1 Isolated from input: Evidence of default mode network support for perceptually-
2 decoupled and conceptually-guided cognition

3

4 Abbreviated Title – Insulated from input

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21 Abstract

22 The default mode network supports a variety of mental operations such as
23 semantic processing, episodic memory retrieval, mental time travel and mind-
24 wandering, yet the commonalities between these functions remains unclear. One
25 possibility is that this system supports cognition that is independent of the
26 immediate environment; alternatively or additionally, it might support higher-
27 order conceptual representations that draw together multiple features. We tested
28 these accounts using a novel paradigm that separately manipulated the
29 availability of perceptual information to guide decision-making and the
30 representational complexity of this information. Using task based imaging we
31 established regions that respond when cognition combines both stimulus
32 independence with multi-modal information. These included left and right
33 angular gyri and the left middle temporal gyrus. Although these sites were within
34 the default mode network, they showed a stronger response to demanding
35 memory judgements than to an easier perceptual task, contrary to the view that
36 they support automatic aspects of cognition. In a subsequent analysis, we showed
37 that these regions were located at the extreme end of a macroscale gradient, which
38 describes gradual transitions from sensorimotor to transmodal cortex. This shift
39 in the focus of neural activity towards transmodal, default mode, regions might
40 reflect a process of isolation from specific sensory inputs that enables
41 conceptually rich cognitive states to be generated in the absence of input.

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43 Key words: transmodal cortex, default mode network, semantic, conceptual
44 processing, stimulus independence.

45 Highlights

46 • Brain regions supporting meaning overlap with stimulus independence.

47 • Bilateral angular gyri and left MTG respond strongly to both features of
48   cognition.

49 • These patterns reflect a shift in activity towards regions of transmodal
50   cortex.

51 • Complex memory representations may emerge in cortical areas distant
52   from input.

1. Introduction

Although initial studies characterized the default mode network (DMN) as "task negative", this network actively supports aspects of cognition (Spreng, 2012), including semantic processing (Binder, Desai, Graves, & Conant, 2009; Krieger-Redwood et al., 2016), episodic recollection (Rugg & Vilberg, 2013), working memory (Konishi, McLaren, Engen, & Smallwood, 2015; Spreng et al., 2014; Vatansever, Menon, Manktelow, Sahakian, & Stamatakis, 2015), autobiographical planning (Spreng, Gerlach, Turner, & Schacter, 2015; Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010), self-generation of emotion (Engen, Kanske, & Singer, 2017) and imagining the future or the past (Schacter & Addis, 2007). Although we lack an over-arching account of the functions of the DMN, many of these situations involve memory retrieval – i.e., a requirement to focus cognition on previously-encoded knowledge, as opposed to information in the external environment. In line with this account, many regions within or allied to the DMN are considered to be heteromodal 'hubs' for memory-related processes, including the posterior cingulate cortex (Leech, Braga, & Sharp, 2012; Leech & Sharp, 2014), angular gyrus (Bonnici, Richter, Yazar, & Simons, 2016; Seghier, 2013), hippocampus (Moscovitch, Cabeza, Winocur, & Nadel, 2016) and anterior temporal lobes (Visser, Jefferies, & Lambon Ralph, 2010). In addition, cognitive states that activate the DMN tend to involve meaningful content that has personal relevance (Gusnard, Akbudak, Shulman, & Raichle, 2001).

The current study was motivated by the hypothesis that there might be common neurocognitive processes underpinning perceptually-decoupled and conceptually-guided cognition in the DMN. During states of episodic recollection, we recreate past experiences that involve places, objects and people not currently present in the environment. Consequently, memory retrieval might necessitate a process of decoupling from sensorimotor systems, allowing cognition to be generated internally in a way that diverges from what is going on around us (Smallwood, 2013). These perceptually-decoupled states might be easier in brain regions whose neural computations are functionally independent, or distant, from systems important for perceiving and acting. This is consistent with the observation that the distributed regions of the DMN are maximally distant from primary visual and motor cortex, both in terms of their distinct patterns of

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86   functional connectivity and their positions along the cortical surface (Margulies et
87   al., 2016).

88   In addition, DMN regions might support higher-order representations with
89   predictive value across multiple situations and modalities, which integrate
90   features from diverse sensorimotor regions. Contemporary accounts of semantic
91   representation (Lambon Ralph, Jefferies, Patterson, & Rogers, 2017) envisage an
92   interaction between unimodal brain regions that support knowledge about
93   specific features (e.g., knowledge that BANANAS are YELLOW and CURVED in visual
94   cortex) and heteromodal regions within or allied to the DMN, which extract deeper
95   similarity structures across these domains (i.e., allow us to understand that
96   BANANA and KIWI are conceptually related, despite salient differences in colour,
97   shape etc.). This view is also consistent with the observation that DMN lies at the
98   extreme end of a gradient from heteromodal to unimodal cortex (Margulies et al.,
99   2016), since increasingly abstract and complex representations might be formed
100   at greater distances along the gradient, where the influence of specific features
101   linked to stimuli in the immediate environment is reduced (Buckner & Krienen,
102   2013; Margulies et al., 2016; Mesulam, 1998). Within the DMN, angular gyrus
103   (Binder & Desai, 2011; Bonner et al., 2013) and anterior temporal cortex (Lambon
104   Ralph et al., 2017; Patterson et al., 2007) are both implicated in heteromodal
105   semantic processing. However, their roles remain controversial since other
106   regions such as left inferior frontal gyrus and posterior aspects of the temporal
107   lobe frequently show stronger task-induced activation in fMRI. Angular gyrus, in
108   particular, typically shows a pattern of task-induced deactivation, which is greater
109   for harder judgements in both semantic and non-semantic tasks (Humphreys et
110   al., 2015; Humphreys & Lambon Ralph, 2015). In addition, despite commonalities
111   in the intrinsic connectivity of these regions, differences in semantic content have
112   been proposed although not broadly accepted (Jackson, Hoffman, Pobric &
113   Lambon Ralph, 2016): the anterior temporal lobes might support object
114   identification, while angular gyrus is potentially more sensitive to thematic
115   associations (Davey et al., 2015; Schwartz et al., 2011).

116   We developed a novel paradigm to identify brain regions important for
117   stimulus independence, more complex memory representations and the
118   combination of both features in cognition. Our experiment builds on prior work

119   by Konishi and colleagues (Konishi et al., 2015). In their study, participants kept

120   track of the location of pairs of simple shapes (triangles, squares and circles)

121   presented either side of fixation. When probed with one shape from a prior trial

122   and asked which side of the screen it was presented on, activity increased in

123   regions including those within the DMN. The current study extended this

124   paradigm by varying the complexity of the information to be encoded and

125   retrieved. In one condition participants keep track of the location of pairs of

126   stimuli that vary on a single feature (colored patches), in a second they keep track

127   of stimuli that vary in a more complex manner (pairs of familiar real world objects

128   such as dogs or cars). Objects place greater demands on memory than do colours

129   because they are distinguished based on a greater number of features. This

130   allowed us to contrast higher and lower levels of representational complexity in

131   the perceptual representations and memories that would be probed. We also

132   manipulated whether these decisions were made when the relevant information

133   is on the screen (0 – back) or when only the identity of the target upon which the

134   decision is based is present (1 – back). In the latter case the relevant spatial

135   information must be retrieved from memory, a manipulation that allowed us to

136   explore the property of stimulus independence in cognition. This paradigm is

137   presented schematically in Figure 1.

