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Abstract

Working memory function changes across development and varies across individuals. The patterns of behavior and brain function that track individual differences in working memory during human development, however, are not well understood. Here we establish associations between working memory, cognitive abilities, and functional MRI activation in data from over 11,500 9–11-year-old children (both sexes) enrolled in the Adolescent Brain Cognitive Development study, an ongoing longitudinal study in the United States. Behavioral analyses reveal robust relationships between working memory, short-term memory, language skills, and fluid intelligence. Analyses relating out-of-scanner working memory performance to memory-related fMRI activation in an emotional *n*-back task demonstrate that frontoparietal activity specifically during a working memory challenge indexes working memory performance. This relationship is domain-specific, such that fMRI activation related to emotion processing during the emotional *n*-back task, inhibitory control during a stop-signal task, and reward processing during a monetary incentive delay task does not track memory abilities. Together these results inform our understanding of individual differences in working memory in childhood and lay the groundwork for characterizing the ways in which they change across adolescence.

Significance statement

Working memory is a foundational cognitive ability that changes over time and varies across individuals. Here we analyze data from over 11,500 9–11-year-olds to establish relationships between working memory, other cognitive abilities, and frontoparietal brain activity during a working memory challenge, but not during other cognitive challenges. Our results lay the groundwork for assessing longitudinal changes in working memory and predicting later academic and other real-world outcomes.

Introduction

1 Working memory—a collection of cognitive processes responsible for storing and manipulating

2 information—is a foundational ability that varies widely across individuals. Individual

3 differences in working memory, which appear to be stable over time (Alp, 1994; Ross et al.,

4 2008; Johnson et al., 2013; Tulsky et al., 2014; Xu et al., 2018), have pronounced real-world

5 significance. Although the direction of causality is unclear, measures of verbal and visuospatial

6 working memory explain approximately 20–30% of the variance in fluid intelligence in children

7 (Engel de Abreu et al., 2010), and visuospatial working memory performance explains more than

8 40% of this variance in adults (Fukuda et al., 2010). Furthermore, working memory function,

9 which is related to executive and visuospatial attention (Kane and Engle, 2002; Huang et al.,

10 2012), short-term memory (Alloway et al., 2006), and inhibitory control (Davidson et al., 2006),

11 predicts consequential outcomes in development, including reading and math skills (Bayliss et

12 al., 2003; De Smedt et al., 2009; Alloway and Alloway, 2010; Nouwens et al., 2017). Despite the

13 theoretical and practical importance of characterizing associations between working memory and

14 other mental processes, much remains to be learned about the nature of these relationships during

15 development.

16   Working memory not only varies across individuals, but also changes across the lifespan.

17 Working memory emerges in infancy and develops rapidly over the first year of life (Diamond

18 and Goldman-Rakic, 1989; Ross-Sheehy et al., 2003; Reynolds and Romano, 2016; Buss et al.,

19 2018). This ability continues to improve during childhood, plateaus in mid-to-late adolescence

20 (Gathercole et al., 2004; Luciana et al., 2005; Conklin et al., 2007; Ullman et al., 2014; Isbell et

21 al., 2015), and declines after age 40–50, albeit less steeply than it changed during early

22 development (Alloway and Alloway, 2013; Nyberg et al., 2013; Eriksson et al., 2015; Swanson,

23 2017). Developmental gains in working memory follow improvements in attention shifting,

24 attentional maintenance, and distractor suppression (Reynolds and Romano, 2016), whereas

25 changes during later childhood accompany increases in domain-general processing speed and

26 memory capacity (Fry and Hale, 1996, 2000; Pailian et al., 2016) with developmental asymptotic

27 performance by adolescence (Casey et al., 2000, 2005; Klingberg et al., 2002; Steinberg et al.,

28 2009). Decrements in older adulthood relate to declines in processing speed, selective attention,

29 and distractor suppression (Salthouse and Babcock, 1991; Gazzaley et al., 2005; McNab et al.,

30 2015).

31   Converging neuroimaging evidence suggests that variation in frontoparietal brain

32   systems, which are involved in processes including attention and cognitive control (Woolgar et

33   al., 2011; Scolari et al., 2015; Assem et al., 2019), accounts for both developmental change in

34   verbal and visuospatial working memory and individual differences in these processes in

35   adulthood. Early work demonstrated that the same aspects of middle and inferior frontal cortex

36   that support working memory performance in adults also support performance in children (Casey

37   et al., 1995). This evidence led to theorizing that the protracted fine-tuning of prefrontal

38   circuitry contributes to working memory improvements during childhood and adolescence

39   (Casey et al., 2000, 2005). Longitudinal studies support this prediction, with evidence that

40   maturation in prefrontal and parietal volume and structural connectivity accompany working

41   memory development (Tamnes et al., 2013; Klingberg and Darki, 2014). Cross-sectional work

42   suggests that increases in frontoparietal activation during working memory tasks are associated

43   with age-related improvements in performance (Klingberg et al., 2002; Kwon et al., 2002; Crone

44   et al., 2006; Satterthwaite et al., 2013). In the developed brain, individual differences in

45   frontoparietal areas' microstructure, function, and structural and functional connectivity track

46   individual differences in working memory (Osaka et al., 2003; Palva et al., 2010; Burzynska et

47   al., 2011; Takeuchi et al., 2011; Ekman et al., 2016). A subset of developmental studies show

48   similar associations between in-scanner working memory performance (a state-like measure of

49   memory function) and frontoparietal activity during working memory tasks when controlling for

50   age (Crone et al., 2006; Satterthwaite et al., 2013). One study comparing adolescents with higher

51   and lower family incomes found that the higher-income group showed greater frontoparietal

52   activity as a function of load in a working memory (*n*-back) fMRI task and higher out-of-scanner

53   working memory capacity (Finn et al., 2017a). However, it is not yet known whether

54   frontoparietal network function during working memory challenges specifically—or during

55   cognitive task challenges more generally—predicts individual differences in working memory

56   during development.

57   Here we examine behavioral and neural signatures of working memory in childhood.

58   Using data from 11,537 9–11-year-olds participating in the Adolescent Brain Cognitive

59   Development study (Casey et al., 2018; Volkow et al., 2018) (ABCD), we first establish

60   relationships between working memory and other cognitive and attentional abilities, including

61   short-term memory, language and verbal skills, fluid intelligence, processing speed, attention,

62   inhibitory control, and reward processing. Because the ABCD Study will follow children

63 longitudinally for ten years, characterizing these associations in childhood not only informs the

64 structure of cognition at a single time point, but also facilitates understanding the ways in which

65 this cognitive structure changes across adolescence. We next ask whether performance on an out-

66 of-scanner working memory test is related to frontoparietal brain activity when measured *(a)*

67 during a working memory challenge and *(b)* during task challenges unrelated to memory.

68 Together our results provide insight into individual differences in working memory in childhood,

69 and underscore the importance of task fMRI as a "stress test" for cognition (Finn et al., 2017b)

70 that can reveal task-specific and task-general neural signatures of a mental process or behavior.

71

72 **Materials and methods**

73 **The Adolescent Brain Cognitive Development (ABCD) Study.** Individual differences in

74 working memory and other cognitive and attentional processes were assessed using data from

75 11,537 9–11-year-olds in the Adolescent Brain Cognitive Development (ABCD) Study, an

76 ongoing multi-site longitudinal study of neurocognitive development (Luciana et al., 2018).

77 Launched in September 2016, the ABCD Study aims to characterize cognitive and neural

78 development with measures of neurocognition, physical and mental health, social and emotional

79 function, and culture and environment. Exclusionary criteria include a diagnosis of

80 schizophrenia, a moderate to severe autism spectrum disorder, an intellectual disability, or a

81 substance use disorder at recruitment. Children with a persistent major neurological disorder

82 (e.g., cerebral palsy, a brain tumor, stroke, brain aneurysm, brain hemorrhage, subdural

83 hematoma), multiple sclerosis, sickle cell disease, or certain seizure disorders (Lennox-Gastaut

84 syndrome, Dravet syndrome, and Landau Kleffner syndrome) were also excluded.

85 ABCD Study data collection includes yearly behavioral assessments, interviews,

86 questionnaires, and biosample collection as well as biennial MRI scans (Casey et al., 2018). Here

87 we analyze year-one (baseline) demographic and behavioral data collected across 22 sites when

88 children were 9–11 years old and made available as part of curated data release 2.0.1 (DOI

89 10.15154/1504041; n = 11,537; 48.4% female). Sample demographics including race, ethnicity,

90 socioeconomic status, and symptoms of internalizing and externalizing disorders are available in

91 Thompson et al. (2018).

92 Data from children diagnosed with autism spectrum disorder or epilepsy were excluded

93 from the current analysis because moderate to severe forms of autism spectrum disorder and

94 other seizure disorders were exclusionary for the ABCD Study (n = 338 of 11,875). Data from

95   children with attention deficit hyperactivity disorder, depression, bipolar disorder, anxiety, and

96   phobias (n = 1,598 of 11,537) were not excluded, as these diagnoses were assessed with a single

97   screening question and we aimed to characterize working memory in a heterogeneous

98   developmental population.

99

100   **Behavioral data.** To characterize associations between working memory and other cognitive

101   abilities, we analyzed performance data from all 15 available neurocognitive (Luciana et al.,

102   2018) and neuroimaging (Casey et al., 2018) tasks, described in detail below (**Table 1**). Working

103   memory ability outside of the scanner was operationalized as performance on the NIH Toolbox

104   List Sorting Working Memory Task. Performance measures were selected based on previous

105   work including reports of ABCD baseline data (Casey et al., 2018; Luciana et al., 2018).

