

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:<https://orca.cardiff.ac.uk/id/eprint/110727/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Phillips, H. N., Cope, T. E., Hughes, L. E., Zhang, J. and Rowe, J. B. 2018. Monitoring the past and choosing the future: the prefrontal cortical influences on voluntary action. *Scientific Reports* 8 , 7247. 10.1038/s41598-018-25127-y

Publishers page: <http://dx.doi.org/10.1038/s41598-018-25127-y>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



1 **Monitoring the past and choosing the future: the prefrontal cortical**
2 **influences on voluntary action**

3 *H. N. Phillips^{a,b}, T. E. Cope^a, L. E. Hughes^{a,b}, J. Zhang^c, J. B. Rowe^{a,b,d}

4 a. Department of Clinical Neurosciences, University of Cambridge, CB2 0SZ, UK

5 b. Medical Research Council, Cognition and Brain Sciences Unit, Cambridge, CB2 7EF, UK

6 c. School of Psychology, University of Cardiff, CF2 2AT, UK

7 d. Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge,
8 UK

9 *Corresponding Author: holly.phillips@mrc-cbu.cam.ac.uk

10

11

12 Choosing between equivalent response options requires the resolution of ambiguity. One could
13 facilitate such decisions by monitoring previous actions and implementing transient or
14 arbitrary rules to differentiate response options. This would reduce the entropy of chosen
15 actions. We examined voluntary action decisions during magnetoencephalography, identifying
16 the spatiotemporal correlates of stimulus- and choice-entropy. Negative correlations between
17 frontotemporal activity and entropy of past trials were observed *after* participants' responses,
18 reflecting sequential monitoring of recent events. In contrast, choice entropy correlated
19 negatively with prefrontal activity, *before* and *after* participants' response, consistent with
20 transient activation of latent response-sets ahead of a decision and updating the monitor of
21 recent decisions after responding. Individual differences in current choices were related to the
22 strength of the prefrontal signals that reflect monitoring of the statistical regularities in
23 previous events. Together, these results explain individual expressions of voluntary action,
24 through differential engagement of prefrontal areas to guide sequential decisions.

25

26 INTRODUCTION

27 The brain is adept at identifying and representing regularities within a dynamic sensory
28 environment, such as the identification of rhythms in auditory streams ^{1,2}, recurrent visual
29 features embedded in complex objects ³, and the transitional relationships between elements in
30 artificial grammars ⁴. Implicit learning of the statistics of event regularity is evident from early
31 in development ⁵. These expectations adaptively influence behavior, and facilitate preferential
32 responses to new events ⁶.

33 Statistical regularities span different timescales, which map onto a rostral-caudal gradient of
34 neural representations ⁷. While the analysis of shorter sequences relies on the basal ganglia ^{8,9},
35 regularities from temporally extended sequences (tens of seconds) have been associated with
36 the prefrontal cortex ^{10,11}. The neural response to regularities is established across multiple
37 sensory modalities ^{12,13}, whether in fixed event blocks ^{14,15}, over all previous events ^{16,17} or
38 during varying time windows ¹¹.

39 Sequential voluntary actions also contain statistical regularities. Where action decisions cannot
40 be explained by objective differences in outcome or reward, individual differences in the
41 degree of regularity provide critical insights into the mechanisms of volition ¹⁸. Volition is
42 integral to normal human behavior, and many neurological disorders are characterized by
43 changes in volition, with corresponding differences in regularity, entropy or stereotypy of
44 behaviors ¹⁹. This study therefore lies in the broader context of willed action and volitional
45 decision making. Voluntary actions encompass everyday decisions that are not by reflex or
46 forced by some external stimulus or specified rule (over and above the willingness to adhere to
47 such instructions) ²⁰. They are sometimes considered internally-driven decisions or consciously
48 attended to ^{21,22} or associated with a sense of agency when making choices between possible
49 options ^{23,24}. However, terms such as “free-will” or “free selection” of action are poorly

50 operationalized, and open to highly variable interpretation: there are often implied or actual
51 constraints on the range of actions from which to choose. Instead, we propose analysing such
52 tasks in terms of decision-making and choice. Cortical regions consistently associated with
53 action selection include parietal ^{25,26} premotor ^{27,28} and prefrontal areas ^{29,30}. Conversely,
54 abnormal statistical dependencies in the form of perseveration and stereotypies are often
55 associated with dysfunction of the prefrontal cortex and its striatal connections ³¹, including
56 Parkinson's disease and progressive supranuclear palsy ³², Tourette syndrome ³³ and
57 frontotemporal dementia ³⁴.

58 Based on an fMRI study of voluntary action selection, we recently proposed two mechanisms
59 by which the prefrontal cortex introduces regularity to sequential voluntary behaviors ¹¹.
60 Firstly, by monitoring serial actions, it introduces a bias towards selection of previously under-
61 represented choices ³⁵. Secondly, it facilitates the implementation of transient and arbitrary
62 response rules. Such rules are not essential for voluntary action, but may serve to reduce the
63 effort required to resolve ambiguity where the selection between action alternatives is not
64 facilitated by differential rewards ³⁶⁻³⁹. A simple rule might be the inhibition of repetition of
65 sequential choices ¹⁸ analogous to inhibition of return demonstrated in attention and saccades
66 ^{40,41}. For example, Zhang et al. (2012) demonstrated that prefrontal cortical activation brakes
67 the activation of premotor representation of recent actions, leading to regularising of behavior.

68 Neuropsychological and fMRI studies are not able to determine whether prefrontal cortical
69 activity related to selection regularity occurs before the selection of action or afterwards.
70 Regularisation activity before the response suggests a constraint on the current choice, for
71 example by a transient rule that reduces effort by minimising uncertainty ⁴². In contrast,
72 regularisation related activity after the response suggests the monitoring of behavior, or the
73 updating of a heuristic response-set.

74 We therefore exploited the temporal resolution of magnetoencephalography (MEG) to
75 investigate how the degree of regularity in past events modulates present evoked responses.
76 Using a task in which participants are instructed to make a specified action or are given a
77 choice of actions to make, we used entropy to measure types of regularity, quantified as the
78 degree of regularity in past trial events (Trial Entropy, TE) and the degree of regularity of
79 participants' voluntary action decisions (Selection Entropy, SE). Entropy measures do not
80 depend on transition probability, which suits the current experiment given the design that
81 interleaves choice and specified trial types.

82 Tobia et al. (2012) puts forward in their fMRI study that entropy quantifies uncertainty, the
83 inverse of predictive mechanisms used in higher cognitive processes. For example, they
84 interpret positive correlations between past randomness neural activity as an increase of
85 prediction error signals⁴³ and negative correlations as regions that monitor predictability of
86 current events given past events^{14,15}. We expected to observe neural correlates of TE and SE in
87 temporal and prefrontal regions in replication of a previous fMRI experiment using a similar
88 multi-choice action selection task¹¹. Crucially, the high temporal resolution of MEG enabled
89 us to test whether (1) entropy-related neural activity in sequential action selection occurs
90 before or after the action; and (2) whether individual behavioural differences can be explained
91 by monitoring of the preceding regularity in either trial type (TE) or subjects' action choices
92 (SE).

93

94 **RESULTS**

95 **Behavioral results**

96 We recorded MEG data from 18 healthy young participants completing a multi-choice action
97 selection task (Figure 1). Participants were instructed to press the button for a specific finger in
98 'Specified' trials or were to make a new fresh choice of which button to press for 'Choice'

99 trials. On average, participants responded in $99.0 \pm 1.2\%$ of action trials and the average total
100 error rate was 3.2% for omission and commission errors. As expected¹⁸, participants' mean
101 reaction times for choice trials was slightly longer than for specified trials ($584\text{ms} \pm 76\text{ms}$ and
102 $566\text{ms} \pm 56\text{ms}$ respectively; two-tailed paired t-test $t(17) = -2.10$, $p = .05$). We assessed the effect
103 of finger selection on reaction times using a repeated-measures ANOVA with two factors:
104 finger selection (index to little finger) and task condition (specified or choice). There was no
105 significant main effect of finger ($F(1.87, 31.7) = 3.32$, $p = .52$), or task condition ($F(1, 17) = 4.45$,
106 $p = .50$), but there was a significant interaction between finger and task condition ($F(2.07,$
107 $35.2) = 11.4$, $p < .001$) such that, during choice trials, participants selected each finger with the
108 following probabilities: index = 26.8% , middle = 28.7% , ring = 27.5% , little = 17% . Post-hoc
109 tests demonstrated that the middle and little finger actions were significantly different from
110 25% chance rate (Middle: $Z = +2.85$, $p = .004$; Little: $Z = -3.72$, $p < .001$, one-sample Wilcoxon
111 signed-rank test).

112 [Figure 1 about here]

113 During choice trials, participants tended to choose a new action rather than repeat the previous
114 action (repetition rate: $12.2 \pm 12.6\%$; $Z = -3.28$, $p < .001$, against chance rate of repetition at 25% ,
115 one-sample Wilcoxon signed-rank test). This inhibition of repetition was concordant with
116 previous studies, and suggests that a current choice is modulated by the previous response
117 history^{18,44}. The repetition rate was not significantly different across fingers ($F(1.96,$
118 $33.6) = 0.28$, $p = .75$) and the probability of finger choices were not different across repeated and
119 non-repeated trials ($\chi^2(17) = 1.67$, $p = .543$, Friedman's test).

