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Reliability of 1 and 20 Hz rTMS in standard clinical application is low to moderate

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Limited evidence for validity and reliability of non-navigated low and high frequency rTMS over the motor cortex

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Introduction

- Repetitive transcranial magnetic stimulation (rTMS) is a common non-invasive brain stimulation technique that evokes neuromodulatory effects and changes cortical excitability.
- Cortical excitability is measured via motor evoked potentials (MEPs) elicited via single pulse transcranial magnetic stimulation (TMS) of the primary motor cortex (M1) (Rossini et al., 2015).
- For **low f**requency protocols these effects are assumed to be **i**nhibitory and for **hi**gh **f**requency protocols **e**xcitatory (**lofi-hife** heuristic) (Maeda et al., 2000b; Fitzgerald et al., 2006; Cohen et al., 2010; Thut and Pascual-Leone, 2010; Beynel et al., 2020).
- Upcoming evidence highlights the inter- and intra-subject variability (Ridding and Ziemann, 2010; Pell et al., 2011; Guerra et al., 2020b) and further questions the reliability of rTMS-induced changes on cortical excitability.

Methods

- In 30 healthy participants, we administered 1 and 20 Hz rTMS on M1 in alternated order and applied TMS before and after (figure 1) during which we derived MEPs from the first dorsal interosseus.

