

Repetitive transcranial magnetic stimulation (rTMS) in the treatment of comorbid somatic and psychiatric disorders and maintenance treatment with rTMS

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Disclosures

- ◆ No possessions in medical companies
- ◆ Honoraria for lectures, consultation fees and royalties
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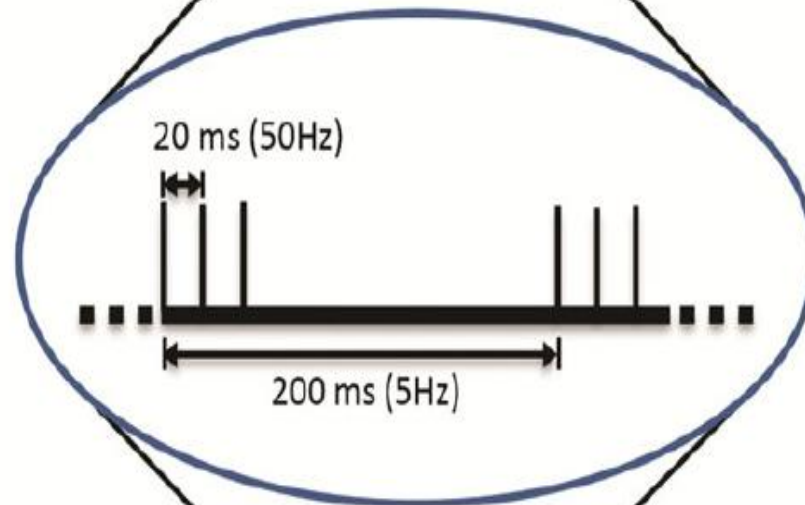
rTMS in comorbid disorders 1

- ◆ Since 2012, we have treated comorbid somatic and psychiatric disorders during the same rTMS-sessions in Turku University Hospital
- ◆ We use navigated, multi-locus rTMS with two or sometimes even three stimulation targets
- ◆ Targets are marked by a specialist in clinical neurophysiology (CN) on the cortical surface of the patients' MRI-image
- ◆ Somatic protocols are planned by a CN and psychiatric protocols by a psychiatrist

The most common targets and protocols

- ◆ Major depression: left BA 46/9 10 Hz or iTBS, right BA 46/9 1 Hz
- ◆ Neuropathic pain: primary target contralateral M1 10 Hz, optional target right parietal operculum ("S2") 10 Hz
- ◆ Anxiety: right BA 46/9 1 Hz
- ◆ Tinnitus: left auditory cortex 1 Hz
- ◆ OCD: bilateral pre-SMA 1 Hz
- ◆ Eating disorder: left BA 46/9 10 Hz or iTBS

cTBS



iTBS

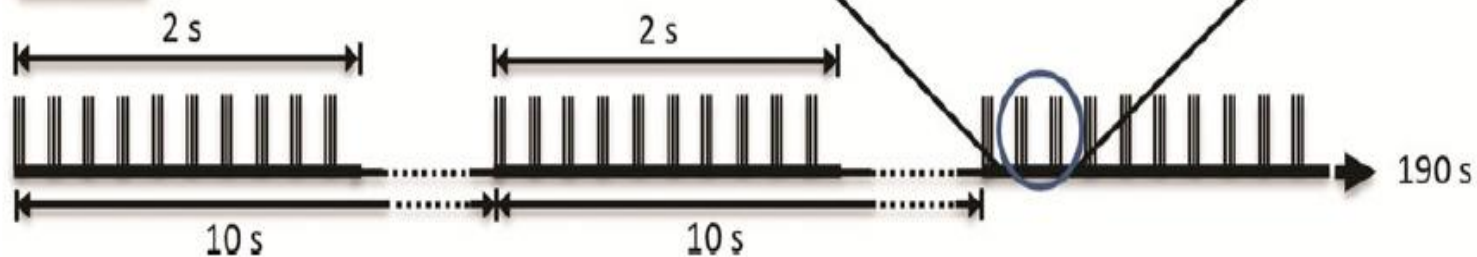
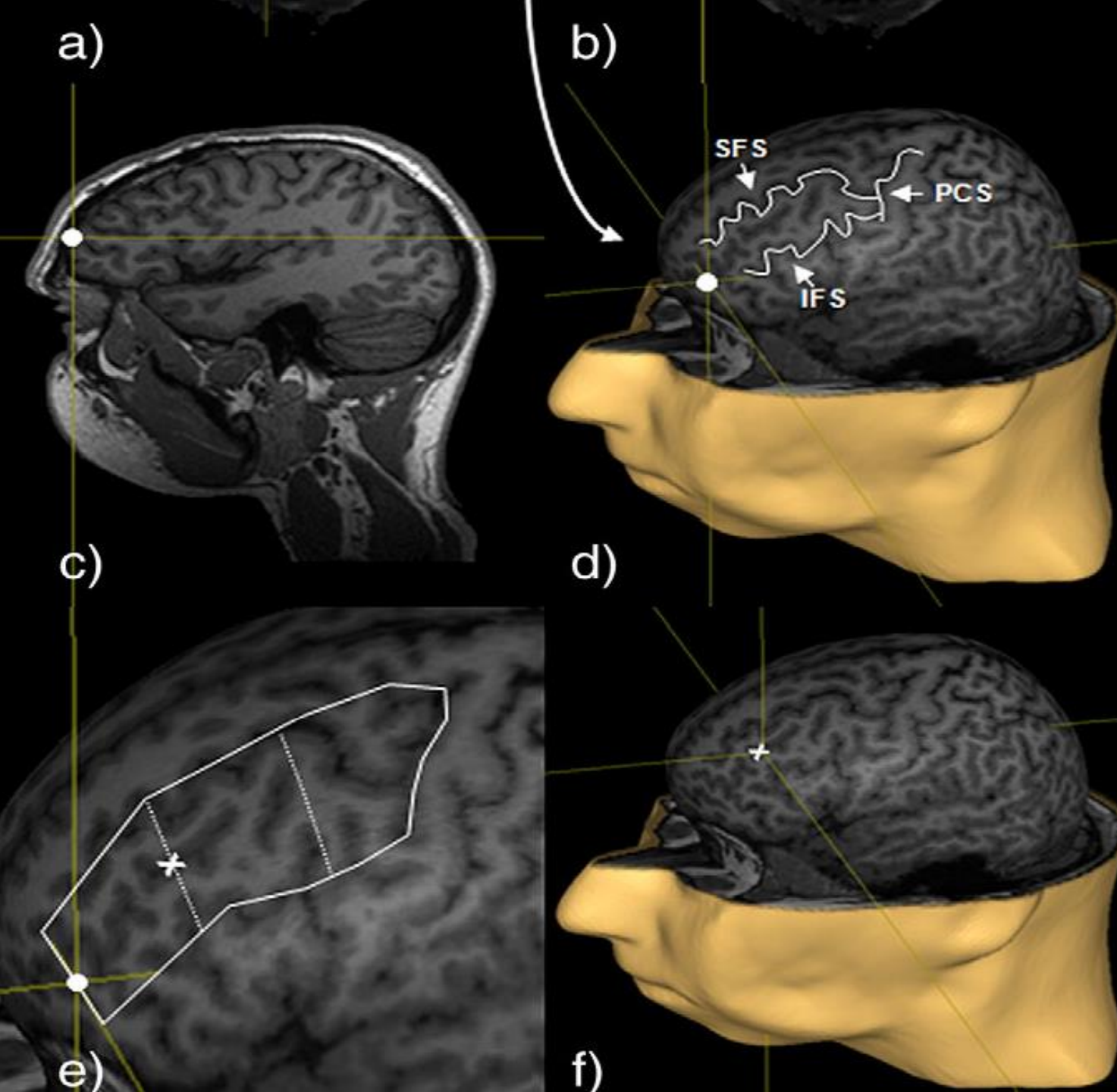


Figure 1. Different TBS protocols. TBS pattern consists of three bursts of pulses given at 50 Hz every 200 ms. When stimulated continuously (cTBS) for either 20 or 40 s, it induces LTD-like effect. However, when stimulated intermittently (iTBS) at 2 s every 10 s for 190 s, it induces LTP-like effect.

