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## **The Variability of Neural Responses to Naturalistic Videos Change with Age and Sex**

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40 **Abstract**

41 Neural development is generally marked by an increase in the efficiency and diversity of neural  
42 processes. In a large sample (N = 114) of human children and adults with ages ranging from 5 - 44  
43 years, we investigated the neural responses to naturalistic video stimuli. Videos from both real-life  
44 classroom settings and Hollywood feature films were used to probe different aspects of attention and  
45 engagement. For all stimuli, older ages were marked by more variable neural responses. Variability  
46 was assessed by the inter-subject correlation of evoked electroencephalographic (EEG) responses.  
47 Young males also had less variable responses than young females. These results were replicated in  
48 an independent cohort (N = 303). When interpreted in the context of neural maturation, we conclude  
49 that neural function becomes more variable with maturity, at least during the passive viewing of real-  
50 world stimuli.

51 **Significance Statement**

52 Naturalistic videos were used to probe response variability with EEG in a large developmental cohort.  
53 Our results are consistent with developmental theories positing that neural variability increases with  
54 maturation, and that neural maturation typically occurs earlier in females. These results differ from  
55 those observed with fMRI, where an increase in stereotyped responses with age is observed during  
56 development.

57 **Keywords**

58 Inter-subject correlation, electroencephalography, naturalistic stimuli, evoked responses, development

59 **Introduction**

60 This study examines the relationship between the variability of neural responses and  
61 development. Over the course of development, the accuracy and stability of behaviors generally  
62 increase. This performance improvement is typically accompanied by a seemingly paradoxical  
63 increase in the variability of neural responses both within and across subjects (Grady, 2012; Dinstein  
64 et al., 2015). More variable electroencephalographic (EEG) responses across trials, characterized by

65 an increase in dimensionality and entropy, are associated with lower reaction time variability and  
66 higher recognition accuracy (Mcintosh et al., 2008). Neural variability often presents as an increase in  
67 the complexity of neural responses. This may be due in part to a developmental increase in the  
68 repertoire of possible brain states (Vakorin et al., 2013) and this increase in complexity may underlie  
69 the integration between distributed neural populations (Vakorin et al., 2011). EEG signal complexity  
70 becomes elevated in late adolescence and is also elevated in females relative to males at this stage,  
71 indicating that females may attain mature brain functioning prior to males (Anokhin et al., 2000).  
72 Anatomical studies generally support the notion that females reach neural maturity prior to males  
73 (Giedd et al., 1999; Lenroot and Giedd, 2006; Lenroot et al., 2007; Marsh et al., 2008).

74 Neural variability does not always accompany proficient behavior, however. Both theta band  
75 coherence, a performance monitoring measure, and behavior are more variable across trials in  
76 children (Papenberg et al., 2013). This suggests that neural variability does not always increase with  
77 maturation. For adults, the variability in “functional connectivity” between different networks measured  
78 with fMRI is elevated during rest and decreases during a cognitive task. The reverse is true for  
79 children, whose brains become more variable during the task, and their performance is expectedly  
80 lower than adults (Hutchison and Morton, 2015).

81 Recently, responses to naturalistic narrative stimuli have been used to examine how variability  
82 in behavior and neural activity change with development. In these cases, variability is measured  
83 across subjects rather than within individuals because it is expected that if an individual has a less  
84 variable neural response across repeated renditions of stimulus, their neural response will also be  
85 more similar to others who are responding to the same stimulus. Adults watch *Sesame Street* more  
86 similarly to each other than infants do, as assessed by where their eyes fixate (Kirkorian et al., 2012).  
87 Additionally, adults have more broadly similar neural responses to *Sesame Street* than children  
88 (Cantlon and Li, 2013). While the neural responses of adults to *Sesame Street* correlate more with  
89 each other in many parietal and frontal regions, children correlate more strongly with each other in a

90 specific region in the superior temporal cortex (Cantlon and Li, 2013). Generally, from ages 18-88, as  
91 humans age, responses to videos increase in variability (Campbell et al., 2015). Taken together, these  
92 studies demonstrate that neural variability changes with age. The nature of this relationship depends  
93 on multiple factors including the metric of neural variability, the developmental stage sampled, and the  
94 brain region(s) of interest.

95 Here, EEG was recorded from subjects with ages ranging from 5 - 44 years as they were  
96 presented with both naturalistic (Dmochowski et al., 2012, 2014) and conventional stimuli. To assess  
97 neural variability, the level of similarity across subjects was assessed with the inter-subject correlation  
98 (ISC) of responses evoked by the stimuli. ISC of the EEG is indicative of attention, engagement, and  
99 memory in healthy adults (Dmochowski et al., 2014; Cohen and Parra, 2016; Ki et al., 2016; Cohen et  
100 al., 2017) . We found that neural responses, indexed by ISC, become more variable with age. Among  
101 children, females have more variable neural responses than males. This increase in variability is not  
102 due to a decrease in evoked response magnitude, and was reproduced in two independent cohorts  
103 consisting of 114 and 303 individuals. These results are consistent with theories positing that  
104 development coincides with an increased repertoire of neural representations (Mcintosh et al., 2008),  
105 and the sex differences are consistent with the idea that young males are less neurally mature than  
106 young females (Giedd et al., 1999; Lenroot and Giedd, 2006; Lenroot et al., 2007; Marsh et al., 2008).  
107 Importantly, this is the first EEG study to report a measure of across-subject neural similarity with clear  
108 age and sex effects.

## 109 **Methods**

### 110 *Subjects*

111 In the main study ages ranged from 6 to 44 years old (N = 114, 14.2 +/- 8.0 years old, 46 females, see  
112 Figure 1A for a full age and sex distribution) as part of the Child Mind Institute - Multimodal Resource  
113 for Studying Information Processing in the Developing Brain (MIPDB;  
114 [http://fcon\\_1000.projects.nitrc.org/indi/cmi\\_eeg/](http://fcon_1000.projects.nitrc.org/indi/cmi_eeg/); (Langer et al., 2017)). In the replication study ages

115 ranged from 5 to 21 years old (N = 303, 11.3 +/- 3.9 years old, 135 females, see figure 1B for a full  
116 age and sex distribution). This data was obtained from the Child Mind Institute Healthy Brain Network  
117 (CMI-HBN; [http://fcon\\_1000.projects.nitrc.org/indi/cmi\\_healthy\\_brain\\_network/](http://fcon_1000.projects.nitrc.org/indi/cmi_healthy_brain_network/); (Alexander et al.,  
118 2017)). Both the main and replication study data come from publically available datasets. All  
119 experiments were performed in accordance with relevant guidelines and regulations. The study was  
120 reviewed and approved by the Chesapeake Institutional Review Board. All subjects presented with  
121 normal or corrected to normal vision.

