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18

Abstract

22

23 Mounting evidence indicates that posterolateral portions of the cerebellum (right Crus I/II) contribute to

24 language processing, but the nature of this role remains unclear. Based on a well-supported theory of

25 cerebellar motor function, which ascribes to the cerebellum a role in short-term prediction through internal

26 modeling, we hypothesize that right cerebellar Crus I/II supports prediction of upcoming sentence content.

27 We tested this hypothesis using event-related fMRI in human subjects by manipulating the predictability

28 of written sentences. Our design controlled for motor planning and execution, as well as for linguistic

29 features and working memory load; it also allowed separation of the prediction interval from the

30 presentation of the final sentence item. In addition, three further fMRI tasks captured semantic,

31 phonological and orthographic processing, to shed light on the nature of the information processed. As

32 hypothesized, activity in right posterolateral cerebellum correlated with the predictability of the upcoming

33 target word. This cerebellar region also responded to prediction error during the outcome of the trial.

34 Further, this region was engaged in phonological, but not semantic or orthographic processing. This is the

35 first imaging study to demonstrate a right cerebellar contribution in language comprehension

36 independently from motor, cognitive and linguistic confounds. These results complement our work using

37 other methodologies showing cerebellar engagement in linguistic prediction, and suggest that internal

38 modeling of phonological representations aids language production and comprehension.

39 **Significance statement**

40 The cerebellum is traditionally seen as a motor structure that allows for smooth movement by predicting

41 upcoming signals. However, the cerebellum is also consistently implicated in non-motor functions such as

42 language and working memory. Using fMRI, we identify a cerebellar area that is active when words are

43 predicted and when these predictions are violated. This area is active in a separate task that requires

44 phonological processing, but not in tasks that require semantic or visuospatial processing. Our results

45 support the idea of prediction as a unifying cerebellar function in motor and non-motor domains. We

46 provide new insights by linking the cerebellar role in prediction to its role in verbal working memory,

47 suggesting that these predictions involve phonological processing.

48

Introduction

The cerebellar role language and cognition has become increasingly apparent over recent decades (Strick et al., 2009). Patient and functional imaging data show that cerebellar regions contributing to language and cognition are largely confined to the posterolateral cerebellum (hemispheric portions of Lobule VII, consisting of Crus I and Crus II). These regions are reciprocally connected with supramodal neocortical areas, as demonstrated using tracer studies in non-human primates (Kelly and Strick, 2003) and by functional connectivity MRI in humans (Buckner et al., 2011; Bernard et al., 2012). A wealth of neuroimaging studies report right posterolateral cerebellar activation in studies that probe language (Stoodley and Schmahmann, 2010; Price, 2012) and working memory processes (Desmond et al., 1997; Hayter et al., 2007; Stoodley and Schmahmann, 2009; Keren-Happuch et al., 2012).

However, the functional contribution of the cerebellum in language remains unclear. In motor control, the cerebellum is thought to acquire and store internal models of the motor system. These internal models predict upcoming reafferent sensory input, and these continuous short-term predictions allow for fluent movements and efficient error correction (Miall et al, 1993, Wolpert and Miall, 1996; Miall, 1998). Based on the homogeneous cerebellar cytoarchitecture, several authors have argued that the cerebellar role in non-motor functions is like that in motor control, performing similar operations on more abstract inputs

66   (Bloedel, 1992; Ramnani, 2006; Ito, 2008). Thus, extrapolating from the internal model motor theory of

67   the cerebellum, the posterolateral areas of the cerebellum might support short-term prediction of future

68   linguistic stimuli.

69

70   A testable hypothesis can be derived from this proposal: the cerebellum, specifically right Crus I/II, should

71   be differentially engaged when processing highly predictable versus unpredictable language. Consistent

72   with this notion, online prediction of upcoming sentence content is slowed after perturbation of the right

73   cerebellum with transcranial magnetic stimulation (TMS; Lesage et al., 2012) and modulated by electrical

74   stimulation (tDCS; Miall et al., 2016; D'Mello et al., 2017). In addition, fMRI studies have reported right

75   cerebellar recruitment in conditions where linguistic prediction is possible (Desmond et al., 1998;

76   Moberget et al., 2014). However, it has been difficult to manipulate linguistic prediction without also

77   introducing differences in speech production processes, linguistic properties of the stimulus, task difficulty

78   (working memory load), or outcome evaluation (prediction error); each of these processes have been

79   shown to recruit the posterior cerebellum (Petersen et al., 1989; Floyer-Lea and Matthews, 2004;

80   Fedorenko et al., 2010; Stoodley et al., 2012; Grimaldi et al., 2014; Argyropoulos, 2015; Moberget and

81   Ivry, 2016). To date, no fMRI study has been able to capture cerebellar responses to linguistic prediction

82   during comprehension while controlling for these confounds.

83

84   Here, we manipulate the predictability of sentences in an event-related fMRI design, and test whether the

85   haemodynamic response in right Crus I/II covaries with predictability. Critically, the time at which a

86   prediction is made was isolated from the outcome of the sentence and from the contextual information

87   that allows a prediction to be made. In addition, we explored whether the cerebellar roles in working

88   memory and linguistic prediction could be reconciled; e.g. perhaps linguistic prediction requires short-term

89   storage of semantic, phonological or orthographic representations. Thus, we further assessed whether

90   cerebellar regions identified in the predictive task were engaged in three additional fMRI tasks which

91   capture semantic, phonological and orthographic (visuospatial) working memory.

92

93   **Materials and methods**

94   *Participants*

95   Eighteen right-handed volunteers (4 male, average age 21 years, range 18-27 years) participated in two

96   fMRI sessions. One male subject was excluded from the second session and from all data analysis due to

97   severe signal dropout in the lateral cerebellum. All participants were native English speakers; none were

98   fluent in any other language. Participants were remunerated for their time. Written informed consent was

99   obtained for each participant. This study was approved by the local ethics committee at the University of

100 Birmingham and was carried out in accordance with the guidelines set out in the Declaration of Helsinki

101 (1964).

102

103 *Prediction task*

104 Participants silently read visually presented sentences with varying degrees of predictability, and pressed

105 an MR-compatible response button to indicate the plausibility of the sentence. Participants were not

106 informed that the predictability of sentences was relevant, and were merely instructed to read the words

107 presented on the screen and judge whether the outcome of the final item was likely given the context.

108 The task consisted of 78 trials, each presenting a unique item (context sentence + stem of a second

109 sentence). Thirty three items were taken from a study by Fitzsimmons and Drieghe (2013) and altered to

110 better suit this fMRI design; 45 items were newly constructed. A behavioral pilot experiment in an

111 independent sample of 43 participants had determined the items' predictability (cloze probability). Cloze

112 probability can be defined as the probability that a sentence will be completed with a given target word

113 (e.g. a cloze probability of 0.90 indicates that 90% of participants will complete the item with the same

114 target word). Cloze probability was used as a continuous parametric modulator in behavioral and fMRI

115 analysis. We also categorized items as neutral (cloze probabilities between 0 and 0.40; 27 items), semi-

116 predictable (cloze probabilities between 0.40 and 0.70; 25 items) and predictable (cloze probabilities

117   between 0.70 and 1.00; 26 items). These discrete levels of predictability were used for easier

118   visualization of the results; all analyses were conducted with cloze probability as a continuous variable.

