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Author(s): Piitulainen, Harri; Illman, Mia Johanna; Jousmäki, Veikko; Bourguignon, Mathieu

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1 **Feasibility and reproducibility of electroencephalography-based**
2 **corticokinematic coherence**

3 **Harri Piitulainen^{1,2}, Mia Illman^{1,2}, Veikko Jousmäki^{2,3}, Mathieu Bourguignon^{4,5,6}**

4 ¹Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland

5 ²Department of Neuroscience and Biomedical Engineering, Aalto University School of Science,
6 P.O. BOX 12200, 00076 AALTO, Espoo, Finland

7 ³Aalto NeuroImaging, MEG Core, Aalto University School of Science, Espoo, Finland

8 ⁴Laboratoire de Cartographie fonctionnelle du Cerveau, ULB Neuroscience Institute (UNI),
9 Université libre de Bruxelles (ULB), Brussels, Belgium

10 ⁵Laboratoire Cognition Langage et Développement, UNI – ULB Neuroscience Institute,
11 Université libre de Bruxelles (ULB), Brussels, Belgium.

12 ⁶BCBL, Basque Center on Cognition, Brain and Language, San Sebastian, Spain.

13

14 **Corresponding author:**

15 Harri Piitulainen, Faculty of Sport and Health Sciences, University of Jyväskylä, P.O. BOX 35,
16 FI-40014, University of Jyväskylä, Finland

17 E-mail: harri.piitulainen@aalto.fi, Tel. +358 505 680 654, Fax. +358 14 260 1021

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19 **Running head:** Reproducibility of EEG-based corticokinematic coherence

20

21 **Abstract**

22 Corticokinematic coherence (CKC) is the phase coupling between limb kinematics and cortical
23 neurophysiological signals reflecting cortical processing of proprioceptive afference, and is
24 reproducible when estimated with magnetoencephalography (MEG). However, feasibility and
25 reproducibility of CKC based on electroencephalography (EEG) is still unclear and is the

26 primary object of the present report. Thirteen healthy right-handed volunteers (7 females, $21.7 \pm$
27 4.3 years) participated two separate EEG sessions 12.6 ± 1.3 months apart. Participants' dominant
28 and non-dominant index finger was continuously moved at 3 Hz for 4 min separately using a
29 pneumatic-movement actuator. Coherence was computed between finger acceleration and three
30 derivations of EEG signals: (1) average reference, (2) bipolar derivations, and (3) surface
31 Laplacian. CKC strength was defined as the peak coherence value at the movement frequency.
32 Intraclass-correlation coefficient values (0.74–0.93) indicated excellent inter-session
33 reproducibility for CKC strength for all derivations and moved fingers. CKC strength obtained
34 with EEG was ~ 2 times lower compared to MEG but the values were positively correlated across
35 the participants. CKC strength was significantly ($p < 0.01$) higher for bipolar (session-1
36 0.19 ± 0.09 ; session-2 0.20 ± 0.10) and surface Laplacian (session-1 0.22 ± 0.09 ; session-2
37 0.21 ± 0.09) derivations than for the average reference (session 1 0.10 ± 0.04 ; session 2,
38 0.11 ± 0.05). We demonstrated that CKC is feasible and reproducible tool to monitor
39 proprioception using EEG recordings, although the strength of CKC was twice lower for EEG
40 compared to MEG. Laplacian and bipolar (CP3-C1/CP3-C3 and CP4-C2/C4-FC2) EEG
41 derivation(s) are recommended for future research and clinical use of CKC method.

42 **Keywords:** proprioception; kinematics; electroencephalography; somatosensory; repeatability

43 **New & Noteworthy**

44 The most important message of this report is that the corticokinematic coherence (CKC) method
45 is feasible and reproducible tool to quantify, map and follow cortical proprioceptive (“the
46 movement sense”) processing using EEG that is more widely available for CKC recordings than
47 previously used MEG designs, especially in clinical environments, but also for basic research.
48 We provide useful recommendations for optimal EEG derivations for cost-effective experimental
49 designs allowing large sample size studies.

50 **Introduction**

51 Corticokinematic coherence (CKC) quantifies the coupling between oscillatory cortical activity
52 measured with electrophysiological recordings and limb kinematics (*e.g.* acceleration) that
53 occurs during repetitive rhythmic voluntary (Bourguignon et al., 2012b, 2011; Jerbi et al., 2007),
54 passive (Piitulainen et al., 2013b, 2015, 2018a), and observed (Marty et al., 2015; Bourguignon
55 et al., 2012a) movements. CKC peaks at movement frequency and its harmonics, and it can be
56 measured using various peripheral movement-related signals and motor tasks (Piitulainen et al.,
57 2013a), and movement rates (Marty et al., 2015; Piitulainen et al., 2015). CKC primarily reflects
58 proprioceptive processing in the primary sensorimotor (SM1) cortex (Bourguignon et al., 2015;
59 Piitulainen et al., 2013b) with an apparent latency of 50–100 ms that corresponds to the timing of
60 the strongest deflection of the cortical movement-evoked field (Piitulainen et al., 2015). CKC
61 has been mainly studied in response upper limb movements but it can also be measured using
62 ankle (Piitulainen et al., 2018a) or toe movements (Piitulainen et al., 2015).

63 CKC is a promising tool for clinical evaluation of the integrity of cortical proprioceptive
64 processing. Passive movements have been previously used to probe the recovery of sensorimotor
65 functions after stroke (Parkkonen et al., 2017), but CKC could provide the clinicians with
66 essential information about changes in the cortical proprioceptive processing to better target
67 stroke rehabilitation to restore upper and lower limb functions. Another potential clinical use is
68 non-invasive pre-surgical functional mapping of SM1 cortex (Bourguignon et al., 2013). CKC
69 can be used to identify the SM1 cortex even in the presence of strong magnetic artifacts arising
70 from cranial clips or tooth braces in magnetoencephalographic (MEG) recordings (Bourguignon
71 et al., 2016). Other potential applications of CKC lay in the investigation of the development of
72 proprioception across the lifespan (Piitulainen et al., 2018a), and its alteration in various
73 sensorimotor impairments, *e.g.*, cerebral palsy, neuropathy, spinal cord injury, Friedreich ataxia,
74 etc. (Naeije et al., 2020; Lamartine Monteiro et al., 2020; Marty et al., 2019).

75 In initial CKC studies, CKC was estimated in response to voluntary or experimenter-evoked
76 passive movements (Bourguignon et al., 2011; Piitulainen et al., 2013a; Piitulainen et al.,
77 2013b). But movements made by humans vary in amplitude, frequency and regularity between
78 sessions, days, and experimenters. These sources of variability are a severe limitation for studies
79 aimed at comparing populations with different motor skills and for longitudinal studies. To
80 overcome this limitation, an accurate computer-controlled and MEG-compatible movement
81 actuator was developed for reproducible movements across time (Piitulainen et al., 2015). Using
82 this actuator, we have shown that CKC can be reproducibly estimated from MEG recordings,
83 with high consistency across sessions performed one year apart, especially at the group level
84 (Piitulainen et al., 2018b). CKC to accurately timed movements is thus a suitable tool for
85 longitudinal studies.

86 Although MEG is likely to be the technique of choice to estimate CKC, its availability is still
87 limited, and it comes at a high cost. Electroencephalography (EEG) is an obvious potential
88 alternative to MEG as it is more widely available, cheaper, and more versatile. Although it has
89 been demonstrated in newborns that CKC can be estimated based on EEG recordings (Smeds et
90 al., 2017b), there are no studies yet to determine the reliability and reproducibility of such
91 estimation. Recommendations for EEG electrode configurations to guide the large-scale
92 utilization of CKC are also missing.

93 Our aim was to examine the reliability and reproducibility of CKC estimated from EEG signals
94 using passive index finger movements evoked by a computer-controlled pneumatic movement
95 actuator in a one-year follow-up study on healthy young adults. A long enough follow-up period
96 was chosen, since detectable changes in cortical proprioceptive processing induced by most
97 pathologies or rehabilitation techniques are expected to occur in time-ranges of months or years.
98 We also aimed to examine if CKC strength and its reproducibility differ between the dominant

99 and non-dominant hand. Finally, we aimed to provide recommendations for recording and
100 computing CKC when using EEG.

