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Tracking thoughts: Exploring the neural architecture of mental time travel during mind-wandering

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Abstract

The capacity to imagine situations that have already happened or fictitious events that may take place in the future is known as mental time travel (MTT). Studies have shown that MTT is an important aspect of spontaneous thought, yet we lack a clear understanding of how the neurocognitive architecture of the brain constrains this element of human cognition. Previous functional magnetic resonance imaging (MRI) studies have shown that MTT involves the coordination between multiple regions that include mesiotemporal structures such as the hippocampus, as well as prefrontal and parietal regions commonly associated with the default mode network (DMN). The current study used a multimodal neuroimaging approach to identify the structural and functional brain organisation that underlies individual differences in the capacity to spontaneously engage in MTT. Using regionally unconstrained diffusion tractography analysis, we found increased diffusion anisotropy in right lateralised temporo-limbic, corticospinal, inferior fronto-occipital tracts in participants who reported greater MTT. Probabilistic connectivity mapping revealed a significantly higher connection probability of the right hippocampus with these tracts. Resting-state functional MRI connectivity analysis using the right hippocampus as a seed region revealed greater functional coupling to the anterior regions of the DMN with increasing levels of MTT. These findings demonstrate that the interactions between

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the hippocampus and regions of the cortex underlie the capacity to engage in MTT, and support contemporary theoretical accounts that suggest that the integration of the hippocampus with the DMN provides the neurocognitive landscape that allows us to imagine distant times and places.

Keywords: Mental time travel, Spontaneous thought, Diffusion MRI, Hippocampus, Mesiotemporal lobe, Default mode network

1. Introduction

Conscious experience is not restricted to events in the here and now. The prominence of states such as daydreaming and mind-wandering in our mental lives illustrates that we often mentally escape from the constraints of the moment and generate thoughts regarding people, places and situations other than those in the immediate environment (Killingsworth and Gilbert, 2010). It is now known that these states are accompanied by a measurable reduction in the processing of external events, indicating a disengagement, or decoupling, of attention from the external environment (Smallwood et al., 2008). Instead of relying on perceptual input for their mental content, it is hypothesised that these experiences are built almost exclusively from representations in semantic and episodic memory (see Smallwood and Schooler 2015 for a review).

Evidence from functional neuroimaging is consistent with the view that memory retrieval is a core process with which we generate spontaneous thought. Prior work has demonstrated that a large-scale brain system known as the default mode network (DMN) is important for the thoughts that are generated during the mind-wandering state (Mason et al., 2007; Christoff et al., 2009). The DMN is generally identified as a distributed regional assembly anchored by hubs in the medial prefrontal cortex, the posterior cingulate cortex and the angular gyrus (Raichle et al., 2001; Raichle, 2015). During tasks that involve retrieving information from memory, the DMN often integrates information from medial and lateral temporal regions known to play a pivotal role in episodic and semantic memory, such as the hippocampus (Sestieri et al., 2011) and the anterior temporal lobe (Patterson et al., 2007). Several studies have linked the DMN, as well as related structures such as the hippocampus, to processes such as imagining events from the future or past (Schacter et al., 2007), which are collectively known as mental time travel (MTT). Studies have shown that MTT is an important element

of the mind-wandering state (Smallwood et al., 2009b; Baird et al., 2011) and a meta analytic study has shown similarities between the neural activation during mind-wandering and episodic future thinking (Stawarczyk and D’Argembeau, 2015). A recent study (Ellamil et al., 2016) has also indicated that the hippocampus is activated early during the spontaneous generation of thoughts while mind-wandering.

Although previous functional magnetic resonance imaging (MRI) studies have established a functional role of the DMN in the mind-wandering state (Mason et al., 2007; Allen et al., 2013; Ellamil et al., 2016), the extent to which the neural architecture of this network and associated regions of cortex constrain naturally occurring spontaneous thought remains uncertain. In the current study, we tested the hypothesis that variations in spontaneous thoughts across participants emerge as a consequence of the large-scale structural network organisation of the brain. We applied regionally unconstrained tractography analysis to diffusion magnetic resonance imaging data in a cohort of healthy adults and assessed whether individual variability in the contents of their thoughts related to markers of structural connectivity. Our analysis approach was complemented with probabilistic connectivity mapping, to identify the cortical grey matter with the highest connection probability to these tracts. Finally, we used seed-based resting-state functional MRI connectivity mapping to identify associated functional networks. Based on functional studies of the role of the DMN and regions in the medial and lateral temporal lobe in thoughts generated during the mind-wandering state (Christoff et al., 2009; Stawarczyk et al., 2011), we anticipated our structural analysis to highlight a constellation of regions, including the medial prefrontal, posterior cingulate, as well as lateral and medial temporal cortices, including the hippocampus.