120 **Trial and Selection entropy**

121 To observe the neural representation of regularity monitoring we measured the entropy of past
122 trials events (Trial Entropy, TE) and of past finger choices (Selection entropy, SE) across
123 temporally extended periods, we examined six windows of 25-50 trials, in steps of 5. These

124 window lengths were chosen to obtain meaningful measures of entropy and encompass those
125 used in previous studies of statistical information representations in the brain for temporally
126 extended event sequences^{11,16,45}. All participants showed fluctuations over time in their SE
127 values. Their TE values also fluctuated over time because trial conditions were pseudo-
128 randomly intermixed. Figure 2a shows an example single participant's TE and SE values for
129 the shortest (25) and longest (50) sliding window lengths. The entropy measures for each
130 window were non-independent, i.e. data from the 25-trial window and 30-trial window overlap
131 in all but five trials. Thus, entropy measures were significantly correlated across time (Figure
132 2b, Pearson's $r > 0.55$ and $r > 0.65$ for TE and SE respectively, $p < .003$, Bonferroni corrected),
133 where neighboring window lengths had highest coefficients.

134 [Figure 2 about here]

135 We tested whether entropy influenced reaction times using a within-participant Pearson's
136 correlation between single-trial reaction times and the corresponding trial and selection
137 entropies. We used reaction times here as an indication of participant's attention across the
138 task, where we would expect slower reaction times with reduced concentration. We observed
139 no significant correlations for any window lengths for either SE or TE ($r < \pm 0.018$, $p > .20$ across
140 all participants), suggesting that TE and SE measures were not significantly confounded by
141 trial-to-trial variations in reaction time and therefore attention.

142 There was a significant negative correlation between TE and SE for each window length ($Z < -$
143 2.67 , $p < .007$, Figure 2c). There was not a significant main effect of window length on the TE-
144 SE correlations ($\chi^2(5) = 2.63$, $p = .76$, Friedman's test). Therefore, although SE was conditional
145 on trial type, the recent specified trials order partially influenced the current trial choice. The
146 strength of this relationship was observed to vary between individuals. For a window length of
147 25, where the overall group correlation between TE and SE was $z = -0.297$, single participant
148 correlations ranged from $z = 0.021$ to $z = -0.605$. Some individuals therefore displayed a strong

149 negative correlation between TE and SE, while others demonstrated a weaker or no
150 relationship (Figure 2d). No participants displayed a significant positive correlation. Hartigan's
151 dip test ⁴⁶ over 10000 iterations confirmed that this represented a unimodal distribution suitable
152 for further parametric analysis, rather than a bimodal distribution of strong and weak
153 responders (dip=0.105, p=.079).

154 **Entropy related MEG responses**

155 Single trial gradiometer sensor MEG data were correlated with TE and SE measures using a
156 first-level statistical parametric mapping (SPM) general linear model. For SE and TE
157 separately, the resulting contrast images were used in a second-level SPM full-factorial model
158 across all participants and all window lengths.

159 For trial entropy, TE, there were significant negative correlations with the MEG responses
160 (Figure 3a, $p < .001$ threshold with $p < .05$ FWE cluster correction). Crucially, these correlations
161 began 30ms *after* the participants' response and continued until the end of the epoch (1500ms).
162 For MEG gradiometer sensors, the measurement at the scalp is maximal over the source of
163 neural activity ⁴⁷, which gives a fair approximation of the location of cortical sources in sensor
164 space. The Figure 3B sensor space t-maps show these correlations were observed over the left
165 frontal sensors throughout the post-response period, and additional right frontotemporal
166 sensors later 656-1356ms period.

167 To visualise the neural sources of these statistically significant sensor space correlations, we
168 performed minimum norm source reconstruction of the single-trial MEG data around the time
169 of peak effect within the significant sensor space clusters. We then correlated the resulting
170 source space images with the trial entropy measures (Figure 3b right, $p < .01$). At 172ms, we
171 observed correlations of trial entropy within the left inferior frontal gyrus (MNI: [-50, 10, 2],
172 Neuromorphometrics Atlas, SPM12), and anterior middle frontal gyrus [-40, 46, 0]. Similar
173 peak locations were observed for both 656ms and 1356ms time points in left anterior middle

174 frontal gyrus ([-36, 52, 2] and [-22, 58, 0] respectively), right superior temporal gyrus ([52, -
175 38, 10] and [54, -44, 12]) and left temporal pole ([-48, -2, -26] and [-50, 0, -28]).

176 We contrasted the short (25) and long (50) window lengths. Figure 3c shows significantly
177 stronger negative correlations in bilateral frontotemporal sensor regions for longer trial
178 windows. The left frontal sensors had negative correlations that peaked after the response at
179 532ms, and were localised to the left anterior middle frontal gyrus [-40, 48, 2] and bilateral
180 superior temporal gyrus ([-42, -8, -14] and [56, -10, -10]). The right frontal sensor negative
181 correlations peaked later at 1112ms, and were localised to the right inferior temporal gyrus [52,
182 -44, -26]. No correlations were greater for short vs. long windows. We observed no significant
183 positive correlations between TE and the MEG response.

184 [Figure 3 about here]

185 For selection entropy, SE, we observed negative correlations both *before* the participants'
186 response at right and polar frontal sensors, and *after* the response at frontal polar sensors
187 (Figure 4a and b), but these did not survive FWE cluster correction threshold. However, the
188 use of such stringent whole-brain correction does not reflect our strong *a-priori* expectation for
189 frontal lobe correlations with SE on the basis of previously published fMRI results¹¹. In Figure
190 4 we therefore present results with the same height threshold but a more lenient 50-pixel
191 cluster defining threshold. We again visualised the sources of these correlations using
192 minimum norm source localisation (Figure 4b, $p < .01$). At -340ms, source peaks were observed
193 in the right central operculum [58, -14, 16] and left inferior frontal gyrus [-54, 20, 18]. At t=
194 16ms, source peaks were observed in right anterior middle frontal gyrus [22, 50, 14], bilateral
195 anterior orbital gyrus ([-24, 44, -12] and [22, 52, -16]) and right superior temporal gyrus [58, -
196 2, -2]. At t=376ms source peaks were observed in the left anterior orbital gyrus [-24, 46, -12],
197 right superior frontal gyrus [12, 62, 20], left inferior frontal gyrus [-38, 14, 24] and left
198 temporal pole [-28, 12, -36].

199 Given our *a-priori* hypothesis of the presence of negative correlations in the frontal pole from
200 previous fMRI observation ¹¹, we assessed the effect of window length within a 20mm box
201 ROI in the frontal pole. The post-response signal in the frontal polar region was significant for
202 the long > short contrast ($p=.009$, $t=3.48$, FWE peak correction, Figure 4c). Source localisation
203 (Figure 4d), suggested that the strongest negative correlations were in the left inferior frontal
204 gyrus [-36, 14, 24], left anterior orbital gyrus [-20, 58, -14] and right superior frontal gyrus [12,
205 58, 22]. There were no significant differences for the reverse contrast or for positive
206 correlations with MEG.

207 [Figure 4 about here]

208 **Inter individual variability**

209 As expected from previous work, we observed that TE and SE were negatively correlated ¹¹.
210 The strength of this relationship differed between individuals (Figure 2d). **In a post-hoc**
211 **exploratory analysis**, we explored the neural correlates of this difference. Figure 5 shows the
212 between-participants relationship between the peak t-score of each entropy-related neural
213 response (Figure 3a and 4a) and the correlations between TE and SE for the 25-event window
214 (Figure 2d). We demonstrated a significant negative correlation for TE (Pearson's $r=-0.55$,
215 $n=18$, $p=.018$) but not for SE (Pearson's $r=0.22$, $n=18$, $p=.38$). We compared these correlations
216 using Meng's z-test for comparing correlations ⁴⁸. The TE and SE correlations were
217 significantly different ($z=2.31$, $p=.011$).

218 **Shapiro-Wilk tests demonstrated that the use of parametric statistics to assess correlations**
219 **between our measures of interest was not rendered inappropriate by deviations from the normal**
220 **distribution in these variables: (TE peak t-score $W=0.92$, $n=18$, $p=0.11$; TE-SE correlation**
221 **$W=0.90$, $n=18$, $p=0.055$). However, to ensure the robustness of this finding, the analyses were**
222 **repeated using non-parametric Spearman's rank correlations. The results were replicated, with**
223 **a significant negative correlation again demonstrated for TE (Spearman's $\rho=-0.56$, $n=18$,**
224 **$p=0.018$) but not for SE (Spearman's $\rho=0.06$, $n=18$, $p=0.80$).**

225 Similarly, the results were robust to different choices in how the strength of neural response
226 related to TE was quantified for each individual. We used a binary mask of group significance
227 to restrict the time and location of the single subject analysis to those clusters demonstrated to
228 have population-level relevance for TE and SE respectively. Repeating the analysis with a
229 much more liberal mask, containing any pixel with $p < 0.001$ correlation at the group level
230 uncorrected for multiple comparisons and therefore resulting in more latitude for individual
231 differences in the scalp location and time of peak response, had very little effect on the
232 negative correlation demonstrated for TE (Pearson's $r = -0.54$, $n = 18$, $p = 0.021$; Spearman's
233 $\rho = -0.54$, $n = 18$, $p = 0.023$). The t-peak values were determined for each individual separately,
234 not on the group t-maps, on the basis that it could not reasonably be expected that all
235 individuals would display the exact time and scalp location of response. However, to assess the
236 uniformity of response we repeated the analysis with a much more stringent mask restricted to
237 the group peak ($[X = 47, Y = 8, \text{time} = 656\text{ms}, F(1,102) = 29.74, p < 0.001]$ +/- 1cm and +/- 50ms;
238 marked with a star in Figure 3b) and took the median individual t-score within this mask as the
239 dependent measure for each individual. This resulted in slightly weaker correlations (Pearson's
240 $r = -0.45$, $n = 18$, $p = 0.061$; Spearman's $\rho = -0.53$, $n = 18$, $p = 0.026$), but a similar pattern.
241 Overall, therefore, individual differences in the strength of the relationship between past events
242 and future choices could be accounted for by the strength of neural monitoring of past events
243 (TE) but not by the strength of monitoring of past choices (SE).

