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1 **Title: EEG Beta desynchronization during hand goal-directed action observation in newborn**  
2 **monkeys and its relation to the emergence of hand motor skills**

3  
4 **Running title: EEG suppression to observed grasping actions in newborn monkeys**

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25

## Abstract

Previous developmental research suggests that motor experience supports the development of action perception across the lifespan. However, it is still unknown *when* the neural mechanisms underlying action-perception coupling emerge in infancy. The goal of this study was to examine the neural correlates of action perception during the emergence of grasping abilities in newborn rhesus macaques. Neural activity, recorded via electroencephalogram (EEG), while monkeys observed grasping actions, mimed actions, and means-end movements during the first (W1) and second week (W2) of life was measured. Event-related desynchronization (ERD) during action observation was computed from the EEG in the alpha and beta bands, two components of the sensorimotor mu rhythm associated with activity of the mirror neuron system (MNS). Results revealed age-related changes in the beta band, but not the alpha band, over anterior electrodes, with greater desynchronization at W2 than W1 for the observation of goal-directed grasping actions. Additionally, desynchronization to observed grasping actions at W2 was associated with infants' motor skills – measured by a separate behavioral task – such that more grasping attempts were associated to greater beta ERD. These findings suggest the emergence of an early action-perception system that relies on motor experience, shortly after birth.

**Keywords:** Development; Mu Rhythm; ERD; Mirror neuron system; Grasping actions; Electroencephalogram

## 48 **1.1 Introduction**

49           The connection between motor development and the emergence of social and cognitive  
50 abilities has been widely investigated in both human and nonhuman primates (Ferrari et al., 2009;  
51 Kaburu et al., 2016; Marshall and Meltzoff, 2014, 2011; Woodward and Gerson, 2014). Human  
52 infants begin to show the capacity to infer others' motor goals at the end of the first year of life, as  
53 developments in their self-produced actions contribute to improved perception of how others interact  
54 with their surrounding environment (Hunnius and Bekkering, 2014; Sommerville et al., 2005;  
55 Woodward and Gerson, 2014). The Mirror Neuron System (MNS), which activates during both the  
56 execution and the observation of goal directed actions, might represent an important neural correlate  
57 of this action-perception coupling. Since the initial discovery of mirror neurons in the premotor and  
58 parietal cortices of the adult macaque (Bonini et al., 2010; di Pellegrino et al., 1992; Fogassi et al.,  
59 2005; Gallese et al., 1996), it has been hypothesized that the MNS might mediate higher cognitive  
60 functions such as action understanding and imitation (Rizzolatti et al., 2001). The proposed  
61 mechanism through which the MNS operates relies on mapping the description of an observed action  
62 onto one's own motor representation. Such sensory-motor mapping would support the observer's  
63 embodied access to the meaning of the observed action; thus making the motor system central to both  
64 controlling the movement of the body in space and supporting cognitive functions related to the  
65 decoding of others' actions (Gallese et al., 1996; Rizzolatti et al., 2001).

66           The electroencephalogram (EEG) is a non-invasive approach to measure brain activity in  
67 developmental populations, and is widely used to investigate infant motor and cognitive development,  
68 in particular through the investigation of a specific sensorimotor rhythm, called the mu rhythm  
69 (Marshall and Meltzoff, 2011; Vanderwert et al., 2013). In human adults, this EEG oscillation falls  
70 within the alpha (8-13 Hz) and beta (15-30 Hz) frequency bands, and is recorded over central scalp  
71 locations, corresponding to sensorimotor areas (Fox et al., 2016; Hari and Salmelin, 1997; Pineda,  
72 2005). The mu rhythm typically desynchronizes (i.e., decreases in spectral power) during both the  
73 execution of intentional motor acts and the observation of actions performed by others (Fox et al.,

74 2016; Neuper and Pfurtscheller, 2001; Pineda, 2005). For this reason, desynchronization of mu  
75 rhythm (of both its components: alpha and beta) has been suggested to reflect the activation of the  
76 motor system and, indirectly, of the MNS, in both humans (Avanzini et al., 2012; Babiloni et al.,  
77 2002; Fox et al., 2016; Muthukumaraswamy and Johnson, 2004; Pineda, 2005) and monkeys (Coudé  
78 et al., 2014; Ferrari et al., 2012; Vanderwert et al., 2015).

79 An analogue of the adult mu rhythm has been described in human infants, starting from about  
80 the sixth month of life (Marshall et al., 2002). The infant mu rhythm peaks at lower frequencies than  
81 the adult mu rhythm (around 6–9 Hz for alpha and 15-17 Hz for beta), has a more diffuse scalp  
82 distribution (Marshall and Meltzoff, 2011; Thorpe et al., 2016) and desynchronizes during both  
83 executed and observed actions (Nyström et al., 2011; Southgate et al., 2010, 2009). Critically, infant  
84 mu suppression is strongly affected by the infant's own motor competences. For example, Cannon et  
85 al. (2016) found that 9-month-old infants' motor proficiency correlated with the strength of the mu  
86 desynchronization during action observation and that desynchronization during action execution was  
87 directly associated with maturity of infants' grasping skills. van Elk and colleagues (2008) studied the  
88 effects of spontaneous EEG variations in 14- to 16-month-old infants while observing movies of other  
89 infants crawling or walking. They found greater desynchronization in both sensorimotor alpha and beta  
90 bands while infants observed crawling, a more developed motor pattern in their repertoire, compared  
91 to walking. Moreover, they found a correlation between infants' experience crawling and their mu  
92 reactivity. Further, Yoo and colleagues (2015) reported that 12- but not 9-month-old infants' motor  
93 competences correlated with their mu desynchronization when they observed goal-directed actions  
94 performed with a tool. Finally, Gerson and colleagues (2015) experimentally manipulated motor  
95 experience by giving 10-month-old infants training observing a novel action and performing a separate  
96 novel action over the course of a week. They found that infants had greater mu desynchronization to  
97 observation of the executed actions compared to the only observed novel actions. Taken together, these  
98 studies show that motor experience, rather than visual experience, is the driving factor in the  
99 development of mu desynchronization.

