Lasting EEG/MEG Aftereffects of Rhythmic Transcranial Brain Stimulation: Level of Control Over Oscillatory Network Activity

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A number of rhythmic protocols have emerged for non-invasive brain stimulation (NIBS) in humans, including transcranial alternating current stimulation (tACS), oscillatory transcranial direct current stimulation (otDCS), and repetitive (also called rhythmic) transcranial magnetic stimulation (rTMS). With these techniques, it is possible to match the frequency of the externally applied electromagnetic fields to the intrinsic frequency of oscillatory neural population activity (“frequency-tuning”). Mounting evidence suggests that by this means tACS, otDCS, and rTMS can entrain brain oscillations and promote associated functions in a frequency-specific manner, in particular during (i.e., online to) stimulation. Here, we focus instead on the changes in oscillatory brain activity that persist after the end of stimulation. Understanding such aftereffects in healthy participants is an important step for developing these techniques into potentially useful clinical tools for the treatment of specific patient groups. Reviewing the electrophysiological evidence in healthy participants, we find aftereffects on brain oscillations to be a common outcome following tACS/otDCS and rTMS. However, we did not find a consistent, predictable pattern of aftereffects across studies, which is in contrast to the relative homogeneity of reported online effects. This indicates that aftereffects are partially dissociated from online, frequency-specific (entrainment) effects during tACS/otDCS and rTMS. We outline possible accounts and future directions for a better understanding of the link between online entrainment and offline aftereffects, which will be key for developing more targeted interventions into oscillatory brain activity.

Keywords: human brain oscillations, offline aftereffects, transcranial alternating current stimulation, repetitive transcranial magnetic stimulation (rTMS), oscillatory transcranial direct current stimulation, entrainment, LTP/LTP-like plasticity

INTRODUCTION

Oscillatory brain activity is thought to reflect the assembly (i.e., synchronization) of neuronal elements into functional networks as an essential component of information processing (e.g., Bütszák, 2006) and has been suggested to play a mechanistic role in normal function (e.g., Fries, 2005; Wang, 2010; Thut et al., 2012; Lopes da Silva, 2013) and dysfunction of the brain (e.g.,...
Schnitzler and Gross, 2005; Uhlhaas and Singer, 2015). This has sparked an interest in specifically interacting with oscillatory activity by means of rhythmic non-invasive brain stimulation (NIBS). Protocols that are promising in this regard are transcranial alternating current stimulation (tACS), oscillatory transcranial direct current stimulation (otDCS), and repetitive/rhythmic transcranial magnetic stimulation (rTMS) (see Box 1). Despite the different mechanisms by which tACS/otDCS and rTMS exert their effect on the brain (weak electrical currents vs. stronger magnetic pulses; see Box 1), there is growing evidence that either technique can be used to impose a rhythmic structure on the underlying brain activity. Recordings in vitro and in vivo have shown that during (i.e., online to) rhythmic electromagnetic stimulation, neuronal spiking activity phase-aligns with the applied periodic electromagnetic force (Fröhlich and McCormick, 2010; Ozen et al., 2010; Ali et al., 2013; see also Reato et al., 2010 and review by Reato et al., 2013b). Converging evidence from human research confirms that, during stimulation, oscillatory brain activity as measured with electroencephalography (EEG) and more recently with magnetoencephalography (MEG), phase-locks to rhythmic trains of stimulation (tACS: Helfrich et al., 2014b; Witkowski et al., 2015; rTMS: Thut et al., 2011b; Romei et al., 2015; see also Rosanova et al., 2009; Herring et al., 2015 for phase-locking to single pulse TMS). Hence, the electromagnetic force can be used to entrain, or synchronize, intrinsic brain oscillations (for reviews see: rTMS: Thut et al., 2011a; tACS: Herrmann et al., 2013; Fröhlich, 2015; otDCS: Marshall and Binder, 2013). Notably, such entrainment effects are more pronounced when the frequency of stimulation coincides with the dominant frequency of the stimulated neurons/areas (Ozen et al., 2010; Ali et al., 2013; Reato et al., 2013b; Schmidt et al., 2014; Romei et al., 2015), suggesting that frequency tuning constitutes a means for interacting with intrinsic neuronal network activity with some specificity. Besides these electrophysiological entrainment effects, corresponding changes in behavioral performance during stimulation have been reported. These consist of oscillatory patterns in performance measures imposed by rhythmic stimulation, or behavioral performance being biased in expected directions when the stimulation frequency matches known, task-related brain oscillations. For tACS/otDCS, such behavioral effects have been shown in various domains including perception (e.g., Feura et al., 2011; Laczó et al., 2012; Neuling et al., 2012a; Brignani et al., 2013; Strüber et al., 2014; Helfrich et al., 2014a,b; Riecke et al., 2015), decision making (e.g., Sela et al., 2012), crossmodal integration (e.g., Cecere et al., 2015), motor control (e.g., Pogosyan et al., 2009; Joudi et al., 2012), and memory/cognition (e.g., Polania et al., 2012; Santar necchi et al., 2013; Vosskuhl et al., 2015). Analogous examples exist for rTMS (Romei et al., 2010, 2011, 2012; Chanes et al., 2013; Hanslmayr et al., 2014; Jaegle and Ro, 2014; Ruzzoli and Soto-Faraco, 2014; Quentin et al., 2015). This shows that tACS/otDCS and rTMS are viable tools to exert control over both brain oscillations and their associated functions. As a consequence, guiding online tACS/otDCS or rTMS by knowledge of task-related oscillatory brain activity may be a promising approach to enhance the specificity and effectiveness of interventions. In addition to these well-documented online effects, prolonged stimulation with tACS/otDCS or rTMS often leads to offline changes in oscillatory brain activity that persist after the end of stimulation. However, oscillations that are entrained during rhythmic stimulation have been reported to remain stable only for maximally a few oscillatory cycles after stimulation offset (Marshall et al., 2006; Reato et al., 2013a, same data; Thut et al., 2011b; Hanslmayr et al., 2014). These short-lived post-tACS/rTMS reverberations that show phase-locking to the entraining field have also been termed “entrainment-echoes” (Hanslmayr et al., 2014). On the other hand, many of the offline effects on brain oscillations can be observed over much longer durations (for TMS, e.g., Thut and Pascual-Leone, 2010; for tACS, e.g., Zaehele et al., 2010), and may not simply reflect continuation of online entrainment. We refer here to these longer lasting offline effects as aftereffects.

One important open question is if and to what extent aftereffects on brain oscillations relate to entrainment effects observed during stimulation (e.g., Vossen et al., 2015). Given that entrainment dominates the online EEG recordings for stimulation at physiological frequencies (e.g., Thut et al., 2011b; Helfrich et al., 2014b; Romei et al., 2015), it is conceivable that some of these aftereffects are conveyed through direct interaction with brain oscillations that match the frequency of stimulation. This would imply that control over oscillatory brain activity during stimulation through entrainment transfers to some extent to the changes observed after stimulation. If this is the case, aftereffects should predominate in narrow frequency bands that match the stimulation frequency and its harmonics or subharmonics (Ali et al., 2013), or extend to other frequency bands through known physiological cross-frequency interactions (e.g., alpha-gamma, Spak et al., 2012). Alternatively, aftereffects of tACS/otDCS and rTMS on brain oscillations may originate in other mechanisms unrelated to interaction with brain oscillations per se. In this case, stimulation would be expected to generate broadband modulations, or effects at frequencies that have no direct or indirect relationship with the stimulation frequency.

