

# Differences in strategic abilities but not associative processes explain memory development

Müller N.C.J.<sup>1</sup>, Kohn, N.<sup>1</sup>, van Buuren<sup>2</sup>, M., Klijn<sup>1</sup>, N., Emmen, H.<sup>1</sup>, Berkers, R.M.W.J.<sup>1,3</sup>, Dresler, M.<sup>1,4</sup>, Janzen, G.<sup>1,5</sup>, Fernández, G.<sup>1\*</sup>

<sup>1</sup> Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Centre, Nijmegen, The Netherlands.

<sup>2</sup> <sup>1</sup>Department of Clinical, Neuro and Developmental Psychology, Faculty of Behavioral and Movement Sciences, Institute for Brain and Behavior Amsterdam, Vrije Universiteit Amsterdam, The Netherlands.

<sup>3</sup> Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany.

<sup>4</sup> Max Planck Institute of Psychiatry, Munich, Germany.

<sup>5</sup> Behavioural Science Institute, Radboud University Nijmegen, The Netherlands

\*Corresponding author: G. Fernández ([guillen.fernandez@donders.ru.nl](mailto:guillen.fernandez@donders.ru.nl))

## 1 Abstract

2 Children’s learning capabilities change while growing up. One framework that describes the cognitive and  
3 neural development of children’s growing learning abilities is the two-component model. It distinguishes  
4 processes that integrate separate features into a coherent memory representation (associative  
5 component) and executive abilities, such as elaboration, evaluation and monitoring, that support memory  
6 processing (strategic component). In an fMRI study using an object-location association paradigm, we  
7 investigated how the two components influence memory performance across development. We tested  
8 children (10-12 yrs., n=31), late adolescents (18 yrs., n=29) and adults (25+ yrs., n=30) of either sex. For  
9 studying the associative component, we also probed how the utilisation of prior knowledge (schemas)  
10 facilitates memory across age groups. Children had overall lower retrieval performance, while adolescents  
11 and adults did not differ from each other. All groups benefitted from schemas, but this effect did not differ  
12 between groups. Performance differences between groups were associated with deactivation of the  
13 dorsal medial prefrontal cortex (dmPFC), which in turn was linked to executive functioning. These patterns  
14 were stronger in adolescents and adults and seemed absent in children. This pattern of results suggests  
15 the children’s executive system, the strategic component, is not as mature and thus cannot facilitate  
16 memory performance in the same way as in adolescents/adults. In contrast, we did not find age-related  
17 differences in the associative component; with activity in the angular gyrus predicting memory  
18 performance systematically across groups. Overall our results suggest that differences of executive rather  
19 than associative abilities explain memory differences between children, adolescents and adults.

## 20 1. Introduction

21 In virtually all contexts learners need to focus on what to learn, avoid distraction, relate information to  
22 each other or keep several types of information online to combine them. These abilities, executive  
23 functions, have been shown to strongly influence the efficiency of ones mnemonic system (Simons and  
24 Spiers, 2003). The maturation of the executive system – especially the prefrontal cortex – during  
25 adolescence (Bunge and Crone, 2009; Crone and Dahl, 2012; Luna et al., 2015) makes it an excellent  
26 candidate to support the development of learning. The relation of executive functions with associative  
27 memory processes have been formalised and extended in a model explaining age-related differences in  
28 episodic memory: the two component model of development (Shing et al., 2008, 2010). It postulates one  
29 associative and one strategic component with differential maturational trajectories. The associative  
30 component “refers to mechanisms of binding together different features of the memory content into  
31 coherent representations” (Shing et al., 2010). The strategic component “refers to control processes that  
32 aid and regulate memory content at both encoding and retrieval” (Shing et al., 2010). Whereas the  
33 strategic component is centred around the prefrontal cortex, the associative component is centred  
34 around the medial temporal lobe. However, the developmental interaction of the two systems and their  
35 underlying neurobiology are still poorly understood.

36 When we learn new information this usually involves prior knowledge. Almost nothing we learn is  
37 fundamentally new in all aspects but mostly relates to something we already know. This entails that when  
38 we form new memory representations, the different features that get integrated via the associative  
39 component of the two-component model also include prior knowledge. That prior knowledge benefits  
40 learning was first formulated by Bartlett (Bartlett, 1932) and Piaget (Piaget, 1936) in the context of  
41 schemas: Our knowledge is organised in schemas which can be used to readily assimilate new information  
42 about the world or provide a foundation that can be modified when we acquire new insight/perspectives.  
43 The idea of schemas had a strong influence on education and educational psychology (Thorndyke and

44 Hayes-Roth, 1979). Throughout our life we continuously acquire, modify, or enrich schemas. This  
45 difference in scope of schemas available to children versus adults might explain developmental memory  
46 differences (Brod et al., 2013). Whereas adolescents and adults have a sophisticated net of knowledge  
47 spanning a large range of topics, children are still in the process of acquiring most of that. Thus, for new  
48 information the children might have fewer opportunities to relate new information to their schemas. On  
49 the other hand, children might be superior in building new knowledge structures of previously  
50 unconnected information due to their generally increased neural plasticity (Ismail et al., 2016).

51 Executive processes and the utilisation of schemas have both been linked to the prefrontal cortex, yet  
52 vary in their precise localisation (Miller and Cohen, 2001; Ridderinkhof, 2004; Tse et al., 2011; van  
53 Kesteren et al., 2012). Generally, the prefrontal cortex shows a protracted maturation trajectory, reaching  
54 a matured state only in the mid-twenties (Gogtay et al., 2004; Shaw et al., 2008). This relatively late  
55 maturation has previously been linked to the development of cognitive control (Luna et al., 2015). Based  
56 on that we tested three age groups that differ strongly in prefrontal maturation: children between the  
57 age of 10-12 years, 18-year-old late adolescents and adults over twenty-five years old. To measure  
58 memory performance we used a game like object-location memory task (van Buuren et al., 2014). A  
59 strength of this paradigm is that it has no verbal requirements, which would have favoured the older  
60 groups as verbal memory itself is still developing in children (Vakil and Blachstein, 2007). The schema was  
61 trained during the first part of our study so that all groups have the same level of prior knowledge available  
62 to facilitate learning.

## 63 2. Materials and Methods

### 64 2.1. Participants

65 Ninety right-handed native Dutch-speaking volunteers participated in this study. As we investigated  
66 developmental differences related to differential maturation of the prefrontal cortex we tested three  
67 different age groups: Thirty adults aged between 25-32 years old ( $M = 26.9$  years,  $SD = 21.9$  months, 12  
68 male), twenty-nine adolescents aged 18 ( $M = 18.5$  years,  $SD = 3.1$  months, 10 male) and thirty-one children  
69 aged between 10-12 years old ( $M = 11.0$  years  $SD = 8.8$  months, 8 male). All subjects had normal hearing  
70 and normal or corrected-to-normal vision. All participants were required to have no history of injury or  
71 disease known to affect the central nervous system function (including neuropsychological disorders such  
72 as dyslexia, autism and ADHD) and to not have MRI contraindications. Assessment of these were based  
73 on self-reports by the participants. Adults and adolescents were recruited from the student population of  
74 Radboud University, Nijmegen, and from the surrounding community. Children were recruited through  
75 presentations and flyers at local schools. The study was approved by the institutional Medical Research  
76 Ethics Committee (CMO Region, Arnhem-Nijmegen). Written informed consent was obtained prior to  
77 participation from all participants who were at least 18 years old; for the children participating both  
78 parents signed the informed consent.

79 Of these 90 participants, 4 children had to be excluded (2 did not want to complete the study, 1 moved  
80 excessively in the scanner, 1 due to an experimenter error); 2 adolescents were excluded as they did not  
81 complete the training at home; 1 adult had to be excluded due to an experimenter error. Of these 83  
82 participants that completed the study, we excluded 11 (6 children, 1 adolescent, 4 adults) participants for  
83 the analysis based on their poor performance – see the fMRI data analysis section for details. All analysis  
84 focussed on this final set of 72 participants (21 children, 26 adolescents and 25 adults).