### 122 *Stimuli*

123 Engaging, naturalistic videos were the primary stimuli. Specific videos were selected because they  
124 contained content relevant to social cognition, classroom anxiety, and attention. Three videos featured  
125 either educational content or depicted classroom scenarios: *Fun with Fractals* (Fract, MIT), a cartoon  
126 that explains fractals with examples (4m 34s), *How to improve at Simple Arithmetic* (Arith, E-How), in  
127 which a math teacher in a typical educational setting explains addition and multiplication (1m 30s),  
128 and *Pre-Algebra Class* (StudT, Pearson Education)), showing an interaction between two students  
129 and a teacher (StudT, for student-teacher interaction) during math problem solving (1m 40s). Two  
130 videos were clips from conventional cinema: *Diary of a Wimpy Kid* (Wimpy, Universal Pictures), a  
131 movie about a preteen starting middle school (1m 57s), and *Despicable Me* (DesMe, Universal  
132 Pictures), which contains infant and toddler characters and emphasizes social interactions (2m 51s).  
133 While the main cohort contains data from all stimuli, the replication cohort only had three stimuli:  
134 Wimpy, Fract, and DesMe. The variability of the neural responses to these videos was measured  
135 across subjects using the inter-subject correlation (ISC) of evoked responses (see below). As a  
136 control condition, a “Rest” condition, during which subjects sat with their eyes-closed for 4m 20s, was  
137 also analyzed. This period establishes the baseline level of ISC, as no time-aligned stimulus  
138 entraining neural activity across subjects was presented. Finally, “Flash”, a stimulus condition without  
139 any narrative content was used. During this stimulus a black and white grating pattern that flashed at

140 25 Hz was presented for three minutes, thus synchronously stimulating neural activity across subjects  
141 (see Steady State Visual Evoked Potentials (SSVEP) Methods section). This stimulus elicits steady  
142 state evoked potentials (Vanegas et al., 2015) and was included to explore the extent to which ISC is  
143 driven by low level evoked responses.

#### 144 *Procedure*

145 While seated in a dimly lit room wearing an EEG net, subjects watched a series of short videos in a  
146 pseudorandom order. Stimuli were presented on a 17-inch CRT monitor (SONY Trinitron Multiscan  
147 G220, display dimensions 330×240 mm, resolution 800×600 pixels, vertical refresh rate of 100 Hz).  
148 Note that some subjects did not experience all stimuli due to time limitations (Langer et al., 2017).  
149 Additionally, as explained below, poor data quality for some recordings caused additional data loss.  
150 For the replication study, only three conditions were used: Wimpy, Fract and DesMe.

#### 151 *EEG recordings and preprocessing*

152 EEG recordings were performed with an EGI Clinical Geodesic 128 channel system (Electrical  
153 Geodesic Inc, Eugene, OR). Of the 128 channels recorded, 105 constituted the EEG recording and 11  
154 represented EOG channels used for eye movement artifact removal. The remaining channels, mainly  
155 recording from the neck and face, were discarded. First, noisy channels were selected by visual  
156 inspection and replaced with by zero valued samples, thus eliminating those channels' contribution in  
157 subsequent calculations of covariance matrices. Recordings, initially at 500 Hz, were then  
158 downsampled to 125 Hz, high-pass filtered at 1 Hz, and notch filtered between 59 and 61 Hz with a  
159 4th-order Butterworth filter. Eye artifacts were removed by linearly regressing the EOG channels from  
160 the scalp EEG channels (Parra et al., 2005). Next, a robust Principal Components Analysis (PCA)  
161 algorithm, the inexact Augmented Lagrange Multipliers Method (Lin et al., 2013), was used to remove  
162 sparse outliers from the data following Ki et al (2016). Briefly, robust PCA recovers a low-rank matrix,  
163  $A$ , from a corrupted data matrix  $D = A + E$ , where some entries of the additive errors  $E$  may be  
164 arbitrarily large. Finally, individual recordings for some stimuli were discarded on the basis of visual



165 inspection because they remained noisy after both automatic and manual noise removal. This was  
166 necessary because these subjects exhibited profound movement artifacts and/or the saline used for  
167 the recordings dried out. Despite these steps taken, the data overall appear to be of poorer quality  
168 than that collected in an electrically shielded room with conductive gel (saline was used here). The  
169 noise in the data may have led to the relatively low ISC values reported in the paper compared to  
170 previous studies (Ki et al, 2016; Cohen et al, 2017). However, it is unlikely that the noise contributed to  
171 our results as under baseline conditions (Rest), there was no difference in power between the cohorts  
172 (see Results). All signal processing was performed offline using MATLAB software (MathWorks,  
173 Natick, MA, USA).