106

107   *NIH Toolbox cognition battery.* The NIH Toolbox[®] cognition battery includes seven tasks

108   measuring multiple aspects of cognition (Gershon et al., 2013) (**Table 1, column 3**).

109   Performance is measured using uncorrected standard scores, as age-corrected scores are currently

110   undergoing revision by the NIH Toolbox (Luciana et al., 2018).

111

112   ***The Toolbox List Sorting Working Memory Test***[®] measures working memory by asking

113   children to recall stimuli in different orders (Tulsky et al., 2014). Children were first shown

114   pictures of two animals, and were asked to repeat them back in order from smallest to largest.

115   They were shown longer lists (with up to seven animals) if they answered correctly. Next,

116   children were shown pictures of both animals and foods, and were asked to repeat the

117   animals in order of size and then the foods in order of size. Interleaved lists increased in

118   length from two to seven if children responded accurately, and performance scores reflect the

119   number of accurate responses. Importantly, this list sorting task was developed to assess

120   working memory function in general rather than verbal or visual working memory in

121   particular (Tulsky et al., 2014). Visuospatial working memory was not measured in the

122   ABCD baseline sample, and reflects a cognitive ability closely related to but dissociable from

123   verbal working memory (Alloway et al., 2006; Swanson, 2017) that is traditionally tested

124   with tasks such as delayed match-to-sample.

125

126 ***The Toolbox Picture Vocabulary Test***® measures language and verbal abilities (Gershon et
127 al., 2014). Children hear a series of words, and are asked to choose which of four pictures
128 most closely matches the meaning of the word.

129

130 ***The Toolbox Flanker Task***®, a flanker task (Eriksen and Eriksen, 1974) used to measure
131 cognitive control and attention, was adapted from the Attention Network Task (Fan et al.,
132 2002; Zelazo et al., 2014). On each trial, children see a row of five arrows. The outer four
133 arrows (distractors, or flankers) all point to the left or right of the screen. The middle arrow
134 (the target) points in the same direction as the flankers on congruent trials, and the opposite
135 direction of the flankers on incongruent trials. Children are asked to indicate whether the
136 center arrow points to the left or to the right. Performance scores are based on speed and
137 accuracy.

138

139 ***The Toolbox Dimensional Change Card Sort Task***® measures cognitive flexibility (Zelazo,
140 2006). On each trial, children see two objects on a screen. They are asked to match a third
141 item with one of the initial two based on either color or shape. Children first match items
142 based on one dimension (e.g., color), then match items based on the other dimension (e.g.,
143 shape), and finally match based on both shape and color in pseudorandom order.
144 Performance scores are based on speed and accuracy.

145

146 ***The Toolbox Pattern Comparison Processing Speed Test***® measures visual processing speed
147 (Salthouse et al., 1991; Carlozzi et al., 2015). Children are shown two pictures and are asked
148 to indicate whether they are the same or different. Scores are based on the number of correct
149 responses within a time limit.

150

151 ***The Toolbox Picture Sequence Memory Test***® measures episodic memory and visuospatial
152 sequencing (Bauer et al., 2013; Dikmen et al., 2014). Children are shown 15 pictures of
153 activities or events and asked to reproduce the presentation order.

154

155 ***The Toolbox Oral Reading Recognition Task***® measures reading abilities by asking children
156 to pronounce a series of written letters and words (Gershon et al., 2014).

157

158   *Matrix reasoning.* The matrix reasoning subtest of the Wechsler Intelligence Test for Children-
159   V (WISC-V; Wechsler, 2014) measures fluid and spatial reasoning, perceptual organization,
160   visual attention, and sequencing. On each trial, children are shown an array of visual stimuli, and
161   are asked to select one of four stimuli that best completes the pattern. The task continues until a
162   child makes three consecutive errors or completes 32 trials. Performance is measured by
163   converting the number of total correct items to a standard score (Luciana et al., 2018).

164

165   *Rey Auditory Verbal Learning.* The Rey Auditory Verbal Learning Test (RAVLT) measures
166   learning and memory. During the test, children hear a list of 15 unrelated words five times. Each
167   time they hear the list, they are asked to recall as many words as possible. After these five
168   learning trials, children hear a distractor list and are again asked to recall as many words as they
169   can. Recall of the initial list is assessed immediately after the distractor list and again 30 minutes
170   later (Van Den Burg and Kingma, 1999; Luciana et al., 2018). Here we measure performance as
171   the number of correctly recalled words on these immediate and delayed memory assessments
172   (i.e., RAVLT trials vi and vii).

173

174   *Intertemporal cash choice.* The intertemporal cash choice task (Wulfert et al., 2002) assesses
175   children's delay of gratification, motivation, and impulsivity (Luciana et al., 2018). Children are
176   asked, "Let's pretend a kind person wanted to give you some money. Would you rather have \$75
177   in three days or \$115 in 3 months?" Smaller-sooner reward choices were coded with a "1",
178   larger-later reward choices were coded with a "2", and infrequent "don't know" responses were
179   excluded from analysis. Positive correlations between cash choice and performance on another
180   task indicate that children who performed better on the other task were more likely to choose the
181   larger-later option, whereas negative correlations indicate that children who performed worse on
182   the other task were more likely to choose the larger-later option.

183

184   *Little Man.* The Little Man task (Acker and Acker, 1982) measures aspects of visuospatial
185   processing including mental rotation. During this task, children see a cartoon of a man holding a
186   briefcase in his left or right hand appear on a computer screen. The man can be right side up or
187   upside down, and can appear facing the child or with his back turned. Children are asked to
188   indicate whether the man's briefcase is in his left or right hand via button press. The task

189   includes practice trials and 32 assessment trials. Performance is measured with efficiency

190   (percent accuracy divided by mean correct-trial response time) (Luciana et al., 2018).

191

192   *Emotional n-back*. The in-scanner emotional *n*-back (EN-back) task engages processes related to

193   memory and emotion regulation (Barch et al., 2013; Casey et al., 2018). During the task, children

194   perform 0-back (low memory load) and 2-back (high memory load) task blocks with four types

195   of stimuli: happy, fearful, and neutral face photographs (Tottenham et al., 2009; Conley et al.,

196   2018) and place photographs. Data are collected during two approximately 5-min functional

197   MRI runs each with four 0-back and 2-back blocks each. Runs included 362 whole-brain

198   volumes after discarded acquisitions. At the start of each 0-back block, children are shown a

199   target stimulus and asked to press a button corresponding to "match" when they see an identical

200   picture and a button corresponding to "no match" when they see a different picture. During 2-

201   back blocks, children are asked to press "match" when they see a picture identical to the one they

202   saw two trials back. Performance is quantified as percent accuracy on 0-back and 2-back blocks.

203

204   *Recognition memory*. After scanning, memory for EN-back task stimuli is assessed with a

205   recognition memory test (Barch et al., 2013; Casey et al., 2018). During this test, children are

206   presented with 48 EN-back stimuli and 48 novel stimuli (i.e., 12 old and new happy, fearful, and

207   neutral face photographs and 12 old and new places), and are asked to rate whether each picture

208   is "old" or "new." Performance is assessed with sensitivity (d') averaged across stimulus types.

209

210   *Stop-signal*. The in-scanner stop-signal task (Logan, 1994) (SST) is designed to measure

211   impulsivity and impulse control (Casey et al., 2018). SST data are collected during two

212   approximately 6-minute functional MRI runs (437 volumes after discarded acquisitions) each

213   with 180 trials each. On each trial, children see an arrow pointing to the left or to the right of the

214   screen (the go signal). They are instructed to indicate the direction of the arrow with a button

215   press as quickly and accurately as possible, except when an upright arrow (the stop signal)

216   appears on the screen (16.67% of trials). The time between go and stop signal onset, the stop-

217   signal delay, is staircased so that each child achieves approximately 50% accuracy on stop trials.

218   Performance is measured with stop-signal reaction time (SSRT), or the mean stop-signal delay

219   subtracted from the mean reaction time on correct go trials. For consistency with other

220   behavioral measures, SSRTs were reverse scored (multiplied by –1) so that higher scores
221   correspond to better performance.

222

223   *Monetary incentive delay.* The in-scanner monetary incentive delay task (Knutson et al., 2000;
224   Yau et al., 2012) (MID) measures aspects of reward processing, including anticipation and
225   receipt of rewards and losses and motivation to earn rewards and avoid losses (Casey et al.,
226   2018). Data are collected during two approximately 5.5-minute, 50-trial functional MRI runs
227   (403 volumes per run after discarded acquisitions). Trials begin with a cue indicating whether the
228   child can win \$.20 or \$5, lose \$.20 or \$5, or earn \$0. After 1500–4000 ms, a target appears for
229   150–500 ms. Target timing is staircased such that each child achieves approximately 60%
230   accuracy. Children must respond during the target presentation to achieve the indicated trial
231   outcome. Trials are followed by feedback indicating the outcome.

232   Response time and accuracy are not used as MID performance measures because target
233   timing was individualized. Overall task performance is instead summarized as the average
234   amount of money earned during both runs. This metric is correlated with mean accuracy (r_s =
235   .68, $p < .001$) and correct-trial RT ($r = –.29$, $p < .001$), but may capture additional variance in
236   reward-related behavior. For example, two children who achieve 60% accuracy could earn
237   different amounts of money if one preferentially responds to win large rewards and avoid large
238   losses, perhaps due to greater reward motivation.

