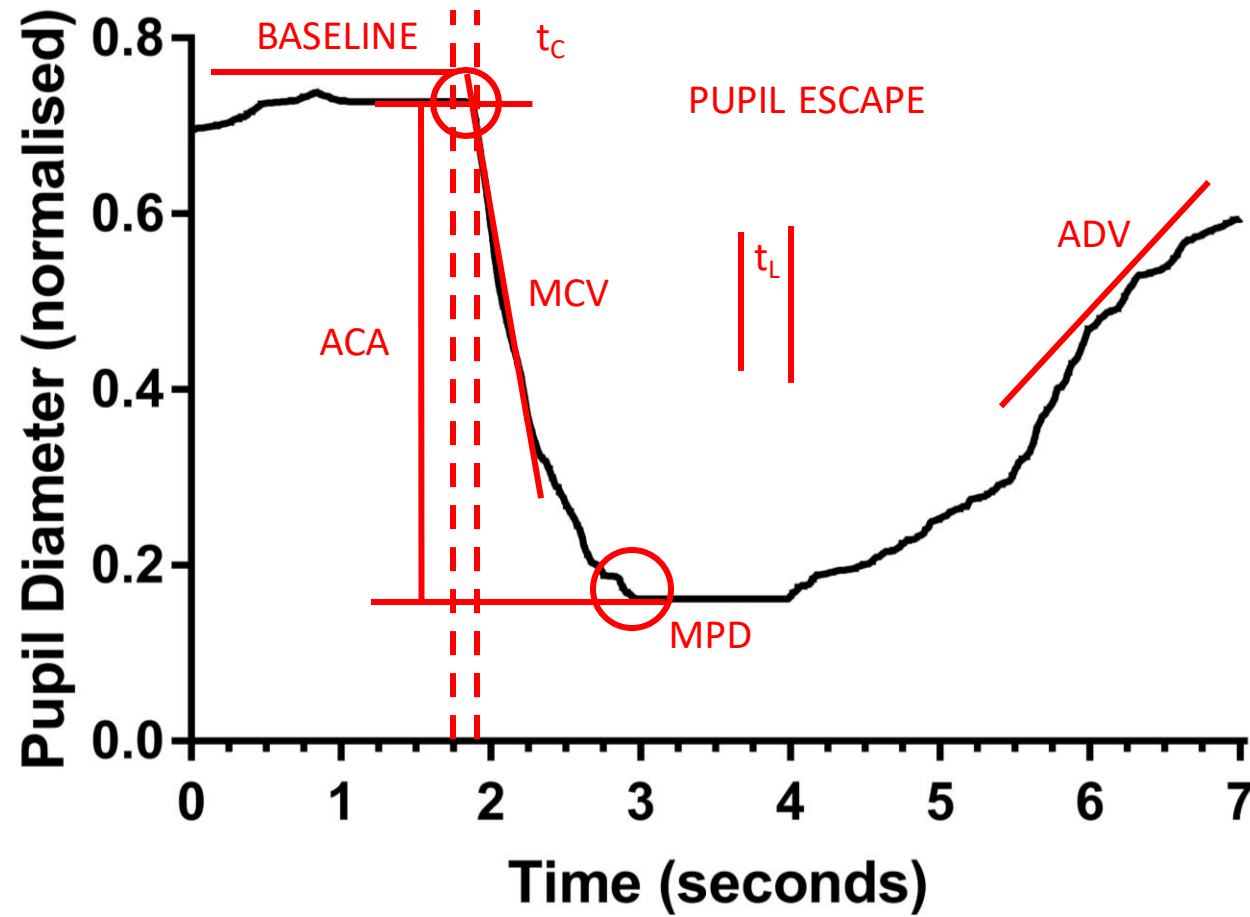
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What is Pupillometry?

