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Socioeconomic status in infancy and the developing brain: Functional connectivity of the hippocampus and amygdala

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Short Title: SES in infancy and the developing brain

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1 **1. Abstract**

2 The development of the hippocampus and amygdala is particularly sensitive to environmental
3 factors, including socioeconomic status (SES). Studies that have investigated associations between
4 SES and brain development markers have rarely focused on connectivity. Accordingly, this
5 longitudinal study examined whether SES in infancy (parental education and income-to-needs ratio)
6 predicts the functional connectivity of the hippocampus and amygdala in late childhood, and in turn
7 whether functional connectivity is associated with child socioemotional adjustment in a middle-class
8 sample. SES indices were measured when children (N = 28) were 7 months old. When children were
9 10 years of age, they underwent a resting-state functional magnetic resonance imaging exam, and
10 their school teachers completed a questionnaire assessing child socioemotional adjustment. Whole-
11 brain regression analyses, including left and right hippocampi and amygdalae as seeds and SES
12 indices as predictors, revealed that higher parental education predicted stronger functional
13 connectivity between the left and right hippocampi and the right amygdala with the dorsal anterior
14 cingulate cortex, and between the left amygdala and bilateral angular gyrus, after accounting for
15 child age and sex. In turn, the connectivity of these regions was associated with higher child prosocial
16 behavior. These findings contribute to the emerging literature suggesting that SES is associated with
17 variability in the neural substrates of social abilities in children.

18

19 2. Introduction

20 Childhood socioeconomic status (SES) is a multidimensional construct that reflects both economic
21 and social resources available to children and their families, and is typically indexed by parental
22 education and family income [1–3]. While poverty implies a threshold that dichotomizes families as
23 being poor or not, SES represents a gradient, and indeed the effects of SES on child outcomes
24 operate across the whole SES continuum [2–4]. Although many effects of SES on child outcomes are
25 attributable to the lower end of the continuum, small variations of SES within the middle-class range
26 can be meaningfully related to child development [2]. The present report investigates whether
27 variation in SES predicts differences in child brain functional connectivity in a low-risk sample of
28 mostly middle-class families.

29 SES is associated with early experiences likely to shape child development and brain maturation [1,5].
30 Children growing up in higher-SES families are more likely to be exposed to stimulating
31 environmental input (e.g., linguistic, cognitive and social stimulation) that is favorable to child
32 development [5,6]. In line with this, numerous studies report that socioeconomic differences in
33 childhood are sources of variation in child development at both the behavioral and neural levels [5–
34 8].

35 Early exposure to higher-SES environments is associated with better child affective and cognitive
36 functioning, including fewer behavioral problems, lower rates of psychopathology, and better
37 cognitive performance and socioemotional adjustment [1,8–12]. Neural differences may underlie
38 these observed behavioral differences. SES-related differences in the morphometry and activity of
39 brain regions important for affective and cognitive processing are reported [see 2,6 for reviews],
40 notably in the hippocampus and the amygdala [13–15], two regions centrally involved in
41 socioemotional processes [16,17].

42 Prior research has provided evidence for the links between SES and individual brain regions, but the
43 relation between SES and brain connectivity is still under-investigated. Yet, complex cognitive and
44 emotional functions depend on the dynamic interplay and exchange of information between
45 distributed brain regions [18–21]. Brain connectivity development is modulated by early experiences
46 that determine to a large degree which synaptic connections persist and are strengthened [22–24].

47 The development of the hippocampus and amygdala is sensitive to early experiences and
48 environmental factors, including SES [1,16,25]. During childhood, the connectivity networks
49 associated with the hippocampus and the amygdala develop and likely underlie the refinement of
50 child socioemotional functioning [25–29]. Consequently, differences in the connectivity networks of
51 the hippocampus and the amygdala may be a mechanism for SES-related variation in child
52 development.

53 Two studies report a positive association between childhood SES and structural connectivity in white
54 matter tracts involved in affective and cognitive processes, including the parahippocampal cingulum
55 bundle and the uncinate fasciculus tracts, which connect the hippocampus and the amygdala with
56 the frontal cortex [30,31]. Structural connectivity between brain regions is presumed to provide the
57 anatomical basis for functional interactions between these regions [32,33]. However, the
58 associations between SES and functional connectivity in children are just beginning to receive
59 empirical attention.

60 The brain is organized into multiple resting-state functional networks that reflect correlated
61 spontaneous activities between two or more brain regions (called resting-state functional
62 connectivity [rsFC]) measured with resting-state functional magnetic resonance imaging (rs-fMRI).
63 RsFC is believed to reflect a history of repeated co-activation between brain regions [18,34,35]. Thus,
64 rsFC reflects functional brain organization and when measured during childhood can provide insight
65 into fundamental organizing principles underlying brain development [35,36].

66 A longitudinal rs-fMRI study reported that higher SES (i.e., higher family income and greater maternal
67 education) was related to more optimal maturation of cortical functional networks during the first
68 year of life [37]. Another study reported that change in family income during adolescence was
69 associated with changes in rsFC [38]. In a study focused on the connectivity of the amygdala and
70 hippocampus, Barch and colleagues [39] reported that higher family income during early childhood
71 predicted stronger rsFC between these regions and the superior frontal cortex and lingual gyrus,
72 which in turn predicted lower negative mood/depression at school age. In addition, higher family
73 income during late childhood predicts greater connectivity between the hippocampus and the
74 posterior cingulate cortex in early adulthood [40].