239

240   **Relationships between behavioral measures.** To characterize associations between working
241   memory and other cognitive abilities, we first cross-correlated all 17 behavioral measures using
242   data from all children meeting inclusion criteria ($n = 11,537$). Although normality was not
243   evaluated with formal tests, which reject the null hypothesis for near-normal distributions in
244   large samples (Ghasemi and Zahediasl, 2012), rank correlation was applied because visual
245   inspection indicated that behavioral measures were not normally distributed (**Fig. 1**). To establish
246   whether relationships were robust to potential confounds such as age, sex, missing data, outliers,
247   and statistical dependence introduced by family structure, data collection method, and site, we
248   subsequently replicated this analysis using:

249   1. data from one child per family, based on self-report ($n = 9,750$). For families with
250   multiple children in the 11,537-participant cohort, the child whose randomly assigned

251   NDAR Global Unique Identifier (GUID) came first in alphabetical order was included in

252   this sample.

2. data from all children meeting inclusion criteria using Spearman partial correlation to control for age and sex

3. data values within 2.5 standard deviations of the group mean (see **Table 1**)

4. data from children with no missing values (i.e., complete cases; $n = 7,504$)

5. data from children who completed the emotional n-back, SST, and MID tasks during MRI data collection rather than on a laptop outside the scanner ($n = 9,452$). (Of the children whose data were analyzed here, 1,102 did not complete any task in the scanner or did not have this information available, 399 completed one task in the scanner, 584 completed two tasks in the scanner, and 9,452 completed all three tasks in the scanner.)

6. data from children without performance flags on the emotional n-back, SST, and MID tasks ($n = 6,441$). Performance flags, available in the curated ABCD data, were assigned based on the following criteria: <60% 0-back or 2-back accuracy on the emotional n-back task; <150 go trials, <60% go trial accuracy, >30% incorrect go trial percentage, >30% late go trial percentage, >30% "no response" go trials, <30 stop trials, or <20% or >80% stop trial accuracy on the SST; <3 positive and negative feedback events for large reward, small reward, large loss, small loss, or no stakes trials on the MID task.

7. data from a conservative subsample excluding outlier values, incomplete cases, children who completed neuroimaging tasks outside of the scanner, children with neuroimaging task performance flags, and related children. Age and sex were controlled with partial correlation ($n = 4,393$)

8. data from each of the 21 data collection sites with more than 100 participants separately ($n = 328–988$; mean $n = 524.4$; $s.d. = 192.1$; 22nd site with 36 children excluded from this analysis)

Due to the presence of missing data, relationships between behavioral measures were evaluated with pairwise correlations rather than with data reduction techniques such as principal component analysis (PCA), which do not typically allow for missing data. 34.96% of children were missing at least one performance measure, and neuroimaging task performance data were missing in 20.14% of the sample on average (**Table 1**; note that recovery of missing data is ongoing). Although Bayesian probabilistic PCA can account for missing data as well as the nesting of participants in families and data collection sites (Thompson et al., 2018), this approach

283 assumes that missing data occur randomly, independent of other sample features (Oba et al.,
284 2003). This assumption is violated in the current sample, as, for example, children with better
285 working memory function are less likely to be missing other behavioral measures (Spearman
286 correlation between list sorting performance and number of missing performance measures = –
287 0.09, $p < 2.2 \times 10^{-16}$). (Of note, Thompson et al. (2018) performed Bayesian probabilistic PCA on
288 a subset of the behavioral measures analyzed here—specifically those collected outside the
289 scanner. A smaller percentage of these data are missing from curated release 2.0.1 [less than 3%
290 per measure; **Table 1**], reducing issues associated with missingness.)
291
292 **Neuroimaging data collection.** ABCD scan sessions included a localizer and acquisition of a
293 high-resolution anatomical scan, two runs of resting state fMRI, diffusion weighted images, 3D
294 T2-weighted spin echo images, two more runs of resting state fMRI, and task-based fMRI. (Sites
295 with Siemens scanners used Framewise Integrated Real-time MRI Monitoring (Dosenbach et al.,
296 2017) [FIRMM] to monitor children's head motion during data collection. Scan operators at
297 these sites may have stopped resting-state data collection after three runs if 12.5 minutes of low-
298 motion resting-state data had been collected.) Image acquisition order was fixed, but fMRI task
299 order was randomized across participants (Casey et al., 2018). Data were collected on Siemens
300 Prisma, Phillips and GE 750 3T scanners, with detailed acquisition parameters reported in
301 previous work (Casey et al., 2018; Hagler et al., 2019). Functional images were collected using a
302 multiband gradient EPI sequence with the following parameters: TR = 800 ms, TE = 30 ms, flip
303 angle = 52°, 60 slices acquired in the axial plane, voxel size = 2.4 mm^3, multiband slice
304 acceleration factor = 6.
305
306 **Image preprocessing.** Task-based data were processed by the ABCD Study Data Analysis and
307 Informatics Center (DAIC) using approaches described in detail in Hagler et al. (2019).
308 Preprocessing steps included motion correction with 3dvolreg in AFNI, B_0-distortion (i.e., field-
309 map) correction, gradient nonlinearity distortion correction, and resampling scans into alignment
310 with cubic interpolation using a mid-session scan as the reference. Registration between T2-
311 weighted spin echo scans, field maps, and T1-weighted structural images was performed using
312 mutual information. Functional images were aligned to T1-weighted images using rigid-body
313 transformation (Hagler et al., 2019).

314   The equivalent of 16 volumes was removed from the start of each run. For Siemens and
315   Philips scanners, 8 volumes were removed because the first 8 volumes were used as the
316   multiband reference scans. For GE scanners running DV25 software, 5 volumes were removed
317   because the first 12 volumes were used as the multiband reference. The images were then
318   combined into a single volume and saved as the initial TR (leaving a total of 5 frames to be
319   discarded). For GE scanners running DV26 software, 16 volumes were removed.
320

321   **Relationships between fMRI activity and working memory function.** After preprocessing,
322   voxel-wise time series data were normalized within run. Task-related activity estimates were
323   generated for each child using general linear models (GLMs) with 3dDeconvolve in AFNI
324   (Hagler et al., 2019). GLMs included nuisance regressors accounting for baseline and quadratic
325   trends as well as motion estimates and their derivatives, temporally filtered to attenuate .31–.43
326   Hz signals related to respiration (Fair et al., 2018). Volumes with framewise displacement values
327   >.9 mm were censored (Siegel et al., 2014).
328   In addition to fixation, the emotional *n*-back task GLM included predictors for happy,
329   fearful, and neutral face as well as place stimuli in the 0-back and 2-back conditions. Task bocks
330   (approximately 24 s) were modeled as square waves convolved with a two-parameter gamma
331   basis function (Hagler et al., 2019). The stop-signal task model included predictors for correct
332   and incorrect stop and go trials, modeled as instantaneous. The monetary incentive delay model
333   included small and large reward and loss cues and feedback and no stakes cues, modeled as
334   instantaneous (Hagler et al., 2019). GLM beta coefficients for cortical gray matter voxels were
335   sampled into surface space. (This step differs from the processing pipeline described in Hagler et
336   al. (2019), in which preprocessed data were sampled onto the cortical surface, but does not affect
337   the beta values.)
338   To characterize relationships between out-of-scanner list sorting working memory
339   performance and fMRI activation in response to a working memory challenge, we first estimated
340   memory-related activity with a linear contrast of 2-back vs. 0-back emotional *n*-back task blocks
341   (6,965 data sets available; $n = 3,750$ after exclusion). Subject-specific beta weights were entered
342   into a multiple regression model, including list sorting performance as a predictor, with FSL's
343   PALM software (Winkler et al., 2014). Covariates were also included in the model: age and sex
344   (to account for effects present in the uncorrected list sorting standard scores) (Luciana et al.,
345   2018), scanner (to account for magnet-related differences between the 26 scanners as well as

346 effects of participant population [e.g., family income, education, race and ethnicity]), fluid

347 intelligence (to account for non-specific effects of cognitive function), and mean frame-to-frame

348 head motion during the *n*-back task. Head motion was measured with *tfmri_nback_all_beta_mm*

349 from curated data release 2.0.1 sheet nback_bwroi02.txt. Degrees of freedom

350 (*tfmri_nback_all_beta_dof*) and number of frames with a framewise displacement of less than .2

351 mm (*tfmri_nback_ab_subthnvols*) were not included as covariates because they were highly

352 correlated with frame-to-frame motion ($r = -.96$ and $-.95$, respectively). Nonparametric

353 significance was assessed with permutation testing using PALM's tail approximation

354 acceleration method (Winkler et al., 2016). For each contrast, 1000 permutations were run, a

355 generalized Pareto distribution (GPD) was fit to the tail of the resulting null distribution, and *p*-

356 values below .10 were computed from the GPD. Regression coefficients surviving a family-wise

357 error-corrected *p*-value threshold of .05 were considered significant.

358 To assess the specificity of relationships between list sorting scores and memory-related

359 fMRI activity, we repeated this analysis using contrast maps related to three other processes:

360 emotion processing, inhibitory control, and reward processing. Subject-specific beta coefficient

361 maps reflecting emotion processing-related activity were computed by contrasting emotional vs.

362 neutral face stimulus blocks on the emotional *n*-back task (6,965 data sets available; $n = 3,750$

363 after exclusion). Beta coefficient maps reflecting inhibitory control-related activity were

364 computed by contrasting successful vs. unsuccessful stop trials on the stop-signal task (6,906

365 data sets available; $n = 4,316$ after exclusion). Beta coefficient maps reflecting activity related to

366 reward sensitivity were computed by contrasting successful vs. unsuccessful reward trials (i.e.,

367 volumes corresponding to positive vs. negative feedback) on the monetary incentive delay task

368 (6,984 data sets available; $n = 4,277$ after exclusion). Multiple regression models including

369 working memory performance, age, sex, scanner, fluid intelligence, and mean frame-to-frame

370 head motion during the relevant task runs were applied to predict subject-specific beta weights.

