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Plasticity and imagery after spinal injury

1 **Neuroplasticity of imagined wrist actions after spinal cord injury: A pilot study¹**

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Attribution-NonCommercial (CC BY-NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

17 **Abstract**

18 Motor imagery (MI, *i.e.*, the mental representation of an action without physically executing it)
19 stimulates brain motor networks and promotes motor learning after Spinal Cord Injury (SCI). An interesting
20 issue is whether the brain networks controlling MI are being reorganized with reference to spared motor
21 functions. In this pilot study, we tested using magnetoencephalography (MEG) whether changes in cortical
22 recruitment during MI were related to the motor changes elicited by rehabilitation. Over a 1-year period of
23 inclusion, C6 SCI participants ($n = 4$) met stringent criteria for inclusion in a rehabilitation program focused on
24 the tenodesis prehension (*i.e.*, a compensatory prehension enabling seizing of objects in spite of hand and
25 forearm muscles paralysis). After an extended baseline period of 5 weeks including repeated MEG and
26 chronometric assessments of motor performance, MI training was embedded to the classical course of
27 physiotherapy for 5 additional weeks. Post-test MEG and motor performance data were collected. A group of
28 matched healthy control participants underwent a similar procedure. The MI intervention resulted in changes in
29 the variability of the wrist extensions, *i.e.*, a key movement of the tenodesis grasp ($p < .05$). Interestingly, the
30 extent of cortical recruitment, quantified by the number of MEG activation sources recorded within Brodmann
31 areas 1-8 during MI of the wrist extension significantly predicted actual movement variability changes across
32 sessions ($p < .001$). However, no such relationship was present for movement times. Repeated measurements
33 afforded a reliable statistical power (range = .70 - .97). This pilot study does not provide straightforward
34 evidence of MI efficacy, which would require a randomized controlled trial. Nonetheless, the data showed that
35 the relationship between action and imagery of spared actions may be preserved after SCI.

36 **Keywords:** Motor imagery, spinal cord injury, rehabilitation, magnetoencephalography.

37 Introduction

38 Motor imagery (MI, *i.e.*, the mental representation of an action without physically executing it) is
39 known to engage overlapping cerebral substrates with physical practice (PP) of the same action, which has been
40 referred to as the “functional equivalence” principle between overt and covert motor performance of the same
41 task (Jeannerod 1994, 2001; Jeannerod and Frak 1999). These include pre-motor, primary somatosensory,
42 primary motor and associative cortices (for reviews, see Lotze and Halsband 2006; Munzert et al. 2009; Guillot
43 et al. 2012). Reduced activation levels, from 30 % to 50 %, are however measured during MI compared to PP
44 (Lotze and Halsband 2006; Porro et al. 1996). Due to structural and functional similarities with PP, repeated MI
45 practice can stimulate motor networks and induce “*activity-dependant*” neuroplasticity (*i.e.*, the capacity of the
46 neural tissue to reorganize its structure of connectivity), thereby positively impacting actual motor performance
47 in healthy subjects (Jackson et al. 2003; Ranganathan et al. 2004; Lacourse et al. 2004; Pascual-Leone et al.
48 1995). Neuroplasticity is crucial for functional recovery after central nervous system (CNS) injuries, and is a
49 major focus of rehabilitative interventions (Dobkin 1993). Interestingly, MI training was found to stimulate
50 cerebral reorganizations and improve motor functions after various CNS disorders (Di Rienzo et al. 2014a;
51 Schuster et al. 2011; Malouin et al. 2013). These effects were primarily described in studies with stroke (*e.g.*,
52 Page et al. 2009; Sun et al. 2013) and Parkinson’s disease participants (*e.g.*, Tamir et al. 2007; Schlesinger et al.
53 2009; Subramanian et al. 2011). Testing the therapeutic effect of MI after other CNS disorders is a matter of
54 interest.

55 After spinal cord injury (SCI), neuroplasticity at the site of injury can mediate some functional recovery
56 (Kakulas 2004). Nonetheless, changes occurring within the spinal circuitry below the lesion and supraspinal
57 structures can also mediate functional improvements (Wirth et al. 2008; Curt et al. 2008). For instance,
58 spontaneous cortical reorganizations may contribute to maximize output to the somatic effectors that retained a
59 voluntary control (Kokotilo et al. 2009; Nardone et al. 2013; Topka et al. 1991; Levy et al. 1990). Jurkiewicz et
60 al. (2007) observed with functional magnetic resonance imaging that concentration of activations within the
61 primary motor cortex during PP of wrist extensions correlated with motor scores on the American Spinal Injury
62 Association during the first year post-SCI (ASIA; Maynard et al. 1997) impairment scale (see also Green et al.
63 1999, 1998). Whether targeting cortical plasticity can contribute to improve functional recovery after SCI is an
64 interesting research avenue considering that the limited number of studies available at this point prevents
65 definitive conclusions

66 Complete SCI at the C6-C7 level elicits paralysis of hand, finger and wrist flexor muscles. Prehension is
67 severely impaired and a major focus of rehabilitation (Snoek et al. 2004). Active elbow and wrist extension are
68 spared in most cases, thus affording motor learning of a compensatory prehension using the “*tenodesis*” effect
69 (Mateo et al. 2013). The tenodesis grasp is a pinch grip achieved through an *active* wrist extension, triggering a
70 *passive* fingers-to-palm and thumb-to-fingers flexion (Fig. 1A). Prehension with tenodesis is thus a different
71 motor skill than healthy prehension and requires motor learning of new upper limb coordination (Hoffmann et al.
72 2002; Mateo et al. 2013).

73 SCI participants are capable to achieve accurate MI of simple actions, and showed preserved functional
74 equivalence with PP of the same movement (Sabbah et al. 2002; Di Rienzo et al. 2013). SCI subjects also
75 appeared to benefit from MI training programs to learn motor sequences executed with intact muscles (Cramer et
76 al. 2007). In clinical settings, single-case pilot experiments yielded that MI practice could improve the tenodesis
77 prehension, *i.e.*, increased movement speed and accuracy associated with smoother hand trajectories were
78 reported (Grangeon et al. 2012; Grangeon et al. 2010). The authors inferred an effect of the technique on brain
79 neuroplasticity, which was recently evidenced using MEG (Di Rienzo et al. 2014b).

