Time-frequency analysis of short-lasting modulation of EEG induced by intracortical and transcallosal paired TMS over motor areas

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Manganotti P, Formaggio E, Storti SF, De Massari D, Zamboni A, Bertoldo A, Fiaschi A, Toffolo GM. Time-frequency analysis of short-lasting modulation of EEG induced by intracortical and transcallosal paired TMS over motor areas. J Neurophysiol 107: 2475–2484, 2012. First published February 1, 2012; doi:10.1152/jn.00543.2011.—Dynamic changes in spontaneous electroencephalogram (EEG) rhythms can be seen to occur with a high rate of variability. An innovative method to study brain function is by triggering oscillatory brain activity with transcranial magnetic stimulation (TMS). EEG-TMS coregistration was performed on five healthy subjects during a 1-day experimental session that involved four steps: baseline acquisition, unconditioned single-pulse TMS, intracortical inhibition (ICI, 3 ms) paired-pulse TMS, and transcallosal stimulation over left and right primary motor cortex (M1). A time-frequency analysis based on the wavelet method was used to characterize rapid modifications of oscillatory EEG rhythms induced by TMS. Single, paired, and transcallosal TMS applied on the sensorimotor areas induced rapid desynchronization over the frontal and central-parietal electrodes mainly in the alpha and beta bands, followed by a rebound of synchronization, and rapid synchronization of delta and theta activity. Wavelet analysis after a perturbation approach is a novel way to investigate modulation of oscillatory brain activity. The main findings are consistent with the concept that the human motor system may be based on networklike oscillatory cortical activity and might be modulated by single, paired, and transcallosal magnetic pulses applied to M1, suggesting a phenomenon of fast brain activity resetting and triggering of slow activity.

single pulse; paired pulse; transcallosal stimulation

IN THE AWAKE STATE, oscillatory human brain activity occurs at different frequencies (Niedermeyer 1999) and can be rapidly modulated over the occipital regions by eyes opening, by movement, or by sensory stimulation over the central parietal regions. Dynamic changes in spontaneous electroencephalogram (EEG) rhythms can be seen to occur with a high rate of variability. An innovative method to study brain function is by triggering oscillatory brain activity with a perturbation method such as direct stimulation.

Recent advances in EEG-transcranial magnetic stimulation (TMS) coregistration have shed new light on EEG reactivity in humans. Most studies have focused on slow EEG responses evoked by a single magnetic stimulus in the time domain (Bonato et al. 2006; Ilmoniemi et al. 1997; Izumi et al. 1997; Komssi et al. 2002, 2004; Paus et al. 1998, 2001; Thut et al. 2003; Thut and Pascual-Leone 2010). Single-pulse TMS (Fuggetta et al. 2005; Paus et al. 2001; Rosanova et al. 2009; Van Der Werf et al. 2006) or a TMS pulse train (Briegel et al. 2008; Fuggetta et al. 2008; Plewnia et al. 2008) induces synchronous rhythmic rapid brain activity that preferably oscillates in the natural frequency of the target site. Although the real meaning and site of rapid oscillatory synchronization evoked by TMS remain to be elucidated, cortical and subcortical sources have been suggested (Rosanova et al. 2009; Van Der Werf et al. 2006). Johnson et al. (2010) provide evidence that a potential approach to understanding the behavioral effects of TMS is by studying oscillatory activity changes due to TMS. A method to better understand the time course of these evoked oscillations for behavioral or clinical investigations is therefore needed. Paired-pulse TMS can be utilized to modulate rapid oscillatory brain activity. The technique (Kujirai et al. 1993) relies on a well-known paradigm to test the intracortical inhibitory/facilitatory balance by means of a subthreshold conditioning stimulus (S1) followed by a suprathreshold test stimulus (S2). The test responses are inhibited at interstimulus intervals (ISIs) of 1–5 ms and facilitated at ISIs of 8–30 ms. These phenomena are referred to as short intracortical inhibition (SICI) and intracortical facilitation (ICF). The effect of S1 on the size of control motor evoked potentials (MEPs) is thought to originate at the cortical level (Orth et al. 2003; Shimizu et al. 1999). A suprathreshold stimulus is, in fact, known to determine a corticospinal output leading to a MEP, while a subthreshold stimulus excites only local cortical interneurons (Di Lazzaro et al. 2002). Thus, by combining a subthreshold pulse with a suprathreshold pulse, one can assess the effects of interneurons on cortical output (Ziemann et al. 1998). Paired-pulse TMS allows for the measurement of SICI (ISI ranging from 1 to 4 ms), which reflects the excitability of short inhibitory interneuronal circuits within the motor cortex (Chen 2004; Di Lazzaro et al. 1999; Kujirai et al. 1993; Ziemann et al. 1996). Similarly, transcallosal paired-pulse TMS investigates the excitability of the transcallosal inhibitory system (Ferbert et al. 1992; Meyer et al. 1995). Corticospinal output gives rise to contralateral MEP (cMEP), and transcallosal output gives rise to inhibition of the contralateral M1. Transcallosal output can be measured as either a period of silence in ongoing electromyographic (EMG) activity [ipsilateral silent period (iSP)] or an inhibition of the amplitude of the cMEP evoked by a TMS pulse over the M1 of the contralateral hemisphere [interhemispheric inhibition (IHI)].
The aim of this study was to investigate the oscillatory activity related to the inhibitory interneuronal circuits on both M1 areas by using different types of TMS (single, paired pulse, and transcallosal). A time-frequency analysis of EEG signals was applied to characterize the rapid modifications of oscillatory EEG rhythms induced by TMS and to understand the physiological mechanism of these induced oscillations. A wavelet method was utilized to detect dynamic changes in the regional neural oscillatory activity of the cortical areas.

