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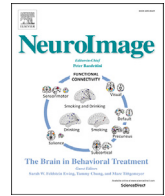
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Comparing MEG and EEG in detecting the ~20-Hz rhythm modulation to tactile and proprioceptive stimulation

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ABSTRACT

Modulation of the ~20-Hz brain rhythm has been used to evaluate the functional state of the sensorimotor cortex both in healthy subjects and patients, such as stroke patients. The ~20-Hz brain rhythm can be detected by both magnetoencephalography (MEG) and electroencephalography (EEG), but the comparability of these methods has not been evaluated. Here, we compare these two methods in the evaluating of ~20-Hz activity modulation to somatosensory stimuli.

Rhythmic ~20-Hz activity during separate tactile and proprioceptive stimulation of the right and left index finger was recorded simultaneously with MEG and EEG in twenty-four healthy participants.

Both tactile and proprioceptive stimulus produced a clear suppression at 300–350 ms followed by a subsequent rebound at 700–900 ms after stimulus onset, detected at similar latencies both with MEG and EEG. The relative amplitudes of suppression and rebound correlated strongly between MEG and EEG recordings. However, the relative strength of suppression and rebound in the contralateral hemisphere (with respect to the stimulated hand) was significantly stronger in MEG than in EEG recordings.

Our results indicate that MEG recordings produced signals with higher signal-to-noise ratio than EEG, favoring MEG as an optimal tool for studies evaluating sensorimotor cortical functions. However, the strong correlation between MEG and EEG results encourages the use of EEG when translating studies to clinical practice. The clear advantage of EEG is the availability of the method in hospitals and bed-side measurements at the acute phase.

1. Introduction

The ~20-Hz beta rhythm, detected over the Rolandic area, is modulated by somatosensory stimuli and motor activity, i.e. tactile stimulation (Cheyne et al., 2003; Gaetz and Cheyne, 2006; Houdayer et al., 2006; Pfurtscheller et al., 2001; Salmelin and Hari, 1994), voluntary movement (Cassim et al., 2001; Feige et al., 1996), passive movement (Alegre et al., 2002; Cassim et al., 2001; Parkkonen et al., 2015), action observation (Hari et al., 1998), motor imagining (Neuper et al., 2005; Schnitzler et al., 1997) or even to distracting auditory and visual stimuli (Piitulainen et al., 2015b). The amplitude of the rhythm is typically reduced soon

after stimulus onset (suppression; event-related desynchronization (ERD), or movement related beta desynchronization (MRBD)), followed by an increase in the strength of the rhythm (rebound; event-related synchronization (ERS), or post movement beta rebound (PMBR)). The 'suppression' is thought to reflect activation (Chen et al., 1998; Pfurtscheller and Lopes da Silva, 1999) and the 'rebound' active inhibition or reduced excitability of the sensorimotor cortex (Cassim et al., 2001; Chen et al., 1998; Gaetz et al., 2011).

The ~20-Hz rebound has been used to assess the functional state of the sensorimotor cortex, and since it reflects changes in inhibitory mechanisms, it has been considered to be a suitable marker of neural

Abbreviations: EEG, electroencephalography; MEG, magnetoencephalography; MSR, magnetically shielded room; PCA, principal component analysis; PSD, power-spectra density; SMI, primary sensorimotor cortex; TFR, time-frequency representations; TSE, temporal spectral evolution.

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plasticity in the brain (Gaetz et al., 2010; Mary et al., 2015). Indeed, the ~20-Hz rebound has been successfully used as a neurophysiological biomarker to evaluate motor recovery after stroke (Laaksonen et al., 2012; Parkkonen et al., 2017), and to characterize neurophysiological changes in Parkinson's disease (Degardin et al., 2009; Hall et al., 2014), schizophrenia (Brookes et al., 2015; Liddle et al., 2016; Robson et al., 2015) and Unverricht-Lundborg type epilepsy (Silen et al., 2000).

Although the modulation of the ~20-Hz rhythm has been studied both with MEG and EEG, there are no studies examining this phenomenon simultaneously using both methods. Both MEG and EEG measure electrical activity generated by tens of thousands of simultaneously active cortical pyramidal cells from outside the head, with the difference that EEG measures electrical potentials and MEG magnetic fields generated by neuronal currents. Both methods have their advantages. In MEG, the magnetic fields propagate through the head almost unchanged and provide thus a less spatially distorted signal, which allows more accurate source localization (Hari, 2011). MEG is also less sensitive to disturbances caused by movements and muscle (Claus et al., 2012; Hämäläinen et al., 1993; Hari and Puce, 2017; Whitham et al., 2007). On the other hand, MEG devices are available only in a few centers, and MEG needs to be recorded in a magnetically shielded room (MSR), that attenuates external electrical interference, thus providing a very low interference environment also for measuring EEG. EEG is cheaper, widely available, and can be brought directly to the patient. The better availability and lower operating costs make EEG an attractive method to be used especially in clinical settings.

We have successfully used the ~20-Hz rebound as a motor recovery-related neurophysiological biomarker in acute stroke patients using MEG (Laaksonen et al., 2012; Parkkonen et al., 2017). In the present study, we aimed to clarify if the ~20-Hz rebound is equally well identified in EEG recordings allowing its use in future clinical studies. The use of EEG would allow to explore larger patient groups, and to include more severely affected stroke patients not suitable for measurements outside the ward.

2. Materials and methods

2.1. Subjects and data availability

Twenty-four healthy participants (11 females, age 19–35, mean 23 ± 4 yrs) volunteered in the experiment. Twenty-two subjects were right-handed, one left-handed and one ambidextrous, according to the Edinburgh Handedness Inventory (Oldfield, 1971).

The local ethics committee of Aalto University approved the experiment in accordance with the Declaration of Helsinki. All subjects gave written informed consent prior to participation.

2.2. Experimental design

In order to modulate the ~20-Hz sensorimotor cortex rhythm, two different stimuli, tactile and proprioceptive stimulation, were applied in separate sessions. The order of the sessions was randomized. The participants were instructed to remain relaxed, not to pay attention to the stimuli, and to fixate on a 12×15 cm picture at a distance of 2.2 m in front of them. The subjects wore earplugs throughout the measurement to attenuate possible weak noise artefacts, caused by the stimulators.