80 Both theoretical and clinical data support the therapeutic relevance of MI in motor learning of tenodesis
81 prehension after SCI. However, whether the cerebral networks of MI are reorganized with reference to actual
82 motor capabilities along the course of rehabilitation remains unexplored. Investigating the time course
83 relationship between actual and imagined actions in a longitudinal design, based on movements that SCI subjects
84 can still perform physically, is of particular interest. Using magnetoencephalography (MEG), we tested in this
85 pilot experiment whether the extent of cortical recruitment during MI of wrist extension (*i.e.*, a key component
86 of tenodesis) mirrored behavioral changes elicited by a rehabilitation program including MI training. A strong
87 hypothesis was, considering that functional equivalence between MI and PP may be well-preserved after SCI (Di
88 Rienzo et al. 2014a), that the reorganizations of MI networks should correspond to the motor changes co-
89 occurring with MI practice, as shown in healthy participants (Lacourse et al. 2004; Jackson et al. 2003).
90 Particularly, we expected a more focused recruitment of brain motor networks during MI, a well-known
91 neurophysiological index of motor learning in healthy controls (HC) (Chang et al. 2011; Milton et al. 2007; Ross
92 et al. 2003).

93 ***Material and methods***

94 ***1. Participants***

95 SCI participants were recruited from the Henri Gabrielle hospital (St Genis Laval, F-69230) over a
96 period of inclusion of 1 year. Inclusion criteria were: *i*) age range 18-55 y, *ii*) quadriplegia elicited by SCI at the
97 C6-C7 level, *iii*) *complete* infra-lesional motor deficit according to the ASIA impairment scale (Maynard et al.
98 1997), with finger and forearm flexor muscles paralysis, *iv*) post-traumatic period > 6 months (since a motor
99 recovery plateau is usually reached at 6 months post-SCI; Waters et al. 1993; Yakura 1996). Exclusion criteria
100 were: *i*) non-stabilized hypertension or pathological autonomic nervous system dysfunction (*e.g.*, orthostatic
101 hypotension), *ii*) cerebral damage and/or cognitive deficit, *iii*) elbow or shoulder joint amplitude restriction,
102 upper limb para osteo-arthritis, *iv*) participation to another study, and *v*) presence of metallic objects within
103 the body incompatible with MEG or fMRI recordings. Four SCI participants met the inclusion criteria over the
104 period of inclusion (Table 1). Four HC matched according to gender, age (\pm 1 year) and handedness were also
105 included.

106 *** *Insert Table 1 about here* ***

107 2. *Ethical considerations*

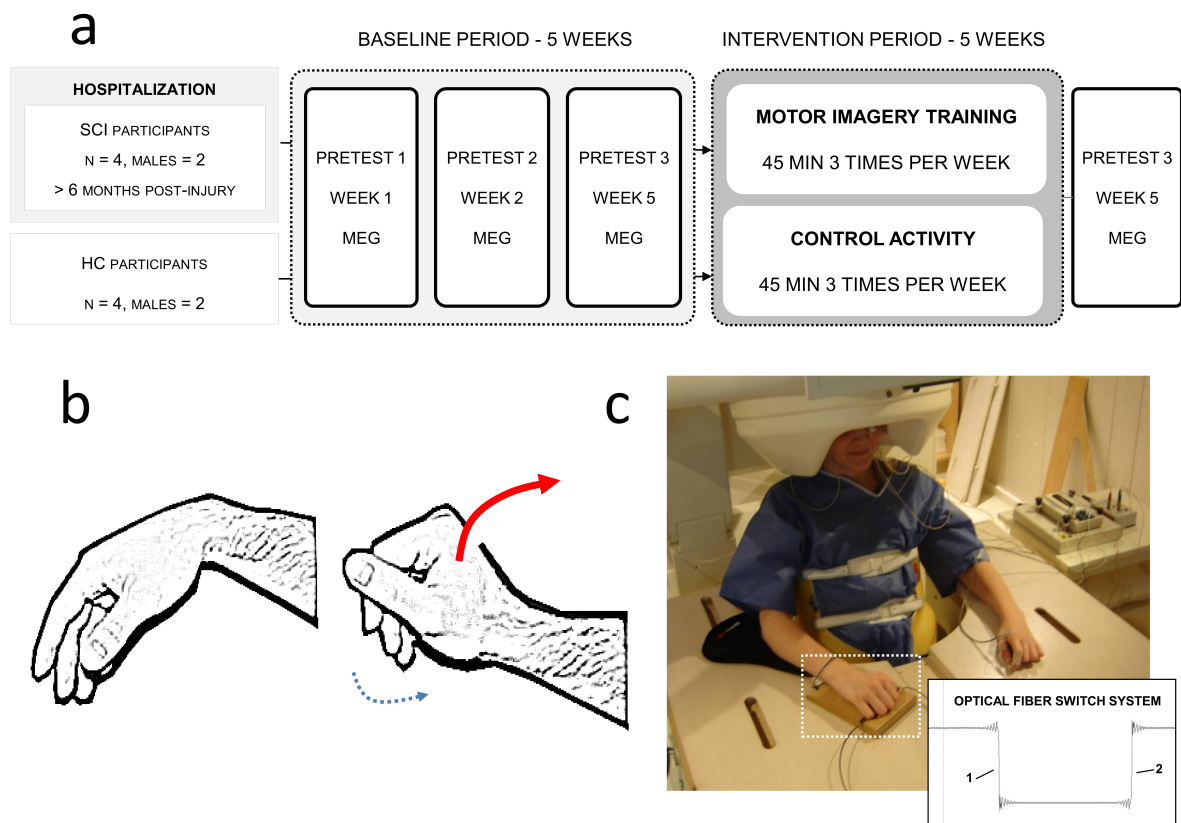
108 All participants provided informed written consent according to the Declaration of Helsinki (1964).
109 This study was performed under approval of the Lyon Civil Hospices ethic committee (CPP 2009-051-B), as part
110 of a Hospital Program for Clinical Research (n° 2010-541/142) prospective-registered under the trial number
111 ACTRN12612001030864. The ethical review board refused the participation of a non-trained SCI group or a
112 SCI group not receiving MI training (*i.e.*, classic physiotherapy targeting prehension recovery only) to this study.
113 It was not deemed acceptable not to issue the same treatments to all SCI participants due to risk of unbalance
114 between the practical costs (*e.g.*, numerous transfers from the site of hospitalization and the site of MEG
115 recordings, *etc.*) and the *potential* clinical benefits associated with the participation to this research.
116 Counterbalanced interventions were also disregarded, again due to an identified risk of inequities between the
117 groups of SCI participants during the early stages of the experimental intervention (*i.e.*, at the point of
118 experiment where some participants would be delivered adjunctive MI training, while others not). These could
119 result in differential effects on motor recovery, greater improvements being usually achieved during the early
120 stages of training.