75 The study by Barch and colleagues (2016) indirectly suggested an association between childhood SES,
76 amygdala and hippocampus rsFC and child socioemotional functioning, in that the authors examined
77 psychological dysfunction (i.e., negative mood/depression). However, they focused their analyses on
78 negative mood/depression in a sample enriched for depression symptoms; hence, the generalization
79 of the results to low-risk samples is unknown. In addition, only one index of SES (family income) was
80 used, and the role of other indices (such as parental education) remains unclear. Family income and
81 parental education, although correlated, represent distinct facets of SES and may have different links
82 to childhood experiences and child neural and behavioral development [1,2,14,41,42]. Higher family
83 income is associated with greater access to resources, including more nutritious foods, enriched
84 home learning environments, higher quality child care and safer neighborhoods [5,41]. Independent
85 of family income, more educated parents spend more time with their children, have higher quality
86 parent-child interactions, use more elaborate language, and are more likely to engage in parenting
87 activities that promote socioemotional development [5,41]. Thus, both family income and parental
88 education may influence children's development, including their neural development.

89 The goal of the present report was to examine whether SES in infancy, indexed by parental education
90 and family income separately, predicts the rsFC of left and right hippocampi and amygdalae in late
91 childhood, and in turn whether differences in rsFC are associated with child socioemotional
92 adjustment in a middle-class sample of typically-developing children. Based upon previous studies
93 [30,31,39], we hypothesized that higher SES (i.e., higher parental education and/or family income)
94 would predict stronger hippocampus and amygdala connectivity with frontal regions. In turn, we
95 expected these patterns of connectivity to be associated with child socioemotional adjustment. As
96 parental education and family income have differential links with child neural and behavioral
97 development [1,41], it was further expected that parental education and family income would
98 predict different patterns of hippocampus and amygdala connectivity (i.e., the brain regions with
99 which the hippocampus and amygdala would be most strongly connected). Given the lack of previous
100 research including the two SES indices, no hypothesis was formulated regarding the exact differences
101 in patterns of connectivity.

102 **3. Materials and Methods**

103 **3.1 Participants**

104 Participants included in the present study ($n = 28$) were followed annually as part of a larger
105 longitudinal prospective cohort project ($N = 272$ at baseline recruited between 2005 and 2011)
106 investigating early relational predictors of child development [43]. In 2016-2017, all families who
107 were still active in the project and whose child was at least 10 years old ($n = 64$ – most children were
108 younger) were invited to take part in a magnetic resonance imaging (MRI) exam. Younger children
109 were not invited to participate because we wanted to maintain a narrow age window for the MRI
110 exam to avoid confounds related to ongoing brain development. Here, we report on SES indices
111 (parental education and family income) assessed when children were 7 months of age and rs-fMRI
112 data as well as child socioemotional adjustment measured around 10-11 years of age. The larger

113 project and current study were approved by the local human research ethics committee and all
114 families provided written informed consent for participation.

115 Families were recruited from birth lists randomly generated by the Ministry of Health and Social
116 Services. Inclusion criteria were full-term pregnancy (i.e., at least 37 weeks) and the absence of any
117 known disability or severe delay in the infant. When children were 10 years of age, they were invited
118 to undergo an MRI exam including an rs-fMRI sequence. Inclusion criteria for the MRI exam were the
119 absence of neurological or psychiatric disorders, traumatic brain injury, psychoactive medication, and
120 standard MRI contraindications. Of the 64 families approached for the MRI exam, 39 (60.94%) agreed
121 to participate. However, four (6.25%) of these children were not eligible due to security reasons (e.g.,
122 wearing braces); thus, 35 children underwent the MRI exam (54.69%). There were no
123 sociodemographic differences between the 35 children who underwent the MRI exam and the 29
124 who did not in terms of family income, parental age, education, ethnicity, language, or child sex (see
125 Table 1, all $ps \geq .21$).

126 Of the 35 children who took part in the MRI exam, four were subsequently excluded because of a
127 diagnosis of anxiety disorder ($n = 1$) or attention deficit hyperactivity disorder treated with
128 psychoactive medication ($n = 3$). In addition, the rs-fMRI data of three children were excluded due to
129 significant motion (translation > 2.5 mm or rotation > 2.5 degrees). Therefore, data from 28 children
130 (17 girls and 11 boys, $\chi^2(1) = 1.29$; $p = .26$) were used in the analyses. There were no
131 sociodemographic differences between the final sample ($n = 28$) and the other families ($n = 36$) in
132 terms of family income, parental age, education, ethnicity, language, or child sex (all $ps \geq .25$).

133 **3.2. Data collection**

134 **3.2.1. SES indices**

135 Parental education and family income were reported by mothers upon enrollment in the larger
136 project, when children were 7 months old ($M = 7.04$ months, $SD = 0.71$, range = 6.0 – 8.5). For the
137 final sample ($n = 28$), mean years of education was 15.79 ($SD = 1.95$, range = 11 – 18) for mothers and
138 15.71 ($SD = 1.88$, range = 11 – 17) for fathers. Parental education ($M = 15.75$, $SD = 1.70$, range = 11.5
139 – 17.5) was calculated by averaging both parents' total years of education completed ($r = .58$, $p =$
140 $.001$). In Quebec (Canada), where this study was conducted, a high school degree corresponds to 11
141 years of education. Thus, all parents in the sample had at least a high school degree.

142 Family income ($M = 4.48$, $SD = 1.48$, range = 1 – 6) corresponded to the total annual raw family
143 income on a 1-6 scale: 1 = less than CAD\$20,000 ($n = 1$); 2 = CAD\$20,000 to CAD\$39,000 ($n = 3$); 3 =
144 CAD\$40,000 to CAD\$59,000 ($n = 2$); 4 = CAD\$60,000 to CAD\$79,000 ($n = 5$); 5 = CAD\$80,000 to
145 CAD\$99,000 ($n = 8$); 6 = CAD\$100,000 and up ($n = 8$). One family declined to report family income.
146 The income-to-needs ratio ($M = 2.37$, $SD = 0.83$, range = 0.7 – 3.5) was calculated for each family by
147 dividing reported annual income by the Canadian low income threshold
148 (<https://cdn.carra.gouv.qc.ca/général/pages/IN99KXXX00A001.aspx>) for a same-size family in the
149 year the data were collected. Because family income was reported in ranges, the median value of
150 each increment was used in the income-to-needs ratio calculation (e.g., CAD\$29,500 for the
151 CAD\$20,000 to CAD\$39,000 category).