#### 174 *Inter-Subject Correlation (ISC)*

175 As variability is the inverse of similarity, we measured the similarity of evoked EEG responses across  
176 subjects. This approach has been used extensively to study concerted, inter-subject changes in blood-  
177 oxygen level dependent (BOLD) signal in fMRI (Hasson et al., 2004, 2009; Kauppi et al., 2010), and  
178 has been adapted to leverage the improved time resolution facilitated by EEG. To determine the  
179 neural similarity across subjects responding to the same stimulus (or in the same condition, in the  
180 case of Rest) the inter-subject correlation (ISC) of the EEG signal was computed, as described  
181 previously (Dmochowski et al., 2012, 2014; Cohen and Parra, 2016; Ki et al., 2016). ISC assesses the  
182 level of correlation in the EEG across time among a group of subjects as they respond to the same  
183 stimulus. Larger ISC values imply more similarity in fast EEG responses across subjects (< 1s). This  
184 indicates that the signals are more reliable due to decreased inter-subject variability. It has also been  
185 found that subjects who pay more attention to the stimulus have higher ISC values (Ki et al., 2016). An  
186 advantage of the technique is that the stimulus need only be presented once to each subject because  
187 evoked responses are compared across individuals. As repeated trials are unnecessary, responses  
188 are more similar to natural situations in which people experience uniquely presented novel stimuli.  
189 Additionally, in contrast to event related potentials, the technique can be applied to continuous and



190 dynamic natural stimuli without the need for specific event markers (Ben-Yakov et al., 2012). As such,  
 191 the approach is data-driven both spatially and temporally. The approach is “data driven” spatially  
 192 because the data from the subjects determines the best combination of electrodes (which are spatially  
 193 distributed across the scalp and therefore may correspond with different anatomical regions) that  
 194 maximize the correlation across subjects. The approach is “data driven” temporally because the  
 195 ultimate correlation values are determined by the temporal fluctuations in the EEG signals. In contrast,  
 196 a more traditional approach to EEG data analysis would be to select electrodes that have previously  
 197 been shown to elicit a certain effect (or ERP) and measure event-locked responses from these  
 198 electrodes. We are not taking this approach. Rather, the electrodes that we chose and the time  
 199 periods that maximize correlation are determined directly by the data itself.

200 ISC utilizes correlated component analysis to identify linear combinations of EEG electrodes  
 201 that capture most of the correlation across subjects (Dmochowski et al., 2012). Correlated component  
 202 analysis is similar to principal component analysis (PCA) except that rather than maximizing variance  
 203 within one dataset, it selects projections,  $v \in \mathbf{R}^D$ , where  $D$  is the number of electrodes, that maximize  
 204 the correlation between multiple datasets. These projections can be thought of as virtual sensors (or  
 205 component sources) of activity that are optimized to capture most of the correlation between subjects.  
 206 They are the eigenvectors of  $R_W^{-1}R_B$ . Where  $R_W$  is the average within-subject covariance:  $\frac{1}{N} \sum_k R_{kk}$ ,  
 207 and  $R_B$  is the average between subjects cross-covariance:  $\frac{1}{N(N-1)} \sum_k \sum_{l, l \neq k} R_{kl}$ , and  $R_{kl} = \sum_t (x_k(t) -$   
 208  $\bar{x}_k) (x_l(t) - \bar{x}_l)^T$  measures the cross-covariance of all electrodes in subject  $k$  with all electrodes in  
 209 subject  $l$ . Vector  $x_k(t)$  is the scalp voltages at time  $t$  in subject  $k$  and  $\bar{x}_k$  is their mean value in time.

210 Following previous research, we use the three components, or eigenvalues of  $R_W^{-1}R_B$ , that  
 211 represent the largest fraction of the correlation across subjects. These components can be optimized  
 212 for all subjects together, or for a subset of the entire cohort. The subsets used in this paper are  
 213 stimulus (Wimpy, DesMe, Fract, Arith, StudT, Flash, and Rest), age group (young vs old), sex (male

214 vs female), and sex and age group combined (young-male, young-female, old-male, and old-female).  
 215 ISC components are computed within subsets of the entire sample to examine potential differences in  
 216 the spatial distribution of activity across groups, although the spatial patterns are largely consistent  
 217 (Figure 7).

218 To calculate the ISC for individual subjects as they respond to the same condition as their  
 219 peers, the correlation between each individual's EEG responses and the responses from all other  
 220 individuals is calculated (Cohen and Parra, 2016; Ki et al., 2016). The ISC values reported throughout  
 221 the paper are this measure of how well each individual correlates with the others. The projections,  
 222  $v \in R^D$ , used to compute this subject-specific ISC value are either computed across all subjects or  
 223 within the subgroups listed above (divided by either stimulus, age, sex, or age and sex). The ISC for  
 224 each subject is therefore:

$$225 \quad C_{ik} = \frac{v_i^T R_{b,k} v_i}{v_i^T R_{w,k} v_i},$$

226 where  $R_{b,k} = \frac{1}{(N-1)} \sum_{l,l \neq k} (R_{kl} + R_{lk})$ , and  $R_{w,k} = \frac{1}{(N-1)} \sum_{l,l \neq k} (R_{kk} + R_{ll})$ . ISC for subject  $k$  is therefore  
 227  $\sum_{i=1}^3 C_{ik}$ . A simplified template for the code to compute the correlated components and the ISC for  
 228 individual subjects is available at <http://www.parralab.org/isc/>

### 229 *Steady state visual evoked potentials (SSVEPs)*

230 To determine the strength of low-level sensory evoked responses across individuals, we leveraged the  
 231 steady state visual evoked potential (SSVEP) paradigm (Flash) that was part of the data collection  
 232 effort (Langer et al., 2017). Stimulus and analysis followed established techniques (Vanegas et al.,  
 233 2015). Briefly, the stimulus consisted of four circular 'foreground' stimuli (vertical grating, radius  $2^\circ$ )  
 234 that were flickered on-and-off at 25 Hz and embedded in a static 'background' grating, which is known  
 235 to generate reliable SSVEPs (Vanegas et al., 2015). This stimulus was presented in trials of 2.4 s  
 236 duration with inter-trial intervals of 1s which included a fixation cross presented for 0.5 s. The stimuli  
 237 were presented in several conditions that varied in their contrast and in the phase relationship

238 between the foreground and the background. A total of 128 trials were present (12 conditions total:  
239 four foreground contrasts - 0% 30%, 60% and 100%, and three background conditions - parallel  
240 phase, orthogonal phase, and no surround stimuli). Artifacts were rejected by removing trials for which  
241 the power (or absolute value) of any electrode exceeded more than three standard deviations above  
242 the mean. EOG activity was regressed out of the EEG, as described above. The initial 200ms of each  
243 trial was removed to eliminate the onset of the visual evoked response. Data were Fourier  
244 transformed for each trial, power in a 0.5 Hz bin surrounding the 25 Hz band was extracted, and then  
245 averaged across all trials, regardless of condition (thus ignoring details of the foreground-background  
246 interaction). Since the EEG activity measured with this paradigm is known to be dominated by primary  
247 visual cortex (V1) responses, power was averaged over the five most relevant occipital electrodes  
248 (O1-O5; (Vanegas et al., 2015)).