121

122 3. *Experimental procedure*

123 Due to ethical limitations (see above), the present study cannot be considered a clinical trial of MI
124 efficacy. However, the ethical board agreed for a design including a long baseline period (5 weeks) including
125 repeated pre-tests assessments to control for the stability of motor performance, implemented after a post-SCI
126 delay superior to 6 months (*i.e.*, a point at which SCI participants have usually achieved a spontaneous motor
127 recovery plateau). This repeated measurements design was considered relevant to address *fundamental* issues
128 related to the preservation of the relationship between MI and action after SCI along the course of rehabilitation,
129 by means of intra-subject comparisons.

130 Three pre-tests including MEG and motor assessments were scheduled over a baseline period of five
131 weeks (Fig. 1B). SCI participants were hospitalized and received daily medical care including physiotherapy
132 (*e.g.*, passive limb mobilization, muscle strengthening above the lesion level, prehensile tasks, etc.). MI training
133 was embedded within the time allocated to motor rehabilitation for five additional weeks, so as to prevent a
134 placebo effect due to increased time in the presence of medical practitioners (Fig. 1B). Participants received
135 three MI training sessions of 45 minutes per week. MI training involved mental rehearsal of prehensile actions
136 with tenodesis, performed in an ecological environment. Motor imagery (MI) sessions were individually
137 delivered in a quiet room at the hospital. SCI participants were seated on their wheelchair, in front of a table, and
138 subjected to a 45 minutes session during which they alternately performed physical practice (PP) and MI of goal-
139 directed grasping actions using the tenodesis grasp. During the first week, the experimenter showed the
140 movement before the participant physically or mentally performed it. Training sessions were of increased
141 complexity along the course of training to avoid boredom effects, based on SCI participants' abilities (*i.e.*, from
142 simple pointing actions to complex sequential prehensile sequences involving more rapid seizing of smaller or
143 heavier objects placed in the contralateral and ipsilateral spaces). Visual and kinesthetic imagery were both used
144 during training to promote analysis of the kinematics and correct inadequate executions, respectively. PP vs. MI
145 training ratio was 1 to 5 during the first week and increased each week up to 1 to 9. Importantly, the amount of
146 PP remained very low and past experiments demonstrated that such minor amounts of PP in MI training designs
147 were insufficient to affect actual motor performance (Malouin and Richards 2010). The intervention period was
148 followed by an immediate post-test (Fig. 1B).



149

150 Fig. 1 Experimental design and settings. a. Experimental sessions including three pre-tests scheduled
 151 over five weeks and one post-test, separated by an intervention period of five weeks. Each experimental session
 152 involved both MEG measurements of MI and motor performance recordings. b. Illustration of the tenodesis
 153 grasp, where active wrist extension (red arrow) triggers passive finger flexion (blue dotted arrow). c. Installation
 154 of participants and detection of movement times using an optical fiber switch system spotting movement start (1)
 155 and end (2). SCI: Spinal cord Injury, HC = Healthy Control, MEG: Magnetoencephalography

156 The HC group underwent a similar testing procedure but did not receive MI training. HC performed a
 157 mental imagery task for an equivalent amount of time in the presence of medical practitioners (*i.e.*, visualization
 158 of geometric forms). The HC group thus controlled for the stability of MI networks in the *absence* of task-
 159 specific MI practice and attested that brain changes during MI (hypothesized in the SCI group during the post-
 160 test) were due to MI training on prehensile tasks and was not due to the repeated MEG measurements.

161 4. Experimental sessions

162 4.1. Motor imagery ability

163 During the first pre-test, participants completed the Kinesthetic and Visual Imagery Questionnaire
164 (KVIQ; Malouin et al. 2007). They rated the vividness of visual and kinesthetic perception associated with MI
165 on a Likert scale ranging from 1 to 5, immediately after their actual execution or observation of the experimenter
166 performing it if the task could not be physically executed.

167 4.2. MEG recordings

168 MEG recordings were performed using a CTF-MEG system (CERMEP, France), with 275 radial
169 gradiometers over the scalp and 33 reference channels for ambient field correction. MEG signals were
170 digitalized at sampling rate of 600 Hz and low pass filtered (0 - 150 Hz). Head position was continuously
171 recorded, using three head coils placed on the nasion and pre-auricular points prior to scanning. Brain MRI for
172 co-registration with MEG data was recorded using a 1.5T Siemens Magnetom scanner (CERMEP, France -
173 Siemens AG, Erlangen, Germany) which computed 3D anatomical T1 weighted pictures covering the whole
174 brain with 1mm³ cubic voxels (TR: 9.7 ms, TE: 4 ms). Individual registration of anatomical MRIs in the
175 Talairach space (Talairach and Tournoux 1988) was performed using AFNI functions(Cox 1996).

176 SCI participants were installed on the MEG seat by two physiotherapists under the supervision of a
177 medical doctor. A wooden table was placed above their knees. Both arms were lying on the table in a
178 comfortable position (Fig. 1C). Participants physically performed a block of 10 wrist extensions (1 per trial) with
179 their dominant arm from a standardized start position, at preferential speed (PP condition). Movement times
180 (MT) and their variability (MV; *i.e.*, the variance of MT) were the dependant variables. Movement speed and
181 movement variability are relevant indexes of motor learning. Compared to novel skills, well-learned sequences
182 are performed more rapidly and more reproducibly, thus indicating greater motor efficiency (Müller and Sternad
183 2004; Davids et al. 2006; Schmidt and Wrisberg 2004; Schmidt and Lee 1988). They also performed 10 MI of
184 the same movement using first-person visual and kinesthetic information (MI condition). Importantly, SCI
185 subjects received MI training focused on complex and goal-directed prehensile actions. Accordingly, both SCI
186 and HC groups received an identical amount of practice of the specific MI task studied with MEG (*i.e.*, MI of an
187 isolated wrist extension), yet the two groups differed in terms of the amount of MI practice of prehensile actions
188 (Fig.1A). Finally, they remained motionless for 10 trials (CONTROL condition). Experimental conditions were
189 randomly presented three times each within a block-design, for a total amount of 30 trials in each condition for
190 each recording. This limited number of trials was expected to preserve SCI participants from deleterious effect of
191 physical and mental fatigue due to repetitive movements executed with an impaired limb. An auditory

192 soundtrack was broadcasted to provide instructions regarding each experimental condition. A distinct auditory
193 stimulus triggered onset of each trial every 10s. Movement duration was recorded using an optical fiber switch
194 system spotting wrist extension start and end (Fig. 1C).