## 85 2.2. Summary of Procedure

86 The study spanned eight days in total. On day one participants came to the lab for a first session. The next  
87 four days they performed additional sessions at home. On day eight they returned to the institute for the  
88 final session. As paradigm we used an adapted version of the memory game task that was used in another  
89 study (van Buuren et al., 2014). Details of the paradigm are explained below. As additional measures we  
90 utilised a short verbal memory task, a fractal n-back task (Ragland et al., 2002), the Wisconsin Card Sorting  
91 task (WCST) (Heaton et al., 1993) and the forward digit span task (Alloway et al., 2008). The rationale for  
92 the additional measures is explained in a separate paragraph below.

93 On day one, participants came to the Donders Centre for Cognitive Neuroimaging and started in a  
94 behavioural lab with a practice of the n-back task, followed by the verbal memory task. Immediately after  
95 completing the verbal memory task, participants were taken into the MRI scanner where we first acquired  
96 a 10-minute resting state scan during which participants were instructed to lie still, think of nothing in  
97 particular and look at a black fixation cross on a white background. After that participants performed the  
98 n-back task and lastly, we acquired a structural scan. As the memory task required the use of a trackball  
99 – because of MRI-compatibility – participants had a practice session with the trackball (Kensington, Orbit  
100 Optical Trackball) that was used for all sessions of the memory task. During all uses of the trackball we  
101 instructed participants to operate the trackball with two hands: the right dominant hand moves the cursor  
102 and the left hand clicks.

103 After the practice, participants performed the first two sessions of the memory game. During the next  
104 four days, participants were instructed to “play” the memory game at home using a provided laptop and  
105 trackball. Participants were instructed to not skip a day and perform the task at roughly the same time of  
106 day. We monitored this online using the times the log files were created. Day six and seven were free of  
107 any experimental tasks. On day eight, the participants came back to the institute for the final session. The  
108 time of day during the two visits differed by maximally two hours to avoid time of day confounds. Day  
109 eight started with the final two parts of the memory task in the MRI scanner. Between the parts, which  
110 took both roughly 17 minutes, there was a break during which the participant could leave the scanner. As  
111 a last scan we acquired a second structural scan. Finally, we conducted the Wisconsin Card Sorting Test  
112 and the digit span in a behavioural lab. The total task time on day eight was around one hour.

## 113 2.3. Memory Paradigm

114 The task mimics the card game “memory/concentration” on two boards of cards and is adapted from (van  
115 Buuren et al., 2014) to make it more suitable for children. It is a 2x2 design (schema/no-schema x  
116 paired/new paired associates): one board was the schema while the other was the no-schema condition.  
117 Each board contained 80 objects in total. 40 of these objects were learnt during the first four days (paired  
118 associates). The remaining 40 objects (new paired associates) were added on day five and filled the  
119 remaining empty positions on each board (see Fig. 1 for an illustration of the task). On the schema board  
120 the place location associations stayed constant across the whole experiment, whereas on the other, the  
121 no-schema board, the associations were randomly exchanged every day. Due to this manipulation,  
122 participants learned the associations on the schema board over the course of four days; forming a schema  
123 that contains the object place association of the first 40 objects. Participants could utilise this schema  
124 when learning the second set – the new paired associations – of associations on day five for the schema  
125 board. The memory for all 160 associations across both boards was tested on day eight in the MRI scanner.

## 126 2.4. Stimuli design, randomisation and presentation

127 In total we used pictures of 160 everyday objects. To ensure that especially the children could name all  
128 the objects effortlessly we selected the objects from a larger set of objects by asking an independent  
129 sample (n=5) of younger children (below the age of 9) to name all the objects. Only objects all children  
130 were able to name were included in the set of 160 pictures. The objects were randomly distributed across  
131 the different conditions (paired associates or new paired associates on the schema or no-schema board).  
132 This randomisation was done individually per participant.

133 Differing from the initial paradigm (van Buuren et al., 2014) we did not use a 10x10 board but a 9x9 board,  
134 furthermore we arranged the 9x9 board into nine visually segregated 3x3 boxes, each containing nine  
135 cards, by increasing the spacing after each third row and column. These changes had two reasons. First,  
136 we aimed to reduce the difficulty and the time required for the task to make it more suitable for children.  
137 Second, we opted to have an additional, more sensitive, measure of memory: instead of only taking into  
138 account the objects where the chosen position was exact, we can also analyse objects where the response  
139 was in the right box. Thus, we would be able to pick on memories where only an approximate location  
140 can be recalled. The two boards were differentiated by the colour of the back of the cards that were  
141 placed on the board. Whether the schema board or the no-schema board was yellow or blue was  
142 randomly assigned per participant in a counterbalanced fashion for each group separately.

143 We randomised the coordinates of the cards in a pseudorandom fashion separately per participant. Each  
144 3x3 box of cards contained either four or five objects per condition (schema and no-schema) to ensure  
145 the cards were spread evenly across the board and there was no particular clustering. Furthermore, within  
146 each box there could not be a row of three objects, preventing particular easy structures from appearing  
147 within the box.

148 All of the memory tasks were implemented using Presentation version 18.1 (Berkeley, CA:  
149 Neurobehavioural Systems). The task at home utilised its web-based license. For tracking compliance with  
150 the study protocol, we used Dropbox (San Francisco, CA: Dropbox Inc.) on the laptops to automatically  
151 receive the log files. This communication was encrypted with a key only available to the researchers of  
152 this study to guarantee participants' privacy.

## 153 2.5. Day 1: Basic training (in the lab)

154 Participants started by learning 40 paired associates on one board. The task started with a 1.5min  
155 presentation of all the 40 objects on their respective location to increase learning speed. After this initial  
156 phase the main task started and only the empty board was visible. One trial consisted of a cue-, a  
157 response- and a feedback phase: Participants saw an object at the bottom of the board in a red frame as  
158 cue. After 3s this frame turned green and a cursor appeared at a random position of the board. To draw  
159 attention to the location of the cursor there was a short animation (around 120ms) when it appeared.  
160 Participants now had to click within 3s on the location that belonged to the cued object using the trackball.  
161 When the response was correct the object was shown for 0.5s at its location. If there was no or a wrong  
162 response the cursor turned red and the object was shown at the correct location for 2.5s. After 40 trials  
163 there was a self-paced pause with a black fixation cross being presented instead of the board. The task  
164 consisted of three cycles. During each of those cycles every object was presented exactly one time.  
165 Participants therefore had three full training cycles for all items. After the three cycles were completed  
166 for the first board, the same procedure was repeated for the second board. Together both sessions took  
167 roughly 35min. We used the laptops and the trackball they would also use at home, showed them how to

168 start the task and explained that the laptop needs an internet connection. To ensure understanding we  
169 had participants start the second part of the task themselves. The order of the boards and their colours  
170 were randomised and counterbalanced across participants per group.

## 171 2.6. Day 2-4: Training (at home)

172 During each of these three days participants would perform training sessions at home. For all sessions  
173 from now onwards the boards were presented in an interleaved fashion. During the initial encoding phase,  
174 first the one board and its 40 objects was presented for 1.5min, then the other board was presented for  
175 1.5min. During the task, the board switched every five trials. This interleaved learning was used to reduce  
176 interference between the boards (McClelland et al., 1995). The start condition was randomised and  
177 counterbalanced across participants. Every day the associations on the no-schema board were shuffled  
178 as described above, preventing learning across days. Participants were instructed to try as hard as possible  
179 to perform well at that board and we showed performance scores at the end of the task to motivate them.

