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Proprioceptive response strength in the primary sensorimotor cortex is invariant to the range of finger movement

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ABSTRACT

Proprioception is the sense of body position and movement that relies on afference from the proprioceptors in muscles and joints. Proprioceptive responses in the primary sensorimotor (SM1) cortex can be elicited by stimulating the proprioceptors using evoked (passive) limb movements. In magnetoencephalography (MEG), proprioceptive processing can be quantified by recording the movement evoked fields (MEFs) and movement-induced beta power modulations or by computing corticokinematic coherence (CKC) between the limb kinematics and cortical activity. We examined whether cortical proprioceptive processing quantified with MEF peak strength, relative beta suppression and rebound power and CKC strength is affected by the movement range of the finger.

MEG activity was measured from 16 right-handed healthy volunteers while movements were applied to their right-index finger metacarpophalangeal joint with an actuator. Movements were either intermittent, every 3000 ± 250 ms, to estimate MEF or continuous, at 3 Hz, to estimate CKC. In both cases, 4 different ranges of motion of the stimuli were investigated: 15, 18, 22 and 26 mm for MEF and 6, 7, 9 and 13 mm for CKC. MEF amplitude, relative beta suppression and rebound as well as peak CKC strength at the movement frequency were compared between the movement ranges in the source space. Inter-individual variation was also compared between the MEF and CKC strengths.

As expected, MEF and CKC responses peaked at the contralateral SM1 cortex. MEF peak, beta suppression and rebound and CKC strengths were similar across all movement ranges. Furthermore, CKC strength showed a lower degree of inter-individual variation compared with MEF strength.

Our result of absent modulation by movement range in cortical responses to passive movements of the finger indicates that variability in movement range should not hinder comparability between different studies or participants. Furthermore, our data indicates that CKC is less prone to inter-individual variability than MEFs, and thus more advantageous in what pertains to statistical power.

1. Introduction

Proprioception is the sense of position, movement, and force of the body where the body and its actions can be seen as the stimuli to itself (Sherrington, 1907). Proprioception is initially generated by proprioceptors in muscles, tendon and joints about the internal state of the locomotive system (Proske and Gandevia 2012). Next stage in generating proprioception, proprioceptive processing in the cortex is not well understood, however. For instance, evoked (i.e., passive) movements of the limbs or extremities have been used to elicit cortical proprioceptive responses, but it is unclear how kinematic features of the stimulus (e.g., movement range) affect the cortical responses reflecting proprioceptive processing. This hinders comparison between studies or participants. Differences in the evoked-movement range may decrease comparability between studies that use different movement actuators or within a study between the participants who possess different limb/extremity

Abbreviations: MEF, movement evoked field; CKC, corticokinematic coherence; MEG, magnetoencephalography; SM1, primary sensorimotor cortex; SII, secondary somatosensory cortex cortex; MANOVA, multivariate analysis of variance; sLORETA, standardized low-resolution electromagnetic tomographic analysis.

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anatomy—being especially apparent when comparing clinical populations to healthy controls due to altered limb morphology or posture.

When a join is flexed (passively or actively), the extensor muscles lengthen and antagonist flexor muscles shorten. The change in the muscle length is detected by muscle spindles that modulate their discharge rate according to muscle elongation and change therein (Matthews, 1933; for a review, see Macefield and Knellwolf, 2018). Muscle spindle afference therefore likely depends on the movement range of the proprioceptive stimulus. Golgi tendon organs located in the muscles and tendons are sensitive to change in muscle tension (Houk and Simon, 1967; Jami, 1992) and contribute to the sense of effort for instance (for a review, see Proske and Gandevia, 2012). In addition, joint receptors are sensitive to forces around the joint and are activated especially near the extremes of the joint range of motion. Proprioceptive afference from the proprioceptors travels primarily via the dorsal column of the spinal cord to the brainstem and cortex via nuclei in the medulla (decussate to contralateral side) and thalamus (for a review, see Proske and Gandevia, 2012). The cerebellum receives proprioceptive input ipsilaterally from cuneate nucleus of medulla (from upper limbs) and Clarke's nucleus of thoracic spinal cord (from lower limbs). From thalamus, the proprioceptive tracts project mainly to the primary (SI; Jennings et al., 1983) and secondary (SII; Fitzgerald et al., 2004) somatosensory cortices, but also to the primary motor (M1) cortex. Thus, SI and M1 cortices are often treated as a single functional unit, the primary sensorimotor cortex (SM1).

Cortical proprioception has been studied in humans both from structural and functional viewpoints, using magnetic resonance imaging (MRI; Jaatela et al., 2022), functional MRI (fMRI; Nurmi et al., 2018, 2021; Yu et al., 2011), positron emission tomography (Weiller et al., 1996), electroencephalography (EEG; Piitulainen et al., 2020; Pittaccio et al., 2013; Qiu et al., 2016; Smeds et al., 2017) and magnetoencephalography (MEG; Alary et al., 2002; Lange et al., 2001; Piitulainen et al., 2015; Vallinoja et al., 2021; Illman et al., 2022a). Proprioceptive stimuli (i.e. evoked movements) elicit cortical responses in contralateral SM1 and SII cortices along with supplementary motor area and posterior parietal cortex (Mima et al., 1996; Reddy et al., 2001), and several spatially independent stimulus-related components can be identified (Vallinoja et al., 2021). Ipsilateral SM1 and SII responses appear to be weaker than contralateral ones and have longer latency, possibly due to callosal conduction delay (Allison et al., 1989). Vast cortical processing of somatosensory afferences may dominate the cortically recorded signals during volitional movements, as the passively evoked and volitional movements activate similar if not identical cortical networks in spatial, temporal and frequency domains (Alegrea et al., 2002; Kornhuber and Lüder, 1965; Piitulainen et. al., 2013).