100 To date, no study has reported EEG mu suppression to execution or observation of actions in  
101 newborn humans; however, there is evidence from recent EEG studies with newborn monkeys.  
102 Ferrari and colleagues (2012) and Vanderwert and colleagues (2015) recorded EEG data from  
103 newborn rhesus macaques during the first week of life and found desynchronization of the 5–7 Hz  
104 frequency band during both imitation and observation of lipsmacking and tongue protrusion gestures,  
105 in electrodes placed approximately over the motor cortex. These findings suggest that, at least in  
106 newborn monkeys, an action-perception coupling system for facial gestures is already active shortly  
107 after birth.

108 During the first month of life, newborn macaques exhibit fundamental developmental changes  
109 in their motor system. Improvements in hand reaching-grasping movements occur from the second  
110 to the fourth week of life, as the precision of grasping actions matures and infants more accurately  
111 move their body in relation to the surrounding space (Sclafani et al., 2015). This suggests that the  
112 first weeks of life are a critical period for infant macaques' sensorimotor development and also marks  
113 a crucial period for the investigation of emerging neural mechanisms underlying the action-perception  
114 coupling. In the current study, we acquired EEG activity from newborn monkeys during the first and  
115 second weeks of life, while they observed grasping actions, mimed grasps and means-end  
116 movements. Based on previous EEG studies investigating the mu rhythm on infant and adult monkeys  
117 (Coudé et al., 2014; Ferrari et al., 2012), we focused on two frequency bands: 1) alpha (5-7 Hz) and  
118 2) beta (15-17 Hz). We also compared, amongst a subset of infants, the relation between infants'  
119 motor experience and their EEG cortical activity during action observation. We hypothesized that  
120 improvements in goal-directed reaching-grasping behaviors over the first two weeks would coincide  
121 with the emergence of the MNS, indexed by desynchronization in the sensorimotor alpha and beta  
122 rhythms, for observed grasping actions.

123

124 **1.2 Materials and methods**

125 **1.2.1 Subjects**

126 We tested a sample of 56 infant rhesus macaques (*Macaca mulatta*), 36 males and 20 females,  
127 born and reared at the Laboratory of Comparative Ethology at the National Institutes of Health. All  
128 infants were separated from their mothers on the first day postpartum and reared in a nursery facility  
129 for unrelated research studies. Infants were individually housed in incubators (51 cm × 38 cm × 43  
130 cm) containing a cloth surrogate mother and various toys (for further details about rearing procedures,  
131 see Simpson et al., (2016)).

132 EEG recordings were performed at two time points: during the first week of life (W1),  
133 between day 3 and day 6 postpartum, and again during the second week of life (W2), between day 7  
134 and day 12 postpartum. Eleven infants were tested twice during W1, thus, the mean EEG value  
135 between the two recording days was calculated for each electrode and each experimental condition.  
136 The remaining 45 infants were tested only once during W1 and once during W2. On average 5.8 days  
137 (SD = 1.6) elapsed between the first and the second EEG recording session.

138 Our final sample included a total of 32 infants (16 males). Twenty infants were excluded from  
139 the initial sample due to insufficient epochs of clean EEG or technical difficulties at the time of testing  
140 (N=12 at W1 and N=8 at W2) and 4 infants were excluded because they were statistical outliers (i.e.,  
141 exceeded +/-2.5 SD from the mean in one or more conditions).

142 All animal care and testing were conducted in accordance with regulations governing the care  
143 and use of laboratory animals and had prior approval from the Institutional Animal Care and Use  
144 Committees of the Eunice Kennedy Shriver National Institute of Child Health and Human  
145 Development (NICHD) and the University of Maryland.

### 146 1.2.2 Behavioral procedures for EEG acquisition

147 At the beginning of each recording session, infant monkeys were removed from their  
148 incubators and brought to a testing room for the EEG procedures. During EEG data acquisition, one  
149 experimenter held the monkey, while a second experimenter served as model and presented the  
150 stimuli in front of the monkey at a distance of approximately 35-45 cm. The experimental paradigm  
151 included three conditions (see Figure 1A): a) Grasping Condition, GC – the model grasped a red ball  
152 (6.5 cm diameter) at the end of a rod; b) Mimicking Condition, MC – the model mimicked a grasping  
153 action, in absence of the target ball; and c) Ball Condition, BC – the model moved a second red ball  
154 at the end of a rod toward the target ball. The MC was introduced to assess possible EEG oscillations  
155 related to simple biological movements rather than to the final goal of the action; the BC was designed  
156 to investigate the possible EEG modulation to the detection of non-biological but means-end motions.  
157 The order of presentation of the experimental conditions was pseudo-randomized between subjects.

158 Each EEG recording session started with a 40-second static baseline where a red target ball  
159 was statically presented, followed by the presentation of the three experimental stimuli. Each stimulus  
160 was repeatedly presented over a period of 20 seconds, at a pace of 0.5 Hz; and the sequence GC-MC-  
161 BC was repeated twice over the recording session, for a total duration of 40 seconds for each stimulus.  
162 The experimental design is illustrated in Figure 1B.