#### 249 *Dimensionality of EEG Responses*

250 To gain a sense of the dimensionality of the EEG responses across subjects, the eigenvalue spectrum  
251 was extracted from each subject's covariance matrix (covariance between all electrodes measured  
252 across time). These covariance matrices measure the correlation between electrodes for each  
253 subject. The sum of the eigenvalues represent the overall power in the data. To assess the  
254 dimensionality of the data, lines were fit to the loglog plot of the eigenvalue spectrum of each subject's  
255 covariance matrix. A shallower slope of the linear fit indicates that there is appreciable power over  
256 a larger number of dimensions. Two-way ANOVAs and subsequent post-hoc t-tests were employed to  
257 compare power and the slopes of these linear fits for each age and sex group both across all stimuli  
258 and within each stimulus.

#### 259 **Results**

260 We sought to determine whether and how the variability of EEG differs across age and gender in  
261 children and adults ranging from 6 – 44 years of age. To assess the variability in EEG signals across  
262 subjects, the intersubject correlation (ISC) between individuals and their peers was assessed in

263 response to both naturalistic videos and artificial stimuli. ISC can be thought of as a measure of the  
264 similarity of neural responses (Dmochowski et al., 2012). If subjects respond more similarly to their  
265 peers, they will have a larger ISC value, which indicates that they have a less variable neural  
266 response.

267 *Intersubject correlation varies between stimuli*

268 ISC is a stimulus-driven measure of attention (Ki et al., 2016) because neural responses are more  
269 correlated across subjects when they naturally attend to a stimulus than when they are engaged in a  
270 dual task. It is therefore expected to be indicative of varying levels of engagement (Cohen et al.,  
271 2017). A one-way ANOVA determined that ISC significantly depended on the stimulus ( $F(7) = 78.26$ ,  $p$   
272  $= 10^{-68}$ ; mean +/- STD ISC values: Wimpy: 0.053 +/- 0.036; DesMe: 0.035 +/- 0.023; Arith: 0.019 +/-  
273 0.013; Fract: 0.026 +/- 0.016; StudT: 0.012 +/- 0.009; Flash: 0.030 +/- 0.019; Rest: 0.001 +/- 0.004),  
274 indicating that the stimuli significantly varied in engagement level (Cohen et al., 2017). It is worth  
275 noting that these ISC values are relatively low compared to previous research (Cohen and Parra,  
276 2016; Ki et al., 2016). There are two factors that contribute to this discrepancy: the lower production  
277 quality and therefore engagement level elicited by these stimuli and the relatively poor quality of the  
278 EEG data (see Methods). Note also that ISC for EEG is generally lower than ISC of fMRI (e.g.  
279 Lahnakoski et al., 2017) which has a slower time scale and higher signal-to-noise ratio, both factors  
280 that can contribute to higher correlations (Haufe et al., 2017). As expected, ISC in the Rest condition  
281 was not significantly different from zero (t-test,  $t(45) = 0.52$ ,  $p = 0.4$ ), confirming the notion that ISC  
282 reflects stimulus-induced correlations (Dmochowski et al., 2012). A one-way ANOVA was therefore  
283 performed on all stimuli excluding Rest, confirming that ISC strongly varies between stimuli ( $F(6) =$   
284  $71.70$ ,  $p = 10^{-55}$ ). Tukey post-hoc pairwise comparisons revealed that ISC was significantly stronger  
285 when evoked by the qualitatively more engaging stimuli (Wimpy and DesMe), than it was for  
286 educational videos (Arith, Fract, StudT; Tukey post-hoc pair-wise comparisons between each pair of  
287 videos, Tukey's HSD:  $p < 10^{-4}$ ). Among the more engaging videos from conventional cinema, Wimpy,

288 a movie trailer for the feature film “Diary of a Wimpy Kid”, evoked a higher level of neural similarity  
289 than DesMe, a scene from the animated film “Despicable Me” (Tukey’s HSD:  $p = 10^{-7}$ ). Among the  
290 relatively less-engaging educational videos, Fract elicited the highest level of ISC, which was  
291 significantly higher than StudT (Tukey’s HSD:  $p = 10^{-6}$ ), but not Arith (Tukey’s HSD:  $p = 0.2$ ).  
292 Interestingly, Arith elicited a level of ISC similar to Flash (Tukey’s HSD:  $p = 0.5$ ), and the level of ISC  
293 elicited by Flash was significantly higher than StudT (Tukey’s HSD:  $p = 10^{-7}$ ).

#### 294 *Intersubject correlation decreases with age*

295 We hypothesized that neural similarity changes with age and therefore examined the correlation  
296 between ISC and age. Here, ISC is computed in individuals by measuring the extent to which each  
297 subject correlated with the other people in the same stimulus condition. For all of the stimuli excluding  
298 Rest, there was a negative relationship between age and ISC (all  $r$ 's = -0.68 +/- 0.09, all  $p$ 's <  $10^{-10}$ , FDR  
299 corrected following Benjamini and Hochberg (1995), Figure 2). ISC did not vary with age during Rest  
300 ( $r = -0.10$ ,  $p = 0.5$ ,  $N = 46$ ). This was expected since Rest contained no stimulus to drive EEG signal  
301 similarly across subjects.

302 These results indicate that ISC decreases with age. However, most of the subjects in the main  
303 study were from the lower half of the age distribution (see Figure 1A). Since the components used to  
304 measure ISC are optimized to capture the correlation across all subjects, the components may have  
305 been biased by these younger subjects who constituted a majority of the sample. The cohort was  
306 therefore divided into two age groups of equal size to eliminate this potential measurement bias. The  
307 median split resulted in groups whose ages ranged from 6-14 (mean age 10.74 +/- 2.03) and 15-44  
308 (mean age 23.65 +/- 8.04). The ISC was then recomputed from components extracted separately in  
309 each group. A two-way ANOVA with factors of age and stimulus revealed that ISC was significantly  
310 modulated by both stimulus (all excluding Rest,  $F(5, 393) = 63.64$ ,  $p = 10^{-47}$ ) and age ( $F(1, 393) =$   
311  $335.46$ ,  $p = 10^{-53}$ , Figure 3A). For all stimuli, ISC was much higher in the younger age group.