101 **Methods**

102 **Participants**

103 We studied 13 healthy right-handed volunteers (mean \pm SD age, 21.7 ± 4.3 years; 7 females)
104 who did not report any history of movement disorders or neuropsychiatric disease. Their
105 Edinburgh handedness inventory score (Oldfield, 1971) was 87.2 ± 11.4 on the scale from -100
106 to 100 . The study had prior approval by the ethics committee of Aalto University. The
107 participants gave informed consent before participation. One participant was excluded due to the
108 presence of intractable artifacts in the EEG recordings. Thus, the results are reported for the
109 remaining 12 participants.

110 We have previously reported the reproducibility of CKC based on the MEG data recorded from
111 the same volunteers (Piitulainen et al., 2018b). The present study focuses on the analysis of the
112 EEG signals that were simultaneously recorded with MEG.

113 **Experimental protocol**

114 A custom-made non-magnetic pneumatic movement actuator (Aalto NeuroImaging, Aalto
115 University, Espoo, Finland) was used to generate passive dominant and non-dominant index
116 finger flexion-extension movements of the metacarpophalangeal joint. The movement actuator
117 has been fully described in (Piitulainen et al., 2015) and similar designs have been successfully
118 used in MEG (Piitulainen et al., 2018b; Smeds et al., 2017a; Bourguignon et al., 2016; Vinding
119 et al., 2019; Illman et al., 2020), EEG (Smeds et al., 2017b) and fMRI (Nurmi et al., 2018; Lolli
120 et al., 2019) studies. Index finger was attached to a pneumatic artificial muscle (DMSP-10-100
121 AM-CM, Festo AG & Co, Esslingen, Germany) that moved downward in vertical direction when

122 its internal air pressure was increased to 4 bar thus flexing the finger, and then extending it back
123 to the initial position when the air pressure was released. In this way, continuous passive
124 flexion–extension movements were generated at 3 Hz for the dominant and non-dominant index
125 finger separately (4 min for each finger in separate sessions). The movement range was ~5 mm.
126 Movement frequency was set to 3 Hz because it has been found appropriate and efficient for
127 robust CKC estimation (Piitulainen et al., 2015).

128 During the MEG/EEG recordings, participants were sitting with the stimulated hand on the upper
129 plate of the movement actuator that was placed on the table in front of them (Fig. 1). The index
130 finger was taped to the aluminum end of the pneumatic muscle. The other hand was resting on
131 the thigh. Earplugs were used to block the slight concomitant auditory noise that arose from the
132 airflow within the pneumatic muscle. A white A3-sized cardboard sheet was taped horizontally
133 to the MEG gantry to prevent the participant from seeing the moving finger. Participants were
134 instructed to fixate, through a rectangular hole in the cardboard sheet, a picture on the wall of the
135 magnetically shielded room, 2.2 m in front of the eyes. In order to estimate reproducibility of
136 CKC, the recordings were performed in two sessions 12.6 ± 1.3 months apart.

137 **Measurements**

138 *EEG/MEG.* The measurements were carried out at the MEG Core, Aalto NeuroImaging, Aalto
139 University (Espoo, Finland) inside a magnetically shielded room (Imedco AG, Hägendorf,
140 Switzerland). EEG signals were recorded simultaneously time-locked with MEG and
141 acceleration signals. The MEG device was a 306-channel whole-scalp neuromagnetometer
142 (Elekta Neuromag™, Elekta Oy, Helsinki, Finland). Reproducibility results for MEG data have
143 been previously reported in (Piitulainen et al., 2018b). EEG was recorded with a MEG-
144 compatible cap (ANT Neuro waveguard™ original), containing 58 Ag-AgCl surface electrodes
145 mounted according to the international 10–20 system with modified combinatorial nomenclature.
146 EEG electrodes were referenced with respect to AFz-electrode. EEG signals were band-pass

147 filtered at 0.1–330 Hz and sampled at 1 kHz. The output impedance of the EEG electrodes was
148 kept below 10 k Ω .

149 *Acceleration.* Index finger acceleration was recorded with a 3-axis accelerometer (ADXL335
150 iMEMS Accelerometer, Analog Devices Inc., Norwood, MA, USA) attached to the nail of the
151 moved finger. Acceleration signals were low-pass filtered at 330 Hz and sampled at 1 kHz, time-
152 locked to the EEG/MEG signals.

153 **Data Processing**

154 *Preprocessing.* EEG data was first visually inspected to identify noisy channels. Then, principal
155 component analysis using MNE-Python toolbox was used to remove two EEG components
156 related to eye blink artefacts (Gramfort et al., 2013). Noisy EEG channels were replaced with the
157 average of all neighboring EEG channels using FieldTrip toolbox function `ft_channelrepair`
158 (Oostenveld et al., 2011). Then the 58 raw EEG signals (referenced to AFz electrode) were
159 spatially filtered using (1) the *average reference* of all EEG channels (excluding the EEG
160 channel of interest), (2) all possible single differential (*bipolar*) combinations between the 58
161 EEG signals (in total 1653 combinations), and (3) surface *Laplacian* derivation. The coherence
162 analysis was performed separately for all the resulting EEG signals (see details below).

163 *Coherence analysis.* For coherence analyses, the continuous data were split into 2-s epochs with
164 1.6-s epoch overlap, leading to a frequency resolution of 0.5 Hz (Bortel and Sovka, 2007). EEG
165 epochs with signals exceeding 200 mV were excluded to avoid contamination of the data by
166 internal or external noise sources. We then performed coherence analysis (Halliday et al.,
167 1995)—yielding cross-, power- and coherence spectra—between EEG signals and the Euclidian
168 norm of the three orthogonal accelerometer signals. Before the coherence analysis, each epoch of
169 acceleration was normalized by its Euclidian norm (Bourguignon et al., 2011). The magnitude
170 squared coherence was chosen as coupling measure as done in our previous CKC studies
171 (Bourguignon et al. 2011, 2015, 2016; Marty et al. 2019; Piitulainen et al. 2013a, 2013b, 2015,

172 2018a, 2018b). Other coupling measures dealing with potential brain-peripheral delays (such as,
173 *e.g.*, phase locking value) are expected to yield similar results.

174 CKC strength was defined as the maximum coherence value at 3 Hz across the 32 EEG
175 electrodes contralateral to the movement for average reference and surface Laplacian approaches
176 or across all the 1653 bipolar EEG signals. The maximum channel (or channel pair) was defined
177 independently for session 1 and session 2 data. Group-level topographic distributions of CKC
178 were visualized for the Laplacian and average reference approaches using FieldTrip toolbox
179 (Oostenveld et al., 2011).

180 *Finger kinematics.* Acceleration signals were extracted and averaged with respect to the
181 movement onsets, separately for each individual, finger, and session. The resulting acceleration
182 signals were filtered through 1–195 Hz. Then, magnitude and regularity of the evoked
183 movements were estimated by computing the mean and coefficient of variation of peak
184 acceleration magnitude (*i.e.* Euclidian norm of the three orthogonal acceleration signals) across
185 all evoked movements.

186 **Statistical analyses**

187 *Statistical significance of coherence.* The statistical significance of individual coherence levels
188 (maximum value across the 32 or 1652 EEG signals of interest) was assessed under the
189 hypothesis of linear independence of Fourier coefficients from epoch to epoch at each frequency
190 of interest, taking into account the use of overlapping epochs (Halliday et al., 1995; Bourguignon
191 et al., 2011). To correct for multiple comparisons, the alpha level was set to $0.05/N_s$, $N_s = 32$
192 (midline and contralateral channels to stimulus) or 1652 (all possible bipolar combinations)
193 being the number of EEG signals included in the analysis. Note that in the case of bipolar
194 derivations, this is an extremely conservative limit as there are naturally much less degrees of
195 freedom than pairs of electrodes.

196 *Reproducibility and analysis of variance.* These statistical analyses were performed in IBM
197 SPSS Statistics software (ver. 25). To enable comparison with other studies, we used common
198 and closely related tests to assess inter-session reproducibility for CKC strength. A two-way
199 mixed-effects model intraclass-correlation coefficient (ICC) and Spearman correlation
200 coefficient were computed between the session 1 and session 2 CKC values. Reproducibility for
201 the evoked passive movements (finger kinematics) has been reported earlier (Piitulainen et al.,
202 2018b).