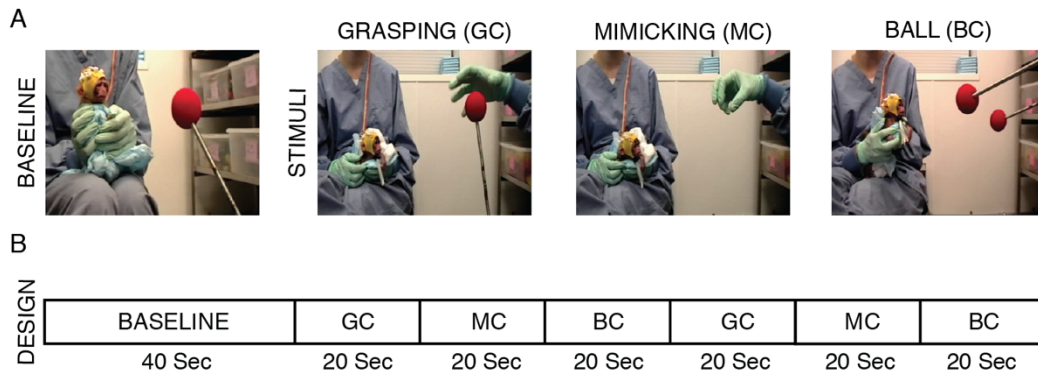
163 An experimenter wearing a surgical mask, cap, and goggles presented stimuli live. The red  
164 ball was presented at the end of a long (35cm) rod. Considering the attire and distance, we believe  
165 the monkeys had limited perception of the model's body/face and that it did not disturb stimuli  
166 presentation. Moreover, we assume that none of the experimental stimuli were perceived as  
167 threatening by the monkeys as, besides being attentive to them during the presentation, they  
168 sporadically attempted to grasp the red ball/s presented during the baseline and experimental  
169 conditions (GC/BC).

170 Each EEG recording session lasted about 10 minutes, which included the time required to cap  
171 the infant and short breaks between each stimulus presentation. Each infant participated in no more



172 than one EEG recording session per day and, if not successfully completed, testing was, if possible,  
173 repeated once within the same week.

174



175

176 **Figure1: Experimental task and design.** A: representation of baseline and experimental conditions.

177 B: description of the experimental design.

178

### 179 1.2.3 Behavioral coding for EEG processing

180 All testing sessions were video recorded. The video signal was recorded using a 30 Hz video  
181 camera (Sony Digital Video Camcorder ZR600, USA), positioned 0.5m behind the model, and time-  
182 stamped with a vertical integrated time code that was synchronized online with the EEG acquisition  
183 software.

184 Subsequently, two coders independently scored both the models and the monkeys' behaviors  
185 in each video. Videos were coded frame-by-frame off-line with the Video Coding System (James  
186 Long Company, NY, USA). The following infants' behaviors, during both baseline and stimuli  
187 presentation, were coded: (a) visual gaze (i.e., looking at the stimulus); (b) arm and hand movements,  
188 and (c) gross body movements. In addition, the following model's behaviors, during each stimulus  
189 presentation, were coded: (a) action begin, corresponding to the first frame in which the  
190 experimenter's hand started moving toward the target ball (GC), started the mimed action (MC) or  
191 started moving the second red ball toward the static target ball (BC), and (b) action completion,  
192 corresponding to the first frame in which the model's whole hand was in contact with the target ball

193 before moving back to the starting position (GC) or the hand was completely still before moving back  
194 to the starting position (MC) or the two balls were touching and still before moving back to the  
195 starting position (BC). Inter-rater agreement, within three frames (about 100 ms), was achieved on a  
196 minimum 85% of each video. The start and the end times of epochs of interest in which the infant  
197 was still and looking at the still target ball (during baseline) or at the presented stimuli were identified  
198 within the EEG signal for data analysis.

199

#### 200 **1.2.4 EEG acquisition and data processing**

201 EEG recordings were performed as previously described in Vanderwert et al. (2015) and  
202 Ferrari et al. (2012). A custom lycra cap (Electro-Cap International, OH, USA) fitted with six tin  
203 electrodes was used. Two anterior electrodes were placed approximately over the motor cortex (A3:  
204 anterior left; A4: anterior right) and two posterior electrodes were placed approximately over the  
205 parietal/occipital cortex (P3: posterior left; P4: posterior right). The vertex served as reference, while  
206 an electrode located on the forehead served as ground. The choice of referencing the EEG signal to  
207 the vertex was mainly due to newborn monkeys' head size resulting in a very limited area for  
208 electrodes placement and thereby in a low density of electrodes.

209 At the beginning of the recording session, the monkey's head was shaved, and a mild abrading  
210 gel was applied to clean the scalp and improve impedances. Impedances were measured and kept  
211 below 20 k $\Omega$ .

212 The EEG signal was band-pass filtered online from 0.1 to 100 Hz, digitized with a 16-bit A/D  
213 converter ( $\pm 5V$  input range) at 1 KHz and recorded on a separate acquisition computer. All data  
214 acquisition was performed with the James Long recording system (James Long Company, NY, USA).

215 The EEG signal was filtered, off-line, using a low pass filter with a cut off of 40 Hz. As in  
216 previous infant monkey EEG studies (Ferrari et al., 2012; Vanderwert et al., 2015) artifacts were  
217 automatically removed using a threshold of  $\pm 250 \mu V$ , in order to capture gross movement artifacts

218 while preserving good EEG signal, and then the signal was visually inspected to remove additional  
219 artifacts not identified in the automatic artifact process. Artifact-free EEG epochs included in both  
220 the baseline and the stimulus presentation period, specifically from the onset to the completion of the  
221 action (for all experimental conditions), were submitted to a fast Fourier transform using a 1000ms  
222 Hanning window, with 50% overlap. Spectral power ( $\mu\text{V}^2$ ) was computed for 1-Hz bins from 2 to 25  
223 Hz. Single hertz bins were then summed to compute two frequency bands: 5-7 Hz, alpha and 15-17  
224 Hz, beta. All data processing was performed using the EEG Analysis System software (James Long  
225 Company, NY, USA).