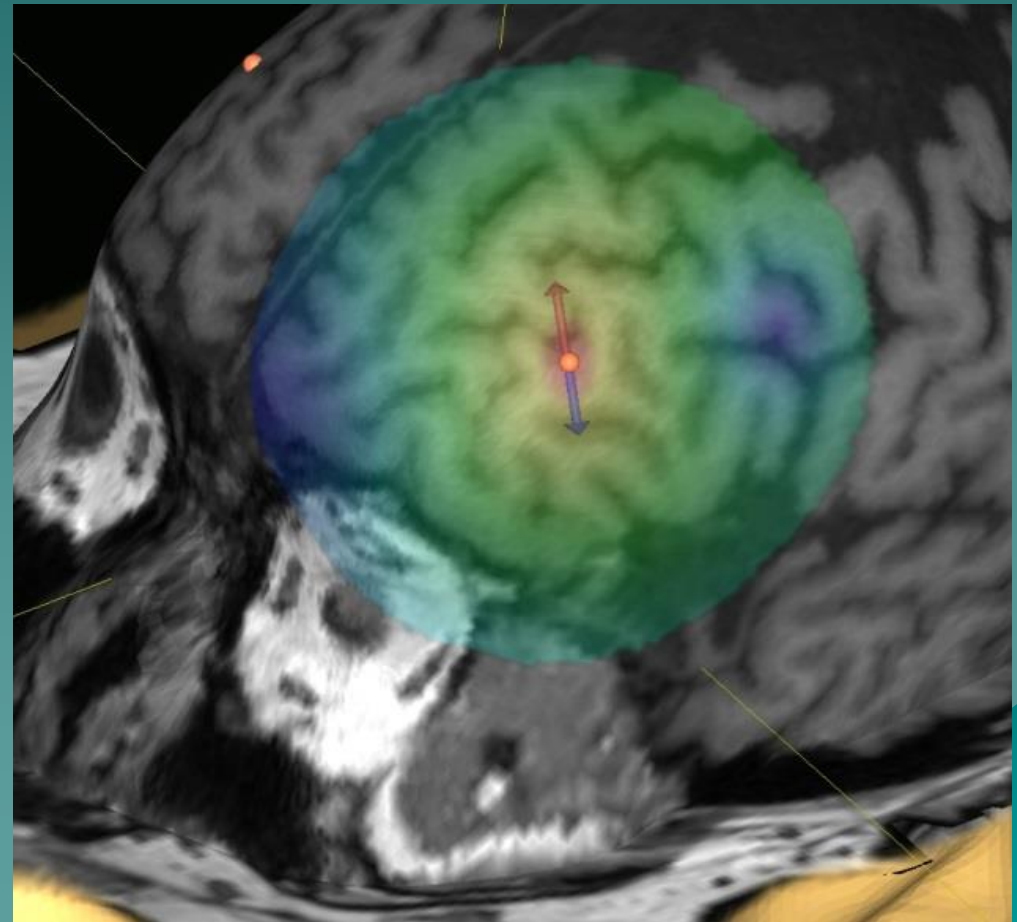
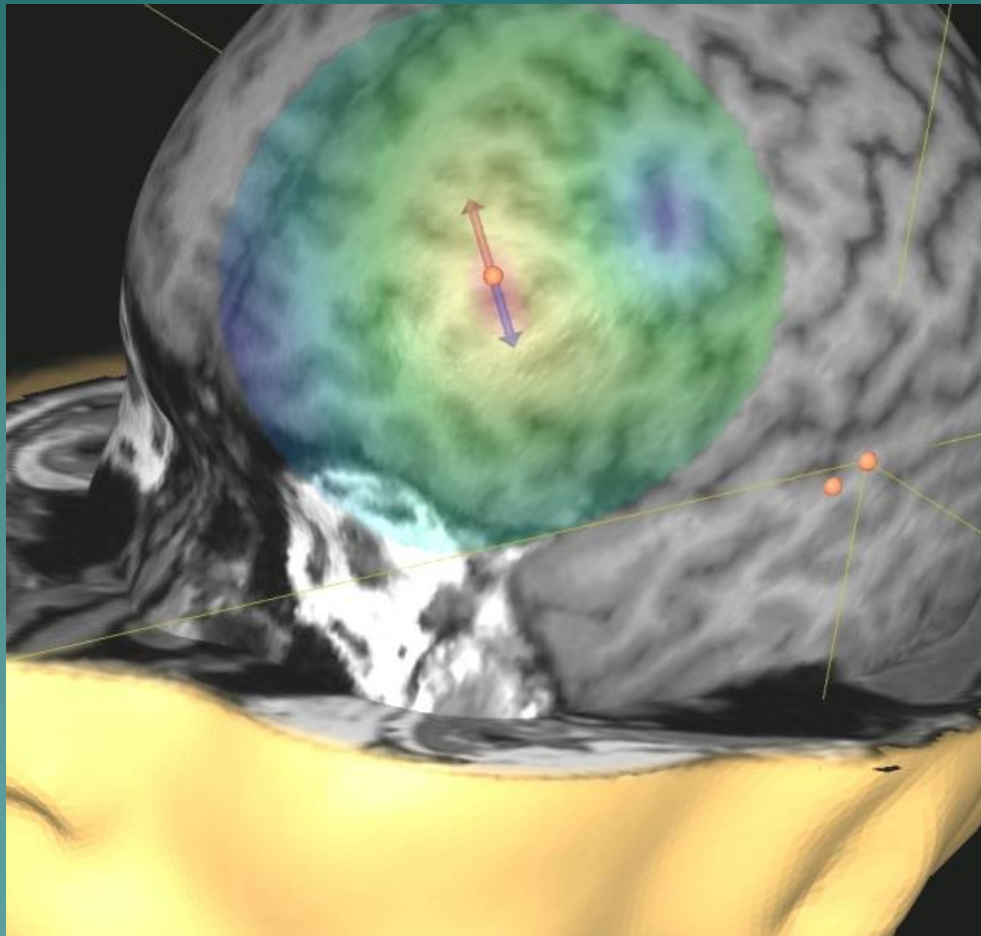
rTMS in comorbid disorders 2