#### 312 *Intersubject correlation is elevated in males*

313 Sex is an important factor that influences the developmental trajectory of the human brain (Giedd et  
314 al., 1999; Lenroot and Giedd, 2006; Lenroot et al., 2007; Marsh et al., 2008). We therefore explored  
315 the relationship between sex and ISC. A two-way ANOVA with factors of sex and stimulus (excluding  
316 Rest) revealed main effects for both sex ( $F(1, 393)=53.11$ ,  $p = 10^{-12}$ ) and stimulus ( $F(5, 393) = 30.12$ ,  
317  $p = 10^{-26}$ , Figure 3B). Tukey's post hoc tests revealed that ISC was consistently higher in males for all  
318 stimuli except for Flash where it was marginally significant (Flash:  $p = 0.06$ ; Wimpy:  $p = 0.03$ ; DesMe:  
319  $p = 10^{-6}$ ; Arith:  $p = 0.003$ ; Fract:  $p = 10^{-4}$ ; StudT:  $p = 10^{-4}$ ). To examine whether the sex difference  
320 depended on age, the data was separated into four groups with the same age division between 14  
321 and 15 years as above (young-male, young-female, old-male, old-female). ISC was measured within  
322 each group and averaged across all stimuli available for each subject to ensure sufficiently large  
323 sample sizes (excluding control conditions - Flash and Rest, Figure 4). A two-way ANOVA with sex  
324 and age as factors confirmed the age effect ( $F(1, 87) = 98.85$ ,  $p = 10^{-16}$ ), and the sex effect was  
325 marginally significant ( $F(1, 87) = 3.83$ ,  $p = 0.05$ ). A direct comparison between the sexes in each age  
326 group revealed that the sex effect was marginally significant among the young ages ( $t(53)=2.02$ ,  
327  $p=0.05$ , 6-14 years), but not present for the old ages ( $t(33)=0.28$ ,  $p=0.8$ , 15-44 years).

328 *The effect of age on inter-subject correlation is not due to evoked response difference*

329 The relationships between ISC, age, and sex may be partially driven by the reduction of evoked  
330 response magnitude with age (Goodin et al., 1978; Tomé et al., 2015). Although correlation, which  
331 ISC measures, is theoretically independent of magnitude, it is possible that a decrease in magnitude  
332 corresponds with a decrease in the signal-to-noise ratio, which would result in a smaller ISC. The  
333 magnitude of evoked responses was therefore assessed with the Flash stimulus which elicited steady-  
334 state visually evoked potentials (SSVEPs, see Methods). SSVEP magnitude weakly declines with age  
335 ( $r=-0.22$ ,  $p=0.02$ ,  $N=109$ , Figure 5A) and a two-way ANOVA with age and sex as factors (the same  
336 age/sex groups as Figure 4) found the age effect to be marginally significant ( $F(1,106)=4.00$ ,  $p=0.05$ ,

337 Figure 5B). There was no significant relationship between sex and SSVEP strength ( $F(1,106)=3.3$ ,  
338  $p=0.08$ ).

339 Since both SSVEP amplitude and ISC decrease with age, we reasoned that SSVEPs could be  
340 used to factor out the effect of evoked response strength (Goodin et al., 1978; Tomé et al., 2015).  
341 Indeed, ISC and SSVEP amplitude are correlated across subjects ( $r = 0.41$ ,  $p = 0.0001$ ,  $N = 84$ ,  
342 Figure 6A). To control for the effect of evoked response strength, each individual's SSVEP amplitude  
343 was linearly regressed against ISC, and the portion that could be explained by the SSVEP was  
344 subtracted (ISC calculated within the same age/sex group as Figure 4). A two-way ANOVA with age  
345 and sex as factors revealed that this residual ISC still significantly varies with age ( $F(1,81)=85.49$ ,  $p =$   
346  $10^{-14}$ ), but does not vary with sex ( $F(1,81)=0.08$ ,  $p = 0.8$ , Figure 6B). Additionally, the sex effect is no  
347 longer present in the younger group when SSVEP strength is controlled for ( $t(49)=0.11$ ,  $p=0.9$ ). The  
348 lack of a sex effect may mean that the relationship between sex and neural variability is due in part to  
349 evoked response magnitude, but the lack of an effect may also result from the reduced number of  
350 subjects for which SSVEP magnitude was available: 84 vs 114. Regardless, neural variability, as  
351 assessed by ISC, does increase with age, regardless of the strength of evoked responses.

352 *Correlated component topographies similar across age and sex groups.*

353 ISC was measured using components of the EEG that maximize correlations between subjects. These  
354 components are linear combinations of electrodes and can be thought of as virtual sensors (See  
355 Methods). To determine if the spatial distribution of the corresponding activity differed across groups,  
356 the “forward model,” which represents how the components look on the surface of the scalp, was  
357 computed for the largest three components which were used to compute ISC (Parra et al., 2005).  
358 These component topographies were very similar across all age/sex groups for the strongest two  
359 components - C1 and C2 (Figure 7, minimum cosine similarity was 0.97 for C1 and 0.78 for C2). The  
360 third component (C3) was less similar across the groups (cosine similarity ranged from 0.89 to 0.31),  
361 but it also constituted a much weaker portion of the ISC ( $C1 = 0.016 \pm 0.009$ ,  $C2 = 0.008 \pm 0.005$ ,



362 and C3 = 0.004 +/- 0.003, computed as in Figure 4 and averaged across all subjects and stimuli).

363 Thus, for the most part, differences in ISC between age and sex groups were not due to differences in  
364 the spatial distribution of neural activity across these groups.

