

Abstracts

Effect of Blue Light on Transcutaneous Auricular Vagus Nerve Stimulation-induced Pupil Dilation

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Rationale: Vagus nerve stimulation (VNS) is an adjunctive treatment for drug-resistant epilepsy. Although the mechanism of action is not fully understood, it is suggested that its efficacy depends on the activation of the Locus coeruleus (LC) and noradrenalin (NE), referred as the LC-NE system. Despite its benefits, a substantial number of patients exhibit an insufficient response to VNS, necessitating strategies to optimize its effectiveness. Recent research highlighted the potential of blue luminotherapy in enhancing cognitive functions and alertness through its influence on brain regions involved in the vagal afferent network, including the LC. Based on the joint action of VNS and blue light on the LC, our hypothesis emerges that combining these two modalities could yield a synergistic effect, resulting in enhanced noradrenergic tone. This combined activation may lead to a more pronounced antiepileptic effect, resulting in larger responses to VNS amongst treated patients. Pupillometry is often used to assess the activity of the LC-NE system: recent studies have shown that VNS could induces pupil dilation in epileptic patients, as well as transcutaneous VNS in healthy subjects, a non-invasive technique suggested to share similar patterns of brain activation with VNS. This exploratory project aims to investigate the potential synergy by evaluating how blue-enriched light modulates the tVNS-induced pupil dilation in healthy subjects compared to control lights.

Methods: 3.4 seconds stimulations of tVNS and sham (pulse width: 200 μ s, frequency: 25 Hz, intensity below pain threshold) were respectively administered to the cymba and tragus zone, and earlobe of the left ear of 23 healthy subjects concomitantly exposed to high-intensity blue (HBL), low intensity blue (LBL) and control lights: orange (OL) and dim light (DL). Dynamic pupil dilations between tVNS and sham for each light condition were analyzed using non-parametric Wilcoxon signed-rank tests. TVNS-induced pupil dilations were also compared between each light condition to determine which light induced the highest pupil dilation.

Results: Results show higher tVNS-induced pupil dilation compared to sham during the stimulation in DL condition (Fig. A1; grey area represents the stimulation period. The top red line indicates statistical

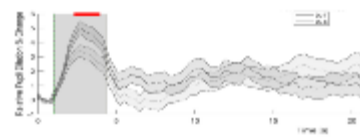
significance, $p < 0.02$). This difference was also observed in LBL condition, where the dilation was sustained up to 3 seconds post-stimulation (Fig. A2; $p < 0.05$). tVNS-induced pupil dilation in LBL was higher to tVNS-induced pupil dilation in dim light during and post-stimulation (Fig. B; $p < 0.05$). Nevertheless, no differences were found between tVNS and sham in orange or high-intensity blue light conditions.

Conclusions: Our results show that tVNS induced the highest pupil dilation in LBL, compared to dim light condition. In low blue light condition, the tVNS-induced pupil dilation response was more sustained. This result supports our synergistic hypothesis regarding blue light and VNS. This innovative project could give new insights into blue luminotherapy as an additive treatment for enhancing the efficacy of VNS in patients with refractory epilepsy.

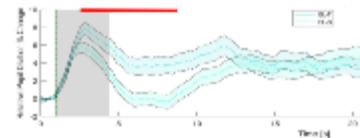
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Neurophysiology

A1. Average tVNS light and sham (grey) pupil dilation (%) in dim light.



A2. Average tVNS light and sham (grey) pupil dilation (%) in low intensity blue light.



B. Average tVNS pupil dilation (%) in low intensity blue light vs dim light.