119

120   Three temporal events per trial were independently modelled to allow separate estimation of the BOLD

121   response to these events (Figure 1). The first was the presentation of a context sentence (CONTEXT),

122   which appeared on the screen for three seconds (e.g. "Sonja wanted to avoid a sunburn in this hot

123   weather."). Context sentences were controlled for the number of syllables and words. The second event

124   was the presentation of the stem of a second sentence (STEM; e.g. "She had brought some …"). The

125   stem was displayed in 4 parts (consisting of one or two whole words), each displayed for 250ms in the

126   center of the screen to avoid eye movements. The stem did not contain the last word of the sentence, and

127   it is inferred that the participant would produce a semantic prediction (e.g. "sunscreen") in a highly

128   predictive item. Thus, prediction and predictability are measured at the time of the STEM event, before

129   the final word. The third event in the trial was the presentation of the final word of the sentence

130   (OUTCOME), which was either likely (50% of trials) or unlikely (50% of trials) given the context.

131   Participants then made a response on a MR-compatible response box to indicate plausibility. Importantly,

132   whether the outcome was likely or unlikely was independent from how predictable the item was. Highly

133   predictable and unpredictable items could be paired with a likely or unlikely outcome. The STEM, and the

9

134 inferred prediction at its end, is the event of interest in this task. Items were constructed in pairs and

135 triplets so that a similar sentence stem was used for different levels of predictability. The length and

136 linguistic properties of the STEM were therefore well-controlled between conditions. Presentation of the

137 outcome and the button-press response were modeled as a single event (OUTCOME, 1s), ensuring that

138 prediction error, motor preparation or motor activity could not contribute to the haemodynamic response

139 at the time of the STEM. Trials with erroneous responses were excluded from the fMRI analysis.

140 Uniformly distributed variable delays were introduced between context and stem (4.5 - 10.5 seconds),

141 between stem and outcome (3 - 7.5 seconds), and between outcome and the context event of the

142 following trial (4-10 seconds). This manipulation ensured that BOLD responses to one event were not

143 contaminated with BOLD response to the previous stimulus (for another example of this technique, see

144 Ramnani and Miall, 2004).

145

146 [Figure 1 about here]

147

148 *Localizer tasks for semantic, phonological and orthographic working memory*

149 When reading a sentence (or a sentence stem), processes in addition to semantic prediction take place.

150 When reading words, one processes the meaning of these words (attention to semantics). When reading

151   words or pronounceable non-words, one processes phonological features of these words (attention to

152   phonology). When looking at words or non-words, one recognizes and processes a visual stimulus with a

153   certain spatial configuration (attention to orthography or visuospatial attention). In order to assess

154   whether any cerebellar areas that differentially respond to predictive sentences were also preferentially

155   engaged when orthographic, phonological or semantic properties were held in short-term store,

156   participants also performed three epoch-related localizing tasks.

157   To maximize comparability between tasks and to have low level of working memory load, all three tasks

158   were 1-back tasks and were contrasted with 0-back versions of the same task. The participants were

159   required press a button on an MRI compatible response box if the current stimulus belonged to the same

160   semantic category as the previous stimulus (semantic 1-back), if the current stimulus rhymed with the

161   previous stimulus (phonological 1-back) or if the current stimulus was identical to the previous stimulus

162   (orthographic 1-back). Similar tasks have previously been used to capture orthographic and phonological

163   processing (Paulesu et al., 1993; Koyama et al., 2013). Three 0-back control conditions required the

164   participants to respond when a known target stimulus appeared. The 0-back controls blocks were

165   performed as separate runs from the 1-back blocks.

166   Semantic 1-back. For the semantic task, stimuli were 50 black-and-white line drawings. Participants were

167   familiarized with the ten stimulus categories (cycles, birds, boats, dogs, fish, fruits, buildings, shoes, tools

168   and furniture) and the five members of each category, as well as with the 0-back task target object, prior

169   to scanning (Figure 2A). In contrasting the 1-back with the 0-back condition, we control for visual

170   processing of the line drawings, and motor activity related to button presses. The requirements that

171   separate the 1-back condition from the 0-back condition are that in the 1-back condition, participants must

172   categorize each stimulus, keep this semantic category in short-term memory, and match it to the semantic

173   category of the subsequent stimulus. In the 0-back condition it is not necessary to process the meaning or

174   semantic category of the line drawing, merely to match it to a target image. We chose line drawings

175   instead of words to avoid automatic phonological processing; line drawings hold meaning but are non-

176   verbal. Nevertheless, we cannot exclude that participants formed a phonological code of the stimulus or

177   the semantic category.

178   Phonological 1-back. For the phonological task, stimuli were 5-letter words that were printed in the middle

179   of the screen (Figure 2C). Before the scanning session, participants were shown some example stimuli

180   for this task, which were not used in the scanning task. They were also shown the target stimulus for the

181   0-back task. The task was constructed such that a small minority of the rhyming pairs ended in the same

182   syllable. This task could therefore not be performed to an acceptable standard by using a visual search

183   strategy. The 1-back and 0-back conditions were controlled for reading requirements (each condition

184   required reading 5-letter words), demands on attention to meaning or semantics (both conditions likely

185   automatically elicited semantic processing but neither condition required it) and motor activity related to

186   the button presses. Unlike the 0-back condition, the 1-back condition required participants to update and

187   hold the phonetic form of each stimulus in short-term storage and match it to the phonetic form of the

188   subsequent stimulus. The 0-back condition merely required the subject to hold in memory and respond to

189   one target word (the word "press") throughout the run.

190   Orthographic 1-back. For the orthographic (visuospatial) task, stimuli consisted of a set of 10 five-letter

191   Punjabi pseudo-words (Figure 2C). These stimuli had a similar configuration as written English words, but

192   held no meaning and were not pronounceable for the participants. Participants were familiarized with all

193   the visual stimuli, as well as with the target stimulus for the 0-back task prior to scanning. Both conditions

194   were matched for low-level visual demands as well as motor activity related to button presses. As in the

195   phonological task, the difference in requirement for the 1-back condition was the higher short-term

196   memory load to retain the visuospatial configuration of each stimulus and compare it to the subsequent

197   stimulus, whereas the 0-back condition required only one easy to identify stimulus to be retained

198   throughout.

199   Each of the six runs (3 tasks, each as 1-back and 0-back) lasted 8 minutes and contained 15 epochs.

200   Each epoch consisted of 10 stimuli and lasted 15 seconds. Stimuli were presented for 500ms, 1000ms

201   apart. Rest periods between blocks lasted 13 to 17 seconds. These rest periods (53% of the scan) were

202   used as an implicit baseline in the analysis.

