TMS@40 Hackathon Briefing

One main aim of TMS@40 is to write a paper. The provisional title of this paper is:

"The experimental psychology of transcranial magnetic stimulation: A consensus paper"

Why do we need a consensus paper on the experimental psychology of TMS?

- There are many existing consensus & guidance papers on TMS. Most are from scientists with neurology, neurophysiology & medical backgrounds
- The main journals that specialise in TMS Clinical Neurophysiology & Brain Stimulation

 again, tend to be edited by & publish work from medical researchers
- By contrast, experimental psychology has had relatively little input or influence on how TMS studies are conducted (but see e.g., <u>Bergmann & Hartwigsen, 2021</u>)
- Since TMS is mostly done on awake, behaving participants(!) experimental psychology
 has much to offer. (We should therefore **not** focus on neurophysiology or (e.g.) EMG)

What is experimental psychology?

Experimental, laboratory-based methods have long been used to understand the relationships between stimuli, (neuro)psychological processes & responses. Arguably, this began with Weber & Fechner's psychophysics in the mid-1800s. Experimental psychology has developed methods to study sensation, perception, attention, associative learning, memory, decision-making, response conflict & much more. It has been an extremely successful paradigm.

TM<u>S</u> is a stimulus like any other, so it follows that the methodological rigour of experimental psychology can be brought to bear on understanding how TMS affects the brain & behaviour. For example, stimulus timing, intensity & location may significantly affect cognition & movement.

How can experimental psychology inform TMS research?

Well, that is what you need to decide, and write about! You should use any and all of your training so far, whether it is in psychology, physiology, neuroscience, biology, statistics or other allied disciplines, to decide. Below are some general examples of what you might discuss. You will be given a more specific briefing for each of the four hackathon topics.

Experimental design: How should TMS experiments be designed to minimise bias, remove confounds, ensure counterbalancing & randomisation, prevent order- & learning-effects?

Analysis: How should data from TMS experiments be analysed to minimise bias & confounds, to ensure all relevant variance is modelled, & to account for individual differences?

Reproducibility: After ~175 years of experimental psychology, what methods work & what don't? What lessons can be applied to the more recent history of TMS research?

TMS@40 Hackathon Briefing: Experimental Design 1

How should TMS experiments be designed to minimise bias, remove confounds, & ensure that we answer the questions we want to answer? What constraints apply to TMS experimental design? What are the trade-offs, pros & cons of each approach?

General design choices

Theoretical

- What kinds of question are we trying to answer?
- How do we choose a protocol that best answers our question?
- How do we estimate the statistical power of TMS studies; do we need large(r) samples?

TMS type

- Offline versus online: what questions can they answer? What are the pros & cons?
- Single pulse versus bursts: what questions can they answer? What are the pros & cons?

TMS timing

- When does a TMS pulse interfere with processing? Can this be before an incoming (e.g., sensory) stimulus is processed by a brain area? Or must it be during processing? Or can it even be after?
- When does a TMS pulse interfere with a brain area's response before, during, or after?
- Should we start by piloting a range of TMS timings ('chronometric' TMS), or are there principled ways to choose a time-point in advance?

Specific design choices

What should we be controlling?

- Participant body, head, arm, & eye position & activity? Should they be relaxed or natural?
- Should we control participant attention with fixation or a (distractor) task?

Primary motor cortex (M1) versus the rest of the brain

- The majority (or largest minority) of TMS has been done on the motor cortex. But the majority of experimental psychology studies are *not* motor.
- How do we generalize M1 protocols to other brain areas?

Electromyography (EMG) versus no EMG

- The majority of experimental psychology TMS studies do *not* measure EMG, so how should we adapt the methods & guidance from TMS studies that measure EMG?
- How should we set stimulus intensity in the absence of EMG? Should we set it relative to motor thresholds like a visible twitch or at a fixed intensity?

Magnetic resonance imaging (MRI) versus no MRI

- The majority of experimental psychology TMS studies do not use MRI scans, so how do
 we adapt the methods to follow guidance from TMS studies that use MRI?
- e-Field modelling without individual MRI is it useful?

TMS@40 Hackathon Briefing: Experimental Design 2

How should TMS experiments be designed when awake, behaving humans are participating? How do we remove bias & confounds, ensure counterbalancing & randomisation, prevent order- & learning-effects?

What is the 'social psychology of the TMS experiment' (Orne, 1962)?

TMS parameters

- How do different TMS timings relative to a stimulus or response change participants' reactions to those stimuli? Does TMS shorten or lengthen reaction times? Do Participants wait until the last TMS pulse in a train?
- Do participants try to predict the TMS? How we we set the intervals between TMS pulses to minimise prediction of the next TMS pulse?
- When can we use block designs & when must conditions be randomised?
- What kinds of TMS work on individual trials? Do some TMS effects build up over time?
- How does TMS change the behaviour we're trying to measure (regardless of brain area!)
- How does TMS intensity and/or randomness affect our studies? better or worse

Control conditions

- What counts as an adequate control for a TMS experiment? What are we controlling?
- What does a control site control for?
- What can control conditions control for? What kind of conditions are needed?
- What kinds of 'sham' condition are there? What do they control for? How do we know?
- Should we be single-blinding our participants? How do we ensure single-blinding?
- Should we be double-blinding our experimenters? Is it possible or desirable?
- How do we minimise 'demand characteristics'? (i.e., when our participants 'play the role'
 of a participant and adjust their responses according to what they think we want)

Participant (dis)comfort

- How do we ask participants to relax? How do these instructions affect the experiment?
- How do we measure participants' perception of the TMS (annoyance, distraction)?
- How does participant perception differ for online versus offline, or other TMS protocols?
- What should we do (or not do) to minimise discomfort? Decrease intensity? Move coil?
- How often should we be providing participants with breaks from tasks or stimulation?
- At what point should TMS experiments on healthy participants not continue?