2. Methods

2.1. Participants

A total of 86 healthy participants were recruited by advert from the Department of Psychology at the University of York (51 women, age range 18 - 31). They were offered either a payment of £20 or a commensurate amount of course credits. Written consent was obtained for all participants and the study was approved by the York Neuroimaging Centre Ethics Committee. Participants were recruited in two cohorts (Sample A, $n = 47$; Sample B, $n = 39$) in different time periods, although there were no differences relevant

66 to the study. While both samples participated in the behavioural session
67 and underwent a resting state (rs) functional MRI scan, we acquired diffu-
68 sion MRI data only for sample A. We excluded 8 out of 39 participants from
69 Sample B due to incomplete brain coverage (whole-brain coverage < 94%).
70 Having two samples gave us the opportunity to treat them separately in our
71 analyses and investigate the robustness of our behavioural and functional
72 MRI results. The behavioural and functional MRI data in this study are the
73 same as those reported in Smallwood et al. (2016).

74 *2.1.1. Independent sample*

75 We also used an independent dataset to provide independent confirmation
76 of functional connectivity results. These data were obtained from a publicly
77 available dataset: the Nathan Kline Institute (NKI)/Rockland Enhanced
78 Sample and contained 141 subjects. Full details of this sample can be found
79 in Gorgolewski et al. (2014).

80 *2.2. Behavioural Methods*

81 *2.2.1. Choice Reaction Time Task*

82 To acquire information about the content of spontaneous thought in a
83 situation conducive to the mind-wandering state, participants performed a
84 simple non-demanding choice reaction time task. This task is routinely used
85 in studies of spontaneous thought because it creates periods when sponta-
86 neous thoughts are generated with as similar a frequency as when participants
87 are not engaging in a task (Smallwood et al., 2009b). Participants sat in a
88 testing booth and were asked to make a parity judgement to numerals that
89 were coloured red. These stimuli were presented in a stream of non-coloured
90 numerals, to which no response was required. Stimuli were presented with a
91 slow inter-stimulus interval (2200-4400 ms) and remained on screen for 1000
92 ms. The task lasted 15 min and participants performed a single run. The
93 occurrence of the target and non-target stimuli was randomly determined
94 with a mean target number of $M = 25.2$, $SE = 0.6$ and a mean non-target
95 number of $M = 109.6$, $SE = 1.1$. Participants responded by using the mouse
96 button. Accuracy was high (mean \pm SD = 0.93 ± 0.08), with a mean response
97 time of 900 ms (SD = 161). Participants performed this task in a laboratory
98 testing session, scheduled one day after the scanning.

2.2.2. Multi-Dimensional Experience Sampling (MDES)

At unpredictable moments while performing the laboratory task, participants were interrupted and asked to rate different aspects of their experience. They were asked to focus their answers on the contents of their experience the moment immediately prior to the interruption, thereby reducing demands on memory. They responded using a continuous Likert scale. The specific questions used are described in Table 1 and they were all asked during each probing. They were selected from prior studies (Smallwood et al., 2016) and examined the content of thoughts (e.g. temporal content relating to the past or future, referent of thought - themselves or another person - and emotional valence), as well as the form these thoughts took (whether the thoughts were in words or images, the level of detail and intrusiveness, etc.).

Whenever experience sampling occurred, the questions were administered in a quasi-random order. The first question was always about task focus, followed by blocks of questions about the content and form of thoughts. On each occasion, the order of each block, as well as the order of questions within each block, was randomised. Participants were probed an average of 8 times during the fifteen-minute task. We used a fully randomised sequence of experience sampling probes to ensure that regularities in our probing schedule did not bias the results of our experiment (Seli et al., 2013).

As in previous studies, data from each individual was concatenated into a single matrix. We z-scored the data from each sample separately to minimise differences between them, and fed them into a principal component analysis (PCA) with varimax rotation, allowing patterns of covariance that broadly correspond to different types of thought to be identified. The decomposition of these data, as well as a replication sample, has previously been reported by Smallwood et al. (2016). The decomposition was performed in separate analyses, one for the content of the experience and one for the form. We chose to decompose the components of content and form separately because our method of experience sampling presented them in these conceptual groups, reflecting our a priori interest in decomposing them as separate factors. In addition, we have successfully employed this technique of experience sampling in several prior studies (Ruby et al., 2013a,b; Engert et al., 2014; Medea et al., 2016) and applying the same procedure in the current study provided the chance to relate our data to these prior investigations. Table S1 in the supplementary materials presents the eigenvalues for the first four components generated from the decomposition of the content and the form

136 questions, where it can be seen that the scores change rapidly after the third
 137 component. For this reason, and to remain consistent with these previous
 138 studies, we opted for a three-component solution.

