Toward Quantitative Neurofunctional Feedback During TMS: A Concurrent TD-NIRS Approach

Michele Lacerenza[1], Costanza Iester[2], Chiara Motto[1], Laura Bonzano[3,4], Marco Bove[2,4], Simone Cutini[5], Sabrina Brigadoi[5].

[1] PIONIRS srl, Milan, Italy; [2] Department of Experimental Medicine, University of Genoa, Genoa, Italy; [3]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy [4] IRCCS Azienda Ospedaliera Metropolitana, Genoa, Italy; [5] Department of Developmental Psychology and Socialization, University of Padova, Padua, Italy.

Email address: lacerenza@pionirs.com

Abstract: Transcranial magnetic stimulation (TMS) and time-domain near-infrared spectroscopy (TD-NIRS) are complementary tools for probing human brain functions, yet their concurrent use remains technically challenging. Most current implementations are based on continuous-wave systems. TD-NIRS offers several advantages, such as depth sensitivity and specificity, and greater flexibility in optode design, which can improve the quality and interpretability of measurements during TMS. We developed and tested a novel hardware and analysis framework for simultaneous TD-NIRS and TMS over the motor cortex. Using a dual-channel TD-NIRS system with retractile spring-loaded optodes and depth-sensitive photon timing analysis, we characterized handgrip-evoked hemodynamic responses and preliminary ipsilateral and contralateral cortical effects during concurrent single-pulse TMS.

Introduction: The combination of TMS and NIRS offers the opportunity to investigate the interplay between cortical excitability and local hemodynamic responses with improved quantitative accuracy [1, 2]. However, concurrent TMS–NIRS measurements remain technically challenging. In this work, we implemented a dedicated TD-NIRS + TMS setup designed to improve probe–scalp coupling through hair, reduce sensitivity to coil-induced perturbations, and enable simultaneous bilateral monitoring of motor cortex hemodynamics during hand motor tasks with and without concurrent TMS stimulation.

Methods: Measurements were performed using the NIRSBOX-DUAL (PIONIRS, Italy) a TD-NIRS device equipped with two dedicated optical probes positioned over the left and right primary motor regions (C3/C4), to investigate ipsilateral and contralateral motor cortical hemodynamic responses. Each probe employs spring-loaded retractile optodes to improve scalp coupling through hair, with a fixed source–detector distance of 2.5 cm. TD-NIRS data were acquired bilaterally at 1 Hz. Photon time-of-flight analysis enabled the extraction of hemodynamic information, improving discrimination between superficial extracerebral contributions and cortical signals. TMS was delivered as a single-pulse stimulation paradigm, with the coil positioned over the motor cortex. Stimulation intensity was adjusted to induce motor evoked potentials (MEPs) of approximately 1 mV in the target hand muscles measured using electromyography (EMG). The experimental design included a series of handgrip tasks at different force levels and durations across three conditions: (i) without TMS, (ii) with the coil placement without stimulation to control for mechanical and pressure-related effects, and (iii) during concurrent TMS.

Results: The proposed setup enabled stable simultaneous TD-NIRS acquisition over bilateral motor areas. Handgrip measurements without TMS produced the expected task-related hemodynamic response functions, supporting the physiological reliability of the recordings. Handgrip with coil placement (both with and without TMS) did not significantly affect hemodynamic estimation. The observed effect was limited to photon count-rate variations, which in TD-NIRS is known to not affect hemodynamic variables retrieval under adequate signal-to-noise conditions. The system demonstrated sufficient robustness for concurrent acquisition under direct coil contact, while the presence of the optical probe beneath the TMS coil did not require any substantial increase in stimulation intensity. A critical aspect remains mechanical stability: if coil placement is not adequately controlled, contact with the optical probe may induce slight repositioning, potentially changing the sampled cortical region during the measurement. Overall, this pilot study generated a dataset of bilateral motor cortex responses during handgrip tasks performed under three conditions (no TMS, coil placement without TMS and with concurrent TMS), enabling a direct comparison of ipsilateral and contralateral responses across different durations and force levels.

Conclusion: This work demonstrates the feasibility of concurrent TD-NIRS and TMS for bilateral monitoring of motor cortex hemodynamics. TD-NIRS obtains absolute estimates of oxy- and deoxyhaemoglobin concentrations and selectively access contributions from different tissue layers. This constitutes a significant methodological advantage particularly in the context of integration with TMS. Furthermore, these preliminary results support the feasibility of TD-NIRS as a quantitative neurofunctional feedback tool during TMS and provide a methodological foundation for future studies in larger cohorts and clinical neurostimulation applications.

[1] Curtin A. et al, A Systematic Review of Integrated Functional Near-Infrared Spectroscopy (fNIRS) and Transcranial Magnetic Stimulation (TMS) Studies. (2019), Front. Neurosci. 13:84. doi: 10.3389/fnins.2019.00084

[2] Bisio A. , Iester C., Biggio M., et al., Frontoparietal network activity during a combined action observation and proprioceptive stimulation protocol reveals long-term plasticity in the primary motor cortex, (2025) NeuroImage, 319, 121432, ISSN 1053-8119, doi: 10.1016/j.neuroimage.2025.121432.