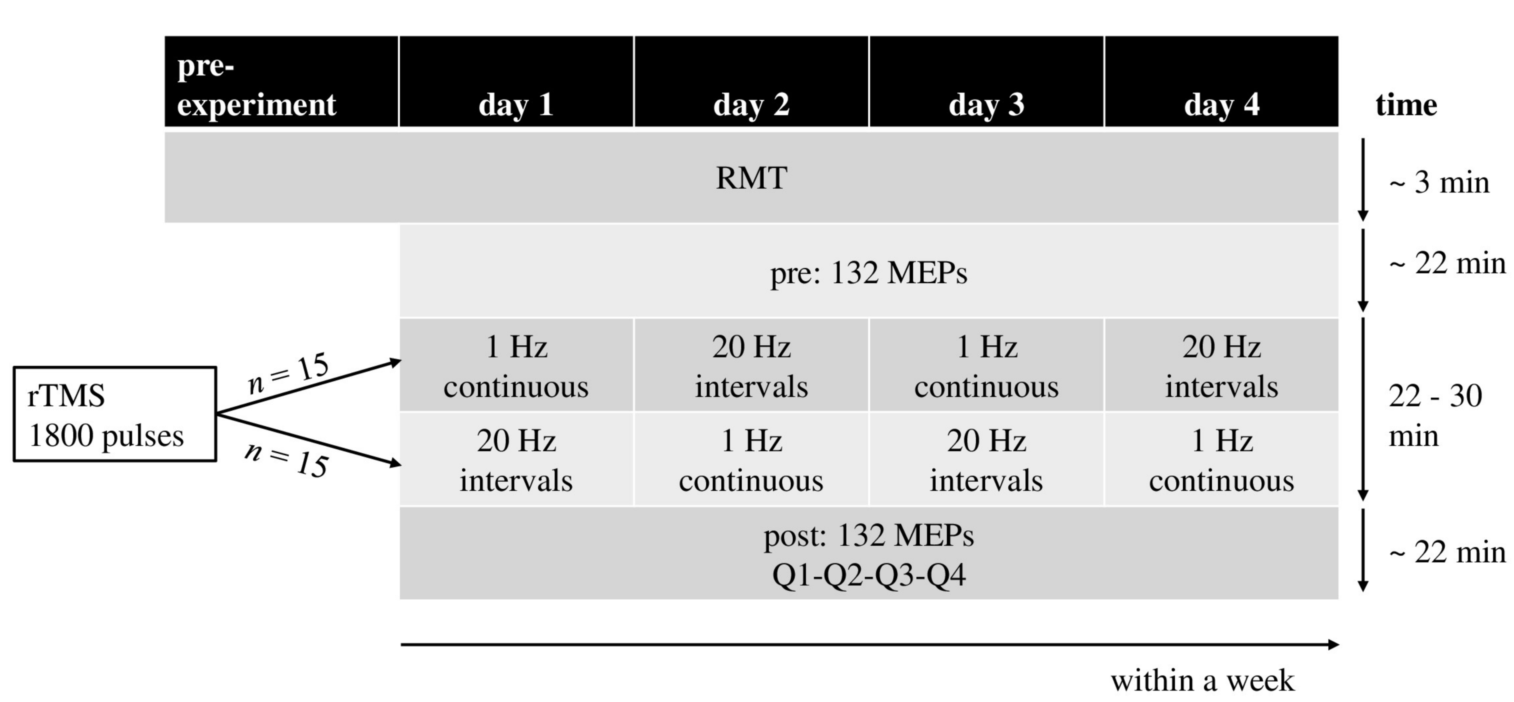

Figure 1. Study procedure. The pre-experiment included a resting motor threshold (RMT) determination. Each day of the main experiment comprised RMT determination, a pre-measurement of cortical excitability with 132 motor evoked potentials (MEPs), a protocol of repetitive transcranial magnetic stimulation (rTMS) (1800 pulses, 1 Hz or 20 Hz) and a post-measurement identical to the pre-measurement. To analyze the time-course after rTMS, we divided the 132 MEPs post-measurement up into quarters of 33 MEPs (Q1-Q4).

- The lofi-hife heuristic was assessed by ANOVAs at group level and by frequency statistics of rTMS-induced changes at single-subject level. Reliability at group level was calculated by using two-way mixed effect intraclass correlation coefficient (ICC) with general agreement and Pearson's correlation coefficient (*r*).

Results

- The heuristic was not evident at group level (figure 3). At single-subject level only four participants responded with heuristic-conform changes, i.e., concomitant decreases for both 1 Hz and increases for both 20 Hz sessions.
- ICCs and *r* for the whole sample were low to moderate (figure 2). Within subgroups of less confounded measures we found good *r* values for 20 Hz rTMS (figure 4).

Discussion

- Results question the validity of the lofi-hife heuristic and show insufficient test-retest reliability for 1 and 20 Hz rTMS under non-navigated conditions.
- Methodological and applicational improvements for the usage of rTMS in research and clinical settings might help to establish a more adequate estimation of validity and reliability of non-invasive brain stimulation.