371

372 **Neuroimaging data exclusion.** Neuroimaging data from all Philips scanners (approximately

373 13% of the sample) were excluded from analysis due to an error in curated ABCD data

374 preprocessing. Neuroimaging data from children with poor structural scan quality, determined

375 with curated data release 2.0.1 sheet freesqc01.txt, were also excluded from analysis. Participants

376 with a score of zero for *fsqc_qc* and/or a score greater than one for *fsqc_qu_motion*,

377 *fsqc_qu_pialover*, *fsqc_qu_wmunder*, or *fsqc_qu_inhomogeneity* were excluded. For each task

378 contrast, participants with fewer than 550 degrees of freedom in preprocessed, concatenated

379 fMRI time series, missing grayordinate (i.e., gray-matter vertex or voxel) values, and/or or

380 extreme values (>3 standard deviations from the group mean) for the mean or standard

381 deviations of beta weights over all grayordinates were also excluded. All fMRI analyses were

382 performed using data from only one child per family to avoid confounds introduced by family

383 structure. We elected to take this conservative approach rather than attempt to control for family

384 structure with multi-level block permutation (Winkler et al., 2015) given the complexity of

385 possible familial relationships (e.g., triplets, monozygotic and dizygotic twins, full siblings, half

386 siblings, cousins, etc.).

387

388

389 **Results**

390 **Working memory performance in childhood.** Working memory function, operationalized with

391 NIH Toolbox List Sorting Working Memory Test performance, approximated the normative

392 population mean (uncorrected standard score mean = 96.7, *s.d.* = 12.0, range = 36–136;

393 normative mean = 100, *s.d.* = 15). Working memory was positively correlated with age (r_s =

394 .148, $p < 2.2 \times 10^{-16}$) and numerically differed by sex, albeit with a negligible effect size (female

395 mean = 96.3; male mean = 97.2; Welch $t_{4339.8}$ = –3.99; $p = 6.8 \times 10^{-5}$; Cohen's d = –.075).

396 Performance on all other neurocognitive measures in the ABCD task battery—which assess short

397 term memory, fluid intelligence, visuospatial attention, reading and language skills, cognitive

398 control, processing speed, flexible thinking, learning, delay of gratification, emotion regulation,

399 impulsivity, and reward processing—is visualized in **Fig. 1**.

400

401 **Behavioral signatures of working memory.** Although a rich literature in cognitive psychology

402 describes relationships between working memory and cognitive and attentional processes in

403 adulthood, how these associations emerge in development is less well understood. Thus, a

404 primary goal of the current work is to characterize these associations in childhood to understand

405 how they change over time.

406 To relate working memory to cognitive and attentional abilities, we computed pairwise

407 Spearman correlations between performance scores on all tasks included in the dataset (i.e., all

408 behavioral measures visualized in **Fig. 1**). Correlation coefficients are reported without

409 corresponding *p*-values because effect sizes as small as $r^2 = 3.34 \times 10^{-4}$ are significant at $p < .05$

410   in a sample of 11,537, and statistical dependence introduced by family relatedness, site effects,

411   and the inclusion of multiple performance measures per test precludes parametric r-to-p

412   conversion. Furthermore, the goal of this analysis is to establish a pattern of behavioral

413   relationships rather than to evaluate the statistical significance of particular associations.

414   Across individuals, working memory was most strongly related to language skills

415   measured with the NIH Toolbox Picture Vocabulary and Oral Reading Recognition tests (r_s

416   values = .40); memory-related performance on the emotional n-back task, Picture Sequence

417   Memory Test, and Rey Auditory Verbal Learning Test (RAVLT); and fluid intelligence

418   measured with matrix reasoning (r_s = .35; **Figs. 2**, **3**).

419   Correlations between list sorting performance and performance on other memory tests

420   also revealed relationships between different aspects of memory. The emotional n-back task,

421   collected during functional MRI, measured performance during high memory load (2-back) and

422   low memory load (0-back) task blocks. During 2-back blocks, children were asked to indicate

423   when they saw a picture identical to the one they saw two trials back. During 0-back blocks,

424   children were shown a target picture and instructed to indicate when they saw a matching image.

425   Working memory was more strongly related to 2-back than to 0-back accuracy (r_s = .36 vs. .32;

426   Steiger's z = 5.36, $p < .0001$), indicating that, as predicted, working memory ability is reflected

427   to a greater degree by performance on high-load vs. low-load n-back blocks. (Interestingly, 2-

428   back and 0-back accuracy scores were highly correlated [r_s = .62], suggesting that common

429   processes such as working memory, attention, and motivation contribute to performance on both

430   tasks.) Recognition memory for emotional n-back stimuli (happy, fearful, and neutral face

431   photographs and place photographs) was tested after fMRI data collection. Although working

432   memory was less highly correlated with recognition memory than with performance on visual

433   attention tasks, including the Flanker task (r_s = .21 vs. .25; Steiger's z = 4.01, p = .0001), this

434   may reflect low overall memory for specific stimuli, especially face photographs, at this age

435   (Casey et al., 2018). Finally, the RAVLT assessed immediate recall of a word list as well as

436   recall after a 30-minute delay, and the NIH Toolbox Picture Sequence Memory Test measured

437   episodic memory and visuospatial sequencing. Working memory was similarly related to

438   immediate and delayed recall on the RAVLT and performance on the Picture Sequence Memory

439   Test (r_s values = .3389, .3372, and .3428, respectively).

440   Of note, correlations between list sorting performance and other behavioral measures are

441   influenced by both the similarity of the constructs they measure and the reliability of the

442   measures themselves. Previous work reports good to excellent reliability for all NIH Toolbox

443   tasks (test-retest intraclass correlation coefficient [ICC] = .61–.90; Dikmen et al., 2014; Gershon

444   et al., 2014; Tulsky et al., 2014; Zelazo et al., 2014; Carlozzi et al., 2015), the WISC-V matrix

445   reasoning test (test-retest r = .78; Luciana et al., 2018), and the RAVLT (test-retest r = ~.60–.70;

446   Van Den Burg and Kingma, 1999; Luciana et al., 2018). In the current sample, ICC, calculated

447   by comparing participants' first and second fMRI runs, is .64 for the 0-back task and .68 for the

448   2-back task. However, the reliability of monetary incentive delay earnings is poor (ICC = .27).

449   Thus, the low correlation between list sorting performance and measures including monetary

450   incentive delay earnings may in part reflect low measure reliability. (Test-retest reliability

451   estimates for the intertemporal cash choice task, Little Man Task, and post-scan n-back stimuli

452   recognition memory test are not available because these tests were only completed once and

453   reliability estimates have not been published elsewhere. Test-retest reliability was not calculated

454   for the stop-signal task because run-specific stop-signal delay values were not available.)

455

456   **Behavioral relationships replicate across independent data releases.** To assess the

457   reproducibility of behavioral relationships, we cross-correlated all performance measures using

458   data from curated ABCD releases 1.1 (n = 4,397) and 2.0.1 (n = 7,140 new individuals)

459   separately. The pattern of relationships was stable across releases (spatial r_s = .982), suggesting

460   that the observed pattern is generalizable rather than idiosyncratic to a particular sample.

461

462   **Behavioral relationships are not influenced by family structure.** The full 11,537-child cohort

463   includes 3,532 related children from 9,750 unique families (based on self-report). Because

464   relatedness affects the independence of behavioral measures and could have affected

465   relationships between them, we replicated correlations between cognitive and attentional abilities

466   in a subset of data from only one child per family. The pattern of behavioral relationships in this

467   unrelated subsample was nearly identical to that observed in the full sample: the Spearman

468   spatial correlation between the two samples' vectorized behavioral cross-correlation matrices

469   was .999.

470   Given the importance of accounting for family structure in big data samples, we next

471   characterized effects of relatedness on behavioral relationships with an additional analysis. First,

472   we computed the absolute difference between all 136 pairwise behavioral correlations in the full

473   sample (n = 11,537) and the unrelated subsample (n = 9,750 after excluding 1,787 related

children). Next, we randomly excluded 1,787 children from the full sample, re-calculated pairwise behavioral relationships, and recorded the difference between the full-sample correlations and these random subsample correlations. We repeated this process 1,000 times to generate a null distribution of correlation coefficient differences for each pair of behavioral measures. Non-parametric p-values were generated by comparing each true correlation difference, $|r(i,j)_{\text{full sample}} - r(i,j)_{\text{unrelated subsample}}|$, to its corresponding null distribution. We used this conservative sub-sampling approach rather controlling for family relatedness with linear mixed models because of the range of possible familial relationships and the fact that relatedness may be inaccurately captured with self-report measures.

Using the subsampling approach, we found that none of the 136 pairwise behavioral relationships differed between the full sample and the unrelated subsample more than they differed between the full sample and the random subsamples (all > Bonferroni-corrected $p = .05/136 = 3.68 \times 10^{-4}$). Therefore, excluding family members from the sample did not disproportionately affect pairwise behavioral relationships, and including related participants does not bias the current results.