203

204   [Figure 2 about here]

205

206   *MRI data acquisition*

207   Each participant underwent two fMRI scanning sessions on separate days. One session consisted of a

208   prediction task, divided into 3 runs each lasting 10min 30s. A high-resolution structural image (T1

209   weighted image, FTE sequence, voxels 1x1x1mm) was also collected during this session. During a

210   second fMRI session, participants performed three localizer tasks, designed to probe attention to

211   semantic, phonological and orthographic features of visually presented stimuli. Localizer tasks were

212   divided into an experimental run (1-back condition) and a control run (0-back condition), with each run

213   lasting 8 mins. Runs were presented in the same order for each participant. All images were acquired on

214   a 3T Philips Achieva scanner using a 32-channel head coil. (Functional: ascending EPI sequence,

215   TR=3s, TE=32ms, 52 axial slices (no gap), voxels 3x3x3 mm, FOV 240x240, flip angle = 85°). Pulse

216   oximetry and breathing measures were collected with a Philips-integrated physiological monitoring

217   system.

14

218

219 *Statistical analysis of the behavior*

220 Behavioral data were processed using custom-made MATLAB scripts (RRID:SCR_001622). Performance

221 in the outcome phase of prediction task, as well as in the localizer tasks was analyzed in R

222 (RRID:SCR_001905) using the packages afex and phia. For the prediction task, a generalized linear

223 mixed model (random intercept, accuracy as binomial dependent variable) was carried out with

224 Predictability (continuous cloze probability) and Outcome (levels: likely and unlikely) as independent

225 variables. For the localizer tasks, a general linear mixed model (random intercept) was used with Task

226 (levels: semantic, phonological, and orthographic) and Condition (levels: 1-back and 0-back). Significant

227 interactions were followed up by post-hoc tests. Average performance was assessed in all conditions to

228 ascertain that participants paid attention to the task, and to allow the exclusion of erroneous trials from

229 the imaging analysis of the prediction task.

230

231 *Statistical analysis of the fMRI data*

232 *Preprocessing.* All analyses were carried out in SPM8 (RRID:SCR_007037). Prior to the first level

233 analysis, raw images were realigned to correct for head motion, slice-time corrected, and co-registered to

234 the anatomical image. First level analyses were carried out in subject-specific space. Contrast images

235   from the first level analysis were normalized to the SPM8 EPI template (whole-brain analysis) and

236   smoothed with an 8mm FWHM Gaussian smoothing kernel before entering group level analysis. To

237   facilitate later region-of-interest analyses, all EPI images were also normalized and smoothed. The BOLD

238   signal around the brainstem and cerebellum can be vulnerable to confounding physiological signals, but

239   this can be accounted for by regressing out heart rate and breathing signals in the GLM model (Schlerf et

240   al., 2012). The Physiological Log Extraction for Modeling (PhLEM) toolbox in SPM (Verstynen and

241   Deshpande, 2011) was used to convert heart rate and breathing traces into SPM regressors with a

242   CETROICOR method (Glover et al., 2000), resulting in eight regressors that were included as regressors

243   of no interest. Physiological measures from one participant during the control sessions were not available;

244   this person's data were excluded from the analysis of the control tasks.

245   *First level analysis.* Prediction task: For the linguistic prediction task, six events per block were modelled

246   at the first level. These were: context, $context_{mod}$ (a parametric modulator of the context by cloze

247   probability), stem, $stem_{mod}$ (a parametric modulator of the stem by cloze probability), $outcome_{likely}$, and

248     $outcome_{unlikely}$. The three blocks were concatenated, thus creating a single first level analysis per person

249   with 18 events of interest. A 19th regressor modeled all trials where an erroneous response was made to

250   ensure that differences in performance could not underlie differences in BOLD activation patterns. The six

251   contrasts of interest (the six events, averaged over the three blocks) were estimated against the implicit

252   baseline.

253   Localizer task: For the localizer tasks, the task blocks were modeled against the implicit baseline in a

254   single t-contrast for each of the six sessions.

255   In all tasks, eight regressors of no interest modelled physiological signals and a further six modelled head

256   movement.

257

258   _Group level analysis._ Normalized first level contrast images for the prediction task were entered into a

259   factorial design. First, the contrast t = [stem] (reading contrast), was estimated to assess which regions

260   were engaged in the processing of written meaningful language, irrespective of predictability. Second, the

261   predictability contrast, t = [$stem_{mod}$] revealed areas where the BOLD signal was modulated according to

262   the predictability of the upcoming sentence ending. A mask of the subjects' brains was created by

263   averaging the normalized skull-stripped anatomical scans co-registered into a 2x2x2mm space (216,611

264   voxels, 1733cm^3). A whole brain cluster-correction at a family-wise error rate (FWE) of 5% for this volume

265   was calculated using the 3dclustsim algorithm (Cox, 1996). This procedure determined a voxel-level

266   correction of p<0.001, with a minimum cluster size of 99 voxels (790mm^3). In addition, we assessed

267   whether cortical activations were in regions that are functionally connected with the cerebellar region of

268   interest. To this end, resting state connectivity maps with right Crus I and right Crus II (Bernard et al.,

269   2012; maps provided by the authors) were summed and smoothed with a 4mm FWHM Gaussian

270   smoothing kernel (Figure 4C). This resulting connectivity map was then overlaid with the activation map

271   from the predictability contrast.

272

273   *Region of interest (ROI) analyses on areas engaged in prediction*

274   We conducted region-of-interest analyses to determine whether any cerebellar areas that are engaged in

275   linguistic prediction also show increased activity when this prediction is violated (i.e. when the outcome is

276   unlikely versus when it is likely; during a prediction error). Moreover, we further assess whether these

277   cerebellar areas were engaged in semantic, phonological or orthographic processing in the three localizer

278   tasks. Region of interest analyses were conduction using the marsbar toolbox in SPM8 (Brett et al.,

279   2002). Regions of interest (ROIs) included cerebellar clusters that were modulated by predictability

280   (predictability contrast), as well as cerebellar areas that were modulated by the presentation of written

281   language (reading contrast). Given our a priori right cerebellar hypothesis, we planned to Bonferroni

282   correct for the number of right cerebellar clusters that are identified in each contrast. In order to explore

283   whether the activation patterns identified in the cerebellum were unique to this structure, or whether

284   cerebral areas also showed the same patterns, we also plotted these parameter estimates of the

285   supratentorial clusters identified in the prediction contrast. These further ROI extractions are strictly

286   exploratory, and their results should not be interpreted. Masks of these areas were created by taking a

287   10mm sphere around the peak coordinate). First-level design matrices were accessed by marsbar to

288   extract the contrasts estimates for the regions of interest defined by the main analysis. This resulted in

289   one parameter estimate per participant per event per ROI.

290   Prediction error analysis. If linguistic internal models are present in the posterolateral cerebellum, one

291   might expect these regions to respond more strongly to the unlikely outcomes (prediction error) than to

292   the likely outcomes, analogous to the high activations seen when movement errors occur in motor tasks

293   (Imamizu et al., 2000; Miall et al., 2001). The first-level design matrix from the main prediction analysis

294   was used to extract parameter estimates for $Outcome_{unlikely}$ and $Outcome_{likely}$ events, which were then

295   compared with a paired t-test. An unlikely outcome does not mean that no prediction was made, it merely

296   means that the outcome violates expectations. A stronger response to unlikely versus likely outcomes

297   indicates that this region processes prediction errors. We hypothesized that those cerebellar areas that

298   are modulated by predictability also respond more strongly when a prediction is violated. A likely or

299   unlikely outcome was equally probable regardless of the item's predictability. This contrast was therefore

300   independent from the predictability contrast.