Tactile stimulation. Tactile stimuli were delivered alternately to both index fingertips by pneumatic diaphragms driven by compressed air (stimulus duration 180 ms, peaking at 40 ms) with an interstimulus interval of 3 s (6 s each finger) controlled by the acquisition computer. During the stimulation, the participants held their hands relaxed on a pillow.

Proprioceptive stimulation. Proprioceptive stimulation was elicited by a pneumatic -artificial muscle embedded in a mechanical movement actuator (Piiitulainen et al., 2015a) causing a fast flexion-extension movement of the index finger. The stimulus was delivered in separate

sessions to the right and left index finger with an ISI of 5 s. The duration (130 ms) and onset (35 ms mechanical delay from the trigger pulse onset to actual movement onset) of the movement were detected with a 3-axis accelerometer (ADXL335 iMEMS Accelerometer, Analog Devices Inc., Norwood, MA, USA), attached to the nail of the index finger. The range of the movement was ~5 mm with the used compressed air pressure of 4 bar. The stimulated hand was supported with pillows to the level of the movement actuator and the tip of the index finger was lightly taped on the artificial muscle. A piece of surgical tape was applied around the fingertip to minimize possible tactile sensation caused by the movement. A visual barrier was used to prevent motion-induced visual contamination.

Resting state recordings. After the stimulation protocols, resting state data with eyes open 3 min was recorded.

2.3. Data acquisition

Rhythmic brain activity was recorded with a 306-channel (204 planar gradiometers, 102 magnetometers) whole-scalp MEG system (Elekta Neuromag, Elekta Oy, Helsinki, Finland) at the MEG Core, Aalto Neuroimaging, Aalto University. EEG was recorded simultaneously with a MEG-compatible EEG cap (ANT Neuro waveguard™original), containing 60 Ag–AgCl surface electrodes mounted according to the international 10–20 system. The measurements were performed in a magnetically shielded room (MSR; Imedco AG, Hägendorf, Switzerland), where the participant was comfortably seated with the head in the helmet-shaped MEG sensor array. Five indicator coils were attached onto the EEG-cap (three to the forehead and one above each ear) to define the subject's head position with respect to the MEG sensors. The location of the indicator coils together with three anatomical landmarks (left and right preauricular points and nasion) and 100–200 additional points from the scalp surface, were determined with a 3-D digitizer (Fastrak 3SF0002, Polhemus Navigator Sciences, Colchester, VT, USA), prior to the measurements. The head position with respect to the sensor array was measured at the beginning of each measurement session (and its stability was monitored across measurement periods). In addition, the head position was tracked with continuous head position monitoring throughout the MEG measurement. Two vertical electro-oculogram electrodes (EOG) were used to detect artefacts caused by eye blinks.

MEG and EEG signals were acquired at a sampling frequency of 1000 Hz, and the signal was band-pass filtered to 0.1–330 Hz. The impedance of the EEG electrodes was kept below 10 k Ω in fifteen subjects and below 5 k Ω in nine subjects (impedance meter changed). The adequacy and quality of the data was evaluated during the measurement based on the raw signals and on-line averaged evoked responses.

2.4. Data processing and analysis

Preprocessing. For each participant, the MEG signals of the different stimulation sessions were transformed to the same head-coordinate system within participant, which in our case was the mean position between tactile and proprioceptive recordings, using a custom made Matlab script. These averaged head coordinates were used as reference head position in the Maxfilter software (v2.2; Elekta Oy, Helsinki, Finland) for coordinate matching and head movement compensation. This procedure enables better comparability between the MEG recordings. To compute grand average topographic maps, the head coordinates of the different stimulation sessions of all participants were transformed to the same standard position with respect to the MEG sensors. Since a larger head-coordinate transformation can increase noise in the MEG data, this transformation was only used to compute the topographic maps. Along with coordinate transfers, the MEG raw signals were preprocessed off-line with the MaxFilter software, using the signal-space separation method with temporal extension (tSSS), including head movement compensation with a threshold of 25 mm (Taulu, 2005; Taulu and Simola, 2006). For tSSS, the length of the data buffer was 16 s, the subspace correlation limit 0.98,

and the inside expansion order 8, and outside expansion 3.

All further analyses were done using custom-written routines in MNE-Python (Gramfort et al., 2013). The individual EEG signals were referenced with respect to the average over all EEG electrodes (excluding bad channels). Since the reference used in EEG analyses may have an effect on the results, we tested a few additional EEG-reference alternatives: (1) a surface Laplacian (SL), using a next-nearest-neighbor derivation, was computed to reduce head volume conduction effects and to obtain a reference-free EEG (Hjorth, 1975; McFarland et al., 1997), and (2) bipolar montage, according to clinical recommendation in somatosensory evoked potential measurements (Cruccu et al., 2008). However, the results of these two alternative references are not presented in this context, as the average reference produced the strongest signals of ~20-Hz modulation and was thus chosen to be used in the final analysis.

Stimulus related evoked responses were removed from the raw data by subtracting the averaged evoked responses from each epoch to better reveal the modulation of the ~20-Hz activity (i.e. induced response). The evoked component can distract the baseline determination of ~20-Hz activity in further analysis (David et al., 2006). Eye movement artefacts were removed using a principal component analysis (PCA) (Uusitalo and Ilmoniemi, 1997), removing two magnetometer, two gradiometer and two EEG components related to eye blinks from the signals.

Spontaneous ~20-Hz activity. To determine the frequencies and amplitudes of spontaneous resting state beta activity, power-spectral densities (PSD) were calculated from the eyes-open resting state data using the Welch method, with a sliding 2048-point fast Fourier transform (FFT) with no overlap and a Hann window function. From the PSD, the peak frequencies in the beta frequency bands (β_1 ~13–19 and β_2 ~19–27) were extracted using automated peak detection for each subject individually for both the right and the left hemispheres. To visually ensure the strongest frequency range of beta rhythm modulation, time-frequency representations (TFRs) were calculated for all conditions in the frequency range of 3–36 Hz for a time window from –700 to 3200 ms with respect to stimulus onset, for each subject. The Morlet wavelet transformation was used in TFR calculation (Tallon-Baudry et al., 1997a, 1997b). The spectral and temporal resolution of the TFRs was balanced by scaling the number of cycles by frequency (number of cycles was set to $f/2$).