Here, we review EEG/MEG studies on changes in oscillatory brain activity after tACS/otDCS and rTMS. In light of the well-documented online entrainment effects that suggest direct and frequency-specific interactions with oscillatory brain activity, we ask to what extent a similar level of control over oscillatory activity and associated behavioral effects can be achieved beyond stimulation. To this end, we surveyed the literature for patterns of aftereffects in favor or against the hypothesis that direct interactions with oscillatory brain activity are at their origin. Because of the analogy between tACS/otDCS and rTMS in terms of evidence for online entrainment, we here considered studies that applied either type of stimulation, despite the differences in basic physiological mechanisms (see Box 1), and despite the rTMS field traditionally guiding the frequency of interventions not based on brain oscillations but on protocols known to induce either long term potentiation (LTP) and long-term depression (LTD) (e.g., Thickbroom, 2007).

We selected those tACS, otDCS, and rTMS studies that investigated EEG/MEG-aftereffects in healthy participants in terms of changes in power or connectivity (e.g., interhemispheric...
coherence) for at least 1 min following stimulation, i.e., when entrainment-echoes likely have ceased. In the following, we will refer to these lasting changes (regardless of the specific measure used) as aftereffects unless otherwise specified. For details please refer to the corresponding Table 1 (tACS/otDCS) and Table 2 (rTMS). Because of our focus on brain oscillations, we did not include studies that used other valuable measures to characterize aftereffects, such as motor evoked potential (MEP) (e.g., Moliadze et al., 2012) or behavioral outcomes (e.g., Laczó et al., 2012), but did not record EEG/MEG. According to the above criteria, we identified 22 tACS/otDCS studies (Table 1, total of 33 experiments) as well as 26 rTMS studies (Table 2, total of 33 experiments) investigating EEG/MEG-aftereffects. We asked three questions: How consistently are aftereffects on brain oscillations reported across studies? Do these aftereffects show replicable patterns across experiments that suggest direct interactions with brain oscillations as their origin (including effects on intrinsic activity at stimulation frequency and/or its (sub)harmonics, or through known cross-frequency interactions)? And to what extent do such aftereffects translate into predictable behavioral consequences?

**HOW CONSISTENTLY ARE AFTERRFECTS ON BRAIN OSCILLATIONS REPORTED?**

**tACS/otDCS Studies**

Oscillatory transcranial electrical stimulation is often accompanied by aftereffects on neural synchrony (Table 1). Of the 22 tACS/otDCS studies included, only three did not report any significant aftereffects (Antal et al., 2008; Krause et al., 2013 in their healthy control group; Strüber et al., 2015). The respective null effects might be explained by insufficient stimulation intensity (Antal et al., 2008), population differences between Parkinson’s disease patients and healthy control participants (Krause et al., 2013), or insufficient stimulation duration (Strüber et al., 2015). All other studies report at least one change in one measure of oscillatory activity (power/coherence, or relative changes thereof).

In terms of duration of tACS/otDCS aftereffects, only few data are available as analyses were mostly restricted to short stimulation-free intervals between successive blocks of stimulation (Marshall et al., 2006; Antonenko et al., 2013; Eggert et al., 2013; Garside et al., 2015), and/or to maximally 3 min after stimulation (Zaehle et al., 2010; Neuling et al., 2012a; Strüber et al., 2014; Helfrich et al., 2014b; Vossen et al., 2015). In those studies that looked at slightly longer intervals, durations of aftereffects are variable, ranging between a few minutes (Chaieb et al., 2014) up to about half an hour (Kirov et al., 2009; Neuling et al., 2013; Wach et al., 2013; Helfrich et al., 2014a), but appear to subside by 60 min after stimulation at the latest (Kirov et al., 2009; Marshall et al., 2011; Sahlem et al., 2015), although in one exception changes only manifested over the course of several hours (Reato et al., 2013a). Notably, aftereffects have also been found to rebound, i.e., an initial power suppression may turn into a power enhancement (Marshall et al., 2011). In addition, analyses of inter-stimulation periods during otDCS revealed that changes observed early into stimulation may wear off before the end of total stimulation time (Marshall et al., 2006; Kirov et al., 2009; Antonenko et al., 2013) or even reverse (Garside et al., 2015), suggesting that homeostatic mechanisms might actively work against aftereffects.

**rTMS-Studies**

For rTMS, aftereffects on brain oscillations are frequently reported as well (Table 2), as only four out of the 26 studies did not report aftereffects (Graf et al., 2001; Grossheinrich et al., 2009 in three out of four experiments; McAllister et al., 2011; Weisz et al., 2014).