203 We assessed the effect of EEG-derivation, moved hand and session on CKC strength. Due to
204 small sample size ($n = 12$), we used non-parametric related samples test to this effect: a
205 Friedman test was used to compare CKC strength between the three different EEG derivations,
206 and a Wilcoxon two-related-samples test was used to compare CKC strength between specific
207 EEG-derivation, hands or sessions.

208 **Results**

209 *Data quality.* The movement actuator and accelerometer did not produce notable artifacts in the
210 EEG signals. The noisy EEG channels (mean \pm SD 6 ± 3 , range 3–13) were replaced with the
211 average of neighboring channels. All recordings were successful with 573 ± 45 (session 1; mean
212 \pm SD) and 572 ± 29 (session 2) artefact-free epochs collected for dominant hand stimulation, and
213 525 ± 58 (session 1) and 566 ± 35 (session 2) for the non-dominant hand. These numbers of
214 epochs did not differ significantly between the hands or sessions ($ps > 0.05$; Wilcoxon tests).

215 The kinematics of the evoked movements were stable. Indeed, in (Piitulainen et al., 2018b) we
216 report a peak acceleration magnitude of 0.93 ± 0.04 m/s² (session 1; mean \pm SD) and 0.92 ± 0.04
217 m/s² (session 2) for dominant hand, and 0.91 ± 0.04 m/s² (session 1) and 0.92 ± 0.04 m/s²
218 (session 2) for non-dominant hand.

219 *Strength of CKC at the group level.* Figure 2 shows the spectra of CKC averaged across subjects
220 for all fingers, spatial filters, and recording sessions. Qualitatively, CKC strength at 3 Hz was
221 strikingly similar between the two measurements separated by 12.6 ± 1.3 months. CKC at
222 harmonic frequencies also appeared very reproducible at the group level. At the individual level,
223 8–12 out of 12 participants showed significant CKC at 3 Hz depending on the EEG-derivation
224 used, hand examined and session (see Table 1). In addition, we did compute CKC for the data
225 referenced to AFz, but it resulted very weak values that were significant in only 3 out of 12
226 participants ($p < 0.05$). Thus, we did not consider the monopolar EEG results further.

227 Table 1 present the CKC strength for all hands, tested derivations, and recording sessions.
228 Figure 3 presents CKC strength when the right and left hands were pooled together. CKC
229 remained at similar level between the *sessions* (Laplacian, $p = 0.81$ and $p = 0.53$; average
230 reference, $p = 0.084$ and $p = 0.70$; bipolar, $p = 0.53$ and $p = 0.31$ for dominant and nondominant
231 hands respectively) and *hands* (Laplacian, $p = 0.81$; average reference, $p = 0.88$; bipolar, $p =$
232 0.75) but differed between the *EEG-derivations* ($ps < 0.002$). CKC strength was higher for
233 Laplacian and bipolar EEG-derivations compared to the average reference approach for both
234 sessions and tested hands ($ps < 0.005$).

235 *Reproducibility of CKC.* Figure 4 illustrates the reproducibility of individual values of CKC
236 strength. In general, participants with strong CKC at session 1 showed strong CKC also at
237 session 2 and *vice versa*. Nevertheless, CKC strength changed by over 0.1 between sessions in
238 1–2 out of 12 participants depending on the EEG derivation and hand. CKC strength based on
239 EEG recordings correlated positively with the CKC strength obtained from simultaneous MEG
240 recordings (Fig. 4b).

241 Table 2 presents the reproducibility values for CKC for the three different derivations tested.
242 ICC values between session 1 and session 2 indicated excellent (≥ 0.74) inter-session
243 reproducibility for CKC strength both for the dominant and non-dominant hand. However,

244 Spearman correlation tests between session 1 and session 2 were significant only for the non-
245 dominant hand when average reference or bipolar approaches were used.

246 *Topographic distribution of CKC at the group level.* Figure 5 shows the topographic
247 distributions of the grand-average CKC values for the dominant and non-dominant hands in
248 session 1 and session 2. As expected for neural sources in the primary sensorimotor cortex, CKC
249 peaked at EEG electrodes close to C3/C4 contralateral to the moved finger.

250 *Optimal bipolar EEG derivation.* Figure 6 presents the EEG-electrode pairs showing the
251 strongest CKC. Among all the possible 1653 bipolar EEG pairs, two appeared to be optimal for
252 CKC estimation. For the dominant hand (right hand stimulation) CKC peaked at the pairs CP3–
253 C1 and CP3–C3 in 58% of the cases (8 and 6 respectively out of 24 cases). For the non-dominant
254 hand, CKC peaked at the pairs C2–CP4 and FC2–C4 in 70% of the cases (10 and 7 respectively
255 out of 24 cases).

256 **Discussion**

257 We examined the reproducibility of CKC derived from EEG recordings for movements elicited
258 by a pneumatic movement actuator. We observed significant CKC in all studied participants, but
259 this depended on the EEG derivation applied, and CKC was generally weaker compared to
260 previous studies using the same stimulus in MEG (Piitulainen et al., 2018b; Piitulainen et al.,
261 2015). The reproducibility of CKC strength was good or excellent at the group level. However,
262 there were several participants who showed some inter-session variation, and thus caution needs
263 to be taken if the aim is to follow CKC in single individuals using EEG. Our results indicated
264 that EEG is a feasible tool to examine and follow cortical proprioceptive processing in
265 longitudinal studies. Finally, a one bipolar EEG-channel approach following our EEG-pair
266 suggestions shows potential as a cost-efficient tool to follow cortical proprioceptive processing
267 in larger populations, *e.g.*, in clinical studies.

268 Reproducibility of CKC when using EEG

269 The reproducibility of CKC strength (tagging cortical proprioceptive processing) at the group
270 level was good to excellent between two sessions 1-year apart. This is an encouraging result, as
271 the test-retest reproducibility of evoked potentials to cutaneous electrical stimulation of the
272 tactile receptors of the fingers has been reported to be low, even in ‘ideal’ condition without
273 detaching the EEG cap between consecutive recordings (Kalogianni et al., 2018). However, the
274 source localizations of evoked potentials to tactile (Schaefer et al., 2002) or median nerve
275 (Kristeva-Feige et al., 1997) stimulations have proven highly reproducible. The topographic
276 distributions for the current proprioceptive stimuli appeared very similar across sessions,
277 suggesting that our protocol could be well suited to compare groups for longitudinal effects.
278 Large longitudinal effects on CKC strength could be expected. Healthy ageing appears to
279 enhance CKC strength by almost 80%, based on cross-sectional comparison of older (~69 years)
280 with young adults (~25 years) (Piitulainen et al. 2018a). Presumably, even larger effects are
281 possible in clinical populations. The change in CKC strength for the current 1-year follow-up
282 was ~5%, thus all intervention effects exceeding this level would presume to be detected.

283 There was no marked difference between the hands in terms of CKC reproducibility. The
284 correlation coefficients between sessions of CKC strength appeared slightly higher for the non-
285 dominant hand, but a non-parametric permutation test (in which values for the dominant and
286 non-dominant hands were randomly permuted within subjects to derive a permutation
287 distribution) indicated that the difference between hemispheres in the inter-session correlation
288 was not statistically significant ($p_s > 0.2$). The reproducibility was very similar for different EEG
289 derivations, although the CKC strength was clearly weaker for the average reference. Thus, it
290 appears that from the reproducibility point of view the choice of EEG derivation is not crucial,
291 but it is natural to recommend using the derivations that maximize the CKC strength (Laplacian
292 or bipolar).

293 The major factor affecting the reproducibility of CKC is most likely the careful preparation of
294 the EEG electrodes maximizing the EEG signal-to-noise ratio. The EEG electrode locations at
295 the scalp should be fixed as well as possible between the sessions, and their impedance should be
296 confirmed to be low enough. We did not use any advanced methods for the placing the EEG cap
297 in our participants but paid particular attention to preparation of the electrode-skin contacts,
298 likely reducing random variability in the data being crucial for all longitudinal studies. The
299 proprioceptive stimuli evoked by the pneumatic movement actuator are shown to be very
300 reproducible from stimulus-to-stimulus, participant-to-participant, and session-to-session
301 (Piitulainen et al., 2018b). Only finger and hand positioning on the stimulator is a potential
302 source of variability in CKC strength attributable to the stimulation procedure. Hence, provided
303 care is taken, the CKC strength should be minimally related to variations in stimulation
304 parameters.