139 *2.3. Neuroimaging Methods*

140 *2.3.1. MRI data acquisition*

141 MRI data were acquired on a GE 3 Tesla Signa Excite HDxMRI scanner,
 142 equipped with an eight-channel phased array head coil at York Neuroimaging
 143 Centre, University of York. For each participant, we acquired a sagittal
 144 isotropic 3D fast spoiled gradient-recalled echo T1-weighted scan ($TR = 7.8$
 145 ms , $TE = \text{minimum full}$, flip angle = 20° , matrix = 256×256 , voxel size =
 146 $1.13 \times 1.13 \times 1 \text{ mm}^3$, $FOV = 289 \times 289 \text{ mm}^2$). Resting-state functional MRI data
 147 based on blood oxygen level-dependent contrast images with fat saturation
 148 were acquired using a gradient single-shot echo-planar imaging sequence (TE
 149 = minimum full ($\approx 19 \text{ ms}$), flip angle = 90° , matrix = 64×64 , $FOV = 192 \times 192$
 150 mm^2 , voxel size = $3 \times 3 \times 3 \text{ mm}^3$). Sample A had a scan duration of 9 min
 151 and the following additional parameters $TR = 3000 \text{ ms}$, 180 volumes, slice
 152 thickness 3 mm, no gap, 60 slices. Sample B had a scan duration of 7 min,
 153 $TR = 2000 \text{ ms}$, 210 volumes, slice thickness 3 mm, 0.5 mm gap and 32
 154 slices. The duration of the diffusion MRI scan was 13 minutes. A single-shot
 155 pulsed gradient spin-echo echo-planar imaging sequence was used with the
 156 following parameters: $b = 1000 \text{ s/mm}^2$, 45 directions, 7 T2-weighted EPI
 157 baseline scans (b_0), 59 slices, $FOV = 192 \times 192 \text{ mm}^2$, $TR = 15 \text{ s}$, $TE = 86 \text{ ms}$
 158 (minimum full), voxel size = $2 \times 2 \times 2 \text{ mm}^3$, matrix = 96×96 .

159 *2.3.2. Structural connectivity analysis*

160 Diffusion MRI data pre-processing involved eddy-current distortion cor-
 161 rection and motion correction using FDT v3.0, part of FSL (Smith et al.,
 162 2004). The fractional anisotropy (FA) was calculated by fitting a tensor
 163 model at each voxel of the pre-processed diffusion data and the resulting
 164 images were brain-extracted using BET (Smith, 2002). Voxel-wise FA maps
 165 were analysed using Tract-Based Spatial Statistics (TBSS) (Smith et al.,
 166 2006). No advanced options were used. After subjects' FA data were non-
 167 linearly aligned to the FMRIB58 template in MNI152 space, the mean FA im-
 168 age was created and thinned to create a mean FA skeleton, which represents
 169 the centres of all tracts common to the group. Using a generalised model,
 170 we assessed correlations between measured FA values across the skeleton and
 171 the mind-wandering PCA scores of each participant. T-statistics maps for

172 contrasts of interest were calculated using FSL’s Randomize (a nonparamet-
 173 ric permutation inference tool) with 5000 permutations (Nichols and Holmes,
 174 2002). Resulting maps were thresholded at a Family-Wise Error (FWE) cor-
 175 rected $p < 0.05$ using Threshold-Free Cluster Enhancement (TFCE) (Smith
 176 and Nichols, 2009).

177 We fitted voxel-wise probabilistic diffusion models using BEDPOSTX
 178 (Behrens et al., 2003) with 2 fibres modelled per voxel and 1000 itera-
 179 tions. Subsequent to BEDPOSTX, probabilistic tractography was performed
 180 using PROBTRACKX (Behrens et al., 2007) to reconstruct fibres pass-
 181 ing through a single-mask or connecting two masks at a time. Tractogra-
 182 phy was performed in native diffusion space. To this end, we transformed
 183 our seed masks from standard space back to diffusion space using the in-
 184 verse of the nonlinear registration calculated in the TBSS pipeline. PROB-
 185 TRACKX was used with standard parameters (5000 samples/voxel, cur-
 186 vature threshold 0.2, step length 0.5 mm, samples terminated after 2000
 187 steps or when they reached the surface as defined by a 40% probabilistic
 188 whole-brain WM mask). In the single-mask case, the connectivity maps of
 189 each individual were thresholded at 1% of total samples sent from the seed
 190 mask, mapped back to standard space using nonlinear registration, and con-
 191 catenated into a single 4D file. Nonparametric voxelwise statistical testing
 192 with 25000 permutations was then performed to obtain a group-level prob-
 193 abilistic tractography map, thresholded using TFCE at $p < 0.05$, FWE-
 194 corrected as above. In the dual-mask case, we performed seed-to-target
 195 analyses, with atlas volumes as the seeds and clusters of significant find-
 196 ings from our analyses as the targets. We also ran seed-to-target analyses
 197 using diffusion imaging data ($b = 1500$ s/mm², 127 directions plus 9 in-
 198 terspersed b0 images, voxel size = 2x2x2 mm³) from a subset ($n = 9$, 4
 199 women, age range 21 - 48) of the Test-Retest Pilot Dataset/enhanced NKI
 200 sample. Full details of this sample, as well as all the parameters of the
 201 diffusion-weighted imaging sequence used, can be found online here: [http:](http://fcon_1000.projects.nitrc.org/indi/pro/eNKI_RS_TRT/FrontPage.html)
 202 [//fcon_1000.projects.nitrc.org/indi/pro/eNKI_RS_TRT/FrontPage.html](http://fcon_1000.projects.nitrc.org/indi/pro/eNKI_RS_TRT/FrontPage.html).