180 On day four, after the task, the training of the 80 paired associates was concluded. Immediately  
181 afterwards, participants performed a recall task testing all the paired associates they had learned. The  
182 trial structure for the recall was identical to the training except that there was no feedback and there was  
183 only one cycle: each object was shown once. The purpose of the recall task was two-fold; first to have a  
184 measure how well the paired associations were learned up until now; second, to familiarise the  
185 participants with the recall task before they would do the final recall in the scanner on day eight. Each  
186 session took around 35 minutes with day four being roughly five minutes longer.

## 187 2.7. Day 5: New learning (at home)

188 On day five the 80 new paired associates were added, 40 to each board. As before, the no-schema board  
189 was shuffled. The session started as usual with an initial encoding phase, however, now all 80 objects per  
190 board were shown and participants had 3min per board to memorise as many associations as possible.  
191 Aside from the number of associations, the session was identical to the previous training sessions. Each  
192 of the 80 objects per board was presented once per cycle leading to 480 trials in total. The boards were  
193 again presented in an interleaved fashion and the randomisation was done in such a way that there were  
194 never more than two paired associates trials or new paired associates trials in a row. The whole session  
195 took approximately 70 minutes. To reduce effects of exhaustion, participants were instructed to take a  
196 more prolonged self-paced break after 240 trials by standing up and moving around in the room, before  
197 resuming.

## 198 2.8. Day 8: Recall (in the MRI)

199 Around 72h later participants returned to the lab for the final recall in the MRI scanner. Participants lay  
200 down in the MRI scanner with the trackball positioned on their abdomen or their right upper thigh at a  
201 comfortable distance. Participants familiarised themselves with using the trackball in the scanner. After  
202 the participant was proficient using the trackball, we started with the recall task. One trial started as usual  
203 with a cue for 3s, followed by a response window of 3s followed by an inter-trial interval with only a black  
204 fixation cross on the screen for 2.5-7.5s. The inter-trial interval was drawn from a uniform distribution.  
205 There was no feedback presented during recall. To keep the trial length and the visual input consistent  
206 across subjects the board would still be presented for the whole duration of the response window,  
207 independent of whether the response was already given. The boards were again interleaved every five  
208 trials. We split the task in two parts (balanced across conditions) so that participants could take a break  
209 from scanning. Each part took roughly 17 minutes.

## 210 2.9. Additional Measures

211 Additional to the memory game we also conducted a short verbal memory task (day one, before scanning,  
212 outside the scanner), a fractal n-back task (Ragland et al., 2002) (day one, in the scanner), the WCST  
213 (Heaton et al., 1993) (day eight, after scanning, outside the scanner) and a forward digit span task (Alloway  
214 et al., 2008) (day eight, after scanning, outside the scanner). The verbal memory task was used to  
215 investigate links between cortical thickness of the prefrontal cortex and verbal memory performance. The  
216 fractal n-back was planned as a control experiment for a planned model-free analysis of the memory  
217 game. The WCST was included as an established measure of executive function. Finally, we included the  
218 digit span measure to control for group differences unspecific to long term memory processes.

## 219 2.10. Behavioural analysis

220 All statistical analyses of behavioural data were conducted in SPSS 21 (Armonk, NY: IBM Corp). Memory  
221 performance was measured as the number of correct responses per condition. The memory game  
222 consisted of four phases: training (day one till day four), recall (day four), integration of the paired  
223 associates (day five) and integration the complete set (day eight). The phases were analysed separately.  
224 To analyse the training (day one till day four) we used a repeated measures ANOVA with the factors  
225 schema (schema, no-schema), session (training day one to four), cycle (one to three) and group (children,  
226 adolescents, adults). For the recall on day four, the repeated measure model included schema and group.  
227 For the integration on day five we used a repeated measure model with the factors schema, cycle, group  
228 and included only the new paired associates. The model for the recall on day eight was identical to the  
229 recall on day four except that we now used the new paired associates instead of the paired associates.  
230 Whenever necessary, results were followed up with simple effect tests.

231 Complementarily, we repeated the analysis using the score for when participants clicked in the correct  
232 box (of the 9 boxes). This analysis is more sensitive, as responding close to the correct location likely also  
233 indicates memory; this heightened sensitivity comes at the cost of a higher chance level (11% versus  
234 1.25%). We report only significant results with  $p < 0.05$ .

## 235 2.11. MRI data acquisition

236 Participants were scanned using a Siemens Magnetom Skyra 3 tesla MR scanner equipped with a 32-  
237 channel phased array head coil. The recall task comprised 935 volumes that were acquired using a T2\* -  
238 weighted gradient-echo, multiecho echoplanar imaging sequence with the following parameters: TR =  
239 2100ms; TE<sub>1</sub> = 8.5ms, TE<sub>2</sub> = 19.3ms, TE<sub>3</sub> = 30ms, TE<sub>4</sub> = 41ms; flip angle 90°; matrix size = 64 x 64; FOV =  
240 224mm x 224mm x 119mm; voxel size = 3.5mm x 3.5mm x 3mm; slice thickness = 3mm; slice gap = 0.5mm;  
241 34 slices acquired in ascending order. As this sequence did not provide whole brain coverage we oriented  
242 the FOV in a way that the hippocampus and the prefrontal cortex were fully inside and that only a small  
243 superior part of the parietal lobe was outside the FOV.

244 For the structural scans we used a T1-weighted magnetisation prepared, rapid acquisition, gradient echo  
245 sequence with the following parameters: TR = 2300ms; TE = 3.03ms; flip angle 8°; matrix size = 256 x 256;  
246 FOV= 192mm x 256mm x 256mm; slice thickness = 1mm; 192 sagittal slices.

## 247 2.12. MRI preprocessing

248 Preprocessing was done using a combination of FSL tools (Jenkinson et al., 2012), MATLAB (Natick, MA:  
249 The MathWorks) and ANTs (Avants et al., 2011a). From the two structural scans we generated an average  
250 using rigid body transformations from ANTs (Avants et al., 2011a), this procedure removed small

251 movement induced noise. From the two scans and the average we always selected the scan with the least  
252 amount of ringing artefacts for all future analysis. If no difference was visible we used the average scan.  
253 These scans were denoised using N4 (Tustison et al., 2010) and generated a study-specific template with  
254 an iterative procedure of diffeomorphic registrations (Avants and Gee, 2004). For the registration of the  
255 functional volumes we resampled the created template to a resolution of 3.5mm isotropic. Using Atropos  
256 (Avants et al., 2011b) the anatomical scans were segmented into 6 tissue classes: cerebrospinal fluid,  
257 white matter, cortical grey matter, subcortical grey matter, cerebellum and brainstem. The segmentation  
258 also produced individual brain masks.

259 For the functional multiecho data we combined echoes using in-house build MATLAB scripts. It used the  
260 30 baseline volumes acquired during the resting period directly before each part of the task to determine  
261 the optimal weighting of echo-times for each voxel (after applying a smoothing kernel of 3mm full-width  
262 at half-maximum to the baseline volumes), by calculating the contrast-to-noise ratio for each echo per  
263 scan. This script also directly realigned the volumes using rigid body transformation. Afterwards the  
264 volumes were smoothed using a 5mm full-width at half-maximum Gaussian kernel and grand mean  
265 intensity normalisation was done by multiplying the time series with a single factor. Younger participants  
266 tend to move more than older ones. For a developmental study it is thus important to minimise the effect  
267 of motion in the data. For this purpose we applied AROMA, a state of the art motion denoising algorithm  
268 that uses independent component analysis decomposition of the data to identify movement and other  
269 noise signals (Pruim et al., 2015b, 2015a). Variance in the BOLD signal that could only be explained by  
270 components identified in this manner was regressed out. Afterwards we regressed out signal stemming  
271 from the cerebrospinal compartments and from the white matter by extracting the signal from individual  
272 generated segmentations using ANTs (Avants et al., 2011b). As a last step a 100s highpass filter was  
273 applied.