Similar to tACS/otDCS, evaluating the duration of the rTMS aftereffects is difficult as the 22 studies reporting significant aftereffects covered different time windows, ranging from a few minutes (Capotosto et al., 2014) to 65 min after stimulation (Schutter et al., 2001), with only eight studies recording brain oscillations in the analysis. Overall, rTMS aftereffects on brain oscillations thus appear to be more variable in duration compared to tACS/otDCS aftereffects. This may be explained by differences in stimulation parameters such as frequency, intensity, target area, etc., and might call for future studies investigating rTMS aftereffects in conjunction with tACS/otDCS to elucidate underlying mechanisms.
| ID/study                  | Method | Stimulation frequency | Montage       | Protocol                                                                 | Effects at stimulation frequency                          | Effects in other frequency bands              | Recording time                                      | Duration of aftereffect |
|--------------------------|--------|-----------------------|---------------|--------------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------|--------------------------------------------------|------------------------|
| 1. Garside et al., 2015  | tACS   | δ 0.75                | F3/F4         | 5 × 5' stimulation with 1-min intervals during sleep; 0.55 mA            | Yes (broadband); suppressed power increase followed by rebound | No                                            | Only 1 min intervals after each stimulation block assessed | At least 1 min          |
| 2. Eggert et al., 2013   | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 1.1) | 5 × 5' with 1' intervals during sleep; 0.26 mA                         | Maybe (n.s.) δ (broadband); power decrease                 | No                                            | Only 1 min intervals after each stimulation block assessed | At least 1 min          |
| 3. Sahlem et al., 2015   | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 0.5) | 5 × 5' with 1' intervals during sleep; 0.6 mA                          | Maybe (n.s.) a: power increase                             | Maybe (n.s.) α: power increase                  | 1 min intervals after each stimulation block and up to 60 min after stimulation | n.s.                   |
| 4. Marshall et al., 2006 | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 0.5) | 5 × 5' with 1' intervals during sleep; 0.26 mA                         | Yes Slow and maybe broadband δ: power increase              | Maybe (n.s.) α: slow spindle activity increase | Max. 1 min after each stimulation block assessed | Only 1st of 5 1 min interstimulation intervals |
| 5. Reato et al., 2013a   | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 0.5) | 5 × 5' with 1' intervals during sleep; 0.26 mA                         | Slow δ: slower decay rate of power/coherence               | Not analyzed                                    | 4.5 h Prolonged changes over the course of 4.5 h    |                       |
| 6. Kirov et al., 2009 (Exp. 1) | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 0.5) | 5 × 5' with 1' intervals during sleep; 0.26 mA                         | Yes Slow δ: power increase                                  | 1 min intervals after each stimulation block and after 30/60 min | Only during 1 min intervals and immediately after stimulation but not 30 or 60 min later |                       |
| 7. Antonenko et al., 2013 | otDCS  | δ 0.75                | F3/F4 (A)/ipsi. mastoids (4 x 0.5) | 5 × 5' with 1' intervals during task; 0.26 mA                         | Yes Slow δ: power increase                                  | Yes β: power increase                           | 1 min intervals after each stimulation block and after 30/60 min | Only during 1 min intervals and immediately after stimulation but not 30 or 60 min later |
| 8. Vosskuhl et al., 2015 | tACS   | δ/θ below ITF         | FPz/Pz (35/35) | 3 × ~6' during cognitive task; 0.4–1.3 mA                                | Yes δ: power increase                                      | Not analyzed                                    | At least up to 10 min                             |                       |
| 9. Pahor and Jaušovec, 2014 | tACS   | θ IAF-5                | F3/Fp2 (35/70) | 5' during rest; 1–2.25 mA                                               | Yes θ: ERD increase                                         | Yes Lower α: power decrease ERD increase         | At least up to 25 min                             |                       |
| “                        |        | “                     | P3/Fp2 (35/70) | “                                                                       | Yes θ: power increase                                      | Yes Lower α: power decrease ERD increase         | “                                              | “                      |
| ID/study          | Method | Stimulation frequency | Montage      | Protocol                                                                 | Effects at stimulation frequency | Effects in other frequency bands                                                                 | Recording time | Duration of aftereffect |
|------------------|--------|-----------------------|--------------|--------------------------------------------------------------------------|----------------------------------|--------------------------------------------------------------------------------------------------|----------------|-------------------------|
| 10. Marshall et al., 2011 | otDCS  | θ 5                   | F3/F4 (A)/ips; mastoids (4 x 0.5) | 5 x 5' with 1' intervals during NREM sleep; 0.26 mA                       | No                               | Yes broadband θ power decrease                                                                  | During 1 min intervals and immediately after stimulation, and after 30/60 min | At least 1 min but followed by rebound within 30 min, no difference after 60 min |
| 11. Vossen et al., 2015 | tACS   | α IAF                 | PO7/9/PO8/10 (35/35) | 11–15’ (intermittent 3 or 8 s on/off pattern) during task; 1.35–2mA         | Yes                              | α: power increase                                                                              | No             | Within 2 min after stimulation | At least 2 min |
| 12. Zaehle et al., 2010 | tACS   | α IAF                 | PO9/PO10 (35/35) | 10’ during task; 0.8–3mA                                                  | Yes                              | Not analyzed                                                                                   | No             | Within 3 min after stimulation | At least 3 min |
| 13. Strüber et al., 2015 | tACS   | α IAF                 | Cz/Oz (35/35) | 10’ (intermittent 1 s on, 4–7 s off pattern) during task; 0.76 (± 0.30) mA | No                               | No                                                                                             | No             | Only between intermittent tACS epochs | – |
| 14. Neuling et al., 2013 | tACS   | α IAF                 | Cz/Oz (35/35) | 20’ during task w/eyes open; ~1.5 mA                                      | Yes                              | α: power increase                                                                              | No             | 30 min | At least 30 min |
| 15. Helfrich et al., 2014b | tACS   | α 10                  | Cz/Oz (35/35) | 20’ during task; 0.8–1 mA                                                  | Yes                              | α: coherence increase                                                                          | No             | Within 3 min after stimulation | At least 3 min |
| 16. Neuling et al., 2012a | otDCS  | α 10                  | T7/T8 (A) (35/35) | 2 x 21’ (on 2 days) during task; ~45 mA AC modulation +1 mA DC offset     | Yes                              | δ: power increase                                                                              | Yes            | Within 3 min after stimulation | At least 3 min |
| 17. Wach et al., 2013 | tACS   | α 10                  | leftM1/ right orbit (35/35) | 10’ during rest; 1mA                                                      | No                               | Yes y: decrease in cortico-muscular coherence during isometric contraction                     | 38 min         | At least 38 min |
| 18. Krause et al., 2013 | tACS   | β 20                  | leftM1/ right orbit (35/35) | 15’ during rest; 1mA                                                      | No                               | Not analyzed                                                                                    | Between 5 and 13 min after stimulation | – |
| 19. Strüber et al., 2014 (Exp. 1) | tACS   | γ 40                  | P7-PO7/P8- PO8 (35/35) | 15’ during task, anti-phase; 1.02 ± 0.62 mA                               | Yes                              | Not analyzed                                                                                    | Within 3 min after stimulation | At least 3 min |
| 17. Wach et al., 2013 (Exp. 2) | tACS   | β 6                   | “             | 15’ during task, anti-phase; 0.50 (±0.19) mA                              | No                               | No                                                                                             | “             | “ | – |

(Continued)
activity up to recovery (Serrien et al., 2002; Strens et al., 2002; Chen et al., 2003; Oliviero et al., 2003; Huber et al., 2007; Veniero et al., 2011; Assenza et al., 2015; Marshall et al., 2015). Longer recording windows have been mostly considered for theta burst stimulation (TBS) protocols (Schindler et al., 2008; Grossheinrich et al., 2009; Noh et al., 2012; Rizk et al., 2013; Vernet et al., 2013) which consistently showed that the aftereffects can outlast the stimulation for 40–60 min. For the rTMS protocols using single frequencies, the results are more varied, with experiments using low frequency rTMS (0.9–1 Hz) reporting aftereffects lasting 15–65 min (Schutter et al., 2001; Strens et al., 2002; Chen et al., 2003) and experiments testing higher frequencies (5–25 Hz) reporting aftereffects of 5–30 min duration (Huber et al., 2007; Veniero et al., 2011). Note that the latter studies varied considerably in number of delivered pulses and intensity of stimulation, whereas TBS studies followed more strictly a standard protocol (usually 50 Hz@5 Hz, 600 pulses, 80% aMT, but see Wozniak-Kwasińska et al., 2013).

In summary, most of the reviewed studies report tACS/otDCS- and rTMS-aftereffects on brain oscillations. In the following section, we examine whether consistent patterns in these aftereffects can be identified across studies, with an emphasis on those patterns that would be suggestive of direct interaction with intrinsic oscillations (entrainment) as their origin.

### DO AFTERT-EFFECTS ON OSCILLATORY BRAIN ACTIVITY SHOW REPLICABLE PATTERNS ACROSS STUDIES?

As an index of control over brain oscillations, we assessed whether a consistent relationship exists between the externally applied stimulation frequency and affected frequencies in intrinsic oscillatory activity. Specifically, we surveyed the literature for evidence that stimulation frequency can predict the observed changes in intrinsic frequencies (i.e., effect frequencies), and vice versa, whether effect frequencies are preferentially associated with specific stimulation frequencies. Patterns that would indicate that the aftereffects primarily originate from direct interactions with oscillatory brain activity are (i) a match between stimulation and effect frequencies (Thut et al., 2011b; Schmidt et al., 2014; Helfrich et al., 2014a,b), (ii) effects at (sub)harmonics (Ali et al., 2013), or (iii) specific cross-frequency changes that have been related to intrinsic network coupling modes in electrophysiological recordings (for review see e.g., Engel et al., 2013), such as amplitude-amplitude coupling (e.g., gamma-alpha, Spaak et al., 2012) or phase-amplitude coupling (e.g., theta-gamma, Canolty et al., 2006), which would point to network effects.