Movement evoked fields (MEFs) in MEG enable precise investigation of the temporal dynamics of cortical proprioceptive processing (Hämäläinen et al., 1993). Additionally, movement induced responses can be used to quantify frequency domain power modulations in the SM1 cortex during and after the movement (Hämäläinen et al., 1993). Proprioceptive or somatosensory stimuli give rise to an initial power reduction ("suppression") in the beta band (i.e. 12–30 Hz) followed by an increase ("rebound") in the same power band (Chen et al., 1998; Ilman et. al., 2020, 2022; Jasper and Penfield, 1949; Salmelin and Hari, 1994). These changes reflect the excitation and active inhibition of the somatosensory system respectively (Neuper and Pfurtscheller, 2001; Salmelin and Hari, 1994). An additional method for studying proprioceptive processing in the frequency domain is the cortico-kinematic coherence (CKC), which is computed between MEG signals and limb kinematics such as acceleration during continuous voluntary (Bourguignon et al., 2011, 2012; Jerbi et al., 2007; Marty et al., 2015; Piitulainen et al., 2013) or passive movements (Piitulainen et al., 2013, 2015; Piitulainen et al., 2018). CKC peaks in the sensorimotor (SM1) cortex at the movement frequency and its harmonics following somatotopy (Bourguignon et al., 2011; Piitulainen et al., 2015). CKC seems to reflect mainly the cortical processing of proprioceptive afference (Bourguignon et al., 2015; Piitulainen et al., 2013). CKC is typically strong and can be detected in almost every individual (Bourguignon et al., 2011, 2013). Both MEFs and CKC have an excellent inter-session reproducibility (Mujunen et al., 2022; Piitulainen et al., 2018, 2020). CKC strength is modulated by the degree of attention directed to the proprioceptive stimulus (Piitulainen et al., 2021), stimulus regularity, (Mujunen et al., 2021) extent (number of fingers) of stimulus (Hakonen et al., 2021) and aging (Piitulainen et al., 2018). For these reasons, both MEFs and CKC are important tools in basic and in clinical research on the brain basis of human proprioception.

Our primary aim was to study whether cortical MEG responses to proprioceptive stimulation is affected by the movement range of the right index finger stimulation. Previously, it has been shown in fMRI that passively evoked movement ranges of 5 mm elicit stronger activation than movement ranges below 5 mm (Nurmi et al., 2018). However, the effect of movement range has not been investigated using MEG or EEG recordings that are reflecting more directly the associated neuronal processing. Here, we aimed to characterize the influence of movement range on proprioceptive response strength quantified with MEF peak amplitude, relative beta suppression and rebound power as well as CKC strength. Our hypothesis was that the cortical responses would strengthen with the movement range, because of more extensive activation of the proprioceptors around the metacarpophalangeal joint and muscles of the index finger. Our secondary aim was to compare the degree of inter-individual variability in MEF and CKC strengths, which are relevant for statistical power estimation to advise future studies. Besides the novel neurophysiological knowledge, this study provides important information about the significance of movement range as a potentially confounding factor. This may be a potential concern when comparing different studies, conditions within a study or different populations (such as clinical populations with limited movement range of a joint) where the movement range may vary.

2. Materials and methods

2.1. Participants

Nineteen healthy adults volunteered in this study. One participant was excluded from the study due to technical problems (i.e. participant hearing the sounds of the movements) during the recording session. Two participants were excluded from the final analysis due to noisy MEG signals and not having structural MRI available. Data analyses were performed with the data from the remaining 16 participants (10 females, mean ± SD age: 27.3 ± 5.3 years, range: 20–40 years, all right-handed; mean Edinburgh handedness test score: 88.3 ± 15.6, range: 60–100). Participants were either employees or students at Aalto University. All participants gave a written informed consent. The protocol was approved by the ethics committee of Aalto University and was conducted according to the Declaration of Helsinki.

2.2. Experimental protocol

2.2.1. Preparation

Prior to the MEG measurements, participants were asked to remove any metallic objects or clothing. The participants were familiarized with the study and asked to fill in a consent form and Edinburgh handedness questionnaire. Five head-position indicator coils were attached to the participant's forehead to continuously measure the head position during the measurements. Vertical electro-oculography (EOG) electrodes were also attached above and below the left eye of the participant to measure eye blinks. Participant's head landmarks (i.e., nasion, inion and ear lobes) and additional scalp surface points (~100) were digitized in view of co-registration with anatomical MRIs.

Participants were sitting inside a magnetically shielded room with the movement actuator on a table in front of them. They wore earplugs