274 Boundary based registration was first calculated from native functional to native structural space using  
275 FLIRT (Greve and Fischl, 2009). We then calculated nonlinear registration from native structural space to  
276 the study template with FNIRT (Smith et al., 2004). The warping was done in a way that every functional  
277 volume was only resliced exactly once after the initial realignment. For displaying the final results we  
278 warped the final maps to MNI space using the nonlinear registration of ANTs (Avants and Gee, 2004).

### 279 2.13. fMRI data analysis

280 After preprocessing the data was analysed using the general linear model framework implemented in  
281 FEAT (Jenkinson et al., 2012). On the first level we included eight separate regressors: four regressors  
282 modelled correct responses for the separate conditions (paired associates vs. new paired associates on  
283 the schema or no-schema board). As duration we used the trial onset of the cue until the participant gave  
284 a response. As a correct response, we counted if the participant clicked in the correct one of the nine  
285 boxes. We used this way of scoring instead of using only the trials in which participants clicked on the  
286 correct card as we would have substantially more power due to the higher amount of trials for the MRI  
287 analysis while still maintaining a fairly low chance level (11%).

288 For all those conditions but the schema paired associates an additional regressor was included to model  
289 incorrect responses. For the schema paired associates condition the performance was designed to be as  
290 close to ceiling as possible leading to only few incorrect trials. These trials were modelled together with  
291 all the trials in which subjects failed to respond in time in a single “miss” regressor. For the miss trials the  
292 full 6s of the cue and response window was used. Regressors were then convolved with a double gamma



293 hemodynamic response function. On the first level the model was fitted separately per run. Using fixed  
294 effect modelling the runs were combined per subject and then the participant specific contrasts were  
295 estimated. To calculate the group level statistics, we warped the participant level results into study  
296 template space and used mixed effect modelling implemented in FSL FLAME2. The results were  
297 thresholded using a cluster forming threshold of  $z > 2.3$  (equal to  $p < 0.01$ ) and a cluster significance  
298 threshold of  $p < 0.05$  at the whole brain level. Our central motivation for this study was to understand  
299 how the neural mnemonic processes differ across different stages of cortical maturation. Therefore, our  
300 imaging analysis was centrally guided by the behavioural results, illuminating the underlying neural  
301 architecture related to behavioural differences. Thus, the contrasts used will be explained while  
302 presenting the imaging results.

303 As a follow up analysis, we conducted moderation analysis based on the results of the general linear model  
304 analysis. For this, we extracted the average betas from the significant clusters on a participant by  
305 participant basis. We then conducted the moderation analysis using the PROCESS macro (Hayes, 2013) for  
306 SPSS.

### 307 3. Results

#### 308 3.1. Training

309 As expected, during the recall on day four schema items were better recalled than no-schema items  
310 ( $F(1,69)=199.05$ ,  $p<.001$ ,  $\eta_p^2=.74$ ). For the training, we observed a significant three-way interaction of  
311 schema x session x cycle ( $F(4.49,309.86)=27.84$ ,  $p<.001$ ,  $\eta_p^2=.29$ ), reflecting the fact that in the schema  
312 condition the paired associates could be learned across days while the shuffling between days prevented  
313 this for the no-schema paired associates.

#### 314 3.2. New Learning

315 The schema new paired associates were learned better compared to the no-schema paired associates  
316 ( $F(1,69)=59.94$ ,  $p<.001$ ,  $\eta_p^2=.47$ ).

#### 317 3.3. Recall day 8

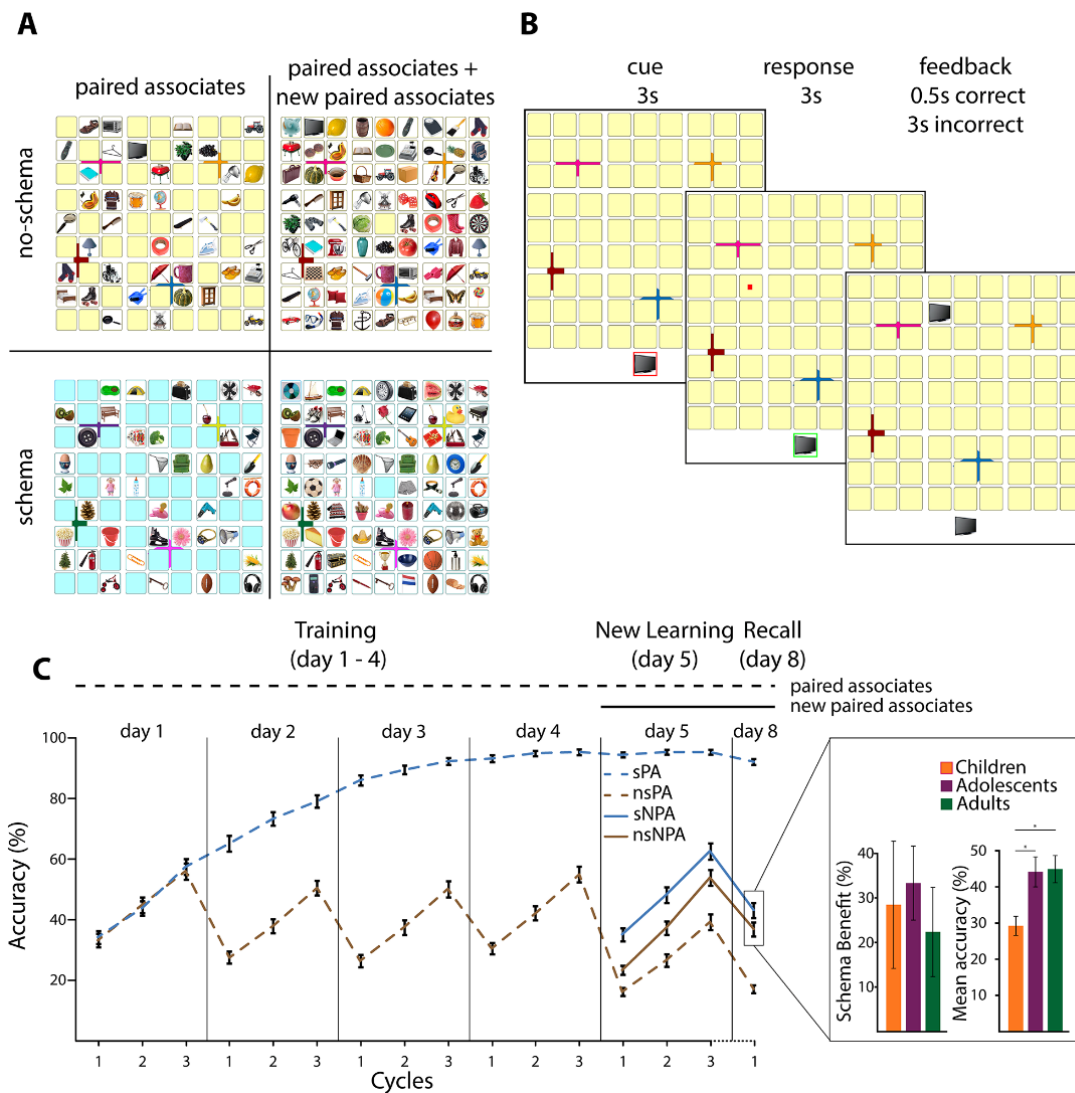
318 In the final recall the schema new paired associates were better retrieved compared to the new no-  
319 schema paired associates ( $F(1,69)=17.09$ ,  $p<0.001$ ,  $\eta_p^2=.2$ ). However, there was a significant effect of group  
320 on the retrieval performance of the new paired associates overall ( $F(2,69)=5.33$ ,  $p=.007$ ,  $\eta_p^2=.13$ ). Children  
321 performed worse than adolescents ( $MD=-5.97$ ,  $p=.006$ ) and adults ( $MD=-5.23$ ,  $p=.005$ ); whereas  
322 adolescents and adults did not differ significantly ( $MD=-.31$ ,  $p=.881$ ).

#### 323 3.4. Precise location correct vs. box correct

324 Analysing the data counting only trials as correct where the response was on the right card instead of the  
325 right box (3x3 cards) did not alter the results: All of the reported effects were also significant for the box  
326 score.