301

302   Localizer tasks: attention to semantics, phonology, and orthography. Given the recruitment of the

303   posterolateral cerebellum in working memory tasks, we were interested to see whether those regions that

304   are differentially engaged in linguistic prediction are also active in tasks that require short-term storage of

305   semantic, phonological or orthographic stimulus features. Such functional overlap can provide us with

306   insight into how the cerebellum contributes to language function, and how linguistic and working memory

307   contributions may be reconciled. First level design matrices were created modeling the six conditions (1-

308   back and 0-back conditions for the three localizing tasks) individually against the implicit baseline.

309   Parameter estimates were extracted using marsbar and paired t-tests assessed whether the regions of

310   interest showed a larger response to the 1-back condition than to the 0-back condition in the semantic,

311   phonological and visual localizer. Data from the localizer tasks resulted from independent datasets (from

312   the same participants). Circularity was therefore not a concern.

313

314   [Figure 3 about here]

315

316   **Results**

317   *Behavioral Results*

318   Overall, participants performed well (average 86% correct, SEM = 2.5%, range 79-90%), indicating that

319   all participants were attentive and able to judge whether a sentence ending was likely or unlikely in the

320   context of the trial. The mixed-model ANOVA showed a significant effect for Predictability (X^2_1=17.69,

321   p<0.001), Outcome (X^2_1=15.48, p<0.001) and their interaction (X^2_1=8.24, p=004). Post-hoc tests reveal

322   that predictability did not affect performance on unlikely trials (X^2_1=0.30, p=0.582), but did affect

323   performance on likely trials (X^2_1=28.69, p<0.001; Figure 3A). These results suggest that a likely sentence

324   ending is less likely to be perceived as such when a prediction is harder to make. Trials with incorrect or

325   missing responses were excluded from the neuroimaging analysis.

326   On the localizer tasks, participants performed well in all conditions (Figure 3B, average hits 92%, SEM =

327   2.3%, range 80-96%). The mixed-model ANOVA revealed significant effects of Condition ($F_{1,80}$= 4.84, p =

328   0.03), Task ($F_{2,80}$=44.76, p<0.001) and the interaction between Condition and Task ($F_{2,80}$ = 17.60,

329   p<0.001). Follow-up tests showed that these effects were driven by overall slightly poorer performance in

330   the orthographic attention task than the other tasks (Orthographic vs. Phonological: X^2_1=63.17, p<0.001;

331   Orthographic vs. Semantic: X^2_1=70.88, p<0.001), and poorer performance in the Orthographic 0-back

332   task than the 1-back task (X^2_1=36.01, p<0.001). No significant differences were present in performance

333   between the phonological and the semantic localizers, or between 1-back and 0-back conditions of these

334   tasks (Figure 3B). These results suggest that the orthographic (visuospatial) localizer was more difficult

335   than the other two tasks.

336

337   *Imaging results*

338   <u>Areas that respond to written meaningful language (reading contrast)</u>

339   The reading contrast revealed a widespread network of cortical and subcortical regions that are

340   classically implicated in language processing, attention and visual processing (Price, 2012; Rodd et al.,

341   2015). Areas engaged when processing the sentence stem were bilateral inferior and middle frontal

342   gyrus, medial frontal gyrus, bilateral middle temporal gyrus extending from the temporal pole into

343   temporoparietal cortex, left thalamus, bilateral posterolateral cerebellum and the cerebellar vermis (Figure

344   4A, Table 1). Activations were more pronounced on the left of the cerebral cortex, and on the right in the

345   cerebellum.

346

347   <u>Areas where activity covaries with predictability (predictability contract):</u>

348   The predictability contrast revealed an area in right posterolateral cerebellum, Crus II, where

349   haemodynamic activity positively correlated with predictability (Figure 4B, 5B, Table 1). Supratentorial

350   clusters were identified in the left inferior frontal gyrus, right middle frontal gyrus, left posterior parietal

351 cortex, pre-supplementary motor area, and right caudate nucleus (Figure 4B, 6, Table 1). No brain areas

352 showed activity that correlated negatively with the predictability of the items. All clusters apart from the

353 right middle frontal gyrus cluster overlapped with a map of regions that are functionally connected to Crus

354 I and Crus II (Figure 4C).

355

356 [Figure 4 about here]

357

358 <u>ROI analyses: cerebellar area that represents prediction also represent prediction error</u>

359 A paired-samples t-test compared the regression weights for unlikely outcomes and likely outcomes for

360 the cerebellar cluster that was modulated by predictability (predictability contrast) and for the cerebellar

361 area that responded to written language (reading contrast). As only one cluster was identified in each

362 contrast, tests were considered significant at $p<0.05$. The Crus II cluster that was modulated by

363 predictability (Figure 5B) also showed a larger response to unlikely than to likely sentence outcomes (MNI

364 28 -86 -48 likely > unlikely: t_{16} = 2.27, p = 0.037). Conversely, the larger area that responded to the stem

365 event (Figure 5A) did not show such a difference (MNI 30 -70 -52: t_{16}=0.33, p=0.743).

366

367 [Figure 5 about here]

23

368

369 <u>ROI analyses: cerebellar area that represents predictability is engaged in phonological processing but not</u>

370 <u>semantic or orthographical processing</u>

371 Paired t-tests compared the activity in 0-back and 1-back conditions for semantic, visual and phonological

372 localizers. This analysis indicates whether the areas that were modulated by predictability were also

373 engaged by attention to semantic content, phonological or visual features. Results showed that right Crus

374 II was significantly engaged in the phonological localizer task (MNI 28 -86 -48; t_{15} = 2.52, p = 0.032), but

375 not in the semantic or orthographic task (Figure 5B). Note that these results do not imply that the Crus II

376 region is more engaged in the phonological task as compared with the other two tasks. The condition

377 effect (1-back minus 0-back) in the phonological task differs from that in the semantic task (t_{15} = 2.49, p =

378 0.025), but not from that in the orthographic task (t_{15} = 1.23, p = 0.238). However, these between-task

379 comparisons do not survive a Bonferroni correction for the three possible post-hoc tests. The Crus II

380 region that responded to written language (reading contrast), was significantly recruited in all three

381 localizer tasks (MNI 30 -70 -52. Semantic: t_{15} = 8.82, p<0.001; Phonological: t_{15} = 9.08, p<0.001;

382 Orthographic: t_{15} = 7.43, p<0.001). This activation pattern is consistent with a region that is engaged in

383 processing written meaningful language, as this entails semantic, phonological and orthographic

384 processing.

385

386   [Figure 6 about here]

387

388   In summary, we found that a discrete region in cerebellar Crus II was significantly modulated by the

389   predictability of the stem sentence, in the interval before the outcome was presented. This area was also

390   active in a contrast that probed phonological processing, but not in contrasts that probed semantic or

391   visual processing. It lay within a broader zone of the cerebellum activated by the reading task (but not

392   modulated by predictability) and that broader zone did overlap with the regions activated by semantic and

393   orthographic processing.