203 2.3.3. Functional connectivity analysis

204 Functional MRI pre-processing and analyses were performed using FSL.
 205 Following the co-registration of functional and structural data, we extracted
 206 the brain using BET and linearly registered them to MNI152 space. Prior to
 207 functional connectivity analysis, resting state data underwent motion correc-
 208 tion using MCFLIRT, slice-timing correction using Fourier-space time-series

209 phase shifting, brain extraction using BET, spatial smoothing using a Gaus-
210 sian kernel with a full width at half maximum of 6 mm, grand-mean intensity
211 normalisation followed by high-pass (sigma = 100 s) and low-pass temporal
212 filtering (sigma = 2.8 s).

213 In each subject, we extracted the time series from seed regions of interest
214 (i.e. atlas volumes or significant clusters identified in previous steps) and used
215 them as explanatory variables in separate functional connectivity analyses
216 that also included 11 nuisance regressors: the top five principal components
217 extracted from WM and cerebrospinal fluid masks in accordance with the
218 CompCor method (Behzadi et al., 2007) and six motion parameters. No
219 global signal regression was performed (Murphy et al., 2009).

220 Group-level statistical modelling was carried out using FEAT/FLAME
221 stage 1 (Woolrich et al., 2004) with automatic outlier detection (Woolrich,
222 2008). A 50% probabilistic GM mask was applied and results were thresh-
223 olded at the whole-brain level using cluster-based Gaussian random field
224 theory, with a cluster-forming threshold of $z > 3.1$ (and $z > 2.3$ when
225 the two samples were analysed independently) and a FWE corrected clus-
226 ter significance level of $p < 0.05$. To further confirm our group-level find-
227 ings we also ran the analysis using permutation testing with the obtained
228 maps thresholded using TFCE at $p < 0.05$, FWE-corrected. Unthresh-
229 olded maps were uploaded onto Neurovault and can be found here: [http: //neurovault.org/collections/1448](http://neurovault.org/collections/1448).
230

231 3. Results

232 3.1. Analysis aims

233 The goal of this experiment was to identify connections between the struc-
234 tural and functional organisation of the brain and variations in different types
235 of spontaneous thought. We first calculated the principal components of
236 the type of spontaneous thoughts as reported in a laboratory session. Next
237 we determined whether there was any relationship between the fractional
238 anisotropy of tractography-derived white matter tracts and inter-individual
239 variation in the content and form of spontaneous thought. Finally, we ex-
240 plored the functional connectivity of grey matter regions that received pro-
241 jections from the tracts identified in the previous step, with the aim of iden-
242 tifying whether the functional connectivity of these regions is modulated by
243 the same aspects of spontaneous thought. The analysis pipeline is outlined
244 in Figure 1.

245 3.2. *Components of spontaneous thought*

246 For the decomposition of content, we focused on questions relating to
 247 temporal focus, referent of thought, task focus, and emotional content. Con-
 248 sistent with prior investigations (Ruby et al., 2013a,b; Engert et al., 2014;
 249 Medea et al., 2016), we found three orthogonal factors: i) Future and self-
 250 focused thoughts: individuals with high weighting on this component were
 251 often thinking about themselves in the future, accounting for 29% of the
 252 observed variance; ii) Past-focused social thoughts: individuals with high
 253 weighting were often thinking about self and others in the past, accounting
 254 for 19% variance; iii) Task-related thoughts: individuals with high weighting
 255 were often thinking about the task itself and experienced fewer negatively
 256 valenced off-task thoughts, accounting for 18% variance. The average of the
 257 future and past components, which we refer to as MTT, accounted for 48%
 258 of the overall variance.

259 Our next step was to decompose the questions regarding the form of
 260 thoughts - such as whether these were experienced as images or words, if they
 261 were detailed and whether they were intrusive - following a similar procedure.
 262 This yielded three components: i) The modality of the thoughts (images or
 263 words): individuals with high weighting often described their thoughts as
 264 containing words rather than images and this reflected 33% of the variance;
 265 ii) The level of intrusiveness of the thoughts: individuals with high weighting
 266 often described their thoughts as intrusive, accounting for 26%; iii) The level
 267 of detail in the thoughts: individuals with low weighting on this reported
 268 more detail in their thoughts accounting for 23%. These patterns of the form
 269 of cognition are consistent with prior investigations (Medea et al., 2016; see
 270 also the replication sample in Smallwood et al., 2016).

271 3.3. *Identifying the relationship between white matter fractional anisotropy* 272 *and the contents of spontaneous thought*

273 Relating component weighting of the mind-wandering PCA scores to
 274 skeleton-wide FA values derived from the TBSS analysis revealed a spe-
 275 cific increase in the fractional anisotropy of a temporo-limbic white mat-
 276 ter region for people engaging more in MTT (Figure 2i-top, Table 2). No
 277 other components showed any significant association. In order to describe
 278 the whole-brain structural connectivity profile of this region, we performed
 279 a probabilistic tractography analysis using it as a seed (Figure 2i-bottom).
 280 This analysis showed (Figure 2ii) that the clusters' structural connectogram
 281 closely overlapped with the right fornix, the right corticospinal tract, and

282 the right inferior fronto-occipital fasciculus, as defined by the Johns Hopkins
283 University DTI-based white-matter atlases (Mori et al., 2005).