Debriefing

- What should we regularly be asking our participants about?
- Should we ask about their tolerance for the stimulation? How? A standard guestionnaire?
- If we used a sham (or multiple TMS sites), did they detect the sham? Did blinding work?

TMS@40 Hackathon Briefing: Analysis 1

How should data from TMS experiments be *pre-processed* to minimise bias & confounds, to ensure all relevant variance is modelled?

Pre-processing is the filtering, de-noising, 'cleaning' and other processing that might be done to a dataset *before* any statistical analysis. It is often not fully-described in scientific papers, but may have substantial consequences for the statistical analysis stage.

(Please avoid focusing on EMG data and MEPs – this is covered by other papers and research fields)

Measures

What do we need to record or measure during the experiment to aid pre-processing?

What can go wrong?

Coil position and movement whether robot/non

If we have coil position measures, do we use them as a covariate? At which level of the analysis?

Or do we set a fixed threshold, e.g., 5mm or 10degrees?

Temporal filtering

Do we expect TMS responses to change over time? With arousal, alertness, learning, association, or plasticity?

If temporal changes are of no interest, should we filter responses (RTs, decisions), to remove these trends?

'Outlier' removal

What is an 'outlier' and why?

When is it acceptable to delete data?

What evidence do we need to justify deleting a data-point?

'Normalisation' of data

When it is appropriate to 'normalise' or 'standardise' data? (this could be as a ratio of a baseline measure per participant, or by using the standard normal distribution to convert to Z-scores) What are the consequences of normalisation?

Should we always present both normalised and raw data analysis?

Transformation of data

Researchers often desire 'normally-distributed' data

If we find non-normal (e.g., logarithmic, exponential, or skewed) data, what should we do? At what level of analysis should transformation be applied? (raw data per participant, summary data across participants, or (as the stats assume) – only the residuals after the analysis)

TMS@40 Hackathon Briefing: Analysis 2

How should data from TMS experiments be *processed* to minimise bias & confounds, to ensure all relevant variance & individual differences are modelled?

The statistical analysis (post-processing) is the final stage of analysis used to draw conclusions about the manipulations, sample and/or population under study. It is usually the main focus of scientific reports.

What covariates should we include in our statistical models (what should we be measuring?)

sham effectiveness/detection
participant annoyance/discomfort/tolerance
e-field model parameters
TMS intensity
fatigue, time-of-day, sleep (eg, during sleep studies @FBreuer)
caffeine, recreational substances Turco et al. 2020
posture; supine vs sitting up
experience of the subject in prior TMS experiments

Post-processing

What meta-data, pre-processing, summary, & group statistical analyses are appropriate?

How can we change our analysis pipelines to maximise fully-open sharing of data & code?

Capturing change over time dynamics learning rate, dynamics washout periods

Stats

If we use ratios as measures (e.g., in conditioned / unconditioned designs), how do we account for the consequences wandering denominators

problem of dynamic range of responses, and where on the input-output curve a stimulation or response is (this applies to MEPs, but also to any psychophysical stimulus-response curve)

going beyond pre/post subtraction methods and beyond ANOVA (i.e., where ANOVA is not enough: multi-level, unbalanced, nested, trials)

multi-level modelling of TMS data (using R, GLMM, etc)

TMS@40 Hackathon Briefing: Reproducibility 1

After ~175 years of experimental psychology, what methods work & what don't? What lessons can be applied to the more recent history of TMS research?

How can we enhance the reproducibility of TMS work within labs & between labs?

What are the challenges?

What does a cumulative, theory-driven science of TMS look like?

We need TWO separate (sets of) sub-themes, so that the two groups are working mostly independently

Consistency (reliability, replicability)

within-person (do the same people show the same effects over sessions?) within-lab (can the same lab show the same effects over studies?) across-lab (can multi-labs show the same effects?)

Reviewing / editing

when reviewing others' work, incorporate best-practice into the process

Pre-registration

does TMS do this (enough?)

How to work out what matters?

start with a list of environmental factors that might affect TMS data; see if people agree / can rule them out

e.g., things like: time-of-day; hormone fluctuations; instructions given; posture/position; lighting...

With minimal reporting standards (e.g., tms-rat.org), we can work this out post-hoc

Between-lab practices

electrode placements... heuristics cargo cults

TMS@40 Hackathon Briefing: Reproducibility 2

After ~175 years of experimental psychology, what methods work & what don't What lessons can be applied to the more recent history of TMS research?	[?

TMS@40 Hackathon Briefing: Implementation 1

Assuming that we develop a series of agreements and recommendations about how TMS experiments should be done, how do we make sure that change happens?

How can we best ensure that TMS methods improve?

How can we ensure that guidance is implemented?

That consensus is put into practice?

We need TWO separate (sets of) sub-themes, so that the two groups are working mostly independently

What should TMSMultiLab do next?

Sharing is a given
Meetings will continue
Hackathons (online vs. in person) - to be arranged
Formalise the organisation (elect officers...) - to be decided...
Disseminate at other events; find people interested in, but not heavy TMS users

SIPS

Symposia at other meetings Satellite meetings at other meetings

headlines to share after the workshop

videos other multimedia social media

For students, avoid starting with 'github'. instead: "here's a wiki you might find useful..." Set up a forum to share advice (eg as psychopy, FSL, others do) - discourse is most user-friendly

tips 'n' tricks

exchange tips in a session, discussion [will be in practical session] rapid fire 3-min presentation -> then follow-up

TMS@40 Hackathon Briefing: Implementation 2

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