Modulation of ~20-Hz rhythm. The modulation of the ~20-Hz sensorimotor cortex rhythm was quantified using the temporal spectral evolution (TSE) method (Salmelin and Hari, 1994), where the continuous data was first band-pass filtered, then rectified and averaged time-locked to the stimulus onset. The pre-stimulus time (–500–100 ms) was set to zero level, to obtain both negative and positive values. TSE curves were computed for three frequency bands (13–23 Hz, 15–25 Hz and 17–27 Hz) for each subject separately, and the individual frequency band with strongest modulation was visually selected for further analysis. This band was used for both MEG and EEG analysis as the strongest modulation occurred at the same band in both methods. The analysis period for both conditions was from –700 to 3200 ms with respect to stimulus onset. In order to quantify the peak amplitudes and latencies of suppression and rebound, the most responsive MEG and EEG channel was selected from the left and right hemisphere separately. If peak suppression and rebound were strongest in different channels, separate channels were selected for further analyses. The peak values were converted into relative values by calculating the percentage of decrease/increase of the rhythm with respect to the pre-stimulus baseline (time period from –500 to –100 ms).

2.5. Statistical analysis

Kolmogorov–Smirnov and Shapiro–Wilkin tests (IBM SPSS Statistics 24) were used to test the normal distribution of the relative values of suppression and rebound. Due to non-normal distribution, correlations between MEG and EEG strengths were calculated with the nonparametric Spearman's correlation coefficient. For the same reason, the nonparametric Wilcoxon signed-rank test was used to analyze significant

differences between MEG and EEG results. A p -value < 0.05 was considered as statistically significant.

3. Results

The quality of the data of MEG/EEG recordings for all twenty-four subjects was good, despite of two MEG and 1–3 bad EEG channels throughout the measurements, which were not located in the sensorimotor cortex area. The number of applied stimuli used in the TSE analysis was 105 ± 11 (mean \pm SD) for tactile and 108 ± 11 for proprioceptive stimuli. Fig. 1 shows the TSE curve in one representative participant for both tactile and proprioceptive stimuli.

3.1. Spontaneous ~20-Hz activity

In the eyes-open resting state condition, the strongest frequency points of β_1 (~13–19 Hz) and β_2 (~19–27 Hz) were detected both in MEG and EEG over the left and right sensorimotor regions. No differences in the frequencies nor strengths of the ~20-Hz peaks at rest were observed between the hemispheres nor between MEG and EEG measurements (Table 1).

3.2. Modulation of the ~20-Hz rhythm

Frequency band. The modulation of the beta rhythm to tactile and proprioceptive stimulation was observed at a frequency range of 13–27 Hz, from which the 10 Hz bandwidth of strongest modulation was individually selected for each subject. The strongest modulation occurred interindividually in slightly different frequency bands, and therefore, the accurate 10 Hz bandwidth was individually selected for further analysis.

Latencies. Both MEG and EEG showed clear modulation of the ~20-Hz rhythm to both tactile and proprioceptive stimulation, as Fig. 2 illustrates. Both stimuli induced an initial suppression at 300–400 ms duration, strongest at around 330 ms, followed by a subsequent rebound of 2000–2500 ms duration, strongest at around 820 ms. The latencies of suppression and rebound were very similar between MEG and EEG recordings (Table 2).

Spatial distribution of the ~20-Hz modulation. Fig. 3 shows the grand averaged ($n = 24$) topographic distribution of the ~20-Hz suppression (at 350 ms after stimulus onset) and rebound (at 800 ms after stimulus onset) for MEG magnetometers and EEG electrodes. Suppression and rebound of the ~20-Hz rhythm was seen bilaterally over the sensorimotor cortices for unilateral stimulations both for MEG and EEG. As demonstrated by earlier (Salmelin et al., 1997; Salmelin and Hari, 1994), the modulation of the rhythm was always strongest in the contralateral hemisphere to the stimulated hand. This was more pronounced in MEG than EEG recordings.

Suppression and rebound amplitudes to tactile and proprioceptive stimulation. Fig. 4 illustrates the relative (%) peak amplitudes of suppression and rebound to tactile and proprioceptive stimulation. To tactile stimulation, the suppression was significantly stronger in MEG than in EEG recordings in the contralateral hemisphere to both left and right finger stimulation ($-28 \pm 2\%$ vs. $-22 \pm 2\%$, $p < 0.01$ for left and $-25 \pm 2\%$ vs. $-20 \pm 2\%$, $p < 0.01$ for right finger stimulation). Also the rebound amplitudes were stronger in MEG than in EEG recordings ($63 \pm 9\%$ vs. $48 \pm 6\%$, $p < 0.05$ for left and $53 \pm 8\%$ vs. $41 \pm 5\%$, $p < 0.07$ for right finger stimulation), albeit the difference for right finger stimulation did not reach significance. Table 2 shows relative peak amplitudes for suppression and rebound.

To proprioceptive stimulation, the suppression was significantly stronger in MEG than in EEG in the contralateral hemisphere to left finger stimulation ($-27 \pm 2\%$ vs. $-21 \pm 2\%$, $p < 0.01$, respectively), and right finger stimulation ($-25 \pm 2\%$ vs. $-21 \pm 2\%$, $p < 0.05$). The rebound amplitudes in the contralateral hemisphere to both left and right finger stimulation were significantly stronger in MEG than in EEG recordings ($53 \pm 9\%$ vs. $39 \pm 5\%$, $p < 0.05$ for left and $53 \pm 9\%$ vs. $39 \pm 5\%$, $p <$

