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

2.1.1. Independent sample

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

2.2. Behavioural Methods

2.2.1. Choice Reaction Time Task

To acquire information about the content of spontaneous thought in a situation conducive to the mind-wandering state, participants performed a simple non-demanding choice reaction time task. This task is routinely used in studies of spontaneous thought because it creates periods when spontaneous thoughts are generated with as similar a frequency as when participants are not engaging in a task (Smallwood et al., 2009b). Participants sat in a testing booth and were asked to make a parity judgement to numerals that were coloured red. These stimuli were presented in a stream of non-coloured numerals, to which no response was required. Stimuli were presented with a slow inter-stimulus interval (2200-4400 ms) and remained on screen for 1000 ms. The task lasted 15 min and participants performed a single run. The occurrence of the target and non-target stimuli was randomly determined with a mean target number of $M = 25.2$, $SE = 0.6$ and a mean non-target number of $M = 109.6$, $SE = 1.1$. Participants responded by using the mouse button. Accuracy was high ($\text{mean}\pm\text{SD} = 0.93\pm0.08$), with a mean response time of 900 ms ($SD = 161$). Participants performed this task in a laboratory 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 questions, where it can be seen that the scores change rapidly after the third component. For this reason, and to remain consistent with these previous studies, we opted for a three-component solution.

2.3. Neuroimaging Methods

2.3.1. MRI data acquisition

MRI data were acquired on a GE 3 Tesla Signa Excite HDxMRI scanner, equipped with an eight-channel phased array head coil at York Neuroimaging Centre, University of York. For each participant, we acquired a sagittal isotropic 3D fast spoiled gradient-recalled echo T1-weighted scan (TR = 7.8 ms, TE = minimum full, flip angle = 20°, matrix = 256x256, voxel size = 1.13x1.13x1 mm^3, FOV = 289x289 mm^2). Resting-state functional MRI data based on blood oxygen level-dependent contrast images with fat saturation were acquired using a gradient single-shot echo-planar imaging sequence (TE = minimum full ($\approx$19 ms), flip angle = 90°, matrix = 64x64, FOV = 192x192 mm^2, voxel size = 3x3x3 mm^3). Sample A had a scan duration of 9 min and the following additional parameters TR = 3000 ms, 180 volumes, slice thickness 3 mm, no gap, 60 slices. Sample B had a scan duration of 7 min, TR = 2000 ms, 210 volumes, slice thickness 3 mm, 0.5 mm gap and 32 slices. The duration of the diffusion MRI scan was 13 minutes. A single-shot pulsed gradient spin-echo echo-planar imaging sequence was used with the following parameters: b = 1000 s/mm^2, 45 directions, 7 T2-weighted EPI baseline scans (b0), 59 slices, FOV = 192x192 mm^2, TR = 15 s, TE = 86 ms (minimum full), voxel size = 2x2x2 mm^3, matrix = 96x96.

2.3.2. Structural connectivity analysis

Diffusion MRI data pre-processing involved eddy-current distortion correction and motion correction using FDT v3.0, part of FSL (Smith et al., 2004). The fractional anisotropy (FA) was calculated by fitting a tensor model at each voxel of the pre-processed diffusion data and the resulting images were brain-extracted using BET (Smith, 2002). Voxel-wise FA maps were analysed using Tract-Based Spatial Statistics (TBSS) (Smith et al., 2006). No advanced options were used. After subjects' FA data were non-linearly aligned to the FMRIB58 template in MNI152 space, the mean FA image was created and thinned to create a mean FA skeleton, which represents the centres of all tracts common to the group. Using a generalised model, we assessed correlations between measured FA values across the skeleton and the mind-wandering PCA scores of each participant. T-statistics maps for contrasts of interest were calculated using FSL's Randomize (a nonparametric permutation inference tool) with 5000 permutations (Nichols and Holmes, 2002). Resulting maps were thresholded at a Family-Wise Error (FWE) corrected $p < 0.05$ using Threshold-Free Cluster Enhancement (TFCE) (Smith and Nichols, 2009).