305 Our results indicate that CKC strength may vary from session-to-session at the level of the
306 individual participant, but the individuals with strong CKC in the first session tended to have
307 strong CKC also in the second session, and *vice versa*. Indeed, the CKC strength correlated
308 positively between the sessions, being significant for 2 in instances out of the 6 (2 hands \times 3
309 derivations). Thus, EEG-based CKC approach is reproducible tool to follow the cortical
310 proprioceptive processing in longitudinal studies, but individual patient results should still be
311 interpreted with some caution. It could be recommended that future studies could measure the
312 same participant multiple times in sessions separated by few hours/days; the rational being that
313 CKC strength should prove more reproducible when assessed based on multiple than single
314 sessions.

315 **Inter-individual variability in CKC strength**

316 In line with previous studies, CKC showed high inter-individual variation (Piitulainen et al.,
317 2015, 2013b, 2018b; Bourguignon et al., 2011). The mechanisms for the variation are unclear but

318 do not seem to be attributable solely to MEG or EEG methodological constraints, as the variation
319 is evident in both methods with different constraints. For example, MEG is more prone to
320 alterations in the head orientation and distance with respect to MEG sensors between the session.
321 CKC strength clearly reflects changes in the brain functions, as older individuals show stronger
322 CKC than younger ones in association to worse postural balance performance (Piitulainen et al.,
323 2018a). However, the sources of the high inter-individual variation in the CKC strength (*i.e.*
324 cortical proprioceptive processing) still need to be clarified.

325 **Impact of EEG derivation scheme on CKC strength**

326 CKC was stronger when estimated from Laplacian and bipolar derivations compared to average
327 reference. These clear differences in CKC strength indicate a difference in the signal-to-noise
328 ratio (SNR) of the EEG signals for these derivations. Indeed, based on simulations, an increase
329 in low SNR signal amplitude increases the level of coherence (Muthukumaraswamy and Singh,
330 2011). Such SNR–coherence relationship is also easily shown from theoretical considerations.
331 The advantage of Laplacian EEG and bipolar derivations are their enhanced spatial selectivity
332 when compared to average reference derivation. Higher spatial selectivity may enhance the SNR
333 arising from the SM1 cortex contralateral to the stimulus. The further advantage of using
334 multiple bipolar electrode-pairs is the exploration of all possible bipolar derivations (in our case
335 1653 pairs of EEG electrodes) that increases the probability of identifying the optimal derivation
336 for a given stimulus and individual. But this approach comes with increased computational
337 burden and increased risks of false positives. In contrast, the Laplacian approach is
338 computationally more straightforward and requires less stringent control for multiple
339 comparisons. The average reference derivation affords a lower spatial selectivity and hence is
340 fraught with poorer SNR and CKC strength. Even worse results were obtained with monopolar
341 EEG, *i.e.*, when referenced to AFz (< 25% of the participants reached the statistically significant
342 CKC).

343 CP3-C1 or CP3-Fz electrode pairs are the recommended derivations to look at somatosensory
344 evoked potentials to right hand stimuli (Cruccu et al., 2008). In line with this recommendation,
345 we identified CP3-C1 as the most common optimal derivation in our population. The CKC did
346 not peak in CP3-Fz electrode pair in our participants, and this electrode pair reached significant
347 CKC level only in 15% of the participants. Therefore, the recommendations by Cruccu et al.
348 (2008) are valid also for CKC recordings but if single channel EEG recordings are used, we
349 recommend the derivation CP3-C1 or CP3-C3 as the electrode placements. However, if
350 abnormal cortical anatomy is expected, e.g. due to cortical lesions, single channel EEG approach
351 may fail to detect significant CKC, and thus it would be recommended to use a larger set of EEG
352 electrodes (minimum 32) and a Laplacian derivation approach to pinpoint the peak CKC
353 channels. Note also that a common feature of most of the optimal derivations is to involve
354 electrode pairs for which one is posterior and lateral to the other.

355 There is one prior CKC study using EEG, although to manually evoked movements in infants at
356 the neonatal intensive-care environment (Smeds et al., 2017b). In the infants, CKC peaked only
357 at first harmonic of movement frequency (Smeds et al., 2017b), whereas adults typically show
358 strong CKC both at the movement frequency and its first harmonic both to experimenter
359 (Piitulainen et al., 2013b) and actuator evoked (Piitulainen et al., 2015, 2018b; Bourguignon et
360 al., 2016) finger movements. This discrepancy may arise from uncompleted neurodevelopment
361 and therefore less discrete movement directional specificity (extension *versus* flexion) in infants.

362 **CKC strength in EEG vs. MEG**

363 CKC strength obtained in the same session and recording with EEG and MEG were highly
364 correlated, although the CKC strength obtained with EEG (most optimal Laplacian derivation)
365 was about two times lower than the one obtained with MEG recordings. This difference in CKC
366 strength between the modalities probably pertains to differences in spatial selectivity of the
367 techniques (Hämäläinen et al., 1993), leading to differences in SNR and estimated coherence

368 strength. Nevertheless, our results indicate that EEG can be used to quantify CKC as surrogate to
369 MEG recordings, which expands clinical utilization of CKC method by providing a more cost-
370 efficient and accessible recordings.

371 Since significance thresholds for coherence estimates decrease asymptotically as the inverse of
372 the number of data epochs (Halliday et al., 1995), it can be inferred that EEG recordings need to
373 be 2 times longer than MEG recordings to uncover significant CKC (Destoky et al., 2019).
374 Similar findings were previously reported for the coupling between brain activity and the
375 temporal envelope of heard speech (Destoky et al., 2019). As fully developed in this latter
376 reference, significant effects in a broad range of cortical functions are typically detectable with
377 EEG if there is 2–4 times longer recording than in MEG.

378 **Perspectives**

379 CKC can extract the somatosensory component of the corticospinal coupling during passive
380 movement stimuli, particularly the proprioceptive processing in the SM1 cortex (Bourguignon et
381 al., 2015; Piitulainen et al., 2013b). Therefore, CKC is applicable also in paralyzed patients and
382 to examine and follow changes in cortical proprioceptive processing, *e.g.*, during stroke
383 recovery, motor-skill acquisition, sensorimotor development, and aging. High reproducibility is a
384 prerequisite for longitudinal studies. The reproducibility of EEG-based CKC at group level was
385 good or excellent, and thus enables its use in the longitudinal studies, but individual patient
386 results should be interpreted with some caution. Another advantage of CKC is that the cortical
387 signals are relative robust, and thus CKC can be detected in most if not all individuals. Finally,
388 the applicability of EEG to measure CKC will expand the research and clinical use of the CKC
389 method.

390 **Conclusions**

391 Our results demonstrate that CKC elicited with a pneumatic movement actuator can be reliably
392 and reproducibly estimated from EEG recordings. Thus, EEG-based CKC approach shows
393 potential as a tool to follow the cortical proprioceptive processing in longitudinal studies.
394 However, some caution needs to be taken if the aim is to follow single individuals. Laplacian
395 and bipolar EEG derivation(s) are recommended for future research and clinical use of the CKC
396 method. A cost effective CKC recording using only few bipolar EEG channels was also
397 suggested. For this purpose, we recommend the use of CP3-C1/CP3-C3 and CP4-C2/C4-FC2
398 bipolar derivations.

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401 actuators at Aalto NeuroImaging, Aalto University, Espoo, Finland.

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405 **Disclosures**

406 None of the authors have potential conflicts of interest to be disclosed.

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515

516 **Figure captions**

517 **Figure 1.** The experimental setup. (A) The participant's index finger was taped to the vertically
518 moving pneumatic muscle, and an accelerometer was taped to the nail of the finger. (B) EEG
519 signals were recorded with a 58-electrode cap. (C) Participants sat on a chair with their head in
520 the MEG sensor array.

521 **Figure 2.** Coherence spectra between finger acceleration and EEG signals averaged across all
522 participants ($n = 12$). Coherence peaked at the 3-Hz-movement frequency and its harmonics.
523 Black solid lines indicate session 1 and grey lines session 2 averages. The number of participants
524 showing significant coherence at 3 Hz are indicated above the 3-Hz peak for session 1 and
525 session 2 separately.