284 As this region falls in an area with a high degree of crossing fibres, we
285 also performed an additional analysis using a model that incorporates fibre-
286 specific measurements (tbss_x) (Jbabdi et al., 2010). We estimated the
287 primary and secondary fibre orientations, together with their partial volume
288 fractions, and found a significant increase in the partial volume fraction of
289 the primary orientation for people engaging more in MTT. No other compo-
290 nent was significant for any of the two orientations. The identified regions,
291 presented in the supplementary materials, include the areas discovered in our
292 original analysis, but being more widespread did not improve their structural
293 classification. For this reason and due to the potential limitations of our dif-
294 fusion imaging sequence in regard to probabilistic analyses and crossing fibres
295 (see Discussion), we did not consider them any further.

296 To identify those grey matter regions most likely to be connected to the
297 temporo-limbic white matter substrate of MTT, we used the seeds-to-target
298 mode of PROBTRACKX with no advanced options and calculated proba-
299 bilistic streamline counts that reach our target mask when seeding from 116
300 regions-of-interest, as defined by the automated anatomical labelling (AAL)
301 (Tzourio-Mazoyer et al., 2002) for a given participant. This generated a 116
302 x 47 connectivity matrix, in which streamline counts were normalised by
303 the total number of generated tracts (waytotal), thus translated to connec-
304 tion probabilities. The results demonstrate that the most likely grey matter
305 region connected with the MTT substrate is the right hippocampus (Fig-
306 ure 3). To quantitatively assess this, we calculated the difference between
307 the hippocampus connection probability to our target mask and the second
308 highest connection probability, per participant. The generated distribution
309 was significantly greater than 0 (one-sample Wilcoxon Signed Ranked test,
310 $p < 0.0001$). Arguably, the TBSS-derived cluster was situated in a white-
311 matter region that may harbour extensive fibre crossing, which may challenge
312 tractography-based fibre reconstruction, particularly when a low number of
313 diffusion directions is used. We therefore repeated the diffusion tractography
314 analyses based on data from the NKI Enhanced repository (see Structural
315 connectivity analysis), which were acquired using a sequence with a substan-
316 tially increased number of diffusion directions. Theoretically, such sequences
317 should better resolve crossing-fibres and thus minimise the risk of erroneous
318 tractography results (see Discussion). Our analyses at this higher angular
319 resolution confirmed that the right hippocampus was the grey matter region

most likely to be connected to the temporo-limbic white matter substrate of MTT, supporting our initial findings.

3.4. Determining the link between the functional connectivity of the hippocampus and the content of spontaneous thought

Having identified the hippocampus as the region with the highest connection probability to our white matter MTT substrate, we assessed its functional connectivity profile and the modulation of these patterns by inter-individual differences in the propensity to engage in MTT. Our motivation for performing this analysis was two-fold. First, we wanted to test the robustness of the diffusion imaging results by investigating whether the selected region had a specific relationship to MTT using data from another scanning modality. Second, we wished to understand whether the mechanism that underlies the role of the hippocampus in MTT was related to its integration into the DMN. To assess these two questions we took advantage of the fact that we had two cohorts of participants for whom resting state functional MRI data were available and who also had MDES descriptions of their thoughts. We calculated the functional connectivity of the AAL mask of the right hippocampus for each participant in each cohort. These maps were used as the dependent variables in a multiple regression analysis with the 6 dimensions from the PCA decomposition of MDES scores used as independent variables, all in the same model.

Group-level functional connectivity of the right hippocampus indicated extensive connections to the ventromedial prefrontal cortex, the retrosplenial cortex, the brain stem and the cerebellum (Figure 4i). Next, we assessed regions whose connectivity with the right hippocampus correlated with individual differences in the content and form of participants' thoughts. This analysis revealed a region of dorsal anterior cingulate cortex/medial pre-frontal cortex as can be seen in Figure 4i (cluster: size 646 voxels, volume 5168 mm³, centre of gravity -4, 48, 11 mm), whose connectivity to the hippocampus increased for individuals with higher MTT scores (MTT+) compared to those with lower scores. These results were thresholded at the whole-brain level with a cluster-forming threshold of $z > 3.1$ and a FWE corrected cluster significance level of $p < 0.05$. The same regions (Figure S3 in supplementary materials) were also highlighted for the MTT+ comparison from our group-level permutation testing analysis. Finally, we observed two significant clusters of functional connectivity that were associated with the modality of

thoughts and their relative levels of detail. These did not survive more stringent analyses, so we do not consider them further, however we present their spatial maps in the supplementary materials, and the unthresholded maps can be found in Neurovault.