MATERIALS AND METHODS

Subjects. The study sample was five healthy subjects [4 men and 1 woman; mean age 25.7 yr ± standard deviation (SD) 4.2 yr], right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield 1971). None of the subjects had a past medical history of neurological disease or was taking any medications. Basal EEG was normal in all subjects. In accordance with the Declaration of Helsinki, all subjects gave written informed consent to participate in the study. The study design and protocol were approved by the Local Ethics Committee of the Verona University Department and Hospital.

EEG recordings. EEG data were acquired with a magnetic resonance (MR)-compatible EEG amplifier (SD MRI 32; Micromed, Treviso, Italy) and a cap providing 32 TMS-compatible Ag/AgCl-coated electrodes (diameter 8 mm; thickness 0.5 mm) with 2-mm slits to interrupt eddy currents, positioned according to a 10/20 system. The reference was placed anterior to Fz and the ground posterior to Fz, as in previous studies (Formaggio et al. 2011; Manganotti et al. 2008) using the same system. The EEG data were acquired at a rate of 1,024 Hz with the SystemPlus software package (Micromed) (Fig. 1). To avoid saturation, the EEG amplifier had a resolution of 22 bits (range ±25.6 mV). An antialiasing hardware band-pass filter was applied with a bandwidth between 0.15 and 269.5 Hz.

TMS stimulation. TMS was performed with a Magstim-Rapid Stimulator in biphasic pulse configuration (Magstim, London, UK), which generates a maximum magnetic field of 1.5 T. TMS was delivered through a figure-of-eight focal coil oriented so that the induced electric current flowed in a posterior-anterior direction over the left M1. MEPs were recorded from the right thenar eminence (TE) muscle with Ag/AgCl surface electrodes fixed to the skin with a belly-tendon montage. The coil was placed tangentially with respect to the scalp, with the handle pointing backward and laterally at a 45° angle away from the midline. The stimulation coil was positioned with the handle pointing backward and over the optimal scalp position to obtain the highest MEP, corresponding approximately to between C3 and P3 in all subjects. Induced currents were directed postero-anteriorly. Stimulus intensity was set at 110% of motor threshold (MT) intensity. The MT intensity was approached from individual suprathreshold levels by reducing the stimulus intensity in 1% steps. MT intensity was defined as the lowest stimulator output intensity capable of inducing MEPs of at least 50-μV peak-to-peak amplitude in relaxed right TE muscles in at least half of 10 trials over the optimal scalp position (Rossini et al. 1994). Stimulus intensities are expressed as a percentage of maximum stimulator output.

The click associated with the coil discharge propagates through air and bone and can elicit an auditory N1-P2 complex at latencies of 100–200 ms (Nikouline et al. 1999; Tiitinen et al. 1999). In this study, we inserted earphones to mask the coil-generated click in all subjects to avoid any effect of clicks in the modulation of cortical oscillatory activities. A loud white noise (90 dB) was played through the insert earphones to mask the coil-generated click (Fuggetta et al. 2005). All subjects indicated that the white noise was sufficient to mask the auditory input.