- ◆ Treatment sessions are carried out by psychiatric nurses or CN-technicians
- ◆ We keep a short pause (10 – 15 min) per site, while changing stimulation target during a session, in an attempt to avoid exhaustion of the effects on synaptic transmission
- ◆ We are preparing a small study (N = 31, Jääskeläinen et al.) testing the hypothesis that rTMS response is determined by constitutional factors, and therefore, the patients would either benefit from the treatment in all conditions or not at all

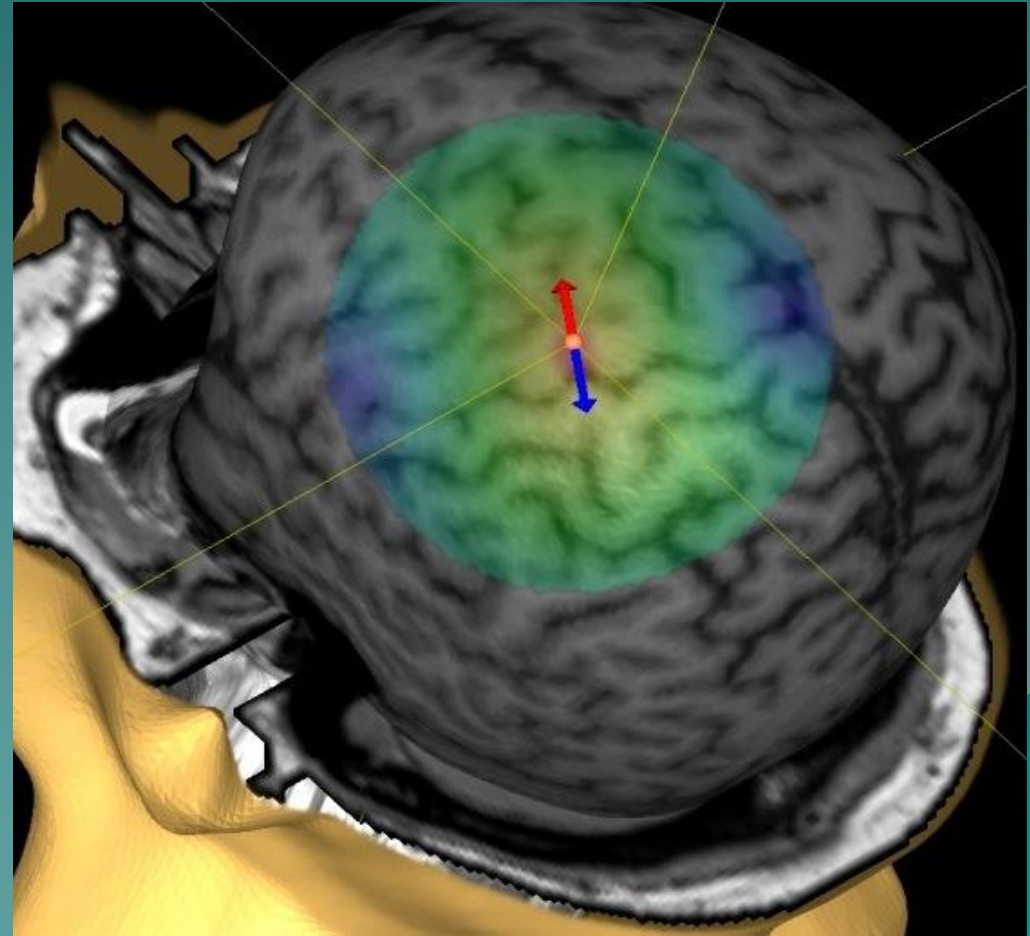
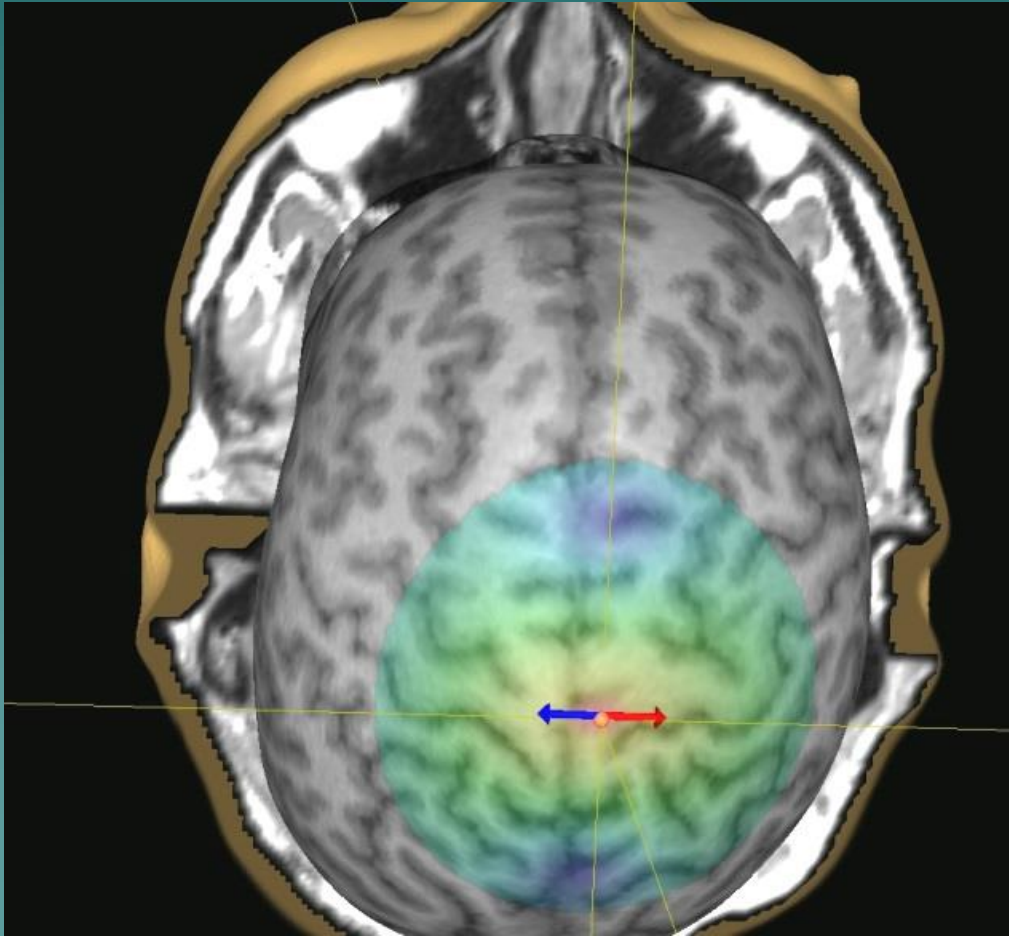


- ◆ Target for major depression : junction between BA9 and BA 46 (Mylius et al. 2013)