152 Parental education and income-to-needs ratio ($r = .40$, $p = .04$) were used as SES indicators in
153 subsequent analyses.

154 **3.2.2. MRI acquisition at 10-11 years**

155 When children were 10-11 years ($M = 10.57$ years, $SD = 0.46$, range = 10 – 11.67) neuroimaging data
156 were collected using a 32-channel head coil on a Siemens 3-Tesla scanner (MAGNETOM Trio,
157 Siemens, Erlangen, Germany). Structural data were acquired using two high-resolution anatomic
158 sequences: a three-dimensional T1-weighted 4-echo magnetization-prepared rapid gradient-echo

159 sequence and a two-dimensional T2-weighted turbo spin echo sequence (see [44] for parameter
160 details). Then, rs-fMRI data were acquired with a two-dimensional T2-star echo planar image
161 sequence (repetition time: 2430 ms; echo time: 30 ms; flip angle: 70°; 40 slices; slice thickness: 3.5
162 mm; gap: 3.5 mm; matrix: 64 × 64; field of view: 224 mm; in-plane resolution: 3.50 × 3.50 mm; 120
163 volumes; duration: 298 sec) during which children were asked to fixate on a dot on a screen. This
164 short 5-minute sequence allowed for a suitable balance between feasibility and reliability of rs-fMRI
165 in children. Short acquisition times such as this are likely to reduce the risk of motion artefacts
166 [45,46], which are especially salient in pediatric imaging [47]. Many of the brain networks that
167 include the hippocampus and amygdala show very good stability even with acquisition times as short
168 as 3 minutes [46].

169 **3.2.3. Child socioemotional adjustment at 10-11 years**

170 Shortly after the MRI exam ($M = 10.99$ years, $SD = 0.32$, range = 10.33 – 11.68), children’s school
171 teachers were asked to complete the Strengths and Difficulties Questionnaire (SDQ; Goodman,
172 1997). The SDQ is a behavioral screening questionnaire describing positive and negative attributes of
173 children aged between 2 and 17 years. This 25-item questionnaire yields scores for five subscales: (1)
174 Emotional symptoms, (2) Conduct problems, (3) Hyperactivity/inattention, (4) Peer problems, and (5)
175 Prosocial behavior. The respondent rates each item on a 3-point scale (0 = “not true”, 1 =
176 “sometimes true” and 2 = “certainly true”). In low-risk or general population samples (as in the
177 present study), an alternative three-subscale division of the SDQ is recommended [49]: ‘Internalizing
178 problems’ (Emotional symptoms + Peer problems), ‘Externalizing problems’ (Conduct problems +
179 Hyperactivity/inattention) and ‘Prosocial behavior’. Given the small sample size, this three-subscale
180 division is used here, so as to reduce the number of comparisons. A higher score is indicative of more
181 child difficulties, except for the Prosocial behavior subscale for which a higher score is indicative of
182 more prosocial behavior. The score for each subscale is the sum of item scores, generating a subscale
183 score from 0-20 for Internalizing problems and Externalizing problems and from 0-10 for Prosocial
184 behavior (see Table 2 for means, SD s, observed ranges).

185 **3.3. Head motion**

186 Motion has deleterious effects on resting-state analyses [45,47]. Thus, the following steps of fMRI
187 data pre-processing and analysis were performed to reduce potential motion effects on the results:
188 (1) All images were inspected for motion artefacts, and only participants who showed no more than
189 2.5 mm in translation or 2.5 degrees in rotation were included in the analyses; (2) pre-processing
190 included volumes realignment to correct for head motions, noise-correction using the ‘aCompCor’
191 strategy, and a band-pass filter between 0.008 and 0.09 Hz that improves control of motion [50]; and
192 (3) the first-level models included the six motion parameters (3 translations, 3 rotations) estimated
193 during realignment as nuisance regressors. Note that the mean framewise displacement ($M = 0.16$
194 mm, $SD = 0.06$ [47]) was not significantly correlated with parental education ($r = -.18$, $p = .35$),
195 income-to-needs ratio ($r = -.13$, $p = .52$) or SDQ scores (Internalizing problems: $r = -.03$, $p = .90$;
196 Externalizing problems: $r = -.34$, $p = .12$; Prosocial behavior: $r = -.05$, $p = .81$).

197 **3.4. Resting-state fMRI pre-processing**

198 After all images were visually inspected for motion artefacts and image quality, data pre-processing
199 was performed with SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK) and the CONN
200 Functional Connectivity SPM Toolbox version 17f [51] running on MATLAB version R2017b
201 (MathWorks, Inc., Natick, MA, USA). Using the SPM platform: (1) the echo planar imaging (EPI)
202 volumes were corrected for slice timing and realigned to the first volume to correct for head
203 motions; (2) the T1, T2 and mean EPI (calculated during realignment) images were co-registered; (3)
204 tissues (grey matter [GM], white matter [WM] and cerebrospinal fluid [CSF]) were segmented and
205 normalized using T1 and T2 images and an age-appropriate stereotaxic template (NIHPD 7.5-13.5
206 asymmetric: www.bic.mni.mcgill.ca/ServicesAtlases/NIHPD-obj1; Fonov et al., 2011); (4) resulting

207 parameters were applied to normalize the co-registered T1 image and EPI volumes with a voxel size
208 of 2 x 2 x 2 mm; and (5) the normalized EPI images were smoothed at 6 mm full width at half-
209 maximum (FWHM). Finally, the noise reduction step was performed to remove unwanted motion,
210 physiological and other artefactual effects from the blood-oxygen-level dependent (BOLD) signal
211 using the anatomical principal component-based noise-correction ‘aCompCor’ strategy [51–53]
212 implemented in the CONN toolbox. The aCompCor strategy accounts for motion, physiological and
213 other artefactual effects based on principal components of the signals from the white matter and the
214 cerebrospinal fluid voxels, along with the six motion parameters estimated during realignment. Then,
215 a band-pass filter between 0.008 and 0.09 Hz was applied.