195 4.3. Data processing

196 Time-frequency analysis of MEG sensor signals was performed using the Brainstorm® application
197 (Tadel et al. 2011). Time-frequency power distributions (0-60 Hz) were normalized over 5 s according to a pre-
198 stimulus period of 1s (Z -score). The normalized time-frequency maps were averaged across sensors and MI
199 trials, for each participant and experimental session. This enabled to estimate the duration and frequencies of
200 event-related perturbations associated with MI, using a threshold of $Z = 2$ (*i.e.*, twice the variance of the pre-
201 stimulus noise; see supplementary material 1 for an illustration). Based on previous studies, MI was expected to
202 elicit a phase-locked desynchronization (*i.e.*, event-related desynchronization; ERD) of sensorimotor mu (8-12
203 Hz) and beta (13-35 Hz) rhythms (Pfurtscheller and Lopes da Silva 1999; Pfurtscheller et al. 2005; Neuper and
204 Pfurtscheller 2010).

205 Synthetic Aperture Magnetometry (SAM) was used to map the brain sources of ERD during MI. SAM
206 is a minimum variance beamformer that emphasizes the MEG activity originating from a defined site while
207 blocking signals from outside (Robinson 2004). SAM displays the sources of event-related power changes within
208 a defined frequency domain using t -paired Jackknife statistics between an active and a control time window. For
209 MI and CONTROL conditions, the control time window was established before stimulus onset, while the active
210 state time window was established immediately after. The time window duration was triggered according to the
211 duration of the ERD elicited during MI, as revealed by the time-frequency analysis. We enumerated the number
212 cortical activation maxima (*i.e.*, ERD sources displaying SAM t -contrast ratios > 2 , corresponding to an $\alpha = .05$
213 threshold of statistical significance for 30 trials).

214 5. Statistical analysis

215 5.1. Motor performance

216 MT and MV were bootstrapped (permutation) and normalized in absolute percentage (*i.e.*, modulus) of
217 the median pre-tests value. We used R (R Core Team 2014) and *lme4* (Bates et al. 2014) to perform a linear
218 mixed effects analysis (see Winter 2013). A rank transformation applied on MT and MV (conversion from
219 numeric to ordinal data) in order to increase the statistical power (see Baguley 2012 for further description). As

220 fixed effect, we entered the interaction between the group and the experimental session. As random effect, we
221 had intercepts by subjects. Visual inspection of the residual plots did not reveal any deviations from
222 homoscedasticity or normality. The p -values were obtained by likelihood ratio tests of the full model against the
223 model without the effect in question. For post hoc investigations, we iterated the procedure on datasets from
224 which classes of the factor group and session were removed to allow dual comparisons. Holm's sequential
225 corrections for multiple comparisons were applied (Holm 1979). We used similar procedure to compare the
226 number of MEG sources between groups across experimental sessions.

227 5.2. Motor performance and MEG sources

228 The relationship between movement parameters and the cortical recruitment during its imagination was
229 tested using a linear mixed effect analysis between movement time parameters (*i.e.*, MT and MV) and the
230 number of SAM activation sources during the MI. This enabled to test the independence hypothesis between the
231 MEG and motor performance variables. An intercept by subjects was entered as random effect. The p -value was
232 obtained using a likelihood ratio test of the full model against the intercept model only.