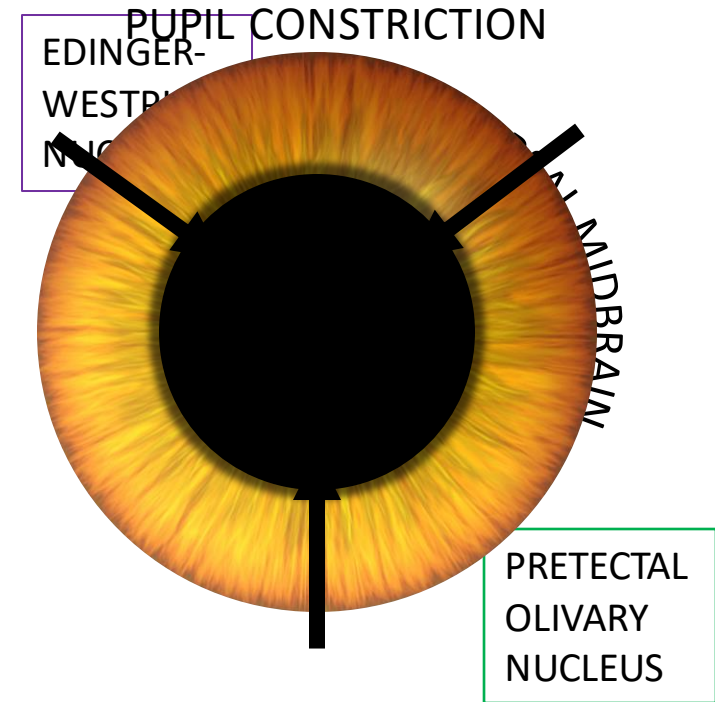
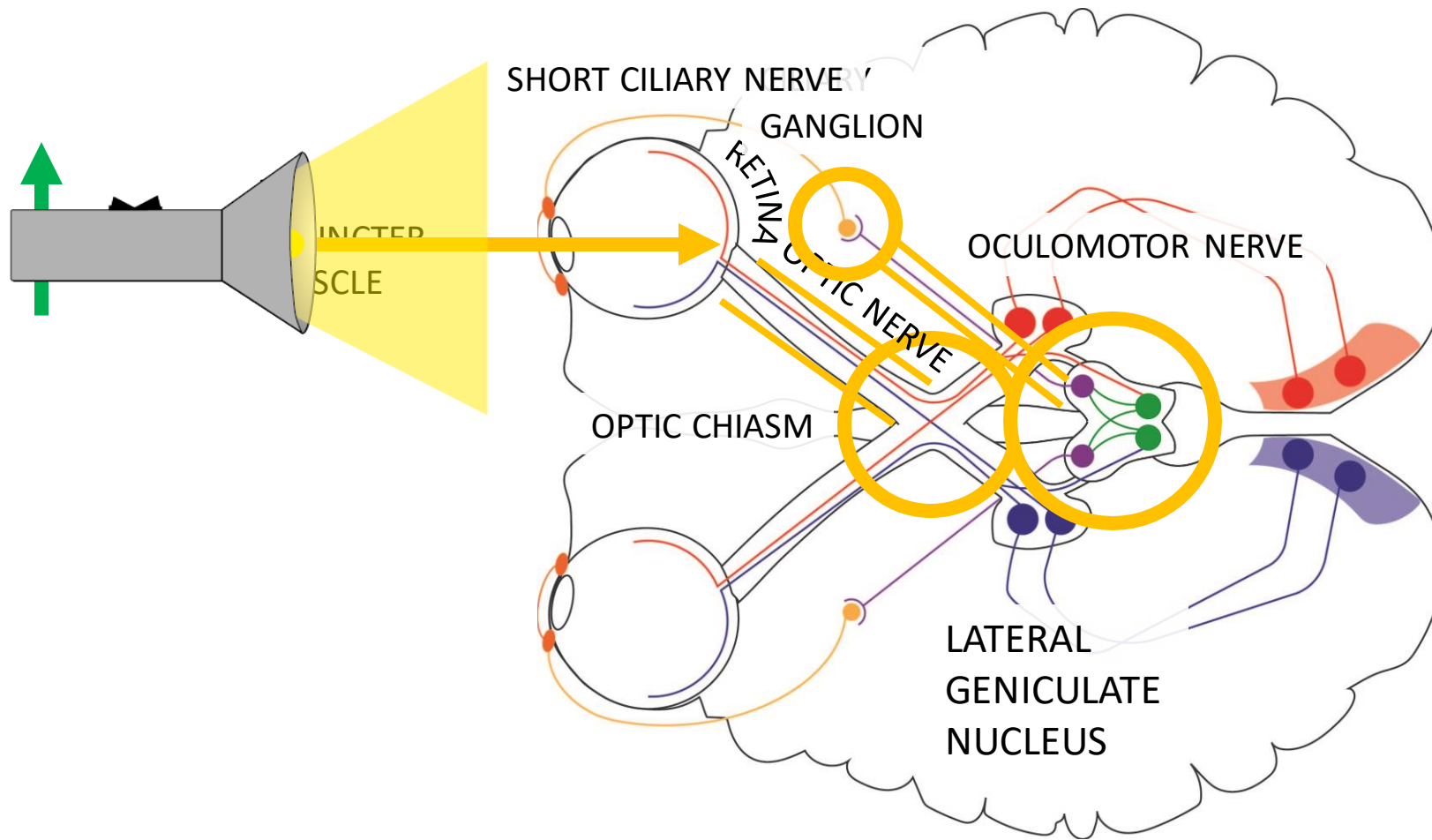
- The measurement of pupil diameter and reactivity in response to a stimulus.
 - LIGHT – Pupillary Light Reflex (PLR)
 - NEAR FIXATION – Pupil Near Response (PNR)
 - COGNITIVE ACTIVITY – Psychosensory Pupil Response (PPR)
- Two main types of Pupillometry:
 - Dynamic Pupillometry
 - Chromatic Pupillometry