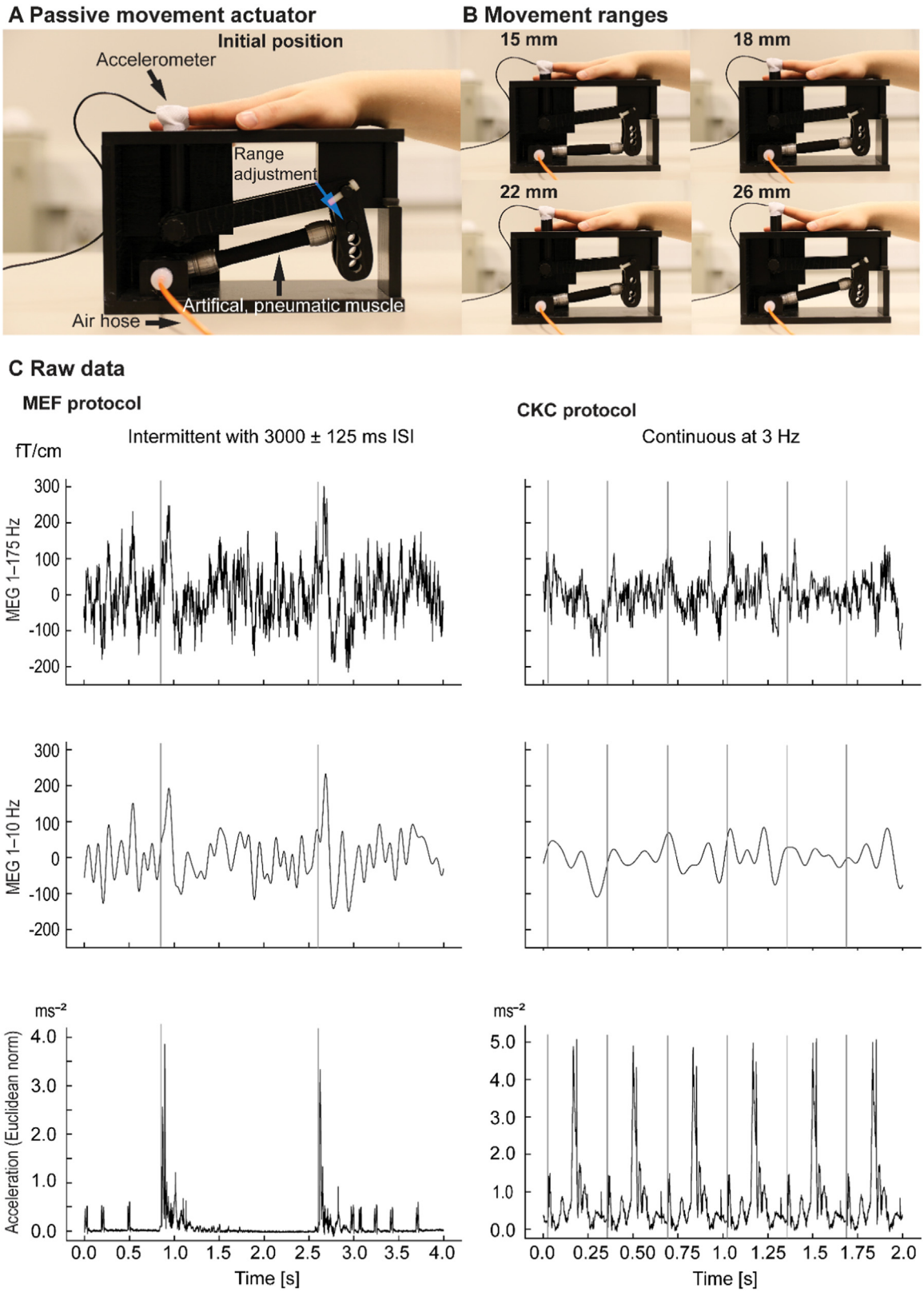

Fig. 1. Experimental setup and representative signals. (A) Proprioceptive stimulator consisting of a pneumatic artificial muscle embedded in a plastic frame and a lever system extending the index finger. An accelerometer was attached to the tip of the index finger. (B) Movement ranges for the intermittent MEF protocol. (C) Representative raw signals of one participant filtered at 1–175 and 1–10 Hz for the MEF and CKC protocols, respectively. Euclidean norm is also shown for the three orthogonal accelerometer signals from the same time window. Gray vertical lines represent the onset of the movement.

and Brownian noise was played through back panel speakers at 70 dB to mask a slight but otherwise perceivable sound from the movement actuator. A cardboard screen with an opening was placed in front of the participants to hide the movement actuator while leaving visible a projection screen onto which was played a video of slowly changing scenes during the MEG recordings. The video ensured comfortable fixation of the gaze and stabilized alertness level of the participant.

A surgical tape was wrapped around the tip of the participant's right index finger to reduce tactile contact between the fingertip and the movement actuator. Thereafter, the right index finger was attached to the movement actuator with tape and an accelerometer was taped to the nail of the index finger (Fig. 1). In the MEF protocol, the largest movement range corresponded to 20.4 ± 5.1° mean range of motion in the metacarpophalangeal joint, i.e., the range between the resting and the most extended position of the index finger. This was measured just prior to the MEG recordings using a manual goniometer.

2.2.2. MEG recordings

Measurements were carried out at the MEG Core of the Aalto Neuroimaging infrastructure in Aalto University (Espoo, Finland). The data was acquired with a 306-channel (102 magnetometers, 204 gradiometers) MEG device (Vectorview 4-D Neuromag Oy, Finland) in a 3-layer magnetically shielded room (Imedco AG, Hägendorf, Switzerland), with a pass-band at 0.1–330 Hz and a sampling rate of 1 kHz.

2.2.3. Kinematics

The acceleration of the right index finger was measured with a 3-axis-accelerometer (ADXL335 iMEMS Accelerometer, Analog Devices Inc., Norwood, MA, USA). The accelerometer data was low-pass filtered at 330-Hz and sampled at 1 kHz, time-locked to MEG signals.

2.2.4. Movement actuator

A pneumatic movement actuator was used to produce extension-flexion movements in the metacarpophalangeal joint of the participant's right index finger. In brief, the opening of an air valve rapidly increased the pressure to 4 Bar inside the pneumatic artificial muscle (DMSP-10–100 AM-CM, Festo AG & Co, Esslingen, Germany) causing the muscle to contract (i.e., the length of the artificial muscle shortened). As a result, a lever was pulled, which raised a vertical cylinder upwards causing a finger extension. When the air valve was closed, the artificial muscle relaxed (back to 1 Bar) returning the finger to the initial position. The movement range of the actuator (i.e., the extent the lever raises) was adjusted by the experimenter by selecting one of the four different effective lever lengths.

2.2.5. Movement protocols

Intermittent (MEF) or *continuous* (CKC) movements were evoked with the pneumatic movement actuator. Each of the movement protocols consisted of four different runs at specific movement ranges: 14.8, 17.8, 21.8 and 25.7 mm (Fig. 1B). The order of the movement ranges was randomized for each movement protocol and participant separately. After each run, the experimenter manually adjusted the range of the movement actuator for the next run. In the *MEF protocol*, intermittent extensions of the right index finger were delivered every 3000 ± 125 ms. The finger remained in the extended position after the movement onset for 1600 ms and then returned to the rest position before the next movement (Fig. 1C). In each run, about 90 stimuli were presented (mean ± SD of clean trials after preprocessing rejections: 90.8 ± 3.6 for 14.8 mm, 89.9 ± 1.1 for 17.8 mm, 91.0 ± 6.2 for 21.8 mm and 89.6 ± 1.9 for 25.7 mm). The duration of each run was 4 min 10 s in the MEF protocol. In the *CKC protocol*, continuous repetitive finger extension-flexions were evoked at 3 Hz for 3 min per run. This frequency was achieved by delivering 120-ms inflations every 333 ms. Inflations were followed with slightly longer deflations of the artificial muscle which lead to continuous flexion-extension movement of the index finger. Movement ranges were 5.7, 6.6, 9.3 and 12.6 mm.

The movement ranges were selected for the *Intermittent* (MEF) movements so that the maximal range was within the range of motion (ROM) of the metacarpophalangeal joint of the index finger (Latz et al., 2019). The largest (26 mm) movement approached the extension ROM limits, and the smallest (15 mm) movement was comparable to those commonly used in previous studies (Onishi et al., 2013; Tsuiki et al., 2019). Therefore, we could not go further towards the extension direction, and it would have not been feasible to position the finger to more flexed position as that would have caused slack in the muscle tendon unit (i.e. finger was in slight passive pre-stretched / tension position), which could potentially affect e.g. muscle spindle sensitivity. CKC movement ranges were smaller *due to pneumatic limitations* of the movement actuator during the stimulation.

2.2.6. MRI recordings

Anatomical T1 MRIs were acquired using a 3-Tesla MRI scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany), a 32-channel head coil and a high-resolution T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) pulse sequence (sagittal orientation, isometric voxel size: 1 × 1 × 1 mm, slices: 176, TR: 2530 ms, TE 3.3 ms, TI 1100 ms, flip angle 7°) in Advanced Magnetic Imaging centre of Aalto University (Espoo, Finland).

2.3. MEG preprocessing

Preprocessing was done semi-manually with visual inspection to identify noisy MEG channels. Next, oversampled temporal projection was applied to the MEG data (OTP; Larson and Taulu, 2018) and an algorithm was used to reduce uncorrelated sensor noise. The OTP step included temporally extended signal space separation algorithm with head movement compensation that was used to mitigate external interferences and interpolate the noisy channels (Maxfilter, version 2.2; Elekta Neuromag Oy, Helsinki, Finland; Taulu and Simola, 2006; buffer length: 16 s, correlation limit: 0.95).