We also repeated these analyses separately in both datasets to investigate whether idiosyncratic features of one sample may have contributed to our findings. Comparing each group separately, only Sample B passed a cluster forming threshold of $z > 3.1$, however both groups produced significant cluster corrected regions at a more lenient value of $z > 2.3$. In both cases these regions fell in the mPFC and are shown in Figure 4ii, alongside their overlap (cluster: size 82 voxels, volume 656 mm³, centre of gravity -4, 47, 11 mm) and separate scatter plots from each sample. These analyses show a robust pattern of strengthened correlation between the right hippocampus and the medial prefrontal cortex for individuals who engage in greater MTT when the sample is treated as a group; however, we also find a converging pattern when both groups are treated as separate populations. These two features of our data suggest that our findings are statistically robust and are reasonably consistent across both groups of participants.

The observation that coupling between the right hippocampus and the medial prefrontal cortex was greater for participants who engaged in increasing levels of MTT suggests that this experience may depend upon integration between the medial temporal lobe and the DMN. To quantitatively assess this possibility, we used the overlap region identified in the previous step as a seed in a functional connectivity analysis of an independent dataset (see 2.1.1 "Independent sample"). This analysis confirmed a pattern of connectivity focused on the posterior cingulate and medial prefrontal cortex, which reflects the canonical DMN (Figure 4iii).

4. Discussion

We demonstrated that the content and form of spontaneous thought is partly constrained by structural and functional brain network organisation. Structural connectivity analyses identified a temporo-limbic white matter region, highly connected to the right hippocampus, for people who spontaneously engaged in more mental time travel (MTT). Using resting state functional connectivity, we found that the temporal correlation of the right hippocampus with the dorsal anterior cingulate cortex, a core region of the default mode network (DMN), was also modulated by inter-individual vari-

392 ation in MTT. These converging lines of evidence provide unambiguous sup-
393 port that the spontaneous thoughts experienced during the mind-wandering
394 state are in fact reliant upon the hippocampus and its integration into the
395 DMN.

396 Component process accounts of the mind-wandering state suggest that
397 this class of experience depends upon distinct neurocognitive components.
398 These include the ability to disengage attention from external input, known
399 as perceptual decoupling, and processes more directly related to the genera-
400 tion and coordination of the experiential content (Smallwood and Schooler,
401 2015). Among them, episodic memory processes have been considered to play
402 a key role in the generation of the mental content during mind-wandering,
403 particularly those episodes that entail imagining distant times and places
404 (MTT). People frequently use MTT to consider autobiographical goals (Baird
405 et al., 2011), solve personal problems (Ruby et al., 2013b), reduce social stress
406 (Engert et al., 2014) and to generate creative solutions to problems (Baird
407 et al., 2012): all tasks that draw on multiple types of memory and involve the
408 hippocampus. The hippocampus has been linked to a broad range of cogni-
409 tive processes, including episodic or autobiographical memory (Eichenbaum,
410 1993; Aggleton and Brown, 1999), spatial navigation (O’keefe and Nadel,
411 1978; O’Keefe et al., 1996) and the binding of temporally extended events
412 into a sequence (for a review see Eichenbaum 2013). These distinct accounts
413 have led to the proposal that the hippocampus may serve an integrative
414 function in cognition by combining information from different domains to
415 form coherent scenes (Hassabis and Maguire, 2007; Maguire et al., 2015),
416 allowing autobiographical information to be placed in a temporal and spatial
417 context (Eichenbaum and Cohen, 2014). Building on this view, it is possible
418 that the hippocampus integrates different aspects of knowledge from mem-
419 ory into an ongoing train of thought. It could do so by its dense structural
420 and functional connectivity profile to multiple areas of cortex (Squire et al.,
421 2004; Moscovitch et al., 2016; Bernhardt et al., 2016; Strange et al., 2014).
422 Our demonstration that the structural and functional connectivity of the
423 hippocampus is important in MTT may reflect a hippocampal contribution
424 to the process through which we use our memory to consciously organise our
425 life goals and evaluate our past experiences. It is worth noting that, although
426 our main diffusion tractography analysis targeted the right hippocampus, our
427 supplementary analysis after accounting for crossing fibres highlighted tracts
428 more symmetrical across hemispheres (see supplementary Figure S1), sug-
429 gesting an involvement of both left and right hippocampi. Thus, while prior

430 studies have found that the right hippocampus is important in mental time
431 travel especially when imagining events (see Arzy et al. 2009, Experiment
432 2, see also Addis and Schacter 2012 for further consideration of this issue),
433 further work is needed to identify the role of the hippocampus in different
434 hemispheres in spontaneous mental time travel.