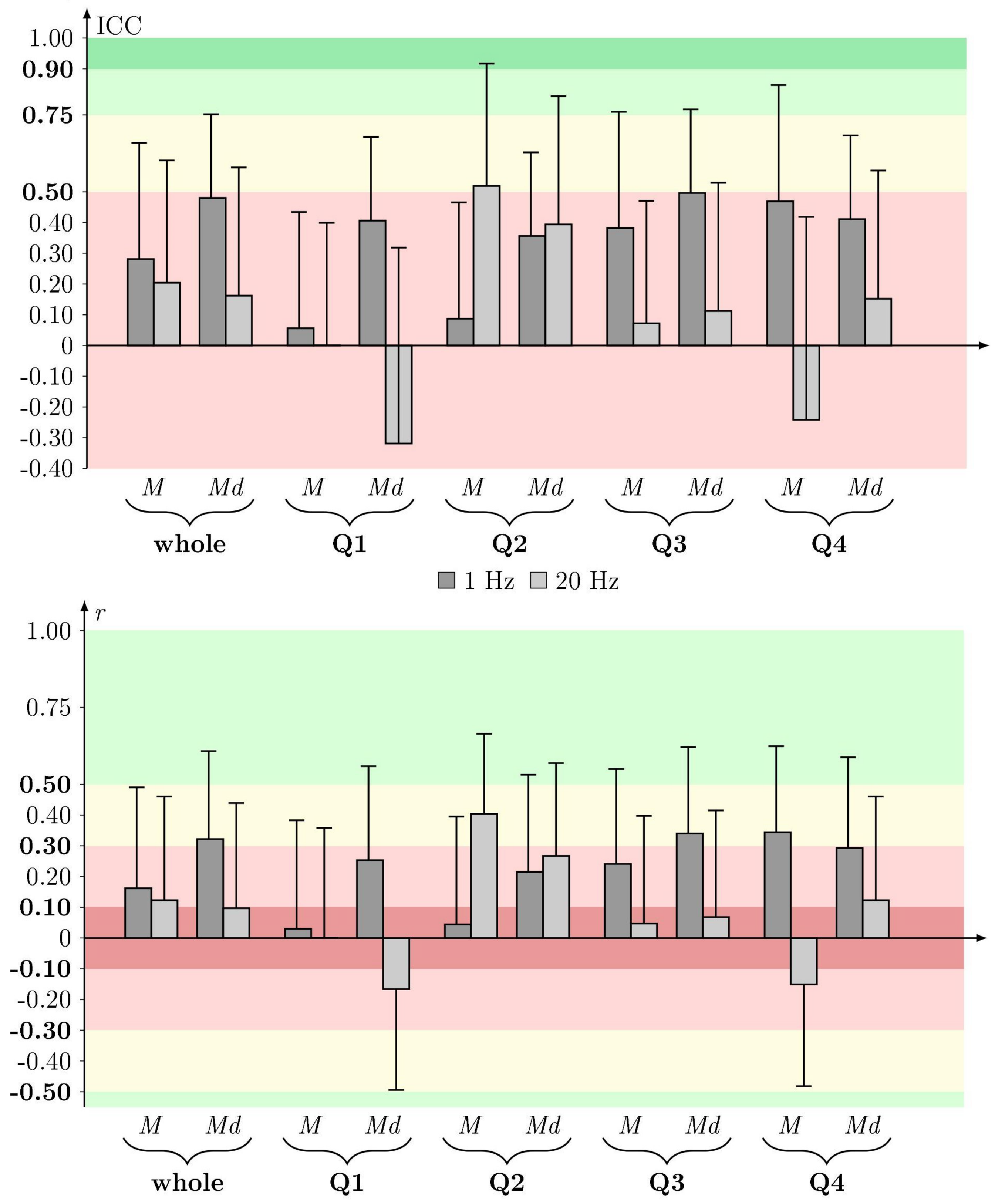

Figure 2. Reliability measures intraclass correlation coefficient (ICC) and Pearson's *r* between sessions 1 and 2 from the whole sample. Error bars represent 95% confidence interval. Colors represent the interpretation of Koo and Li (2016) for ICC and Cohen (1992) for *r*.

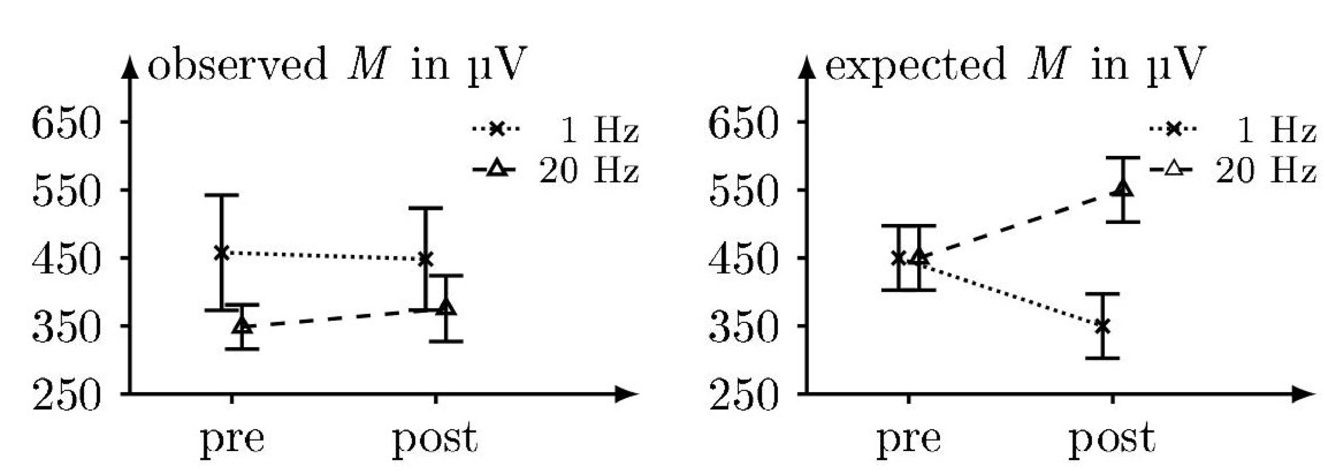

Figure 3. "Frequency" x " within-session time" interaction vs. expectation. Error bars represent standard error. M = Mean.