Eye blink and heart beat artifacts were suppressed using the fast independent component analysis (ICA; Hyvarinen, 1999; implementation: MNE Python, version 0.17.0) with 30 ICA components and the data was filtered between 1 and 40 Hz using a zero-phase finite impulse response filter (firwin in SciPy 1.2.1; Hamming window; see Table 1 for more specific filter parameters). ICA components corresponding to heartbeat or eye-blink artifacts were identified through visual inspection and subtracted from the data.

2.4. Data processing

2.4.1. Sensor space data processing

Event timings were extracted from the accelerometer data by defining start of the movement (i.e., y-intercept of an epoch) being 4 ms before the main peak of the Euclidean norm of accelerometer signal. Next, the data was epoched based on the event timings from 400 ms before to 1100 ms after the stimulus onset. Epochs for which the maximal value exceeded 5000 fT for magnetometers or 700 fT/cm for planar gradiometers were excluded. The remaining epochs were averaged. For each pair

Table 1
Filter parameters.

Filter parameter	Parameter value
Filter	Windowed time-domain design (firwin) method
Hamming window parameters:	
Passband ripple	0.0194
Stopband attenuation	53 dB
Lower passband edge:	1
Lower transition bandwidth:	1.00 Hz (−6 dB cutoff frequency: 0.5 Hz)
Upper passband edge	40 Hz
Upper transition bandwidth:	10 Hz (−6 dB cutoff frequency: 45 Hz)
Filter length (order):	3301 samples (3.301 s)

of planar gradiometers, we retained the vector sum at each time point to eliminate the effect of sensor polarity and to combine sensors placed at the same location. The gradiometer pair showing the maximum vector sum response within 0–160 ms (i.e., realistic upper bound for the primary SM1 response latency; the validity of this threshold was also inspected visually for each participant) were selected.

2.4.2. MEF analysis

Source-localized MEFs were obtained for all runs. The concatenated raw data (initially the different conditions were in different runs and therefore in different raw data files) was epoched and averaged using the processed sensor space data. Rejection thresholds for the epochs were 5000 fT for magnetometers and 700 fT/cm for planar gradiometers. Magnetometer data was not used for analyses. For a crude visualization of the software and procedures used in data processing and analyses, see Fig. 2.

The source localization was performed using the standardized low-resolution electromagnetic tomographic analysis (sLORETA). To compute the forward model for source localization, cortical surfaces were first reconstructed from the original T1 images using Freesurfer's recon-all algorithm (Freesurfer software v. 6.0; Dale et al., 1999). A single-compartment boundary-element model (BEM) of the inner skull was generated with the FreeSurfer's watershed algorithm (Ségonne et al., 2004). MEG sensor locations and the anatomical MRI images were also co-registered using the ficidual points and additional head-points. Thereafter, the forward model was computed using the BEM model, co-registration matrix and a volumetric source space with a 6 mm spacing between the grid points. The inverse model was generated based on the forward solution. Finally, source estimates were obtained by applying the inverse model on epoched data using sLORETA.

The SI cortex activation was estimated as the maximum sLORETA value within Brodman area 3a (Freesrufer Brodmann Area Maps; annotation file: "BA_exvivo"). The sLORETA time-series at the location of maximum value was visually inspected to identify the timing of early activation peaks at 0–160 ms.

2.4.3. Beta suppression and rebound analysis

First, evoked responses were subtracted from the unaveraged data epochs to obtain purely induced responses. Then, the average power of beta frequency band (13–30 Hz) was calculated (MNE-Python function: source_induced_power using Wavelets) withing Brodman area 3a sources using sLORETA. Then, the relative beta suppression defined as the relative minimum value to the mean baseline of the time-series between 0 and 950 ms after the movement whereas the beta rebound was defined as the maximum value between the time of the beta suppression valley and 950 ms. Using this method, credible beta suppression and rebound latencies were obtained (see results).

2.4.4. CKC analysis

Continuous MEG data was divided into 2-s epochs with 1.6-s overlap between the epochs, yielding a frequency resolution of 0.5 Hz (Bortel and Sovka, 2007). The same rejection thresholds for MEG amplitude as that used for MEFs was applied here. CKC was estimated with the Euclidean norm of the three orthogonal accelerometer signals filtered at 1–195 Hz (Bourguignon et al., 2015), directly in the source space using dynamic imaging of coherent sources (DICS) implemented in a custom

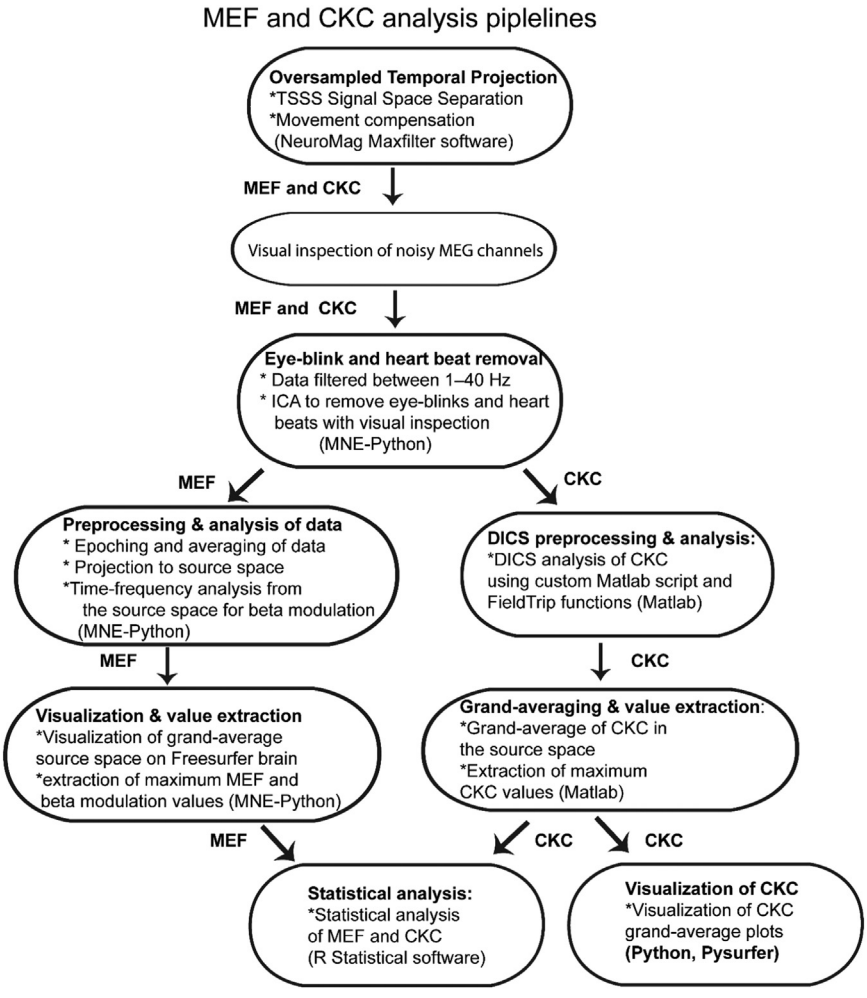

Fig. 2. MEF and CKC analysis pipelines. A flowchart representing the analysis pipelines of MEF and CKC including tool boxes and software as well as procedures used.