233

234 **Results**

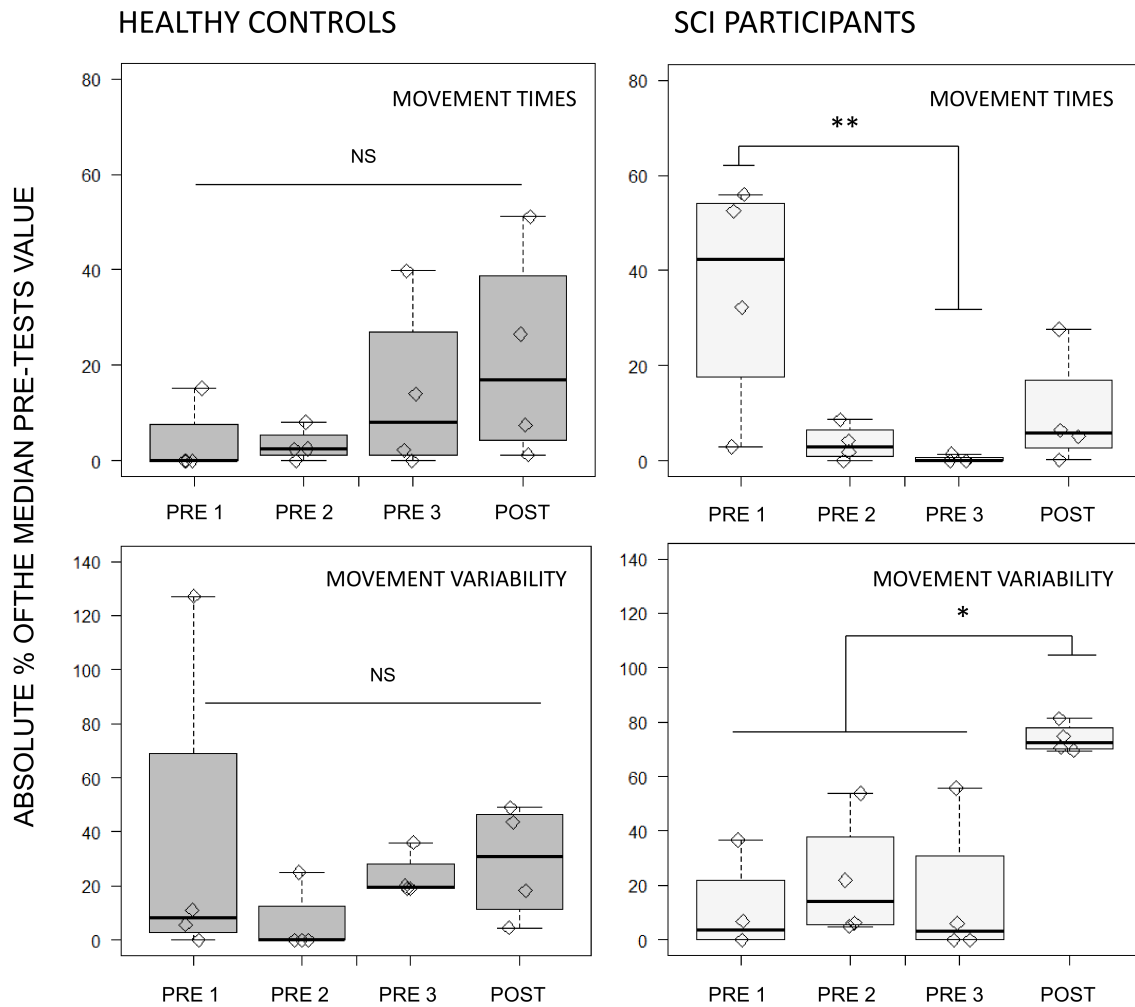
235 1. MI ability

236 KVIQ scores are dependant variables derived from ordinal scales. Median KVIQ score in the SCI group
237 was 3.0 ($IQR = .63$) and 4.0 in the HC group ($IQR = .30$). Median KVIQ visual score was 3.0 ($IQR = .5$) in SCI
238 participants and 4.0 in all HC participants. Median KVIQ kinesthetic score was 4.0 ($IQR = .5$) in SCI
239 participants and 4.0 ($IQR = .25$) in HC participants. Wilcoxon's tests yielded no statistically significant
240 differences between groups on KVIQ scores or subscores (all $p > .05$).

241 2. Motor performance

242 MT and MV raw data and their normalization in absolute (*i.e.*, modulus) percentage of the pre-test
243 median are provided in the supplementary material 2. Mixed linear modeling revealed that the group by
244 experimental session interaction was significant for both MT ($\chi^2(3) = 8.81, p = .03$) and MV ($\chi^2(3) = 13.67, p <$
245 $.01$). The power of these tests was respectively $.97$ and $.84$. MT were superior by $.73$ s in SCI participants during
246 the first pre-test compared to the third pre-tests of the design ($p < .01$), but not in HC ($p > .05$, NS) (Fig. 2). In

247 SCI participants, post-test MV was 12.3-18 % superior to the median pre-tests value ($p < .05$), whereas such
 248 differences were not present in HC ($p < .01$). This accounted for the significance of the group by experimental
 249 session interaction (Fig. 2).



250

251 Fig. 2 Boxplot of movement times and their variance, expressed in absolute percentage (*i.e.*, “modulus”)
 252 of difference with the median value of the pre-tests across experimental sessions in both groups. * $p < .05$, ** $p <$
 253 $.01$

254 2.1. Magnetoencephalography

255 2.1.1. Time-frequency analysis

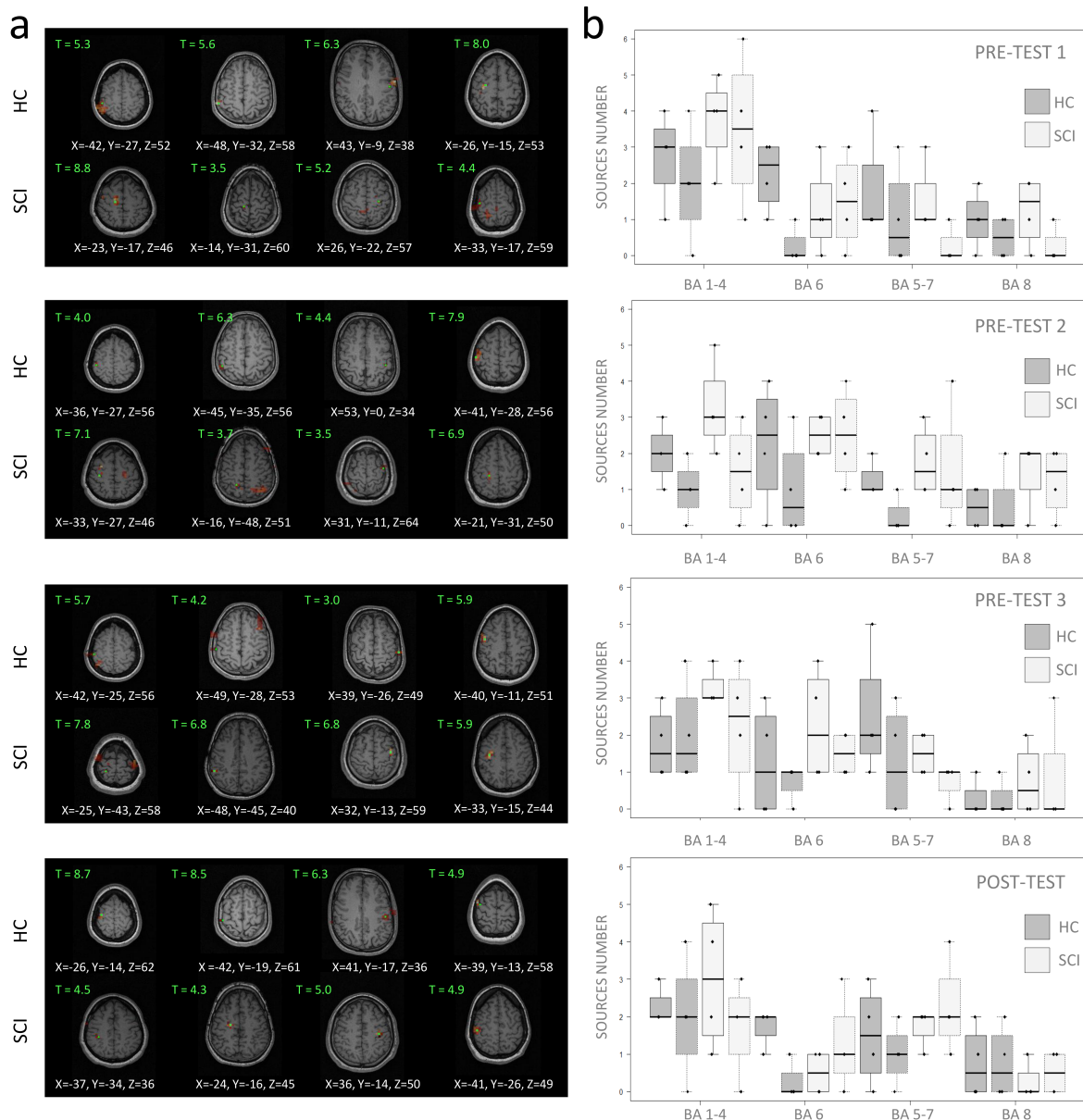
256 Time frequency analysis revealed that the strongest ERD occurred within the beta (13-30 Hz) frequency
 257 domain in both SCI and HC groups. Beta desynchronization was immediately followed by a power increase that

258 exceeded the pre-movement level (*i.e.*, the post-movement beta rebound) (Pfurtscheller 2000; Neuper and
259 Pfurtscheller 2010). ERD duration ($M = 1.12s$, $SD = .42$) was similar in HC and SCI groups across experimental
260 sessions (repeated measures ANVOA; $F(3, 18) = 1.81$, $p = .18$). No specific changes were observed between the
261 pre- and post-test, which, at the sensors level, might account for the unchanged nature and duration of the task.