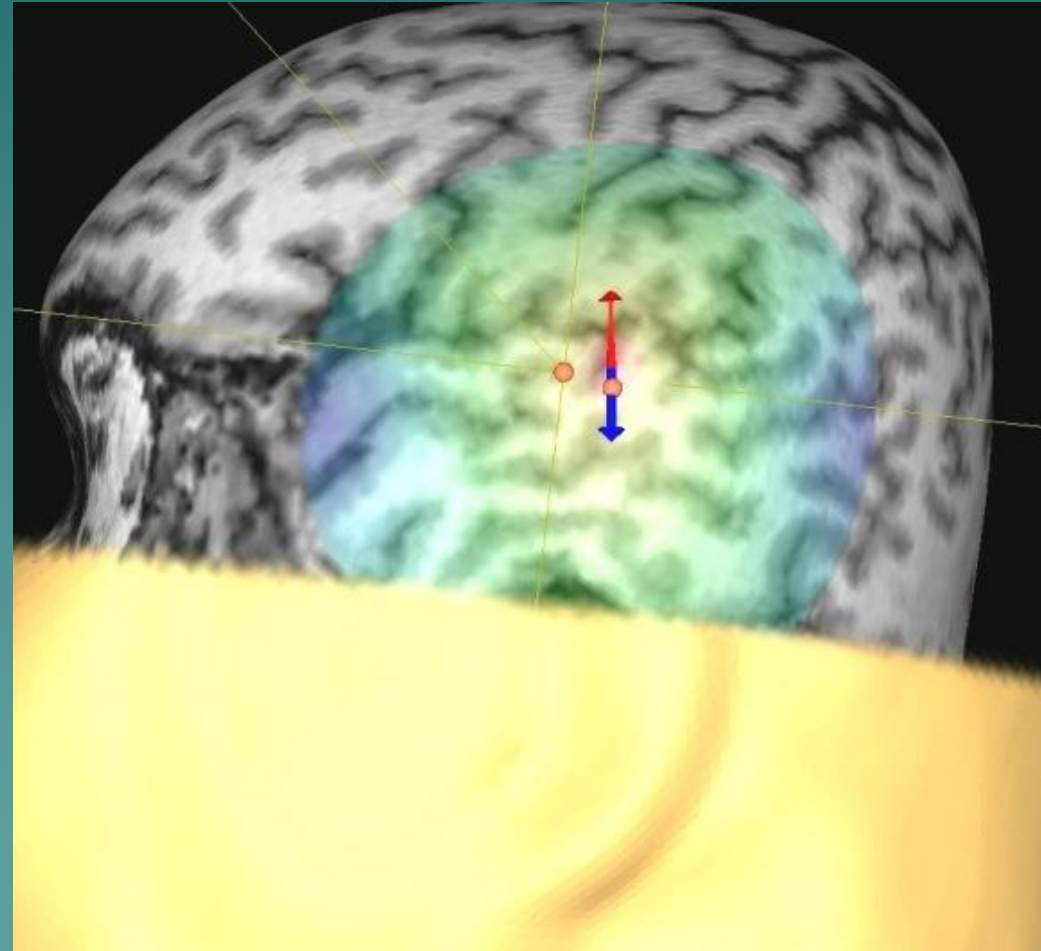
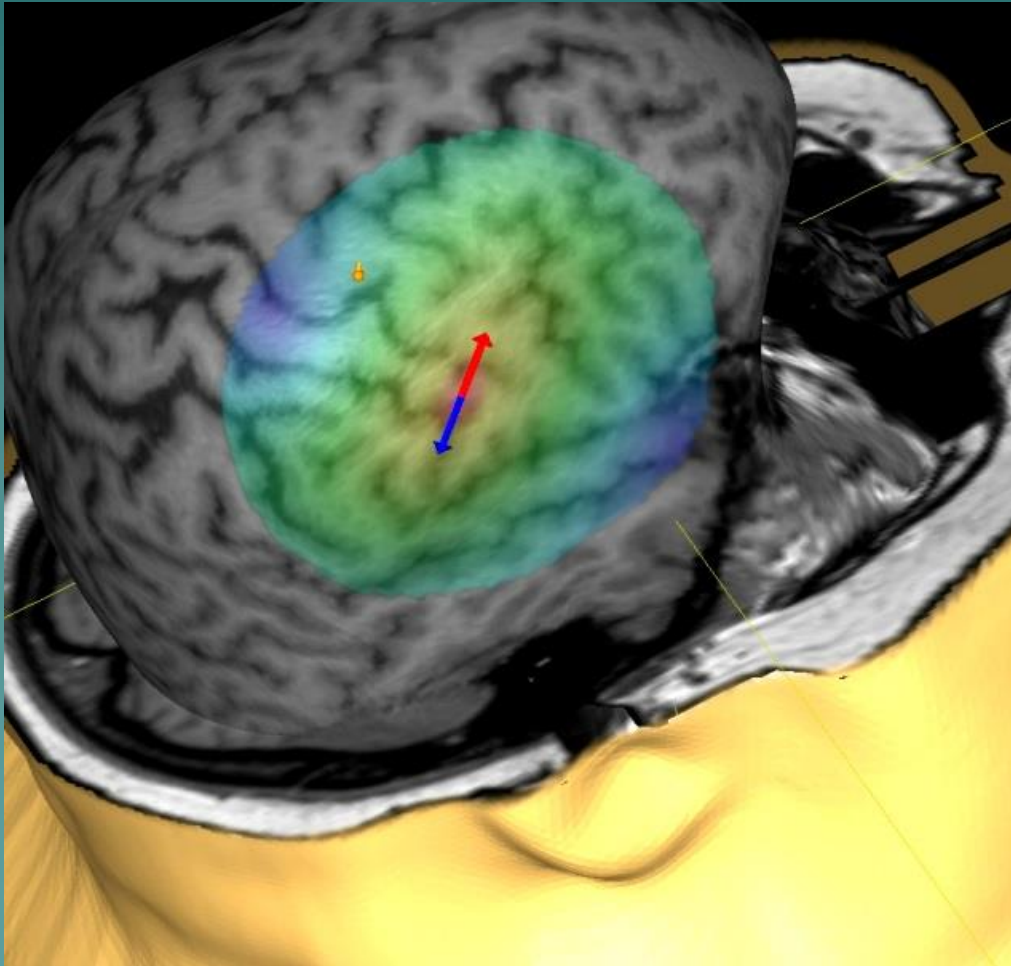
Left BA 46/9 (DLPFC) – target for major depression with either 10 Hz or iTBS



Treatment of neuropathic pain by stimulating M1: on the left, left foot treatment; on the right, right hand treatment by 10 Hz



Left: optional target for neuropathic pain – right parietal operculum (“S2”) Right: target for tinnitus – left superior temporal gyrus (auditory cortex)



rTMS in comorbid disorders 3

- ◆ Both vulnerability to comorbidity (Taiminen et al. 2011) and treatment response (Jääskeläinen et al. 2014) may be partly genetic
- ◆ The most common combination in our clinic has been major depression and neuropathic pain
- ◆ 81 % of patients (N = 31) responded to multi-locus rTMS in at least one indication
- ◆ 74 % of our patients either benefitted in both treatment indications or not at all