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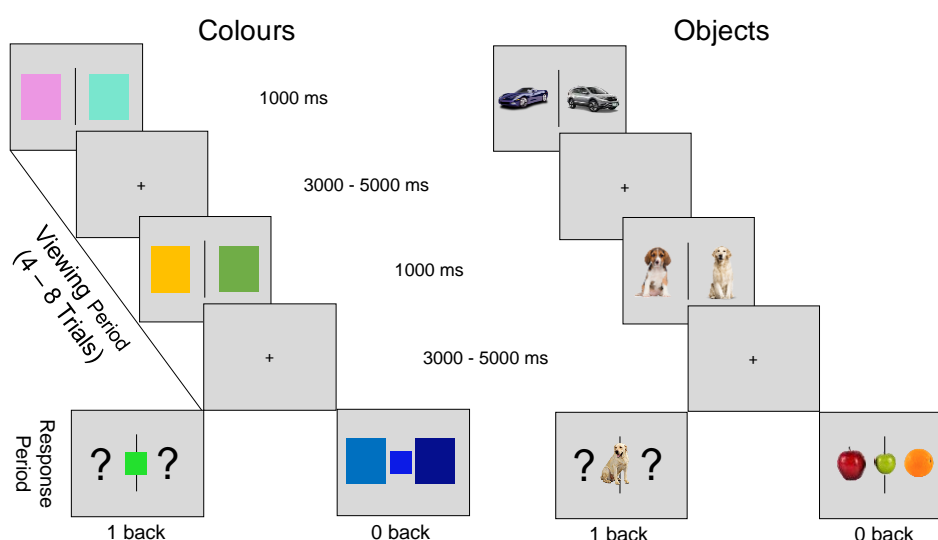
Figure 1. *Experimental design.* The four different judgments that participants
made in this experiment.

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142   We used this paradigm in a functional magnetic resonance imaging (fMRI)

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143   experiment to localize the brain regions that support the properties of stimulus

144   independence and representational complexity. Our aim was to establish whether

145   regions sensitive to perceptual decoupling and conceptual retrieval fall within the

146   DMN, and whether these effects were located in overlapping or distinct regions.

147   We identified regions of cortex that respond: (i) to stimuli with a rich multi-modal

148   structure by comparing the response of objects to colors, (ii) when decision

149   making has a higher reliance on memory by comparing decisions that are made in

150   the 1-back condition with those made in the 0-back conditions, and (iii) to

151   conditions that require a combination of both elements of cognition. We tested

152   these hypotheses using both standard whole brain univariate analyses, as well as

153   characterizing neural activity in each condition in terms of its position on the

154   macroscale gradient from unimodal to heteromodal cortex described by Margulies

155   et al. (2016).

156   If regions in the DMN are activated when spatial decisions are guided by

157   information from memory, this would support a role in stimulus independent

158   decision making. Alternatively, if DMN regions respond to decisions made

159   regarding objects rather than colours, this would reflect a role in the processing of

160   information with a high degree of representational complexity. Finally, if DMN

161   regions show the strongest response when spatial decisions are made based on

162   objects from memory, these regions would support more complex stimulus

163   independent representational states. This latter pattern would be consistent with

164   the hypothesis that decoupling from perceptual input enables cognition to

165   represent information that diverges from what is going on around us (Smallwood,

166   2013). Moreover, if this processing emerges in regions located towards the

167   transmodal end of the principle gradient, this would support the hypothesis that

168   the "distance" from systems important for perceiving and acting, provides a

169   cortical mechanism that underpins the processing of complex representations

170   derived from memory (Lambon Ralph et al., 2016; Margulies et al., 2016).

171

172   <u>2. Material and Methods</u>

173

174   2.1 Participants

175   Thirty right-handed native British-speaking participants with normal or

176   corrected-to-normal vision were recruited from the University of York (16 female;

177   mean age 22.68, range 18-34 years). One participant's data was excluded due to

178   excessive motion artefacts, leaving twenty-nine subjects in the final analysis for

179   (15 female; mean age 22.57, range 18-24 years). In a subsequent analysis we used

180   a set of 60 participants' resting state data, including the same individuals who

181   performed the task (34 female; mean age 20.32, range 18-29 years). Both studies

182   were approved by the York Neuroimaging Centre (YNIC) Ethics Committee.

183   Participant's provided informed consent prior to the start of the experimental

184   session.

185

186   2.2 Stimuli

187   The task paradigm had four conditions: (A) Object 0-back, (B) Object 1-

188   back, (C) Colour 0-back and (D) Colour 1-back using a block design. In all

189   conditions, pairs of items were presented separated by a central line. In the colour

190   conditions, these were different coloured squares, while in the object conditions,

191   these were familiar and meaningful objects, taken from the same semantic

192   category (i.e., different types of cars, fruit, dogs; see Figure 1). Items were

193   presented once with no repetition. The contrast between object and colour

194   conditions allowed us to investigate regions that are important for the retrieval of

195   conceptual information. The colour patches only varied on one feature (their

196   colour), while the objects were meaningful multi-featural concepts. In addition,

197   the contrast of 0-back and 1-back conditions allowed us to investigate the effect of

198   stimulus-independent processing (1 back > 0 back).

199

200   2.3 Procedure

201   In the scanner, participants completed a total of four functional runs

202   (average run time 8 min 32 s). Within each run, there were two blocks related to

203   each of the 4 conditions (Object 1-back; Object 0-back; Colour 1-back; Colour 0-

204   back). Each block began with written instructions stating the task type (0-back or

205   1-back). Blocks consisted of observing pairs of items (1000 ms); each pair was

206   separated by a jittered inter-stimulus interval (ISI; 3000-5000 ms) in which a

207   fixation cross was presented. At random intervals (4-8 trials), a third item was

208   presented in the centre of the screen and participants were asked to indicate the

8

209 location of one of the pair (left or right) that was most similar to this probe (see
210 Figure 1). This paradigm also required participants to match items that were
211 present and compared this with items in memory. In the 0-back catch-trials
212 participants had to decide which stimulus (left or right of the screen) was most
213 similar to this centrally-presented probe (i.e., all items were present on the
214 screen). In the 1-back catch-trials, participants had to decide which stimulus (left
215 or right of the screen) had been most similar to this centrally-presented probe on
216 the previous trial (i.e., the critical stimulus was absent). Blocks consisted of 5
217 probes in total and lasted on average 64 s.

218

219 2.4 MRI Acquisition

220 Data for both experiments were acquired using a GE 3 T HD Excite MRI
221 scanner at the YNIC. A Magnex head-dedicated gradient insert coil was used in
222 conjunction with a birdcage, radio-frequency insert coil tuned to 127.4 MHz. A
223 gradient-echo EPI sequence was used to collect data from 38 bottom-up axial
224 slices aligned with the temporal lobe (TR = 2s, TE = 18ms, FOV = 192x192mm,
225 matrix size = 64x64, slice thickness = 3mm, slice-gap = 1mm, flip-angle = 90°).
226 Voxel size was 3x3x3mm. Functional images were co-registered onto a T1-
227 weighted anatomical image from each participant (TR = 7.8s, TE = 3ms, FOV =
228 290x290mm, matrix size = 256x256mm, voxel size = 1.13x1.13x1mm) using
229 linear registration.