244 [Figure 5 about here]

245 **DISCUSSION**

246 When faced with a choice between similar alternative actions, our decisions are constrained by
247 the history of recent experience and choices. These constraints vary over time, leading to slow
248 fluctuations in the regularity of behavioral decisions. This study makes three key contributions.
249 First, we replicate the finding that frontal and temporal neural responses relate to the regularity
250 in the sequence of recent events (trial entropy). But, by exploiting the temporal resolution of

251 MEG, we demonstrated that these correlations occur *after* the response, suggesting the
252 updating of a monitor of recent stimulus events, occurring after the new action is made.
253 Second, we replicate the finding that rostral frontal activity correlated negatively with the
254 entropy of participants' own chosen actions (selection entropy), but here we demonstrated that
255 the physiological response occurred both *before* and *after* the response. Third, the degree to
256 which individuals manifested a link between the variability of the preceding experimental
257 context and their current behavior was related to the strength of their neural correlates of trial
258 entropy but not selection entropy. We interpret this as evidence that the constraints on current
259 behavioral choices are driven more strongly by the degree of monitoring of recent events than
260 by the instantiation of arbitrary rules.

261 The prefrontal cortex facilitates optimal interactions with a dynamic environment^{10,49,50}. By
262 virtue of its connectivity, this region is well placed to integrate sensory information from
263 multiple domains, defining behavioral goals, maintaining the response sets necessary to
264 achieve them, and predicting the outcomes of action^{49,51}. The value of a given course of action
265 may be learned by subjects, either in association with specific stimuli or in terms of a current
266 task set or rule³⁸. However, there are situations in which current stimuli do not in themselves
267 provide the evidence necessary to make a choice. Whether the choice refers to the action itself,
268 how to select it, when or whether to make it^{52,53} the resolution of ambiguity is time consuming
269 and effortful, with extensive activations observed for what might otherwise be seen as trivial or
270 inconsequential choices²⁷. In neuroeconomic terms, there is a cost of ambiguity, to resolve a
271 choice when the expected rewards are too similar between response options⁵⁴.

272 One solution to the problem of ambiguity is stochastic decision-making, competing 'first past
273 the post' between response options^{11,44}. An arguably simpler strategy is to assign differential
274 value according to a local arbitrary rule, thereby replacing the ambiguity by a value based
275 decision process⁵⁵, even without attributing stable or causal relationships between decision
276 and outcome⁵⁶. The presence of an arbitrary 'rule' would also reduce the differential reaction

277 time between trial types, and support the observed attribution of value to freely chosen
278 responses⁵⁷.

279 As a result, a participant would have *a-priori* response preferences that determine the
280 inequality in the distribution of ostensibly equivalent choices, despite the experimental
281 neutrality over the response options. Such an arbitrary ‘rule’ would also reduce the differential
282 reaction time between trial types. Rules and response-sets can be chosen⁵³, but more usually
283 they are specified experimentally. Multiple studies show the prefrontal and frontopolar cortical
284 representations of such rules^{36,38,53} and the impact of prefrontal lesions on rule-guided or goal-
285 directed action. The specific rule need not be directly determined, and may change over time,
286 but such rules would reduce the entropy of responses.

287 We observed the neurophysiological correlate of selection entropy at right frontal sensors
288 *before* the action was made. Source localisation of these correlations revealed peak responses
289 in the right supramarginal gyrus at -340ms, and right frontopolar prefrontal cortex and left
290 orbitofrontal cortex at -16ms. The prefrontal cortex is known to be active when learning or
291 retrieving rules and when implementing or switching rules^{37,44}. We suggest that the application
292 of a local rule, by prefrontal cortex, is embedded in the current sequence of trial types and
293 choices, whether a simple rule (e.g. the avoidance of repetition) or a more complex statistical
294 dependency between events. Premotor and supplementary motor areas may also show
295 activation in respond to arbitrary rules and in volitional actions^{22,58} but these areas were not
296 observed for selection entropy correlations. We also observed activity related to selection
297 entropy *after* the response in left orbitofrontal cortex and right frontopolar prefrontal cortex.
298 We suggest this activity might be updating a monitor of past responses, although it could
299 represent the reinforcement of the transient response set^{36,38}. The prefrontal cortical
300 correlations with selection entropy increased with longer window lengths, which argues
301 against a within-trial ‘surprise’ signal^{11,59}. Further studies could directly assess whether this
302 activity is monitoring past responses by testing whether the activity predicts if the participant

303 switches or repeats the previous response on the next response. However, with only 12.2%
304 probability of repetition in trials we did not have enough trials to do this.

305 We consider the importance of these results in regards to the broader issue of a predictive brain
306 that is sensitive to odd and unexpected events (e.g. the mismatch response ^{2,60}), regularities in
307 stimulus patterns and sequence learning ⁶¹ and here we show that such sensitivity also extends
308 to regularity in action choices. Changes in neural responses to regularities in sensory sequences
309 are shown to correlate with changes in different neurological and psychiatric disorders ⁶².
310 Therefore, it is of importance to conduct further studies into whether monitoring regularity in
311 action choices also change in different disorders. We interpreted our MEG negative
312 correlations in terms of a monitor of statistical regularities in sensory and motor events.
313 However, the representation of statistical regularities equates to forming beliefs, including
314 implicitly the beliefs used to make predictions about sensory inputs in a hierarchical predictive
315 model of our actions and the environment. Indeed, it has recently been shown that mechanisms
316 for monitoring prior stimulus statistics are represented at the neural level in rodents ⁶³,
317 demonstrating that such processes have significant evolutionary relevance.

318 The experimental modulation of trial entropy was analogous to earlier studies of audio-visual
319 sequence entropy ^{12,64}. Our negative MEG correlations were concordant with evidence for
320 activation-entropy associations for auditory and visual sequences ^{15,65}. The negative
321 correlations between neural activity and trial entropy replicated those demonstrated by Zhang
322 and Rowe (2015). However, their fMRI study could not establish whether the activity occurred
323 before or after the response. Here we demonstrate that neural activations related to trial entropy
324 were limited to the post-response period and therefore represent the monitoring of recent
325 events rather than an action selection process.

326 In contrast to previous studies that used either short fixed event lengths or entire sequences
327 ^{14,16,59,66}, we varied windows lengths from 25 to 50 trials, in line with the neural representations

328 of information theoretic measures such as entropy ^{11,15,66}. This length is in keeping with the
329 predictive value of events on remote future choices observed in non-human primate decisions
330 ⁶⁷. We observed increased negative correlations between prefrontal regions and trial and
331 selection entropy for the longer trial windows, suggesting that stronger frontal activity supports
332 the updating or consolidation of response sets over multiple trials.

333 Additionally, **in a post-hoc analysis** we observed an interaction between monitoring of events
334 and the selection of action. For some individuals, periods of irregular events (high trial
335 entropy) were associated with more regularity of action selection (low selection entropy). This
336 behavioural interaction was significantly related to individual differences in the strength of
337 activity related to monitoring recent trials (Figure 5). This provided a neurophysiological
338 marker of individual differences in the degree to which recent behaviors and stimuli constrain
339 subsequent voluntary actions. **The importance of frontal brain regions for monitoring volitional
340 decisions and influencing future decisions is clear from the behavioural consequences of
341 damage or degeneration of the regions we identify in association with action selection. These
342 may impair the self-initiation of actions, as a feature of apathy ⁶⁸, reduce a sense of agency for
343 one's own actions ²⁴, or lead to perseverative and stereotyped behaviours.**

344 **The implication of the negative relationship between TE and SE is that the more entropic
345 previous events have been, the less entropic an individual's arbitrary choices tend to be. This
346 can be seen as an analogous observation to inhibition of return in saccadic choices. Therefore,
347 if the constrained trials are already highly entropic, it is not necessary to introduce entropy in
348 one's selections to avoid returning time and again to the same arbitrary choice. If a goal of the
349 nervous system in arbitrary choices is to diversely sample selections to gain information about
350 the relative merit of seemingly equivalent choices and thus constrain future choices in the
351 optimal manner ^{69,70}, it is more informative in determining the optimal choice at any one
352 instant, to use the fidelity with which one has monitored previous sampling not previous
353 unconstrained choices. This view is supported by our observation that individual differences in**

354 the strength of the relationship between past events and future choices could be accounted for
355 by the strength of neural monitoring of past events (TE) but not by the strength of monitoring
356 of past choices (SE).

357 There are potential limitations this study. First, participant's attention may have varied across
358 the length of the task. We tested correlations between reaction times and selection entropy,
359 hypothesising that reaction times increase with reduced attention: there was not a significant
360 correlation. Second, we analyzed the differences between trial window lengths using a full
361 factorial model and corrected for non-sphericity because of the high correlations between
362 regressors of the different window lengths that were nested within sequence. An alternative
363 approach could use a separate regression model for each window length, followed by a
364 disjunction test to estimate the temporal specific MEG activation associations. Both methods
365 were used by Zhang and Rowe (2015), with similar results. However, the disjunction test
366 would only show regions that correlate in one trial window and not the other, rather than
367 directly testing the hypothesis that window length is itself a determinant of neural activity.
368 Third, the selection entropy correlations were only observed using a more lenient whole-head
369 statistical correction than trial entropy correlations. However, the location of selection entropy
370 correlates were in agreement with anatomical priors based on the fMRI study of this task ¹¹ and
371 analogous correlates of regularity in other tasks ^{15,16}. Fourth, our study was designed and
372 powered to examine main effects of the association between activity and TE/SE but we
373 acknowledge that power was limited for our post-hoc assessment of the neural correlations
374 with individual differences: we were powered to detect large effects (similar studies using
375 fMRI range from 12-16 participants ^{11,15,16,45}). Despite this, we have demonstrated a robust
376 statistical relationship between the degree to which individuals avoid repetition in their
377 selected actions and the strength with which they neurally monitor the entropy of past events
378 (trial entropy, Figure 5a). We did not demonstrate a relationship between individuals' actions

379 and the strength with which they monitored their previous choices (selection entropy, Figure
380 5b).