435 Our functional data showed that the region with heightened hippocam-
436 pal coupling for increased mental time travel fell outside of the group con-
437 nectivity map of the hippocampus (see Figure 4). This suggests that the
438 contribution of the hippocampus to MTT involves integration with the me-
439 dial prefrontal cortex, a core node of the DMN (Gusnard and Raichle, 2001;
440 Greicius et al., 2003; Buckner et al., 2008). Contemporary accounts of this
441 network (Andrews-Hanna et al., 2014a) propose that the DMN consists of
442 discrete subsystems, whose coupling to the medial core - the medial pre-
443 frontal cortex and posterior cingulate cortex - influences ongoing cognitive
444 processing (Andrews-Hanna et al., 2014b). In concordance with this view,
445 it has been shown that, during memory retrieval, the hippocampus couples
446 with other DMN regions more strongly than it does at rest (Huijbers et al.,
447 2011), while hippocampal - DMN interactions have also been highlighted in
448 conceptual processing (Constantinescu et al., 2016). Our demonstration that
449 increased functional connectivity between the hippocampus and the medial
450 prefrontal cortex is associated with increased MTT supports this component
451 process view of the DMN function, suggesting that engaging in spontaneous
452 episodic thought is a situation when the hippocampus and the DMN act to-
453 gether in an integrated fashion. Our data from the domain of spontaneous
454 thought provides further evidence that the DMN is important in attending
455 to distant times and places (Peer et al., 2015), perhaps because it functions
456 to integrate information from across the cortex (Margulies et al., 2016). This
457 hypothesis could be further explored by looking at the content of thought
458 while ongoing measures of neural function are recorded (Tusche et al., 2014).
459 In addition, as recent studies have demonstrated ways of measuring activity
460 in white matter from a functional MRI acquisition (Gawryluk et al., 2014;
461 Ding et al., 2016), it could be of interest to explore the temporal correla-
462 tions along white matter tracts and how these might relate to spontaneous
463 thoughts and DMN connectivity.

464 There are some limitations that should be borne in mind when considering
465 our data. First, we only measured the functional and structural organisation
466 of neural functioning in the participants on one occasion. Although the con-
467 verging evidence produced by two independent imaging methodologies, and

468 especially the diffusion data, show that these data are most parsimoniously
 469 described as reflecting a trait, there remains a possibility that the experience
 470 sampling observations are partly influenced by state related changes. Future
 471 studies may gain greater power by measuring experience across several
 472 days, which would provide measures of the content of mind-wandering that
 473 are more closely tied to an individual’s trait. Also, our study explored the
 474 neural correlates of latent patterns within a multi dimensional experience
 475 sampling space by performing a data reduction using principal components
 476 analysis. This allows us to characterise the largest patterns within the experience
 477 sampling data in a statistically robust manner; however, its weakness
 478 is that it does not provide the specificity to determine whether it is the self-
 479 relevant or temporal aspects of cognition, or a combination of both, that our
 480 data capture. Future work with a larger sample size could profitably explore
 481 this issue by modelling the interactions at the level of each question. In addition,
 482 our whole-brain tractographic findings did not survive a superordinate
 483 Bonferroni correction additionally adjusting family-wise error levels for the
 484 number of different contrasts included in our model. We believe that this is
 485 quite possibly due to the sample size of our diffusion MRI data and unlikely
 486 to be a Type 1 error, as the MTT score was found to be a significant predictor
 487 of a fractional anisotropy increase in a white matter region highly connected
 488 to the hippocampus, a region for which there are strong a priori reasons to
 489 expect it to play an important role in the mind-wandering state (Schacter
 490 et al., 2007). Moreover, the functional connectivity of the hippocampus to
 491 core regions of the DMN showed a similar pattern of modulation by MTT
 492 across two datasets. Finally, it is also important to note that the current
 493 study was carried out using a conventional diffusion imaging sequence with
 494 45 diffusion directions and only one b-value shell. While it has been argued
 495 previously (Jones, 2004; Jones et al., 2013) that 30 or more unique orientations
 496 allow to obtain robust estimates of tensor-derived properties (fractional
 497 anisotropy and principal eigenvector orientation), tractographic analysis and
 498 estimation of tensor parameters may generally be challenged when different
 499 fibre populations cross in a given voxel. These limitations motivate more
 500 targeted follow-up diffusion MRI studies on the observed relation, that can
 501 take advantage of increased angular resolution by moving to higher fields, using
 502 longer scans, and/or by utilizing accelerated image acquisition techniques
 503 (Feinberg et al., 2010).

504 In conclusion, our study highlights that although spontaneous thoughts
 505 seem to emerge independently of external input, they are nonetheless con-

strained by the structure of the cortex. Our results provide evidence that the connections between the hippocampus and other areas of the cortex support the contribution of episodic content during spontaneous thought. These findings complement prior studies linking individual differences in spontaneous thought to (i) neural measures such as cortical thickness (Bernhardt et al., 2014), functional connectivity (Smallwood et al., 2013a; Tusche et al., 2014; Smallwood et al., 2016), and (ii) psychological measures such as executive control (Smallwood et al., 2013b; Kane et al., 2007; Levinson et al., 2012; McVay and Kane, 2009) and personality (McVay et al., 2009; Diaz et al., 2014; Golchert et al., 2016). Together, these complimentary lines of research demonstrate that although the specific content our thoughts take is doubtlessly influenced by our current concerns (Klinger and Cox, 1987) or our mood (Smallwood et al., 2009a; Killingsworth and Gilbert, 2010; Poerio et al., 2013), aspects of how they emerge may be determined by more stable aspects of a person. Thus, even though our clear sense is that spontaneous thoughts emerge from nowhere (Schooler, 2002), the manner in which this process occurs is likely influenced by the organisation of our neurocognitive system.