230

231 2.5 Pre-processing

232 All imaging data were pre-processed using a standard pipeline and
233 analysed via FMRIB Software Library (FSL Version 6.0). Images were skull-
234 stripped using a brain extraction tool [BET, (Smith, 2002)]. The first five volumes
235 (10s) of each scan were removed to minimize the effects of magnetic saturation,
236 and slice-timing correction with Fourier space time-series phase-shifting was
237 applied. Motion correction (MCFLIRT, (Jenkinson, Bannister, Brady, & Smith,
238 2002)) was followed by temporal high-pass filtering (cut-off = 0.01Hz). Individual
239 participant data was registered to their high-resolution T1-anatomical image, and

240   then into a standard spare (Montreal Neurological Institute); this process included

241   tri-linear interpolation of voxel sizes to 2x2x2 mm.

242   The resting state functional data used were pre-processed and analysed

243   using the FMRI Expert Analysis Tool (FEAT). The individual subject analysis

244   involved: motion correction using MCFLIRT; slice-timing correction using Fourier

245   space time-series phase-shifting; spatial smoothing using a Gaussian kernel of

246   FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a

247   single multiplicative factor; high-pass temporal filtering (Gaussian-weighted

248   least-squares straight line fitting, with sigma = 100 s); Gaussian low-pass temporal

249   filtering, with sigma = 2.8s

250

251   2.6 Task based fMRI

252   For our task-based analysis, the time points of interest were the probe

253   trials where participants had to make a decision about something present (0-

254   back) or absent (1-back) from the screen. We therefore used a box-car regressor

255   to model the probe trial for each condition and another one to model the entire

256   block. Modelling the entire block ensured any effect detected from our analysis

257   can be attributed to the probe itself and not the general effect of the block. Box-car

258   regressors for each probe/block, for each condition, for each run, were convolved

259   with a double gamma hemodynamic response function. Regressors of no interest

260   were included to account for head motion. We computed four contrasts: (1) 0-back

261   > 1-back, (2) 1-back > 0-back, (3) Object > Colour and (4) Colour > Object. A fixed

262   effect design (FLAME, http://www.fmrib.ox.ac.uk/fsl) was conducted to average

263   the four runs, within each individual. Individual participant data were then

264   entered into a higher-level group analysis using a mixed effects design (FLAME,

265   http://www.fmrib.ox.ac.uk/fsl) whole-brain analysis. Finally, our analysis

266   focused on a conjunction of 1-back > 0-back and Object > Colour to identify regions

267   engaged in both stimulus independent processing and conceptually abstract

268   representations.

269

270   2.7 Resting-state fMRI

271   We extracted the time series from regions identified by univariate analysis

272   and used these as explanatory variables in a connectivity analyses at the single

10

273 subject level. In each analysis, we entered 11 nuisance regressors; the top five

274 principal components extracted from white matter (WM) and cerebrospinal fluid

275 (CSF) masks based on the CompCor method (Behzadi, Restom, Liau, & Liu, 2007),

276 six head motion parameters and spatial smoothing (Gaussian) was applied at

277 6mm (FWHM). WM and CSF masks were generated from each individual's

278 structural image (Zhang, Brady, & Smith, 2001). No global signal regression was

279 performed, following the method implemented in Murphy, Birn, Handwerker,

280 Jones, & Bandettini (2009).

281 All whole brain analyses were cluster corrected using a z-statistic

282 threshold of 3.1 to define contiguous clusters. Multiple comparisons were

283 controlled using Gaussian Random Field Theory at a threshold of $p < .05$ [34]. All

284 statistical maps produced in these analyses are freely available at Neurosynth at

285 the following URL: http://neurovault.org/collections/2296/.

286

287 <u>3. Results</u>

288 Table 1 presents behavioural performance, in the form of response

289 efficiency (RT/ACC), for each of the four conditions of our task. Response

290 efficiency controls for speed-accuracy trade-offs. These data were compared using

291 a 2 (task; 0-back vs. 1-back) by 2 (condition; object vs. colour) repeated-measures

292 analysis of variance (ANOVA). There was no significant differences between

293 stimulus type ($F(1,28) = 2.55$, $p = .116$) but a significant main effect of task

294 ($F(1,28) = 15.38$, $p < .001$). There was no significant interaction ($p > .05$). These

295 analyses demonstrate that performance on the 1-back task was less efficient than

296 for the 0-back task but that object and colour conditions were well matched in

297 terms of overall task difficulty.

298   Table 1. Behavioural results.

Condition	Response Efficiency	
	Mean	**SE**
Colour 1-back	1028	206
Colour 0-back	829	287
Object 1-back	1041	229
Object 0-back	841	295

299   Footnote: SE = standard error. Response efficiency = reaction time in milliseconds / percent
300   accuracy.

301   We next generated statistical maps describing patterns of neural activity at
302   the moments when participants responded in each of our four conditions. These
303   maps were compared at the group level using a GLM (see Methods). The contrast
304   of 0-back > 1-back decisions captures perceptually-guided decision-making,
305   revealing increased activity in the bilateral ventral visual stream, from occipital
306   pole through to posterior fusiform cortex (presented in cool colours in the upper
307   panel of Figure 2). These regions have a well-documented role in online visual
308   processing. The contrast of 1-back > 0-back reflects stimulus independence in
309   decision-making. This comparison revealed greater activation in bilateral angular
310   gyrus and anterior temporal lobes, as well as medial structures in the posterior
311   cingulate cortex and medial prefrontal cortex (these are presented in warm
312   colours in the middle panel of Figure 2). Many of these regions fall within the DMN
313   (58.44% of voxels fell within the DMN as defined by Yeo et al., 2011) and are
314   spatially similar to the 'general recollection network' proposed by Rugg and
315   Vilburg (2013). The comparison of Objects > Colours identifies brain areas that
316   support the processing of multi-featural conceptual representations. These are
317   presented in warm colours in the lower panel in Figure 2. This contrast revealed
318   a similar set of regions to the stimulus independence contrast (medial pre frontal
319   cortex, left and right angular gyrus and anterior temporal lobe) with the addition
320   of the right dorsolateral cortex (52.49 % of voxels fell within the DMN as defined
321   by Yeo et al., 2011). The contrast of Colours > Objects yielded no significant whole-
322   brain corrected results. To allow comparison with previous research, the spatial
323   maps for the contrast of 1-back > 0-back from Konishi and colleagues are also

324   displayed: similarities can be seen in posterior cingulate cortex, medial prefrontal

325   cortex, right angular gyrus and dorsolateral cortex.
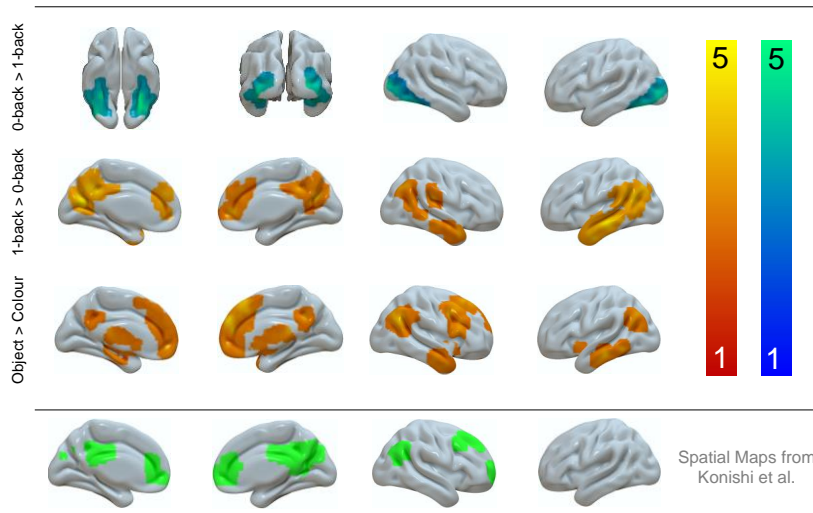
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327   **Figure 2.** *Neural activity produced when making decisions based on meaningful*

328   *objects and when decisions are made from memory.* (a) Activity elicited when

329   decisions were made based using information from perception (b) Activity when

330   decisions were made on the basis of information from memory and (c) when

331   information from memory was more complex. Spatial maps were cluster

332   corrected at Z = 3.1 FWE.