327

328



329

330 **Figure 1 Task design and behavioural performance.** (A) Participants needed to learn object-location associations (paired  
 331 associates) in the memory game. For two boards (one schema, one no-schema board) there were two sets of associations to  
 332 learn. During the first four days participants learned the paired associates on both boards (40 associations each). For the schema  
 333 board participants could thus systematically learn the layout of the board. For the no-schema board on the start of every day the  
 334 paired associates switched places with each other, therefore preventing systematic learning. On day five the new paired  
 335 associates were added (again 40 associations per board). In the final session on day eight both the paired and the new paired  
 336 associates were tested in a recall session in the MRI. (B) During a trial, participants first saw an object (cue) at the bottom of the  
 337 board. After 3s the box in which the cue was presented turned green and a mouse cursor appeared. Participants then responded  
 338 within 3s with the location corresponding to the object. If the response was correct the object was only shown very briefly (0.5s)  
 339 whereas if they responded wrongly or not at all the object was shown for 3s. Each object was repeated three times for participants  
 340 to have ample opportunity to learn the layout. Additionally, at the start of each session the whole board (during training the 40  
 341 paired associates, during new learning the whole 80 associations) was presented. (C) During the training phase participants  
 342 systematically learned the schema paired associates (sPA) on the schema board whereas the performance on the no-schema  
 343 paired associates (nsPA) on the other board dropped at the start of every day due to the shuffling of locations. The schema new  
 344 paired associates (sNPA) that were added during the new learning were better learned compared to the no-schema new paired  
 345 associates (nsNPA) ( $F(1,69)=59.94$ ,  $p<.001$ ,  $\eta_p^2=.47$ ). In the recall on day eight we observed a reduced performance in the children  
 346 compared to both older groups ( $F(2,69)=5.33$ ,  $p=.007$ ,  $\eta_p^2=.13$ ). Schema benefit refers to how many items participants had correct  
 347 in the schema new paired associates over the no-schema new paired associates. All error bars indicate the standard error of the  
 348 mean. A star indicates a significance of  $p<.05$ .

349 **3.4. fMRI: Developmental differences**

350 Our central behavioural finding is that children show lower memory performance than adolescents and  
351 adults while the latter two groups did not perform significantly differently. To understand the neural  
352 changes across development, we contrasted the activation during retrieval of the new paired associates  
353 for the correctly retrieved trials minus the trials in which a wrong response was given. As all groups seem  
354 to have profited to a similar degree from schema, we averaged across schema and no-schema trials to be  
355 more sensitive for developmental differences. The contrast between hits and misses was then compared  
356 between the children versus the average of the two older groups; this was done because the latter two  
357 groups did not differ in performance. As we used mixed modelling on the group level analysis the fact that  
358 the adolescent-adult group is twice as big as the children does not bias the results.

359 We observed increased activation in children in midline structures, including the dorsomedial prefrontal  
360 cortex (dmPFC). Increased activation in the adolescent-adult groups was most pronounced bilaterally in  
361 the angular gyrus (Fig. 2). For a complete list of all clusters please see Table 1.

362

363

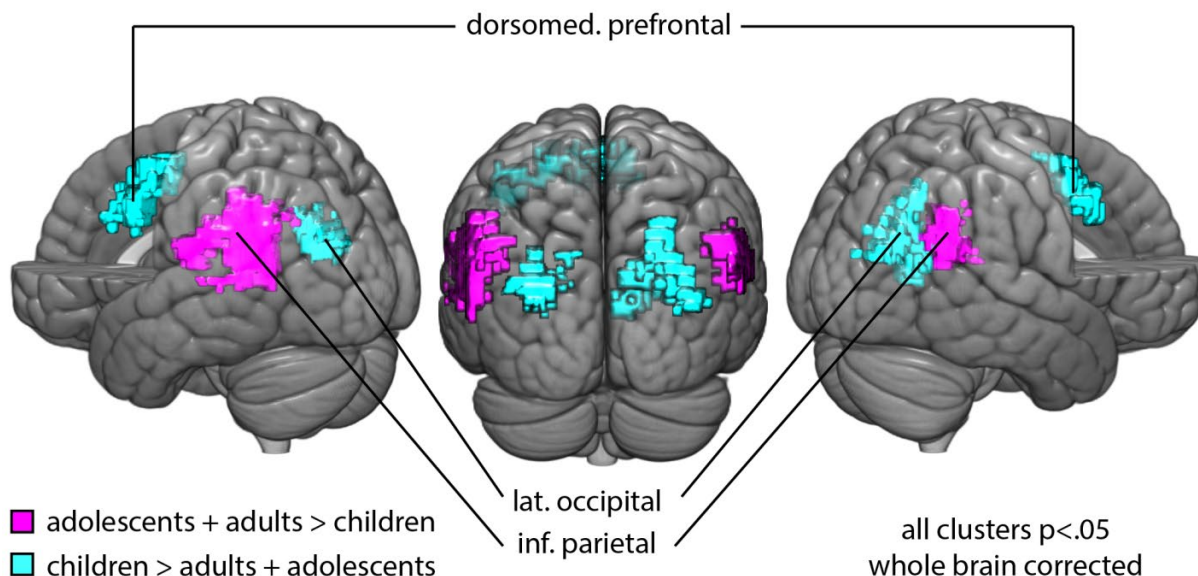
Region	MNI Coordinates			z-Score	Voxels
	x	y	z		
<b>Children &gt; Adolescents + Adults</b>					
R dorsomed. prefrontal cort.	3	15	46	4.04	243
L dorsomed. prefrontal cort	-7	-14	43	3.74	
R dorsomed. prefrontal cort	4	22	42	3.72	
L precentral gyrus	-40	3	40	3.54	
R middle frontal gyrus	-25	2	55	3.48	
L dorsomed. prefrontal cort	-4	5	55	3.34	
R lat. sup. occipital cort	25	-67	41	4.73	151
R precuneus	15	-58	25	3.5	
R lat. sup. occipital cort	42	-83	24	3.34	
R lat. sup. occipital cort	30	-80	29	3.3	
R Precuneus	9	-59	9	3.26	
R med. occipital cort	38	-76	19	3.17	
L lat. sup. occipital cort	-29	-84	32	4.2	103
L lat. sup. occipital cort	-26	-81	24	3.9	
L lat. sup. occipital cort	-30	-74	22	3.82	
L precuneus	-15	-72	38	3.39	
L precuneus	-19	-81	35	2.68	
L lat. sup. occipital cort	-45	-85	27	2.54	
<b>Adolescents + Adults &gt; children</b>					
L lat. sup. Occipital cort	-54	-61	44	4.89	227
L angular gyrus	-51	-59	32	4.14	
L lat. sup. occipital cort	-46	-72	38	4.01	
L par. operculum	-63	-34	22	3.85	
L lat. sup. Occipital cort	-58	-64	16	3.61	
L mid. temp. gyrus	-69	-48	6	2.83	
R lat. sup. occipital cort	60	-61	33	3.44	227
R lat. sup. occipital cort	48	-61	42	3.34	
R lat. sup. occipital cort	56	-60	42	3.27	
R angular gyrus	64	-53	25	3.07	
R angular gyrus	54	-47	23	2.82	
R lat. sup. occipital cort	60	-61	21	2.8	103

364

365 **Table 1 Developmental differences in activation for the correct retrieval of the new paired associates.** The listed clusters here  
 366 and their local maxima show differences between the children, the adolescent and the adult groups for the retrieval of the new  
 367 paired associates in which both older groups outperformed the children. The coordinates were always of the global/local  
 368 maximum. The voxel-count as well as the z-score of the peak voxel were taken from study space. The MNI coordinates were  
 369 obtained by warping the results into MNI space. All labels refer to regions on the cortex.