Behavioral relationships are robust to age, sex, outliers, and missing data. Control analyses confirmed that behavioral relationships were robust to other potential confounds. Specifically, the overall pattern of relationships was consistent after controlling for age and sex with partial correlation ($n = 11,537$; $r_s = .995$), excluding outlier values (> 2.5 standard deviations from the group mean; $n = 11,537$; $r_s = .995$), excluding children with any missing behavioral scores ($n = 7,504$; $r_s = .997$), excluding children who completed any neuroimaging task (i.e., the emotional n-back, stop signal, or monetary incentive delay task) on a laptop outside the scanner ($n = 9,452$; $r_s = .997$), and excluding children with neuroimaging task performance flags provided by the ABCD Study ($n = 6,441$; $r_s = .982$). The overall pattern of relationships was replicated to a lesser degree in a conservative subsample of children excluding relatives, outlier values, incomplete cases, children who completed neuroimaging tasks outside the scanner, and children with neuroimaging task performance flags, and controlling for age and sex ($n = 4,393$; $r_s = .973$). Finally, associations between behavioral measures were similar across data collection sites despite differences in target sociodemographics (Garavan et al., 2018). Similarity between site-specific behavioral cross-correlation patterns ranged from $r_s = .80$–$.94$ (mean $r_s = .86$, $s.d. = .03$).

506 **Neural signatures of working memory.** To identify a vertex-wise map of associations with

507 working memory, we related out-of-scanner list sorting working memory performance to fMRI

508 activation in response to a working memory challenge. Working memory was significantly

509 related to 2-back vs. 0-back (i.e., high vs. low memory load) activation in regions of frontal and

510 parietal cortex including bilateral intraparietal sulci, dorsal premotor cortex/frontal eye fields,

511 dorsolateral prefrontal cortex, anterior insula, dorsal anterior cingulate cortex extending into the

512 pre-supplementary motor area, and precuneus (**Fig. 4**). In line with previous work highlighting

513 the importance of frontoparietal regions for working memory in development (Klingberg et al.,

514 2002; Satterthwaite et al., 2013; Klingberg and Darki, 2014), children with better out-of-scanner

515 working memory performance showed increased activity during high relative to low memory

516 load task blocks in this distributed set of regions that overlap with frontoparietal and dorsal

517 attention networks (Power et al., 2011; Yeo et al., 2011) (**Fig. 5**).

518

519 **Relationships between working memory and fMRI activity are domain-specific.** Are

520 patterns of fMRI activation that track individual differences in working memory driven by

521 general task demands, or are they driven by working memory engagement *per se*? We performed

522 two analyses to disentangle these alternatives. First, we examined the association between

523 individual differences in working memory performance and activation revealed by a contrast of

524 emotional vs. neutral face blocks in the *n*-back task. Although these emotion-related activation

525 patterns were measured during a working memory task, the contrast of these two types of face

526 blocks does not reflect a working memory challenge. Therefore, significant relationships

527 between these patterns and working memory would suggest that neural signatures of working

528 memory are domain-general rather than domain-specific. Second, we examined the relationships

529 between individual differences in working memory and activation patterns reflecting distinct

530 cognitive processes in distinct task contexts: inhibitory control during a stop-signal task and

531 reward processing during a monetary incentive delay task.

532   Results revealed that working memory was not significantly associated with emotion-

533 related activation during the emotional *n*-back task, inhibitory control-related activation during

534 the stop-signal task, or reward-related activation during the monetary incentive delay task (**Fig.**

535 **4**). Although we did not compare regression coefficients across conditions because participant

536 samples were overlapping but not identical, more participants and time points were available for

537 the stop-signal and monetary incentive delay tasks than for the emotional *n*-back task.

538 Furthermore, within-subject reliability of fMRI task activations (characterized by comparing beta

539 weights in regions of the Desikan cortical brain atlas from participants' first and second task

540 runs, as included in curated data release 2.0.1) was numerically highest for the monetary

541 incentive delay task contrast. Thus, the presence of significant effects for the working memory

542 contrast—but not the inhibitory control or reward processing contrasts—is not attributable to

543 sample size, amount of data per individual, or increased within-subject fMRI activation

544 reliability for the working memory contrast, and results suggest that frontoparietal activity is a

545 domain-specific rather than a domain-general signature of working memory.

546

547 **Memory-related frontoparietal activity reflects in-scanner and out-of-scanner working**

548 **memory performance.** One potential explanation of the current results is that in-scanner

549 emotional *n*-back performance—a state-like measure of working memory and task engagement

550 rather than a measure of individual differences in working memory *per se*—drives the selective

551 relationship between working memory and 2-back vs. 0-back frontoparietal activation. To

552 evaluate this possibility, we replicated the analysis relating out-of-scanner working memory

553 performance to 2-back vs. 0-back activation with age, sex, scanner, fluid intelligence, mean

554 frame-to-frame head motion during the *n*-back task, and 0-back and 2-back accuracy included in

555 the model as covariates. Results revealed significant clusters in frontoparietal regions (**Fig. 6**),

556 demonstrating that memory-related activation reflects both in-scanner and out-of-scanner

557 working memory performance.

558   As an exploratory analysis, we next related 2-back vs. 0-back activity to behavior with a

559 multiple regression model that included all 17 behavioral measures reported in Fig. 1 as well as

560 age, sex, scanner, fluid intelligence, and mean frame-to-frame head motion during the *n*-back

561 task. As expected, *n*-back activity predicted in-scanner 2-back and 0-back accuracy, even when

562 controlling for performance on all out-of-scanner cognitive tasks. In addition, significant (albeit

563 qualitatively weaker) relationships were observed between 2-back vs. 0-back activity and

564 performance on the list sorting task and the out-of-scanner measures with which it was most

565 highly correlated—the NIH Toolbox Picture Vocabulary and Oral Reading Recognition tasks

566 and the WISC-V matrix reasoning test. Activity was also significantly related to performance on

567 the Little Man task. Together these results suggest that frontoparietal activity reflects both in-

568 and out-of-scanner measures of working memory as well as behavioral performance on

569 statistically related measures. Given that a limitation of this exploratory analysis is strong

correlation among predictor variables, future work relating independent measures of cognitive and attentional processes to frontoparietal activity observed in multiple task contexts can inform the degree to which working memory-related activity specifically reflects working memory behavioral performance.

Neuroimaging findings replicate across independent data releases. To assess the reproducibility of observed brain–behavior relationships, we repeated fMRI analyses using data from participants first included in ABCD releases 1.0 and 2.0.1 separately. Consistent with the full-sample findings, list sorting working memory task performance was significantly related to 2-back vs. 0-back activity in frontoparietal regions in both subsamples. List sorting performance was not significantly related to emotional vs. neutral face, successful vs. unsuccessful stop, or successful vs. unsuccessful reward activity in either subsample (**Fig. 7**). When controlling for in-scanner n-back accuracy, the pattern of results was qualitatively similar, but significant relationships were observed in release 2 data only (release 1 n = 1412; release 2 n = 2338; **Fig. 6**).

Discussion

Working memory is a foundational cognitive function that changes over development and varies across individuals. Here we characterize relationships between working memory, cognitive and attentional processes, and task-related brain activity in childhood using behavioral and functional MRI data from the largest developmental neuroimaging sample to date. Behavioral analyses demonstrate that children with stronger working memory abilities perform better on a range of cognitive tasks, and revealed close relationships between working memory, performance on other memory tasks, language abilities, and fluid intelligence. Functional MRI analyses of emotional n-back, stop-signal, and monetary incentive delay task data provide evidence that frontoparietal activation in response to an explicit working memory challenge—but not in response to general task demands—is a reliable marker of working memory ability. Finally, a control analysis suggests that memory-related frontoparietal activity reflects individual differences in working memory above and beyond ongoing task performance.

601   Positive associations between working memory, language abilities, and fluid intelligence
602 replicate previous work on the structure of cognition in children and adults (Engle et al., 1999;
603 Gathercole, 1999; Thompson et al., 2018). As expected, children with stronger working memory
604 performance (measured with the List Sorting Working Memory Test) also showed better
605 performance on tests of episodic memory (Picture Sequence Memory), short-term memory (Rey
606 Auditory Verbal Learning), and low- and high-load working memory (emotional n-back 0- and
607 2-back conditions, respectively). Correlations between these measures in the full sample of
608 11,537 children ranged from .32–.36, suggesting that they reflect both distinct and overlapping
609 aspects of memory function. Somewhat surprisingly given established links between working
610 memory and processing speed (Conway et al., 2002), working memory was less closely related
611 to performance on the Pattern Comparison Processing Speed Test than to performance on every
612 cognitive task except the stop-signal, monetary incentive delay, and intertemporal cash choice
613 tasks. Although the strength of the relationship between working memory and processing speed
614 (r_s = .20) is numerically similar to previous findings with the same tasks in 8-to-12-year-olds (r =
615 .26; Carlozzi et al., 2015), individual differences in working memory were more strongly related
616 to processes including executive attention and cognitive flexibility than to processing speed in
617 the current cohort. Together these results reveal relationships between working memory and
618 cognitive and attentional processes in childhood.

619   This behavioral cross-correlation pattern was consistent after controlling for age and sex
620 and excluding statistical outliers, incomplete cases, and neuroimaging task data collected outside
621 the scanner. These behavioral patterns remained unchanged when measured in a subsample of
622 the data that did not include relatives (i.e., only including one child per identified family). Thus,
623 although it is important to account for these factors in large datasets such as the ABCD sample,
624 the current results appear robust to effects of statistical dependence and outliers. Furthermore,
625 the results are not biased by the inclusion of related children.