333

334   Our next analysis formally identifies regions that show a response to both

335   stimulus independence and memory complexity. Figure 3 shows the results of a

336   formal conjunction of the contrasts of Object > Colour and 1-back > 0-back,

337   revealing three regions – bilateral angular gyrus and lateral medial temporal gyrus

338   in the left hemisphere. The left hand panel of Figure 3 summarizes the parameter

339   estimates from each of these regions in each condition of our task. In every case

340   the strongest response was when decisions were made in the Object 1-back

341   condition. Importantly, although these regions fell within the DMN (88.07% of

342   voxels within the conjunction mask fell within the DMN as defined by Yeo et al.,

343   2011), their response profile indicated greater responding during a demanding

13

344   condition (i.e. Object 1-back) ruling out a task-negative interpretation of these
345   results.

Object > Colour ∧ 1 Back > 0 Back   □ 0 Back   ■ 1 Back   C – Colour; O - Object
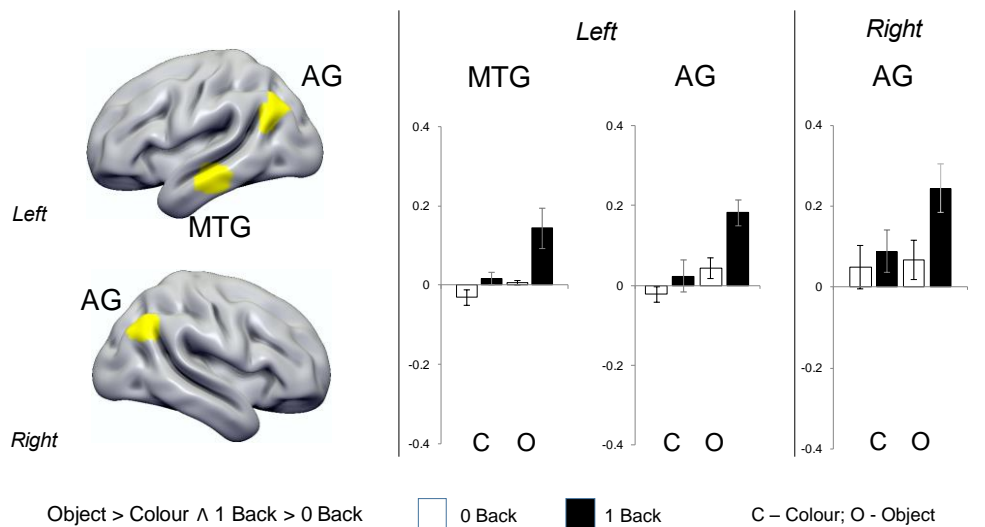
346

347   **Figure 3.** *Locating peak activity during stimulus independent decisions regarding*
348   *complex objects.* (a) A conjunction of the neural activity when making decisions
349   based on meaningful categories and when decisions are made in the absence of
350   perceptual input revealed three regions: bilateral angular gyrus and in the left
351   middle temporal gyrus. (b) Percent signal extracted from these regions confirmed
352   an additive effect (i.e. these regions responded significantly more to the object
353   condition when information was not present on the screen compared to all other
354   conditions). The conjunction analysis was based on whole-brain cluster corrected
355   spatial maps from Figure 2. Error bars indicated 95% confidence intervals.

356

357   We also explored the intrinsic architecture of conjunction regions
358   responding to Object > Colour and 1-back > 0-back in an independent resting-state
359   data set (see Methods). The results of this analysis are presented in Figure 4 and
360   reveal coupling beyond the seed regions to the posterior cingulate cortex,
361   dorsolateral prefrontal cortex and pre-supplementary motor area bilaterally.
362   Some of these regions fall outside the DMN, as defined by Yeo and colleagues, and

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363 instead are members of the frontoparietal network linked with cognitive control

364 (Yeo et al., 2011).

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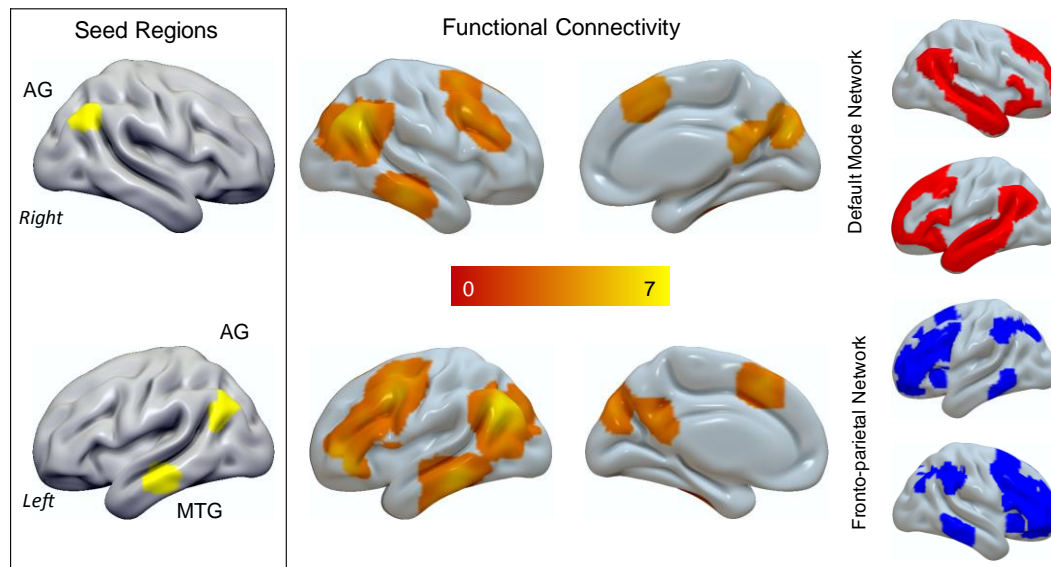
366

367 **Figure 4.** *Peak areas during stimulus independent decision regarding*

368 *complex stimuli involve both regions of the default mode network (DMN) and the*

369 *fronto-parietal network (FPN).* These regions show functional connectivity at rest

370 with both the pre-supplementary cortex and the dorsolateral pre-frontal cortex.

371 Although the regions identified in our conjunction analysis fall within the DMN

372 they show functional communication with regions in the FPN, including the right

373 dorsolateral prefrontal cortex. The spatial networks in the grey panel are from the

374 decomposition of Yeo and colleagues. The conjunction analysis was based on

375 whole-brain cluster corrected spatial maps from Figure 1. For the connectivity

376 analyses spatial maps were cluster corrected at Z = 3.1 FWE.