370

371 As we hypothesised that performance differences might be due to differences in executive abilities in  
372 children, we tested whether there is a link between the (de)activation of the dmPFC and measures of  
373 executive function. Activation in the dmPFC was negatively correlated with performance in the WCST  
374 ( $r(70)=-.31$ ,  $p=.008$ ), as measured by the amount of correct categories, but not significantly related to the  
375 forward digit span score ( $r(70)=.04$ ,  $p=.72$ ). The correlation of dmPFC activation and WCST performance  
376 was driven by a negative correlation across the two adult groups ( $r(49)=-.31$ ,  $p=.026$ ). This association  
377 between dmPFC activity and WCST performance for the children was reduced compared to the  
378 adolescent-adult group ( $z=2.08$ ,  $p=.038$ ) and in itself not significant ( $r(19)=.26$ ,  $p=.27$ ).



**Figure 2 Age-related differences in mean memory performance for the new paired associates.** During the recall of both the schema and the no-schema new paired associates children showed an increased activation in the dorsal medial prefrontal cortex (dmPFC) overlapping with the cingulate and paracingulate gyrus; a second cluster around the lateral occipital cortex showed the same effect. Adolescents and adults showed higher bilateral activation of the angular gyrus.

### 379 3.5. fMRI: Schema effect

380 Participants across all age groups remembered schema new associates better than the no-schema new  
381 associates. To illuminate the neural architecture behind this schema effect we calculated the contrast  
382 between the hits and the misses between the schema new paired associates (sNPA) and the no-schema  
383 new paired associates (nsNPA):  $sNPA (hits - misses) - nsNPA (hits - misses)$ . However, there was no  
384 significant activation that survived whole brain correction. More specifically, we tested the angular gyrus,  
385 as the region had previously been found to be important for integrating different parts of a schema  
386 (Wagner et al., 2015) and in the paradigm utilised here in same the schema x memory contrast (van  
387 Buuren et al., 2014). When separately contrasting sNPA (hits - misses) and nsNPA (hits - misses), we  
388 observed that both angular gyri were significantly activated in both contrasts ( $p < .05$ ). To test whether  
389 there was activation specificity for schema, we extracted the betas for voxels that were significantly  
390 activated for the sNPA's; we extracted both the values for sNPA (hits - misses) and nsNPA (hits - misses).  
391 The difference between those contrasts was positively correlated ( $r(70)=.34$ ,  $p=.003$ ) to the magnitude of  
392 the schema benefit. There was no indication that this relation is significantly modulated by age group  
393 ( $F(2,66)=.95$ ,  $p=.39$ ).

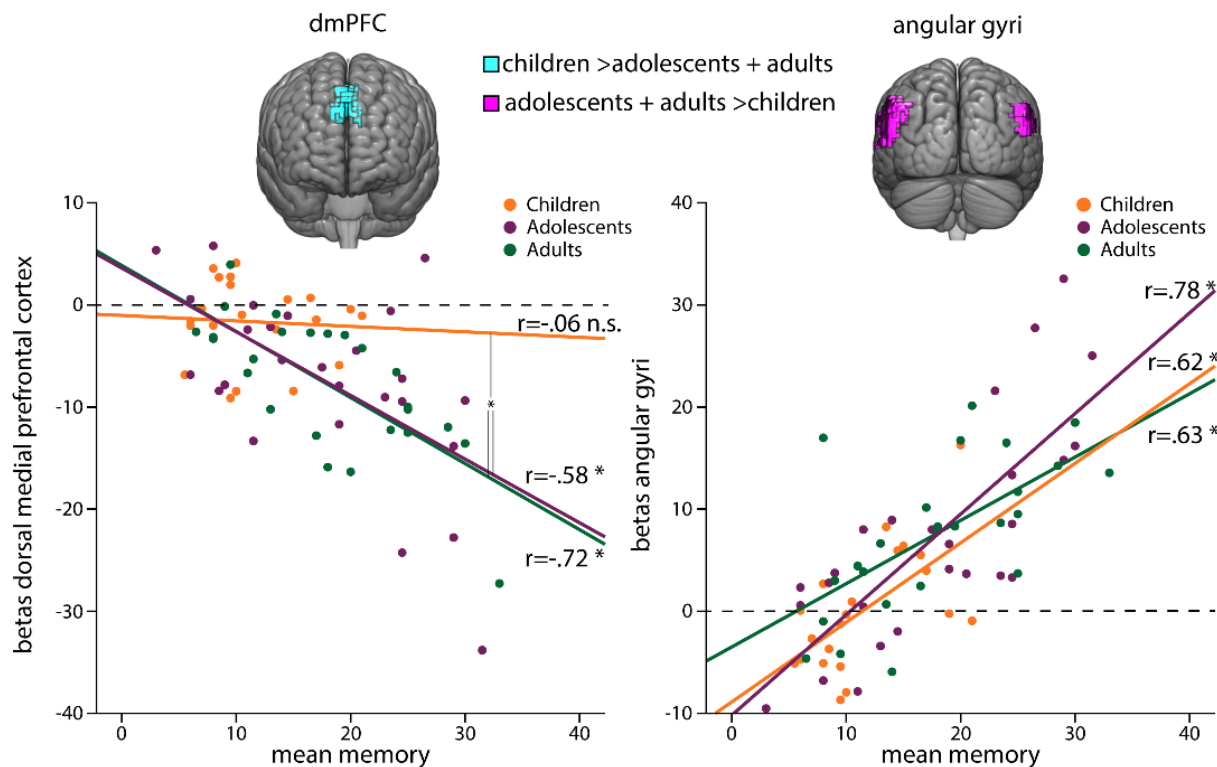


Figure 3 Developmental differences in brain-behaviour relation. For both the activation in the dmPFC and the angular gyri we found a relation to the mean memory performance across the age groups. For the dmPFC this relation was negative ( $r(70) = -.63$ ,  $p < .001$ ). For the angular gyri it was positive ( $r(70) = .75$ ,  $p < .001$ ). Most notably we found an age-related dissociation: whereas the brain-behaviour relation was consistent across age for the angular gyri; Activation in the dmPFC showed a moderation with age  $F(1,68) = 4.19$ ,  $p = .045$ ). Participants in both adult groups varied in the degree they deactivated the dmPFC, the stronger the deactivation the better the performance. Children showed neither a deactivation of the dmPFC nor a relation to recall performance. Mean memory performance refers to the average across the schema and no-schema paired associates. A star indicates a significance of  $p < .05$ .

#### 394 4. Discussion

395 We tested how differences in the associative and the strategic component of the two-component model  
 396 of memory development (Shing et al., 2008, 2010) contribute to memory performance differences  
 397 between children, adolescents and adults. We found that both the adolescent and adult group had higher  
 398 memory performance than children, independent of the conditions, while all groups profited equally from  
 399 utilising schemas (Fig. 1). Performance differences between groups were associated with deactivation of  
 400 the dmPFC, which in turn was linked to executive function. In contrast, activation of the angular gyrus was  
 401 consistently correlated with memory performance across all groups (Fig. 3). This suggests that age-related  
 402 differences in memory are rather driven by differences in the strategic component, but not the associative  
 403 component.

404 The two component model helps us to test whether the age-related differences we observed are driven  
 405 by immaturity of the associative or the strategic component. Memory differences linked to associative  
 406 regions, such as the angular gyrus, or to the utilisation of schema would indicate differences in the  
 407 associative component. Memory differences that are not linked to the associative memory regions but  
 408 rather to regions involved in executive function would suggest a stronger role for the strategic component.  
 409 To corroborate the links between task activation and executive function we used the independently  
 410 acquired WCST performance as a general measurement of executive function (Greve et al., 2005):

411 Participants with high levels of executive function in the WCST can likely use those functions strongly to  
412 facilitate their retrieval performance.