226 Computation of event-related desynchronization (ERD) and/or event-related synchronization  
227 (ERS) was based on previous studies (Cannon et al., 2014; Pineda and Oberman, 2006) that used the  
228 natural log of the ratio of event to baseline activity [i.e.  $\ln$  (“Event”/“Baseline”)], where “Event” is  
229 the absolute power in a particular frequency band while the monkey was still and observing the  
230 presented stimulus, and “Baseline” is the absolute power in a particular frequency band in which the  
231 monkey was still and observing the static target ball. Negative values indicate desynchronization (i.e.,  
232 decrease in band power relative to the baseline) and positive values indicate synchronization (i.e.,  
233 increase in band power relative to the baseline).

234

### 235 1.2.5 Data analysis and statistical approach

236 Our analyses focused on two different EEG frequency bands: 5-7 Hz and 15-17 Hz, hereafter  
237 referred as alpha and beta, respectively. While the choice of focusing on frequencies falling in the alpha  
238 band was driven by previous investigations in newborn monkeys, showing EEG desynchronization in this  
239 frequency band, during imitation and observation of facial gestures (Ferrari et al., 2012), the analysis of  
240 the beta band was based on more recent EEG findings showing that in adult monkeys the beta band  
241 desynchronizes during the observation and execution of grasping actions (Coudé et al., 2014; Bimbi et  
242 al., *under revision*).

243 EEG data were analyzed by means of within-subjects repeated measures ANOVAs.  
244 Significant main effects and interactions were followed up using 2-tailed paired t-tests. The regions  
245 analyzed were as follows: anterior (A3 and A4) and posterior (P3 and P4).

246 A preliminary analysis was run by means of an omnibus ANOVA with Band (Alpha, Beta),  
247 Condition (GC, MC and BC), Region (Anterior, Posterior), Hemisphere (Left, Right) and Week (W1,  
248 W2) as factors. This analysis revealed a main effect of Band ( $F(1, 31) = 7.576, p = 0.010, \eta_p^2 =$   
249  $0.196$ ), with desynchronization in the beta band ( $M = -0.125, SE = 0.040$ ) but not in the alpha band  
250 ( $M = 0.042, SE = 0.049$ ). One sample t-tests compared to zero confirmed the absence of  
251 desynchronization in the alpha band in all conditions (GC, MC, BC), regions (Anterior and Posterior)  
252 and at both W1 and W2 (all  $ps > 0.05$ ) except for MC at W2 which showed a significant  
253 synchronization over posterior scalp locations ( $p = 0.038$ ). Therefore, we focused our remaining  
254 analyses on the beta band.

255

## 256 1.2.6 Correlation between infants' ERD and motor proficiency

257 Some infants showed attempts to reach and grasp during EEG testing, however the presence  
258 of excessive motor artifacts which contaminated EEG data during action execution, together with the  
259 short-term duration of each recording session and the low number of grasping actions exhibited by  
260 each infant, made it impossible to acquire the minimum number of trials required to analyze the EEG  
261 data. However, a subset of monkeys ( $N = 14$ ) from our sample also completed a separate behavioral  
262 *Reaching-grasping task*, originally designed to investigate infants' space perception in relation to  
263 their grasping behavior maturation over the first month of life (for details on infants' behavioral  
264 grasping capacities, see Sclafani et al. (2015). Briefly: monkeys were tested twice a week from the  
265 second to the fourth week postpartum. Each monkey was presented with a series of small and large  
266 balls, either at a reachable distance (infant's peripersonal space) or at a non-reachable distance  
267 (infant's extrapersonal space). If the infant made no grasping attempt with the ball within 20 seconds,

268 the ball was removed and the trial was terminated. Infants were presented with one ball at a time, and  
269 completed up to 8 trials (2 trials for each ball size and distance). Infants could attempt to grasp with  
270 different effectors, hand or mouth, and different motor strategies, stepping toward the target ball  
271 before attempting to grasp it or simply extending their arm/mouth to approach the ball. In the present  
272 study, we considered the number of hand grasping attempts—both successful and unsuccessful—  
273 exhibited by each infant at two weeks of age, as an index of infants' grasping **propensity**. We chose  
274 to include both successful and unsuccessful attempts in our analyses because, at this age, infants make  
275 a high proportion of unsuccessful attempts as they initially develop their manual reach-grasping skills.  
276 There were, however, significant individual differences in the frequencies of attempts overall, so we  
277 focused on this measure. The choice of investigating hand grasping skills in relation to the EEG  
278 activity only in the second week of life and not in the first week was motivated by the fact that in the  
279 first week of life almost no infants attempted to reach the ball. Only in the second week of life did  
280 infants start to develop a rudimentary form of grasping, even though there were significant individual  
281 differences (Sclafani et al., 2015), with some individuals making attempts and others not yet  
282 displaying any attempt to reach the object. **We therefore considered this transition phase, from week**  
283 **1 to week 2, as an ideal time to capture emerging neural activity during action observation. While**  
284 **empirically interesting, further longitudinal measurements at week 3 and 4 post partum were not**  
285 **feasible as the monkeys became too active by these ages.**

286 Since data were not normally distributed we used Spearman's correlation to explore the  
287 possible association between the number of hand grasping attempts exhibited by each infant at W2,  
288 **during the *Reaching-grasping task***, and the EEG activity recorded at the same age during the  
289 observation of grasping, mimed actions and means-end movements. Bonferroni corrections were  
290 applied to account for multiple comparisons.