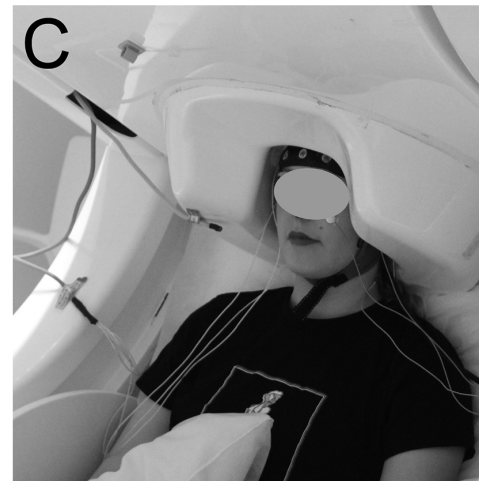
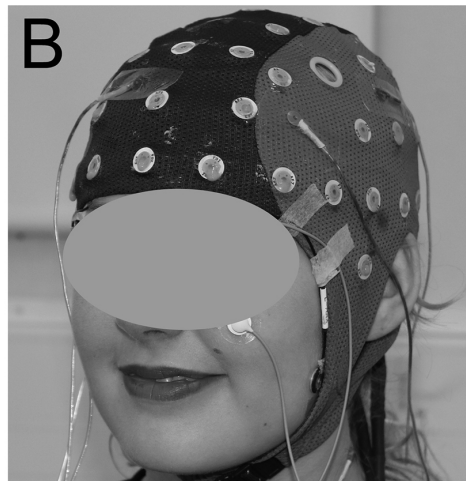
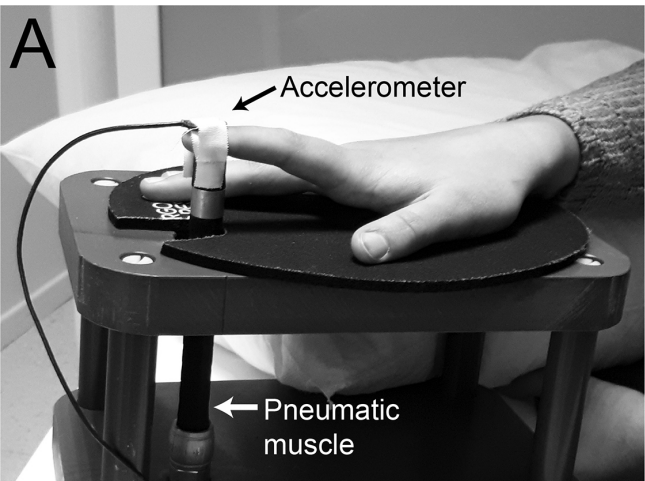
526 **Figure 3.** Mean CKC strength when the hands were pooled together for the three EEG
527 derivations at session 1 and session 2. The error bars represent standard deviation. Horizontal
528 bars indicate the significance of the difference between derivations.

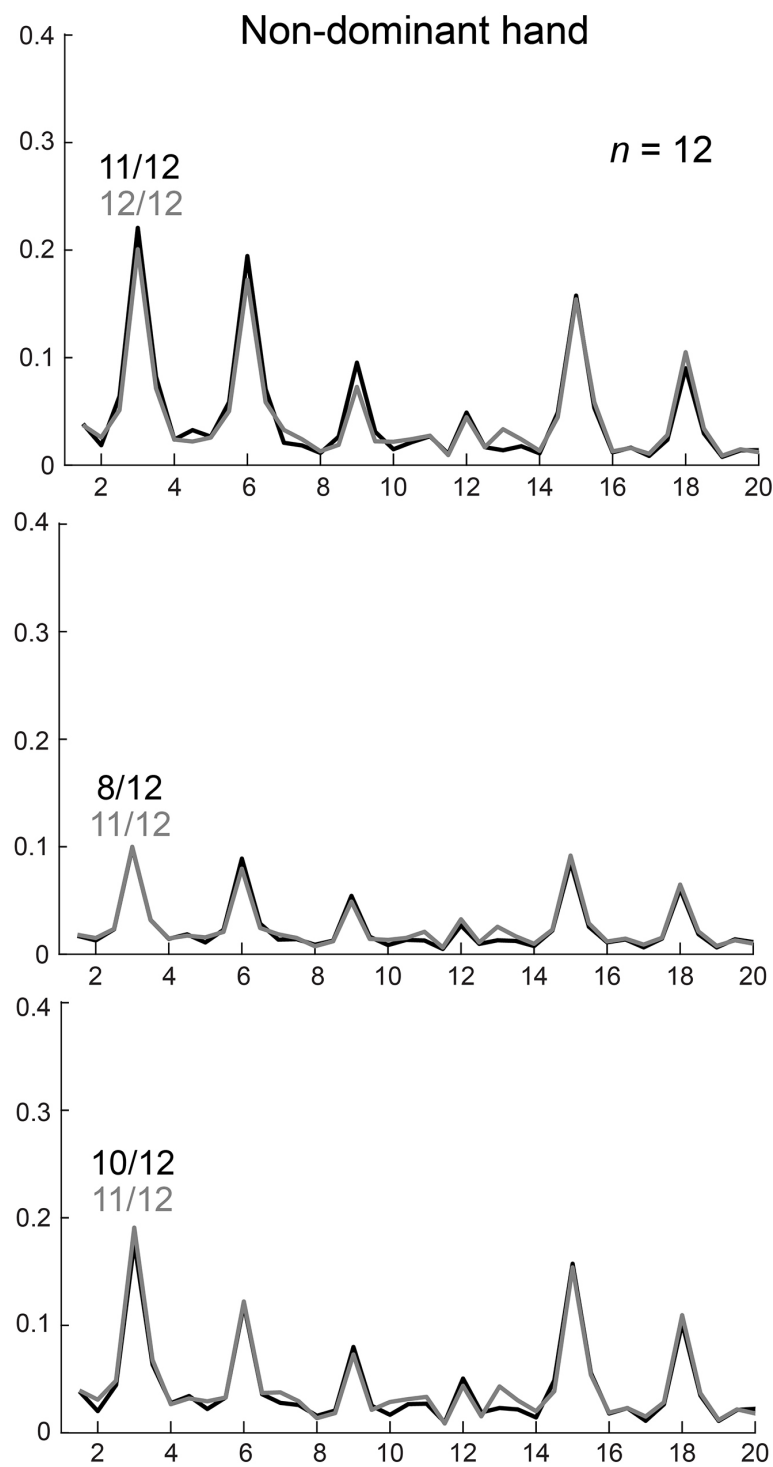
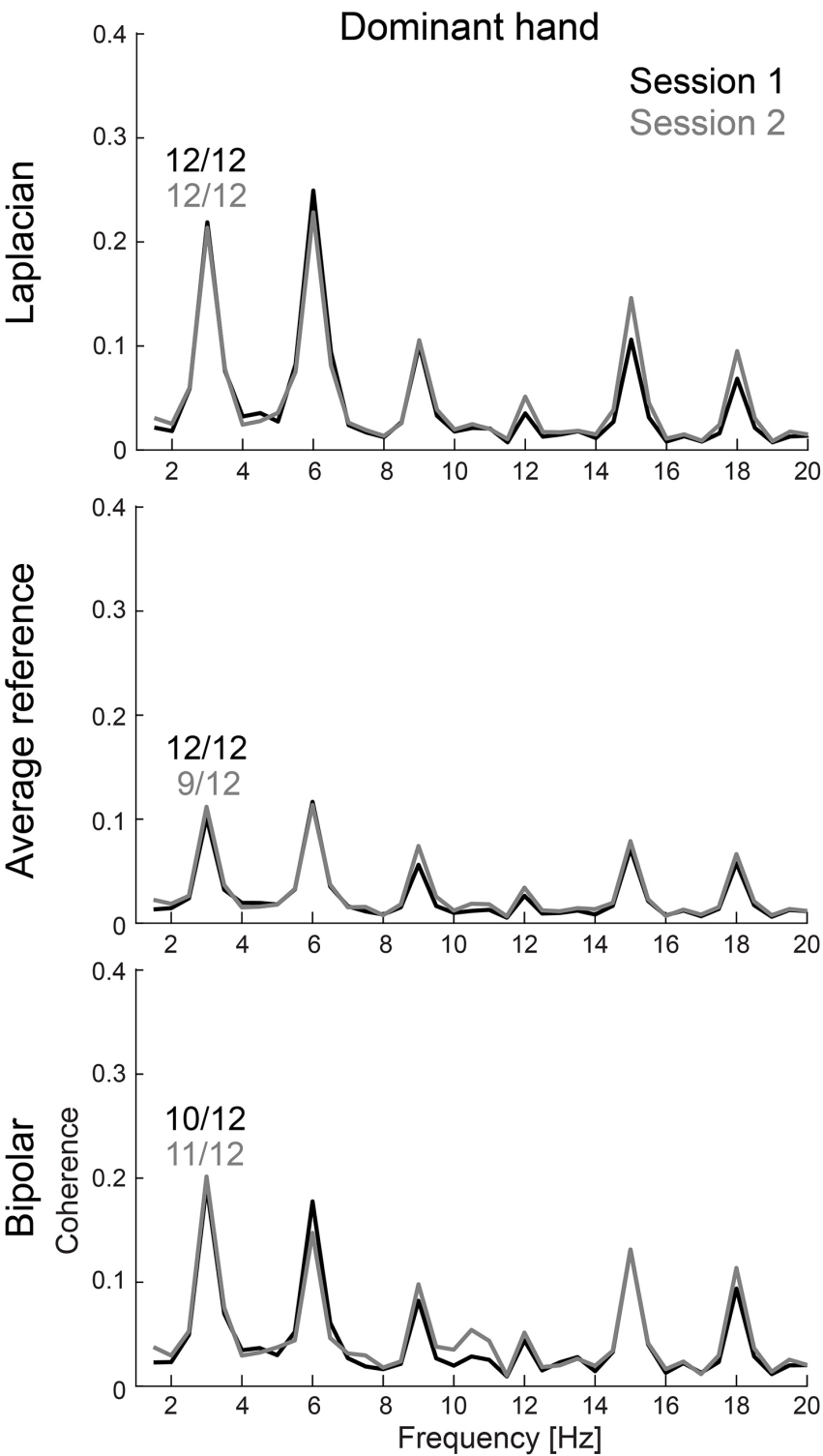
529 **Figure 4.** Inter-session and method correlations. A: Scatterplots for individual CKC values in
530 session 1 and 2 for dominant and non-dominant hands separately. B: Scatterplots for individual
531 CKC values pooled across the hands in session 1 for EEG (the three derivations) and MEG.
532 Corresponding linear regression lines and Spearman correlation coefficients are given.