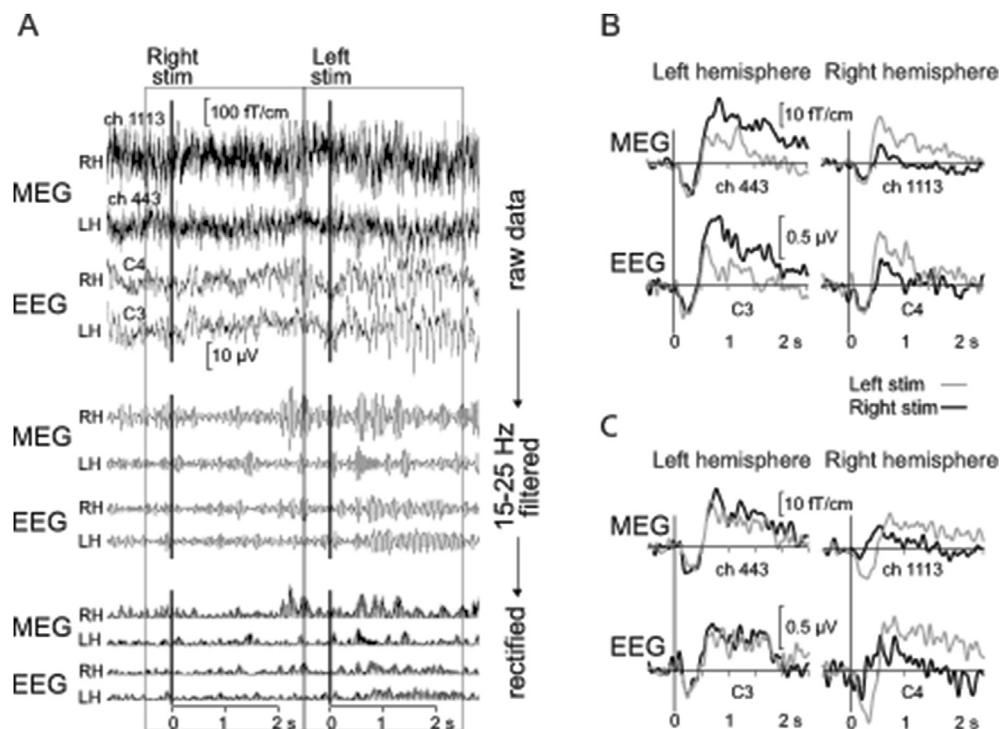


Fig. 1. Modulation of the ~20-Hz rhythm in one participant. (A) In TSE analysis, MEG and EEG raw data was filtered to the beta band (15–25 Hz), then rectified and averaged with respect to the (B) tactile and (C) proprioceptive stimulation. The most representative channels over the SMI region from the right (RH) and left hemispheres (LH) are shown. Stimulus onset is indicated by a vertical line at 0 s.

Table 1

Frequencies and amplitudes ($n = 24$) of the strongest point (mean \pm SEM) of the spectral β_1 (~13–19 Hz) and β_2 (~19–27 Hz) frequencies in the eyes-open condition.

	β_1		β_2	
	RH	LH	RH	LH
Peak frequency (Hz)				
MEG	16.3 \pm 0.3	16.2 \pm 0.3	21.3 \pm 0.3	21.1 \pm 0.3
EEG	16.1 \pm 0.4	16.2 \pm 0.4	21.8 \pm 0.5	21.7 \pm 0.5
Peak amplitude				
MEG (fT/cm) ²	12.7 \pm 2.8	12.3 \pm 2.6	14.0 \pm 2.8	11.9 \pm 2.2
EEG (μ V) ²	1.2 \pm 0.2	1.4 \pm 0.3	1.0 \pm 0.1	1.4 \pm 0.3

LH, left hemisphere.

RH, right hemisphere.

0.05 for right finger stimulation).

The amplitudes of suppression and rebound in the ipsilateral hemisphere to the stimulated hand did not differ between MEG and EEG measurements neither to tactile nor to proprioceptive stimuli. More detailed values are shown in Table 2.

3.3. Correlation between MEG and EEG measurements

The suppression and rebound strengths correlated strongly between MEG and EEG measurements both to tactile and proprioceptive stimulation. Fig. 5A illustrates the correlations of suppression in the hemisphere contralateral to the stimulated hand between MEG and EEG recordings. To tactile stimulation, the correlation was $r = 0.70$ ($p < 0.01$) for left and $r = 0.70$ ($p < 0.01$) for right finger stimulation, and to proprioceptive stimulation $r = 0.64$ ($p < 0.01$) for left and $r = 0.70$ ($p < 0.01$) for right finger stimulation (Table 3).

Correlations of the rebound strengths in the hemisphere contralateral to the stimulated hand between MEG and EEG measurements are shown in Fig. 5B. The correlation to tactile stimulation was $r = 0.62$ ($p < 0.01$)

for left and $r = 0.80$ ($p < 0.01$) for right finger, and to proprioceptive stimulation $r = 0.84$ ($p < 0.01$) for left and $r = 0.81$ ($p < 0.01$) for right finger stimulation. Table 3 shows more information about correlation.

4. Discussion

To our knowledge, this is the first study that compares the modulation of the ~20-Hz rhythm in simultaneously measured MEG and EEG. This comparison is of clinical significance, as the ~20-Hz modulation could be used as an indicator of recovery potential after stroke if the measurements were easily available. Our results demonstrate that the modulation of the ~20-Hz rhythm is well detectable both using MEG and EEG; the suppression and rebound of the rhythm to both tactile and proprioceptive stimulation peaked at similar latencies and locations in both MEG and EEG recordings. However, the modulation of the rhythm was stronger in MEG than in EEG recordings.

4.1. ~20-Hz modulation in MEG vs. EEG

In the present study, the ~20-Hz rhythm modulation to sensory stimulation detected with MEG and EEG was in good agreement with previous studies using MEG and EEG (Alegre et al., 2002; Houdayer et al., 2006; Laaksonen et al., 2012; Neuper and Pfurtscheller, 2001; Parkkonen et al., 2015; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1996a, 1996b; Salmelin and Hari, 1994). The rebound amplitudes in the contralateral hemisphere to the stimulated hand were stronger in MEG than in EEG recordings. Magnetic fields propagate through the head almost unchanged and provide thus a less spatially distorted signal, whereas in EEG the membranes, skull, scalp and spinal fluid greatly modify the electrical current measured from the surface of the head (Antonakakis et al., 2019). For this reason, MEG typically has better spatial resolution than EEG, and thus it can separate simultaneously active sources more precisely. This was evident also in the current topographical maps. As MEG is biased towards tangential currents, it is a particularly suitable method to detect activity arising from the fissural