291

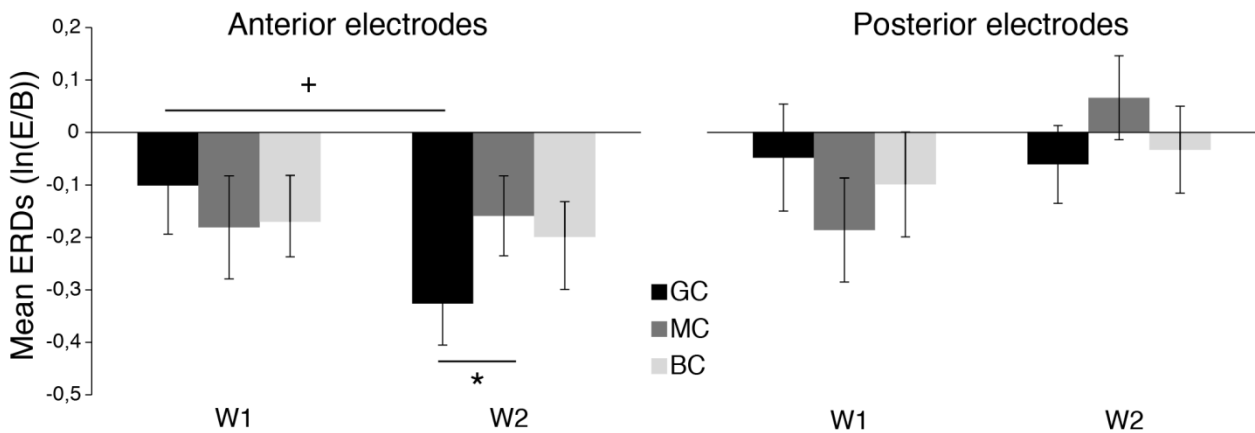
### 292 1.3 Results

293 Preliminary analyses revealed the presence of desynchronization in the beta band but not in  
294 the alpha band. Therefore, results reported in this section will be focused on beta band only.

295 To examine whether there was EEG desynchronization during GC, MC, and BC, one-sample  
296 t-tests compared with zero were run. Analyses revealed significant ERD over anterior electrodes  
297 during W2 (GC:  $t_{(31)} = -4.141, p < 0.001, d = 0.73$ ; MC:  $t_{(31)} = -2.084, p = 0.045, d = 0.37$ ; BC:  $t_{(31)} =$   
298  $-2.967, p = 0.006, d = 0.52$ ) but not during W1 (GC:  $t_{(31)} = -1.085, p = 0.286$ ; MC:  $t_{(31)} = -1.850, p =$   
299  $0.074$ ; BC:  $t_{(31)} = -1.940, p = 0.062$ ), and no significant ERD either at W1 (GC:  $t_{(31)} = -0.483, p =$   
300  $0.632$ ; MC:  $t_{(31)} = -1.888, p = 0.068$ ; BC:  $t_{(31)} = -0.994, p = 0.328$ ) or at W2 (GC:  $t_{(31)} = -0.829, p =$   
301  $0.413$ ; MC:  $t_{(31)} = 0.811, p = 0.424$ ; BC:  $t_{(31)} = -0.411, p = 0.684$ ) for posterior electrodes. Figure 2  
302 shows mean ERDs in the beta band over anterior and posterior electrodes.

303 To explore the possible presence of any longitudinal effects, from W1 to W2, we implemented  
304 further analyses. Because the effect of hemisphere in preliminary analyses was not significant, we  
305 averaged ERD and ERS values across the left and right hemisphere. We implemented a 3 Condition  
306 (GC, MC and BL) x 2 Region (Anterior and posterior) x 2 Week (W1, W2) within-subject ANOVA,  
307 which revealed a main effect of Region ( $F(1, 31) = 5.881, p = 0.020, \eta_p^2 = 0.159$ ), with greater  
308 desynchronization in anterior electrodes ( $M = -0.189, SE = 0.42$ ) than posterior electrodes ( $M = -0.061,$   
309  $SE = 0.053$ ), and a Condition x Week interaction ( $F(2, 62) = 4.021, p = 0.026, \eta_p^2 = 0.156$ ). Follow-up  
310 paired comparisons focused only on anterior electrodes and revealed no differences between W1 and  
311 W2 in MC ( $t_{(31)} = -0.183, p = 0.856$ ;  $MC_{W1}: M = -0.181, SE = 0.098$ ;  $MC_{W2}: M = -0.159, SE = 0.076$ )  
312 and BC ( $t_{(31)} = -0.253, p = 0.802$ ;  $BC_{W1}: M = -0.170, SE = 0.088$ ;  $BC_{W2}: M = -0.198, SE = 0.067$ ),  
313 while a trend was found in GC ( $t_{(31)} = -1.86, p = 0.071, d = 0.33$ ), with more ERD in W2 ( $M = -0.329,$   
314  $SE = 0.079$ ) than W1 ( $M = -0.101, SE = 0.093$ ) (Figure 2). Follow-up paired comparisons also showed a  
315 significant difference between GC and MC at W2 ( $t_{(31)} = -2.06, p = 0.048, d = 0.36$ ) (Figure 2), but  
316 not at W1 ( $t_{(31)} = 0.79, p = 0.435$ ). No difference between GC and BC were found at both W1 and

317 W2 ( $W1:t_{(31)} = 0.63, p = 0.535$ ;  $W2:t_{(31)} = -1.46, p = 0.158$ ). MC and BC did not differ at either time  
 318 point ( $W1: t_{(31)} = 0.14, p = 0.891$ ;  $W2: t_{(31)} = -0.494, p = 0.624$ ).



319  
 320 **Figure 2: Beta Event-related desynchronization.** Means and standard errors of EEG beta event-  
 321 related desynchronizations (ERDs) for anterior and posterior electrodes in each condition (GC, MC,  
 322 BC) and week (W1, W2). E: Event, B: Baseline. \* $p < 0.05$ , + $p = 0.071$ .

323

### 324 1.3.1 Motor competence and ERD during observation of grasping actions

325 To investigate the relation between infants' motor competence at 2 weeks of age and beta  
 326 ERD recorded during action observation at W2, Spearman correlations were run for a subset of 14  
 327 monkeys.