626   Neuroimaging results likewise align with previous work, providing evidence that
627 frontoparietal activity reflects differences in working memory function during development
628 (Klingberg et al., 2002; Satterthwaite et al., 2013). The narrow age range of the current sample,
629 however, allowed us to disentangle individual differences from developmental changes,
630 providing novel evidence that frontoparietal brain function underlies variability in working
631 memory both within and across individuals. Furthermore, assessing relationships between
632 working memory and fMRI activity related to memory, emotion processing, inhibitory control,

633 and reward processing demonstrated that frontoparietal activation is a domain-specific rather

634 than a task-general neural signature of working memory. Accounting for in-scanner emotional *n*-

635 back performance, which reflects individual differences in working memory and attentional

636 processes as well as transient attentional state, revealed relationships between out-of-scanner

637 working memory performance and memory-related fMRI activation in regions of superior

638 parietal and pre-supplementary motor cortex. Children with stronger working memory abilities,

639 therefore, show increased frontoparietal activation during high relative to low memory load task

640 blocks in part because they simply perform better on these tasks, but also because of individual

641 differences in their ability to hold and manipulate information in mind.

642 The current results suggest that frontoparietal activation is a domain-specific neural

643 signature of working memory in that individual differences in working memory are selectively

644 reflected in 2-back versus 0-back frontoparietal activity. Results of an exploratory analysis also

645 suggest some degree of specificity in the reverse direction: 2-back versus 0-back frontoparietal

646 activity is uniquely related to both in- and out-of-scanner working memory measures, as well as

647 a subset of measures correlated with working memory task performance. Importantly however,

648 frontoparietal activity does not *only* support working memory function, but is also related to

649 processes including attention and cognitive control (Corbetta and Shulman, 2002; Vincent et al.,

650 2008; Spreng et al., 2010, 2012; Ptak, 2011). Recent work has emphasized the multifunctional

651 nature of the frontoparietal network, proposing that it represents a domain-general "cognitive

652 core" of the brain (Assem et al., 2019). Our results are not inconsistent with this

653 conceptualization. Rather, they demonstrate that a high versus low memory load contrast reveals

654 a frontoparietal activity signature of working memory, and leave open the possibility that an

655 attention or cognitive control contrast could reveal a frontoparietal activity signature of attention

656 or cognitive control. Future work that expands the collection of attention and control tasks and

657 varies their cognitive demands will provide additional insights into the functional significance of

658 overlapping and distinct patterns of frontoparietal activity across psychological tasks with

659 development.

660 A neural signature of working memory based on task activation data complements a

661 growing body of work identifying neuromarkers of individual differences from functional brain

662 connectivity. In particular, patterns of task-based and resting-state functional connectivity, or

663 statistical dependence between two brain regions' activity time courses, have been used to

664 predict individual differences in abilities including attention, fluid intelligence, and aspects of

memory (Finn et al., 2015; Galeano Weber et al., 2017; Rosenberg et al., 2017; Lin et al., 2018; Rudolph et al., 2018; Yamashita et al., 2018; Avery et al., 2019). Recent work suggests that models based on task connectivity generally outperform those based on resting-state connectivity for predicting behavior, potentially because tasks engage circuits related to a process of interest to magnify individual differences in behaviorally relevant neural phenotypes, thereby improving predictions (Finn et al., 2017b; Greene et al., 2018; Rosenberg et al., 2018; Yoo et al., 2018). It is an open question, however, whether tasks selectively enhance the prediction of task-relevant behaviors. Here, motivated by previous work relating frontoparietal activation to developmental change in working memory (Klingberg et al., 2002; Kwon et al., 2002; Crone et al., 2006; Satterthwaite et al., 2013), we address this question with task activation rather than functional connectivity analyses. The current result—that frontoparietal activity indexes working memory *only when working memory is explicitly taxed*—suggests that task challenges may reveal neural signatures of task-relevant behaviors, and underscores the importance of multi-task or multi-condition data for elucidating state-specific and state-general biomarkers of behavior.

The goal of the current work was to characterize a brain-based biomarker and behavioral signature of working memory in childhood not just for the sake of understanding these relationships at a single point in time, but also for ultimately understanding their trajectories across development. Because the ABCD study will follow children from age 9–11 to age 19–21, longitudinal work can provide new insights into associations between working memory, cognitive and attentional processes, and real-world outcomes across adolescence and young adulthood. Biennial MRI sessions—during which participants will complete the same emotional *n*-back, stop-signal, and monetary incentive delay tasks that they completed at ages nine through eleven—will also facilitate the discovery of changing neural signatures of abilities and behavior. For example, will there be changes in the distinct and overlapping brain activity patterns associated with working memory, inhibitory control, and reward processing with age? Will the domain-specificity and domain-generality of these signatures vary over time? Are there different developmental trajectories for frontoparietal organization of function across these processes? A fruitful way to frame the current findings is as a single point along a nonlinear trajectory rather than as a summary of working memory function in development as a whole.

Finally, as sample sizes in psychology and human neuroscience rapidly increase, it is important to note limitations of big data cohort-based approaches. First, behavioral and neuroimaging task batteries for these studies are determined by committee to address specific

697   scientific goals. Although the resulting task sets often assess a range of mental processes, they

698   may not be optimal for answering all questions. In the ABCD Study neuroimaging battery, for

699   example, cognitive control demands and task difficulty are not equated across the emotional *n*-

700   back, stop-signal, and monetary incentive delay tasks. Thus, the 2-back vs. 0-back contrast may

701   reflect processes such as cognitive control and attention that are not reflected in the three control

702   contrasts. In addition, the individualized nature of the stop-signal and monetary incentive delay

703   tasks (which results in different timing parameters for different children) may obscure activation

704   patterns related to individual differences in behavior. Future work relating individual differences

705   in working memory to fMRI activity reflecting cognitive control, attentional engagement, and

706   other processes in contexts matched for task difficulty will further inform the domain-specificity

707   and -generality of neural signatures of working memory. Second, large samples are not

708   necessarily representative samples, and the ABCD cohort, while geographically,

709   demographically, and socioeconomically diverse, should not be considered representative of the

710   country or the world as a whole (Garavan et al., 2018). Looking ahead, future work relating

711   cognitive and neural measures in weighted samples (LeWinn et al., 2017) can complement

712   existing studies of single- and multi-site datasets. Third, just as the ABCD participant population

713   may not represent youth as a whole, the structure of neurocognition in nine- and ten-year-olds

714   likely does not reflect that of children at other ages. Longitudinal analyses of the ABCD cohort

715   can inform changes in brain–behavior relationships across adolescence, and data collection

716   efforts such as the Human Connectome Project (HCP) Development Study (Somerville et al.,

717   2018) and HCP Aging study (Bookheimer et al., 2019) can inform these associations in younger

718   and older individuals. Finally, because even small effects can reach significance when samples

719   are large, it is helpful to distinguish statistical from practical significance. Here we focused on

720   statistical significance as a proof-of-principle demonstration that memory-related frontoparietal

721   activity tracks individual differences in working memory in childhood. Future work can evaluate

722   practical or applied significance by testing whether models based on task activation patterns

723   generalize to predict real-world outcomes including academic performance or changes in these

724   outcomes over time.

725   Despite these limitations, the current results provide the most well powered

726   characterization of relationships between working memory, cognitive and attentional processes,

727   and task-based fMRI activation in development to date. Overall, they replicate established

728   findings that children with stronger working memory function perform better on a variety of

729 cognitive tasks, particularly those assessing other aspects of memory, language skills, and fluid

730 intelligence. Furthermore, they provide evidence that frontoparietal network activation in

731 response to an explicit working memory challenge is a robust and domain-specific marker of

732 individual differences in working memory ability at age nine through eleven. Together these

733 results inform understanding of the structure of neurocognition in childhood, and highlight the

734 importance of evaluating brain–behavior relationships in multiple task contexts to demarcate the

735 specificity and generality of neural signatures of abilities and behavior.

736

737

	Description	Cognitive process(es)	Performance measure(s)	Data file	Variable name(s)	Percent missing	Percent outliers
Demographics	Age in months			abcddemo01	*interview_age*	.02	0
	Sex			abcddemo01	*sex*	.07	0
	Autism, epilepsy			abcd_screen01	*scrn_asd, scrn_epls*	0	
	Family ID			acspsw03	*rel_family_id*	0	0
	Site ID			abcd_lt01	*site_id_l*	0	0
	Scanner ID			abcd_mri01	*mri_info_deviceserialnumber*	1.01	
Neurocognitive battery	NIH Toolbox cognition battery	working memory	List Sorting Working Memory Test uss	abcd_tbss01	*nihtbx_list_uncorrected*	1.71	1.23
		language	Picture Vocabulary Test uss	abcd_tbss01	*nihtbx_picvocab_uncorrected*	1.32	1.76
		cognitive control, attention	Flanker Test uss	abcd_tbss01	*nihtbx_flanker_uncorrected*	1.37	2.67
		flexible thinking	Dimensional Change Card Sort Test uss	abcd_tbss01	*nihtbx_cardsort_uncorrected*	1.35	2.94
		processing speed	Pattern Comparison Processing Speed Test uss	abcd_tbss01	*nihtbx_pattern_uncorrected*	1.51	.81
		visuospatial sequencing, memory	Picture Sequence Memory Test uss	abcd_tbss01	*nihtbx_picture_uncorrected*	1.40	.59
		reading	Oral Reading Recognition Test uss	abcd_tbss01	*nihtbx_reading_uncorrected*	1.42	2.75
	Matrix reasoning task	fluid reasoning	WISC-V matrix reasoning total scaled score	abcd_ps01	*pea_wiscv_tss*	2.18	1.40
	Rey Auditory Verbal Learning Test (RAVLT)	learning, memory	total correct on immediate and delayed recall trials	abcd_ps01	*pea_ravlt_sd_trial_vi_tc,* *pea_ravlt_ld_trial_vii_tc*	1.87 2.31	1.95 1.68
	Intertemporal cash choice task	delay of gratification	choice of smaller-sooner or larger-later reward	cct01	*cash_choice_task*	1.83	0
	Little Man task	mental rotation	efficiency ratio (% accuracy ÷ mean correct-trial RT)	lmtp201	*lmt_scr_efficiency*	2.85	1.49
Functional MRI tasks	Emotional *n*-back (EN-back) task	memory, emotion regulation	% correct on 0-back and 2-back blocks	abcd_mri nback02	*tfmri_nb_all_beh_c0b_rate,* *tfmri_nb_all_beh_c2b_rate*	20.08 20.08	3.19 3.19
	Post-scan EN-back stimuli recognition memory test	memory	sensitivity (*d′*)	mribrec02	mean of *tfmri_rec_all_beh_posf_dpr,* *tfmri_rec_all_beh_neutf_dp,* *tfmri_rec_all_beh_negf_dp,* *tfmri_rec_all_beh_place_dp*	24.24	1.41
	Stop-signal task	impulsivity	−1*stop-signal RT	abcd_sst02	*tfmri_sst_all_beh_total_meanrt*	18.97	2.51
	Monetary incentive delay task	reward processing	mean earnings	abcd_mid02	mean of *tfmri_mid_r1_beh_t_earnings,* *tfmri_mid_r2_beh_t_earnings*	17.26	1.95