#### tACS/otDCS-Studies

Figure 1A summarizes the relationship between stimulation- and effect frequencies for tACS/otDCS (illustrating the data of Table 1, 5 kHz-tACS not included). The largest body of research has focused on the aftereffect of slow frequency (0.75 Hz) stimulation over frontal areas (also called transcranial slow

| Method | Frequency | Montage | Protocol | Effects at stimulation frequency | Effects in other frequency bands | Duration of aftereffect |
|--------|-----------|---------|----------|---------------------------------|---------------------------------|-------------------------|
| tACS | 10-30 Hz | C3/C4/O1/O2 | 1-2 mA, 50/100/200 Hz | No | No | Between 2 and less than 7 min |
| otDCS | 5-10 Hz | C3/C4/O1/O2 | 0.1-0.5 mA, 50/100 Hz | No | No | Between 2 and less than 7 min |

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### TABLE 2 | Aftereffects of repetitive (also called rhythmic) transcranial magnetic stimulation (rTMS) as assessed by EEG/MEG.

| ID/study          | Method   | Stimulation frequency | Target | Protocol                     | Effects at stimulation frequency | Effects in other frequency bands | Recording time | Duration of aftereffects |
|-------------------|----------|-----------------------|--------|------------------------------|----------------------------------|---------------------------------|----------------|--------------------------|
| 1. Schutter et al., 2001 | Single frequency | δ 1 Hz | DLPC | 1 × 20 min train; 2000 p; 130% MT | Not analyzed                  | Yes a: power increase          | 65 min          | 65 min                   |
| 2. Wozniak-Kwasnienska et al., 2013 | Single frequency | δ 1 Hz | DLPC | 4 trains × 3.33 min ITI 33 s; 800 p; 120% rMT | Yes a: power decrease           | Yes a, b: power decrease, c: power in-& decrease | 10 min          | 10 min                   |
|                   |          | α 10 Hz               |        |                              | No                              |                                 | 10 min          | 10 min                   |
|                   | iTBS     | γ/θ 50 Hz@5 Hz        | DLPC   | 6 × 2 trains × 4 ITI 229 s; 792 p; 80% rMT | Yes a: power in-& decrease, b: power decrease | Yes a, b: power decrease, c: power in-& decrease | 25 min          | 25 min intra-hemispheric coh, few minutes inter-hemispheric coh |
|                   | cTBS     | γ/θ 50 Hz@5 Hz        | DLPC   | 4 × 17 s trains ITI 280 s; 792 p; 80% rMT | Yes a: power in-& decrease, b: power decrease | Yes a, b: power decrease, c: power in-& decrease | 10 min          | 10 min                   |
| 3. Chen et al., 2003 | Single frequency | δ 0.9 Hz | PM | 1 × 15 min train; 818 p; 90% aMT | Not analyzed                        | Yes a: power increase (AG), intra-hemispheric coherence increase (rAG) | 30 min          | 15 min                   |
| 4. Strems et al., 2002 | Single frequency | δ 1 Hz | M1 | 1 × 25 min train; 1500 p; 90% aMT | Not analyzed                        | Yes a: intra and inter-hemispheric coherence increase (rest, task) | 50 min          | 25 min intra-hemispheric coh, few minutes inter-hemispheric coh |
| 5. Tamura et al., 2005 | Single frequency | δ 1 Hz | M1 | 1 × 10 min train; 600 p; 95% rMT | Not analyzed                        | Yes a: reduction of movement-related rebound | 10 min          | 10 min                   |
| 6. Capotosto et al., 2014 | Single frequency | δ 1 Hz | l/rAG; l/r FEF; l/r IPS | 1 × 1 min train; 60 p; rMT | Not analyzed                        | Yes a: (IAF-2): power increase (AG), intra-hemispheric coherence increase (rAG) | 2 min           | 2 min                    |
| 7. Thut et al., 2003 | Single frequency | δ 1 Hz | V1/V2 | 1 × 10 min train; 600 p; 110% PT | Not analyzed                        | Yes a: reduction of visual-induced desynchronization | 8 min           | 8 min                    |
| 8. Serrien et al., 2002 | Single frequency | θ 5 Hz | SMA | 1 × 10 s train; 50 p; 90% rMT | No                               | Yes a, b: interhemispheric coherence decrease between M1s | 25 min          | Few min after stimulation |
| 9. Oliviero et al., 2003 | Single frequency | θ 5 Hz | M1 | 1 × 10 s train; 50 p; aMT | Not analyzed                        | Yes a: (10.7–13.6 Hz): intra-hemispheric coherence decrease (task) | 50 min          | Few min after the end of stimulation |
| 10. Huber et al., 2007 | Single frequency | θ 5 Hz | M1 | 5 × 6 × 10 s trains ITI 5 s; 1500 p; 90% rMT | No                               | Yes a: SWA (1–4.5 Hz); power increase (sleep) | First NREM sleep cycle (60 min) | 30 min                  |
| 11. Jing and Takigawa, 2000 | Single frequency | α 10 Hz | DLPC | 2 × 3 s trains ITI 5 min; 60 p; rMT | Yes a: direct coherence increase | No                               | 5 min           | 5 min (not studied longer) |

(Continued)
### TABLE 2 | Continued

| ID/study          | Method | Stimulation frequency | Target | Protocol | Effects at stimulation frequency | Effects in other frequency bands | Recording time | Duration of aftereffects |
|-------------------|--------|-----------------------|--------|----------|---------------------------------|---------------------------------|----------------|-------------------------|
| 12. Okamura et al., 2001 | Single frequency | α 10 Hz | DLPC | 2 × 3 s trains ITI 300 s; 60 p; rMT | Yes: change in peak frequency and power | Yes; t, i, β; change in peak frequency and power | 5 min | 5 min |
| 13. Griskova et al., 2007 | Single frequency | α 10 Hz | DLPC | 100 × 2 s trains ITI 10 s; 2000 p; 110% rMT; 90% rMT sham | No | Yes; t: power increase | 10 min | 10 min |
| 14. Weisz et al., 2014 | Single frequency | α iAF | Auditory cortex | 20 × ± 5 trains; 100 p; 50% MSO | No | No | 5 min | NA |
| 15. Graf et al., 2001 | Single frequency | β 20 Hz | DLPC | 40 × 2 s trains ITI 28 s; 1600 p; 90% rMT | No (waking or sleep EEG) | No (waking or sleep EEG) | 10 min | NA |
| 16. Veniero et al., 2011 | Single frequency | β 20 Hz | M1 | 10 × 0.45 s trains ITI 14.55 ms; 400 p; rMT | No | Yes; α: power increase (ERS) | 10 min | 5 min |
| 17. Schutter et al., 2003 | Single frequency | β 25 Hz | Cerebellum | 80 × 10 s trains ITI 5 s; 2000 p; MT | No | Yes; γ: change in prefrontal asymmetry | 15 min | 15 min |
| 18. Grossheinrich et al., 2009 | cTBS | γ/θ | DLPC | 1 × 40 s train; 600 p; 80% rMT | No | γ not analyzed | No | 50 min |
| 19. McAllister et al., 2011 | cTBS | γ/θ | mPFC | 1 × 40 s train; 600 p; 80% rMT | No | γ not analyzed | No | NA |
| 20. Noh et al., 2012 | cTBS | γ/θ | M1 | 1 × 20 s train; 300 p; 80% aMT | Yes; α: power increase (ERS); γ: not analyzed | Yes; α: power increase (ERS); γ: not analyzed | 50 min | 50 min (not studied longer) |
| 21. Vernet et al., 2013 | cTBS | γ/θ | M1 | 1 × 40 s train; 600 p; 80% aMT | No | γ not analyzed | No | NA |
| 22. Shafi et al., 2014 | cTBS | γ/θ | M1 | 1 × 40 s train; 600 p; 80% aMT | Yes; α: clustering coefficient increase; γ: not analyzed | Yes; α: connectivity decrease; high-γ: connectivity increase | 10 min | 10 min |
| 23. Assenza et al., 2015 | iTBS | γ/θ | M1 | 20 × 2 s trains ITI 8 s; 600 p; 80% rMT | No | γ NA | Yes | 5 min |
| 24. Rick et al., 2013 | cTBS | γ/θ | rPPC | 1 × 33 s train; 801 p; 90% rMT | Yes; 30 Hz coherence decrease | Yes; α: coherence decrease (PPC-rest of the brain); increase (PPC-rest of the brain) | 40 min | 30–40 min |

