Reliability and optimization of somatosensory afferent inhibition (SAI) as a clinical biomarker in healthy aging

Award type: Multi investigator award for feasibility studies
Amount awarded: £64539.54
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Summary:

Activity in the regions of the brain relating to movement and touch can be measured by applying stimulation to the wrist, and non-invasive magnetic stimulation to the head. These measures can improve understanding into what happens during neurological conditions, including Parkinson's disease and dystonia. However, first, we need to know how well these approaches work in healthy adults of different ages. Specifically, we need more research into people over 35 years old, as these techniques are often based on work from younger adults.

Across three study sites we developed and unified methodology combining non-invasive brain stimulation and electroencephalography (EEG) to improve understanding of how the healthy brain ages. Some key outcomes of the project include developing a new approach to measuring integration of sensory and motor inputs, collecting a unique new dataset, and knowledge exchange activities. Going forward we hope this new information will provide a unique and valuable reference for the assessment of clinical disorders of touch and movement.

Methodology:

When peripheral nerve stimulation precedes a transcranial magnetic stimulation (TMS) pulse over the motor cortex by 20-30ms, short-latency afferent inhibition (SAI) can be produced. SAI is a potential clinical biomarker for brain function in dementia, neurological disorders including Parkinson's and dystonia, and healthy ageing. It is relatively easy to administer and provides high quality data with large effect-sizes. However, clear understanding of underlying mechanisms and the influence of participant demographics/neuroanatomy are lacking. SAI can be personalised by adjusting the strength of stimulating pulses, however, factors such as stimulus timing are often based on small studies of healthy, younger adults. This is problematic, because several factors including ageing may alter the speed at which signals are propagated, which is not well accounted for in current guidelines. Consequently, conclusions about differences between health, disease, old and young could be erroneously derived due to inadequate parameter selection.

Guided by an extensive systematic review/meta-analysis (conducted by NH), we selected a range of parameters to measure to study SAI in healthy aging. Our approach includes assessing SAI using a set of conventional parameters in addition to a new approach that allows us to explore the potential time course in significantly more depth. In 2/3 sites we also collected EEG measures which gives us additional opportunities to explore how sensorimotor signals are altered as a factor of age. Our approach had several stages as follows:
1: Data driven parameter selection (based on meta-analysis), and development of a new approach to SAI measurement based on piloting from NH site.
2: Harmonization of methods across our 3 sites including training of RAs and visits between sites.

3: Data collection with a target of 40 participants at each site, total sample 120.
4: Analysis, outreach and publication.

Outcomes/ impact:

Commitment to open science: Our study is preregistered and can be found here.

Development of new dataset: We have collected 108/ 120 participants. We will continue data collection to reach this sample size. The dataset will be made available with publication. The dataset includes a subset of ~80 participants with EEG. This is a unique healthy aging dataset.

Development of unified analysis pipelines: We are in the process of writing code to combine and analyse the data across our three different sites. TMS-EEG analysis is well underway with new code to distinguish between peripheral and central contribution and the role of inhibition/facilitation balance has been created.

Knowledge exchange -conferences: Funding allowed the applicants and RAs (supported by the project) to attend numerous conferences to present aspects of this work. For the three RAs (all Early career researchers) this also offered an excellent opportunity for networking and additional career development. Conferences attended include International Multisensory Research Forum, Durham; Experimental Psychology Society Conference, London; British Association for Cognitive Neuroscience, Edinburgh; Non-invasive neuromodulation workshop, Nottingham; TMS@40 (ECR event), Birmingham; TMS at 40, London and the European Workshop on Cognitive Neuropsychology, Brixen, Italy.

Knowledge transfer, networking opportunities and co-creation of future TMS projects: In conjunction with funding obtained from the experimental psychological society (EPS) we organised TMS@40, a three-day workshop for early career researchers using TMS. The event was attended by approximately 57 researchers and involved a mixture of talks, hackathons and demonstrations.

Additional funding: data and developments from this project have contributed to a substantial bid by NH to BBSRC (£1M – outcome pending). KD also obtained a small internal award from University of Nottingham (£3026) to extend some of this work into a clinical group, with the aim of using this pilot data in a wider MRC bid.

Pending: We will complete the final few datasets by February and then continue to analyse and publish our new findings. Several additional papers will also be submitted which align with this work.

Alignment with network priorities:

Collaboration: across 3 sites we have aligned protocols, shared training and collected a new pooled dataset.
Sharing: We will provide our data and code open source and have preregistered the study. We provided training to ECRs in our labs, shared knowledge between sites, and facilitated a knowledge exchange event (TMS@40).
Outcomes: our study is preregistered. It is a large and comprehensive dataset of healthy aging which explore pre-existing and new approaches to measuring sensorimotor integration. Methods development is at the heart of this work, aiming to understand how parameters ay change with age.

Techniques & mechanisms: We have paired TMS, EEG and median nerve stimulation to study the underlying mechanisms through which healthy aging may influence sensorimotor integration.