Jääskeläinen et al., in preparation, N = 31

Distribution of diagnostic combinations

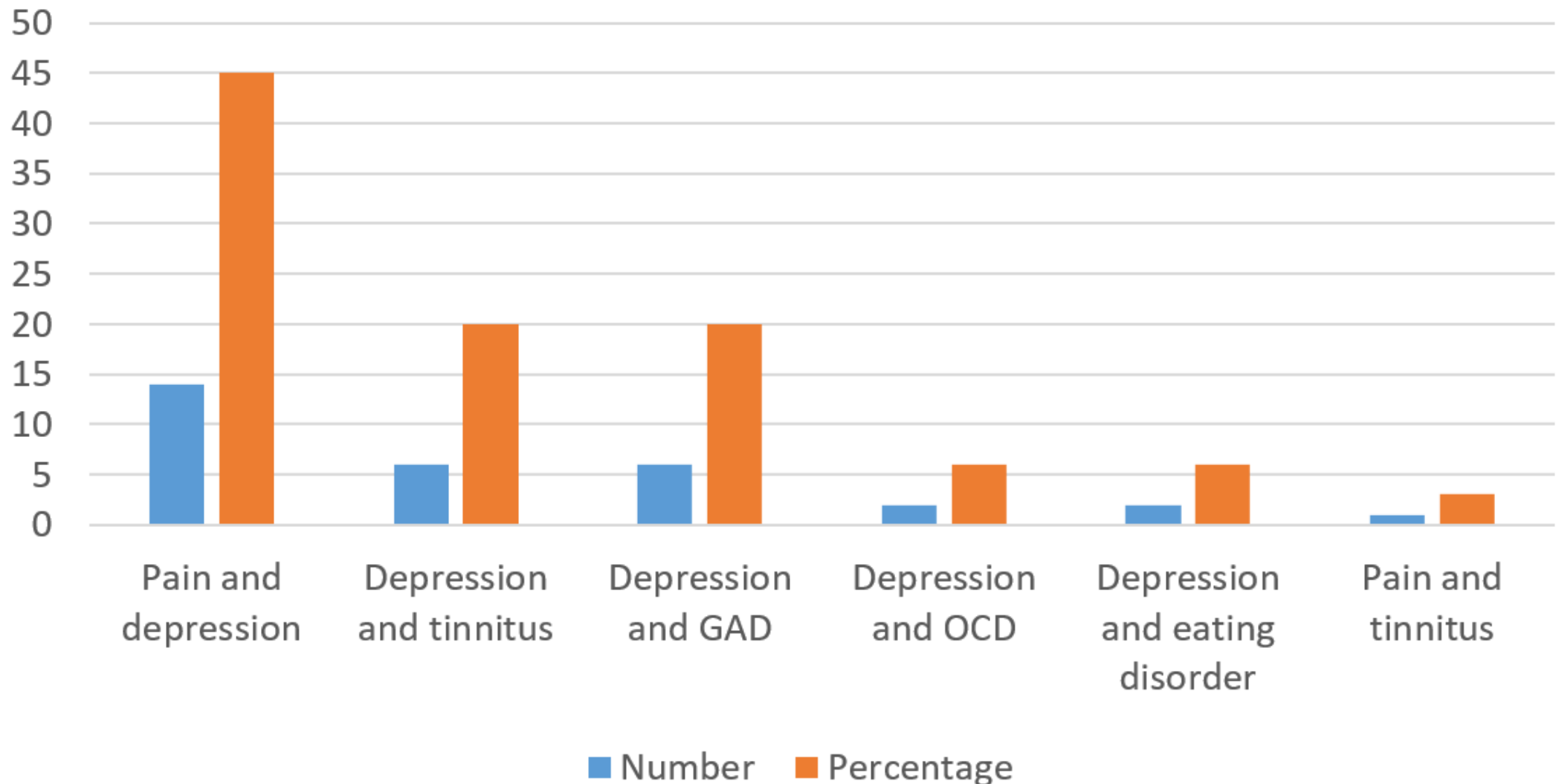
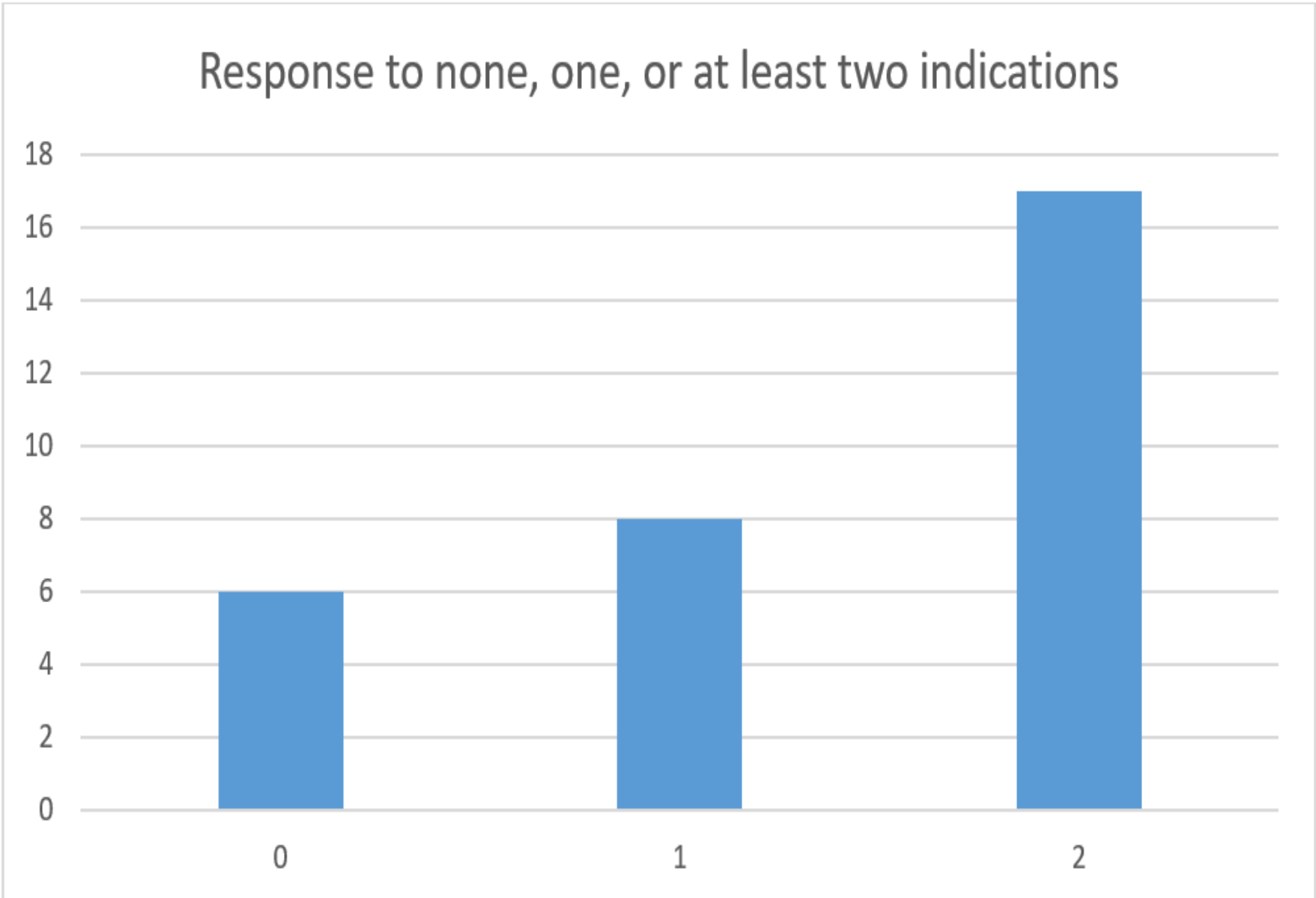
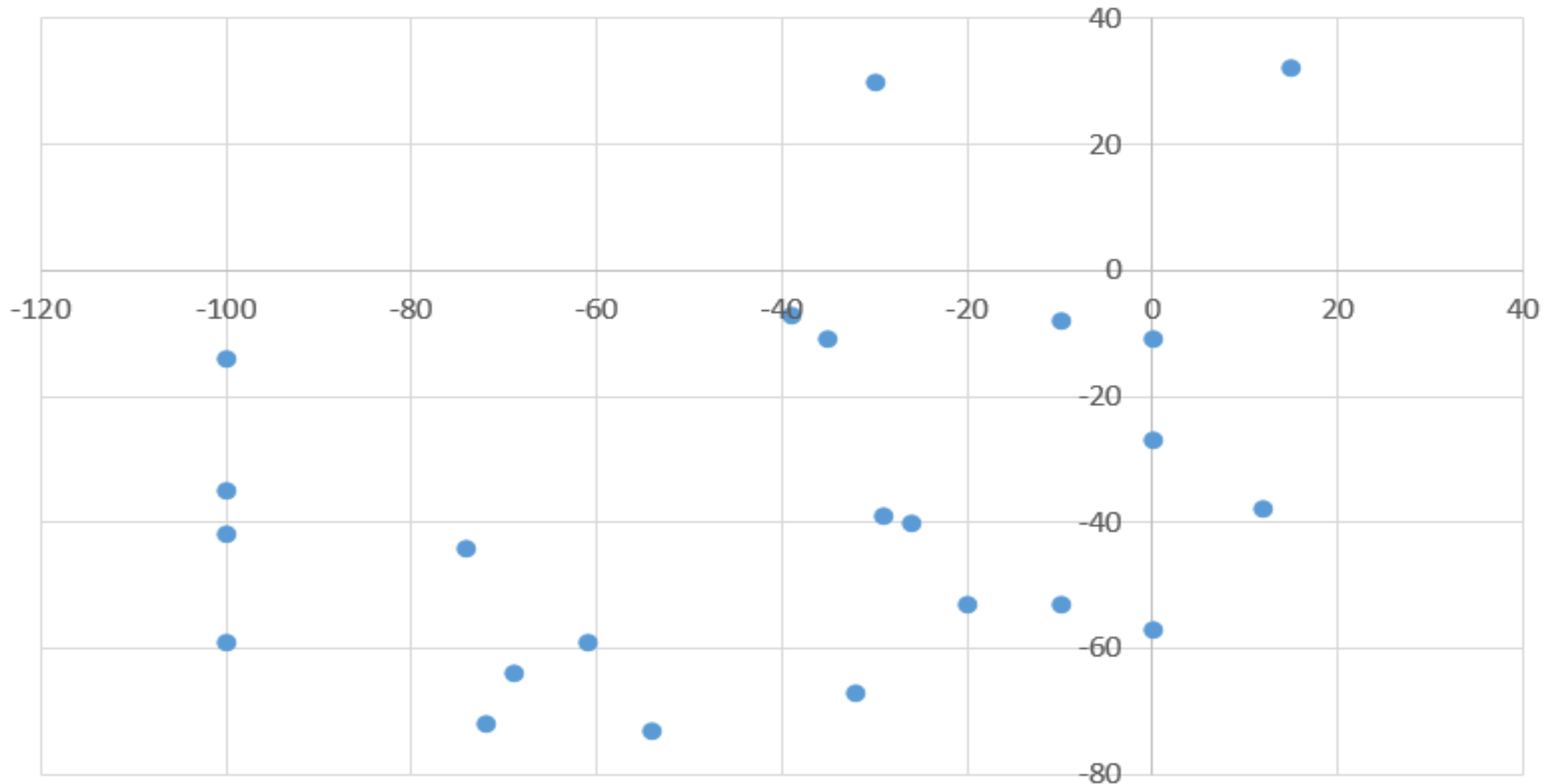