413 Children had a lower retrieval performance than adolescents and adults for the schema and the no-  
414 schema new paired associates. We found for both the adolescents and the adults, the level of the  
415 deactivation of the dmPFC during trials in which they recalled the correct location predicted their overall  
416 recall performance: the stronger the deactivation was, the better was the performance (Fig. 3). This  
417 deactivation also predicted the WCST performance. Furthermore, the dmPFC cluster we found overlaps  
418 with a core cluster previously observed during performance of the WCST (Specht et al., 2009) and is also  
419 contained within the Executive Control Network, a resting state network that is involved across many  
420 aspects of executive function (Smith et al., 2009). The link to the WCST, the involvement of our dmPFC  
421 cluster in the WCST and the dmPFC's important role in executive function (Ridderinkhof, 2004; Domenech  
422 and Koechlin, 2015), suggests to us that it reflects executive function benefitting retrieval performance.  
423 Participants with strong deactivation in the dmPFC could use executive function to improve their task  
424 performance, whereas participants that showed little or no deactivation could not. In contrast to the other  
425 groups, children did not seem to exhibit this behaviour: they neither showed a systematic deactivation of  
426 the dmPFC nor was the dmPFC activity related to memory or WCST performance, in which children  
427 performed worse than adolescents and adults. We take all this as an indication that the strategic  
428 component in children is not as mature as in adolescents and adults: Whereas adolescents and adults can  
429 use their strategic abilities to enhance their memory performance, children did not seem to be able to do  
430 this. These results are nicely in line with recent work demonstrating that age-related increases in  
431 mnemonic strategies is linked to the development of the PFC (Yu et al., 2018).

432 With regard to the associative component, we did not find any indications for differences between age-  
433 groups. Activity of the angular gyrus was correlated with successful memory performance consistently  
434 across groups. Additionally, schema effect was indistinguishable across groups. All groups performed  
435 between 20 and 30 percent better in the schema over the no-schema condition. We interpret this absence  
436 of any developmental differences for associative processes as an indication for a weaker role of the  
437 associative component to explain age-related memory differences in our sample.

438 The consistent relation of the activation from the angular gyrus across groups suggests an important role  
439 in the task that is stable across the tested ages. This stability is consistent with previous work  
440 demonstrating that the angular gyrus has the same functional boundaries in school children (7 to 10 years  
441 old) compared to adults (Barnes et al., 2012); suggesting a relative early functional maturation. In recent  
442 years, the contribution of the angular gyrus to memory has received increased attention. There is now  
443 substantial evidence for it being an amodal convergence zone (Bonnici et al., 2016; Yazar et al., 2017) that  
444 integrates input from different modalities to create higher level representations. With this facility it lays  
445 the basis for abstract representations and thus semantic memory (Binder and Desai, 2011). The ability to  
446 combine several modalities seems ideally suited for the memory game task where spatial information  
447 (location) needs to be combined with semantic information (identity of the card). Another capacity of the  
448 angular gyrus that explains its involvement is the ability to guide attention during memory retrieval relying  
449 on retrieval cues or recovered memories (Cabeza et al., 2008; Vilberg and Rugg, 2008).

450 We replicated that schemas facilitate memory (Tse et al., 2007; van Kesteren et al., 2010; van Buuren et  
451 al., 2014; Liu et al., 2017) as indicated by the higher performance for the schema new paired associates.  
452 This effect did not show any differences across development, in line with a previous study investigating

453 children in a similar age range (Brod et al., 2016). Neurally, we found that not the mPFC but the angular  
454 gyrus distinguished the retrieval of schema versus no-schema associations. Both the angular gyrus and  
455 the mPFC were activated in both the schema and no-schema condition, however the angular gyrus was  
456 significantly more strongly activated whereas the activity of the mPFC did not differ significantly. This  
457 pattern is consistent with results previously found using this paradigm (van Buuren et al., 2014), but it  
458 appears at odds with the typical pattern that the mPFC orchestrates the utilisation of schemas (van  
459 Kesteren et al., 2012; Fernández, 2017; Genzel and Battaglia, 2017). We speculate that the mPFC did not  
460 differentially activate as there were too many associations at the same time that needed to be assimilated  
461 in the schema. If either there would have been less associations to learn or there would have been more  
462 time for learning the associations and stabilising their memories, we speculate that the mPFC would have  
463 been more strongly activated for the correctly retrieved schema new paired associates.

464 In summary, we investigated whether memory differences between children, adolescents and adults  
465 would stem from developmental changes in executive abilities, the strategic component, or rather from  
466 differences in mechanisms related to binding different features together into a memory representation,  
467 the associative component. We found that adolescents and adults outperformed children in memory. The  
468 performance within the adolescents and adult group was associated to their individual executive abilities,  
469 thus providing evidence that a maturation of the strategic component was driving the age-related  
470 differences we observed. In contrast, we did not find differences in the associative component that help  
471 to explain the differences in memory between the age groups.

472

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475



## 476 6. References

- 477 Alloway TP, Gathercole SE, Kirkwood H, Elliott J (2008) Evaluating the validity of the Automated Working  
478 Memory Assessment. *Educ Psychol* 28:725–734.
- 479 Avants BB, Gee JC (2004) Geodesic estimation for large deformation anatomical shape averaging and  
480 interpolation. *Neuroimage* 23:139–150.
- 481 Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC (2011a) A reproducible evaluation of ANTs  
482 similarity metric performance in brain image registration. *Neuroimage* 54:2033–2044.
- 483 Avants BB, Tustison NJ, Wu J, Cook PA, Gee JC (2011b) An open source multivariate framework for N-  
484 tissue segmentation with evaluation on public data. *Neuroinformatics* 9:381–400.
- 485 Barnes KA, Nelson SM, Cohen AL, Power JD, Coalson RS, Miezin FM, Vogel AC, Dubis JW, Church JA,  
486 Petersen SE, Schlaggar BL (2012) Parcellation in left lateral parietal cortex is similar in adults and  
487 children. *Cereb Cortex* 22:1148–1158.
- 488 Bartlett FC (1932) *Remembering : A Study in Experimental and Social Psychology*. Cambridge: Cambridge  
489 University.
- 490 Binder JR, Desai RH (2011) The neurobiology of semantic memory. *Trends Cogn Sci* 15:527–536.
- 491 Bonnici HM, Richter FR, Yazar Y, Simons JS (2016) Multimodal Feature Integration in the Angular Gyrus  
492 during Episodic and Semantic Retrieval. *J Neurosci* 36:5462–5471.
- 493 Brod G, Lindenberger U, Shing YL (2016) Neural activation patterns during retrieval of schema-related  
494 memories: Differences and commonalities between children and adults. *Dev Sci*.
- 495 Brod G, Werkle-Bergner M, Shing YL (2013) The Influence of Prior Knowledge on Memory: A  
496 Developmental Cognitive Neuroscience Perspective. *Front Behav Neurosci* 7:1–13.
- 497 Bunge S, Crone E (2009) Neural correlates of the development of cognitive control. *Neurosci Res*:22–37.
- 498 Cabeza R, Ciaramelli E, Olson IR, Moscovitch M (2008) The parietal cortex and episodic memory: an  
499 attentional account. *Nat Rev Neurosci* 9:613–625.
- 500 Crone EA, Dahl RE (2012) Understanding adolescence as a period of social – affective engagement and  
501 goal flexibility. *Nature* 13:636–650.
- 502 Domenech P, Koechlin E (2015) Executive control and decision-making in the prefrontal cortex. *Curr Opin*  
503 *Behav Sci* 1:101–106.
- 504 Fernández G (2017) The Medial Prefrontal Cortex is a Critical Hub in the Declarative Memory System. In:  
505 *Cognitive Neuroscience of Memory Consolidation*, pp 45–56. Springer International Publishing.
- 506 Genzel L, Battaglia FP (2017) Cortico-Hippocampal Circuits for Memory Consolidation: The Role of the  
507 Prefrontal Cortex. In: *Cognitive Neuroscience of Memory Consolidation*, pp 265–281. Springer  
508 International Publishing.
- 509 Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis a C, Nugent TF, Herman DH, Clasen LS,  
510 Toga AW, Rapoport JL, Thompson PM (2004) Dynamic mapping of human cortical development  
511 during childhood through early adulthood. *Proc Natl Acad Sci* 101:8174–8179.
- 512 Greve DN, Fischl B (2009) Accurate and robust brain image alignment using boundary-based registration.  
513 *Neuroimage* 48:63–72.
- 514 Greve KW, Stickler TR, Love JM, Bianchini KJ, Stanford MS (2005) Latent structure of the Wisconsin Card  
515 Sorting Test: A confirmatory factor analytic study. *Arch Clin Neuropsychol* 20:355–364.
- 516 Hayes A (2013) *Introduction to mediation, moderation, and conditional process analysis*. New York, NY  
517 Guilford:3–4.
- 518 Heaton R, Chelune G, Curtiss G, Kay G, Talley J (1993) Wisconsin card sorting test. *Psychol Assess Resour*.
- 519 Ismail FY, Fatemi A, Johnston MV (2016) Cerebral plasticity: Windows of opportunity in the developing  
520 brain. *Eur J Paediatr Neurol* 21:23–48.
- 521 Jenkinson M, Beckmann CF, Behrens TEJ, Woolrich MW, Smith SM (2012) Fsl. *Neuroimage* 62:782–790.
- 522 Liu ZX, Grady C, Moscovitch M (2017) Effects of Prior-Knowledge on Brain Activation and Connectivity  
523 During Associative Memory Encoding. *Cereb Cortex* 27:1991–2009.