216 **3.5. Statistical analyses**

217 **3.5.1. ROI-to-Voxels resting-state fMRI analyses**

218 ROI-to-Voxels rsFC analyses were performed using the CONN toolbox. Amygdala and hippocampus
219 ROIs (right and left) were selected from the FSL Harvard-Oxford Atlas maximum likelihood subcortical
220 atlas [54,55] implemented in the CONN toolbox to create connectivity maps between ROIs and all
221 brain voxels.

222 At the first level of analysis, Pearson’s correlations were calculated between the mean BOLD signal
223 time-courses of each ROI and each voxels. This provided a ROI-to-Voxels rsFC map for each
224 participant, in which positive and negative correlation coefficients defined positive and negative rsFC,
225 respectively. The six motion parameters (3 translations, 3 rotations) estimated during the
226 realignment step of pre-processing were added as nuisance regressors. Then, Fisher’s r-to-z
227 transformation was applied to allow for parametric testing.

228 For the second-level analysis, multiple regression was performed between each ROI-to-Voxels rsFC
229 map (left and right hippocampus and amygdala) and each SES index (parental education and income-
230 to-needs ratio) separately, controlling for child age and sex. Analyses were masked using a GM mask
231 based on the means of the GM, WM and CSF normalized images (see [44] for calculation details).
232 Resulting statistical maps were thresholded at $p < .001$ uncorrected at the voxel-level, and $p < .05$
233 corrected by family-wise error rate (FWE) at the cluster level using random-field-theory (RFT)
234 assumptions [56,57]. These thresholds ensure that parametric assumptions are valid and the rate of
235 false positives is acceptable [57,58].

236 **3.5.2. Correlations between functional connectivity and child socioemotional adjustment**

237 To examine the associations between rsFC and child socioemotional adjustment, we performed
238 correlations between relevant connectivity coefficients and SDQ scores. To do so, we extracted the
239 connectivity coefficients in significant clusters (previous analysis) for each participant and computed
240 partial correlations between connectivity coefficients and SDQ scores, adjusting for child age and sex.

241 Although mediation analysis is the optimal statistical approach to examine the presumed three-way
242 relation between SES, brain connectivity, and child adjustment, the current study is under-powered
243 to properly test for mediation. Accordingly, these preliminary correlational analyses are exploratory
244 and presented in the spirit of encouraging larger-scale hypothesis-driven investigations.

245 **4. Results**

246 **4.1. Predicting functional connectivity from parental education**

247 ROI-to-Voxels multiple regression analyses were performed to examine whether parental education
248 predicted rsFC of the bilateral hippocampi and amygdalae at 10 years (Table 3; Fig. 1 and 2). The
249 analyses revealed that after accounting for child age and sex, higher parental education was
250 associated with significantly stronger positive connectivity between the bilateral hippocampi and the
251 dorsal anterior cingulate cortex (dACC, also known as the mid-cingulate cortex [MCC]) and between

252 the right amygdala and the dACC. Higher parental education was also associated with significantly
253 stronger negative connectivity between the left amygdala and bilateral angular gyri. The link
254 between parental education and the connectivity of the right hippocampus and the right amygdala
255 with the dACC remained significant when income-to-needs ratio was covaried, whereas the
256 connectivity of the left hippocampus with the dACC and of the left amygdala with the angular gyrus
257 did not.

258 To test whether the results may have been driven by the three children of parents with lower
259 education (<13 years of education), we conducted a secondary regression analysis between
260 connectivity coefficients extracted in each significant cluster and parental education, adjusting for
261 child age and sex, excluding the data from these three children (Table S1, Fig S1). Higher parental
262 education remained significantly associated with stronger positive connectivity between the bilateral
263 hippocampi and the dorsal anterior cingulate cortex (all β s > .49, p s < .02). Higher parental education
264 also tended to be associated with stronger positive connectivity between the right amygdala and the
265 dACC ($\beta = .39$, $p = .06$; this marginal finding can likely be explained by the decrease in statistical
266 power ensuing from the smaller sample size for these analyses). Overall, these secondary analyses
267 suggest that the findings apply broadly and are not due to a few unusual cases.

268 On an exploratory basis, we examined the unique contributions of maternal and paternal education
269 to brain connectivity using a secondary ROI-to-Voxels multiple regression with maternal and paternal
270 education entered separately. The connectivity between the right hippocampus and the dorsal
271 anterior cingulate cortex was predicted by maternal education *beyond* paternal education (Figure
272 S2). There was no significant effect of paternal education *beyond* maternal education.

273 **4.2. Predicting functional connectivity from income-to-needs ratio**

274 ROI-to-Voxels regression analyses were performed to examine whether income-to-needs ratio
275 predicted rsFC of the right and left amygdala and hippocampus at 10 years. The analyses revealed no
276 significant results.

277 **4.3. Associations between functional connectivity and child socioemotional adjustment**

278 Partial correlations (adjusted for child age and sex) between functional connectivity coefficients and
279 child socioemotional adjustment indices are displayed in Table 4 (see also Fig. 3). Overall, the results
280 suggest that children with stronger positive connectivity of bilateral hippocampi and the right
281 amygdala with the dACC, and stronger negative connectivity of the left amygdala with the right
282 angular gyrus, displayed higher prosocial behavior.