381 In conclusion, we propose that when choosing between alternative response options, healthy
382 adults make their decision in part based on a monitor of past events. Statistical regularities in
383 the preceding actions are updated over successive trials, represented in prefrontal areas, and
384 thereby influence subsequent choices between otherwise equivalent responses. We suggest this
385 strategy reduces cognitive effort, and obviates a pause of ongoing behavior during decision-
386 making under uncertainty ⁴². We show that individual differences in sequential decisions relate
387 to the strength of prefrontal monitoring of regularities in previous actions more than to the
388 neural effort associated with the instantiation of such rules. Damage to these monitoring and
389 selection processes may contribute to the stereotypies, inflexible predictions or chaotic
390 behavioral patterns arising from frontal-lobe neurological disorders ⁷¹⁻⁷⁴.

391

392 **METHODS**

393 **Participants, data collection and preprocessing**

394 Twenty healthy, right-handed adults participated in the study (10 females, mean age 26.0 ± 4.9
395 years, range 18-37). Two participants were excluded from further analysis due to error rates
396 greater than three standard deviations from the group mean. Participants gave informed written
397 consent. The study was approved by the Cambridge 2 Research Ethics Committee and the
398 methods were carried out in accordance with the relevant guidelines and regulations.
399 Participants had no history of psychiatric or neurological illness, and no previous experience of
400 the task.

401 **Task**

402 We measured statistical regularities over temporally extended stimulus and action sequences
403 using a multi-choice action selection task that allows participants to choose between action
404 responses without explicit or learned rewards or feedback. The task has been used to study
405 action decisions in healthy individuals ¹¹, in ageing ⁷⁵, and in Parkinson's disease ⁷¹, with
406 robust patterns of activation at group- and single-subject levels ²⁷. In brief, participants
407 watched an image of a hand with empty circles above the fingers. In 'specified' trials, a single
408 circle was filled, cueing the participant to press the corresponding finger on a manual button
409 box. In 'chosen' trials all four circles were filled, directing the participant to make a choice to
410 press any one of their four fingers (**Figure 1a**). Participants were asked to make a "fresh
411 choice, regardless of what they had done before", as quickly as possible. There were no reward
412 differences between action choices, no feedback, and no suggestion of rules for particular
413 modes of response (such as to be 'random'). Null trials appeared identical to a prolonged inter-
414 stimulus interval, with no response required of participants (to keep the paradigm identical to
415 that used in previous fMRI studies, in which the null trials facilitate modelling). Stimuli were
416 displayed for 1 second with 2.5 second stimulus onset asynchrony. The task contained 320

417 specified trials, 320 choice trials and 320 null events, were pseudo-randomly intermixed. The
418 trials were split into four ten-minute blocks with short breaks (30s) for the participant to rest.
419 The task was presented using E-Prime® software (Psychology Software Tools Inc.).

420 **MEG data acquisition and processing**

421 MEG data were collected using a magnetically shielded 306-channel Vectorview system
422 (Elekta Neuromag), with a magnetometer and two orthogonal planar gradiometers at each of
423 the 102 sensor positions. Vertical and horizontal eye movements were recorded using paired
424 EOG electrodes, and the head position was monitored using five head-position indicator coils.
425 A 3D digitizer (Fastrak; Polhemus) was used to record the three-dimensional locations of the
426 coils, three anatomical fiducials (nasion and left and right preauricular points) and
427 approximately 100 scalp points. We used Maxfilter software to make adjustments for head
428 movement⁷⁶, and to downsample the data from 1kHz to 250Hz.

429 The remaining pre-processing steps were completed using SPM12 software (Wellcome
430 Department of Imaging Neuroscience, London, UK). We high-pass filtered at 0.1 Hz and low-
431 pass filtered at 40 Hz using Butterworth filters. We epoched the data around the participant's
432 action response from -1500ms to 1500ms. We applied a baseline correction from -1500 to -
433 1000ms to ensure a baseline before the cue presentation. We used baseline correction because
434 of our interest of how the evoked response is modulated by context of SE and TE, rather than
435 the mean effect of these entropy measures over time. We applied automatic trial artefact
436 rejection by thresholding the EOG electrodes at 200 μ V. Omission and commission error trials
437 were rejected, as were trials on which the participant's reaction time was less than 150ms or
438 longer than 1500ms.

439 **Sliding window entropy measures of randomness**

440 To investigate neural monitoring of temporal events, we calculated the entropy measures of
441 previous trials and of previous action selection events, replicating Zhang and Rowe (2015). We

442 correlated these entropy measures with single-trial MEG responses. We calculated the entropy
 443 over a sliding window of previous stimuli ($C_j=\{a, b, c, d, e\}$, **Figure 1b**) or previous choice
 444 selection responses ($A_j=\{1, 2, 3, 4\}$, for each finger). Iterating through each trial i , the window
 445 included the range of trials: $[i-n+1, i]$, where n was the length of the window (**Figure 1c**). The
 446 entropy measure was then assigned to the i^{th} trial and correlated with that trial's MEG
 447 response. Though error trials were excluded from imaging statistics, they were included in the
 448 measurement of trial entropy (TE) to obtain the complete measure of stimulus trial variability.
 449 Choice trial omission errors were not included in the calculation of selection entropy (SE). The
 450 entropy values were calculated for six trial windows ($n=25-50$ trials, step size =5), to examine
 451 whether any brain regions were sensitive to the fluctuations of entropy over different
 452 timescales ¹¹.

453 TE was defined by Shannon's entropy. TE quantitatively measures the degree of randomness
 454 in the presented stimuli within the sliding window. Higher TE values indicated higher
 455 randomness within the window. The TE at the i^{th} trial is given by:

$$456 \quad TE(i) = H(Stimuli) = -\sum_{k=(a,b,c,d,e)} p(C_j = k) \log p(C_j = k), \quad (i - n + 1 \leq j \leq i) \quad (1)$$

457 SE was measured from the degree of randomness in participants' responses in the choice trials.
 458 SE was defined by conditional entropy ¹⁵, calculating the probability of each action given the
 459 stimuli was a choice trial. The SE at the i^{th} trial is given by:

$$SE(i) = H(Actions|Stimuli = \{e\}) \\
 = - \sum_{\substack{k=(e) \\ m=\{1,2,3,4\}}} p(A_j = m, C_j = k) \log p(A_j = m|C_j = k), \quad (i - n + 1) \leq j \leq i \quad (2)$$

460 TE and SE values were not calculated for the trials occurring before the end of the first sliding
 461 window of interest because there were not enough trials to calculate the entropy measure. Both
 462 TE and SE were calculated for every following trial, whether specified or choice, because we

463 assumed each measure to be a sustained state representation of the degree of order based on
464 recent trials ¹¹.

465 **Entropy-related MEG responses**

466 For each participant, their trial-by-trial TE and SE measures were mean centred and used as
467 regressors within a first-level general linear model to correlate with the single-trial planar-
468 gradiometer MEG data. We firstly completed our analyses in MEG sensor space to be able to
469 observe the correlations across all space and all time. This analysis was repeated for each
470 sliding window. For both TE and SE, we included the first-level contrast images across all six
471 windows within a second-level full-factorial model to examine neural correlations of entropy
472 for all trial window lengths and to contrast these correlations across window lengths. The data
473 were adjusted for unequal variance and for non-sphericity with dependence between measures.
474 Note that a repeated measures design was not appropriate for the multiple window lengths, as
475 the measures reflected nested sequences and were not independent repeated samples. We
476 analyzed trials locked to the participants' responses to investigate temporal precedence of these
477 neural correlations in relation to the action response.

478 **Source Localisation of Entropy correlations**

479 Additionally, we performed single-trial MEG source localisation to make inferences of the
480 neural sources that correlated with the measures of entropy. Firstly, we estimated the forward
481 leadfield model using the participant's individual structural MRI scan to construct a realistic
482 single-shell head model, normalised to MNI standard space (MRI: 3T Siemens Tim Trio, T1-
483 weighted 3D MPRAGE sequence, TR =2250 ms, TE =2.99 ms, flip angle 9°, field-of-view
484 240x256x160, 1 mm slice thickness). The head model was co-registered to digitised
485 anatomical fiducial markers and scalp points. We computed the inverse source reconstruction
486 for every trial using the minimum norm algorithm ⁷⁷ for 20ms time windows around the time
487 of peak significance for each of the significant clusters observed in the sensor space analysis.

488 The resulting single-trial source reconstructed images were smoothed using an 8 mm FWHM
489 Gaussian kernel and then correlated with the trial and selection entropy values, replicating the
490 statistical analysis steps used in the sensor space correlations. As the goal of the
491 reconstructions was to visualise the location of the neural sources already statistically
492 demonstrated in sensor space, correlation maps were displayed at a voxelwise threshold of
493 $p < .01$.