394

395   **Discussion**

396   The right posterior cerebellum is consistently implicated in language processing, but its precise

397   contribution remains unclear. In parallel with the predictive function of cerebellar motor regions through

398   internal models of movements (Courchesne and Allen, 1997; Miall, 1998; Ebner and Pasalar, 2008),

399   internal model prediction may generalize to non-motor cerebellar regions, particularly Crus I/II (Ramnani,

400   2006; Ito, 2008). Thus, language-sensitive right cerebellar regions may assist linguistic processing by

401   predicting upcoming sentence content. Here, we tested this hypothesis with a closely controlled event-

402   related fMRI study. We compared activity time-locked to the presentation of identical sentence fragments

403   that varied in the degree to which they predicted the final word of the sentence (their cloze probability).

404   Crucially, this sentence fragment was modeled independently from a context sentence, through which

405   predictability was manipulated, and from the final word (outcome) of the sentence. We were thus able to

406   capture effects of prediction in the absence of outcome evaluation or prediction error, while also avoiding

407   motor, linguistic, and working memory confounds. Further, using separate fMRI localizer tasks, we

408   assessed whether identified prediction-sensitive areas were also engaged in semantic, phonological, or

409   orthographic processing.

410

411   As hypothesized, activity in right Crus II increased with the predictability of the upcoming sentence

412   ending. Further consistent with the presence of internal model predictions, the same Crus II area was

413   more active during an unexpected outcome (prediction error) than an expected outcome. Finally, this area

414   was also engaged when attending to phonological information, but not semantic or orthographic

415   information.

416

417   This study is the first to identify a right cerebellar region that represents predictability independently from

418   motor demands or error processing. Our findings complement and extend existing evidence on linguistic

419   prediction in the right posterolateral cerebellum. Previous fMRI evidence indicates that right posterior

420   cerebellar regions are engaged when a linguistic prediction is possible (Desmond et al., 1998; Moberget

421   et al., 2014). We have previously shown that low-frequency right cerebellar rTMS disrupts the prediction

422   of upcoming sentence content in a language comprehension task (Lesage et al., 2012), a finding we

423   recently replicated using cathodal tDCS (Miall et al., 2016). In the language production domain, rTMS

424   over right, but not left cerebellum impairs higher level speech monitoring – including internal prediction of

425   upcoming speech (Runnqvist et al., 2016), and a recent study found that right cerebellar tDCS improved

426   performance in a sentence completion task (D'Mello et al., 2017). Such neurostimulation evidence

427   dovetails nicely with the present data to show that the right posterior cerebellum is causally involved in

428   linguistic prediction to aid both language comprehension and language production.

429

430   A posterolateral cerebellar contribution to language processing is consistent with the region's connectivity

431   fingerprint. Viral tracer studies in non-human primates (Middleton and Strick, 1998; Kelly and Strick, 2003;

432   Akkal et al., 2007; Bostan et al., 2013), resting-state functional connectivity and meta-analytic connectivity

433   mapping in humans (Habas et al., 2009; Krienen and Buckner, 2009; Buckner et al., 2011; Bernard et al.,

434   2012; Balsters et al., 2013) have identified connectivity between Crus I/II and higher-order cognitive and

435   language regions, including inferior frontal, dorsolateral prefrontal, posterior parietal, and anterior

436   cingulate cortices. In the present data, cerebral areas where the haemodynamic response scaled with

437   linguistic predictability included the left inferior frontal gyrus, pre-SMA and left posterior parietal lobe, right

438   middle frontal gyrus and bilateral caudate nucleus. These areas are all implicated in lexico-semantic or

439   phonological language processing (Fedorenko et al., 2010; Wu et al., 2012; Martin et al., 2015), and all

440   except the right DLPFC cluster were within the network of regions functionally connected to right Crus I/II

441   (Bernard et al., 2012).

442

443   Our findings support the idea that cerebellar internal models aid language comprehension by predicting

444   upcoming stimuli. Internal models are prominent in theories of motor cerebellar function (Miall, 1998;

445   Wolpert et al., 1998), and it has long been hypothesized that cognitive and linguistic internal models could

446   be present in prefrontal-projecting cerebellar areas (Leiner et al., 1989; Ramnani, 2006; Ito, 2008).

447   Internal model prediction has been incorporated into psycholinguistic accounts more recently (Hickok,

448   2012; Rothermich and Kotz, 2013; Kotz et al., 2014; Pickering and Garrod, 2014). One fairly

449   comprehensive theoretical frameworks posits that comprehension is achieved using the speech

450   production apparatus, with both speech production and comprehension aided by internal model prediction

451   (Pickering and Garrod, 2013; Pickering and Clark, 2014). This model aligns well with our present findings

452   and previous neurostimulation and neuroimaging evidence (Lesage et al., 2012; Moberget et al., 2014;

453   Miall et al., 2016; D'Mello et al., 2017), which indicate that prediction of upcoming words may occur in or

454   depend upon the cerebellum.

455

456   A major challenge in determining the function of prefrontal-projecting cerebellar areas is their involvement

457   in processes that are difficult to manipulate separately. Notably, the Crus I/II area implicated in language

458   is also consistently implicated in verbal working memory, where recruitment scales with cognitive load

459   (Hayter et al., 2007; Lesage et al., 2010; Marvel and Desmond, 2010, 2013). Indeed, it has been

460   proposed that the posterior cerebellum may act as the Baddeley and Hitch's (1974) phonological store,

461   encoding verbal content and keeping this information online (Chen and Desmond, 2005; Marvel and

462   Desmond, 2010). However, the involvement of the posterior cerebellum in language cannot be explained

463   entirely by working memory demands. The right posterolateral cerebellum is recruited consistently in

464   lexico-semantic processing (Vandenberghe et al., 1996; Fedorenko et al., 2010; Price, 2012; Lesage et

465   al., 2015), even in relatively undemanding conditions, such as reading meaningful sentences as

466   contrasted with more cognitively demanding scrambled sentences (Moberget et al., 2014). To explore

467   functional overlap between working memory and language processes, we assessed cerebellar

468   recruitment in three 1-back tasks that each captured a component of reading; attention to a semantics

469   (semantic categorization), attention to phonology (rhyming judgment) or attention to orthographic features

470   (visuospatial matching). In the present data, we found that the prediction-sensitive cerebellar cluster was

471   engaged in the phonological task, but we did not find that this area was engaged in the semantic or

472   orthographic tasks. This area's recruitment in a phonological task aligns with a cerebellar role in the

473   phonological store and inner speech (Ackermann et al., 2004, 2007, Marvel and Desmond, 2010, 2013).

474   The absence of this area's significant engagement in the semantic task is somewhat surprising,

475   especially as evidence for cerebellar linguistic prediction is largely derived from semantic prediction tasks,

476   including the task used here (Lesage et al., 2012; Argyropoulos, 2015; Miall et al., 2016; D'Mello et al.,

477   2017). However, our data do not necessarily mean that internal models exclusively predict the

478   phonological form of upcoming content, or that this prediction cannot be semantic. For example, semantic

479   predictions may be represented in a common code to the representations needed in the phonological

480   task. Alternatively, the semantic task, which used line drawings, may have captured semantic processes

481   distinct from those in the prediction task, and a different localizer task might have recruited the prediction-

482   sensitive cerebellar region.