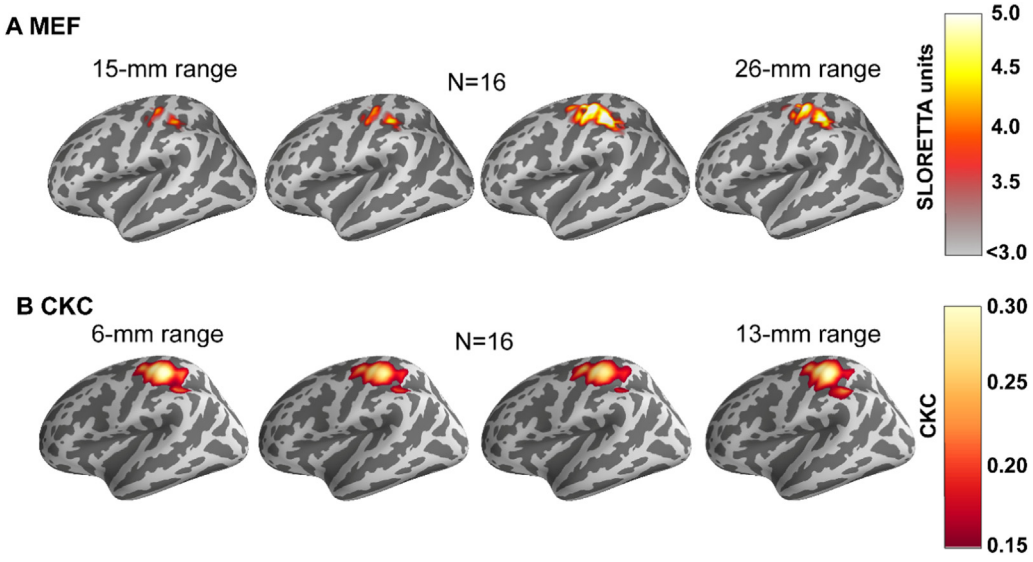

Fig. 3. MEF (A) and CKC (B) group-level sources projected on inflated brain.

Matlab script. CKC was calculated following the procedure described in Gross et al. (2001):

(a) $C(f) = X(f)Y*(f)$, where C(f) denotes cross-spectral density at frequency f for Fourier transformed signals X(f) and Y(f) and Y*(f) denotes complex conjugate of Y(f). and (b) $M_{i,j}(f) = \frac{|C_{i,j}(f)|^2}{C_{ii}(f)C_{jj}(f)}$, where $M_{i,j}(f)$ is the CKC at frequency f for signals i and j. The power spectrum of i is denoted with the diagonal element $C_{ii}$and coherence is the squared magnitude of cross spectrum divided by power spectra of both time series."

In brief, a FFT was applied to epochs of MEG and acceleration data to estimate the cross-spectral density matrix including all combinations of MEG and acceleration signals. Then, the inverse operator was used to project these values in the source-space and estimate CKC at F0 (3 Hz). Importantly, the same inverse models were used here as in the MEF source localization.

The maximum CKC values in the source space were identified, along with the corresponding location, which we visually ensured was in the SM1 cortex. PySurfer toolbox (version 0.11.0) for Python (version: 3.9.2) was used for the group-level CKC maps. First, the individual-level maps in the MNI space were projected on Freesurfer template brain using a registration file made specifically for this purpose ("mni152.register.dat"). The individual-level maps were then averaged to yield a group-average map.

2.5. Statistical analysis

2.5.1. MEF peak amplitude, beta suppression, rebound and CKC strength

Repeated measures MANOVA (SPSS Statistics, version 27, IBM Corp., Armonk, NY, United States) was used to test whether the movement range affects MEF and CKC strengths as well as beta suppression and rebound in the source space. In the case of significant main effects, post-hoc tests with Šidák correction (Sidak, 1967) were used to determine between which specific movement ranges the results differed. If the main effect was not significant (i.e. $p > 0.05$), one sample analog of Hotelling T^2 test with Mahalanobis distance of 1 (i.e. corresponding to 1 standard deviation) was used to determine if all of the ranges were equivalent (R software version 4.0.2; library "cribbie/equivalencetests", function: "eq.hotT2"; Wellek, 2010). If either Hotelling T^2 test was non-significant (i.e. no significant equivalence between all of the ranges) or there were significant differences between the movement ranges, individual ranges that had non-significant differences (determined by ANOVA post-hoc testing) were tested for equivalence using the TOST-procedure (R-library:'TOSTER', function: 'TOSTtwo.raw'). TOST was performed with equivalence bounds of one standard deviation and ℓ-correction (Lauzon and Caffo, 2009) for multiple comparison correction.

Repeated measures Bayes analysis (R-function: rmBayes; Nathoo and Masson, 2016) was also conducted. This function estimated the probability of null hypothesis, i.e. movement range having no effect on cortical proprioceptive response variable. The effect of movement range on MEF and CKC strength as well as beta suppression and rebound are tested using this method (i.e. $p[H_0 \mid data]$, where H_0: $m_1 = m_2 = m_3 = m_4$ and m_x is the mean of response strength or beta suppression and rebound for each of the four movement ranges in MEF or CKC protocols).. This function also gives Bayes factors for equivalence (*BF01*). If the alternative hypothesis was more likely or BF01 was below 3, Bayes test for ANOVA designs with equality constraints (i.e. Bayes equivalent of post-hoc testing) was used to discern which of the specific movement ranges differed in term of response strength and which were equivalent (R-library: 'BayesFactor', function: 'anovaBF').

2.5.2. Inter-individual variability in MEF and CKC strengths

The dispersion of CKC and MEF strength distributions were compared to estimate which protocol and measures yielded more robust measures in the statistical sense at the group level (i.e., the statistical power increases as the dispersion of the distribution decreases). For this purpose, the coefficient of variation (i.e., the ratio of the standard deviation to the mean) was calculated for the maximum values in the source-space of each movement range in the CKC and MEF protocols. Differences between MEF and CKC pooled coefficients of variation (i.e. all values from every movement range were combined to a single vector and the coefficient was calculated and compared between MEF and CKC) were tested using Modified signed-likelihood ratio test (Krishnamoorthy and Lee, 2014).