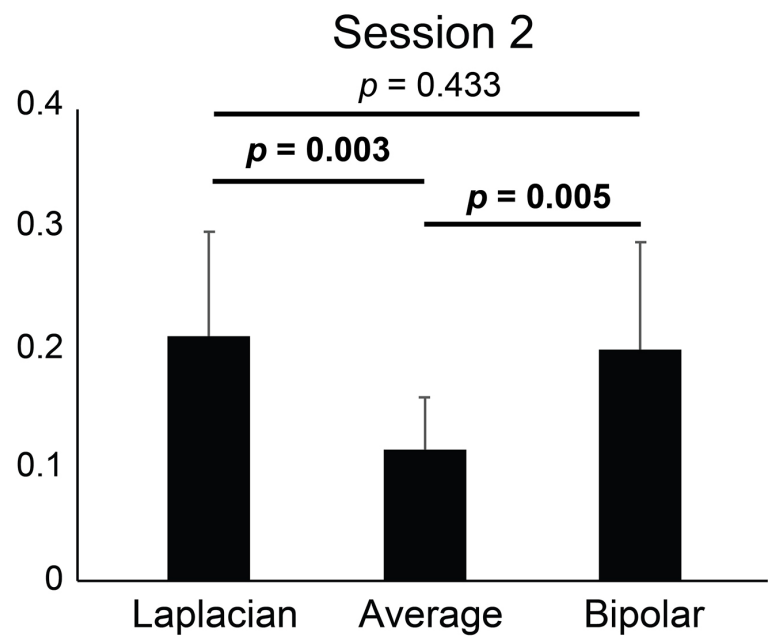
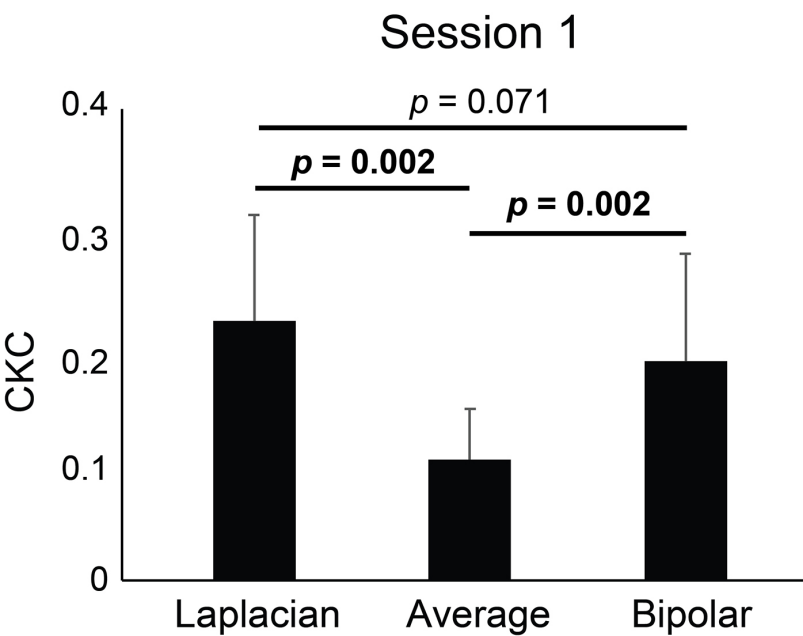
533 **Figure 5.** Topographic distributions of the mean CKC at 3 Hz across subjects ($n = 12$). There is
534 one topography for each possible combination of derivation (surface Laplacian and average

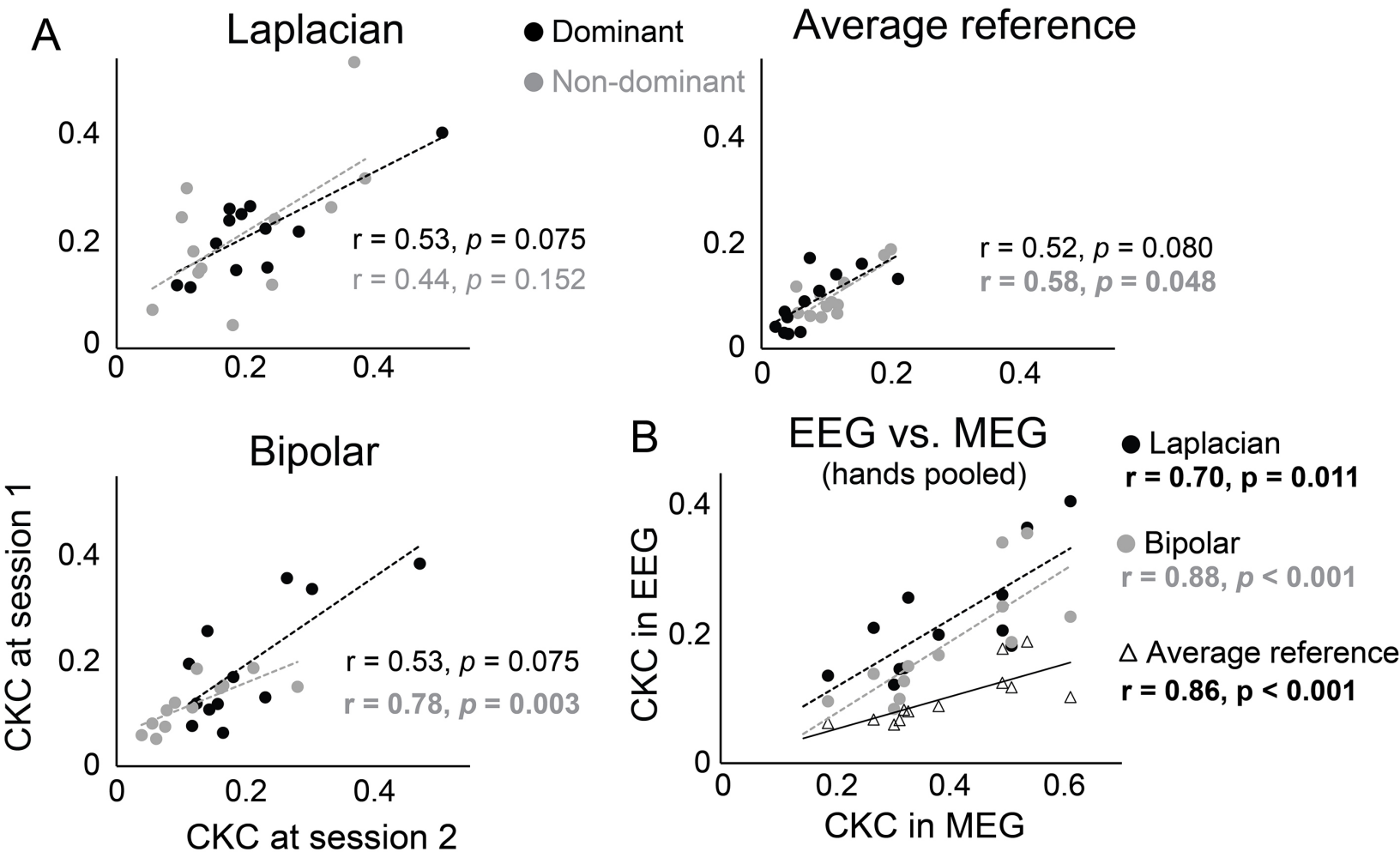
535 reference), moved finger and session. The overlaid numbers indicate the count of participants
536 showing peak CKC in each EEG electrode.