To ensure wakefulness throughout the recording sessions, the subjects were required to keep their eyes open and to fix on a target over the opposite wall. All subjects were naive to TMS prior to the
study. In all conditions of TMS, the computer triggered the magnetic pulses by insertion of a marker in a track of the multichannel EEG recording system.

Experimental design. EEG-TMS coregistration was performed during the same experimental session, which consisted of four conditions (steps): 1) baseline acquisition (5 min), rest motor threshold (rMT) and hot-spot detection over the left M1 area; 2) single-pulse stimulation over the left M1 area; 3) paired-pulse stimulation over the left M1 area with an ISI of 3 ms; and 4) transcallosal stimulation over the left and right M1 areas with an ISI of 10 ms.

The data acquired in step 1 were used to compute the rest power values, which were then exploited to analyze the development of the power spectrum of the EEG signals following the TMS pulse. The subsequent protocols were delivered in random order across the subjects. For each step, 35–40 stimuli were delivered randomly at an interval of 8–15 s.

In single-pulse stimulation (step 2), registration involves delivering 35–40 stimuli at 110% of rMT over the left M1 area. Double-pulse stimulation requires a second device to generate two stimuli and control their intensity and the interval between them. During the registration, the stimuli are delivered through a focal coil over the left M1 area and the interval between them is set to 3 ms. The intensity of the first stimulus is set to 80% and the second stimulus to 110% of rMT. Under the transcallosal protocol, the stimuli are delivered from different coils, one set over the left M1 area and the other over the right M1 area, both at an intensity of 110% of rMT and with the interval between them set to 10 ms.

Wavelet analysis. EEG data were analyzed with a time-frequency procedure to characterize TMS-induced oscillations. Since magnetic artifacts were contained in the first 30 ms, the EEG traces were analyzed 35 ms after magnetic stimulation. All EEG recordings were visually inspected; trials with artifacts produced by environmental noise, muscle activity, or eye movement were rejected.

Time-frequency analysis was performed with continuous Morlet wavelet transform, as previously described (Storti et al. 2010), which provides a time course after magnetic stimulation of the relative power in the main frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (7–12 Hz), and beta (15–22 Hz). Only the most representative channels (F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4) were considered in the analysis. To show the specificity of motor network alterations induced by TMS and demonstrate that effects are specific for areas connected with the motor cortex, frequency band alterations of temporal (T5 and T6) and occipital (O1 and O2) electrodes were also explored.

In the first part of the analysis, ~20 epochs of basal EEG devoid of artifacts were selected for each subject. The mean and the SD of relative power for each channel were computed. In all subjects in baseline conditions, we noted a symmetrical, well-developed alpha rhythm over the posterior and central electrodes reactive to eyes opening and to hand motor activity (Formaggio et al. 2008a, 2008b; Storti et al. 2010).

The relative power for each poststimulus signal (~20–30 epochs) was computed for each subject, averaged among the trials, and normalized to the baseline value (expressed as 1). To check whether

![Wavelet analysis of EEG responses to TMS](http://jn.physiology.org/)

Fig. 2. Average \(N = 5\) relative wavelet power \(P_{\alpha}\) in alpha range \(7–12\) Hz after single (green), paired (red), and transcallosal (black) TMS pulse. Asterisks above bars indicate values significantly different from basal level.
the poststimulus activity differed significantly from the basal level, an unpaired-samples t-test was performed at each sampling time ($P < 0.05$) to evidence the intervals during which the relative power differed significantly from baseline.

RESULTS

Alpha band. The power of the frontal electrodes (F3-Fz-F4) decreased ($\sim$40%) in the 1-s period after single and paired-pulse stimulation (significant decrease in Fz), followed by a more evident increase lasting from 1 to 3 s on the Fz (Fig. 2). After transcallosal stimulation, the power decrease was even more evident (70% in F3 and Fz; 80% in F4), lasting $>1.5$ s but with a less clear rebound. Statistically significant differences between the poststimulus activity and the basal value are indicated by asterisks in Figs. 2–6.

A similar pattern was observed in the central electrodes (C3-Cz-C4): After single and paired-pulse stimulation, the power significantly decreased (50% in C3) from baseline in the 1-s period, followed by an increase lasting from 1 to 3 s, which was clearly visible on all electrodes. After transcallosal stimulation, the power decreased significantly by $\sim$80% in C3 and C4, lasting $>1.5$ s but with a less clear rebound.