3. Results

In line with previous studies, MEF and CKC responses peaked in the SM1 cortex contralateral to the stimulated fingers (Fig. 3; Piitulainen et al., 2015). In the MEF protocol, the number of trials did not significantly differ between the movement ranges (repeated measures ANOVA: $p = 0.43$). See Table 2 for mean ± SD number and percent of accepted and rejected trials for different movement ranges of MEF and CKC protocols.

Table 2
Mean ± SD number and percent of accepted and rejected trials as well as bad channels for different movement ranges for the MEF and CKC protocols.

Movement range (MEF/CKC)	15 / 6 mm	18 / 7 mm	22 / 9 mm	26 / 13 mm
Number of accepted trials (MEF)	90.8 ± 3.6	89.9 ± 1.1	91.0 ± 6.2	89.6 ± 1.9
Number of accepted trials (CKC)	531.3 ± 27.3	528.8 ± 24.0	520.6 ± 14.3	520.9 ± 22
Number of rejected trials (MEF)	0.29 ± 0.59	0.29 ± 0.77	0.35 ± 0.86	0.35 ± 0.79
Number of rejected trials (CKC)	4.0 ± 5.2	2.4 ± 5.2	2.8 ± 5.2	6.7 ± 10.2
Percent of rejected trials (MEF)	0.32 ± 0.65	0.32 ± 0.85	0.39 ± 0.96	0.39 ± 0.86
Percent of rejected trials (CKC)	0.76 ± 0.98	0.45 ± 1.01	0.54 ± 1.0	1.27 ± 1.92
Bad Channels (MEF)	5.13 ± 4.13	3.75 ± 2.21	4.63 ± 2.39	6.63 ± 5.68
Bad Channels (CKC)	5.25 ± 3.45	3.88 ± 3.26	3.5 ± 2.39	4.75 ± 2.70
Removed ICA components (MEF)	2.5 ± 0.51	2.38 ± 0.63	2.5 ± 0.72	2.56 ± 0.63
Removed ICA components (CKC)	2.5 ± 0.62	2.25 ± 0.68	2.25 ± 0.68	2.38 ± 0.52

Table 3
MEF and CKC amplitude. The values are means and standard deviations across subjects.

MEF protocol				CKC protocol	
Range (mm)	MEF (SLORETA units)	Beta suppression (%)	Beta rebound (%)	Range (mm)	Source space (CKC)
15	6.91 ± 3.31	−28.8 ± 13.5	65.3 ± 65.6	6	0.51 ± 0.10
18	7.54 ± 3.70	−31.3 ± 13.8	54.4 ± 46.1	7	0.52 ± 0.11
22	9.06 ± 3.71	−35.8 ± 14	44.6 ± 48.8	9	0.50 ± 0.12
26	8.10 ± 3.77	−36.6 ± 13.2	49.1 ± 33	13	0.48 ± 0.095

Table 4
Equivalence test statistics.

	MEF protocol			CKC protocol
	MEF strength	Beta suppresion	Beta Rebound	CKC strength
Hotelling T^2	$T^2[5.5]<F[7.3]$	$T^2[6.4]<F[7.3]$	$T^2[2.1])<F[7.3]$	$T^2[4.12]<F[7.3]$
Bayes repeated measures $p(H_0 \mid data)$	82%	73%	98%	98%
Bayes Factor (BF01)	4.5	2.7	48	48.26

T^2 and F values are shown inside the brackets. When T^2 is less than the critical value of F, equivalence is significant. Bayes probabilities and factors (BF01) for equivalence are also shown. Bolded values indicate significant equivalence (i.e. T^2 values less than F-values, Bayes probability of or greater than 75% or Bayes factor of or greater than 3).

3.1. Movement range did not affect MEF strength

Grand-averaged MEFs appeared to be of similar shape across conditions (determined qualitatively; Fig. 4). The latency of maximum beta suppression and rebound were 260 ± 70 ms (mean ± SD across participants; range: 143 – 479 ms) and 719 ± 120 (range: 486 – 950 ms) respectively. The main effect of movement range was non-significant in repeated measures ANOVA for MEF strength, beta suppression and rebound ($F_{3,45}$ = 2.2; p = 0.11; $F_{3,45}$ = 2.5; p = 0.07; $F_{3,45}$ = 0.80; p = 0.50 respectively). All the movement ranges elicited MEF response peaks, beta suppression and rebound of similar magnitudes (i.e. significant equivalence) according to Hotelling T^2 test and repeated measures Bayes test. One exception to this equivalence was beta suppression for which the repeated Bayes test gave Bayes factor slightly below 3 (i.e. 2.7) while the Hotelling T^2 indicated equivalence. For the specific results, see Table 3 for mean and SD of the MEF responses and beta modulation and Table 4 for the equivalence test statistics.

3.2. Movement range did not affect CKC strength

Movement range did not have a significant main effect to CKC strength in repeated measures ANOVA (F = 0.65; DF=3; p = 0.59; Fig. 5). All the movement rages elicited similar CKC strengths according to Hotel T^2 and repeated measures Bayes test (see Table 3 for mean and SD of the CKC responses and Table 4 for specific equivalence test statistics).

3.3. Inter-individual variation was smaller for CKC than MEF strength

Across all 4 movement conditions, the coefficient of variation for MEF ranged in 41–49% and for CKC in 20—24%. A pooled coefficient of variation across the movement ranges was significantly larger for MEFs compared with CKC (p < 0.01).

4. Discussion

We examined whether the movement range of proprioceptive stimulation affects the respective cortical response strength quantified using MEFs, beta modulation and CKC in MEG. Contrary to our hypothesis, we did not observe discernible differences in the MEF, beta modulation or CKC strength due to variation in movement range. Inter-individual variation was smaller for CKC than MEF strength, suggesting that CKC might be a more robust measure of proprioceptive processing in statistical sense.