537 **Figure 6.** Bipolar EEG-electrode pairs with peak CKC value among all 1653 combinations. Line
538 thickness and darkness reflects occurrence (out of $n = 12 \times 2$ sessions) of peak CKC in the given
539 electrode pair among the participants across both sessions. The narrowest and lightest line
540 indicates that there was only one occurrence of the peak CKC value.





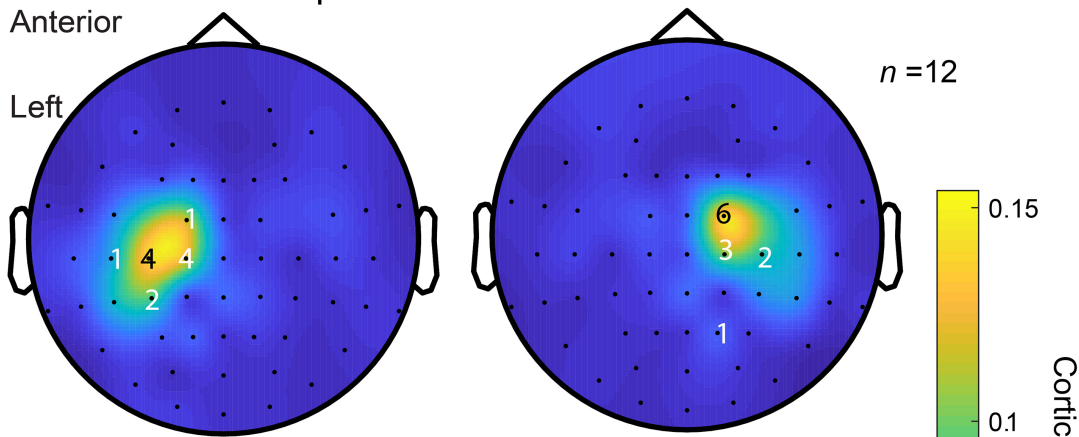




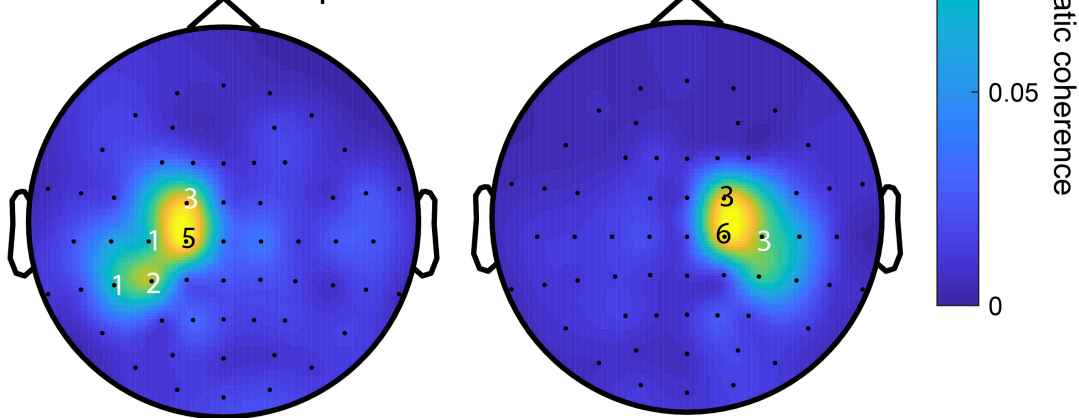
Dominant hand

Non-dominant hand

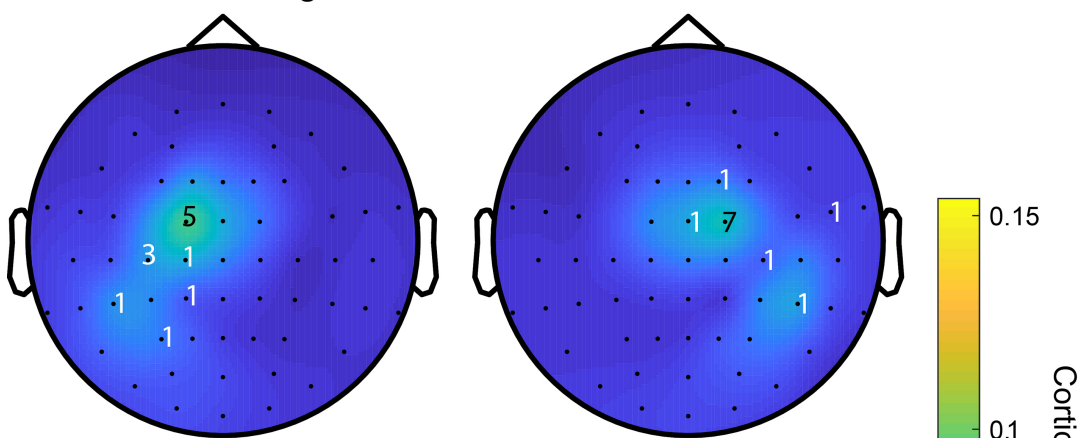
Laplacian at session 1



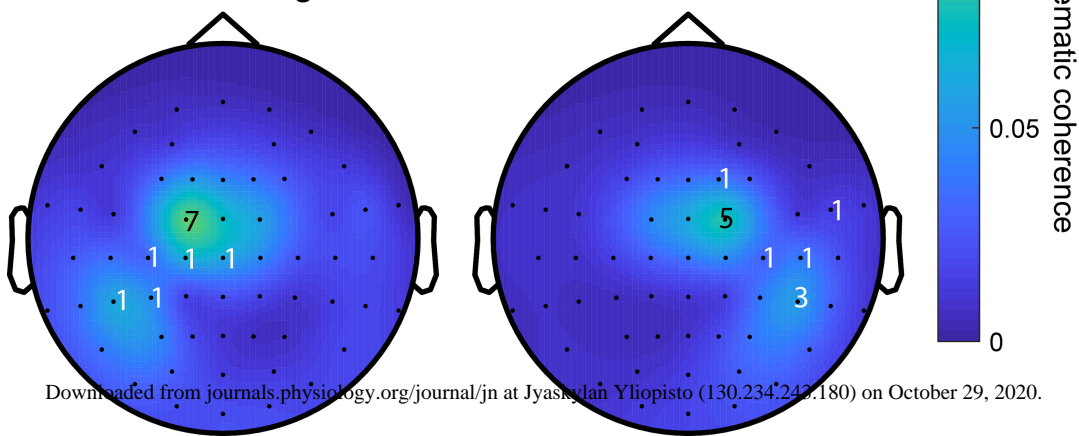
Laplacian at session 2



Average reference at session 1



Average reference at session 2



Dominant hand

Non-dominant hand

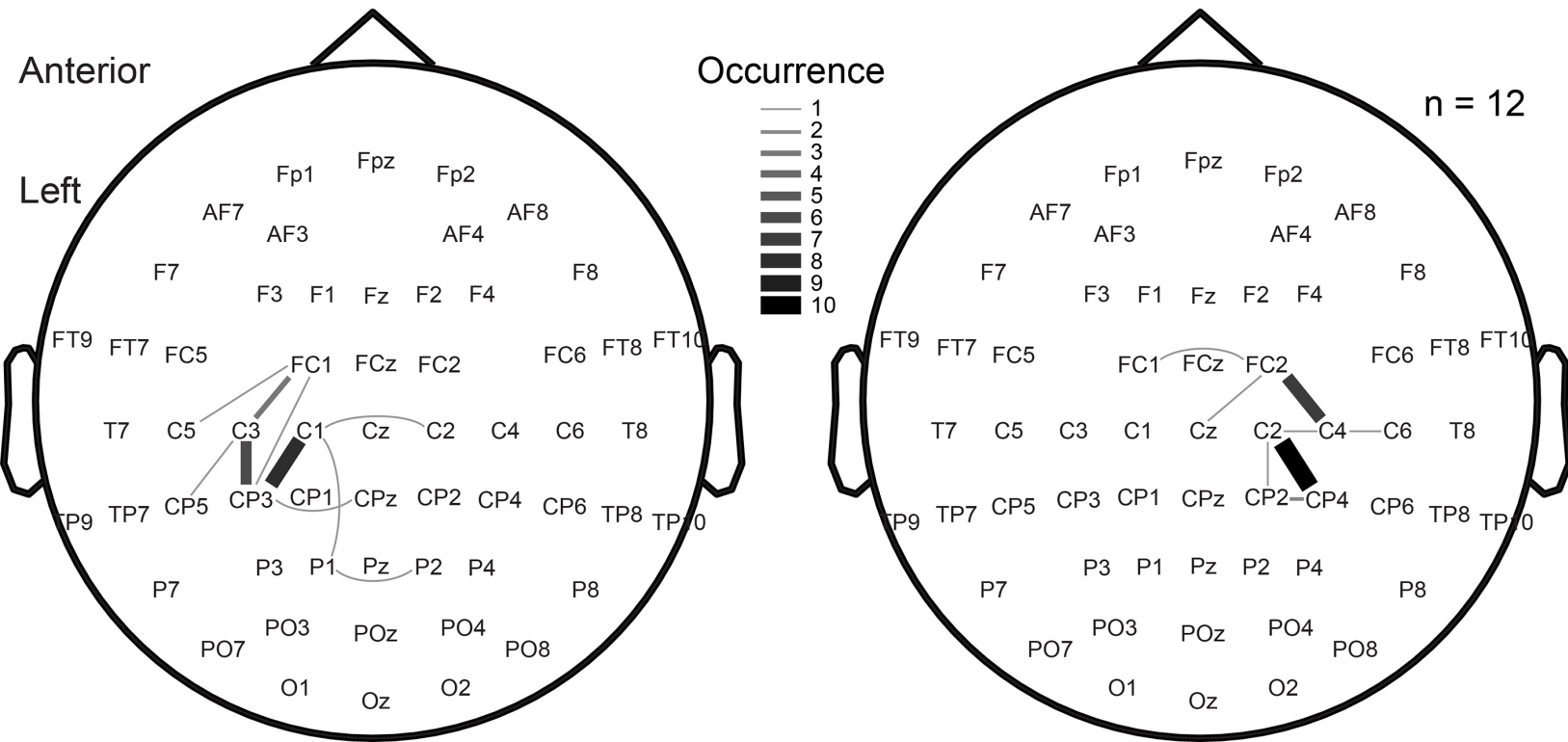


Table 1. CKC strength and number of subjects showing significant CKC (n-sig)

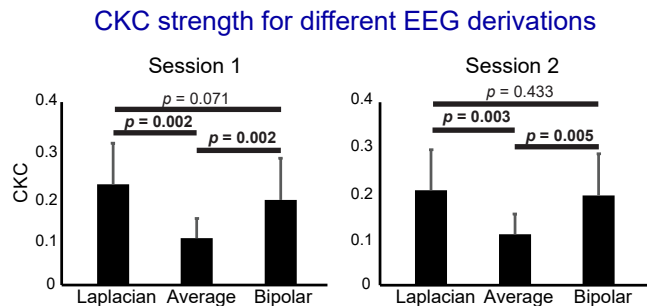
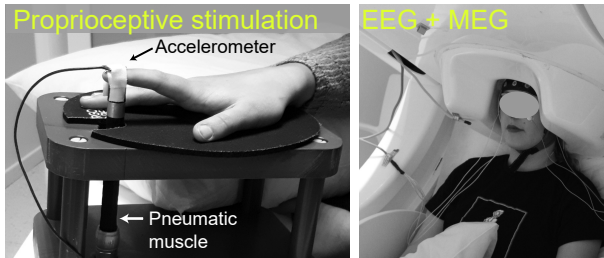
Approach	Dominant			Non-Dominant		
	Mean \pm SD	Range	#($p < 0.05$)	Mean \pm SD	Range	n-sig
Session 1						