(Continued)
oscillation stimulation/(tSOS) mostly during sleep (Marshall et al., 2006, 2011; Antonenko et al., 2013; Eggert et al., 2013; Reato et al., 2013a; Garside et al., 2015; Sahlem et al., 2015; see also Table 1, rows 1–9). Using similar experimental protocols (anodal stimulation over F3/F4 at 0.75 Hz), these studies showed that delta-otDCS/tACS leads to somewhat reliable and replicable EEG effects in the delta band, often alongside changes in other frequency bands (see Figure 1A, “effect frequency” in “stimulation frequency” delta bin). Conversely, effects in the delta band were rarely observed with other stimulation frequencies (Marshall et al., 2006 [5 Hz]; Marshall et al., 2011 [5 Hz]; Neuling et al., 2012a [individual alpha frequency/IAF]; Chiae et al., 2014 [5 kHz]) (see Figure 1A, “stimulation frequency” in “effect frequency” delta bin). This points to a reasonable match between stimulation and effect frequency for slow frequency stimulation and suggests a direct interaction of frequency-tuned tACS/otDCS with intrinsic brain activity through resonance of a slow oscillating network. However, mixed results have been reported regarding the direction of modulation (i.e., enhancement: Marshall et al., 2006; Kirov et al., 2009; Antonenko et al., 2013; Sahlem et al., 2015; vs. suppression: Eggert et al., 2013; Garside et al., 2015), and regarding accompanying spectral changes (e.g., alpha increase after otDCS during sleep: Marshall et al., 2006; vs. theta increase during wakfulness: Kirov et al., 2009). This has been suggested to reflect dependence of the response on population characteristics (Eggert et al., 2013), on whether both hemispheres are stimulated in-phase or in anti-phase (see Box 1 for definition; Garside et al., 2015), as well as on brain state (Marshall et al., 2006; Kirov et al., 2009).

Another series of studies investigated the aftereffects of posterior alpha tACS on spectral measures (Zaehle et al., 2010; Neuling et al., 2012a, 2013; Helfrich et al., 2014b; Vossen et al., 2015; see Table 1, rows 15–21). This reliably resulted in alpha power increases (see Figure 1A), again suggesting a good match between stimulation- and effect frequency. However, sometimes alpha-activity has also been found to increase after frontal slow delta stimulation (Figure 1A; Marshall et al., 2006; Sahlem et al., 2015), and to decrease after theta stimulation (Figure 1A; Marshall et al., 2006, 2011; Pahor and Jaušovec, 2014). Some alpha changes may thus reflect other mechanisms than specific oscillatory interactions (see also rTMS section below and Veniero et al., 2011).

Theta tACS/otDCS has rarely been followed by lasting changes in theta activity (Pahor and Jaušovec, 2014; Vosskuhl et al., 2015). Rather, a variety of responses in other frequency bands is observed (Marshall et al., 2006, 2011; Pahor and Jaušovec, 2014), without any obvious consistent pattern (Figure 1A). Theta changes have instead been observed after frontal slow frequency stimulation in awake participants (Marshall et al., 2011).

Finally, recent posterior gamma tACS studies (Helfrich et al., 2014a; Strüber et al., 2014) found that 40 Hz (but not 6 Hz) tACS either enhanced or weakened interhemispheric coherence in the gamma range depending on whether bilateral occipital stimulation is delivered in-phase or in anti-phase, again suggesting some match between stimulation- and effect frequency, although with a discrepancy between the narrow frequency bin of stimulation (40 Hz) and the rather broadband gamma effect (Helfrich et al., 2014a; Strüber et al., 2014).

With respect to cross-frequency tACS/otDCS-aftereffects that may be indicative of targeted interventions into oscillatory network activity, some studies reported that delta-otDCS during sleep enhanced alpha spindles (Marshall et al., 2006; Sahlem et al., 2015). Because these spindles are thought to be driven by slow oscillations during slow wave sleep (Steriade, 2006; Mölle et al., 2011), this may constitute supporting evidence for otDCS interactions with oscillatory network activity. However, other studies with similar stimulation parameters but arguably different state variables failed to observe this effect (Kirov et al., 2009; Antonenko et al., 2013; Eggert et al., 2013). Recently, Helfrich et al. (2014a) observed reduced alpha-power during stimulation with 40 Hz (gamma-)tACS, in line with the known inverse gamma-alpha relationship (e.g., Fries et al., 2001; Spaak

| ID/study | Method | Stimulation frequency | Target | Protocol | Effects at stimulation frequency | Effects in other frequency bands | Recording time | Duration of aftereffects |
|----------|--------|-----------------------|--------|----------|-------------------------------|-------------------------------|----------------|------------------------|
| 25. Marshall et al., 2015 | cTBS | γ/α | 50 Hz@6 Hz | rFEF | 1 × 40 s train; 600 p; 80% aMT | Yes: induced stimulus synchronzation | Yes: α decreased stimulus induced desynchronzation | 30 min | 30 min |
| 26. Schindler et al., 2008 | cTBS | γ/α | 30 Hz@10 Hz | rFEF | 1 × 33 s train; 600 p; 80% rMT | Yes: γ/α increase | Yes: α, β decrease | 60 min | 60 min |

Studies are order from top to bottom according to stimulation frequency and target site (from anterior to posterior brain). Aftereffects are expressed in terms of effects at stimulation frequency, other frequencies and duration. DLPFC, dorsolateral prefrontal cortex; mPFC, medial prefrontal cortex; PM, premotor cortex; M1, primary motor cortex; rAG, right angular gyrus; FEF, frontal eye field; IPS, intraparietal sulcus; PPC, posterior parietal cortex; SMA, supplementary motor area; V1, V2, early visual cortex; MT, motor threshold; r/aMT, resting/active motor threshold; MSO, maximum stimulator output; PT, phospine threshold; ITI, intertrain interval; p, pulses; NA, not applicable.
et al., 2012). However, this interaction did not lead to stable alpha aftereffects.