4.1. Movement range of proprioceptive stimulus does not affect cortical response strength

All movement ranges produced similar MEF peaks, beta modulation and CKC strengths for the respective intermittent and continuous stimulations, suggesting that variation in movement range of proprioceptive stimulation does not significantly affect the quantification of cortical proprioceptive processing with either movement protocol. Varying the

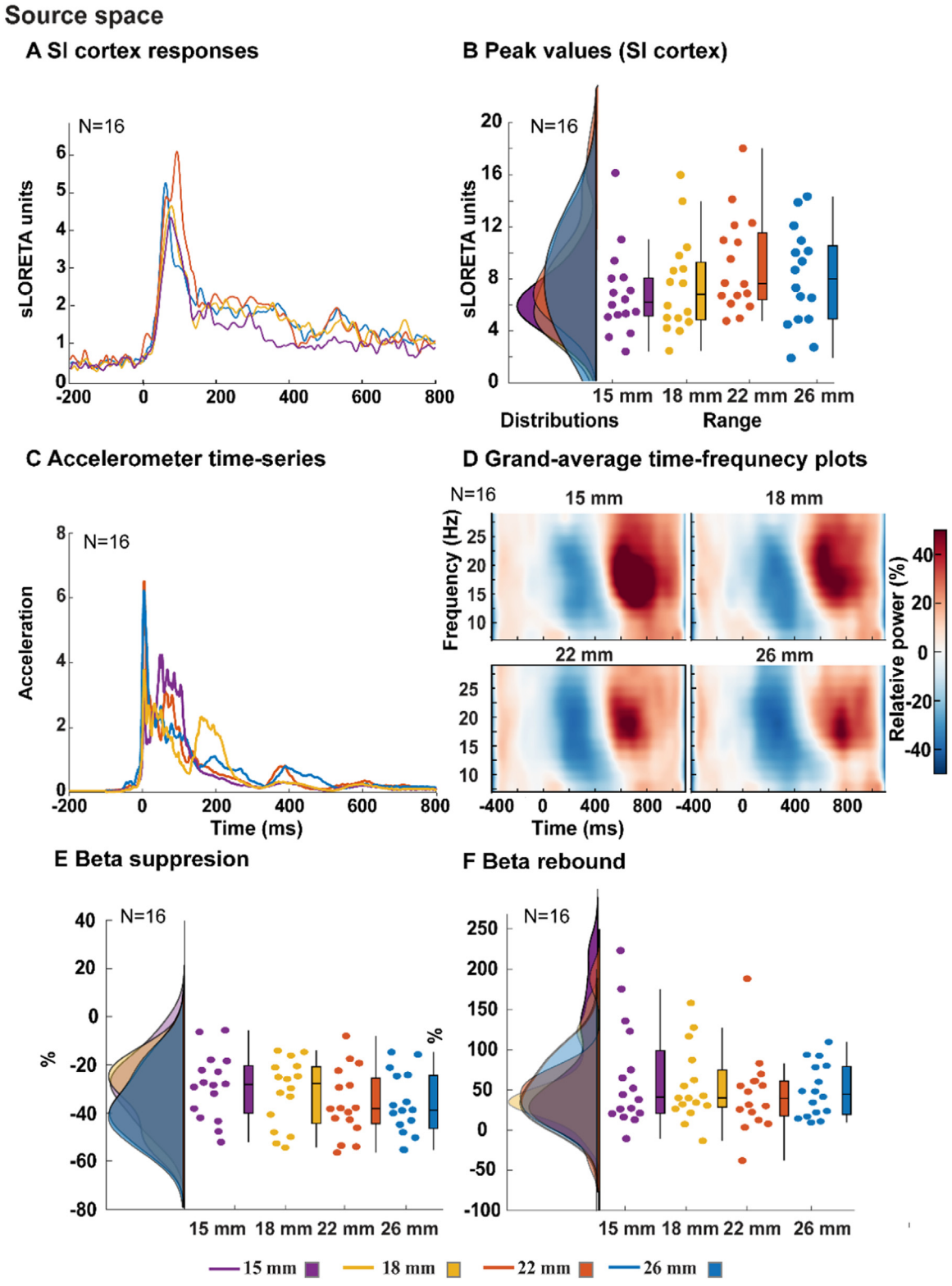

Fig. 4. Results for discrete movements. (A) Time-series of the SI responses for the 4 movement ranges. (B) Peak values of the SI responses. (C) Grand-average acceleration magnitude time-series. (D) Grand-average time-frequency relative power in the SI cortex. (E) Peak relative beta suppression in SI cortex (F). Peak relative beta rebound in SI cortex.