483   A larger area of right Crus II that was consistently activated during reading (when meaningful language

484   was presented) but not specific to prediction, was robustly engaged in all three localizer tasks. This is

485   consistent with imaging evidence for semantic processing in posterolateral cerebellum (Price, 2012) and

486   with meta-analyses of cerebellar recruitment in various tasks, where clusters responding to verbal

487   working memory and language tasks overlap (Stoodley and Schmahmann, 2009, 2010; Keren-Happuch

488   et al., 2012; Stoodley et al., 2012).

489

490   This study is not without limitations. First, stimulus type differed between the localizer tasks. Even though

491   the contrasts used controlled for such lower-level differences, it is possible that a semantic localizer using

492   written language might have produced different results, potentially recruiting the cerebellar area that

493   scaled with predictability. Second, the analysis on the localizer tasks is unable to speak to whether

494   regions are recruited differently in different localizer tasks. Third, the order of the localizer task runs was

495   not counterbalanced. We can therefore not exclude fatigue or learning effects. However, given the lack of

496   performance differences, we think it unlikely that order affected the phonological or semantic localizer

497   tasks. Lower performance in the 0-back condition of the orthographic localizer may be partially

498   attributable to fatigue, but it is not clear what outcome such an order effect would have on cluster location.

499

500   Future research can further elucidate how working memory and linguistic prediction are represented in

501   the cerebellum and whether internal model prediction could be an underlying mechanism to support these

502   functions. Tasks using different stimulus types may further shed light on how linguistic prediction takes

503   place in the cerebellum. Finally, study of the interaction between supratentorial areas that are functionally

504   connected to the cerebellum and also represent predictability, can elucidate how linguistic internal model

505   prediction is achieved.

506

Conclusions

508   We identified an area in cerebellar Crus I/II where BOLD response scales with the predictability of

509   upcoming sentence content. Activity in this region was larger when an unexpected sentence ending was

510   evaluated compared to an expected sentence ending, consistent with processing prediction errors.

511   Interestingly, the cerebellar area modulated by predictability was also recruited in a phonological

512   processing task, but not in orthographic or semantic processing tasks. Thus, results support the presence

513   of linguistic internal models during language comprehension and suggest that this process may rely on

514   phonological processing.

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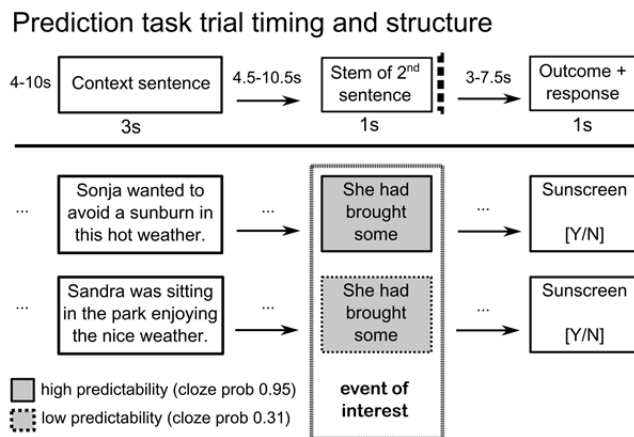647   physiological artifacts in the BOLD signal. Neuroimage 55:1633–1644.

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653 **Figures**

Prediction task trial timing and structure

4-10s	Context sentence	4.5-10.5s →	Stem of 2nd sentence	3-7.5s →	Outcome + response
	3s		1s		1s

| ... | Sonja wanted to avoid a sunburn in this hot weather. | ... → | She had brought some | ... → | Sunscreen [Y/N] |
| ... | Sandra was sitting in the park enjoying the nice weather. | ... → | She had brought some | ... → | Sunscreen [Y/N] |

▢ high predictability (cloze prob 0.95)
⬚ low predictability (cloze prob 0.31)

event of interest

654

655   Figure 1. Trial structure of the prediction task. The stem and the outcome stimuli are matched for high-

656   and low-cloze trials, and the context sentences are matched for length. Here, two items with the same

657   stem, where one has a very predictable sentence ending (cloze probability 0.95) and the other does not

658   (cloze probability 0.31). Three temporal events are independently modeled in the analysis: the context

659   (3s), the stem (1s) and the outcome (1s). Ellipsis indicate variable delay/temporal jitter.
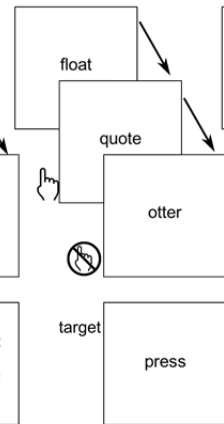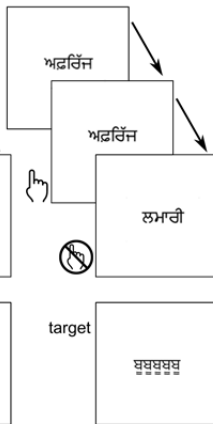
42

A. Localizer task trial structure
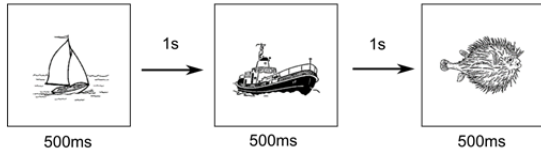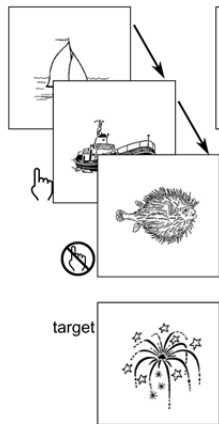
B. Semantic   C. Phonological   D. Orthographic

660

Figure 2. Trial structure and typical stimuli for the localizer tasks. A. Stimulus timing. B-D. The upper

overlapping panels show typical stimulus displays (stimuli presented 500ms, 1s apart), illustrating first a