Table 1. Demographic, neurocognitive, and neuroimaging task performance measures. Data were acquired from publicly available ABCD data release 2.0.1 (DOI 10.15154/1504041). Percent missing values represent the percentage of values missing in the full sample of 11,537 children meeting inclusion criteria, although note that recovery of missing data is ongoing.

Percent outlier values represent the percentage of data values more than 2.5 standard deviations from the group mean. uss = uncorrected standard score.

Figure 1.
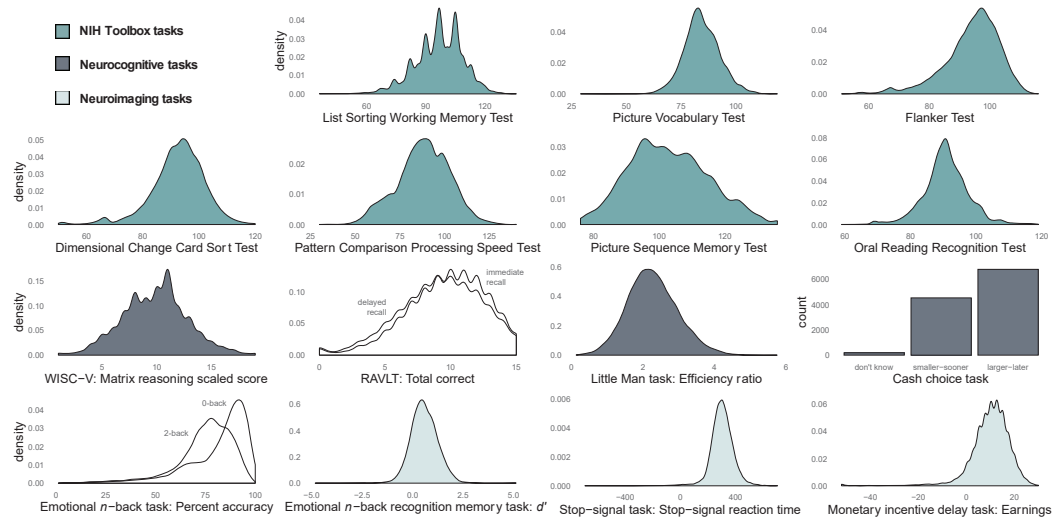
Figure 1. Kernel density estimates, or smoothed histograms, show performance in the full sample of 11,537 9–11-year-olds, including statistical outliers. NIH Toolbox performance is measured with uncorrected standard scores. Responses on the cash choice task—whether a child preferred to receive a smaller–sooner reward, a larger–later reward, or couldn't choose—are visualized with a histogram. Although "don't know" responses on this task are included here, they were excluded from formal analysis.

Figure 2.
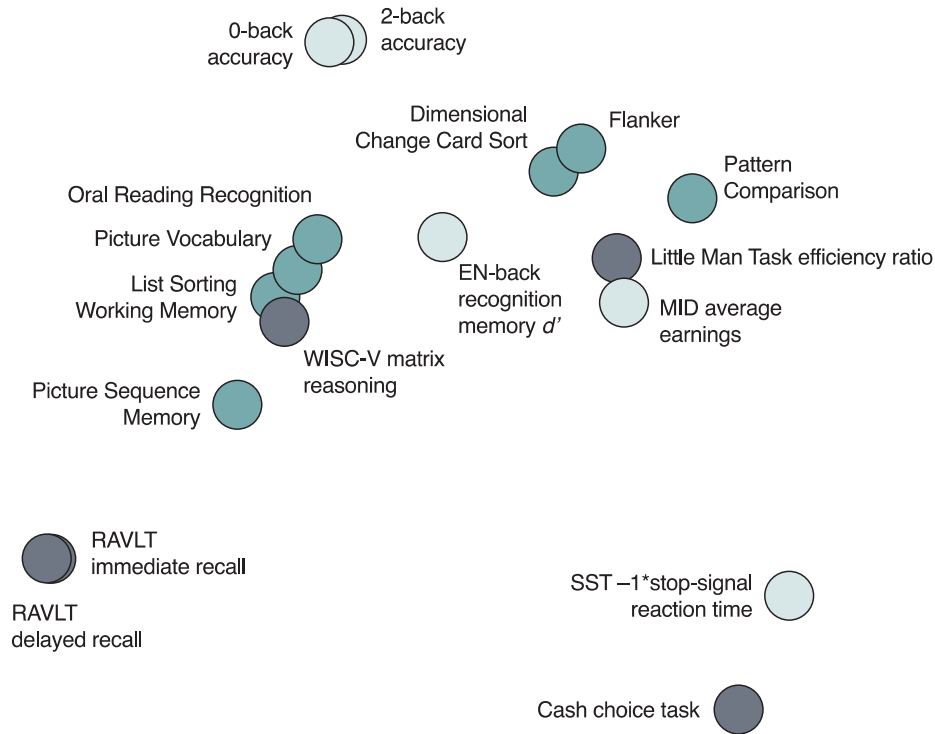
Figure 2. Multidimensional scaling plot illustrating two-dimensional distance between behavioral metrics in children with no missing data (n = 7,504). Classical multidimensional scaling was applied to the complete-case sample to avoid assumptions associated with imputing missing values. Distance was calculated as the Euclidean distance between each pair of behavioral measures after mean-centering and scaling each measure across participants. NIH Toolbox measures are shown in dark green, other neurocognitive measures in dark gray, and neuroimaging task measures in light green.

Figure 3.
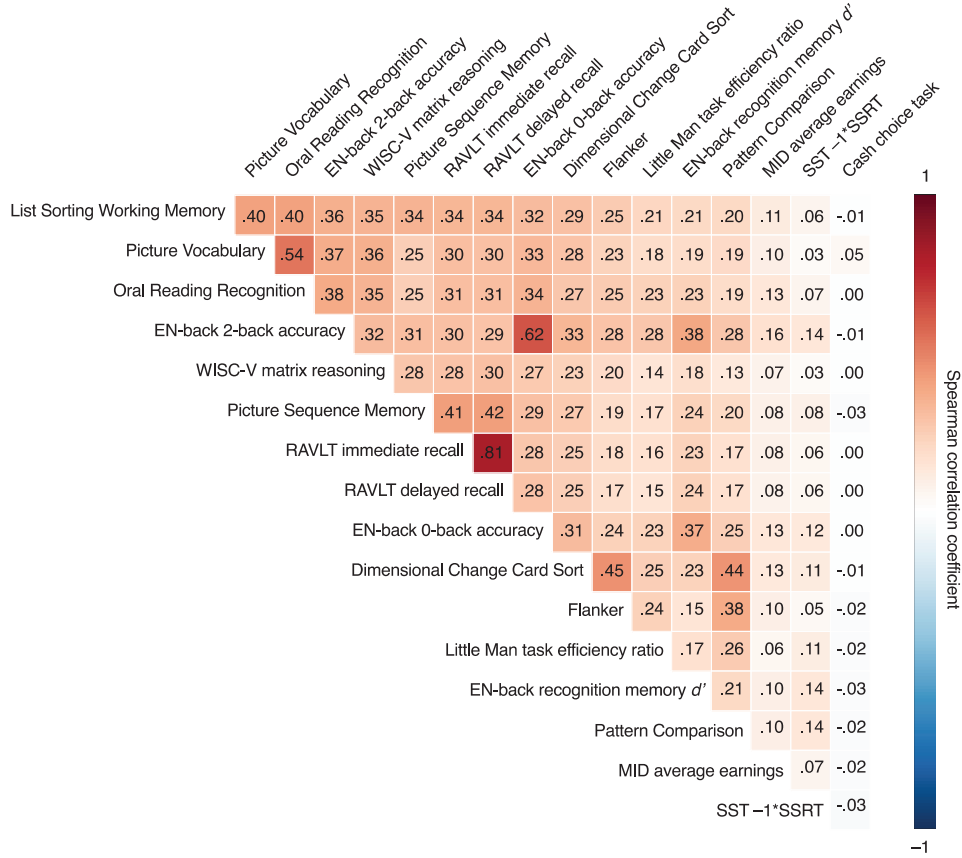
Figure 3. Spearman correlations between performance measures in the full 11,537-child sample. Measures are ordered according to the strength of their relationship with working memory, operationalized as NIH Toolbox List Sorting Working Memory Test. Because the outcome of the cash choice task is binary, relationships with performance on this measure are equivalent to point-biserial Spearman correlation coefficients.

