Paired Associative Stimulation as an Assessment of Neuroplasticity: A Pilot Study

Matthew Picard-Fraser PT, DPT[1], Catherine Cahill[1], Aidan Kimberley[1], Richard Hardstone PhD[2,3], David Lin MD[1,2,3, 4], Teresa Kimberley PT, PhD, FAPTA[1,3]

[1]MGH Institute of Health Professions, Boston MA, USA, [2]Laboratory for Translational Neurorecovery, Massachusetts General Hospital, Boston, MA, USA, [3]Center for Neurotechnology and Neurorecovery, Massachusetts General Hospital, Boston MA, [4]Department of Neurology, Massachusetts General Hospital, Harvard Medical School; Division of Neurocritical Care

Background

- Paired Associative Stimulation (PAS) combines pulses of transcranial magnetic stimulation (TMS) with peripheral nerve stimulation in a precisely timed manner to induce neurophysiological changes
- PAS has been widely used in stroke rehabilitation as an intervention with variable responses
- Recent studies have shown the potential of leveraging response to PAS as an assessment to increase precision in intervention prescription since PAS driven changes share neural substrates with motor learning
- Response to PAS can be assessed using common TMS measures of cortical excitability
- Response to PAS may be a key predictor of response to interventions that promote motor learning following stroke, such as Paired Vagus Nerve Stimulation (VNS)

Purpose

- To demonstrate that PAS can drive quantifiable, transient neurophysiological changes

Methods

- A healthy, 19 year-old, left-handed female underwent 3 sessions of PAS (PAS-LTP, PAS-LTD, PAS-Sham)
- Participant's baseline level of cortical excitability and peripheral sensory threshold was assessed prior to each PAS session
- Follow-up measurements of cortical excitability were completed immediately after the PAS session and up to 30 minutes afterwards

PAS Parameters

- All PAS sessions consisted of 225 pulse pairs of synchronized peripheral nerve pulses and TMS pulses delivered at .25 hZ
- TMS pulses were delivered at 130% of the participant's motor threshold and targeted the left motor cortex for all PAS conditions
- Peripheral nerve stimulation was delivered on their right median nerve at 300% of their sensory threshold for all PAS conditions
- The inter-stimulus interval (ISI) was different for each PAS condition, however sensory stimulation always preceded the TMS pulse
    - PAS-LTP: ISI of 25 ms
    - PAS-LTD: ISI of 15 ms
    - PAS-Sham: ISI of 25 ms

PAS can be used to drive transient Long-Term Potentiation (LTP)-like or Long-Term Depression (LTD)-like changes in the motor cortex

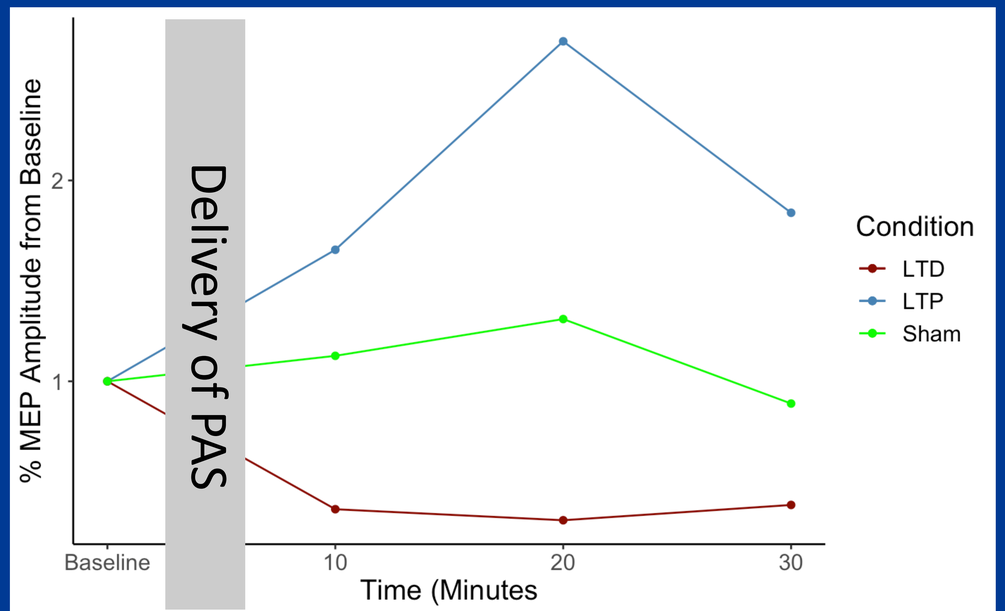

Figure 1. Changes in cortical excitability from baseline as measured by peak-to-peak Motor Evoked Potential (MEP) Amplitude at baseline prior to PAS and every ten minutes after completion of PAS protocol. Each Time Point represents the average of 30 MEPs.

Results

- Clear differences were seen in assessments of cortical excitability following each session of PAS
- PAS-LTP resulted in increased cortical excitability
- PAS-LTD resulted in decreased cortical excitability
- PAS-Sham resulted in no difference in cortical excitability
- Participant's cortical excitability began to return towards their baseline level within 30 minutes following PAS-LTP and PAS-LTD
- No side effects were reported following any PAS session

Limitations

- N of 1 study so no ability to compare variability in response to any PAS conditions across individuals
- ISI used were not personalized for the participant and instead based on physiological norms
- Follow up assessments only lasted 30 minutes due to time constraints and did not fully capture participant's return to baseline

Conclusions

- Participant's response to PAS-LTP and PAS-LTD were as expected for LTP-like and LTD-like changes respectively
- Differences between the three PAS conditions highlights potential of PAS as an assessment of neuroplastic capacity
- Correct ISI is vital to obtaining desired effect from PAS
- PAS may serve as a feasible, effective method to assess baseline capacity for neurological changes in healthy and impaired populations

Future Studies

- Assess PAS response to all three conditions in additional healthy individuals to demonstrate variability in response to PAS protocols
- Assess PAS-LTP response in individuals following a stroke and correlate their response to PAS to motor improvements following an intervention, such as Paired-VNS

References

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