283 **5. Discussion/Conclusion**

284 The goal of this report was to investigate whether SES in infancy, namely parental education and
285 family income, predicted rsFC of bilateral hippocampi and amygdalae in late childhood, and whether
286 this connectivity was associated with child socioemotional functioning in a middle-class sample.
287 Although the findings of this small-scale preliminary study require replication in larger samples to be
288 generalized, we observed that higher parental education during infancy predicted stronger rsFC of
289 the hippocampus and the amygdala with the dACC and the angular gyrus in late childhood, which in
290 turn was associated with higher prosocial behavior. No significant findings emerged with family
291 income. These findings are the first to provide evidence of an association between parental
292 education and subcortical-cortical rsFC, and contribute to the emerging literature suggesting that
293 childhood SES is associated with the development of the neural substrates of social abilities in
294 childhood [7].

295 Higher parental education during infancy predicted stronger positive connectivity of the bilateral
296 hippocampi and the right amygdala with the dACC (also known as the mid-cingulate cortex [MCC]),
297 and stronger negative connectivity between the left amygdala and bilateral angular gyrus at 10 years

298 of age. In adults, the dACC has positive connectivity with the hippocampus and the right amygdala
299 [59–61], and the angular gyrus (inferior parietal lobe) is negatively coupled with the amygdala
300 [29,61]. Subcortical-cortical connectivity undergoes protracted maturation throughout childhood and
301 adolescence characterized by changes in both the valence and the strength of connectivity [28,29].
302 Specifically, studies report age-related increases in rsFC strength (which becomes more positive with
303 age) between the hippocampus and the dACC, and between the amygdala and the dACC, and
304 reversal in rsFC valence (from positive to negative) between the amygdala and the inferior parietal
305 cortex from childhood to adulthood [28,29]. Gabard-Durnam et al. [29] suggest that changes in
306 amygdala-cortical connectivity are likely to occur at the transition between childhood and
307 adolescence (around age 10 years, age at which MRI acquisition was performed in the present
308 study). Based on adult patterns of connectivity and these developmental trends, our results,
309 although preliminary, appear to indicate that rsFC is more mature in children whose parents have
310 higher levels of education.

311 The enhanced connectivity of the right hippocampus and the right amygdala with the dACC appears
312 to be robustly associated with parental education, in that these links hold above and beyond family
313 income. In contrast, the connectivity of the left hippocampus with the dACC, and of the left amygdala
314 with the angular gyrus, appears to be associated with the variance shared by parental education and
315 family income, rather than to variance unique to each. Consistent with the multidimensional nature
316 of SES that reflects both economic and social facets of the familial environment and previous findings
317 suggesting that each may bear differently on child development [1,2,14,41,42], the present findings
318 highlight that parental education may have both unique effects on neural development and
319 combined effects with income.

320 Stronger parental education-related connectivity (i.e., hippocampus-dACC, right amygdala-dACC and
321 left amygdala-right angular connectivity) was associated with higher child prosocial behavior.
322 Prosocial behaviors include voluntary actions that respond to another's need or improve their
323 welfare (i.e., helping, consoling, sharing) and are mutually dependent on socio-cognitive abilities such
324 as empathy and mentalizing [62–65]. The amygdala, hippocampus, dACC and angular gyrus are
325 interconnected brain regions involved in empathy and mentalizing [64–68]. In older adolescents and
326 young adults, SES has been associated with the neural substrates of socio-cognitive abilities.
327 However, in children, while higher SES is associated with higher performance on mentalizing tasks
328 [69–71], no study to date has explored the neural correlates of this association [7]. Thus, the current
329 findings are the first to suggest that higher parental education may promote the development of the
330 neural substrates of child social abilities, with higher parental education predicting stronger rsFC
331 associated with prosocial behavior in 10 year-old children.

332 Children growing up in higher-SES families are more likely to be exposed to positive early experiences
333 promoting their development and brain maturation [5,6]. More educated parents generally provide
334 richer linguistic, cognitive and social stimulation [5]. Although speculative, it is possible that such
335 stimulation promotes the development of the neural substrates underlying child social abilities
336 through experience-dependent processes that regulate synaptogenesis and synaptic pruning (i.e.,
337 micro-mechanisms that underlie the maturation of brain connectivity). Through experience-
338 dependent processes, experience determines the strength and effectiveness of synaptic connections
339 based on their recruitment [24,72]. Parents who have higher levels of education may be better
340 equipped (e.g., access to and tendency to look for educational resources and information) to expose
341 their children to a variety of cognitively and socially stimulating situations. Such situations may
342 increase child prosocial behaviors resulting in frequent coactivation of brain regions involved in
343 prosociality, and in turn, strengthening the connectivity of these regions. Thus, the links between
344 brain connectivity and child prosociality observed here may be bidirectional.

345 Contrary to Barch and colleagues [39], who reported that higher family income during childhood
346 predicted stronger rsFC of the amygdala and hippocampus, no association between family income

347 and rsFC was found in the present study. This discrepancy may come from the different sample sizes
348 and populations. Barch and colleagues' sample was much larger than the current one (N = 105 vs. 28)
349 and thus provided better-powered analyses. Further, there was more income variability in their
350 sample: about 21% of their families were below the poverty line (as defined by an income-to-needs
351 ratio < 1; income-to-needs ratio range = 0 – 3.93) compared to 11% in the current sample (income-
352 to-needs ratio range = 0.7 – 3.5). These parameters may have limited our ability to detect family
353 income effects. Age effects may also explain the difference in the findings; Barch and colleagues
354 assessed family income when children were between 3 and 6 years old (vs. 7 months in the present
355 study). Another explanation for the absence of association between family income and rsFC in the
356 present study is that family income has been shown to be volatile and can change substantially from
357 early to late childhood [41]. Consistent with this, a recent study reported that mean 7-year family
358 income during adolescence was not associated with brain rsFC, but change in income across
359 adolescence predicted rsFC [38].