Laplacian	0.22 \pm 0.08	0.12–0.41	12	0.22 \pm 0.13	0.04–0.58	11
Average reference	0.10 \pm 0.04	0.06–0.19	12	0.10 \pm 0.06	0.03–0.24	8
Bipolar	0.19 \pm 0.11	0.06–0.38	10	0.18 \pm 0.09	0.06–0.33	10
Session 2						
Laplacian	0.21 \pm 0.11	0.09–0.51	12	0.20 \pm 0.11	0.06–0.39	12
Average reference	0.11 \pm 0.05	0.05–0.20	9	0.10 \pm 0.05	0.02–0.19	11
Bipolar	0.20 \pm 0.10	0.11–0.47	11	0.19 \pm 0.11	0.06–0.36	11

= number of subjects (out of 12) that reached statistical significance in level of $p < 0.05$ in CKC.

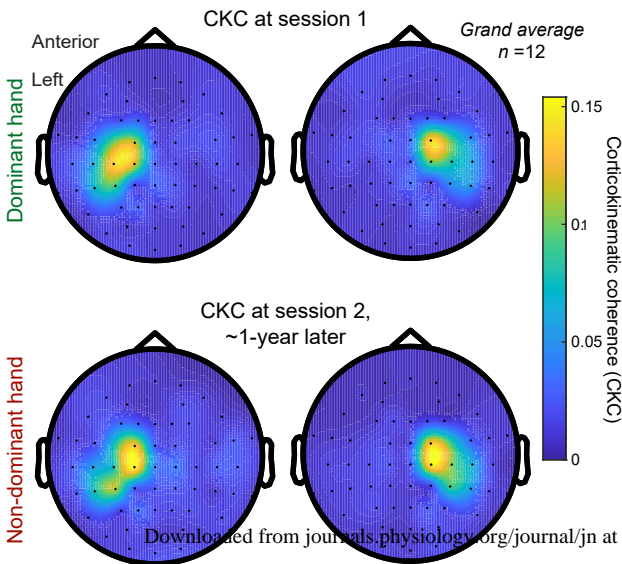
Table 2. Inter-session reproducibility of CKC.

Approach	Dominant		Non-Dominant	
	ICC	Spearman r	ICC	Spearman r
Laplacian	0.88	0.53	0.76	0.44
Average reference	0.88	0.52	0.74	0.58*
Bipolar	0.87	0.53	0.93	0.78**

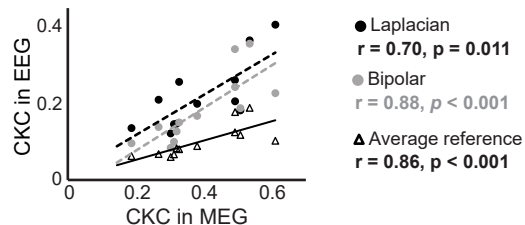
* = $p < 0.05$, ** = $p < 0.01$ for Spearman correlation coefficient.



Cortico-kinematic coherence (CKC) for EEG (Laplacian derivation)



CKC in EEG vs. MEG (hands pooled together)



Bipolar electrode pairs showing peak CKC