match and then a non-match trial, for the 1-back runs. The separate lower panel shows the target item for
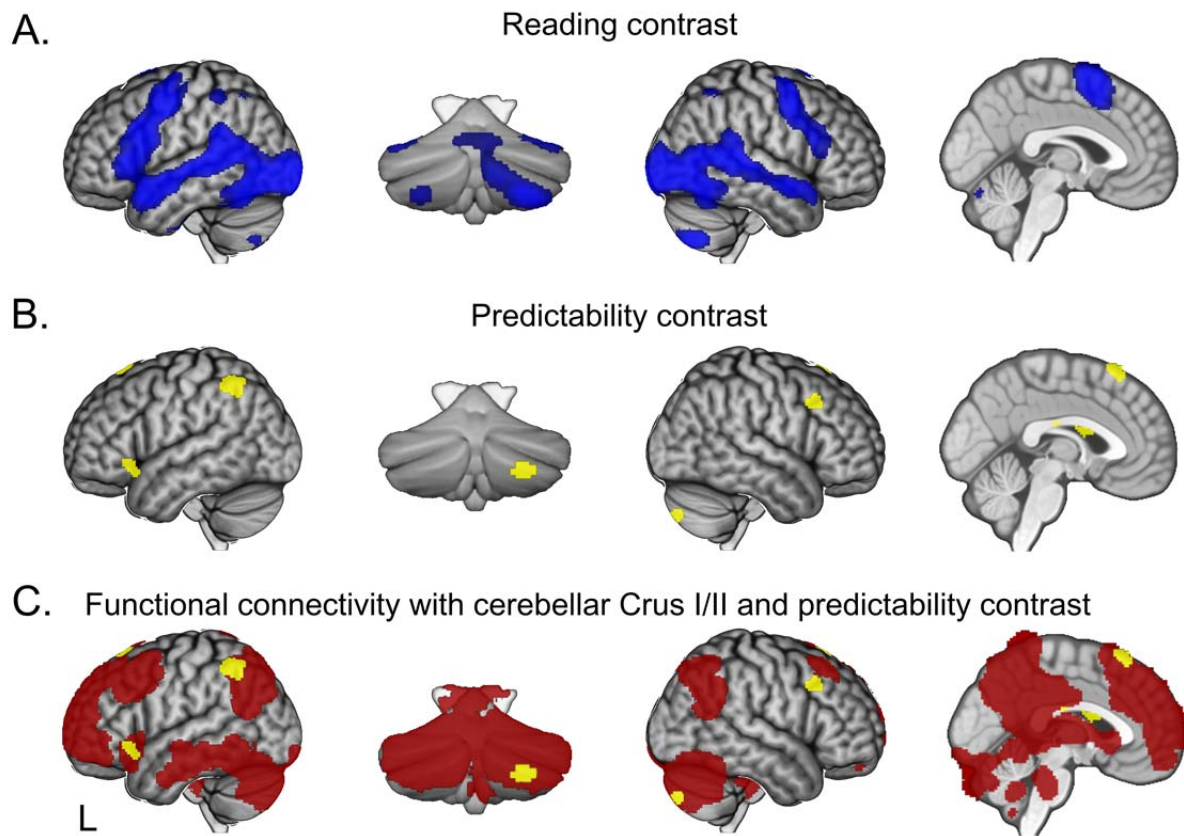
the 0-back runs.
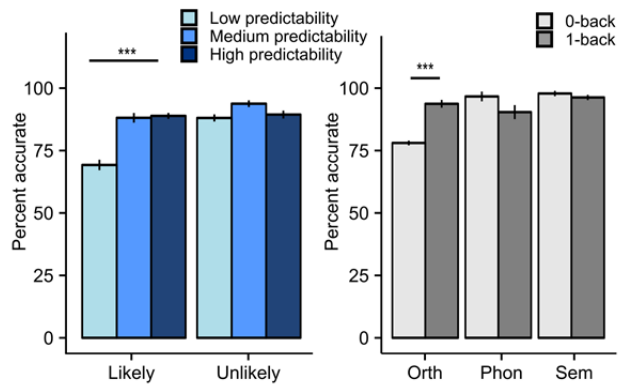
665

666   Figure 3. Behavioral performance. A. Percentage accurate responses in prediction task. Discrete levels of

667   predictability were used for display purposes only; analyses were conducted using predictability as a

668   continuous variable. B. Percentage accurate responses in localizer tasks. Error bars indicate +/- 1 SEM.

669   ***: $p < 0.001$.

A. Reading contrast

B. Predictability contrast

C. Functional connectivity with cerebellar Crus I/II and predictability contrast

670

671 Figure 4. Imaging results A. Areas activated over baseline when reading (reading contrast). B. Areas

672 where BOLD response is modulated by predictability of future outcome (predictability contrast). Contrasts

673 family-wise error corrected at alpha<0.05 (voxelwise p<0.001, cluster size > 99 voxels). C. Areas

674 functionally connected to right Crus I and Crus II, based on Bernard et al. (2012) in red, with the results

675 from the predictability contrast (yellow) overlaid to indicate overlap.
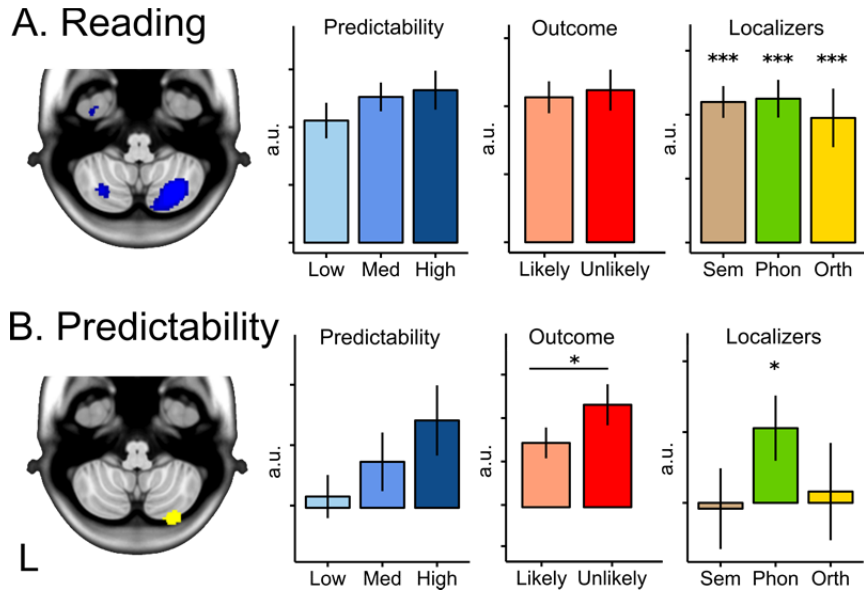
676

677 Figure 5: Parameter estimates for right cerebellar activations. First column: Cerebellar clusters in reading

678 contrast (A, blue) and predictability contrast (B, yellow), whole-brain corrected at FWE p<0.05. Column 2

679 – Predictability. Parameter estimates extracted for different levels of predictability. Regression weights

680 were extracted from the clusters identified in the imaging analysis where predictability (cloze probability)

681 was a continuous variable; they are plotted to aid interpretation only – no statistical inference should be
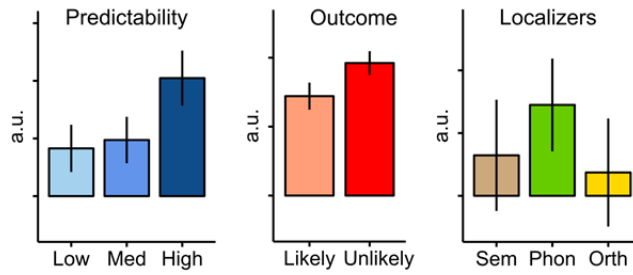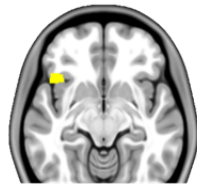
682 drawn. Column 3 – Outcome. ROI analysis for prediction error, using clusters as ROIs. Column 4 -