We fitted voxel-wise probabilistic diffusion models using BEDPOSTX (Behrens et al., 2003) with 2 fibres modelled per voxel and 1000 iterations. Subsequent to BEDPOSTX, probabilistic tractography was performed using PROBTRACKX (Behrens et al., 2007) to reconstruct fibres passing through a single-mask or connecting two masks at a time. Tractography was performed in native diffusion space. To this end, we transformed our seed masks from standard space back to diffusion space using the inverse of the nonlinear registration calculated in the TBSS pipeline. PROBTRACKX was used with standard parameters (5000 samples/voxel, curvature threshold 0.2, step length 0.5 mm, samples terminated after 2000 steps or when they reached the surface as defined by a 40% probabilistic whole-brain WM mask). In the single-mask case, the connectivity maps of each individual were thresholded at 1% of total samples sent from the seed mask, mapped back to standard space using nonlinear registration, and concatenated into a single 4D file. Nonparametric voxelwise statistical testing with 25000 permutations was then performed to obtain a group-level probabilistic tractography map, thresholded using TFCE at $p < 0.05$, FWE-corrected as above. In the dual-mask case, we performed seed-to-target analyses, with atlas volumes as the seeds and clusters of significant findings from our analyses as the targets. We also ran seed-to-target analyses using diffusion imaging data ($b = 1500$ s/mm^2, 127 directions plus 9 interspersed b0 images, voxel size = 2x2x2 mm^3) from a subset ($n = 9$, 4 women, age range 21 - 48) of the Test-Retest Pilot Dataset/enhanced NKI sample. Full details of this sample, as well as all the parameters of the diffusion-weighted imaging sequence used, can be found online here: http://fcon_1000.projects.nitrc.org/indi/pro/eNKI_RS_TRT/FrontPage.html.

2.3.3. Functional connectivity analysis

Functional MRI pre-processing and analyses were performed using FSL. Following the co-registration of functional and structural data, we extracted the brain using BET and linearly registered them to MNI152 space. Prior to functional connectivity analysis, resting state data underwent motion correction using MCFLIRT, slice-timing correction using Fourier-space time-series phase shifting, brain extraction using BET, spatial smoothing using a Gaussian kernel with a full width at half maximum of 6 mm, grand-mean intensity normalisation followed by high-pass (sigma = 100 s) and low-pass temporal filtering (sigma = 2.8 s).

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

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

3. Results

3.1. Analysis aims

The goal of this experiment was to identify connections between the structural and functional organisation of the brain and variations in different types of spontaneous thought. We first calculated the principal components of the type of spontaneous thoughts as reported in a laboratory session. Next we determined whether there was any relationship between the fractional anisotropy of tractography-derived white matter tracts and inter-individual variation in the content and form of spontaneous thought. Finally, we explored the functional connectivity of grey matter regions that received projections from the tracts identified in the previous step, with the aim of identifying whether the functional connectivity of these regions is modulated by the same aspects of spontaneous thought. The analysis pipeline is outlined in Figure 1.

3.2. Components of spontaneous thought

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

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

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

Relating component weighting of the mind-wandering PCA scores to skeleton-wide FA values derived from the TBSS analysis revealed a specific increase in the fractional anisotropy of a temporo-limbic white matter region for people engaging more in MTT (Figure 2i-top, Table 2). No other components showed any significant association. In order to describe the whole-brain structural connectivity profile of this region, we performed a probabilistic tractography analysis using it as a seed (Figure 2i-bottom). This analysis showed (Figure 2ii) that the clusters' structural connectogram closely overlapped with the right fornix, the right corticospinal tract, and the right inferior fronto-occipital fasciculus, as defined by the Johns Hopkins University DTI-based white-matter atlases (Mori et al., 2005).

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

To identify those grey matter regions most likely to be connected to the temporo-limbic white matter substrate of MTT, we used the seeds-to-target mode of PROBTRACKX with no advanced options and calculated probabilistic streamline counts that reach our target mask when seeding from 116 regions-of-interest, as defined by the automated anatomical labelling (AAL) (Tzourio-Mazoyer et al., 2002) for a given participant. This generated a 116 x 47 connectivity matrix, in which streamline counts were normalised by the total number of generated tracts (waytotal), thus translated to connection probabilities. The results demonstrate that the most likely grey matter region connected with the MTT substrate is the right hippocampus (Figure 3). To quantitatively assess this, we calculated the difference between the hippocampus connection probability to our target mask and the second highest connection probability, per participant. The generated distribution was significantly greater than 0 (one-sample Wilcoxon Signed Ranked test, $p < 0.0001$). Arguably, the TBSS-derived cluster was situated in a white-matter region that may harbour extensive fibre crossing, which may challenge tractography-based fibre reconstruction, particularly when a low number of diffusion directions is used. We therefore repeated the diffusion tractography analyses based on data from the NKI Enhanced repository (see Structural connectivity analysis), which were acquired using a sequence with a substantially increased number of diffusion directions. Theoretically, such sequences should better resolve crossing-fibres and thus minimise the risk of erroneous tractography results (see Discussion). Our analyses at this higher angular 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 mm^3, 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 mm^3, 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 variation in MTT. These converging lines of evidence provide unambiguous support that the spontaneous thoughts experienced during the mind-wandering state are in fact reliant upon the hippocampus and its integration into the DMN.