360 The current results must be interpreted in the context of some limitations. The links between SES
361 and child brain connectivity and socioemotional functioning may be underestimated because of the
362 limited statistical power, as well as the conservative use of covariates and severe *p*-value thresholds
363 and statistical corrections. Hence, these results should be considered preliminary and examined in
364 larger samples to test their generalizability, notably in samples including parents with very low
365 education levels (all parents in the current sample had at least a high school degree). Although the
366 short 5-minute rs-fMRI sequence used here was chosen to reduce the risk of motion artefacts in this
367 pediatric population and is sufficient to capture connectivity between the hippocampus and the
368 amygdala with the rest of the brain [45,46], the present results need to be replicated with longer rs-
369 fMRI sequences. Although longitudinal, the non-experimental design precludes causal inference and
370 notably does not allow us to rule out that child brain connectivity may be a genetic inheritance from
371 parents. However, a recent study reported that connectivity between the amygdala and the
372 prefrontal cortex is largely influenced by environmental factors [73], suggesting that brain
373 connectivity may be subject to only modest genetic influences. Finally, the lack of direct assessment
374 of stimulating environment input (e.g., linguistic, cognitive and social stimulation) prevented us from
375 testing the hypothesis that richer stimulation, presumably provided by more educated parents, may
376 promote the development of the neural substrates underlying child social abilities. Future studies
377 should assess such aspects of the familial environment to better understand the interactive
378 mechanisms through which parental education may promote child brain development.

379 **5.1. Conclusion**

380 This report suggests that higher parental education during infancy predicts more mature subcortical-
381 cortical rsFC in late childhood, which in turn is associated with higher concurrent prosocial behavior
382 in children. These findings are congruent with a growing literature suggesting that childhood SES is
383 associated with the development of the neural substrates of child social abilities [7]. In addition, they
384 re-emphasize the idea that small variations of SES within the normative range meaningfully relate to
385 child neural and socioemotional functioning. Nevertheless, child brain development is influenced by
386 many environmental factors inside and outside the family environment (e.g., siblings, daycare and
387 school experience, peers, etc.), and the present findings should in no way be taken to imply that only
388 higher parental education may promote better brain development. While the present results need
389 be replicated in larger and more diverse samples, this study provides rare evidence that parental
390 education may contribute to the development of rsFC between brain regions important for social
391 abilities in typically developing children.

392 **6. Appendix**

393 None

394 **7. Supplementary Material**

395 Secondary analyses are presented in supplementary Table S1 and Figures S1 and S2.

396

397 **8. Statements**

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407 **8.2. Statement of Ethics**

408 The present study has been approved by the local human research ethics committee and all families
409 have provided written informed consent for participation.

410 **8.3. Disclosure Statement**

411 The authors have no conflicts of interest to declare.

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416 **8.5. Author Contributions**

417 A.B., F.D. and M.B. conceived and designed the research; É.L. and V.D. collected the data; F.D.
418 analyzed the data and drafted the manuscript; all authors edited and revised the paper.

419

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10. Figure Legends

Fig. 1. Parental education during infancy predicts stronger positive functional connectivity between the left and right hippocampi and the right amygdala seeds with the dorsal anterior cingulate cortex (A, B, D), and stronger negative connectivity between the left amygdala and bilateral angular gyrus (C).

Fig. 2. Association between parental education and functional connectivity of the left hippocampus (A), right hippocampus (B), left amygdala (C) and right amygdala (D). Scatter plots are presented for descriptive purposes to illustrate the direction of the association. Abbreviations: dACC, dorsal anterior cingulate cortex; Lamyg, left amygdala; Lang, left angular gyrus; Lhipp, left hippocampus; Ramyg, right amygdala; Rang, right angular gyrus; Rhipp, right hippocampus.

Fig. 3. Scatter plots of partial correlations between functional connectivity and child social-emotional adjustment. Only significant associations are represented. Abbreviations: dACC, dorsal anterior cingulate cortex; Lamyg, left amygdala; Lhipp, left hippocampus; Rang, right angular gyrus; Rhipp, right hippocampus.

Fig. S1. Association between connectivity coefficients and parental education, adjusting for child age and sex, excluding the data from the three children of parents with lower education (<13 years of education). Scatter plots are presented for descriptive purposes to illustrate the direction of the association. Abbreviations: dACC, dorsal anterior cingulate cortex; Lamyg, left amygdala; Lang, left angular gyrus; Lhipp, left hippocampus; Ramyg, right amygdala; Rang, right angular gyrus; Rhipp, right hippocampus.

Fig. S2. Maternal education predicts stronger functional connectivity of the right hippocampus with the left superior frontal gyrus ($xyz = -14\ 3\ 74$, $k = 432$, $F = 50.46$, $p\text{-FWE} < .01$), the left inferior OPER frontal gyrus ($xyz = -48\ 10\ 6$, $k = 325$, $F = 33.84$, $p\text{-FEW} = .02$) and the dorsal anterior cingulate cortex ($xyz = 3\ 8\ 48$, $k = 432$, $F = 31.38$, $p\text{-FWE} < .01$).