In summary, the collective evidence for frequency-specificity of otDCS/tACS aftereffects is mixed at best. Although aftereffects at the stimulation frequency or a physiologically related frequency band have been observed after stimulation at delta, alpha, and gamma frequencies, experimental conditions and outcomes have overall been too variable, and identically performed replications too few, to unequivocally establish either direct frequency-matched modulation originating in entrainment, or cross-frequency phenomena which would indicate interactions through intrinsic coupling modes. In addition, it needs to be pointed out that the coverage of frequency bands is incomplete in several studies (especially for alpha stimulation) (see Table 1; “effects in other frequency bands”), with a considerable number of studies focusing on selective frequency bands. This may skew the conclusions favorably toward frequency specificity.

rTMS-Studies

Figure 1B summarizes the relationship between stimulation and effect frequencies across rTMS studies (illustrating the data of Table 2). With one exception (Weisz et al., 2014), none of these studies specifically tested the idea that rTMS can interact with brain oscillations in a controlled manner, but investigated electrophysiological aftereffects of rTMS in light of evidence that patterned transcranial magnetic stimulation can lead to long term potentiation/depression (LTP/LTD)-like phenomena (e.g., Thickbroom, 2007). Accordingly, many papers often refer to the classical distinction between excitatory and inhibitory rTMS (low vs. high frequency rTMS, continuous TBS vs. intermittent TBS) rather than to canonical frequency bands. As a result, not all papers did consider EEG effects at stimulation frequency. Collapsing the results across all studies (see Figure 1B) reveals that rTMS at one frequency typically leads to broadband aftereffects spanning more than one frequency band, as summarized below.

rTMS at delta and theta frequencies (0.9–1 vs. 5 Hz) has been reported to generally induce broadband EEG power modulations, with the exception of rTMS over motor areas which seems to affect activity in a more restricted (alpha/beta) frequency band (Serrien et al., 2002; Strens et al., 2002; Chen et al., 2003; Oliviero et al., 2003; Tamura et al., 2005). The only study investigating changes in the delta band after delta-rTMS reported a power decrease (Wozniak-Kwasniewska et al., 2013).

Conflicting results have been reported for rTMS at alpha frequency, i.e., alpha-rTMS. Some studies described increases in alpha power or connectivity (Jing and Takigawa, 2000; Okamura et al., 2001), although not exclusively so (Okamura et al., 2001). Others did not find any aftereffect in the alpha band (Griskova et al., 2007; Weisz et al., 2014). Alpha power increase has also been reported after beta-rTMS (Veniero et al., 2011), which has led to the suggestion that alpha-band increases may be a generic response of cortical areas cycling at alpha frequency independent of stimulation protocol (Veniero et al., 2011).

Several studies using continuous theta-burst stimulation (cTBS), consisting of gamma bursts applied at theta frequency, reported aftereffects in the theta-band on both connectivity (Shafi et al., 2014) and power (Noh et al., 2012; Vernet et al., 2013; Wozniak-Kwasniewska et al., 2013), albeit in opposite directions. When aftereffects were probed for changes in the gamma band (n = 4 studies) a complex pattern of gamma power and connectivity modulation was observed (Schindler et al., 2008; Rizk et al., 2013; Vernet et al., 2013; Marshall et al., 2015). Yet, aftereffects of cTBS were not restricted to the theta and gamma bands, and effects in these frequency bands were also reported across many other studies using other frequencies of stimulation. A similarly inconsistent picture
emerges for intermittent theta-burst stimulation (iTBS), for which decreases in gamma/theta power have been reported in one out of three papers (Wozniak-Kwasniowska et al., 2013) alongside increases in alpha (Groseleinrich et al., 2009), beta (Wozniak-Kwasniowska et al., 2013) and delta power (Wozniak-Kwasniowska et al., 2013; Assenza et al., 2015).

In summary, many rTMS-studies did not analyse the aftereffects at stimulation frequency. Of those that did, a considerable fraction did not report any effects in this frequency band (Graf et al., 2001; Serrien et al., 2002; Schutter et al., 2003; Griskova et al., 2007; Huber et al., 2007; Grosseinrich et al., 2009; McAllister et al., 2011; Veniero et al., 2011; Weisz et al., 2014; Assenza et al., 2015). Whilst not providing much evidence for targeted interactions with brain oscillations per se, these results are relevant for two reasons. They suggest that rTMS, and possibly NIBS in general (see also discussion), is likely to lead to aftereffects in brain oscillations that are largely frequency-unspecific, and by extension, represent confounds for those attempting to control brain oscillations and associated functions through direct interaction via externally applied stimulation.

**ARE EEG AFTEREFFECTS ACCOMPANIED BY BEHAVIORAL CHANGES, IN LINE WITH KNOWN CORRELATIVE EEG-BEHAVIORAL LINKS?**

The most promising evidence for behavioral aftereffects that correspond to the reported tACS/otDCS-induced EEG modulations has been provided by those studies using frontal 0.75 Hz tACS/otDCS aiming to either enhance or disrupt slow waves during sleep, a rhythm that has been associated with memory consolidation (e.g., Rasch and Born, 2013). As expected based on the known correlation between EEG slow wave activity and memory, several of these studies reported changes in declarative memory performance after frontal slow wave tACS/otDCS (Marshall et al., 2006, 2011; Kirov et al., 2009; Antonenko et al., 2013; Garside et al., 2015), while others failed to find an effect (Eggert et al., 2013; Sahlem et al., 2015).

Of note, Garside et al. (2015) reported a negative correlation between the individual changes in slow/alpha power and the performance on a verbal learning task (in the absence of a group effect on task performance), although it has to be pointed out that their sample was too small ($n=7$) to allow strong conclusions. Collectively, these findings are promising but given that the neural and behavioral measures were generally obtained up to several hours apart, it is debatable whether the behavioral changes reflect a neural aftereffect or rather the interaction with an ongoing process in the acute phase of the experiment.

Behavioral effects were also studied using gamma-tACS (40 Hz) (Helfrich et al., 2014a; Strüber et al., 2014). These studies aimed to induce an oscillatory signature that has been associated in previous EEG studies with the prevalence of a specific apparent motion percept (Helfrich et al., 2014a; Strüber et al., 2014). Neither Strüber et al. (2014), nor Helfrich et al. (2014a) found aftereffects on perception, despite an online modulation of interhemispheric connectivity in the latter study. Yet, it has to be noted that Helfrich et al. (2014a) assessed the perceptual aftereffects long after the EEG modulation had subsided.

In studies on the cognitive impact of theta-tACS, short term memory performance did not improve beyond stimulation despite an online effect on memory (Vosskuhl et al., 2015), whereas Pahor and Jaušovec (2014) reported lasting improvement on tasks presumed to assess fluid intelligence for up to 25 min that coincided with a decrease in alpha activity. All other reviewed studies either did not assess whether the observed EEG/MEG aftereffects were correlated with meaningful behavioral consequences (Zaehler et al., 2010; Neuling et al., 2012a; Wach et al., 2013; Chaieb et al., 2014; Vossen et al., 2015), or found no such behavioral changes (Neuling et al., 2013).