Pupillogram

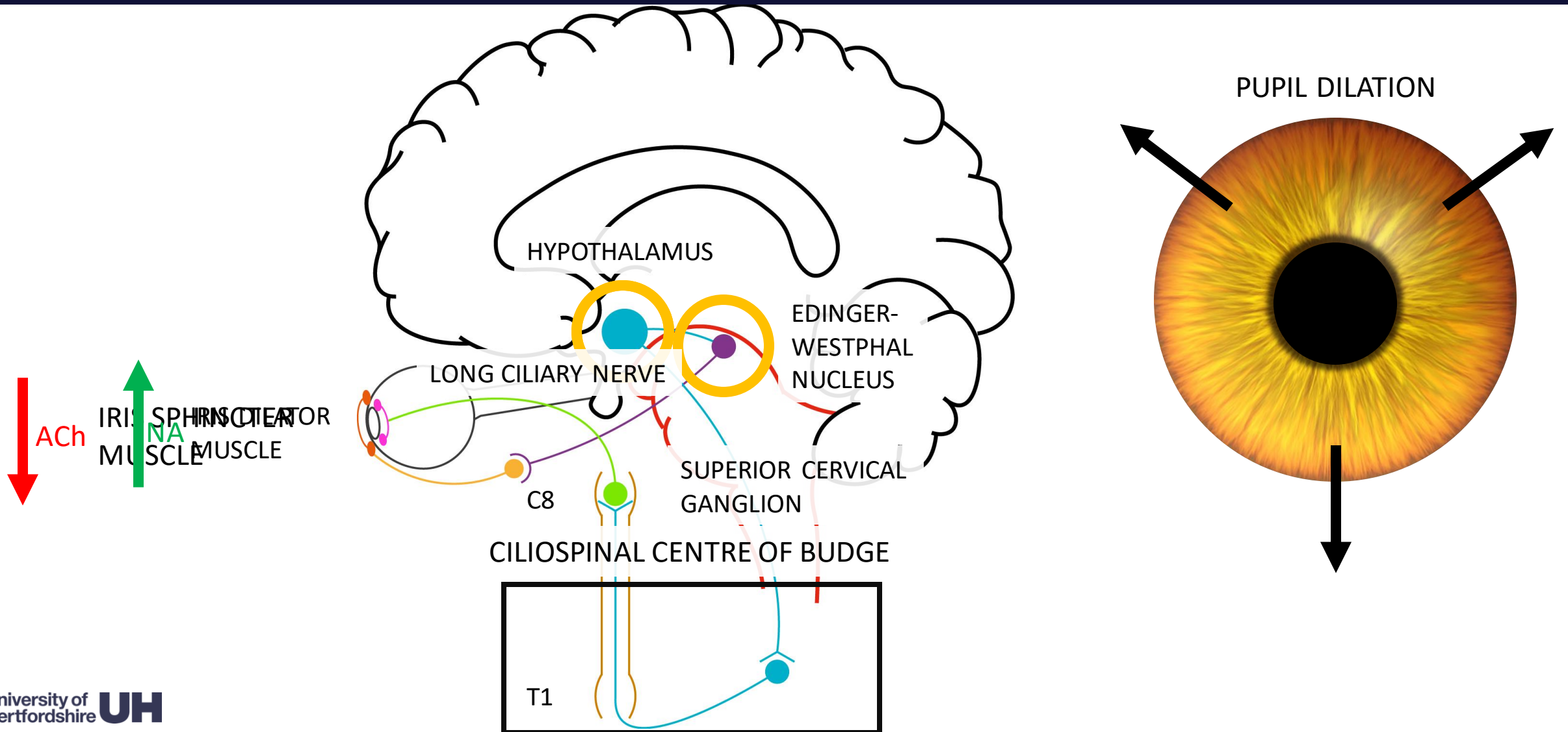


- Latency (t_L)
- Minimum Pupil Diameter (MPD)
- Constriction time (t_c)
- Maximum Constriction Velocity (MCV)
- Absolute Constriction Amplitude (ACA)
- Absolute Dilation Velocity (ADV)

Neurophysiology of the PLR (Constriction Pathway)



Neurophysiology of the PLR (Dilation Pathway)



Summary of PLR



Anything that can affect the ACh/NA balance within the CNS will have an effect on the Pupillary Light Reflex.