For the parietal electrodes (P3-Pz-P4), the effects of TMS stimulation were less evident: After single and paired-pulse stimulation, the power decreased significantly (20% in P4) in 1 s, followed by an increase lasting from 1 to 3 s and a significant rebound from 3 to 5 s in P4 and Pz. This pattern, though also observable in P3, was not significant. After transcallosal stimulation, the power decreased significantly by $\sim$50%, lasting $>0.2$ s and followed by a rebound lasting from 3 to 5 s in P4.

Beta band. The trend of the frontal electrodes was not consistent across the recordings (single, paired, and transcallosal stimulation) except for Fz, which showed a decrease in power of $\sim$20% from the baseline value, lasting 0.5 s and followed by a rebound of $\sim$20% lasting until 1 s (Fig. 3). In none of the three electrodes were the changes significant.

After both single and paired-pulse stimulation, the power of the central electrodes (C3-Cz-C4) decreased (significant decrease of 30% in C3) from the baseline value and lasted 0.4 s, followed by an evident rebound on all electrodes. Figure 2 shows the same pattern also in Cz (paired-pulse stimulation), with significant changes in power from 3 to 5 s, and in C4 (single stimulation), with a significant increase from 0.5 to 1.5 s. After transcallosal stimulation, the power decreased significantly only in C3 and lasted 0.2 s, followed by a rebound.

After single and paired-pulse stimulation, the power of the parietal electrodes (P3-Pz-P4) decreased significantly from the baseline value only in P4 and lasted <0.5 s without a consistent rebound in power.

Fig. 3. Average ($N = 5$) relative wavelet power ($P_{\omega}$) in beta range (15–22 Hz) after single (green), paired (red), and transcallosal (black) TMS pulse. Asterisks above bars indicate values significantly different from basal level.
**Delta band.** After single and paired-pulse stimulation, the power of the frontal electrodes (F3-Fz-F4) increased significantly by ~50% in Fz from the baseline value, with a maximum at 0.5 s and lasting 1 s (Fig. 4). This pattern was also observed in F3 and F4. A significant decrease in power from 3 to 5 s after paired-pulse stimulation was observed for all three electrodes. After transcallosal stimulation, the power increased significantly from 50% to 100% in Fz, with a maximum after 0.5 s but lasting >1 s.

After single and paired-pulse stimulation, the power of the central electrodes (C3-Cz-C4) increased from the baseline value, with a maximum at 0.5 s and lasting 1 s. There was a significant increase in C3 and C4 after paired-pulse stimulation. After transcallosal stimulation, the power increased significantly from 60% to 100%, with a maximum after 0.5 s but lasting >1 s in C3 and C4.

After single and paired-pulse stimulation, the power of the parietal electrodes (P3-Pz-P4) decreased slightly from the baseline value only in Pz and lasted <0.3 s, followed by an increased rebound of 20% lasting until 1 s. After transcallosal stimulation, the power decreased (20% in P3), lasting <0.3 s, but followed by a significant increase in Pz and P4.

**Theta band.** After single, paired-pulse and transcallosal stimulation, the power of the frontal electrodes (F3-Fz-F4) increased markedly but not significantly from the baseline value, with a maximum at 0.2 s and lasting 0.5 s (Fig. 5). The power decreased significantly from 0.5 s to 1 s in Fz after all three stimulation modes. An increase in power from 4.8 s to 5 s in F4 after single-pulse stimulation was also noted.

After single and paired-pulse stimulation, the power of the central electrodes (C3-Cz-C4) increased significantly from the baseline value only in C3, with a maximum at 0.2 s and lasting 0.5 s. After transcallosal stimulation, the power increased significantly from 30% to 100% in C3, with a maximum after 0.2 s and lasting to 0.5 s. The power decreased significantly from 0.5 s to 1 s in Cz.

After single and paired-pulse stimulation, the power of the parietal electrodes (P3-Pz-P4) increased significantly from 70% to 100% over the baseline value, lasting >0.5 s (more evident in P3); after transcallosal stimulation, it increased significantly from 50% to 90% in P3 and P4.