### 365 *Dimensionality of EEG Responses*

366 To determine whether the differences in ISC across groups was due to diverse responses across  
367 subjects or to more highly dimensional responses within subjects, the eigenvalue spectra of the EEG  
368 covariance matrices were analyzed (Figure 8). The sum of these spectra represents the overall power  
369 of the data. In general, the younger age group (using the same median split as above) had more  
370 power than the older age group across all stimuli ( $F(1,438) = 452.13, p = 10^{-69}$ ). This suggests that  
371 there was more overall power in the EEG of the young group. This power difference was only present  
372 during the stimuli, not during rest ( $t(44) = 0.6, p = 0.5$ ), suggesting that younger subjects have stronger  
373 stimulus driven evoked responses. To assess the dimensionality of the EEG responses, a linear  
374 model was fit to each subject's eigenvalue spectrum (see Methods), and the slopes were compared  
375 between the groups. A difference in dimensionality is reflected by a difference in this slope, with a  
376 shallower slope indicating that there is a higher number of dimensions with appreciable signal. The  
377 slopes of the linear fit did not differ across the age groups (across all stimuli:  $F(1,438) = 2.74, p = 0.1$ ).  
378 This suggests that the stimulus evoked responses are not inherently higher dimensional in the young.  
379 For the sex comparison, males had higher overall power (across all stimuli:  $F(1,438) = 71.25, p = 10^{-16}$ ),  
380 for all stimuli and not during rest ( $t(44) = 0.9, p = 0.3$ ). Here females had a shallower slope than  
381 males (across all stimuli:  $F(1,438) = 152.12, p = 10^{-30}$ ). This suggests a greater complexity of  
382 responses within females.

### 383 *Replication of results*

384 To confirm these findings, the results were replicated in an independent cohort (N=303) with a  
385 reduced stimulus set: Wimpy, Fract, and DesMe. Replicating the results above, ISC also decreased  
386 with age in this cohort (Wimpy:  $r = -0.44, p = 10^{-14}, N = 276$ ; Fract:  $r = -0.37, p = 10^{-10}, N = 270$ ;

387 DesMe:  $r = -0.41$ ,  $p = 10^{-12}$ ,  $n=281$ , Figure 9A). A two-way ANOVA with age and condition as factors  
388 revealed that ISC is modulated by age ( $F(1,799) = 35.33$ ,  $p = 10^{-9}$ ) and stimulus ( $F(2,799) = 272.903$ ,  
389  $p = 10^{-91}$ , Figure 9B). A two-way ANOVA with sex and stimulus as factors revealed that ISC was also  
390 significantly modulated by sex ( $F(1,823) = 11.12$ ,  $p = 0.0009$ , Figure 9C), and stimulus ( $F(2,823) =$   
391  $430.95$ ,  $p = 10^{-129}$ ). Finally, a two-way ANOVA which divided the data across age and sex groups, and  
392 averaged ISC across stimuli, replicated the main effect of age ( $F(1,291) = 17.68$ ,  $p = 10^{-5}$ ), and did not  
393 find an effect of sex ( $F(1,291) = 2.59$ ,  $p = 0.1$ , Figure 9D). Follow up analyses that examined a  
394 potential sex difference in ISC in each age group revealed that the difference in ISC was present  
395 among the young ages ( $t(224)=2.29$ ,  $p=0.02$ , 5-14 years), but not the old ages ( $t(67)=0.59$ ,  $p=0.6$ , 15-  
396 21 years). When the median was calculated according to the median of the replication distribution  
397 (split at 10/11 years, see Figure 1B for age distribution), the above results were unchanged. In  
398 summary, all results from the main experiment replicated in this independent cohort.

#### 399 **Discussion**

400 The present work demonstrated age- and sex- related variability among individuals with respect to  
401 their neural responses to complex naturalistic stimuli. Specifically, ISC was significantly correlated with  
402 age for both naturalistic videos and artificial visual flashes. Younger subjects (6-14 years) exhibited  
403 less variable neural responses than older subjects (15-44 years). A parallel finding revealed that  
404 young males exhibited more similar responses to the stimuli than young females, a difference which  
405 was only present in the younger cohort. These age and sex effects may result from neural  
406 development, consistent with the notion that neural maturation occurs later in males than in females  
407 (Lenroot et al., 2007; Marsh et al., 2008; Mous et al., 2017). A quantitative analysis of the spatial  
408 distribution of the correlated activity revealed that the observed age and sex differences are largely  
409 driven by the same neural components, lending more weight to the idea that the observed differences  
410 in age and sex stem from a common developmental feature. Finally, a replication study with 303  
411 participants yielded similar results.

412 A possible confound for the present results is that the neural correlations found across  
413 subjects are due to correlations in overt behaviors such as eye movements. However, it is unlikely that  
414 eye movements follow the same developmental trajectory as neural responses because eye  
415 movement trajectories evoked by videos actually become more similar with age (Kirkorian et al.,  
416 2012). Thus, although the gaze patterns evoked by videos seem to converge with maturity, potentially  
417 driving similar bottom-up neural processes, neural similarity as measured by ISC, *decreases* with age.  
418 This indicates that patterns of neural activity may potentially increase in their diversity with age as top-  
419 down factors relating to the interpretation of naturalistic stimuli develop. Even in the condition where  
420 subjects were instructed to maintain a fixed gaze position (Flash), ISC decreased with age. Future  
421 studies with fine-grained eye-tracking during EEG could more definitively answer this question.