377

378 We also conducted a supplementary analysis contrasting Object and Colour

379 decisions separately in the 1-back and 0-back conditions to confirm regions

380 important for stimulus-independent decisions (see Supplementary Figure 1). This

381 analysis showed that 1-back trials involving meaningful objects activated regions

382 including angular gyrus, middle temporal gyrus and right dorsolateral prefrontal

383 regions more than colours. In contrast, the comparison of Objects > Colours in the
384 0-back condition only revealed greater activity in fusiform cortex.

385

386 Together these analyses highlight a network of regions that are important
387 when spatial decisions are made in the absence of external sensory support, and
388 when they involve multi-feature concepts (Figure 5). Common regions responding
389 to the two task contrasts (1-back > 0-back; Object > Colour), include angular gyrus
390 and middle temporal gyrus. In the right hemisphere, two of the three maps also
391 include the right dorsolateral cortex. All of these right hemisphere regions
392 responded to a similar 1-back > 0-back contrast involving abstract shapes (circle,
393 triangle, square) in the study by Konishi and colleagues (2015).

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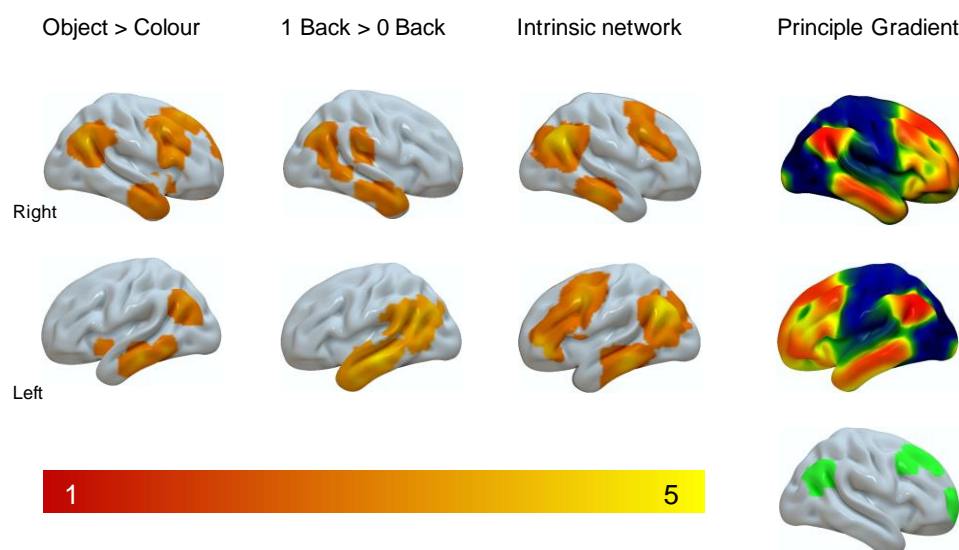
395
396 **Figure 5.** *Regions linked to during stimulus independent decisions regarding*
397 *complex stimuli form localized clusters in transmodal cortex.* Regions in the main
398 panel reflect data generated in this experiment. The grey sub panel presents the
399 spatial distribution of the principle gradient from Margulies and colleagues (2016)
400 coloured blue-red, and the cluster corrected map from Konishi and colleagues
401 (2015) coloured green.

402

403 In Figure 5, we summarise the spatial maps produced by this experiment
404 and present these alongside the principal gradient from Margulies and colleagues
405 (2016), which describes a functional spectrum of intrinsic connectivity across the
406 cortical surface, extending from primary sensorimotor systems to regions of the

407   DMN at the other extreme. More similar colours on this gradient reflect greater

408   similarity in connectivity. It can be seen that common regions implicated in

409   stimulus-independent and conceptual processing are all localized towards the

410   transmodal end of the principal gradient.

411

412   Our final analysis characterizes the similarity between the neural patterns

413   captured by our task and the spatial distribution of the principle gradient from

414   Margulies et al., (2016) in a more formal manner. Following Margulies et al., we

415   divided the principle gradient into 20 equally sized bins. Next for each participant

416   we calculated the average signal in each bin for each condition of our task. The left

417   hand panel in Figure 6 presents these data plotted across the principle gradient

418   separately for each condition; the shaded bars represent the 95% confidence

419   intervals. It can be see that the conditions are most distinct towards the

420   transmodal end, with the highest values when participants made judgments about

421   objects from memory. To quantify these patterns, we compared their distribution

422   using a 2 (stimulus independence) X (stimulus complexity) X 20 (Gradient Bin)

423   ANOVA. This revealed a significant 3-way interaction [$F_{(19, 532)} = 5.136$, $p <$

424   .001]. To follow up this interaction, we performed a principle components analysis

425   (PCA) on the condition level data, describing the dynamics captured in the left

426   hand panel of Figure 6. The results revealed two components with eigenvalues

427   greater than 1 accounting for over 86% of the variance (component 1 = 70.49%;

428   component 2 = 15.73%) across the principal gradient bins. The first two

429   components are presented in the right hand panel of Figure 6. The second

430   component describes a gradual transition showing increasing levels of BOLD

431   activity from the unimodal end of the gradient towards the transmodal end.

432   Projecting the values from component 2 back onto the task conditions, and

433   averaging them at the group-level, revealed that this pattern of variance loaded

434   almost exclusively on the 'object' 1-back condition. There was a significant

17

435 positive fit between the spatial map of the principle gradient and recruitment in

436 the Object 1-Back task, but not other conditions.

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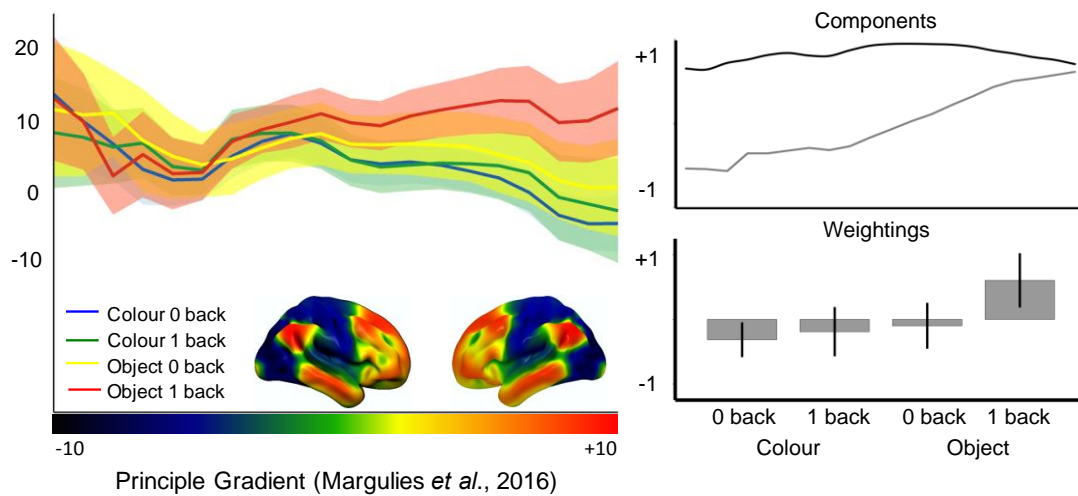
Figure 6. *Stimulus independent decisions regarding meaningful objects leads to a whole-brain shift towards the transmodal-end of the gradient.* (a) A regions-of-interest analysis using bins of the principal gradient revealed that the decisions that are made on objects rather than colours when these stimuli are not available to perception led to higher activity towards the transmodal-end of the principal gradient. (b) Decomposition using PCA revealed that this difference was related to a gradual shift in the locus of neural activity away from regions on the principal gradient related to perception and action and towards transmodal regions of cortex. Error bars indicated 95% confidence interval.