Figure 1

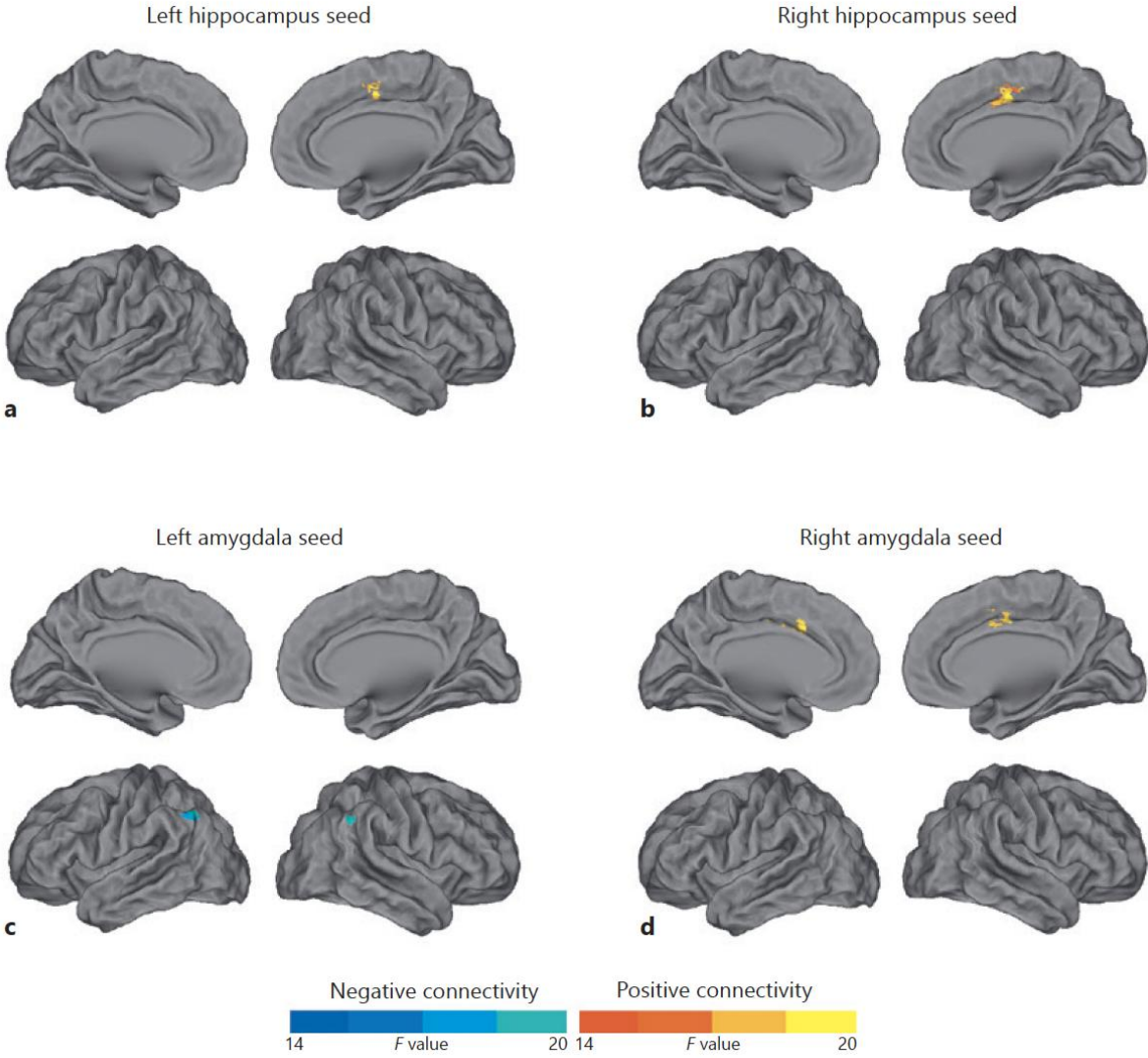
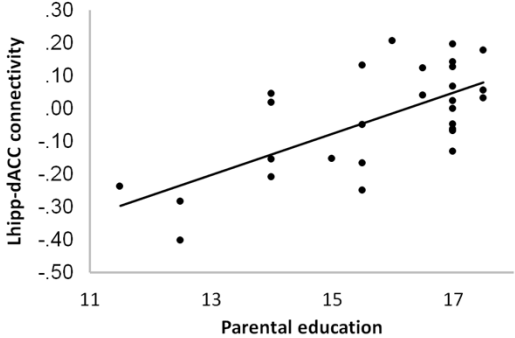
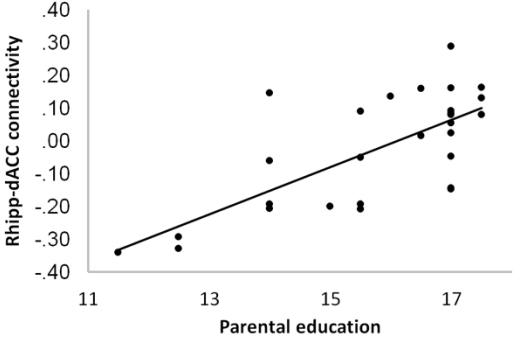