494 **Inter individual variability**

495 TE and SE are negatively correlated¹¹. We observed that the strength of this relationship
496 differs between individuals (Figure 2d). To assess whether this coupling between TE and SE
497 related to the strength of entropy-related neural activity, we undertook a further three step **post-**
498 **hoc analysis**. First, we separately extracted binary masks of the scalp topology of neural
499 activity related to TE and SE from the general linear model described above (Figure 3a and
500 4a). Second, using these masks as a region of interest, for each individual we separately
501 extracted the peak t-score between neural coupling and both TE and SE, **reflecting the strength**
502 **of the neural response associated with these measures. T-scores are a more appropriate**
503 **measure here than beta estimates, as they are less vulnerable to differences in noise between**
504 **scalp locations at the single pixel level⁷⁸, and in overall response amplitude between brain**
505 **areas⁷⁹**. Finally, we correlated these extracted values, which represented the individual
506 strengths of coupling between neural activity and either TE or SE, with subjects' behavior
507 calculated as follows: to account for the possibility of a delayed relationship between TE and
508 SE, for each individual we aligned the TE and SE signals by maximising the normalized cross
509 correlation within a lag window of ± 10 trials. At this optimal lag, we then calculated the
510 Pearson's product moment correlation co-efficient between TE and SE at the window length of
511 25 trials. **This window length was chosen because, as shown in Figure 2c, the absolute value of**
512 **the TE-SE correlation was relatively unaffected by increasing window length but the**
513 **variability of the measure increased. As can be appreciated from Figure 2a and 2b, at longer**

514 window lengths much of the trial-to-trial variability in TE and SE is reduced by temporal
515 smoothing. A short window length therefore allows the most robust measure of TE-SE
516 correlation. These data were then Fisher Z-transformed for correlation with the measure of
517 neural activity.

518 **Data availability**

519 The data that support the findings of this study are available from the corresponding author
520 upon reasonable request, for academic (non-commercial) purposes.

521 **REFERENCES**

- 522 1. Näätänen, R., Gaillard, A. W. & Mäntysalo, S. Early selective-attention effect on evoked
523 potential reinterpreted. *Acta Psychol. (Amst)*. **42**, 313–329 (1978).
- 524 2. Phillips, H. N., Blenkmann, A., Hughes, L., Bekinschtein, T. A. & Rowe, J. B. Hierarchical
525 Organization of Frontotemporal Networks for the Prediction of Stimuli across Multiple
526 Dimensions. *J. Neurosci*. **35**, 9255–9264 (2015).
- 527 3. Ewbank, M. P. *et al.* Changes in ‘Top-Down’ Connectivity Underlie Repetition Suppression in
528 the Ventral Visual Pathway. *J. Neurosci*. **31**, 5635–5642 (2011).
- 529 4. Cope, T. E. *et al.* Artificial grammar learning in vascular and progressive non-fluent aphasias.
530 *Neuropsychologia* **104**, 201–213 (2017).
- 531 5. Saffran, J. R., Johnson, E. K., Aslin, R. N. & Newport, E. L. Statistical learning of tone
532 sequences by human infants and adults. *Cognition* **70**, 27–52 (1999).
- 533 6. Friston, K. J., Daunizeau, J., Kilner, J. M. & Kiebel, S. J. Action and behavior: a free-energy
534 formulation. *Biol. Cybern.* **102**, 227–60 (2010).
- 535 7. Kiebel, S. J., Daunizeau, J. & Friston, K. J. A hierarchy of time-scales and the brain. *PLoS*
536 *Comput. Biol.* **4**, e1000209 (2008).
- 537 8. Grahn, J. A. & Rowe, J. B. Feeling the beat: premotor and striatal interactions in musicians and
538 nonmusicians during beat perception. *J. Neurosci*. **29**, 7540–8 (2009).
- 539 9. Cope, T. E., Grube, M., Singh, B., Burn, D. J. & Griffiths, T. D. The basal ganglia in perceptual
540 timing: Timing performance in Multiple System Atrophy and Huntington’s disease.
541 *Neuropsychologia* **52**, 73–81 (2014).
- 542 10. Barascud, N., Pearce, M., Griffiths, T., Friston, K. J. & Chait, M. MEG responses in humans
543 reveal ideal-observer-like sensitivity to complex acoustic patterns. *Proc. Natl. Acad. Sci.* **113**,
544 E616–E625 (2016).
- 545 11. Zhang, J. & Rowe, J. B. The neural signature of information regularity in temporally extended
546 event sequences. *Neuroimage* **107**, 266–276 (2015).
- 547 12. Huettel, S. A., Mack, P. B. & McCarthy, G. Perceiving patterns in random series: dynamic
548 processing of sequence in prefrontal cortex. *Nat. Neurosci.* **5**, 485–490 (2002).

- 549 13. Friston, K. J., Kilner, J. M. & Harrison, L. M. A free energy principle for the brain. *J. Physiol.*
550 **100**, 70–87 (2006).
- 551 14. Bischoff-Grethe, A., Martin, M., Mao, H. & Berns, G. S. The context of uncertainty modulates
552 the subcortical response to predictability. *J. Cogn. Neurosci.* **13**, 986–93 (2001).
- 553 15. Tobia, M. J., Iacovella, V. & Hasson, U. Multiple sensitivity profiles to diversity and transition
554 structure in non-stationary input. *Neuroimage* **60**, 1–59 (2012).
- 555 16. Strange, B. A., Duggins, A., Penny, W., Dolan, R. J. & Friston, K. J. Information theory, novelty
556 and hippocampal responses: unpredicted or unpredictable? *Neural Networks* **18**, 225–230
557 (2005).
- 558 17. Mars, R. B. *et al.* Trial-by-trial fluctuations in the event-related electroencephalogram reflect
559 dynamic changes in the degree of surprise. *J. Neurosci.* **28**, 12539–12545 (2008).
- 560 18. Zhang, J., Hughes, L. & Rowe, J. B. Selection and inhibition mechanisms for human voluntary
561 action decisions. *Neuroimage* **63**, 392–402 (2012).
- 562 19. Rowe, J. B. & Wolpe, N. in *The Sense of Agency* (eds. Haggard, P. & Eitam, B.) 389–414
563 (2015).
- 564 20. Haggard, P. Human volition: towards a neuroscience of will. *Nat. Rev. Neurosci.* **9**, 934–46
565 (2008).
- 566 21. Frith, C. D., Friston, K. J., Liddle, P. F. & Frackowiak, R. S. J. Willed Action and the Prefrontal
567 Cortex in Man: A Study with PET. *Proc. R. Soc. London. Ser. B Biol. Sci.* **244**, 241–246 (1991).
- 568 22. Lau, H. C., Rogers, R. D., Ramnani, N. & Passingham, R. E. Willed action and attention to the
569 selection of action. *Neuroimage* **21**, 1407–15 (2004).
- 570 23. Forstmann, B. U. *et al.* When the choice is ours: Context and agency modulate the neural bases
571 of decision-making. *PLoS One* **3**, 2–7 (2008).
- 572 24. Haggard, P. Sense of agency in the human brain. *Nat. Rev. Neurosci.* **18**, 197–208 (2017).
- 573 25. Shadlen, M. N. & Newsome, W. Neural basis of a perceptual decision in the parietal cortex (area
574 LIP) of the rhesus monkey. *J. Neurophysiol.* **86**, 1916–1936 (2001).
- 575 26. Roitman, J. D. & Shadlen, M. N. Response of neurons in the lateral intraparietal area during a
576 combined visual discrimination reaction time task. *J. Neurosci.* **22**, 9475–89 (2002).
- 577 27. Rae, C. L., Hughes, L., Weaver, C., Anderson, M. C. & Rowe, J. B. Selection and stopping in

- 578 voluntary action: A meta-analysis and combined fMRI study. *Neuroimage* **86**, 381–91 (2014).
- 579 28. Hoffstaedter, F., Grefkes, C., Zilles, K. & Eickhoff, S. B. The ““What”” and ““When”” of Self-
580 Initiated Movements. *Cereb. Cortex* **23**, 520–530 (2013).
- 581 29. Forstmann, B. U. *et al.* Function and structure of the right inferior frontal cortex predict
582 individual differences in response inhibition: a model-based approach. *J. Neurosci.* **28**, 9790–6
583 (2008).
- 584 30. Cunnington, R., Windischberger, C., Robinson, S. & Moser, E. The selection of intended actions
585 and the observation of others’ actions: a time-resolved fMRI study. *Neuroimage* **29**, 1294–302
586 (2006).
- 587 31. Kranick, S. M. & Hallett, M. Neurology of volition. *Exp Brain Res* **229**, 313–327 (2013).
- 588 32. Rowe, J. B. *et al.* Parkinson’s disease and dopaminergic therapy--differential effects on
589 movement, reward and cognition. *Brain* **131**, 2094–105 (2008).
- 590 33. Moretto, G., Schwingenschuh, P., Katschnig, P., Bhatia, K. & Haggard, P. Delayed experience
591 of volition in Gilles de la Tourette syndrome. *J. Neurol. Neurosurg. Psychiatry* **82**, 1324–1327
592 (2011).
- 593 34. Snowden, J. S., Neary, D. & Mann, D. M. A. Frontotemporal dementia. *Br. J. Psychiatry* **180**,
594 140–143 (2002).
- 595 35. Baddeley, A. D. Random Generation and the Executive Control of Working Memory. *Q. J. Sect.*
596 *A* **51A**, 819–852 (1998).
- 597 36. Sakai, K. & Passingham, R. E. Prefrontal interactions reflect future task operations. *Nat.*
598 *Neurosci.* **6**, 75–81 (2003).
- 599 37. Bunge, S. A. How we use rules to select actions: A review of evidence from cognitive
600 neuroscience. *Cogn. Affect. Behav. Neurosci.* **4**, 564–579 (2004).
- 601 38. Sakai, K. & Passingham, R. E. Prefrontal Set Activity Predicts Rule-Specific Neural Processing
602 during Subsequent Cognitive Performance. *J. Neurosci.* **26**, 1211–1218 (2006).
- 603 39. Ridderinkhof, K. R., Span, M. M. & van der Molen, M. W. Perseverative Behavior and
604 Adaptive Control in Older Adults: Performance Monitoring, Rule Induction, and Set Shifting.
605 *Brain Cogn.* **49**, 382–401 (2002).
- 606 40. Posner, M. I., Rafal, R. D., Choate, L. S. & Vaughan, J. Inhibition of return: Neural basis and