328 For anterior electrodes, this analysis revealed a trend-significance negative correlation  
 329 between the total number of hand grasping attempts exhibited by each infant at W2, during the  
 330 behavioral *Reaching-grasping task*, and EEG desynchronization to observed grasping actions  
 331 (Spearman correlation:  $r_s(14) = -0.616, p_{corr} = 0.057$ ). Specifically, greater ERD in GC were  
 332 associated with more grasping attempts, suggesting that infants with more mature manual motor  
 333 abilities may also be exhibiting stronger sensorimotor neural activation during observation of  
 334 grasping actions. No significant correlations were found between the total number of hand grasping  
 335 attempts exhibited by each infant at W2 and EEG desynchronization to observed mimed actions

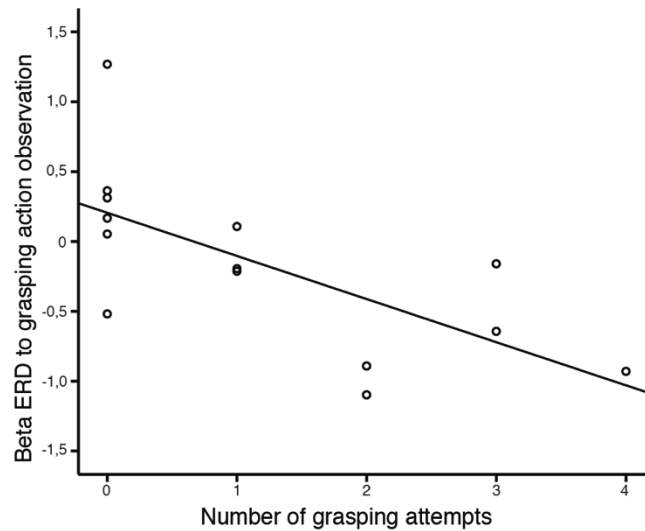
336 (Spearman correlation:  $r_s(14) = -0.242, p = 0.404$ ) or observed means-end movements (Spearman  
337 correlation:  $r_s(14) = 0.174, p = 0.560$ ).

338 Similarly, no significant correlations were found between the total number of grasping  
339 attempts exhibited by each monkey during the *Reaching-grasping task* and EEG values over posterior  
340 electrodes in GC (Spearman correlation:  $r_s(14) = 0.104, p = 0.723$ ), MC (Spearman correlation:  $r_s$   
341  $(14) = 0.586, p_{corr} = 0.102$ ) and BC (Spearman correlation:  $r_s(14) = 0.202, p = 0.508$ ).

342 We further explored the possible relations between EEG activity recorded during grasping  
343 action observation (GC) and the number of grasping attempts exhibited by each infant, during the  
344 behavioral *Reaching-grasping task*, when the object was presented in the peripersonal or in the  
345 extrapersonal space. In fact, compared to the peripersonal space trials, the extrapersonal space trials  
346 required the infant to engage in not only grasping, but also locomotion, moving toward the ball, which  
347 involve a more elaborate encoding of the surrounding space and evaluation of their body representation  
348 in it. The number of grasping attempts made when the target ball was presented in the infant's  
349 peripersonal space was correlated with EEG desynchronization, recorded during grasping action  
350 observation (GC) (Spearman correlation:  $r_s(14) = -0.735, p_{corr} = 0.009$ ) (Figure 3). Specifically,  
351 greater desynchronization was associated with more grasping attempts. No relation was found  
352 between EEG activity and the number of attempts executed in the extrapersonal space (Spearman  
353 correlation:  $r_s(14) = -0.210, p = 0.471$ ).

354 Together, these results suggest that grasping motor abilities, particularly when objects are  
355 available within reaching distance, are associated with EEG reactivity while observing others'  
356 grasping actions.





357

358 **Figure 3: Correlation between EEG beta desynchronization over the anterior scalp region and**  
 359 **infants' propensity to grasp: Negative** correlation between ERD values and the number of hand  
 360 grasping attempts exhibited in the peripersonal space at W2 ( $p < 0.05$ ). The x-axis corresponds to the  
 361 number of grasping attempts **exhibited by each monkey- during a separate behavioral task- when the**  
 362 **object was presented** in the infant's peripersonal space. The y-axis is the beta ERD recorded over  
 363 anterior electrodes at W2.

364

#### 365 1.4 Discussion

366 In the current study, we acquired EEG data on newborn macaque monkeys while they  
 367 observed grasping actions, mimed actions and means-end motions. In a subset of monkeys, we also  
 368 examined the relations between EEG reactivity and the emergence of infants' manual motor skills.  
 369 To track any possible longitudinal development, we performed EEG recordings at two different time  
 370 points: during the first and second week postpartum (W1 and W2) and, following previous EEG  
 371 studies in human infants (Cannon et al., 2016; Southgate et al., 2010; van Elk et al., 2008; Yoo et al.,  
 372 2015) and, in infant (Ferrari et al., 2012) and adult (Coudé et al., 2014) monkeys, we focused analyses  
 373 on two specific frequency bands, representing the main components of the mu rhythm: alpha, 5-7Hz,  
 374 and beta, 15-17Hz.

375 In newborn monkeys, the first month of life represents a crucial transitional stage for  
376 developing reaching-grasping movements, with the greatest motor changes occurring between the  
377 second and the third week. During this period, infants start showing successful motor strategies to  
378 reach and grasp objects in the surrounding environment (Sclafani et al., 2015). Therefore, we  
379 hypothesized that rudimentary cortical mechanisms underlying the perception of others' manual  
380 actions may emerge and operate in parallel with improvements in infants' hand motor skills. In  
381 particular, our goal was to observe the possible emergence of neural modulations to action  
382 observation, from the first week of life, when there is almost total absence of grasping abilities  
383 (Sclafani et al., 2015), to the second week of life, when a rough propensity to approach objects  
384 emerges.