Figure 2

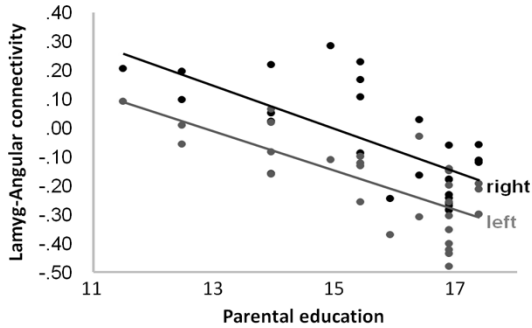
A. Left hippocampus seed



B. Right hippocampus seed



C. Left amygdala seed



D. Right amygdala seed

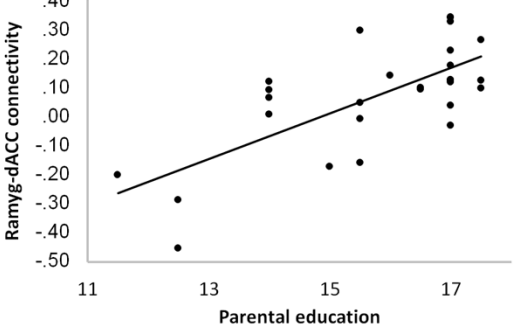


Figure 3

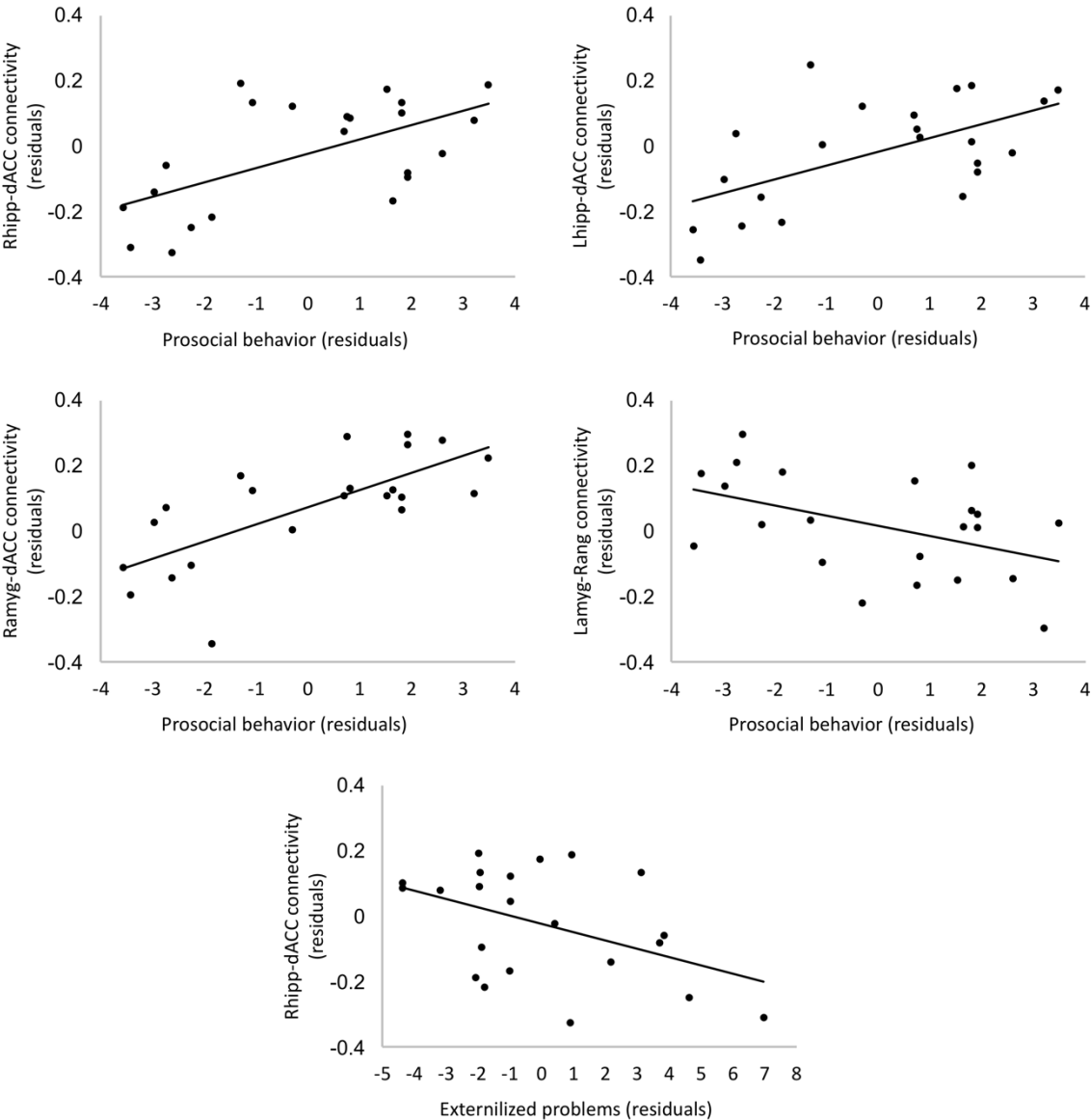
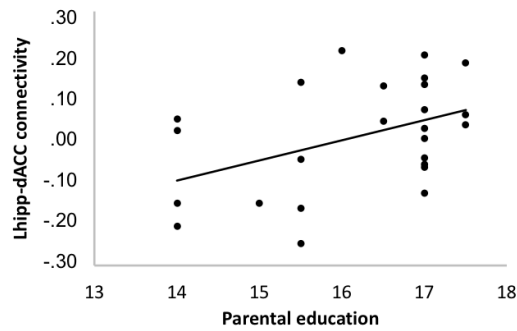
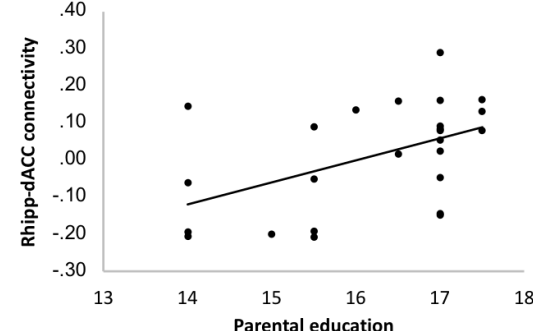


Figure S1

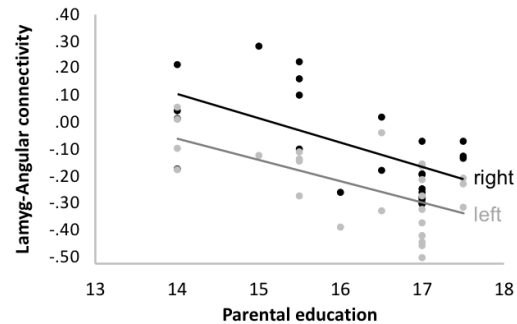
A. Left hippocampus seed



B. Right hippocampus seed



C. Left amygdala seed



D. Right amygdala seed

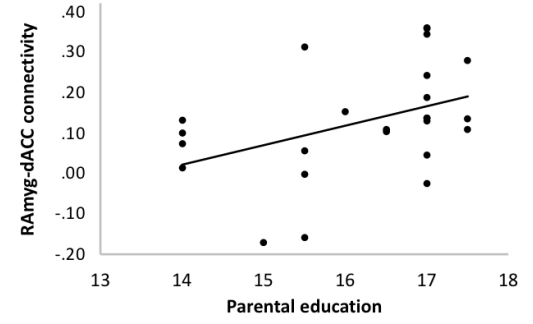


Figure S2