262 2.2. Sites of activity during MI

263 SAM t -values during the CONTROL condition were systematically inferior to $t = 2$.

264 The total number of SAM sources elicited during MI was similar in HC and SCI groups across
265 experimental sessions (repeated measures ANVOA; $F(3, 18) = 0.20$, $p = .89$). Participants generally had
266 maximal SAM t -values ranging between $t = 3.5-8.8$ and $t = 3.0-7.9$ (Fig. 3A). SAM maxima were primarily
267 located in central regions, including the primary somatosensory and motor cortices [*i.e.*, Brodmann areas 1-4]
268 (Fig. 3A). Sources were also present within Brodmann areas 5-8. SCI participants exhibited overall very
269 comparable patterns of cortical recruitment as HC when the number and distribution of SAM sources across
270 Brodmann areas was considered (Fig. 3B).



271

272

Fig. 3 Magnetoencephalography data. a. Maximal SAM t -contrast ratios location (green dots) between active and control state time windows during MI. The maximal SAM t -values are indicated and their Talairach coordinates (X, Y, Z) provided. A threshold of $t = 90\%$ t -max was applied to the SAM maps for purposes of visual display. b. Boxplot of the number of SAM sources during MI ($t > 2$). SAM sources were present within Brodmann areas 1-4 (primary somatosensory and motor cortices); 6 (pre-motor cortex); 5-7 (parietal cortex extending to precuneus) and 8 (frontal cortex). The dotted boxplots represent ipsilateral sources. SCI: Spinal cord injury, HC: Healthy controls, BA: Brodmann area

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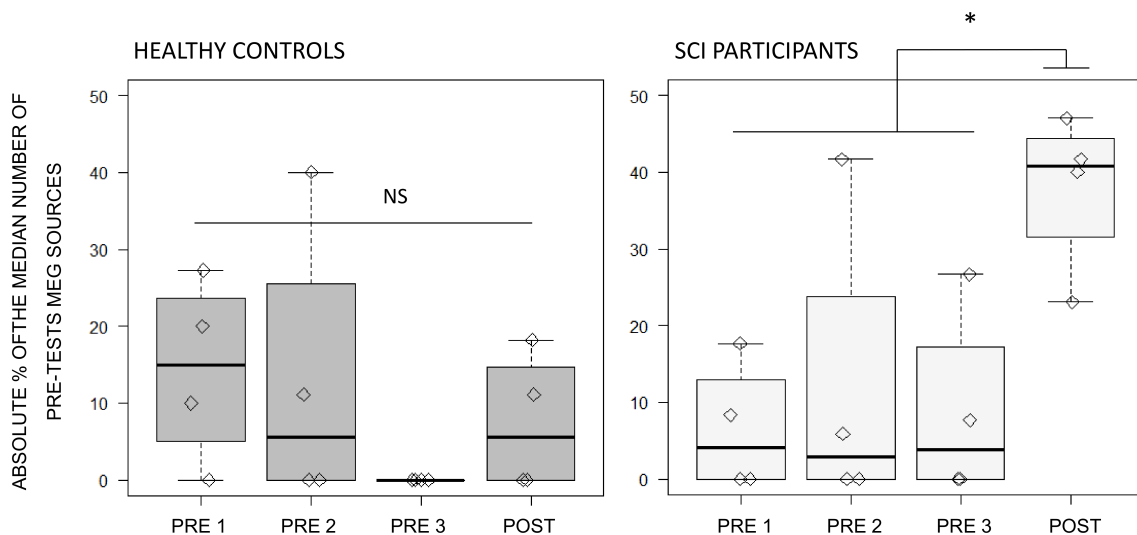
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278

279

2.3. Cortical recruitment during MI

280 Mixed linear modeling yielded to significance for group by experimental session interaction when
 281 considering the number of SAM sources during MI [*n. b.*, normalized in absolute (*i.e.*, modulus) percentage of
 282 the pre-tests median] ($\chi^2(3) = 8.54, p = .03$). Post-test values were significantly higher than those recorded
 283 during the pre-tests in the SCI group (9.45-10.60 % of post-test increase; all $p < .01$), whereas no such
 284 differences occurred in HC ($p > .05$) (Fig. 4).