- 524 Luna B, Marek S, Larsen B, Tervo-Clemmens B, Chahal R (2015) An Integrative Model of the Maturation of  
525 Cognitive Control. *Annu Rev Neurosci* 38:151–170.
- 526 McClelland JL, McNaughton BL, O'Reilly RC (1995) Why there are complementary learning systems in the  
527 hippocampus and neocortex: insights from the successes and failures of connectionist models of  
528 learning and memory. *Psychol Rev* 102:419–457.
- 529 Miller EK, Cohen JD (2001) An integrative theory of prefrontal cortex function. *Annu Rev Neurosci* 24:167–  
530 202.
- 531 Piaget J (1936) *Origins of intelligence in children*. London: Routledge & Kegan Paul.
- 532 Pruim RHR, Mennes M, Buitelaar JK, Beckmann CF (2015a) Evaluation of ICA-AROMA and alternative  
533 strategies for motion artifact removal in resting state fMRI. *Neuroimage* 112:278–287.
- 534 Pruim RHR, Mennes M, van Rooij D, Llera A, Buitelaar JK, Beckmann CF (2015b) ICA-AROMA: A robust ICA-  
535 based strategy for removing motion artifacts from fMRI data. *Neuroimage* 112:267–277.
- 536 Ragland JD, Turetsky BI, Gur RC, Gunning-Dixon F, Turner T, Schroeder L, Chan R, Gur RE (2002) Working  
537 memory for complex figures: an fMRI comparison of letter and fractal n-back tasks. *Neuropsychology*  
538 16:370–379.
- 539 Ridderinkhof KR (2004) The Role of the Medial Frontal Cortex in Cognitive Control. *Science* 306:443–447.
- 540 Shaw P, Kabani NJ, Lerch JP, Eckstrand K, Lenroot R, Gogtay N, Greenstein D, Clasen L, Evans A, Rapoport  
541 JL, Giedd JN, Wise SP (2008) Neurodevelopmental trajectories of the human cerebral cortex. *J*  
542 *Neurosci* 28:3586–3594.
- 543 Shing YL, Werkle-Bergner M, Brehmer Y, Müller V, Li S-C, Lindenberger U (2010) Episodic memory across  
544 the lifespan: the contributions of associative and strategic components. *Neurosci Biobehav Rev*  
545 34:1080–1091.
- 546 Shing YL, Werkle-Bergner M, Li S-C, Lindenberger U (2008) Associative and strategic components of  
547 episodic memory: a life-span dissociation. *J Exp Psychol Gen* 137:495–513.
- 548 Simons JS, Spiers HJ (2003) Prefrontal and medial temporal lobe interactions in long-term memory. *Nat*  
549 *Rev Neurosci* 4:637–648.
- 550 Smith SM, Fox PT, Miller KL, Glahn DC, Fox PM, Mackay CE, Filippini N, Watkins KE, Toro R, Laird AR,  
551 Beckmann CF (2009) Correspondence of the brain's functional architecture during activation and  
552 rest. *Proc Natl Acad Sci* 106:13040–13045.
- 553 Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TEJ, Johansen-Berg H, Bannister PR, De  
554 Luca M, Drobnjak I, Flitney DE, Niazy RK, Saunders J, Vickers J, Zhang Y, De Stefano N, Brady JM,  
555 Matthews PM (2004) Advances in functional and structural MR image analysis and implementation  
556 as FSL. *Neuroimage* 23:S208–S219.
- 557 Specht K, Lie CH, Shah NJ, Fink GR (2009) Disentangling the prefrontal network for rule selection by means  
558 of a non-verbal variant of the wisconsin card sorting test. *Hum Brain Mapp* 30:1734–1743.
- 559 Thorndyke PW, Hayes-Roth B (1979) The Use of Schemata in the Acquisition and Transfer of Knowledge.  
560 *Cogn Psychol* 11:82–106.
- 561 Tse D, Langston RF, Kakeyama M, Bethus I, Spooner PA, Wood ER, Witter MP, Morris RGM (2007) Schemas  
562 and memory consolidation. *Science* 316:76–82.
- 563 Tse D, Takeuchi T, Kakeyama M, Kajii Y, Okuno H, Tohyama C, Bito H, Morris RGM (2011) Schema-  
564 dependent gene activation and memory encoding in neocortex. *Science* 333:891–895.
- 565 Tustison NJ, Avants BB, Cook P a., Zheng Y, Egan A, Yushkevich P a., Gee JC (2010) N4ITK: Improved N3  
566 bias correction. *IEEE Trans Med Imaging* 29:1310–1320.
- 567 Vakil E, Blachstein H (2007) Rey AVLT : Developmental norms for adults and the sensitivity of different  
568 memory measures to age. *Clin Neuropsychol* 7049:37–41.
- 569 van Buuren M, Kroes MCW, Wagner IC, Genzel L, Morris RGM, Fernandez G (2014) Initial Investigation of  
570 the Effects of an Experimentally Learned Schema on Spatial Associative Memory in Humans. *J*  
571 *Neurosci* 34:16662–16670.

- 572 van Kesteren MTR, Rijpkema M, Ruiters DJ, Fernandez G, Fernández G (2010) Retrieval of associative  
573 information congruent with prior knowledge is related to increased medial prefrontal activity and  
574 connectivity. *J Neurosci* 30:15888–15894.
- 575 van Kesteren MTR, Ruiters DJ, Fernández G, Henson RN (2012) How schema and novelty augment memory  
576 formation. *Trends Neurosci* 35:211–219.
- 577 Vilberg KL, Rugg MD (2008) Memory retrieval and the parietal cortex: A review of evidence from a dual-  
578 process perspective. *Neuropsychologia* 46:1787–1799.
- 579 Wagner IC, van Buuren M, Kroes MCW, Gutteling TP, van der Linden M, Morris RG, Fernández G (2015)  
580 Schematic memory components converge within angular gyrus during retrieval. *Elife* 4:1–28.
- 581 Yazar Y, Bergström ZM, Simons JS (2017) Reduced multimodal integration of memory features following  
582 continuous theta burst stimulation of angular gyrus. *10*:1–16.
- 583 Yu Q, McCall DM, Homayouni R, Tang L, Chen Z, Schoff D, Nishimura M, Raz S, Ofen N (2018) Age-  
584 associated increase in mnemonic strategy use is linked to prefrontal cortex development.  
585 *Neuroimage* 181:162–169.
- 586