Component process accounts of the mind-wandering state suggest that this class of experience depends upon distinct neurocognitive components. These include the ability to disengage attention from external input, known as perceptual decoupling, and processes more directly related to the generation and coordination of the experiential content (Smallwood and Schooler, 2015). Among them, episodic memory processes have been considered to play a key role in the generation of the mental content during mind-wandering, particularly those episodes that entail imagining distant times and places (MTT). People frequently use MTT to consider autobiographical goals (Baird et al., 2011), solve personal problems (Ruby et al., 2013b), reduce social stress (Engert et al., 2014) and to generate creative solutions to problems (Baird et al., 2012): all tasks that draw on multiple types of memory and involve the hippocampus. The hippocampus has been linked to a broad range of cognitive processes, including episodic or autobiographical memory (Eichenbaum, 1993; Aggleton and Brown, 1999), spatial navigation (O'keefe and Nadel, 1978; O'Keefe et al., 1996) and the binding of temporally extended events into a sequence (for a review see Eichenbaum 2013). These distinct accounts have led to the proposal that the hippocampus may serve an integrative function in cognition by combining information from different domains to form coherent scenes (Hassabis and Maguire, 2007; Maguire et al., 2015), allowing autobiographical information to be placed in a temporal and spatial context (Eichenbaum and Cohen, 2014). Building on this view, it is possible that the hippocampus integrates different aspects of knowledge from memory into an ongoing train of thought. It could do so by its dense structural and functional connectivity profile to multiple areas of cortex (Squire et al., 2004; Moscovitch et al., 2016; Bernhardt et al., 2016; Strange et al., 2014). Our demonstration that the structural and functional connectivity of the hippocampus is important in MTT may reflect a hippocampal contribution to the process through which we use our memory to consciously organise our life goals and evaluate our past experiences. It is worth noting that, although our main diffusion tractography analysis targeted the right hippocampus, our supplementary analysis after accounting for crossing fibres highlighted tracts more symmetrical across hemispheres (see supplementary Figure S1), suggesting an involvement of both left and right hippocampi. Thus, while prior studies have found that the right hippocampus is important in mental time travel especially when imagining events (see Arzy et al. 2009, Experiment 2, see also Addis and Schacter 2012 for further consideration of this issue), further work is needed to identify the role of the hippocampus in different hemispheres in spontaneous mental time travel.

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

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

In conclusion, our study highlights that although spontaneous thoughts seem to emerge independently of external input, they are nonetheless constrained 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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Figure captions

Figure 1. *Overview of analysis pipeline.*
The upper panel describes the analysis steps which allow the dimensions that underlie the trial level experience sampling data to be calculated. The middle panel describes how the functional connectivity maps for our regions of interest are calculated from the resting state functional Magnetic Resonance Imaging data (MRI). The lower panel describes how the fractional anisotropy maps are calculated from the whole-brain diffusion MRI data.

Figure 2. *Identifying the relationship between structural connectivity and the contents of spontaneous thought.*
i: The upper panel shows the results of the whole-brain diffusion MRI analysis. The clusters where a significant increase in fractional anisotropy was found for participants engaging more in mental time travel are indicated in red and are overlaid on the mean fractional anisotropy skeleton. Results were thresholded at a Family-Wise Error (FWE) corrected $p < 0.05$ using Threshold-Free Cluster Enhancement. The lower panel presents these significant clusters along with the probabilistic streamline that was found to pass through them. The streamline was thresholded using Threshold-Free Cluster Enhancement at $p < 0.05$, FWE-corrected.
ii: This panel demonstrates the overlap of the probabilistic streamline with the right fornix, the right corticospinal tract, and the right inferior fronto-occipital fasciculus.
Acronyms: FA - fractional anisotropy , MTT+ - increased mental time travel, PS - probabilistic streamline, rFX - right Fornix, rCST - right corticospinal tract, riFOF - right inferior fronto-occipital fasciculus.

Figure 3. *Identifying the grey matter regions connected to the temporo-limbic white matter substrate of mental time travel.*
The box plots in the upper panel show the connection probability of each one of the 116 grey matter volumes of the Automated Anatomical Labelling atlas with the white matter substrate of mental time travel found in our whole-brain tractography analysis. In the lower panel, the volumes are presented with each region coloured according to its average connection probability among participants. It is clear in both panels that the right hippocampus has the highest number of streamlines connecting it to the cluster obtained in the prior step of our analysis.

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

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

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

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

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