422 The observed ISC magnitude changes with age and sex may also be partially dependent on  
423 evoked response magnitudes which typically decrease with age. While the amplitudes of auditory  
424 event related potentials and their components decline with age (Goodin et al., 1978; Tomé et al.,  
425 2015), other components increase with age (Dinteren et al., 2014), or remain stable across  
426 development (Kujawa et al., 2013). Although correlation, as measured by ISC, is in principle  
427 insensitive to magnitude, it is possible that weaker stimulus evoked responses in adults may be  
428 overpowered by non-stimulus related neural activity (i.e., “noise”) (Hammerer et al., 2013). In this  
429 case, a smaller fraction of the signal would correlate across adults in comparison to children. To  
430 control for the effect of age, the magnitude of steady state visual evoked potentials (SSVEPs) was  
431 regressed from the ISC. The result indicates that SSVEP amplitude cannot explain the age effect, but  
432 it may explain the sex effect, indicating that males have stronger evoked responses than females  
433 (Figure 3B and 6B). However, it is worth noting that ISC and SSVEPs measure very different facets of  
434 neural activity. SSVEPs, extracted from early visual processing areas in V1, likely represent low-level  
435 visual processes. ISC, on the other hand, may be driven by higher level cortical areas since the spatial  
436 distributions of the two dominant components (Figure 7) do not resemble low-level sensory evoked

437 responses. Parallel work indicates that the first component (C1), which captures the majority of the  
438 correlated activity, is a supramodal component that is driven by both auditory and visual stimuli  
439 (Cohen and Parra, 2016).

440         It is also possible that ISC decreases with age because adults process the world with more  
441 diverse brain activity. In this view, adults have more highly variable stimulus-evoked responses and  
442 their neural activity is therefore less similar across subjects. In this case, it would be likely that the  
443 dimensionality of neural responses, a measure of their complexity, increases with age (Anokhin et al.,  
444 2000; Mcintosh et al., 2008; Vakorin et al., 2013). There was no clear trend, indicative of a difference  
445 in the dimensionality between the young and old group. However, it does appear that females have  
446 more diverse responses than males, a result that deserves further exploration and could possibly  
447 underlie the reduction in ISC in this group.

448         The present results appear to be consistent with Campbell et al. (2015), who using fMRI also  
449 found a decrease of ISC with age. However, while we study an age range dominated by development  
450 and corresponding improvements in cognitive performance (between 6-44 and 5-23 years in each  
451 cohort), Campbell et al. (2015) examined a range (18-88 years) that exhibited a deterioration in fluid  
452 intelligence and reaction time. These measures correlated with a decrease in ISC. While Cantlon and  
453 Li (2013) studied a cohort that was more comparable to ours in age (4 to 25 years), they find that ISC  
454 of fMRI was generally higher among adults (above age 18) than it was in children (below age 11). In  
455 total, it appears that ISC as assessed by fMRI increases with development and declines in older age,  
456 which potentially opposes our result with EEG. These differences may be due to important  
457 methodological discrepancies between these studies and ours. To more definitively establish the  
458 effect of age on ISC more work should be done using both fMRI and EEG.

459         The idea that maturity is marked by variability is not new (Campbell et al., 2015). It aligns with  
460 theories from neural systems modeling and human studies (Mcintosh et al., 2008; Vakorin et al.,  
461 2011). In these models, moderate amounts of noise or variability facilitate efficient responses in

462 complex environments. Increased variability may be the reason for reduced evoked response  
463 magnitudes since event related potentials are obtained by averaging across many events that are  
464 inherently sensitive to signal noise. It is therefore possible that the increased variability of evoked  
465 responses across trials with age results in reduced ERP magnitudes.

466         In the age range examined, neural development is a dynamic process. At the macro level,  
467 longitudinal structural neuroimaging shows that cortical thinning occurs from childhood through early  
468 adulthood, progressing in a caudal to rostral pattern (Gogtay et al., 2004; Giedd et al., 2015). At the  
469 micro level, synaptic pruning and myelination, particularly in the frontal lobe, are ongoing during this  
470 period (Rakic et al., 1994; Huttenlocher and Dabholkar, 1997; Cox et al., 2016). From a functional  
471 perspective, studies of functional connectivity and task-based fMRI suggest that functional maturation  
472 tends to follow a “diffuse to focal pattern” (Durston et al., 2006; Grill-Spector et al., 2008; Fair et al.,  
473 2009; Kelly et al., 2009), and may correspond to the extraordinary advances in behavior during  
474 childhood (Xiao et al., 2016). Speculatively, the decreased ISC strength in older ages may reflect  
475 greater inter-individual variability that results from the interplay of structural and functional  
476 “streamlining” of neural architecture with distinct life experiences (e.g. cortical thinning, synaptic  
477 pruning and diffuse-to-focal shifts in functional patterns). However, one limitation of the present study  
478 is that it is cross-sectional rather than longitudinal, it is therefore difficult to make developmental  
479 claims based on the age-based differences demonstrated here (Kraemer et al., 2000).

480         The age-related effect, may also be echoed by the sex difference in neural variability.  
481 Longitudinal studies have demonstrated that females mature prior to males in a range of anatomical  
482 measures (Lenroot et al., 2007; Lim et al., 2015). However, differences in developmental trajectories  
483 between males and females may be complicated by the fact that the sexes ultimately differ in their  
484 mature neuroanatomy (Marsh et al., 2008). Here, sex-related differences in neural variability were only  
485 seen among younger subjects, suggesting that this is a development-related difference. Prepubescent  
486 and early teenage years are marked by sex differences in behavioral maturity that may not be present

487 in later years (Mous et al., 2017). The difference in neural variability may also be due to pubertal stage  
488 since it is known that females reach pubertal maturity 2-3 years prior to males (Sisk and Foster, 2004).  
489 However, physiological pubertal stage was not measured here, and it is therefore not possible to  
490 determine whether the sex differences were related to this factor.

491         Among the different stimuli used, the clips from conventional cinema (Wimpy and DesMe)  
492 evoked a higher level of ISC than the educational videos (Arith, Fract, and StudT). The Hollywood  
493 clips were rich with scene cuts and dynamic visual cues and are therefore expected to elicit strong  
494 levels of ISC (Poulsen et al., 2017). However, previous research has also shown that engagement  
495 with narrative stimuli modulates ISC, and it is therefore likely that these Hollywood clips are more  
496 effective at engaging attention and thus elicit stronger ISC (Dmochowski et al., 2014; Ki et al., 2016;  
497 Cohen et al., 2017). Although the ISC differences between age and sex may be due to each cohort's  
498 average level of attention, no independent measures of engagement or attention were collected. It is  
499 therefore not possible to determine whether the present effects are driven by attention or differences  
500 in low-level stimulus features. Most of the videos were aimed at younger audiences (i.e., Despicable  
501 Me, Diary of a Wimpy Kid), and older subjects may have therefore been less interested in them.  
502 However, this was not uniformly the case, for instance, the video about Fractals (Fract) may have  
503 been equally interesting to both children and adults, while the Flash stimulus may be equally boring for  
504 all ages. Thus, these two stimuli provided an important control for attentional effects on the age-  
505 related differences in ISC. Future work may benefit from looking at objective measures of engagement  
506 (Cohen et al., 2017) in the different cohorts studied here. An understanding of such factors, and their  
507 impact on behavior, may be of relevance to models of media-based addiction (e.g., internet addiction,  
508 pornography addiction), as well as commercial neuroscience enterprises. Regardless, it is of note that  
509 the age effect seen for the naturalistic videos was echoed in the SSVEP condition. Since this stimulus  
510 should be equally (un)engaging for all ages, this favors an interpretation based on neural maturation  
511 rather than attention.