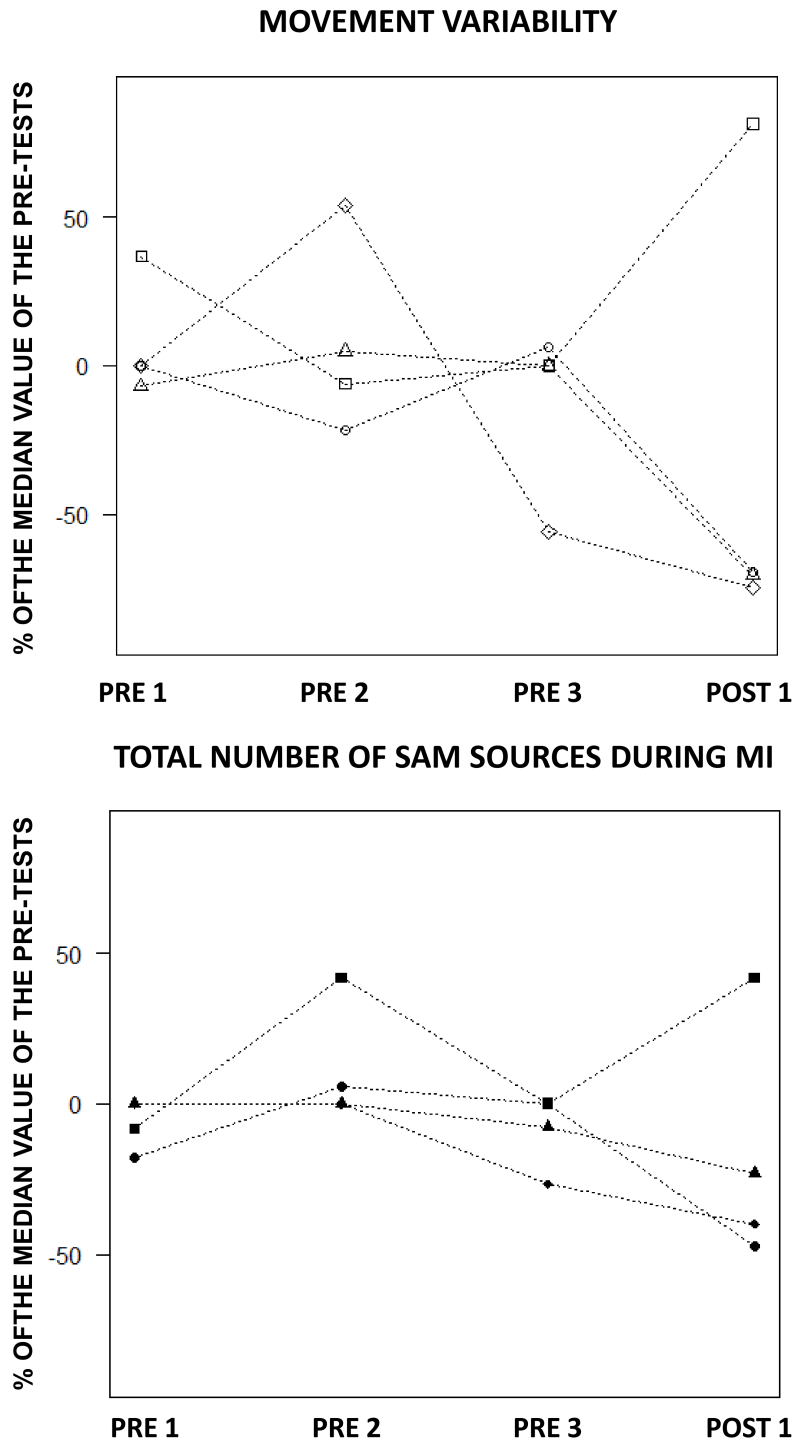
285
 286 Fig. 4 Boxplot of the number of MEG sources recorded during MI across groups and experimental
 287 sessions, expressed in absolute percentage (*i.e.*, “modulus”) of difference with the median pre-tests value. * $p <$
 288 .05

289 2.4. Motor performance and MEG sources during MI

290 Individual data in SCI subjects revealed individual patterns of MV and changes during the pre-tests as
 291 compared to the post-test (Fig. 5, upper panel). Three SCI subjects showed reduced MV during the post-test
 292 (69.4-74.6 % of the median pre-tests value), whereas one showed increased MV (81 % of the median pre-tests
 293 value) (Fig. 5). The motor performance analysis did not consider individual patterns of response, since MT and
 294 MV data were normalized in *absolute* percentage of difference with the pre-test median. This quantified the
 295 magnitude of the effect elicited by the intervention, independently from whether an increase or a decrease was
 296 present at the individual level (see Fig. 2)². The same applies to MEG data.

² For a figure of raw MEG and motor performance data plotted as in Fig. 5, see supplementary material 3.

297 MT did not account for the variance of the number of MEG sources during MI across experimental
298 sessions in both SCI and HC groups, as revealed by mixed linear modeling ($\chi^2(1) = .51, p = .47$; $\chi^2(1) = .01, p$
299 $= .93$, respectively). By contrast, MV was statistically predicted by the number SAM sources activated during
300 MI in the SCI group ($\chi^2(1) = 11.92, p < .001$, likelihood ratio test power = .70) (Fig. 5). Linear modeling
301 coefficient was 1.33. Such statistical relationship was absent in HC ($\chi^2(1) = .97, p = .32$). Accordingly, for each
302 SCI participant, MV changes (*i.e.*, increase or decrease during the post-test) were tightly paralleled by changes in
303 cortical recruitment during the motor representation of the action.



304

305 Fig. 5 Movement times variability and SAM sources number during MI in SCI subjects (individual
 306 data) expressed in percentage of the median of pre-tests value. Mixed linear modeling revealed a significant
 307 relationship between the two dependant variables across sessions ($p < .01$). Different patterns were present. One
 308 SCI participant presented increased movement times variance associated with an increased number of MI
 309 sources. SAM: Synthetic aperture magnetometry

310 *Discussion*

311 The present study was not, due to ethical reasons (see methods), a controlled study and thus cannot be
312 considered a study of the efficacy of MI training on the recovery of tenodesis grasp. The experiment was
313 primarily intended to provide pilot data concerning the state of preservation of the relationship between overt
314 and covert motor performance for spared actions in SCI subjects, using a longitudinal design (*i.e.*, here along the
315 course of a rehabilitation program). Past experiments addressed this issue in transversal designs (*e.g.*, Alkadhi et
316 al. 2005; Hotz-Boendermaker et al. 2008). Here, we tested whether cortical activity during MI related to the
317 changes in motor performance elicited by a rehabilitation program which included MI training. Repeated pre-
318 tests sessions including both MEG measurements and motor performance recordings enabled to rigorously
319 define the baseline level and assess the stability of motor performance before the MI intervention. Repeated
320 assessments, presumably, reinforced the statistical power of the study in spite of its limited sample size (*i.e.*, the
321 power ranged between .70 and .97). Main results are: *i*) Changes in MV, but not MT, were recorded in SCI
322 participants after the experimental intervention period, *ii*) MI of the wrist extension elicited comparable patterns
323 of cerebral activity between SCI and HC participants (activation sources being localized within associative and
324 primary sensorimotor cortical regions; Fig. 3), and *iii*) Pre-tests vs. post-test change in the number of cortical
325 sources recruited during MI statistically predicted MV changes (based on mixed linear modeling).

326 We chose the wrist extension as the reference task. It is the triggering movement of the tenodesis grasp
327 (Mateo et al. 2013). MT and MV are relevant indexes of skill learning (Müller and Sternad 2004; Davids et al.
328 2006; Schmidt and Lee 1988), albeit these remain more limited than a full kinematic analysis of upper limb
329 performance (*e.g.*, Mateo et al. 2013; Hoffmann et al. 2006; Laffont et al. 2000). SCI and HC groups showed
330 stable MT and MV across pre-tests, albeit MTs were higher during first compared to the third pre-test in SCI
331 participants. A similar pattern was present in HC, even though the difference was not statistically significant.
332 This might account for a learning effect as participants underwent the same experimental design several times
333 within a restricted time period. MT remained unchanged during the post-test in both groups. This was not
334 expected for SCI subjects. MI training has been shown to improve movement speed during tenodesis actions, yet
335 in single-case experimental designs (Grangeon et al. 2012). Greater sample size in the present design should
336 have enabled to detect meaningful effects. At the meantime, MI training sessions here focused on the control of
337 the tenodesis prehension realized in an ecological environment, and actual and imagined wrist extension
338 performance during MEG recordings was executed at preferential speed. Accordingly, the absence of post-test
339 changes on movement speed is not surprising. Changes in actual movement speed are indeed dependant from the