Figure 3. Responders and non-responders in the whole sample (N=31 patients), based on numerical ratings, clinical observations and patients' global impression of change (GIC)



Correlation (Pearson) $r = 0.34$

Response (%) to disease 2 vs disease 1



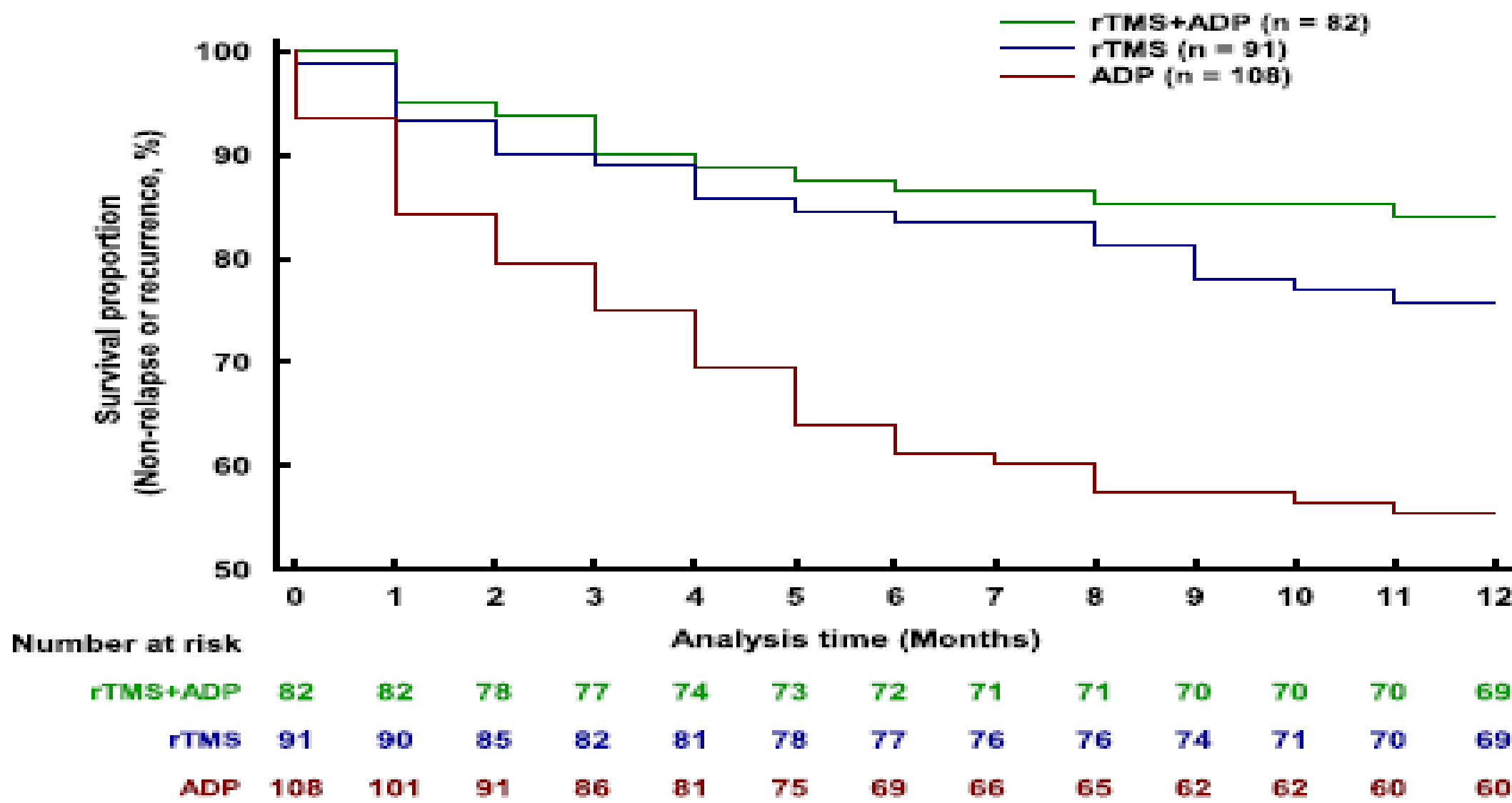
rTMS in comorbid disorders - conclusions

- ◆ Simultaneous rTMS-treatment for somatic and psychiatric disorders is patient-friendly, because positive response seems to be more probable compared to treating only one disorder
- ◆ rTMS-response to one disorder is a strong predictor for a response also to other comorbid disorders
- ◆ Neural plasticity of the brain may be dependent of constitutional factors, independent of the disorder

Prevention of depression relapse – rTMS maintenance treatment?