**DISCUSSION**

This study sheds new light on the functional behavior of the human brain as investigated by TMS-induced modulation of EEG oscillations. Insight on the intracortical inhibitory sources of brain rhythms can be gained from the effects of single-pulse, paired-pulse, and transcallosal TMS on brain oscillations. Methods to induce synchronization of rapid brain rhythms (Fuggetta et al. 2005; Paus et al. 2001; Rosanova et al. 2009;...
Van Der Werf et al. (2006) and the effect of paired TMS on slow evoked transcranial potentials have been variously described (Ferreri et al. 2011). The novelty of the present method, however, resides in the application of a time-frequency analysis to the time course of rapid and slow brain oscillations induced by TMS. The main study finding is that low-intensity single, paired, and transcallosal TMS, applied on the sensorimotor areas, induces early desynchronization over the frontal and central-parietal electrodes, followed by a rebound of synchronization in the alpha and beta bands, and early synchronization in delta and theta activities. The power decrease in the alpha and beta bands is significantly evident (P \leq 0.05) in C3 and C4, with a well-defined time course. In contrast, in the midline and temporal and occipital electrodes this trend is less evident. In the alpha range there is a significant power decrease in O1 and O2 from \(-0.4\) s to \(0.8\) s, a shorter interval than that observed in C3 and C4 (Fig. 6). The lack of a significant modification in Cz, especially after single and paired pulses, is evidence for a noneffect of volume conducted. Synchronization of delta rhythm is more evident in the frontal and central electrodes than in the occipital electrodes, suggesting a physiological source of the rhythm reactive to TMS. In contrast, theta rhythm has the same stereotyped pattern for all the electrodes, probably due to the widespread scalp EEG oscillations induced by TMS. These findings indicate differences in the behavior of brain oscillations and suggest that the effect of ICI or transcortical inhibition can be studied by measuring MEP amplitude modulation. In all subjects we obtained a marked ICI with the paired TMS at \(3\) ms with an amplitude decrease from single to paired pulse (from a mean of \(350\) \(\mu\)V to a mean of \(30\) \(\mu\)V), as well as finding a decrease in amplitude from single to transcallosal stimulation (from a mean of \(350\) \(\mu\)V to a mean of \(250\) \(\mu\)V) in all subjects (Fig. 7).

Even if the number of subjects is limited, the results obtained in this pilot study are reproducible among subjects and the modifications of the EEG patterns are supported by \(t\)-test. Therefore the power decrease in alpha and beta bands is evident over the sensorimotor areas, and the synchronization of delta rhythm is more localized in frontal and central electrodes than in occipital electrodes. The research hypothesis is that cortical stimulation of an inhibitory network can induce the modulation of oscillatory activity.

Oscillatory activity and TMS. Early research on EEG-TMS coregistration reported only synchronization in beta activity after single magnetic stimulation and linked it to a sort of resetting or disruption of the ongoing oscillatory activity of M1 produced by external magnetic stimulation of the brain (Paus et al. 2001). Fuggetta et al. (2005) observed that single-pulse TMS produces an increase in power in both beta and alpha bands, unlike the self-motor finger movement, which produces
a well-known decrease in alpha and beta powers. We observed that the effect of a power increase was more evident with increasing stimulation from subthreshold to 130% rMT intensity. Moreover, we noted a significant effect using the threshold and minimal intensity stimulation on EEG activity (Fuggetta et al. 2005), which suggests an effect of magnetic stimulation on the cortical sources. The use of inhibitory paired stimulation is indeed more detailed and is known to primarily produce a cortical effect. Since the second pulse is the stronger one and activates not only intracortical neurons, it might prevent observation of the effect of the first pulse on the EEG. The effect of the first subthreshold stimulus without the second pulse should be explored, in order to show an effect of TMS-induced activation on intracortical systems. However, we cannot apply this type of analysis because the ISI is low (3 ms) and the effects of the two stimuli are not discernible; we can analyze only the EEG response after the second stimulus. Therefore, an increase in beta power has been observed by others (Rosanova et al. 2009; Van Der Werf et al. 2006). In this study we used wavelet-based methods to detect the temporal modulation of brain oscillations in the main frequency bands. The initial decrease of power in the alpha and beta bands, followed by a more prominent increase of power in beta activity over the ipsilateral and contralateral M1, is simultaneously associated with an early increase in delta power over the central and frontal areas, followed by a slow return to background activity. These patterns are visible in single and paired-pulse TMS, with greater diffusion on the hemisphere ipsilateral to stimulation, and also after transcallosal TMS, with a larger and more bilateral distribution probably related to the bilateral sites of stimulation and the diffusion of the callosal pathways.