340 instructed timing of mental rehearsal (*i.e.*, movement speed changes only occurred when participants were asked
341 to mentally rehearse the skill more slowly or rapidly than its preferential execution duration; Louis et al. 2008).
342 Post-test MV values significantly differed from those recorded during the pre-tests' in SCI subjects, but not in
343 HC. Notably, the wrist extension is a key component of prehension after SCI, but does not serve such specific
344 functions in HC. MV was reduced in three SCI participants ($\approx 70\%$), whereas 81% of increase was measured in
345 one SCI subject. While we only focused on the tenodesis grasp, Grangeon et al. (2012) reported reduced
346 variability of hand trajectories during point-to-grasp actions after 5 weeks of rehabilitation with MI. Here, the
347 baseline period was of equivalent duration to the intervention period in SCI participants with stabilized motor
348 deficits. Post-test changes in motor performance in SCI subjects thus *co-occurred* with the inclusion of MI
349 training to classical physiotherapy programs. No causal effect of MI training on motor recovery can be directly
350 established as the present experiment is not a controlled study of efficacy but a longitudinal insight on the
351 relationship between the neural correlates of MI and the behavioral indexes of motor performance after SCI.
352 Whether MV changes related to the neurophysiological correlates of MI required specific MEG investigations.

353 Using MEG, we recorded task-specific changes in neural oscillations occurring during MI. MEG is
354 particularly sensitive to signals originating from pyramidal neurons of the neocortex (Lopes da Silva 2010). ERD
355 of neural oscillations is of specific relevance to perform functional mapping during motor task (Pfurtscheller
356 2001). Time-frequency analyses ensured a phase-locked reconstruction of brain sources, ERD features of MI
357 yielded by the time-frequency analysis were highly congruent with previous MEG reports in both HC and SCI
358 subjects (*e.g.*, Burianova et al. 2013; Di Rienzo et al. 2013). The sources of ERD primarily located within the
359 sensorimotor and associative regions of the cortex in both groups (Fig. 3B). Such MEG results corroborate the
360 conclusions of previous brain imaging experiments in both SCI and HC (*e.g.*, Lotze et al. 1999; Alkadhi et al.
361 2005). The extent of cortical recruitment during MI (quantified by the number of activation sources) showed
362 clear changes during the post-test in the SCI group. These brain activation changes closely paralleled those
363 recorded on MV (Fig. 5). The reduced cortical recruitment in three SCI participants suggests a more selective
364 activation of the brain motor system. Guillot et al. (2008) provided evidence that the focused recruitment of the
365 brain motor system was a neurophysiological correlate of both motor and MI expertise. Top performers elicited
366 reduced motor network activations during MI of high-automated motor skills as compared to novices (Ross et al.
367 2003; Milton et al. 2007; Chang et al. 2011). Generally speaking, the extent of cortical recruitment during MI
368 can be considered an index of the involvement of mental resources in the generation of motor representations
369 (Debarnot et al. 2014). When present, reduced cortical recruitment in SCI subjects was systematically associated

370 to a reduction of MV. This hypothetically reflects greater motor efficiency during the control of wrist actions,
371 considering that the skill was being performed with a higher level of reproducibility and more selectively
372 engaged the brain motor system during its mental rehearsal (*i.e.*, an index of motor program consolidation). In
373 the SCI subject who exhibited an increase in MV during the post-test, the cortical sources recruited during MI of
374 the wrist extension were more numerous. This participant started the experiment 2.6 years after injury, and had
375 developed habits of sizing objects without using tenodesis. She grasped objects with both arms, and used passive
376 index to thumb pinch grip whenever seizing small and light objects was required. Hypothetically, extensive
377 training focusing on tenodesis elicited a competing process with anterior motor strategies that could account for
378 the pattern of response to the intervention. Increased MV during the post-test supports this view, as it is an index
379 recently learned motor skills (Eckert 1974). Independently from individual patterns of response, the data overall
380 confirmed the assumption of parallel changes in brain correlates of MI and behavioral indexes of motor
381 performance after SCI.

382 Importantly, this pilot study did not enable to determine whether brain changes in response to MI
383 training were similar in HC and SCI participants. We did not involve a HC group performing MI in the design.
384 Issuing a similar MI training program to HC and SCI groups (*i.e.*, focusing on the kinematics of goal-directed
385 prehensile actions) was not relevant as normal prehension does emphasizes the role of the wrist extension during
386 grasping (contrary to the tenodesis grasp in SCI participants). Hence, no transfer to the wrist extension studied
387 with MEG due to its functionality during tenodesis prehension in individuals with SCI could be expected,
388 furthermore as HC had no specific knowledge of the tenodesis grasp. Likewise, MI training focused on the
389 tenodesis prehension was not relevant as HC had no need to learn this skill and, presumably, *could not* since the
390 upper limb is not impaired. In other words, various forms of MI training in HC would not have enabled any
391 conclusive comparisons with changes observed during MI of wrist extension in SCI participants³.

392 Present results extend previous findings in the field of MI research in individuals with SCI. The
393 reorganization of MI networks appeared related to motor performance changes elicited by rehabilitation. The
394 data support the hypothesis of a spared relationship between overt and covert motor performance for movements
395 that can still be performed physically after SCI. These findings have meaningful implications for researchers,

³ Hence, including a group healthy participants performing MI represents further development of the present design.

396 clinicians and physiotherapists, particularly with regards to future implementations of MI training as an
397 adjunctive technique in prehension recovery after C6-C7 SCI.

398

399 **Conflict of Interest**

400 The authors declare no conflict of interest.

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Subject	Age/ Sex	Time post- injury (months)	ASIA level (dominant side)	UEMS score (dominant side) /25	Handedness (Edinburgh inventory)
SCI participant 1	33/F	32	C6	12	Right
SCI participant 2	24/M	6	C6	11	Right
SCI participant 3	21/M	14	C6	9	Left
SCI participant 4	32/F	6	C6	11	Right

405

406 Table 1 Clinical characteristics of SCI participants. No residual motor functions caudal to C6 were
407 present in the dominant upper limb. SCI: Spinal Cord Injury, ASIA: American Spinal Injury Association,
408 UEMS: Upper Extremity Motor Score.

409

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