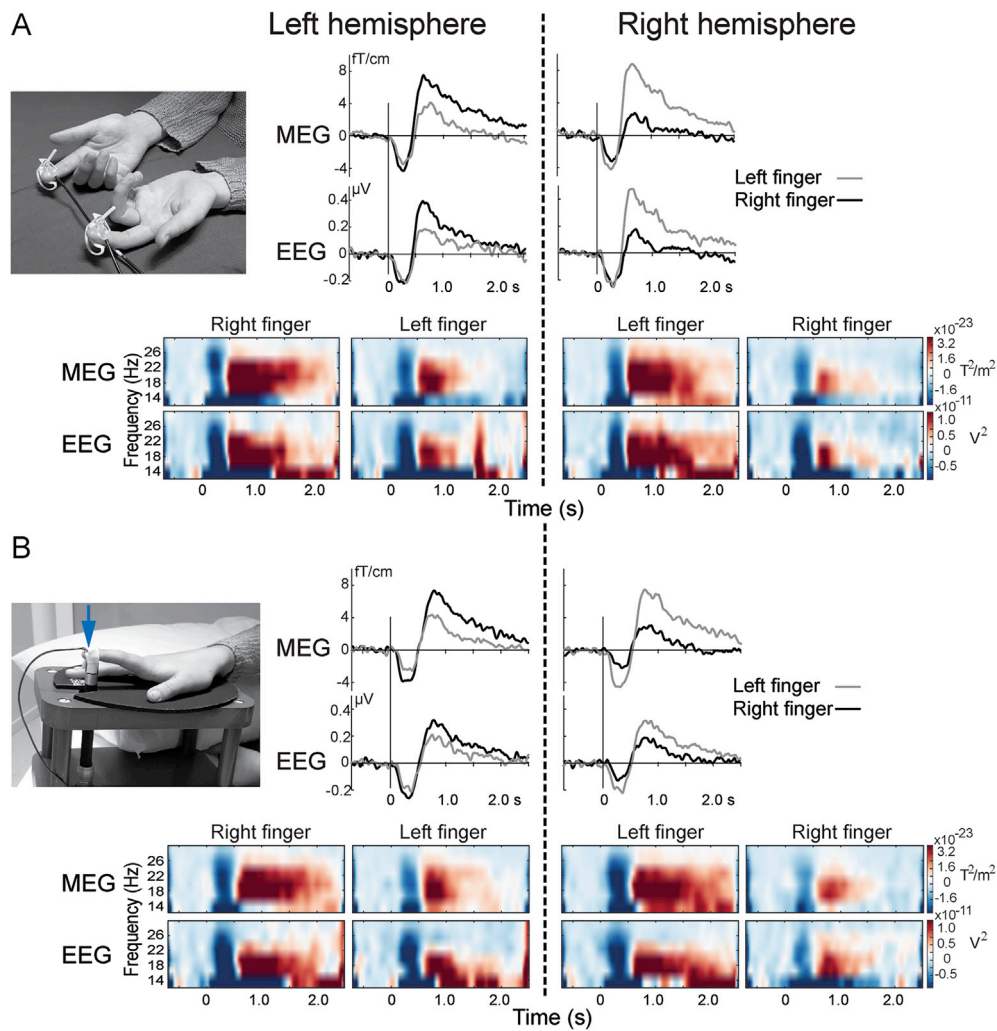


Fig. 2. ~20-Hz rhythm modulation to (A) tactile and (B) proprioceptive stimulation. Grand averaged (N = 24) TSE curves from one most representative channel over the left and right sensorimotor areas are shown on the right side of stimulus setup images, and corresponding time frequency representations (TFR) are presented below them. The vertical line at 0 s indicates the onset of the stimulus.

Table 2

The relative amplitudes and latencies (mean ± SEM) of the ~20-Hz suppression and rebound (n = 24) with respect to the baseline level elicited by tactile and proprioceptive stimulation.

Tactile stim	Left finger				Right finger			
	MEG IH	EEG IH	MEG CH	EEG CH	MEG CH	EEG CH	MEG IH	EEG IH
Suppression								
Relative amplitude (%)	-20 ± 2	-18 ± 2	-28 ± 2	-22 ± 2	-25 ± 2	-20 ± 2	-20 ± 2	-21 ± 2
Peak latency (ms)	319 ± 19	297 ± 19	303 ± 15	313 ± 20	314 ± 14	300 ± 21	321 ± 17	330 ± 21
Rebound								
Relative amplitude (%)	28 ± 5	23 ± 3	63 ± 9	48 ± 6	53 ± 8	41 ± 5	22 ± 4	21 ± 2
Peak latency (ms)	837 ± 43	792 ± 54	725 ± 37	741 ± 42	788 ± 40	739 ± 44	827 ± 48	768 ± 42
Proprioceptive stim	Left finger				Right finger			
	MEG IH	EEG IH	MEG CH	EEG CH	MEG CH	EEG CH	MEG IH	EEG IH
Suppression								
Relative amplitude (%)	-18 ± 2	-19 ± 2	-27 ± 2	-21 ± 2	-25 ± 2	-21 ± 2	-15 ± 2	-17 ± 1
Peak latency (ms)	357 ± 22	339 ± 21	332 ± 17	315 ± 16	360 ± 18	316 ± 14	362 ± 21	349 ± 17
Rebound								
Relative amplitude (%)	36 ± 7	29 ± 4	53 ± 9	39 ± 5	53 ± 9	39 ± 5	25 ± 4	23 ± 3
Peak latency (ms)	831 ± 46	874 ± 38	853 ± 33	856 ± 34	869 ± 36	879 ± 55	821 ± 44	817 ± 42

IH, ipsilateral hemisphere with respect to stimulus.

CH, contralateral hemisphere with respect to stimulus.