With regard to rTMS, only few studies assessed its effects on cognitive tasks in relation to the outcome on brain oscillations. Marshall et al. (2015) showed that gamma/theta cTBS over frontal eye fields can modulate alpha and gamma power over the parieto-occipital cortex and concurrently impair performance in a cued spatial attention task for 16 min. Applying the same stimulation protocol, Rizk et al. (2013) also showed that posterior parietal cortex stimulation can induce neglect-like behavior during a visual exploration task lasting at least 15 min (not tested longer).

This was however associated with a change of alpha connectivity between stimulated cortex and its homologous area and between both parietal areas and the rest of the brain, not with any effect at the stimulation frequencies. Interestingly, the behavioral effect of the stimulation was dependent on individual alpha band connectivity strength prior to stimulation.

In summary, only few studies looked at both behavioral and oscillatory aftereffects simultaneously. In those that did, many did not observe lasting behavioral changes. Only one study (Garside et al., 2015) reports a direct correlation between individual neural and behavioral aftereffects. Hence, at present, there is too little information about the behavioral impact of rhythmic stimulation-induced aftereffects to draw firm conclusions.

**DISCUSSION**

Our review suggests that aftereffects on oscillatory brain activity are common after otDCS, tACS, and rTMS, yet do not reveal a consistent pattern across studies relative to frequency of stimulation. For tACS/otDCS, only a fraction of studies have reported aftereffects that would be expected if they were related to entrainment of frequency-matched brain oscillations during stimulation, such as corresponding (cross-)frequency changes in EEG/MEG and associated behavior. For rTMS, the reported EEG/MEG aftereffects are broadband throughout, and range across multiple canonical frequency bands. Collectively, these data illustrate that despite some promising reports of controlled interventions into brain oscillations beyond stimulation, the overall evidence so far is weak. Below, we discuss some of the challenges that need to be overcome in order to test whether such interventions are viable. We suggest ways to optimize existing stimulation protocols, and outline future research directions to close the gaps in the existing evidence.
Competing Mechanisms of Action of NIBS Techniques

The most promising attempts to induce aftereffects in directly targeted brain oscillations and their associated functions have been made in tACS/otDCS studies. However, collectively, the tACS/otDCS results are mixed, with a considerable number of studies reporting effects that are independent of stimulation frequency. This illustrates that neural oscillations are responsive to electrical stimulation in general, in line with frequently reported changes in oscillatory brain activity after NIBS with other non-rhythmic protocols such as transcranial direct current stimulation (e.g., Lapenta et al., 2013; Puanhuvan et al., 2013; Spitoni et al., 2013; Hsu et al., 2014) or even static magnetic stimulation (Gonzalez-Rosa et al., 2015). Hence, frequency-tuned modulation of oscillatory brain activity will likely be accompanied by effects on brain oscillations that originate from mechanisms other than entrainment (e.g., forms of plasticity). In order to enhance control over aftereffects, the relative contribution of these different (possibly competing) mechanisms of action needs to be investigated. In addition, it remains to be established whether stimulation parameters can be optimized to favor one mechanism over another.

The idea that entrainment, or resonance, of cortical networks cannot explain all aftereffects on brain oscillations is in line with recent data from our group (Vossen et al., 2015). We found that tACS-induced aftereffects around stimulation frequency were observed even when the optimal condition for entrainment (i.e., continuous stimulation with a periodic field at the intrinsic frequency) was explicitly disrupted, and despite the absence of lasting phase alignment after tACS offset. One candidate mechanism that could lead to lasting aftereffects independently of entrainment are LTP- or LTD-like processes akin to those suggested to operate during non-rhythmic NIBS, such as tDCS (Nitsche et al., 2008, 2009; Ziemann and Siebner, 2008; Fritsch et al., 2010). Notably however, there is evidence from tACS-studies that online entrainment and aftereffects on brain oscillations may not be entirely unrelated (Helfrich et al., 2014a,b). Helfrich et al. (2014a,b) found the strength of entrained oscillatory power to be positively correlated with the strength of the aftereffects across participants. This important result (reproduced across two experiments using different stimulation frequencies, Helfrich et al., 2014a,b) suggests that entrainment effects online to tACS may influence the aftereffects, and hence may provide an opportunity for targeted intervention lasting beyond stimulation. Importantly also, Helfrich et al. (2014b) showed that these online and offline effects are of different quality, with the online effects observed at a narrow frequency peak, and the offline effects seen in a broader band around this peak discounting the trivial explanation that the correlated online and offline effects may simply reflect the same phenomenon measured at two time points. In line with these considerations, some accounts propose that entrainment of brain oscillations may specifically strengthen (or weaken) the targeted neuronal circuits by spike-timing dependent plasticity (STDP), which constitutes a hybrid account between immediate entrainment and longer lasting LTP/LTD-mechanisms (see Zaehle et al., 2010, for a computational model; Vossen et al., 2015 for a conceptual extension). The general idea is that small timing differences between tACS-imposed (entrained) and intrinsic cortical rhythms may lead to strengthening or weakening of the corresponding oscillatory neuronal circuit by modifying the efficacy of its component synapses. More specifically, the tACS-induced periodic hyper- and depolarization of neural membranes could impose a temporal window that modulates the spiking activity of stimulated neurons by raising or lowering the probability of an action potential as a function of phase in the stimulation cycle (as compared to a direct induction of action potentials). This would result overall in greater regularity in firing patterns and allow the modification of specific recurrent loops, involving feedback from relay neurons. As the stimulated neurons are more likely to fire at a specific point in the stimulation cycle, only feedback potentials that arrive in close temporal proximity to this time point (i.e., with a period slightly longer or shorter than the stimulation period) will result in synaptic strengthening/LTP or weakening/LTD, respectively.

Please note that so far, the only evidence available for this idea stems from a computational model (Zaehle et al., 2010). Experiments on cell cultures and in-vivo animal studies provide no insight as none of them have observed effects that last beyond stimulation offset (reviewed in Reato et al., 2013b; see also Strüber et al., 2015, for a discussion). The STDP account is only one of several possible models, some of which include more complex biologically plausible modeling (Fröhlich, 2015). Future studies will need to provide further insight into how and to what extent online entrainment contributes to offline effects at the neuronal level if we want to capitalize on frequency-tuned interventions that modulate specific oscillatory networks also beyond the duration of stimulation.

rTMS vs. tACS/otDCS

Compared to the tACS/otDCS-literature, the evidence for a controlled lasting modulation of brain oscillations is particularly thin for rTMS, with aftereffects ranging across several frequency bands without any evidence for frequency specificity. This discrepancy may be explained by the difference in the physiological mechanisms by which tACS/otACS and rTMS affect neuronal activity: whereas tACS/otACS modulates membrane potentials without discharging neurons (Paulus, 2011), TMS elicits action potentials (Barker et al., 1987). Moreover, the stimulation techniques also differ in terms of spatial resolution, with tACS/otDCS affecting a significantly larger neural population than rTMS (e.g., Sparing and Mottaghy, 2008). Accordingly, it is conceivable that electrical and magnetic stimulation induce fundamentally different long-term plasticity effect. Nonetheless, rTMS has been shown to cause online entrainment (Thut et al., 2011b; Hanslmayr et al., 2014; Romei et al., 2015; see also Rosanova et al., 2009; Herring et al., 2015), analogous to tACS/otDCS. Yet, only one rTMS study on aftereffects (Weisz et al., 2014) optimized the design by tailoring stimulation frequency to underlying brain oscillations, which therefore may constitute another explanation of the discrepant patterns of rTMS vs. tACS/otDCS aftereffects. In addition,
information about effects at stimulation frequency is often missing as several rTMS studies did not analyse aftereffects in this frequency band due to their focus on LTD and LTP-like effects. Finally, as most tACS/otDCS studies were designed to interact with oscillatory activity, experiments that failed to find frequency effects may be more likely to end up in the file drawer, i.e., might be more prone to publication bias. rTMS studies with different design rationales and hypotheses may suffer less from this particular problem.