**Muscle
mechanism**

**Nervous system
control**

**Main
neurotransmitter**

Some Known Effects of CO...

- Binding to haemoglobin.
- Changes in visual function (Blumenthal, 2001).
- Central nervous system dysfunction
 - Disturbances of normal pupillary reactions (Wilmer, 1921).
 - Dysfunction of acetylcholinergic neurons (Nabeshima *et al.* 1991).

Other Toxicological Examples...

- Organophosphates including Sarin (Gore *et al.*, 2014), Soman (Genovese *et al.* 2010) and Dichlorvos (Taylor *et al.*, 2008).
- Botulinum toxin (Zheng and Azar, 2014).
- Solanaceae/Nightshades including Devil's snare (Hansen and Clerc, 2002) and Angel trumpet (Andreola *et al.*, 2008).
- Mercury intoxication (Miloni *et al.*, 2017).

Summary

- Pupillometry offers insight into nervous system health.
- Disruptions to the ACh/NA balance can affect the PLR.
- Carbon monoxide intoxication can impair CNS function.

THEREFORE...

Central nervous system disruption is likely to be reflected in the PLR of a patient exposed to CO.

Current/Future work...



P.E.E.C.O

Pupillary Evaluation of Exposure to Carbon Monoxide

- Evaluating the use of a novel pupillometer as a sensitive indicator of low-level CO exposure.
 - Chromodynamic Pupillometry

Present research

- Reproducibility of CDP.
- Optimisation of CDP stimuli.

Future research

- Investigate dose response of CO.
- Investigate age effects.

- Project funded by the CO Research Trust.

References:

- Andreola, B., Piovan, A., da Dalt, L., Filippini, R., & Cappelletti, E. (2008). Unilateral mydriasis due to Angel's Trumpet. *Clinical Toxicology*, *46*(4), 329–331. <https://doi.org/10.1080/15563650701378720>
- Blumenthal, I. (2001). Carbon monoxide poisoning. *Journal of the Royal Society of Medicine*, *94*(6), 270–272. <https://doi.org/10.1177/014107680109400604>
- Genovese, R. F., Benton, B. J., Oubre, J. L., Fleming, P. J., Jakubowski, E. M., & Mioduszewski, R. J. (2008). Determination of miosis threshold from whole-body vapor exposure to sarin in African green monkeys. *Toxicology*, *244*(2), 123–132. <https://doi.org/https://doi.org/10.1016/j.tox.2007.11.004>
- Gore, A., Bloch-Shilderman, E., Egoz, I., Turetz, J., & Brandeis, R. (2014). Efficacy assessment of a combined anticholinergic and oxime treatment against topical sarin-induced miosis and visual impairment in rats. *British Journal of Pharmacology*, *171*(9), 2364–2374. <https://doi.org/10.1111/bph.12586>
- Hansen, P., & Clerc, B. (2002). Anisocornia in the dog provoked by a toxic contact with an ornamental plant: *Datura stramonium*. *Veterinary Ophthalmology*, *5*(4), 277–279.
- Milioni, A. L. v, Nagy, B. v, Moura, A. L. A., Zachi, E. C., Barboni, M. T. S., & Ventura, D. F. (2017). Neurotoxic impact of mercury on the central nervous system evaluated by neuropsychological tests and on the autonomic nervous system evaluated by dynamic pupillometry. *NeuroToxicology*, *59*, 263–269. <https://doi.org/https://doi.org/10.1016/j.neuro.2016.04.010>
- Nabeshima, T., Katoh, A., Ishimaru, H., Yoneda, Y., Ogita, K., Murase, K., Ohtsuka, H., Inari, K., Fukuta, T., & Kameyama, T. (1991). Carbon monoxide-induced delayed amnesia, delayed neuronal death and change in acetylcholine concentration in mice. *Journal of Pharmacology and Experimental Therapeutics*, *256*(1), 378–384.
- Taylor, J. T., Davis, E., Dabisch, P., Horsmon, M., Li, M., & Mioduszewski, R. (2008). Alterations in autonomic function in the guinea pig eye following exposure to dichlorvos vapor. *Journal of Ocular Pharmacology and Therapeutics: The Official Journal of the Association for Ocular Pharmacology and Therapeutics*, *24*(5), 473–479. <https://doi.org/10.1089/jop.2008.0020>
- Wilmer, W. H. (1921). Effects of Carbon Monoxid upon the Eye. *American Journal of Ophthalmology*, *4*(2), 73–90.
- Zheng, L., & Azar, D. (2014). Angle-closure glaucoma following periorbital botulinum toxin injection. In *Clinical & experimental ophthalmology* (Vol. 42, Issue 7, pp. 690–693). <https://doi.org/10.1111/ceo.12293>

Thank you!