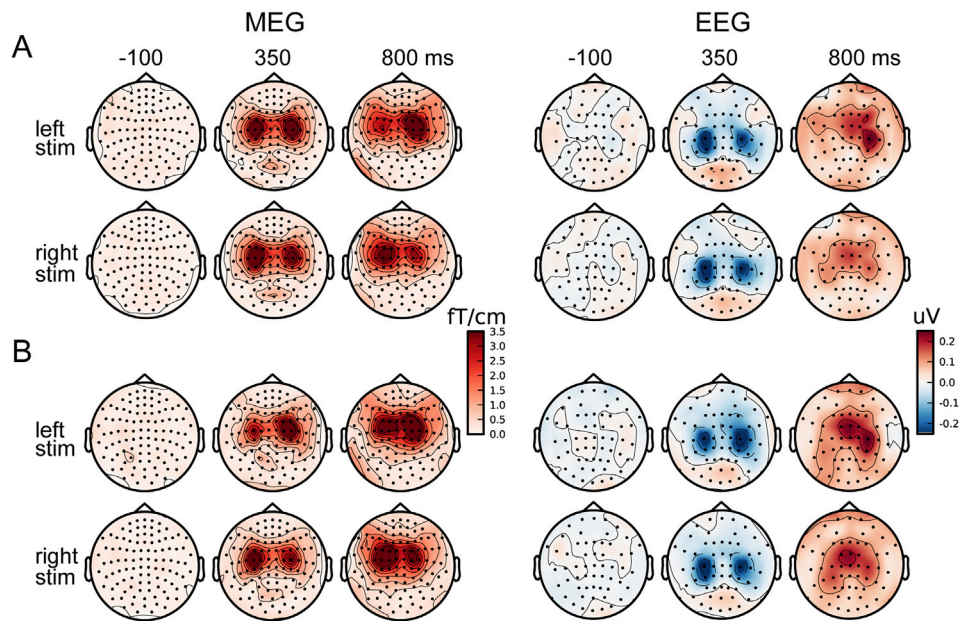


Fig. 3. Topographic maps showing group averaged ($n = 24$) field strengths of the ~ 20 -Hz rhythm modulation to (A) tactile and (B) proprioceptive stimulation both in MEG and EEG (magnetic field vs. electric scalp potential). Note that MEG topoplots shows vector sums of gradiometers (positive value) in each location.

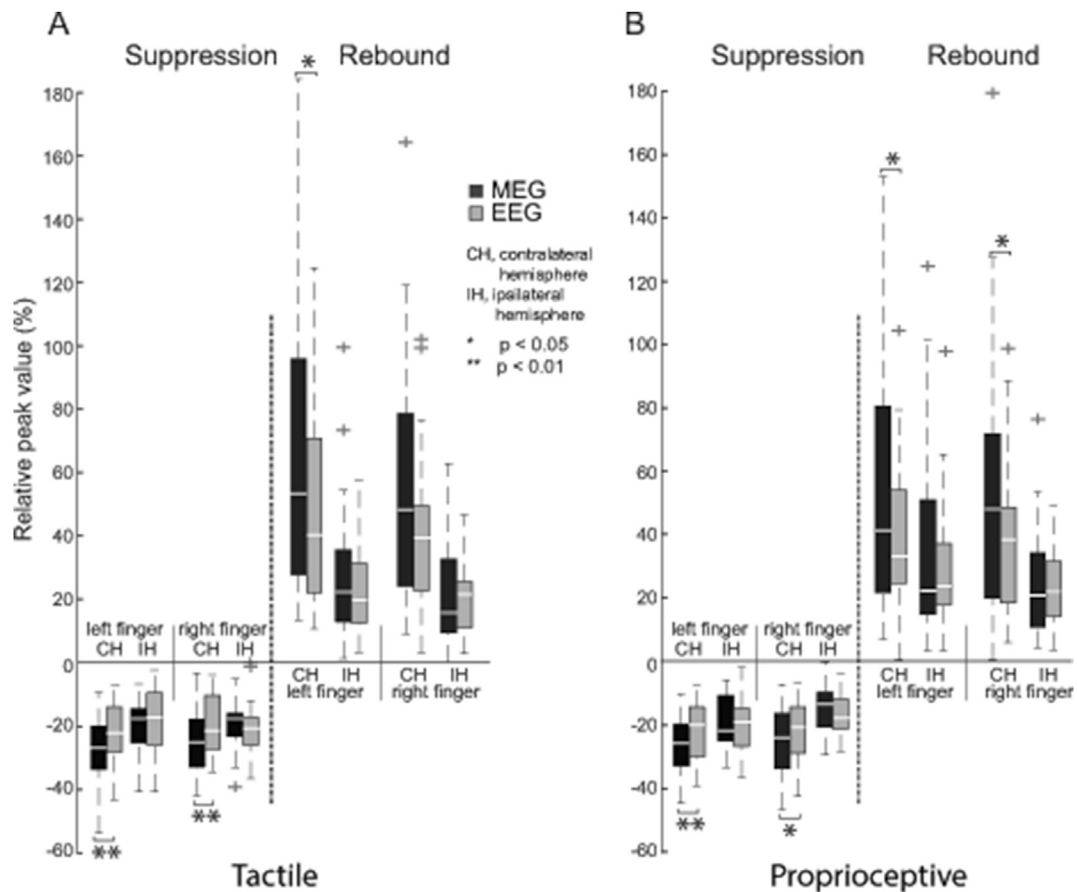


Fig. 4. Peak amplitudes of ~ 20 -Hz rhythm suppression and rebound to (A) tactile and (B) proprioceptive stimulation. Note that values are relative amplitudes with respect to baseline. The boxes include 50% of the data points and horizontal lines inside boxes indicates median values. The whiskers show data range without outliers, which are shown by the crosses. The outliers were defined as a value more than 1.5 times the interquartile range away from the top or bottom of the box. Statistical significances, based on Wilcoxon signed-rank test, are denoted as * $P < 0.05$ and ** $P < 0.01$.