- 607 function. *Cogn. Neuropsychol.* **2**, 211–228 (1984).
- 608 41. Farrell, S., Ludwig, C. J. H., Ellis, L. A. & Gilchrist, I. D. Influence of environmental statistics
609 on inhibition of saccadic return. *PNAS* **107**, 929–934 (2010).
- 610 42. Frank, M., Samanta, J., AA Moustafa, A. & SJ Sherman, S. Hold Your Horses: Impulsivity,
611 Deep Brain Stimulation, and Medication in Parkinsonism. *Science (80-.)*. **318**, 1309–1312
612 (2007).
- 613 43. Rao, R. P. N. & Ballard, D. H. Predictive coding in the visual cortex: a functional interpretation
614 of some extra-classical receptive-field effects. *Nat. Neurosci.* **2**, 79–87 (1999).
- 615 44. Rowe, J. B., Hughes, L. & Nimmo-Smith, I. Action selection: a race model for selected and non-
616 selected actions distinguishes the contribution of premotor and prefrontal areas. *Neuroimage* **51**,
617 888–96 (2010).
- 618 45. Harrison, L. M., Duggins, A. & Friston, K. J. Encoding uncertainty in the hippocampus. *Neural*
619 *Networks* **19**, 535–546 (2006).
- 620 46. Hartigan, J. A. & Hartigan, P. M. The Dip Test of Unimodality. *Ann. Stat.* **13**, 70–84 (1985).
- 621 47. Parkkonen, L. in *MEG: An Introduction to Methods* (eds. Hansen, P., Kringelbach, M. &
622 Salmelin, R.) 24–64 (Oxford University Press., 2010).
- 623 48. Meng, X.-L., Rosenthal, R. & Rubin, D. B. Comparing correlated correlation coefficients.
624 *Psychol. Bull.* **111**, 172–175 (1992).
- 625 49. Passingham, R. E. & Wise, S. P. *The Neurobiology of the Prefrontal Cortex: Anatomy,*
626 *Evolution and the Origin of Insight.* (Oxford University Press, 2012).
- 627 50. Behrens, T. E. J., Woolrich, M. W., Walton, M. E. & Rushworth, M. F. S. Learning the value of
628 information in an uncertain world. *Nat. Neurosci.* **10**, 1214–21 (2007).
- 629 51. Rushworth, M. F. S., Kolling, N., Sallet, J. & Mars, R. B. Valuation and decision-making in
630 frontal cortex: one or many serial or parallel systems? *Curr. Opin. Neurobiol.* **22**, 946–55
631 (2012).
- 632 52. Brass, M. & Haggard, P. To do or not to do: the neural signature of self-control. *J. Neurosci.* **27**,
633 9141–5 (2007).
- 634 53. Zhang, J., Kriegeskorte, N., Carlin, J. D. & Rowe, J. B. Choosing the rules: distinct and
635 overlapping frontoparietal representations of task rules for perceptual decisions. *J. Neurosci.* **33**,

- 636 11852–62 (2013).
- 637 54. Glimcher, P. W., Camerer, C. F., Fehr, E. & Poldrack, R. A. *Neuroeconomics. Annu. Rev.*
638 *Psychol.* (Elsevier Inc., 2014).
- 639 55. Daw, N. D., O’Doherty, J. P., Dayan, P., Seymour, B. & Dolan, R. J. Cortical substrates for
640 exploratory decisions in humans. *Nature* **441**, 876–9 (2006).
- 641 56. Jocham, G. *et al.* Reward-Guided Learning with and without Causal Attribution. *Neuron* **90**,
642 177–190 (2016).
- 643 57. Cockburn, J., Collins, A. G. E. & Frank, M. J. A Reinforcement Learning Mechanism
644 Responsible for the Valuation of Free Choice. *Neuron* **83**, 551–557 (2014).
- 645 58. Fried, I., Mukamel, R. & Kreiman, G. Internally generated preactivation of single neurons in
646 human medial frontal cortex predicts volition. *Neuron* **69**, 548–62 (2011).
- 647 59. Bestmann, S. *et al.* Influence of Uncertainty and Surprise on Human Corticospinal Excitability
648 during Preparation for Action. *Curr. Biol.* **18**, 775–780 (2008).
- 649 60. Friston, K. J. A theory of cortical responses. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* **360**, 815–
650 36 (2005).
- 651 61. Wacongne, C., Changeux, J.-P. & Dehaene, S. A neuronal model of predictive coding
652 accounting for the mismatch negativity. *J. Neurosci.* **32**, 3665–78 (2012).
- 653 62. Näätänen, R. *et al.* The mismatch negativity (MMN)--a unique window to disturbed central
654 auditory processing in ageing and different clinical conditions. *Clin. Neurophysiol.* **123**, 424–58
655 (2012).
- 656 63. Akrami, A., Kopec, C. D., Diamond, M. E. & Brody, C. D. Posterior parietal cortex represents
657 sensory history and mediates its effects on behaviour. *Nature* **554**, 368–372 (2018).
- 658 64. Nobre, A. C., Coull, J. T., Frith, C. D. & Mesulam, M. M. Orbitofrontal cortex is activated
659 during breaches of expectation in tasks of visual attention. *Nat. Neurosci.* **2**, 11–12 (1999).
- 660 65. Nastase, S., Iacovella, V. & Hasson, U. Uncertainty in visual and auditory series is coded by
661 modality-general and modality-specific neural systems. *Hum. Brain Mapp.* **35**, 1111–1128
662 (2014).
- 663 66. Harrison, L. M., Bestmann, S., Rosa, M. J., Penny, W. D. & Green, G. G. R. Time scales of
664 representation in the human brain: weighing past information to predict future events. *Front.*

- 665 *Hum. Neurosci.* **5**, 37 (2011).
- 666 67. Churchland, A. K., Kiani, R. & Shadlen, M. N. Decision-making with multiple alternatives. *Nat.*
667 *Neurosci.* **11**, 693–702 (2008).
- 668 68. Levy, R. & Dubois, B. Apathy and the Functional Anatomy of the Prefrontal Cortex-Basal
669 Ganglia Circuits. *Cereb. Cortex* **16**, 916–928 (2005).
- 670 69. *Information sampling and adaptive cognition.* (Cambridge University Press, 2006).
- 671 70. Hsu, M., Bhatt, M., Adolphs, R., Tranel, D. & Camerer, C. F. Neural Systems Responding to
672 Degrees of Uncertainty in Human Decision-Making. *Science* (80-.). **310**, 1689–1683 (2005).
- 673 71. Hughes, L., Altena, E., Barker, R. A. & Rowe, J. B. Perseveration and Choice in Parkinson’s
674 Disease: The Impact of Progressive Frontostriatal Dysfunction on Action Decisions. *Cereb.*
675 *cortex* 1–10 (2012). doi:10.1093/cercor/bhs144
- 676 72. Kayser, A. S. & D’Esposito, M. Abstract rule learning: The differential effects of lesions in
677 frontal cortex. *Cereb. Cortex* **23**, 230–240 (2013).
- 678 73. Gleichgerrcht, E., Ibanez, A., Roca, M., Torralva, T. & Manes, F. Decision-making cognition in
679 neurodegenerative diseases. *Nat Rev Neurol* **6**, 611–623 (2010).
- 680 74. Cope, T. E. *et al.* Evidence for causal top-down frontal contributions to predictive processes in
681 speech perception. *Nat. Commun.*
- 682 75. Rowe, J. B. *et al.* The val158met COMT polymorphism’s effect on atrophy in healthy aging and
683 Parkinson’s disease. *Neurobiol. Aging* **31**, 1064–8 (2010).
- 684 76. Taulu, S., Simola, J. & Kajola, M. Applications of the signal space separation method. *Signal*
685 *Process. IEEE* **53**, 3359–3372 (2005).
- 686 77. Hauk, O. Keep it simple: a case for using classical minimum norm estimation in the analysis of
687 EEG and MEG data. *Neuroimage* **21**, 1612–1621 (2004).
- 688 78. Misaki, M., Kim, Y., Bandettini, P. A. & Kriegeskorte, N. Comparison of multivariate classifiers
689 and response normalizations for pattern-information fMRI. *Neuroimage* **53**, 103–118 (2010).
- 690 79. Smith, A. T., Kosillo, P. & Williams, A. L. The confounding effect of response amplitude on
691 MVPA performance measures. *Neuroimage* **56**, 525–530 (2011).
- 692

693 **Acknowledgments**

694 J.B.R and H.N.P. were supported by the James S. McDonnell Foundation 21st Century Science
695 Initiative, Scholar Award in Understanding Human Cognition. J.B.R. and L.E.H were
696 supported by Wellcome Trust [Senior Fellowship to JBR; 103838]. J.Z. was supported by the
697 Medical Research Council [MC-A060-5PQ30]. T.E.C was supported by The Patrick Berthoud
698 Charitable Trust and the Association of British Neurologists.

699 **Author contributions**

700 H.P. contributed acquisition, analysis and interpretation of the data and writing of this
701 manuscript. T.E.C. contributed analysis and interpretation of the data and writing of this
702 manuscript. L.E.H. contributed design of the paradigm and the acquisition of data. J.Z.
703 contributed analysis and interpretation of the data. J.B.R. contributed design of this study and
704 paradigm, interpretation of the data and writing of this manuscript.