448

449 4. Discussion

450 Our experiment contrasted judgments when stimuli to be decided upon

451 were present in the current trial (stimulus-dependent 0-back decisions) with

452 identical decisions where the information was from the previous trial (stimulus-

453 independent 1-back decisions, see Figure 1). We also varied whether decisions

454 were made on uni-dimensional stimuli (colour patches) or more complex multi-

455 dimensional stimuli (objects in conceptual categories). In each task, the items to

456 be matched were not perceptually identical: participants selected the closest hue

457 or the closest concept from similar distractors. This allowed us to identify regions

458 that capture cognitive processes important for representing (i) information that

459   is decoupled from stimulus input, (ii) representations that are complex and multi-
460   dimensional in nature and (iii) a combination of both.

461   Using conventional whole brain analyses we identified overlapping regions
462   in the DMN that are sensitive to both perceptual decoupling (i.e., the requirement
463   to make decisions based on memory, as opposed to the immediate environment)
464   and when these decisions regarded more complex conceptual categories of stimuli
465   (i.e., decisions based on objects rather than colours). We also used a novel analytic
466   approach to demonstrate that these isolated clusters of activity can be seen as part
467   of a whole brain shift in the locus of neural activity towards the extreme end of a
468   gradient from unimodal to heteromodal cortex (Margulies et al., 2016). These
469   findings have broad implications for the role of DMN in cognition, and also
470   contribute to our understanding of specific DMN regions, particularly angular
471   gyrus and lateral temporal lobe. We first consider the results in terms of their
472   implications for functional accounts of these regions. Secondly, we consider the
473   macroscale organisation of the cortex, focusing on approaches which can explain
474   the functional similarity of these distributed clusters and their relative position on
475   the cortical surface.

476   <u>Functional implications for the angular gyri</u>: There were stronger
477   responses in left and right angular gyri, as well as in left middle temporal gyrus,
478   when conceptual decisions were based on information that was no longer present
479   in the environment. These findings are inconsistent with several existing accounts
480   of the contribution of angular gyrus to memory and semantic cognition. First, they
481   do not easily align with the proposal that specific aspects of meaning are
482   represented in angular gyrus – namely thematic associations, but not item identity
483   (Davey et al., 2015; Schwartz et al., 2011). Our conceptual task involved matching
484   items on the basis of their identity, yet it robustly activated this region. Secondly,
485   the findings are at odds with the proposal that the angular gyri only activate
486   during contrasts of easier versus harder tasks, and for "automatic" and not
487   "controlled" patterns of retrieval (Humphreys et al., 2015; Humphreys & Lambon
488   Ralph, 2017). The 1-back condition was harder than the 0-back condition and still
489   elicited a greater response.

490   Instead, our findings are consistent with suggestions that the role of the
491   angular gyri role is to allocate attention to complex memory representations. The

492   angular gyri show a stronger response to a range of memory retrieval situations

493   in which the retrieved representations are detailed, specific or precise (Binder et

494   al., 2005; Price, et al., 2015; Bonnici et al., 2016; Davey at al., 2015). In our study,

495   the 1-back trials required attention to switch from an encoding mode, to a

496   retrieval mode when task relevant information is represented internally. This

497   pattern of responding in the angular gyrus is consistent with the purported role of

498   inferior parietal cortex in focusing attention on memory (Cabeza et al., 2011). In

499   our study, the angular gyri did not activate to the same extent when stimuli were

500   matched on colour, suggesting this region is especially important when

501   heteromodal representations from long-term memory are retrieved.

502   Functional implications for temporal cortex: Angular gyrus shows strong

503   intrinsic connectivity with ventral anterior temporal cortex (Davey et al., 2016;

504   Jackson et al., 2016), which is proposed to support the integration of multiple

505   features and modalities to capture 'deep' conceptual similarities between items

506   with diverse 'surface' features (e.g., items such as PINEAPPLE and KIWI that have

507   different colours, sizes, shapes, phonology etc.; for a review see Lambon (Ralph et

508   al., 2017). Semantic dementia patients with atrophy focussed on this region show

509   highly consistent degradation of conceptual knowledge across tasks (Bozeat et al.,

510   2000; Jefferies & Lambon Ralph, 2006), while neuroimaging studies of healthy

511   participants localise the response during heteromodal conceptual processing to

512   ventral anterior temporal lobes and anterior middle temporal gyrus (Murphy et

513   al., 2017; Visser et al., 2011). Word meaning can be decoded within anterior

514   middle and inferior temporal gyri, while patterns of activation in superior

515   temporal gyrus instead reflect the presentation format (Murphy et al., 2017).

516   The ventral anterior temporal lobes are thought to provide a "graded hub"

517   in which different unimodal features are gradually integrated to form

518   heteromodal concepts, with visual information reaching this region along the

519   ventral visual pathway (fusiform cortex), auditory and motor information arriving

520   from superior temporal gyrus and frontal cortex, and social/emotional

521   information merging from the temporal pole (Lambon Ralph et al., 2017).

522   Nevertheless, the peak response in the anterior temporal lobes in the current

523   study was in lateral MTG, and not in the site of the putative hub in ventral anterior

524   temporal cortex (Murphy et al., 2017). Visser et al. (2012) observed evidence

20

525 compatible with two gradients of information convergence in the temporal lobes:
526 first, there is a posterior-to-anterior axis: posterior temporal lobe regions
527 proximal to visual and auditory cortex show largely unimodal responses, while
528 more anterior regions integrate across these types of input to support
529 heteromodal conceptual processing. Secondly, there may be integration from
530 superior and inferior regions, implicated in auditory and visual processing
531 respectively: towards middle temporal gyrus response become more heteromodal
532 response along the length of the temporal cortex. The site we observed in the
533 conjunction of semantic and perceptually-decoupled decisions in the current
534 study corresponds to the extreme heteromodal end of *both* of these temporal lobe
535 gradients.

536   Implications for the default mode network: We replicated prior
537 demonstrations that transmodal regions in the DMN are engaged when
538 participants make decisions that rely on information from memory rather than
539 input from perception, even though the 1-back task was more difficult than the 0-
540 back task (Konishi et al., 2015). This pattern of task-positive behaviour adds to a
541 growing body of evidence that the DMN contributes in an active manner to
542 demanding external cognitive tasks (Konishi et al., 2015; Krieger-Redwood et al.,
543 2016; Spreng et al., 2014; Spreng et al., 2015; Spreng et al., 2010; Vatansever et al.,
544 2015). The contribution of DMN to controlled cognitive states appears to reflect
545 situations in which DMN regions work in tandem with the frontoparietal network.
546 Prior work has established the combination of these networks is important for
547 tasks including controlled semantic retrieval (Krieger-Redwood et al., 2016),
548 working memory (Vatansever et al., 2015), autobiographical planning (Spreng et
549 al., 2014; Spreng et al., 2015), retrieving memories of close personal friends (de
550 Caso et al., 2017) and the control of spontaneous thoughts in a deliberate manner
551 (Golchert et al., 2017). Our study shows that right angular gyrus, within the DMN,
552 and right dorsolateral prefrontal cortex, a member of the frontoparietal network,
553 activate together when participants make judgments about meaningful objects
554 from memory rather than colours (see Supplementary Figure 1). Our functional
555 connectivity analysis also demonstrates that these regions are correlated at rest,
556 suggesting they form an intrinsic network. The right dorsolateral cluster
557 replicates the spatial distribution observed from the prior study by Konishi et al.