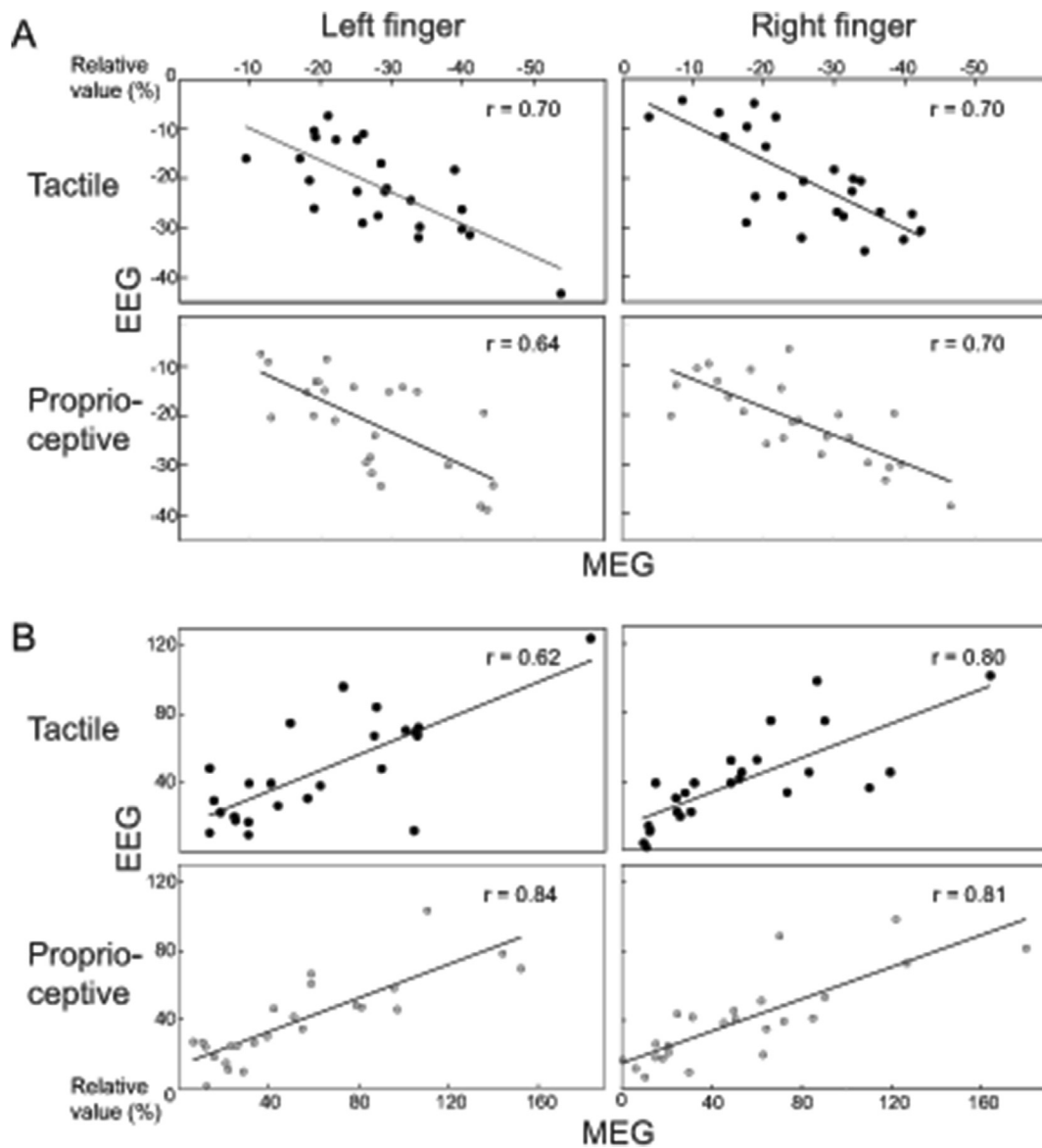


Fig. 5. Correlation of the relative amplitude values (%) of the ~20-Hz rhythm to (A) suppression and (B) rebound between MEG and EEG recordings. Correlations are shown only for the contralateral responses with respect to the stimulated finger. Please note that the correlation is positive for both the suppression and rebound responses.

Table 3
Spearman’s correlation coefficients (r) of the ~20-Hz rhythm suppression and rebound amplitudes with respect to baseline level between MEG and EEG results.

Tactile stim	Left finger		Right finger	
	LH	RH	LH	RH
Suppression	0.72**	0.70**	0.70**	0.36
Rebound	0.81**	0.62**	0.80**	0.81**
Proprioceptive stim	Left finger		Right finger	
	LH	RH	LH	RH
Suppression	0.66**	0.64**	0.70**	0.33
Rebound	0.73**	.84**	0.81**	0.88**

LH, left hemisphere.
RH, right hemisphere.
**p < 0.01.

cortex, such as large parts of the primary sensorimotor (SMI) cortex, but at the same time the sensitivity to deeper sources is weaker (Hari and Puce, 2017; Hillebrand and Barnes, 2002). The depth and orientation of

the source significantly affect its measurability with MEG and EEG; MEG detects better tangential sources, while EEG detects better radial as well as deeper sources (Hunold et al., 2016). Since the ~20-Hz rhythm is mainly generated in the pre-and postcentral walls of the central fissure, MEG provides an excellent tool to detect this rhythm, which was also observed in our results of the stronger ~20-Hz suppression and rebound in MEG than EEG. Combining MEG and EEG could also provide valuable additional information on source localization of the ~20-Hz suppression and rebound (Antonakakis et al., 2019), as well as improve overall SNR (Goldenholz et al., 2009).

Our main objective was to compare the strength of ~20-Hz modulation between MEG and EEG recordings. In line with our hypothesis, we observed stronger modulation in MEG compared to EEG in some of the examined variables, most likely due to better overall signal-to-noise ratio in MEG signals. However, we did not correct for multiple comparisons because use of e.g. Bonferroni correction carries the risk of a Type II error, and some clear differences are possibly removed (Perneger, 1998).

In EEG studies, the reference location affects the analysis results, in contrast to the reference-free MEG, making MEG analyses more

straightforward. As the purpose of this study was to compare EEG with MEG results, it was important to ascertain whether the references methods commonly used in the ~ 20 -Hz rhythm modulation studies has an effect on the EEG results (Pfurtscheller and Lopes da Silva, 1999). The average reference was decided to be used in the final comparison between MEG and EEG, as the suppression and rebound came out more strongly and the overall noise decreased, compared to the original reference (AFz) in the on-line measurement. The surface Laplacian derivatives were tested as well, but as it reduced the peak amplitude strength of suppression and rebound, the results are not presented here. Likewise, analyses were also performed according to the clinical recommendations used in somatosensory evoked potential (SEP) measurements (Crucchi et al., 2008), but also here the modulations were weaker and are hence not discussed further in this context.

Although the measurements were made in a highly undisturbed environment in a MSR, both MEG and EEG data contain unavoidable noise from the human physiology and devices in use. The overall noise level can be even higher in a hospital than in the MSR environment, affecting the results of EEG in clinical settings. In principle, more averaged responses would improve the signal-to-noise ratio, but the problem with long measurement sessions and extensive repetitions of stimuli is the attenuation of brain responses, due to short-term habituation and changes in vigilance.