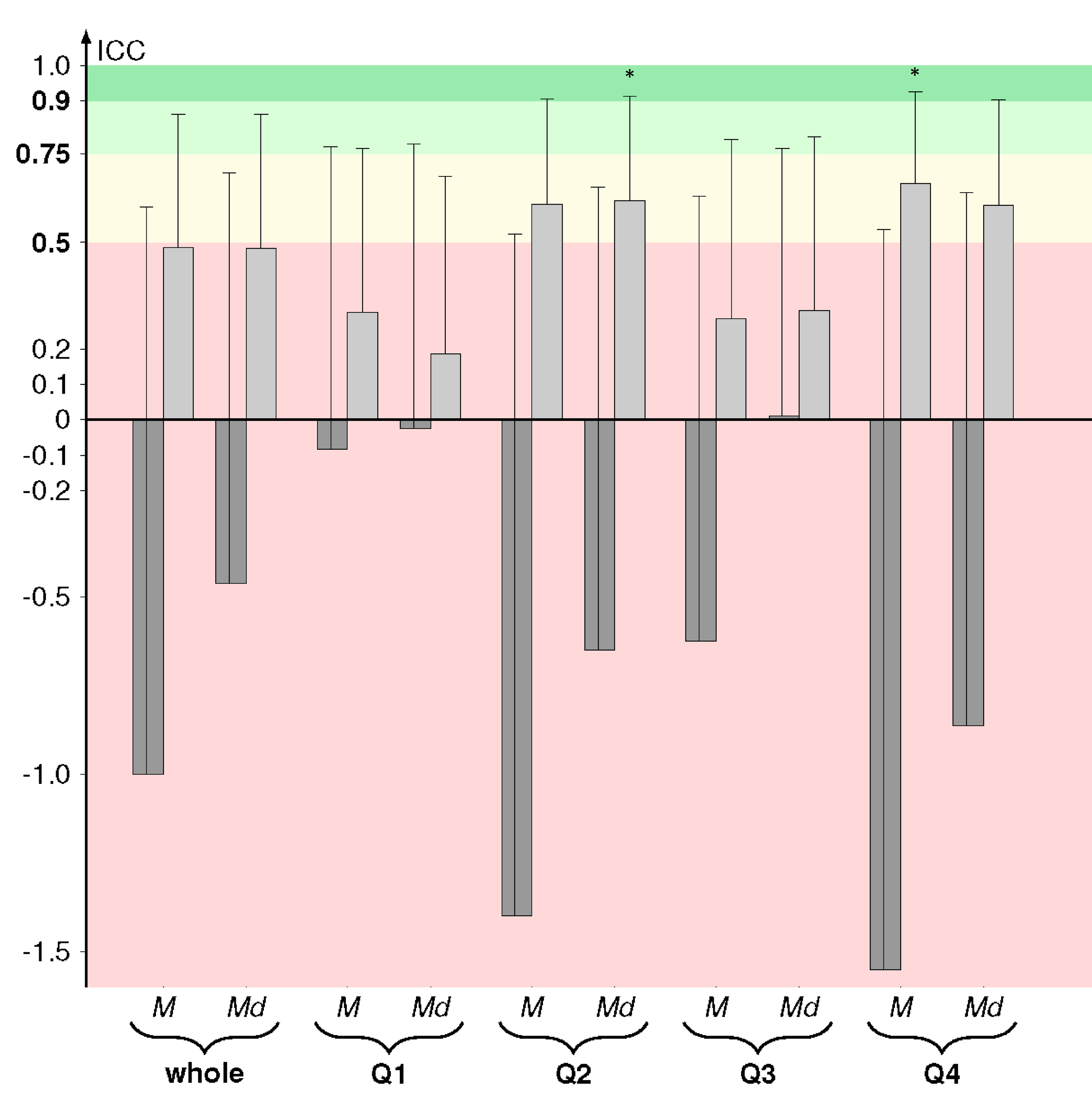

Figure 4. Reliability measure ICC between sessions 1 and 2 from the subsample of participants with at least 75% valid MEPs (n = 9). Error bars represent 95% confidence interval. Asterisks indicate significance after FDR correction.

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modular extended transcranial magnetic stimulation

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