385 Our results confirmed our hypothesis identifying desynchronization in the beta band in  
386 anterior electrodes during the observation of grasping actions that is enhanced between the first and  
387 second week of life. Importantly, this desynchronization coincided with the emergence of the  
388 propensity to engage with objects, between the first and the second week and was greatest for  
389 observation of grasping actions compared to the observation of mimed action or means-end motions.

390 These results are consistent in both their spectral and topographical characteristics with  
391 previous human EEG studies, involving infants or adults, in which EEG mu desynchronization to  
392 action observation has been described in electrodes placed over motor areas and in frequencies  
393 belonging to the beta band range (Avanzini et al., 2012; Babiloni et al., 2002; van Elk et al., 2008).  
394 Findings in the present study are also consistent with EEG investigations in adult monkeys showing  
395 that the observation of grasping actions produces EEG desynchronization over frontal and central  
396 scalp regions in the beta band more than in the alpha band (Coudé et al., 2014).

397 Importantly, our data represent the first evidence showing EEG reactivity to the observation  
398 of hand goal-directed actions as early as the second week of life. The only other neurophysiological  
399 evidence concerning the emergence of a neural system underlying action and perception right after birth  
400 comes from previous EEG investigations in neonate monkeys (Ferrari et al., 2012; Vanderwert et al.,

401 2015). These studies showed a distinct EEG suppression of the 5-7 Hz band during imitation and  
402 execution of communicative facial gestures (i.e., lip smacking and tongue protrusion). Thus, it has been  
403 proposed that a rudimentary mirror mechanism underlying imitation may operate very early in  
404 development and may even be pre-formed in utero (Casile et al., 2011; Simpson et al., 2014;  
405 Vanderwert et al., 2013). However, it is important to note that, compared to oro-facial movements, the  
406 development of arm and hand movements requires a more complex and longer maturation processes  
407 after birth. For example, in both humans and monkeys, the myelination process of the corticospinal  
408 tract, which plays a primary role in the development of voluntary arm movements (Galea and Darian-  
409 Smith, 1995; Lemon, 1999) is completed only between the second and the third year of life (Olivier  
410 et al., 1997). Although newborn monkeys display only exploratory movements in the first week of  
411 life, such space exploration greatly contributes to the initial development of their visual-motor  
412 coordination, proprioception and internal representation of space (Sclafani et al., 2015; von Hofsten,  
413 2004), and all these factors together may contribute to the later development of successful goal-  
414 directed reaching-grasping actions (Nelson et al., 2011; Sclafani et al., 2015). Further, these  
415 neurodevelopmental processes likely contribute to the emergence of desynchronization in the beta  
416 band during observation of actions in anterior scalp locations, along with the emerging cortical  
417 networks involved in action execution.

418 Our results also support the idea that the observation of others' actions recruits mirror neuron  
419 populations hosted in the ventral premotor cortex, in the primary motor cortex, and in the posterior  
420 parietal lobe (Bonini et al., 2010; Fogassi et al., 2005; Gallese et al., 1996; Vigneswaran et al., 2013),  
421 and therefore raise the possibility that, even at this early developmental stage, a mirror mechanism,  
422 probably still broadly tuned, may be emerging. This hypothesis remains speculative, however, two  
423 lines of evidence support this conclusion. First, beta desynchronization is greater for goal-directed  
424 actions than for observed mimed action and, although we did not find any significant differences in  
425 the beta desynchronization between grasping action observation and means-end movement  
426 observation, it is plausible that this latter condition relies on multiple factors, including the final goal,

427 the presence of multiple objects (two red balls versus one), and the movement of an interesting object  
428 rather than the model's hand. Evidence at the single cell level in adult monkeys reveals that F5 and  
429 PFG mirror neurons respond predominantly to goal-directed action rather than mimed actions (Ferrari  
430 et al., 2005; Gallese et al., 1996; Rozzi et al., 2008). Data at the single cell level are not available in  
431 infant monkeys and therefore we cannot infer whether the neuronal activation to specific visual  
432 stimuli is similar to that of adults. Our EEG data, however, suggest that the cortical network recruited  
433 in infants during action observation shares similar stimulus-response properties in frequency and  
434 distribution of activity recorded from the scalp in adults.

435         Second, not surprisingly, we did not find any desynchronization during the first week of life  
436 when reaching-grasping attempts are very sporadic and movements do not appear to be voluntarily  
437 controlled (Sclafani et al., 2015). Our data, thus, reflect the changes occurring at the behavioral and neural  
438 levels, suggesting that a rudimentary cortical system involved in action observation and execution starts  
439 operating along with significant improvements in motor skills as well as the development of specific  
440 cortical visual-motor integrations. As infant macaques start developing reach and grasp skills by the  
441 second week of life, the EEG brain responses become more tuned for goal-directed actions and this,  
442 according to our hypothesis, reflects a more mature organization of cortical motor areas which are  
443 capable not only of supporting hand actions, but also involved in the decoding of others' actions in  
444 terms of goals.

445         Unfortunately, we were unable to analyze the EEG data during action execution. Limited  
446 testing time and the excessive artifact contamination that characterized the EEG signal during infants'  
447 spontaneous reaching-grasping movements resulted in an inability to assess whether  
448 desynchronization occurred in the same frequencies for action execution and observation. However,  
449 the relation between EEG beta desynchronization, found during observation of grasping actions and  
450 infants' motor skills (i.e., *grasping attempts*) in a subset of monkeys, provides some clues to a pairing  
451 of execution and observation of actions at the neural level. Our analysis showed that infants who  
452 made more reaching-grasping attempts to the target ball had greater beta desynchronization over