4.2. ~ 20 -Hz modulation to tactile vs. proprioceptive stimulation

Passive movement, e.g., proprioceptive stimulus has rarely been used to modulate the beta rhythm, and there are only a few comparative studies between different somatosensory stimuli. The results have been variable; passive movement has been shown to produce a similar strong rebounds as tactile stimulation (Alegre et al., 2002; Muller et al., 2003), whereas, other studies have reported stronger rebounds to both passive and active self-paced movement than tactile stimulation (Houdayer et al., 2006; Parkkonen et al., 2015). ~ 20 -Hz rhythm modulation to self-paced movement has been explored more extensively, and based on these studies, it can be concluded that the ~ 20 -Hz rebound is quite sensitive to variations in kinematics of the movement. Faster movement, as well as a wider movement range or a larger group of active muscles have been shown to produce stronger (Cassim et al., 2000; Fry et al., 2016; Pfurtscheller et al., 1998). These factors underlie the importance to use well-known or standardized stimuli in forthcoming patient studies. In our study, the tactile and proprioceptive stimuli of the index finger generated clear and relatively well comparable rebounds and suppressions, although the range of the passive movement was rather small. In the present study, the passive movement was carried out by the computer-controlled mechanical device that was easy to control and features (e.g., like timing, duration, and intensity) are constant and adjustable. Based on the results, both stimulus modalities used in the present study are useful and easy to implement in future clinical studies, as patients may not be capable to perform a volitional or complex task. In addition, it is recommended to keep the stimulus as simple as possible as complexity of the movement is shown to reduce the rhythmic activity of the brain (Manganotti et al., 1998). Tactile stimulation can be recommended to be used to modulate the ~ 20 -Hz rhythm, especially in clinical studies. It is easy to implement pneumatically or by simple electrical stimulation of the fingertip (Stancak et al., 2003). However, the electrical stimulation may activate also the pain receptors and potentially cause electromagnetic artefacts.

4.3. Frequency band of ~ 20 -Hz modulation

The frequency band of strongest ~ 20 -Hz modulation differed slightly between participants and stimuli, in line with earlier studies (Houdayer et al., 2006; Laaksonen et al., 2012; Pihko et al., 2014), but was consistent for MEG and EEG data at individual level. The resting state power

spectra with eyes open showed mainly two ~ 20 -Hz rhythm components (~ 13 – 19 Hz and ~ 19 – 27 Hz) over the sensorimotor region, varying in shape and intensity between individuals, as found in previous study (Leppäaho et al., 2019). Our study did not show hemispheric differences in the amplitudes of the β_1 (~ 13 – 19 Hz) and β_2 (~ 19 – 27 Hz) peaks, similarly to previous studies (Laaksonen et al., 2012; Parkkonen et al., 2015). The selection of the strongest frequency band was not unambiguous for each participant from their power spectra and TFRs. For this reason, we calculated TSE in three different frequency bands and selected the frequency band with the strongest modulation. In most participants, the modulation of ~ 20 -Hz rhythm peaked in 13–23 Hz band for both tactile and proprioceptive stimulation, but 15–25 Hz band was also very common. Earlier studies have shown that there are at least two distinct beta rhythms with different frequencies and functional roles. For example, rebound peaks at a lower frequency band than suppression (Cassim et al., 2000; Feige et al., 1996; Hall et al., 2011; Jurkiewicz et al., 2006; Laaksonen et al., 2012; Pfurtscheller et al., 1997; Szurhaj et al., 2003). This was also evident in our study; the rebound strength increases when the lower (13–23 Hz) frequency band was selected, but it has no effect on the suppression strength.

In addition to possible functional differences, several studies have also shown that the ~ 20 -Hz suppression and rebound have different generator areas in SMI cortex (Bardouille and Bailey, 2019; Jurkiewicz et al., 2006; Pfurtscheller et al., 1997; Salmelin and Hari, 1994; Salmelin et al., 1995). Both suppression and rebound are primarily generated in the SMI cortex, but the peak rebound has been detected more anterior, mainly in the precentral gyrus, than the suppression, that is peaking more posteriorly in the postcentral gyrus (Bardouille and Bailey, 2019; Feige et al., 1996; Fry et al., 2016; Jurkiewicz et al., 2006; Salmelin et al., 1995). In our study, the maximum amplitude of suppression and rebound were often detected in different MEG sensors or EEG electrodes in the respective TSE curves. This was evident especially for MEG. However, the variation was not spatially systematic across the participants.

5. Conclusions

Our results suggest that both MEG and EEG are feasible methods for objective detection of the SMI cortex ~ 20 -Hz modulation. However, the strength of suppression and rebound in the contralateral hemisphere to the stimulated hand was stronger in MEG than in EEG. Based on these results, MEG is recommended to be used in studies evaluating alterations in sensorimotor rhythm, whenever MEG is readily available. Due to its strongest signal-to-noise ratio, MEG may also be more sensitive in detecting changes of ~ 20 -Hz rhythm in longitudinal studies. In addition, patient measurements are often more sensitive to various interfering factors, resulting in higher noise levels in the registration, which further advocates the use of MEG. However, as the correlation between MEG and EEG results were strong, the use of EEG is supported in clinical studies due to its better availability and possibility to bedside measurements of EEG.

This study presented two easy-to-implement stimuli for modulating the ~ 20 -Hz rhythm using either MEG or EEG. Particularly, in patient studies, there is a need to use well-standardized stimulation methods to make the different studies easily comparable.

CRedit statements

Mia Illman: Conceptualization, Investigation, Data curation, Writing - Original draft, Visualization, Methodology, Validation. **Kristina Laaksonen:** Conceptualization, Supervision, Writing - Review & Editing, Methodology. **Mia Liljeström:** Software, Writing - Review & Editing. **Veikko Jousmäki:** Resources, Writing - Review & Editing. **Harri Piitulainen:** Writing - Review & Editing, Conceptualization, Methodology, Funding acquisition, Supervision, Project administration. **Nina Forss:** Funding acquisition, Writing - Review & Editing.

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