705 We have no competing interests

706

707 **Figure Legends**

708 **Figure 1.** The four-choice action selection experiment design. a) An example trial sequence
709 with specified (one circle filled), choice (four circles filled) and null trials (no circles filled).
710 The image of the hand with unfilled circles remains on screen between trials for 1.5 seconds.
711 Each stimulus trial is presented for 1 second, with 2.5 second stimulus onset asynchrony. b)
712 The experimental stimuli used in the action selection task. Trials (a)-(d) are the specified trial
713 cues where the participant was cued to press the specified finger. Trial (e) is the choice trial
714 cue where the participant was cued to make an action with a finger of their choice. c) We show
715 an example of a trial window incrementally sliding over trial stimuli (a-e in B) to calculate the
716 entropy of stimuli or actions preceding the current trial. The trial entropy (TE) and selection
717 entropy (SE) values were assigned to the last trial within the window as the arrows show.
718 Figure adapted with permission from ¹¹.

719 **Figure 2.** Entropy measures. a) Trial entropy (TE, left) and selection entropy (SE, right) for a
720 single participant. The blue lines are entropy measures using the 25-trial sliding-window and
721 the red lines are the 50-trial entropy measures. b) Correlation of the different sliding windows
722 for TE (left) and SE (right), averaged across all participants. All correlations were significant
723 ($p < .003$, even with conservative Bonferroni correction, noting that the entropy measures are
724 not independent tests between sliding windows of different length). c) The mean Fisher
725 transformed correlations between TE and SE with standard error bars. Each correlation was
726 significant. d) A histogram showing frequency of TE-SE correlation across participants for the
727 25-trial window. Some individuals displayed a strong negative correlation between TE and SE,
728 while others demonstrated a weaker or no relationship.

729 **Figure 3.** Trial entropy correlations with MEG. a) The significant negative correlations
730 between TE and planar gradiometer data, averaged across all TE windows in sensor-time space
731 (voxel threshold: $p < .001$, $t > 3.17$ with FWE cluster thresholded at $p < .05$). The scalp plot shows

732 the sensor space clusters collapsed across time and the figure above shows the x plane of
733 sensor space against time. Note that all significant correlations were observed after the
734 response time at $t=0$ ms. b) The t-maps (left) show those scalp locations at which negative
735 correlations were above threshold at the peak time point of each cluster. **The location of peak**
736 **overall group response across the whole of scalp-time space is indicated by a red star.** We
737 visualised the location of the neural sources (right) within a 20ms time window around each of
738 these time-points ($p<.01$, $t>2.36$). At $t=172$ ms, source peaks were observed in the left inferior
739 frontal gyrus, and anterior middle frontal gyrus (Neuromorphometrics atlas). Similar peak
740 locations were observed for $t=656$ ms and $t=1356$ ms in left anterior middle frontal gyrus, right
741 superior temporal gyrus and left temporal pole. c) Clusters in sensor-time space with
742 significantly greater negative correlations for longer trial windows (thresholding as panel a). d)
743 The t-maps (left) show the scalp location of the significant differences between window
744 lengths at the peak time point for each cluster. For the $t=532$ ms peak, the sources were
745 localised to the left anterior middle frontal gyrus and bilateral superior temporal gyrus
746 (thresholding as panel b). For the $t=1112$ ms peak, the largest cluster was localised to the right
747 inferior temporal gyrus.

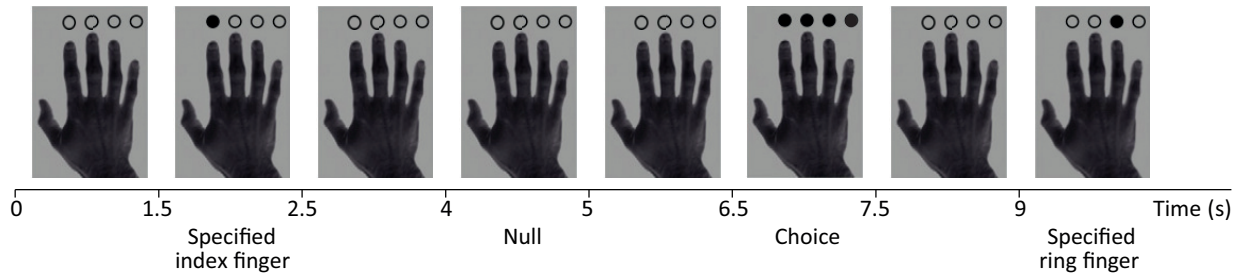
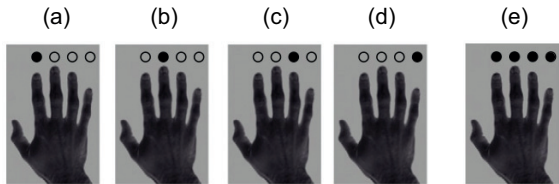
748 **Figure 4.** Selection entropy correlations with MEG. a) The significant negative correlations
749 between SE and planar gradiometer data, averaged across all SE windows in sensor-time space
750 (voxel threshold: $p<.001$, $t>3.17$ with 50 voxel cluster thresholding¹¹). Negative correlations
751 were observed both before and after the response at $t=0$ ms. B) The t-maps (left) show the scalp
752 location of the significant correlations at the peak time point of each cluster. We visualised the
753 location of the neural sources (right) within a 20ms time window around each of these time-
754 points ($p<.01$, $t>2.36$). At $t=-340$ ms, source peaks were observed in the right central operculum
755 and left inferior frontal gyrus. At $t=-16$ ms, source peaks were observed in right anterior middle
756 frontal gyrus, left bilateral anterior orbital gyrus and right superior temporal gyrus. At $t=376$ ms
757 source peaks were observed in the left anterior orbital gyrus, right frontopolar prefrontal

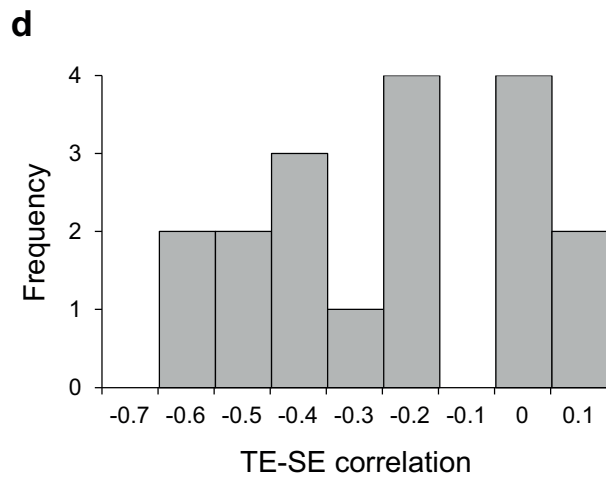
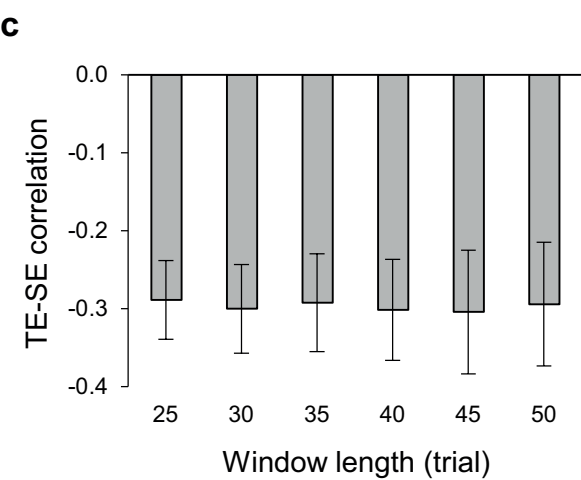
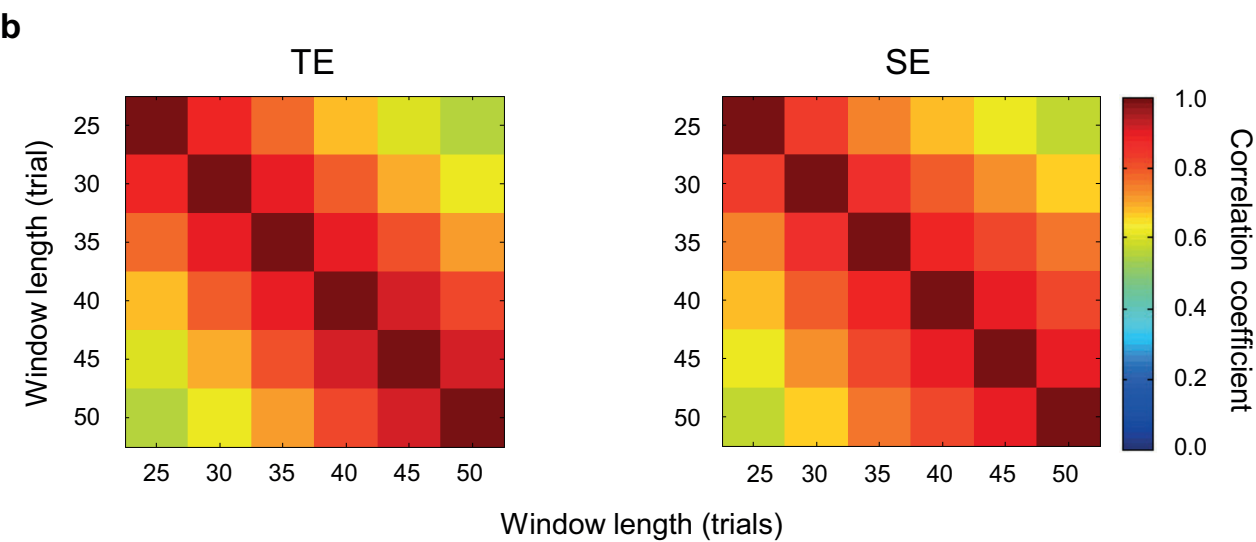
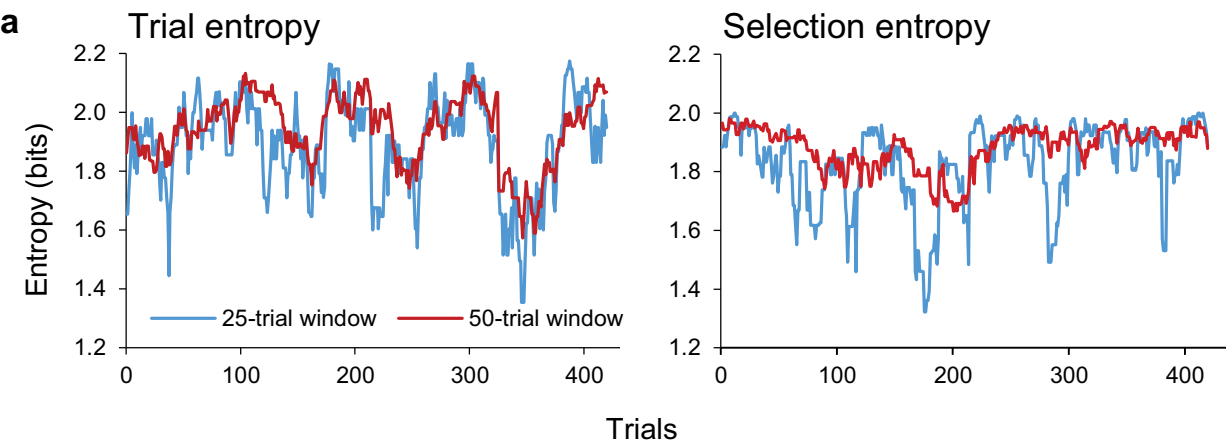
758 cortex, left inferior frontal gyrus and left temporal pole. c) Clusters in sensor-time space with
759 significantly greater negative correlations in the frontal pole for longer trial windows
760 (thresholding as panel a). d) The t-maps (right) show location of the significant differences
761 between window lengths at the peak time point of the significant cluster. This was localised
762 (right) to the left inferior frontal gyrus, left anterior orbital gyrus and right superior frontal
763 gyrus (thresholding as panel b).