- ◆ Constant maintenance: session interval from one to two weeks (O'Reardon et al. 2005)
- ◆ Gradual decrease in session frequency, c.f. ECT (Connolly et al. 2012)
- ◆ Clustered maintenance: e.g. 5 sessions during a weekend, once a month (Fitzgerald et al. 2012, Wang et al. 2017)
- ◆ Level of evidence is still B

Clustered (10 X 1100 pulses / 3 – 5 days) relapse prevention vs. medication (Wang ym. 2017)



TRANSCRANIAL DIRECT CURRENT STIMULATION

Some studies show that stimulating the brain with electricity can immediately boost memory, focus, energy, and vigilance. Researchers say that it also shows promise as a means of treating drug-resistant mental illness like depression, as well as conditions like epilepsy and chronic pain. Here's how it works:

ANODE

The anode, or positively charged electrode, can stimulate neuronal activity in different parts of the brain.

CATHODE

The cathode, or negatively charged electrode, can inhibit brain-cell activity.

WIRES

Two electrodes can provide different types of stimulation, depending on where they are placed. Together, they make a complete circuit.

DEVICE

A battery-powered device delivers a constant electrical current of up to 2 mA (milliamperes). Researchers have demonstrated that it's safe to apply this much current for up to 30 minutes a day. DIY brain stimulators frequently use a 9-volt battery as a power source.