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799 **Figure captions**

800 **Figure 1.** *Overview of analysis pipeline.*

801 The upper panel describes the analysis steps which allow the dimensions that
 802 underlie the trial level experience sampling data to be calculated. The mid-
 803 dle panel describes how the functional connectivity maps for our regions of
 804 interest are calculated from the resting state functional Magnetic Resonance
 805 Imaging data (MRI). The lower panel describes how the fractional anisotropy
 806 maps are calculated from the whole-brain diffusion MRI data.

807
 808 **Figure 2.** *Identifying the relationship between structural connectivity and
 809 the contents of spontaneous thought.*

810 **i:** The upper panel shows the results of the whole-brain diffusion MRI anal-
 811 ysis. The clusters where a significant increase in fractional anisotropy was
 812 found for participants engaging more in mental time travel are indicated in
 813 red and are overlaid on the mean fractional anisotropy skeleton. Results
 814 were thresholded at a Family-Wise Error (FWE) corrected $p < 0.05$ using
 815 Threshold-Free Cluster Enhancement. The lower panel presents these signif-
 816 icant clusters along with the probabilistic streamline that was found to pass
 817 through them. The streamline was thresholded using Threshold-Free Cluster
 818 Enhancement at $p < 0.05$, FWE-corrected.

819 **ii:** This panel demonstrates the overlap of the probabilistic streamline with
 820 the right fornix, the right corticospinal tract, and the right inferior fronto-
 821 occipital fasciculus.

822 **Acronyms:** FA - fractional anisotropy , MTT+ - increased mental time
 823 travel, PS - probabilistic streamline, rFX - right Fornix, rCST - right corti-
 824 cospinal tract, riFOF - right inferior fronto-occipital fasciculus.

825
 826 **Figure 3.** *Identifying the grey matter regions connected to the temporo-
 827 limbic white matter substrate of mental time travel.*

828 The box plots in the upper panel show the connection probability of each one
 829 of the 116 grey matter volumes of the Automated Anatomical Labelling atlas
 830 with the white matter substrate of mental time travel found in our whole-
 831 brain tractography analysis. In the lower panel, the volumes are presented
 832 with each region coloured according to its average connection probability
 833 among participants. It is clear in both panels that the right hippocampus
 834 has the highest number of streamlines connecting it to the cluster obtained
 835 in the prior step of our analysis.

836

837 **Figure 4.** *Determining the link between the functional connectivity of the*
838 *hippocampus and the content of spontaneous thought.*

839 **i:** The group-level functional connectivity of the right hippocampus (left),
840 the region showing a stronger temporal connectivity with it for individuals
841 with higher MTT (middle) and the scatter plot (right) showing the average
842 beta values extracted from this region plotted against the mental time travel
843 scores for each participant. Maps were thresholded at the whole-brain level
844 with a cluster-forming threshold of $z > 3.1$ and a FWE corrected cluster
845 significance level of $p < 0.05$.

846 **ii.** The upper panel shows the regions with increased functional connectivity
847 with the right hippocampus for individuals with higher MTT, when each
848 sample is analysed separately (top left and top middle), as well as their
849 overlap (top right). The lower panel presents an axial slice of the overlap
850 cluster and the two scatter plots from each sample that illustrate the average
851 beta values extracted from this region plotted against the mental time travel
852 scores for each participant. It is apparent that this relationship is consistent
853 across both datasets. Maps were thresholded at the whole-brain level with a
854 cluster-forming threshold of $z > 2.3$ and a FWE corrected cluster significance
855 level of $p < 0.05$.

856 **iii:** The relationship between the default mode network as defined in the
857 Yeo et al. (2011) study and the group-level functional connectivity of the
858 mental time travel conjunction cluster produced through the analysis of an
859 independent dataset. Maps were thresholded at the whole-brain level with a
860 cluster-forming threshold of $z > 3.1$ and a FWE corrected cluster significance
861 level of $p < 0.05$.

862 **Acronyms:** MTT - mental time travel, DMN - default mode network.

Table 1: Experience sampling questions used in this experiment.

Dimension	Question (My thoughts ...)	Left	Right
Task	... were focused on the task I was performing	Not at all	Completely
Future	... involved future events	Not at all	Completely
Past	... involved past events	Not at all	Completely
Self	... involved myself	Not at all	Completely
Other	... involved other people	Not at all	Completely
Emotion	The content of ... was	Negative	Positive
Images	... were in the form of images	Not at all	Completely
Words	... were in the form of words	Not at all	Completely
Intrusive	... were intrusive	Not at all	Completely
Detail	... were vague and non-specific	Not at all	Completely

Table 2: Clusters showing a significant association between the MTT weights and the FA of the whole-brain, corrected for multiple comparisons with a family-wise error rate of $p < 0.05$.

Cluster size (voxels)	Cluster centre of gravity X,Y,Z (mm)
481	25, -18, 9
172	32, -22, -5
8	27, -31, -3