683 Localizer task responses. ROI analysis for semantic, phonological and orthographic processing (1-back
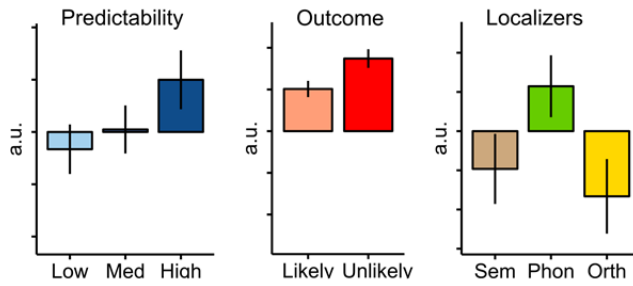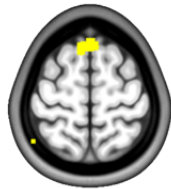
684 minus 0-back), using the same cluster masks. Paired t-tests. * p<0.05, *** p<0.001. a.u.: arbitrary units.
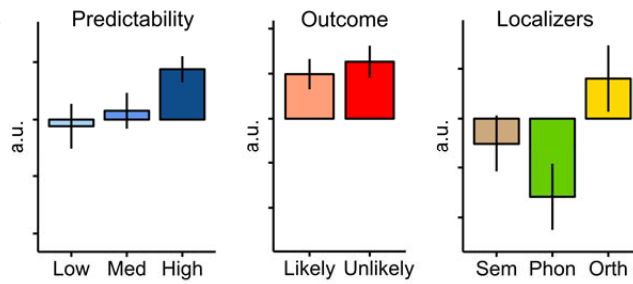
685 Error bars denote SEM.

A. L IFG — Predictability (Low, Med, High); Outcome (Likely, Unlikely); Localizers (Sem, Phon, Orth)

B. SMA — Predictability (Low, Med, High); Outcome (Likely, Unlikely); Localizers (Sem, Phon, Orth)

C. R DLPFC — Predictability (Low, Med, High); Outcome (Likely, Unlikely); Localizers (Sem, Phon, Orth)

D. L SPL — Predictability (Low, Med, High); Outcome (Likely, Unlikely); Localizers (Sem, Phon, Orth)

E. Caud. Nc. — Predictability (Low, Med, High); Outcome (Likely, Unlikely); Localizers (Sem, Phon, Orth)

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687   Figure 6: Parameter estimates for cerebral areas engaged in prediction. Left column: Supratentorial brain
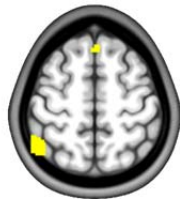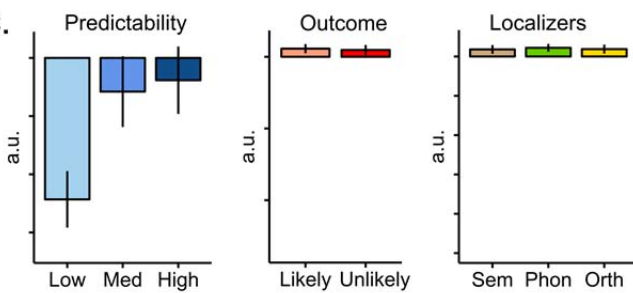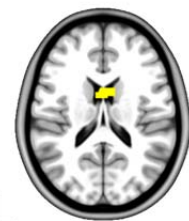
688   areas that relate to predictability, whole-brain corrected at FWE $p<0.05$. Column 2 – Predictability.

689   Parameter estimates extracted for varying levels of predictability. Regression weights were extracted from

690   the clusters identified in the imaging analysis where predictability (cloze probability) was a continuous

691   variable; they are plotted to aid interpretation only – no statistical inference should be drawn. Column 3 –

692   Outcome. Parameter estimates for prediction errors; as these areas were not part of an a priori

693   hypothesis, no statistical inference should be drawn. Column 4 – Localizers. Parameter estimates (1-back

694   minus 0-back) for semantic, phonological and orthographic processing; again, as these areas were not

695   part of an a priori hypothesis, no statistical inference should be drawn. a.u.: arbitrary units. Error bars

696   denote SEM.

697

Tables

699 Table 1. Table of results. Cluster corrected (FWE corrected alpha <0.05: voxel-wise p<0.001, clusters

700 size > 99 voxels). For clusters that encompass multiple peaks, the volume of the entire cluster is given,

701 with the index of the sub-peak in parenthesis.

Gross anatomical region	volume (mm3)	T	MNI coordinates x	y	z	Cytoarchitectonic region
STEM						
Frontal						
Left Inferior Frontal Gyrus	179,384 (5)	10.57	-50	12	24	BA 44
Left Precentral Gyrus	179,384 (6)	9.87	-50	-6	52	BA 6
Right Inferior Frontal Gyrus	32,440 (1)	6.03	48	18	24	BA 44
Right Middle Frontal Gyrus	32,440 (2)	8.48	50	2	56	BA 6
Left Superior Frontal Gyrus	17,592	13.19	-6	8	56	BA 6/SMA
Parietal						
Right Inferior Parietal Lobule	12,608	8.94	32	-52	46	BA 7
Left Inferior Parietal Lobule	12,472	6.21	-34	-58	50	BA 7
Occipital						
Left Middle Occipital Gyrus	179,384 (1)	14.69	-36	-94	-4	hOC4v (V4)
Left Inferior Occipital Gyrus	179,384 (3)	11.98	-44	-60	-14	BA 37
Right Inferior Occipital Gyrus	118,064 (1)	12.25	42	-92	-2	hOC3v (V3v)
Right Inferior Occipital Gyrus	118,064 (3)	11.3	28	-94	-4	BA 18
Temporal						
Left Inferior Temporal Gyrus	179,384 (2)	13.14	-40	-46	-16	BA 37
Left Middle Temporal Gyrus	179,384 (4)	11.65	-54	-50	12	BA 21
Right Inferior Temporal Gyrus	118,064 (2)	12.56	44	-62	-12	BA 37
Right Middle Temporal Gyrus	118,064 (4)	9.99	54	-36	4	BA 22
Right Superior Temporal Gyrus	118,064 (6)	6.92	60	2	-14	BA 22
Left Temporal Pole	179,384 (7)	9.33	-52	10	-20	BA 38
Left Middle Temporal Gyrus	179,384 (8)	8.99	-56	-6	-12	BA 22
Insular regions						

Right Insula Lobe	2,552	6.15	34	24	4	
Cerebellum						
Right cerebellum	118,064 (5)	9.59	30	-70	-52	Lobule VIIb (Hem)
Right cerebellum	118,064 (7)	6.37	30	-62	-26	Lobule VI (Hem)
Left cerebellum	1,304	5.68	-30	-70	-52	Lobule VIIb (Hem)
Other subcortical						
Left Thalamus	840	4.55	-8	-16	12	

STEM COVARIATE

Frontal						
Left Superior Frontal Gyrus	1,584	4.43	0	28	62	BA8/pre-SMA
Left Inferior Frontal Gyrus	1,592	4.14	-42	22	-10	BA47
Right Middle Frontal Gyrus	1,360	4.66	44	20	40	BA 9/46
Parietal						
Left Superior parietal lobule	1,600	4.04	-50	-58	56	BA 7
Cerebellum						
Right Cerebellum	1,072	4.19	28	-86	-48	Lobule VIIa Crus II (Hem)
Other subcortical						
Right caudate nucleus	2,664	4.76	6	4	18	

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