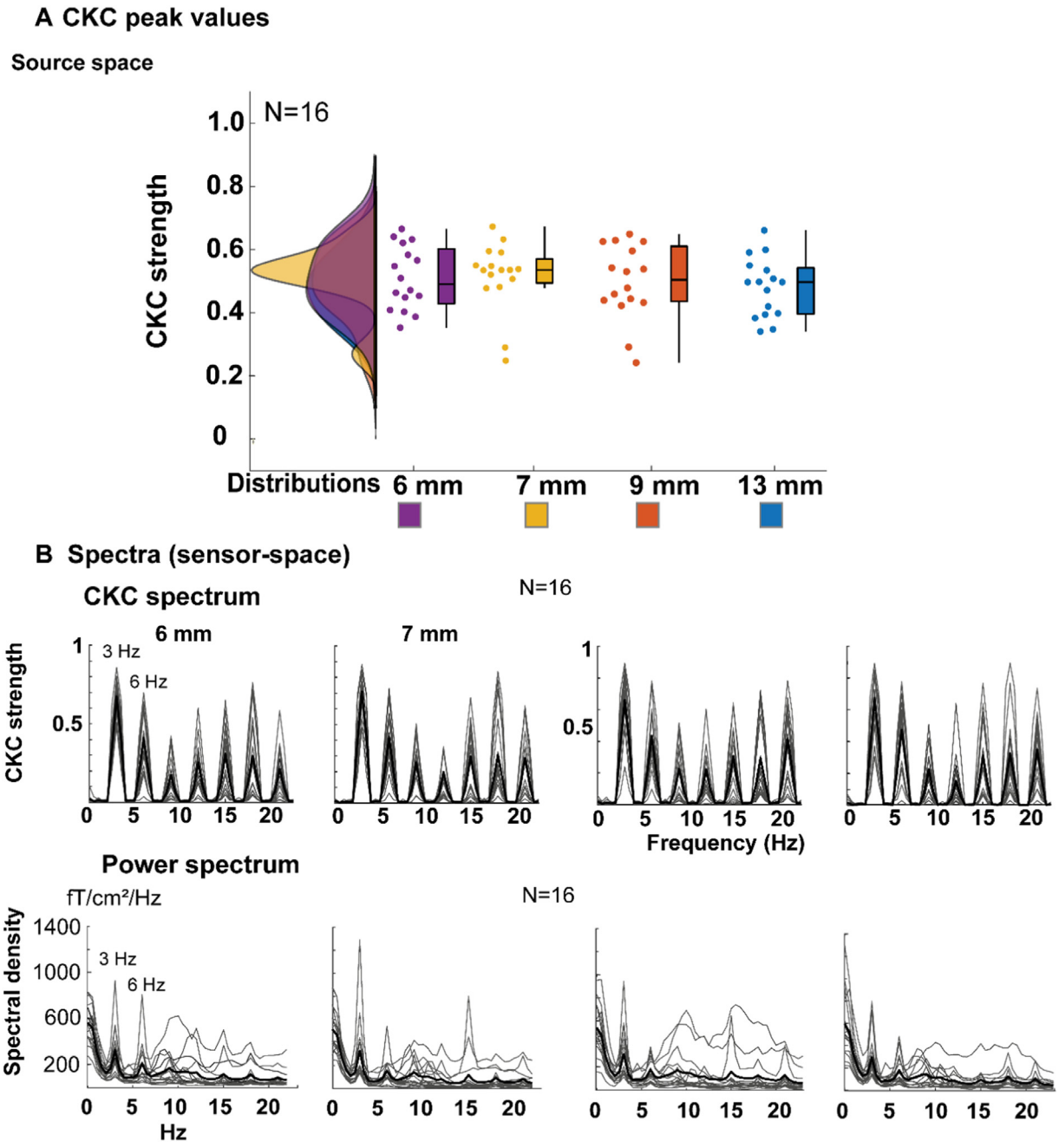

Fig. 5. Results for the continuous mouvements. (A) CKC strength group distributions and boxplots for the peak gradiometer pair at 3 Hz for each movement range in source space. The line in the middle of the box represents the median and upper and lower sides of the boxes 25% quartiles. All CKC strengths were equivalent according to Hotelling T^2 test. (B) Coherence and power spectra for the peak CKC gradiometer pair for each participant (thin gray lines) and group mean (thick black line).

movement range during the intermittent movements did not influence the MEF peak value, beta suppression or rebound according to equivalence testing—although Bayes factor with beta suppression was below (i.e., 2.7) equivalence threshold of 3. This may indicate that movement range has a minimal impact on the proprioceptive processing in SI cortex. The degree of beta suppression and rebound have been suggested to indicate the degree of excitation during the movement and active inhibition after the movement in the somatosensory cortex respectively (Pfurtscheller et al., 1997; Cassim et al., 2000; Neuper and Pfurtscheller 2001; Takemiet al. 2013). The similarity of relative beta suppression and rebound strengths would therefore indicate that the excitatory and inhibitory processes are similar regardless of the movement range.

CKC strength is a robust and reproducible method to study proprioception (Piitulainen, et al., 2018, 2020) with negligible additional effects from concomitant tactile stimulation (Piitulainen et al., 2013) or from simultaneous motor processing due to volitional movements (Marty et al., 2015). However, attention to or away from the stimulus may slightly modulate CKC strength (Piitulainen et al., 2021). The current results extend the knowledge on CKC by indicating that similarly to MEF response strength, variation in the movement range within the normal range of index finger motion does not affect CKC strength significantly.

Our results imply that the effect of movement range on cortical responses could be minimal also for conditions where voluntary move-

ments are used, as we have previously shown that both continuous evoked passive and voluntary movements elicit similar coherent activation patterns in the cortex (Piitulainen et. al., 2013). This negligible effect of movement range might apply also for intermittent movements, and is promising evidence for future studies where the standardization of movement range is difficult due to the variable kinematics of voluntary movements. However, this hypothesis should be confirmed with a direct comparison between passive and voluntary movement conditions, and especially for the intermittent movement designs aimed to quantify evoked and induced responses.

The current results indicate that standardization of the movement range is not crucial when comparing MEF, CKC strength, and SM1 beta modulation between conditions or studies. Results from studies using different movement ranges are therefore comparable in terms of response strength. This information is especially beneficial for clinical studies where it is not always possible to use the same movement range across participants, e.g., due to limited range of motion in the fingers (e.g., spasticity) or altered finger morphology. However, it is noteworthy that proprioceptive stimulation in the extremes of the joint range of motion might possibly activate the proprioceptors differently compared to stimulation at a more moderate ranges of motion of a given joint used in this study, and thus can affect the cortical responses.

4.2. Inter-individual variation was smaller for CKC than MEF strength

Coefficient of variation (indicating normalized deviation around the mean) across the participants was 71 – 145% larger for MEF compared with CKC strengths for all movement ranges. From a purely statistical viewpoint, this suggests that CKC strength is a more robust measure than MEF strength because of its smaller relative inter-individual variability that yields better statistical power. Studies using CKC might therefore find a significant effect with smaller sample sizes than those using MEFs assuming otherwise similar sensitivity for the effect (for sample size planning using coefficient of variation, see Kelley, 2007). However, it should be noted that this assessment of better CKC sensitivity does not take into account how CKC or MEFs differ under different experimental conditions. Moreover, the better statistical sensitivity of CKC might not be solely due to CKC as a measure having less inter-individual variation as other aspects in the MEF and CKC protocols differed as well, such as movement range and continuous vs. intermittent nature of the movements.

4.3. Limitations

Transient MEF and continuous CKC movements were considerably different in terms of the movement ranges used. During the continuous movements, the artificial muscle did not deflate completely due to pneumatic limitations, and the movement range was therefore smaller than in the transient movement condition. For this reason, we did not directly compare these conditions, but rather report the effect of movement range separately in this report. This is one limitation of our experimental design since identical movement ranges allowing direct comparison of MEF and CKC responses might have yielded additional interesting results.

We did not use electromyography (EMG) during the measurements to obtain data concerning muscle activity during the evoked movements. This might be a potential concern since the potential contaminant muscle activity during the evoked movements is unknown due to the lack of EMG data. However, the participants were healthy adults and based on previous studies, healthy adults are well able to remain relaxed during the evoked movements. In addition, the movements were not fast enough to elicit stretch reflex that is often the case for the lower limb movements for which this reflex is more sensitive. Regarding CKC, we have previously shown that EMG and accelerometer provide very similar information for active movements (Piitulainen et. al., 2013).

5. Conclusion

Variation in the movement range of proprioceptive stimulation of the index finger only negligibly affected cortical proprioceptive processing quantified with MEF and CKC strengths in MEG. These results imply that slight-to-moderate variations in movement range of the fingers between participants or studies are not a large cause of concern when comparing participants or studies. Moreover, CKC seems to be a robust measure when using continuous evoked movements with slightly less individual variability than MEFs with single movements.

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Credit authorship contribution statement

Timo Nurmi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft. **Maria Hakonen:** Formal analysis, Software, Writing – original draft. **Mathieu Bourguignon:** Formal analysis, Software, Writing – original draft. **Harri Piitulainen:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft.

Data availability

Data will be made available on request.

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