453 **motor-related brain regions**. Moreover, this correlation was specific for grasping attempts made in  
454 the peripersonal but not the extrapersonal space, confirming what has been previously demonstrated  
455 in monkeys (Sclafani et al., 2015) and in human infant studies (Rochat & Goubet, 1995) showing that  
456 although infants progressively increase their body representation in the space along with their motor  
457 abilities, they might detect the distance at which an object can be reached concurrently with the  
458 emergence of the motor reaching and grasping skills. Attempts to grasp, thus, represent a marker of  
459 neurodevelopment in infants revealing the capacity to coordinate movements requiring complex  
460 visual processing and visuomotor coordination in space. This capacity is known to heavily rely on  
461 parietal-premotor circuits and on the maturation of the corticospinal tract (Lemon, 1999; Olivier et  
462 al., 1997; Rizzolatti and Luppino, 2001). It is possible that individuals who show reaching-grasping  
463 **propensity** have more mature cortical circuits compared to those who are unable or uninterested in  
464 attempting to grasp; consistently with an emerging body of evidence from human developmental EEG  
465 studies (Cannon et al., 2016; van Elk et al., 2008; Yoo et al., 2015). Our data suggest that parietal and  
466 premotor circuits start their maturation and refinement between the first and second week, as reflected  
467 in the emergence of EEG responses during grasping observation, and their association with infants'  
468 readiness to attempt to grasp, especially when objects are located in peripersonal space. **It is in fact**  
469 **reasonable to think that at this developmental stage grasping attempts made within the peripersonal**  
470 **space would better correlate with ERD to grasping observation, as they would reflect the activation**  
471 **of more refined neural circuits also hypothetically activated during action observation. In contrast,**  
472 **attempts to grasp when an object is presented in the extrapersonal space are more sporadic at this age**  
473 **(Sclafani et al., 2015) and this might reflect the fact that some of the parietal-premotor circuits**  
474 **involved in reaching and in space coding are not yet fully developed and still require sensorimotor**  
475 **experience to be refined and become functional.**

476 In contrast to previous newborn monkey EEG investigations (Ferrari et al., 2012; Vanderwert  
477 et al., 2015), we did not find any significant desynchronization in the sensorimotor alpha band. A  
478 possible explanation for this apparent discrepancy might be related to the type of effector used (hand

479 versus mouth) and/or the value (social versus non-social) of the actions assessed in the two different  
480 studies. While Ferrari and colleagues (2012) recorded EEG during a facial neonatal imitation task,  
481 the current study included stimuli involving hand reaching-grasping actions. Thus, the  
482 desynchronization in the alpha band might reflect the recruitment of pre-formed circuits activated by  
483 oro-facial gestures with communicative values (i.e., lipsmacking and tongue protrusion); conversely  
484 the observation of goal-directed actions may reflect the activation of circuits still under development,  
485 involving premotor and motor hand cortical regions requiring a longer period of maturation before  
486 becoming adult-like. Electrophysiological studies in adult monkeys show that mouth and hand mirror  
487 neurons are distributed in different, yet partially overlapping, neuroanatomical sectors within the  
488 ventral premotor cortex, with the hand represented predominantly in the most medial part of F5 and  
489 the mouth neurons distributed in the lateral sector of the F5 convexity (Ferrari et al., 2003; Maranesi  
490 et al., 2012). Neuroimaging studies in human adults report that observing mouth actions activates a  
491 more lateral sector of the premotor cortex than observing hand actions (Buccino et al., 2001). Thus,  
492 although highly interconnected, mouth and hand mirror neurons could rely on different and only  
493 partially overlapped cortical networks, very early in development (Casile et al., 2011).

494 From a developmental perspective, it is possible that cortical mouth circuits are already  
495 present at birth and subsequently shaped by *social* experience (Casile et al., 2011; Tramacere and  
496 Ferrari, 2016; Vanderwert et al., 2015) while hand cortical circuits, although present at birth, may  
497 undergo finer and slower development relying more heavily on body maturation and *motor*  
498 experience (Gerson et al., 2015). **This interpretation would also be partially in line with more recent  
499 views on the development of mirror neuron systems which support the idea that action observation  
500 might benefit from experience as a result of associative learning processes and maturational processes  
501 that are canalized during development (Cook et al., 2014; Del Giudice et al., 2009; Ferrari et al.,  
502 2013; Heyes, 2013, 2010; Tramacere and Ferrari, 2016). Therefore, ERD to grasping action  
503 observation emerging at the second week of life would be sustained by the emergence of grasping  
504 motor skills and modulated by grasping experience.**

505           The functionality of the alpha and beta bands may further represent developmental markers  
506 for maturation of the mirror neuron system. The alpha band, therefore, may reflect the activation of  
507 broader parieto-frontal circuits integrating the activity of other areas besides the motor regions that  
508 might require a longer period of time for myelination processes. Thus, it is possible that the reactivity  
509 of alpha frequencies to others' hand actions might emerge at later ages as a result of greater motor  
510 experience, compared to the beta band. In line with this hypothesis, it has been shown that the two  
511 frequency bands originate from different cortical sources, with beta band having its cortical source in  
512 the motor cortex and the alpha band originating from the post-central gyrus (Hari and Salmelin,  
513 1997). This suggests that local circuits, restricted to the motor and premotor cortex, may develop and  
514 integrate information reflected in the EEG modulation earlier than later developing complex networks  
515 involving fronto-parietal connections. Moreover, a recent neurophysiological investigation using  
516 simultaneous EEG and single neurons recordings (Bimbi et al., *under revision*) in adult monkeys,  
517 demonstrated that F5 mirror neurons activity correlated with EEG desynchronization to grasping  
518 action observation in the beta band but not in the alpha band. Thus, it is possible that the major  
519 contribution of mirror neurons to the beta band desynchronization recorded over anterior and central  
520 scalp locations is already present at this early developmental stage.

521           In conclusion, our findings suggest that EEG beta band suppression recorded over the scalp  
522 may represent a marker of the activation of cortical networks, probably including mirror neurons,  
523 underlying goal-directed hand action perception, starting from the second week of life, and develop  
524 along with the emergence of grasping motor skills.

525

526

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