764 **Figure 5.** The correlations between MEG peak t-scores for TE (a) and SE (b) and the TE-SE
765 correlations for individual participants. Best fit linear regression lines and their standard errors
766 are superimposed. There is a significant negative correlation for TE (Pearson's $r=-0.55$, $n=18$,
767 $p=.018$) but not for SE (Pearson's $r=0.22$, $n=18$, $p=.38$).

768

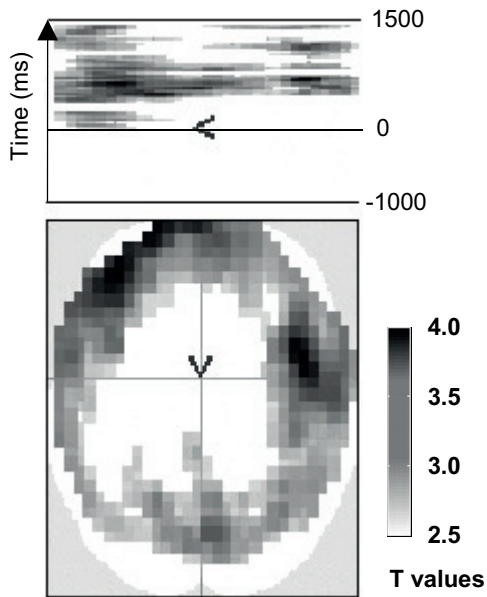
769

a**b****c**

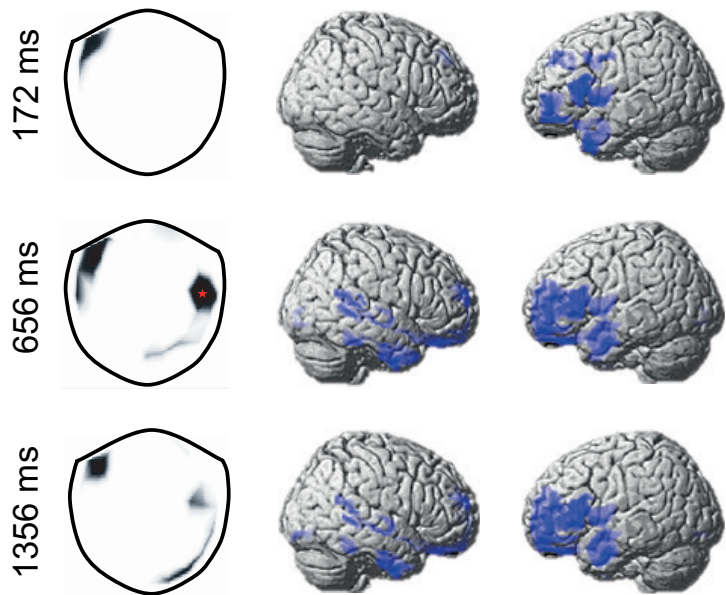


Trial entropy negative correlation

a

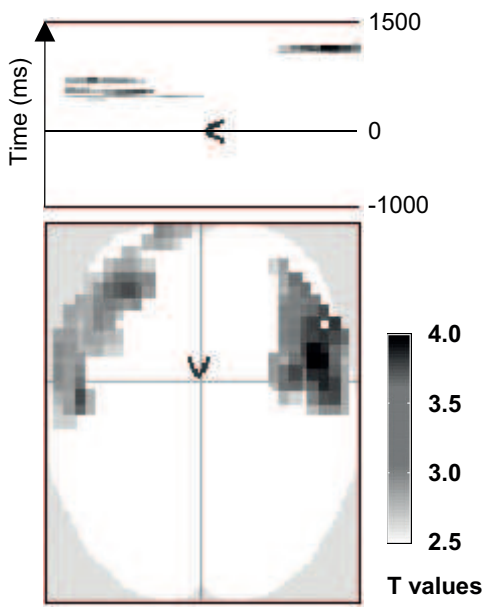


b

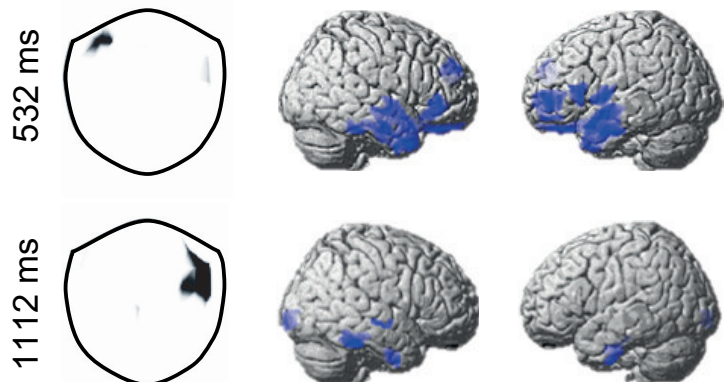


Long > short negative correlation

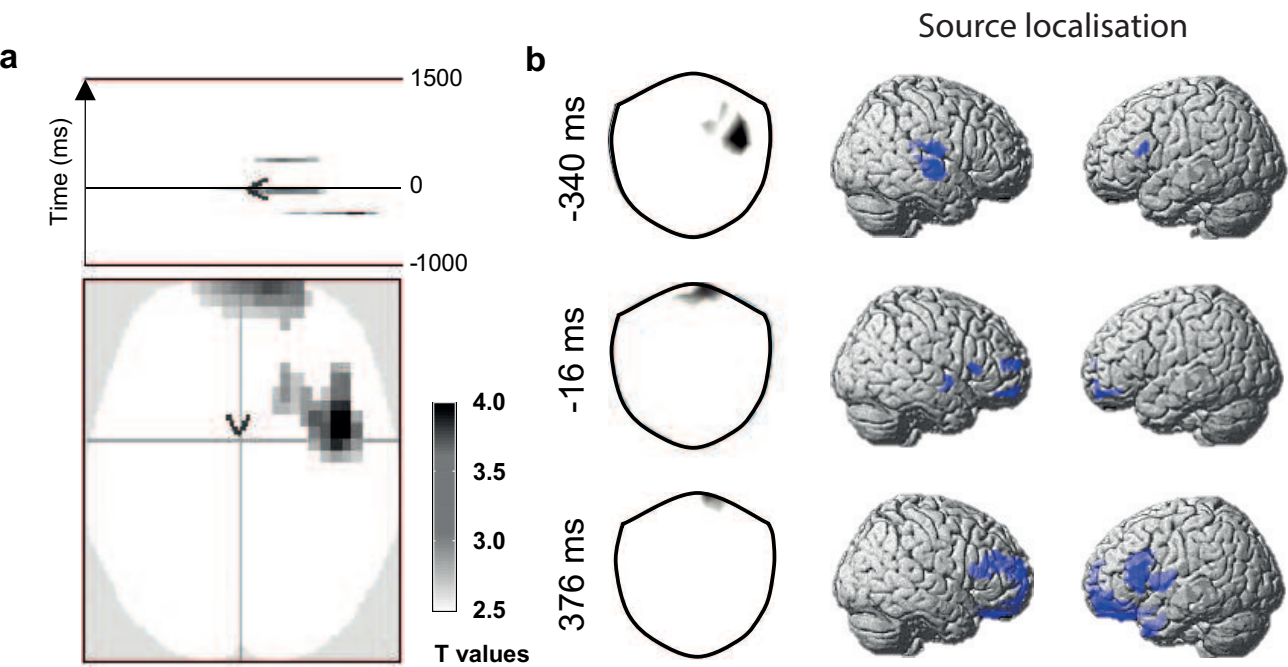
c



d



Selection entropy negative correlation



Long > short negative correlation