558 (Konishi et al., 2015) and overlaps with a region of greater grey matter associated

559 with more deliberate mind-wandering (Golchert et al., 2017). Both 1-back

560 retrieval in our paradigm, and more deliberate spontaneous thought, require

561 memory retrieval to be shaped in a goal-directed fashion. It is possible that a range

562 of states requiring the goal-directed control of memory depend on co-operation

563 between these two large-scale networks.

564   At the most general level our study supports the hypothesis that the

565 capacity for complex memory representations to influence cognition emerges

566 from the topographical arrangement of neural processes across the cortex. Prior

567 work highlighted regions of transmodal cortex, such as the default mode network,

568 as having the greatest distance from uni-modal sensorimotor cortex in both

569 functional and structural space (Margulies et al., 2016). Our finding builds on this

570 observation by showing an association between ongoing neural activity and this

571 dimension of connectivity under situations when the demands placed on cognition

572 require a combination of memory complexity and stimulus independency. Using

573 both standard and novel methods of analysis, we demonstrated that the neural

574 activity associated with this type of activity is prevalent in transmodal regions

575 (Figure 5) and can be represented as a whole brain shift in the balance of neural

576 activity, away from sensorimotor regions cortex and towards the transmodal end

577 of the gradient (Figure 6). This topographical shift in the distribution of neural

578 processing is consistent with theoretical accounts that assume that more abstract

579 cortical functions are facilitated through functional isolation from incoming input

580 (Buckner & Krienen, 2013; Margulies et al., 2016; Mesulam, 1998; Smallwood,

581 2013). Consistent with this interpretation of DMN function, a recent study found

582 that strong connectivity within the DMN (including an overlapping region of left

583 temporal cortex) was linked to poor performance on tasks which depend on

584 encoding information from the environment but not for those that depended on

585 retrieving information from memory (Poerio et al., 2017). The findings of Poerio

586 and colleagues, in combination with those from the current study, provide

587 converging evidence that regions of the DMN support a state where cognition is

588 guided by memory rather than input, regardless of whether it is beneficial to the

589 task or not.

590　　　　There are a number of limitations that should be borne in mind when
591　considering the results of this study. First, our comparison of semantic and colour
592　decisions allowed us to demonstrate a neural pattern associating conceptual
593　processing with stimulus independency. This comparison is too crude a
594　manipulation to determine which aspects of the semantic judgements gave rise to
595　this response in the DMN; for example, is it the richness of concepts such as
596　Labrador or apple, their heteromodal nature or the fact that they are acquired over
597　a lifetime, which dissociates them from colours? Future studies could probe
598　different features of retrieval, such as whether the target is a concrete or abstract
599　concept, whether it has to be identified at a specific or superordinate level, and
600　whether there are differences according to the modality of the representation
601　being probed. Second, the nature of our design precludes the ability to separate
602　different aspects of memory retrieval engaged during 1-back decisions. In our
603　paradigm, these decisions require both the integration of appropriate information
604　from memory, as well as the inhibition of the memory representation for the non-
605　probed item. Interestingly, studies have implicated dorsolateral prefrontal cortex
606　in the suppression of memories (Anderson et al., 2004) whereas the angular gyrus
607　has been linked to the integration of appropriate semantic features (Wagner et al.,
608　2015) and the retrieval of specific information (Davey et al., 2015). It is possible
609　that the angular gyrus and dorsolateral prefrontal region are performing distinct
610　roles in integration of relevant associations and suppression of irrelevant
611　information during retrieval in our paradigm. Future work could address this
612　question by manipulating the level of featural overlap between target and probe
613　during retrieval in a similar paradigm as in this experiment.
614

620 **References**

621 Anderson, M. C., Ochsner, K. N., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S. W., . .
622 . Gabrieli, J. D. (2004). Neural systems underlying the suppression of
623 unwanted memories. *Science, 303*(5655), 232-235.
624 doi:10.1126/science.1089504
625 Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise
626 correction method (CompCor) for BOLD and perfusion based fMRI.
627 *Neuroimage, 37*(1), 90-101. doi:10.1016/j.neuroimage.2007.04.042
628 Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the
629 semantic system? A critical review and meta-analysis of 120 functional
630 neuroimaging studies. *Cereb Cortex, 19*(12), 2767-2796.
631 doi:10.1093/cercor/bhp055
632 Bonnici, H. M., Richter, F. R., Yazar, Y., & Simons, J. S. (2016). Multimodal Feature
633 Integration in the Angular Gyrus during Episodic and Semantic Retrieval. *J
634 Neurosci, 36*(20), 5462-5471. doi:10.1523/JNEUROSCI.4310-15.2016
635 Buckner, R. L., & Krienen, F. M. (2013). The evolution of distributed association
636 networks in the human brain. *Trends Cogn Sci, 17*(12), 648-665.
637 doi:10.1016/j.tics.2013.09.017
638 Cabeza, R., Mazuz, Y. S., Stokes, J., Kragel, J. E., Woldorff, M. G., Ciaramelli, E., . . .
639 Moscovitch, M. (2011). Overlapping parietal activity in memory and
640 perception: evidence for the attention to memory model. *J Cogn Neurosci,
641 23*(11), 3209-3217. doi:10.1162/jocn_a_00065
642 Davey, J., Cornelissen, P. L., Thompson, H. E., Sonkusare, S., Hallam, G., Smallwood,
643 J., & Jefferies, E. (2015). Automatic and Controlled Semantic Retrieval: TMS
644 Reveals Distinct Contributions of Posterior Middle Temporal Gyrus and
645 Angular Gyrus. *J Neurosci, 35*(46), 15230-15239.
646 doi:10.1523/JNEUROSCI.4705-14.2015
647 de Caso, I., Karapanagiotidis, T., Aggius-Vella, E., Konishi, M., Margulies, D. S.,
648 Jefferies, E., & Smallwood, J. (2017). Knowing me, knowing you: Resting-
649 state functional connectivity of ventromedial prefrontal cortex dissociates
650 memory related to self from a familiar other. *Brain Cogn, 113*, 65-75.
651 doi:10.1016/j.bandc.2017.01.004
652 Engen, H. G., Kanske, P., & Singer, T. (2017). The neural component-process
653 architecture of endogenously generated emotion. *Soc Cogn Affect Neurosci,
654 12*(2), 197-211. doi:10.1093/scan/nsw108
655 Golchert, J., Smallwood, J., Jefferies, E., Seli, P., Huntenburg, J. M., Liem, F., . . .
656 Margulies, D. S. (2017). Individual variation in intentionality in the mind-
657 wandering state is reflected in the integration of the default-mode, fronto-
658 parietal, and limbic networks. *Neuroimage, 146*, 226-235.
659 doi:10.1016/j.neuroimage.2016.11.025
660 Gusnard, D. A., Akbudak, E., Shulman, G. L., & Raichle, M. E. (2001). Medial
661 prefrontal cortex and self-referential mental activity: relation to a default
662 mode of brain function. *Proc Natl Acad Sci U S A, 98*(7), 4259-4264.
663 doi:10.1073/pnas.071043098
664 Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved optimization
665 for the robust and accurate linear registration and motion correction of
666 brain images. *Neuroimage, 17*(2), 825-841.
667 Konishi, M., McLaren, D. G., Engen, H., & Smallwood, J. (2015). Shaped by the Past:
668 The Default Mode Network Supports Cognition that Is Independent of