512 Future work should recruit a larger sample of subjects above age 15 to determine whether the  
513 age-related decline in ISC observed in later teenage years continues in adulthood, or might even  
514 reverse in older age (Grady, 2012; Campbell et al., 2015). Future studies with clinical cohorts could  
515 explore the potential link between ISC and behavioral markers of neural development. It is possible  
516 that neural variability is not only a marker of maturity, but it is also a marker of neuropsychiatric  
517 disorders (Dinstein et al., 2015). The methods used here provide a novel way of assessing such  
518 markers under complex, naturalistic conditions.

519 Overall, the current results regarding intersubject correlation in children and adults are  
520 interpreted in the context of neural maturation. Although males are delayed in the development of the  
521 neural variability that appears to be a mark of maturity, the data presented here indicate that with  
522 normal development they are no different than females as adults. Thus, with maturity, neural function  
523 becomes more variable.

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#### 678 **Figure Legends**

679 Figure 1: Age and sex distributions for the main study (A) and replication study (B). A: Subjects in the  
680 main study (N=114) had data for all of the stimuli. B: Subjects in the replication study (N=303) had  
681 only three stimuli (Wimpy, Fract, DesMe) and contribute to the results in Figure 9.

682 Figure 2: Neural similarity, measured as the intersubject correlation (ISC) of neural activity, decreased  
683 with age. Correlation values ranged from  $r=-0.58$  to  $r=-0.78$ , indicating a consistent relationship  
684 between maturity and neural variability. ISC was computed for each individual by correlating neural  
685 responses from individual subjects with the neural responses from all other subjects for that stimulus  
686 (regardless of age and sex).

687 Figure 3: ISC, a measure of neural similarity, was consistently higher among younger ages and males.  
688 A: Across all stimuli, ISC was higher for younger subjects (6-14 years, light green) than older subjects  
689 (15-44 years, dark green). B: Across all stimuli, ISC was higher for males (blue) than females (red).  
690 For both A and B, ISC was computed separately within each age and sex group. Black lines indicate  
691 the median.

692 Figure 4. Sex differences in the young do not exist in the old. Young males were more neurally similar  
693 to each other than young females. This sex difference is absent in the older group. Here, ISC was  
694 computed within each sex and age group separately and averaged across all stimuli except for Flash  
695 and Rest. Black lines indicate the median.

696 Figure 5: Steady state visual evoked potential (SSVEP) magnitude depended on age, but not on sex.  
697 A: SSVEP strength was weakly correlated with age across subjects, but it was no different between  
698 males and females. B: SSVEP strength was no different between males and females. Black lines  
699 indicate the median.

700 Figure 6: Relationship between ISC magnitude and SSVEP strength. A: SSVEP strength, a measure  
701 of the magnitude of evoked responses, correlated with ISC strength, calculated using all stimuli except  
702 for Flash and Rest. B: Comparison of ISC strength after SSVEP magnitude was regressed out (ISC -  
703 SSVEP) between males and females in the young age and old age groups. While there was a  
704 significant difference between the age groups, a difference between the sex groups was not present.  
705 Black line indicates the median.

706 Figure 7: Spatial distributions corresponding to the three strongest components of intersubject  
707 correlation (ISC: C1 - C3). Red and blue colors indicate positive and negative correlation of the  
708 voltages on the scalp surface with the component activity. These maps are unitless due to an arbitrary  
709 scale on the projection vectors. Here, the projections have been computed separately for the  
710 combination of the two sex and age groups. As the scalp topographies were relatively consistent



711 across the groups, the differences in ISC across these groups was not due to differences in the spatial  
712 topography of correlation within the group.

713 Figure 8: Eigenvalue spectra of the average covariances for each demographic group. Eigenvalues  
714 measure the power of the signal in principal components of the EEG (correlated across time for each  
715 stimulus). Each curve is the average eigenvalue spectrum for each group averaged across all stimuli  
716 and subjects. A: Young subjects have more power than Old subjects in all dimensions. This is  
717 represented by the upward shift in their average eigenvalue spectrum. B: The eigenvalue spectrum of  
718 Females has a shallower slope than that for Males indicating that they have a more diverse set of  
719 neural responses.

720 Figure 9: The results from the main study replicated in an independent cohort (N=303). A: ISC  
721 decreased with age in the replication cohort. ISC was computed for each individual by correlating  
722 responses from individual subjects to those from all other subjects (regardless of age and sex) for that  
723 stimulus. Correlation values ranged from  $r=-0.37$  to  $r=-0.44$ . Note that for every stimulus a different  
724 number of subjects was available. B: Across all stimuli, ISC was higher for younger subjects (6-14  
725 years, light green) than it was for older subjects (15-44 years, dark green) in the replication cohort. For  
726 consistency, the split between the ages was consistent between this study and the main study C:  
727 Across all stimuli, ISC was higher for males (blue) than females (red) in the replication cohort. For  
728 both B and C, ISC was computed separately within each age and sex group. Black lines indicate the  
729 median. D: Sex differences in the young disappeared with age in the replication cohort. Young males  
730 were more neurally similar to each other than young females, and this sex difference was absent in  
731 the older group. Here, ISC was computed within each sex and age group separately and averaged  
732 across all stimuli used in the replication cohort. Black lines indicate the median.



