EEG reactivity to perturbation of TMS can be explained by a different hypothesis. The spontaneous EEG signal is the indistinguishable summation of the activation of both fast and slow excitatory postsynaptic potentials (fEPSPs and sEPSPs, respectively) as well as fast and slow inhibitory postsynaptic potentials (fIPSPs and sIPSPs, respectively) (Rosenthal et al. 1967). fEPSPs are mediated by non-\textit{N}-methyl-\textit{d}-aspartate (NMDA), AMPA/kainate receptors with a rise time of 0.5–1.9 ms and sEPSPs are mediated by NMDA receptors with a rise time of 4–9 ms, while fIPSPs are mediated by \textit{\gamma}-aminobutyric
acid (GABA) postsynaptic receptors lasting \(~20–30\) ms (Davies et al. 1990; Deisz et al. 1999). sIPSPs are related to presynaptic and postsynaptic GABA\(_B\) receptors, with an inhibition that peaks around 100–200 ms, starting around 50 ms. TMS can stimulate different levels and different systems of neural tissue (Amassian et al. 1989; Pascual-Leone et al. 1994; Ruohonen et al. 1995, 1996a, 1996b). Threshold and low TMS intensities produce both direct and indirect excitation of pyramidal neurons in the gray matter through transsynaptical volleys (Rothwell 1991), but most importantly, TMS can explore the inhibitory system of the motor areas. SICI (as evaluated by means of MEP amplitude modulation at ISI 3 ms) is thought to explore the net effect of the activation of inhibitory GABA\(_A\) circuits in M1. The main finding of this study suggests that SICI is able to synchronize different patterns of oscillatory activity: the early and transitory decrease in alpha and beta activity and the long-lasting increase in delta and theta activity. While the early pattern could be related to the rapid GABA\(_A\) circuits, the long-time effect could be related to the suprathreshold single pulse, suggesting involvement of GABA\(_B\) receptor activity. We cannot exclude that vasomotor cerebral reactivity might influence brain rhythm desynchronization/synchronization, as found by using high-frequency repetitive TMS (rTMS) (Vernieri et al. 2009), although we used low-intensity single and paired TMS stimulation in this study. Furthermore, we cannot exclude a possible sensory feedback effect on the oscillatory activity of motor areas; nonetheless, the peripheral effect of paired and transcallosal stimulation on muscle twitch is minimal or absent, while its effect on brain oscillation remains significant.

Modulation of brain oscillations by transcallosal TMS. The decrease in alpha and beta bands is observed also on the contralateral hemisphere after transcallosal TMS with ISI of 10 ms, consistent with the transcallosal conduction time of 12–15 ms found with the use of electrical stimulation and TMS (Ferbert et al. 1992). Transcallosal projections synapse onto local inhibitory circuits mediating SICI within the target hemisphere (Daskalakis et al. 2002). Recently, homologous connections and their preferential inhibitory effects in humans were indirectly observed at latencies of 10 ms (Ferreri et al. 2011; Mochizuki et al. 2004). The early decrease in alpha and beta activity, followed by the rebound of synchronization, and the increase in power of delta activity on both sides after transcallosal TMS at ISI 10 ms again suggest GABAergic neurotransmission in both the generation and modulation of delta, beta, and alpha frequency oscillations within the transcallosal pathways and distributed over both hemispheres.

Fig. 7. Representative motor evoked potential (MEP) evoked by single, paired, and transcallosal pulse TMS (4 traces for each stimulus). Traces are aligned to the second stimulus [paired-pulse stimulation: interstimulus interval (ISI) = 3 ms, transcallosal stimulation: ISI = 10 ms].
Single-pulse TMS induces a population of neurons within the stimulated volume of the sensorimotor cortex to oscillate in the entire range of frequencies. The time-frequency approach provides timing of low-frequency brain rhythms that have a synchronization pattern different from that of high-frequency brain rhythms, but most importantly, inhibitory paired-pulse TMS over the primary motor areas or transcallosal stimulation probably activates “idling” neurons that, owing to their membrane properties or intracortical connectivity, begin to oscillate. EEG-TMS is a promising tool to characterize the neuronal circuits as well as the neural mechanisms regulating inhibition within the cortices.

Further studies, with an increased number of subjects, are necessary to confirm these preliminary observations and to improve the significant differences between electrode positions and stimulation protocols. The data could be insufficient to define the different effects of the stimulations; however, they add important information on the pattern of oscillatory activity during stimulations and allow a possible use of this new method of analysis in clinical neurophysiology.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

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