Given that most of the reported rTMS aftereffects on brain oscillations are probably not driven by entrainment, could the classical dichotomy between excitatory and inhibitory rTMS [using high (>5 Hz) vs. low (<1 Hz) rTMS frequencies, respectively] account for the variability in oscillatory aftereffects? This alternative explanation is also unlikely, given for instance that alpha-power enhancement after motor cortex stimulation has been observed across a wide variety of rTMS frequencies that cross the excitatory-inhibitory parameter divide (Veniero et al., 2011; see also Figure 1B). As recently highlighted by Huang et al. (2011), the classification of rTMS designs into high frequency/low frequency (or inhibitory/excitatory) protocols may also not be able to explain aftereffects on MEP amplitude. As for tACS/otDCS, it is therefore likely that the broadband aftereffects which seem to be independent from the stimulation frequency, might reflect LTP/LTP-like phenomena (see also Thickbroom, 2007), for which however a detailed mechanistic account is lacking. Huang et al. (2011) recently proposed a model that takes known cellular mechanisms of LTP/LTD into account to explain rTMS (specifically cTBS/iTBS) aftereffects on MEPS. This model shows that the pattern of stimulation (i.e., the interaction between number of pulses, intertrain interval, total stimulation time and the stimulation frequency) determines whether rTMS leads to a potentiation or depression of cortical excitability.

In light of the general lack of knowledge about effective rTMS targets (and by extension rTMS protocols) for controlled interventions, we believe it is worthwhile to design future rTMS studies to examine more explicitly the opportunity that direct interventions with brain oscillations may provide (see also Luber and Lisanby, 2014). This requires moving beyond the classical low vs. high frequency approach toward stricter frequency tuning of rTMS to underlying brain oscillations to allow comparisons between rTMS and otDCS/tACS aftereffects.

**Gaps in Existing Evidence**

Interest in brain oscillations as potential targets for NIBS has only recently gained momentum from studies demonstrating online entrainment (e.g., Fröhlich and McCormick, 2010; Reato et al., 2010; Thut et al., 2011b; Helfrich et al., 2014b). It is therefore unsurprising that our knowledge of possible oscillatory aftereffects, and optimal stimulation parameters for targeting specific oscillatory network activity, is still limited. In the following, we highlight what we believe are critical gaps in the existing evidence.

First, one largely unexplored aspect is the tailoring of the stimulation frequency to endogenous rhythms. The importance of a frequency match between external fields and underlying neural activity for maximum impact has been identified empirically in slice electrophysiology (Schmidt et al., 2014), and may be a crucial factor for guiding targeted interventions into intrinsic oscillatory activity. Yet, only six of the reviewed tACS/otDCS-studies tailored stimulation frequency to individual intrinsic frequencies (Zaehle et al., 2010; Neuling et al., 2013; Pahor and Jaušovec, 2014; Strüber et al., 2015; Vossen et al., 2015; Vosskuhl et al., 2015), vs. 16 tACS/otDCS-studies that did not take this factor into account. For rTMS, this ratio is even more unfavorable with one study (vs. 25) using frequency-tailored rTMS (Weisz et al., 2014). Note, however, that frequency matching alone does not guarantee aftereffects (Strüber et al., 2015), and that due to a tendency of intrinsic frequencies to fluctuate over time, deviations between stimulation frequency and intrinsic frequencies may affect the overall outcome (Vossen et al., 2015).

Second, there is often fragmentary coverage of frequency space, both in terms of applied stimulation and analyzed effect frequency. Many studies focus on one stimulation frequency (i.e., a control frequency is lacking) and limit their EEG/MEG analyses to one or few, broad frequency bands. This often effectively precludes the assessment of (sub-)harmonic changes that would be expected to be limited to narrow frequency bands.

Third, we note a substantial variability in stimulation montages/sites across studies, even for a given brain oscillation/network of interest. Especially for tACS/otDCS, little is known about optimal electrode sites and configurations, and how different montages might lead to different results with otherwise identical stimulation parameters. A systematic effort is required to compare different montages with respect to an intended manipulation, using guidance from modeling of effective field strength in the cortex (Dmochowski et al., 2011; Neuling et al., 2012b; Saturnino et al., 2015).

Fourth, besides the lack of information on associated behavioral changes discussed above, even with comparable external parameters the initial activation state of the cortex is likely to influence the system’s response (state-dependency; e.g., Marshall et al., 2006; Kirov et al., 2009; Marshall et al., 2011; Neuling et al., 2013; Rizk et al., 2013) and will have to be taken into account. For example, aftereffects appear in different frequency bands when the same otDCS protocol is applied during NREM vs. REM sleep (Marshall et al., 2011), and alpha-tACS enhances alpha power only when participants have their eyes open but not closed (reflecting different baseline levels of alpha activity) (Neuling et al., 2013). Through mapping the state-dependency of stimulation outcomes, we might be able to improve NIBS efficacy, e.g., by capitalizing on closed loop approaches tracking fluctuations in specific ongoing spectral features to guide stimulation parameters (e.g., Brittain et al., 2013). For the latter, advances in algorithms for online tACS artifact correction are a prerequisite, as currently the analysis of EEG/MEG data obtained during stimulation can only be obtained offline (EEG: Helfrich et al., 2014b; for new developments with MEG see Garcia-Cossio et al., 2015; Neuling et al., 2015; Witkowski et al., 2015).

Fifth, inter- and intraindividual variability in the response to stimulation is a general and not trivial problem for NIBS
CONCLUSION

While there is mounting evidence that oscillatory or rhythmic NIBS allows to control brain oscillations and associated functions during (online to) stimulation, we find mixed evidence for the controllability of NIBS-induced aftereffects on brain oscillations. We argue that while online mechanisms must be at the origin of offline effects, there is little evidence that the offline effects can be considered proxies of the online effects. Future studies will need to investigate the link between these online and offline effects to advance our understanding of rhythmic NIBS techniques and their potential for neuromodulation via controlled intervention into brain oscillations. Because a growing number of studies indicate that neurological and mental diseases are characterized by abnormal pattern of specific brain oscillations (the so called oscillopathies; Schnitzler and Gross, 2005; Light et al., 2006; Hammond et al., 2007; Edgar et al., 2015; Uhlhaas and Singer, 2015; for a review see Buzsáki and Watson, 2012), increasing our level of control over these aftereffect, and their direction and duration, will represent a decisive step to plan new strategies for neurorehabilitation.

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