669   Immediate Perceptual Input. *PLoS One, 10*(6), e0132209.
670   doi:10.1371/journal.pone.0132209
671 Krieger-Redwood, K., Jefferies, E., Karapanagiotidis, T., Seymour, R., Nunes, A., Ang,
672   J. W., . . . Smallwood, J. (2016). Down but not out in posterior cingulate
673   cortex: Deactivation yet functional coupling with prefrontal cortex during
674   demanding semantic cognition. *Neuroimage, 141*, 366-377.
675   doi:10.1016/j.neuroimage.2016.07.060
676 Leech, R., Braga, R., & Sharp, D. J. (2012). Echoes of the brain within the posterior
677   cingulate cortex. *J Neurosci, 32*(1), 215-222.
678   doi:10.1523/JNEUROSCI.3689-11.2012
679 Leech, R., & Sharp, D. J. (2014). The role of the posterior cingulate cortex in
680   cognition and disease. *Brain, 137*(Pt 1), 12-32. doi:10.1093/brain/awt162
681 Margulies, D. S., Ghosh, S. S., Goulas, A., Falkiewicz, M., Huntenburg, J. M., Langs, G.,
682   . . . Smallwood, J. (2016). Situating the default-mode network along a
683   principal gradient of macroscale cortical organization. *Proc Natl Acad Sci U*
684   *S A, 113*(44), 12574-12579. doi:10.1073/pnas.1608282113
685 Mesulam, M. M. (1998). From sensation to cognition. *Brain, 121 (Pt 6)*, 1013-1052.
686 Moscovitch, M., Cabeza, R., Winocur, G., & Nadel, L. (2016). Episodic Memory and
687   Beyond: The Hippocampus and Neocortex in Transformation. *Annu Rev*
688   *Psychol, 67*, 105-134. doi:10.1146/annurev-psych-113011-143733
689 Ralph, M. A., Jefferies, E., Patterson, K., & Rogers, T. T. (2017). The neural and
690   computational bases of semantic cognition. *Nat Rev Neurosci, 18*(1), 42-55.
691   doi:10.1038/nrn.2016.150
692 Rugg, M. D., & Vilberg, K. L. (2013). Brain networks underlying episodic memory
693   retrieval. *Curr Opin Neurobiol, 23*(2), 255-260.
694   doi:10.1016/j.conb.2012.11.005
695 Schacter, D. L., & Addis, D. R. (2007). The cognitive neuroscience of constructive
696   memory: remembering the past and imagining the future. *Philos Trans R*
697   *Soc Lond B Biol Sci, 362*(1481), 773-786. doi:10.1098/rstb.2007.2087
698 Seghier, M. L. (2013). The angular gyrus: multiple functions and multiple
699   subdivisions. *Neuroscientist, 19*(1), 43-61.
700   doi:10.1177/1073858412440596
701 Smallwood, J. (2013). Distinguishing how from why the mind wanders: a process-
702   occurrence framework for self-generated mental activity. *Psychol Bull,*
703   *139*(3), 519-535. doi:10.1037/a0030010
704 Smith, S. M. (2002). Fast robust automated brain extraction. *Hum Brain Mapp,*
705   *17*(3), 143-155. doi:10.1002/hbm.10062
706 Spreng, R. N. (2012). The fallacy of a "task-negative" network. *Front Psychol, 3*,
707   145. doi:10.3389/fpsyg.2012.00145
708 Spreng, R. N., DuPre, E., Selarka, D., Garcia, J., Gojkovic, S., Mildner, J., . . . Turner, G.
709   R. (2014). Goal-congruent default network activity facilitates cognitive
710   control. *J Neurosci, 34*(42), 14108-14114. doi:10.1523/JNEUROSCI.2815-
711   14.2014
712 Spreng, R. N., Gerlach, K. D., Turner, G. R., & Schacter, D. L. (2015).
713   Autobiographical Planning and the Brain: Activation and Its Modulation by
714   Qualitative Features. *J Cogn Neurosci, 27*(11), 2147-2157.
715   doi:10.1162/jocn_a_00846
716 Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L.
717   (2010). Default network activity, coupled with the frontoparietal control

718   network, supports goal-directed cognition. *Neuroimage, 53*(1), 303-317.
719   doi:10.1016/j.neuroimage.2010.06.016
720 Vatansever, D., Menon, D. K., Manktelow, A. E., Sahakian, B. J., & Stamatakis, E. A.
721   (2015). Default mode network connectivity during task execution.
722   *Neuroimage, 122*, 96-104. doi:10.1016/j.neuroimage.2015.07.053
723 Visser, M., Jefferies, E., & Lambon Ralph, M. A. (2010). Semantic processing in the
724   anterior temporal lobes: a meta-analysis of the functional neuroimaging
725   literature. *J Cogn Neurosci, 22*(6), 1083-1094.
726   doi:10.1162/jocn.2009.21309
727 Wagner, I. C., van Buuren, M., Kroes, M. C., Gutteling, T. P., van der Linden, M.,
728   Morris, R. G., & Fernandez, G. (2015). Schematic memory components
729   converge within angular gyrus during retrieval. *Elife, 4*, e09668.
730   doi:10.7554/eLife.09668
731 Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M.,
732   . . . Buckner, R. L. (2011). The organization of the human cerebral cortex
733   estimated by intrinsic functional connectivity. *J Neurophysiol, 106*(3),
734   1125-1165. doi:10.1152/jn.00338.2011
735 Zhang, Y., Brady, M., & Smith, S. (2001). Segmentation of Brain MR Images Through
736   a Hidden Markov Random Field Model and the Expectation-Maximization
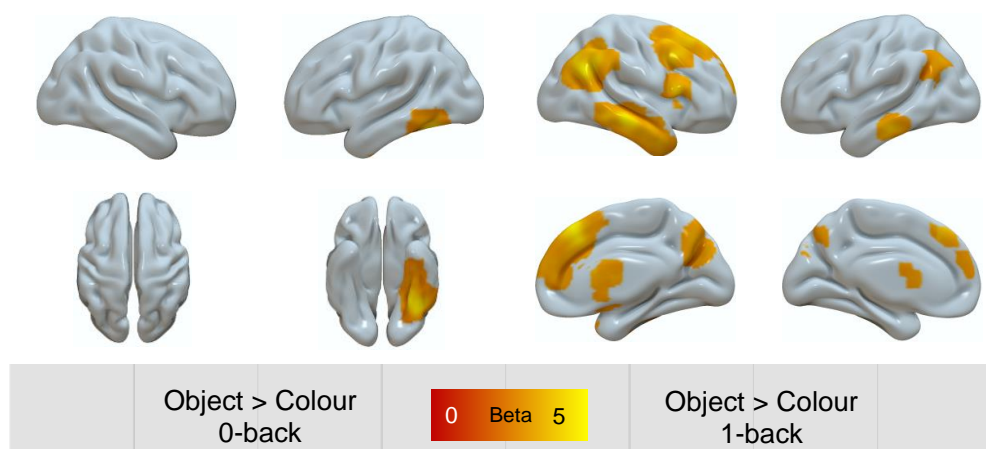737   Algorithm. *IEEE Transactions on Medical Imaging, 20*(1), 45-57.
738

Figure S1. *Comparison of complex memory representation in the presence or absence of relevant perceptual input.* Spatial maps were cluster corrected at Z = 3.1 FWE.