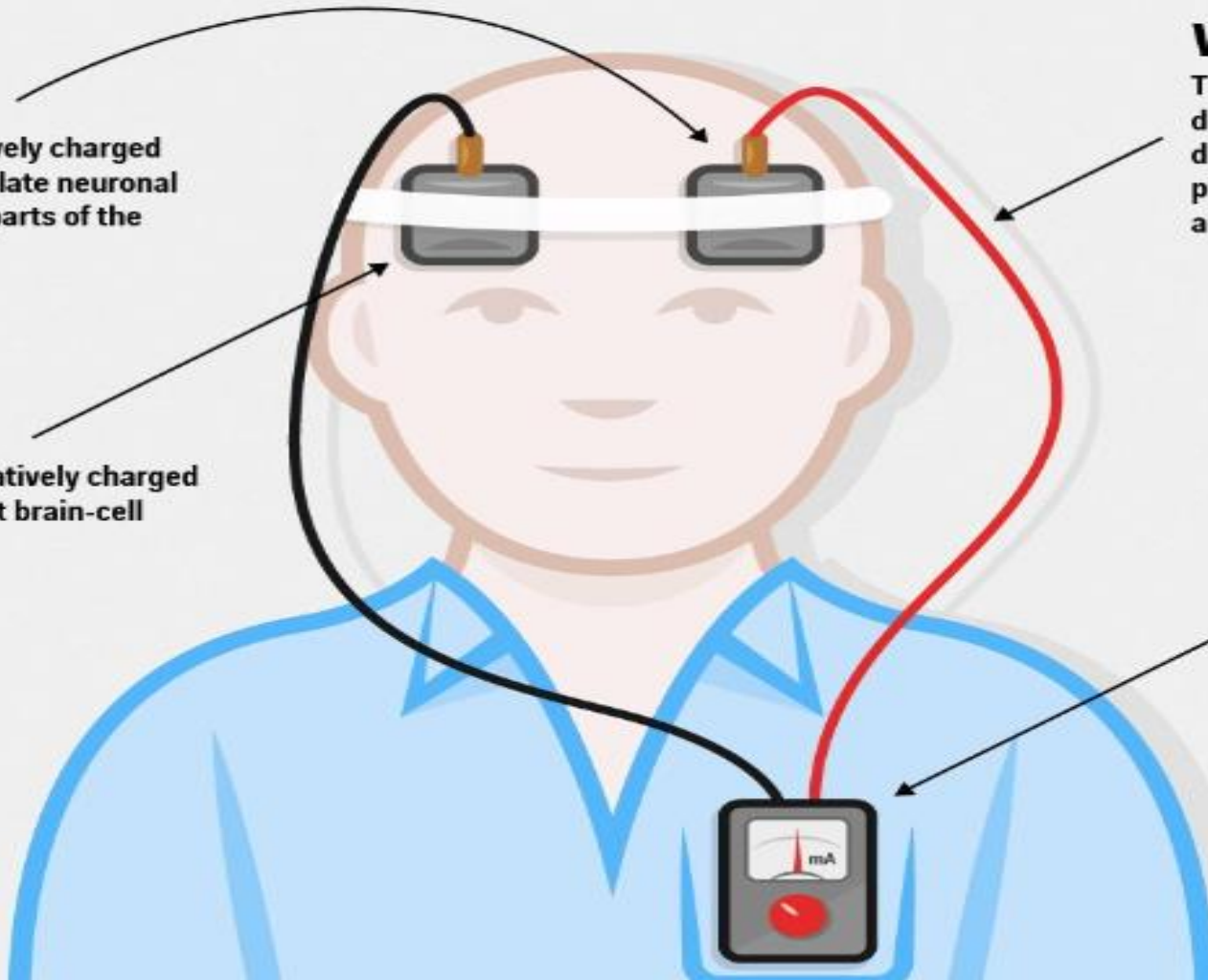
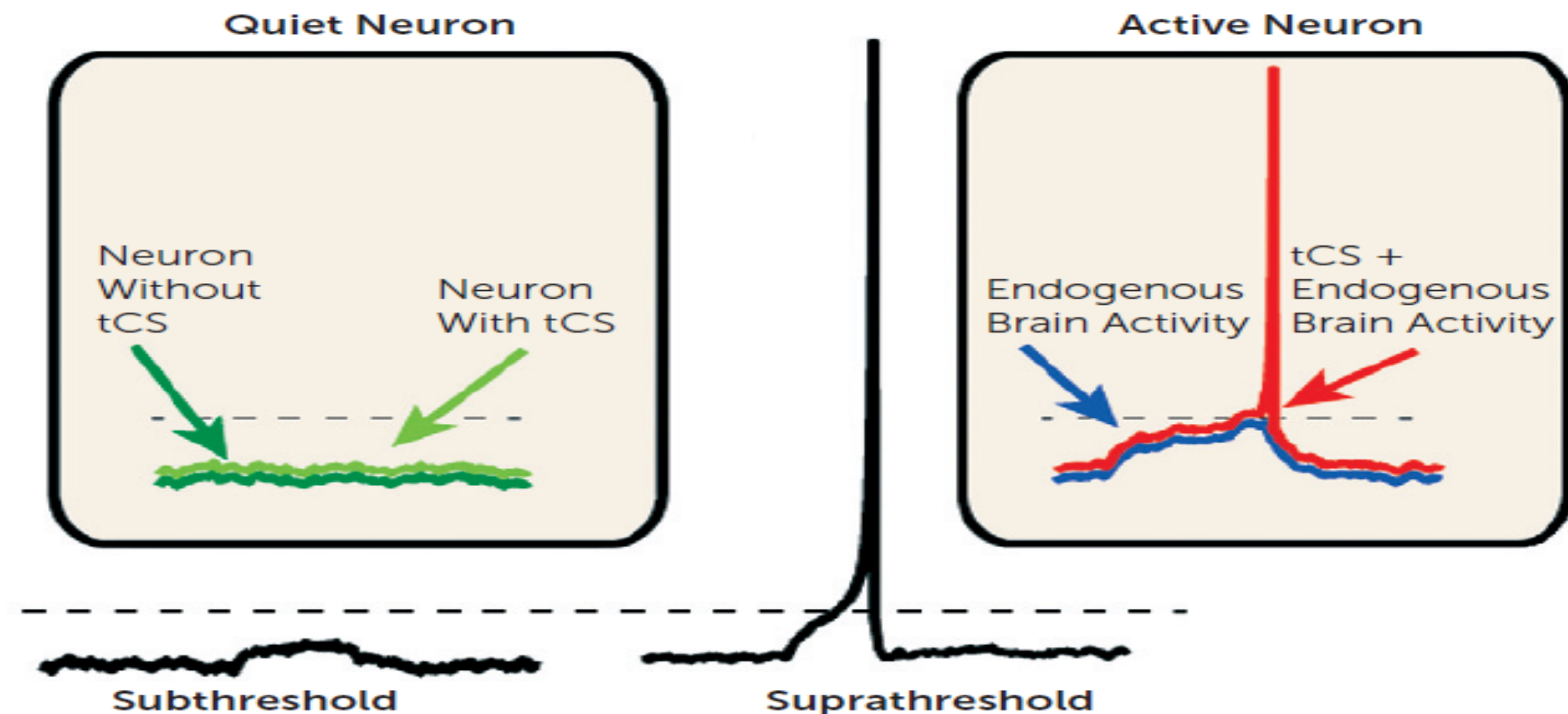
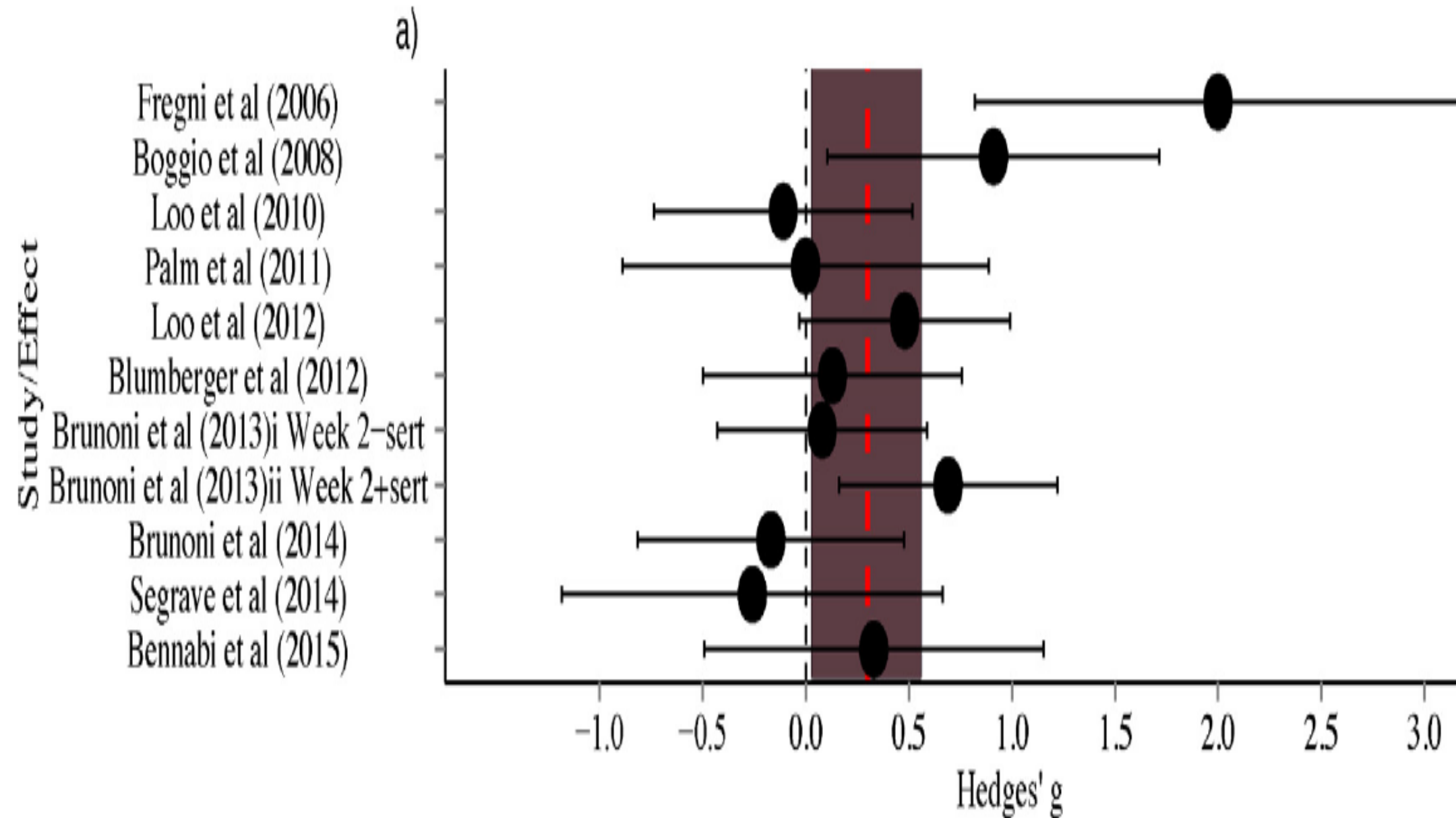


FIGURE 1. Sub- and Suprathreshold Energy Input on Neuronal Action Potentials^a



^a Subthreshold membrane fluctuations are not sufficient to generate an action potential (left). However, if intrinsic fluctuations in a neuron's membrane voltage move it closer to its threshold, application of an inherently subthreshold input, such as low-intensity transcranial current stimulation (tCS), can trigger an action potential (right). Dashed line indicates threshold.

Meron et al. (2015): $g = 0.30$



rTMS maintenance treatment may be replaced by tDCS

- ◆ Our experience in Turku: the majority of weekly or fortnightly rTMS maintenance treatments for depression can be replaced by daily 25 min tDCS
- ◆ tDCS is much cheaper than rTMS
- ◆ tDCS can be carried out by a patient at his or her home