Figure 4.

Emotional *n*-back task:
2-back vs. 0-back

Emotional *n*-back task:
emotional vs. neutral faces

Stop-signal task:
correct vs. incorrect stop

Monetary incentive delay task:
successful vs. unsuccessful reward

t-statistic

−11   11

negatively related to
working memory ability

positively related to
working memory ability
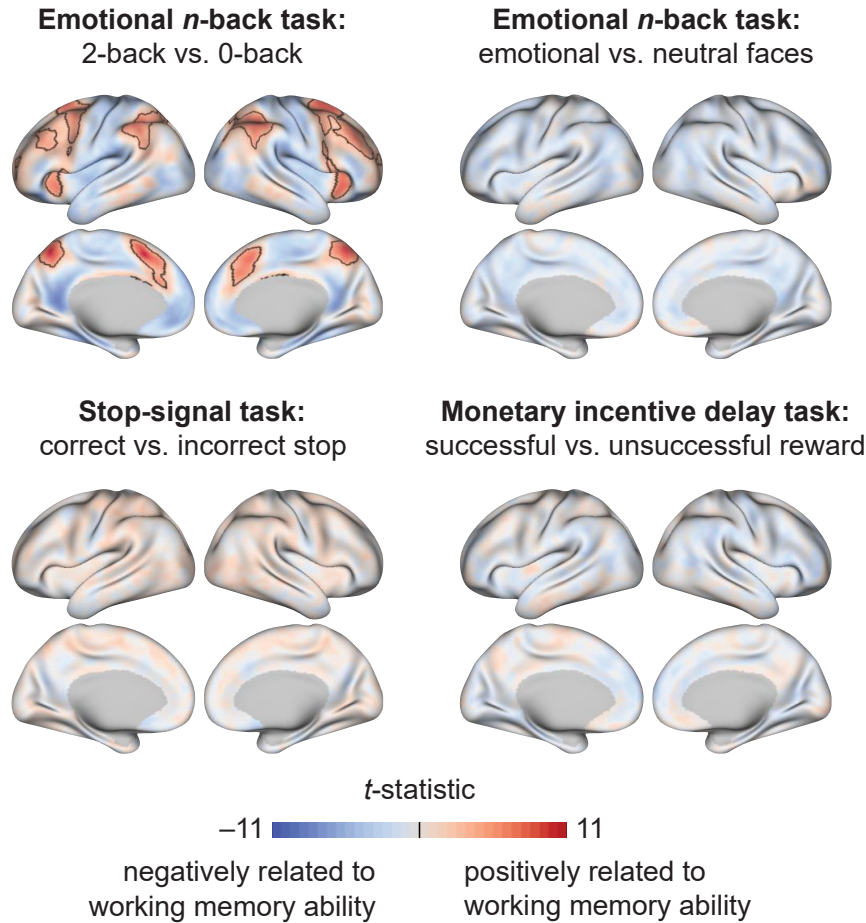
Figure 4. Relationships between fMRI activation and working memory function, measured with an out of scanner list sorting task, across individuals. Analyses control for age, sex, scanner, fluid intelligence, and mean frame-to-frame head motion during the relevant fMRI runs. Unthresholded *t*-statistics (regression coefficients divided by their standard error) are visualized on the inflated cortical surface. Black outlines indicate vertices significant at family-wise error-corrected, two-tailed $p < .05$.

Figure 5.
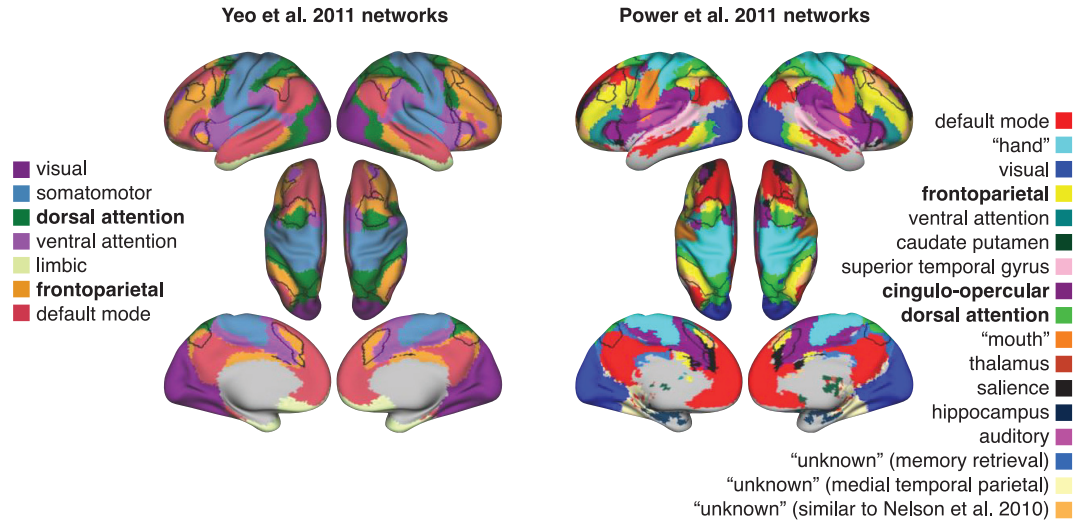
Figure 5. Overlap between neural signatures of working memory in childhood and canonical resting-state functional networks from Yeo et al. (2011) and Power et al. (2011). Black outlines indicate significant relationships between 2-back vs. 0-back activation and working memory function across individuals (family-wise error-corrected, two-tailed $p < .05$).

Figure 6.

Emotional *n*-back task:
2-back vs. 0-back

full sample (*n* = 3750)   release 1 (*n* = 1412)   release 2 (*n* = 2338)

t-statistic

–7 ▰▰▰ | ▰▰▰ 7

negatively related to   positively related to
working memory ability   working memory ability
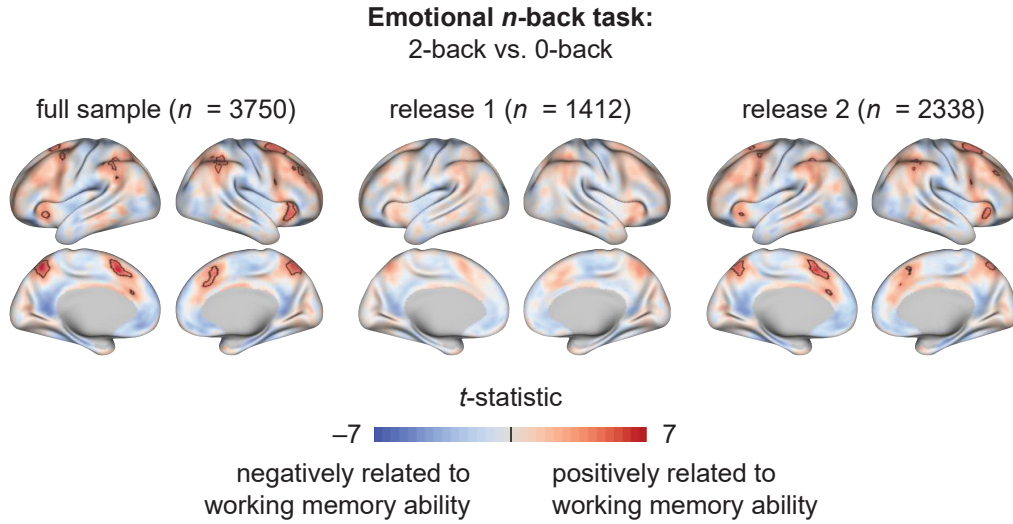
Figure 6. Relationships between 2-back vs. 0-back activation and out-of-scanner working memory performance across individuals, controlling for age, sex, scanner, fluid intelligence, mean frame-to-frame head motion, and in-scanner 0-back and 2-back accuracy, in the full sample and in ABCD data releases 1.1 ("release 1") and 2.0.1 ("release 2") separately. Black outlines indicate vertices significant at family-wise error-corrected, two-tailed p < .05. Results demonstrate that frontoparietal activation in 2-back vs. 0-back contrasts reflects trait-like in addition to state-like working memory abilities.

Figure 7.

Emotional *n*-back task:
2-back vs. 0-back

release 1 (*n* = 1412)   release 2 (*n* = 2338)

Emotional *n*-back task:
emotional vs. neutral faces

release 1 (*n* = 1412)   release 2 (*n* = 2338)

Stop-signal task:
correct vs. incorrect stop

release 1 (*n* = 1578)   release 2 (*n* = 2738)

Monetary incentive delay task:
successful vs. unsuccessful reward

release 1 (*n* = 1572)   release 2 (*n* = 2705)

t-statistic

−11 ▮▮▮▮▮ | ▮▮▮▮▮ 11

negatively related to   positively related to
working memory ability   working memory ability

**Figure 7.** Relationships between task activation and out-of-scanner working memory performance across individuals, controlling for age, sex, scanner, fluid intelligence, and mean frame-to-frame head motion. Black outlines indicate vertices significant at family-wise error-corrected, two-tailed p < .05. Analyses were run using data from each release separately. Participants included in the full sample were included in the "release 1" analysis if they appeared in curated ABCD data release 1.1, and were included in "release 2" otherwise.

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