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Dynamic functional connectivity of the default mode network tracks daydreaming ☆

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ABSTRACT

Humans spend much of their time engaged in stimulus-independent thoughts, colloquially known as "daydreaming" or "mind-wandering." A fundamental question concerns how awake, spontaneous brain activity represents the ongoing cognition of daydreaming versus unconscious processes characterized as "intrinsic." Since daydreaming involves brief cognitive events that spontaneously fluctuate, we tested the hypothesis that the dynamics of brain network functional connectivity (FC) are linked with daydreaming. We determined the general tendency to daydream in healthy adults based on a daydreaming frequency scale (DDF). Subjects then underwent both resting state functional magnetic resonance imaging (rs-fMRI) and fMRI during sensory stimulation with intermittent thought probes to determine the occurrences of mind-wandering events. Brain regions within the default mode network (DMN), purported to be involved in daydreaming, were assessed for 1) static FC across the entire fMRI scans, and 2) dynamic FC based on FC variability (FCV) across 30 s progressively sliding windows of 2 s increments within each scan. We found that during both resting and sensory stimulation states, individual differences in DDF were negatively correlated with static FC between the posterior cingulate cortex and a ventral DMN subsystem involved in future-oriented thought. Dynamic FC analysis revealed that DDF was positively correlated with FCV within the same DMN subsystem in the resting state but not during stimulation. However, dynamic but not static FC, in this subsystem, was positively correlated with an individual's degree of self-reported mind-wandering during sensory stimulation. These findings identify temporal aspects of spontaneous DMN activity that reflect conscious and unconscious processes.

Introduction

Humans spend nearly half their time engaged in cognitions that represent stimulus-independent thoughts, colloquially known as "daydreaming" or "mind-wandering" (Killingsworth and Gilbert, 2010). A set of brain regions that could reflect daydreaming is the default mode network (DMN), which has ongoing activity during task-free and stimulus-free states that is suppressed during externally-oriented tasks (Raichle and Snyder, 2007). Evidence from functional MRI (fMRI) coupled with thought probes suggests that the DMN is activated during mind-wandering (Christoff et al., 2009; Kucyi et al., 2013). One DMN subsystem anchored in the dorsomedial prefrontal cortex is thought to subserve self-referential thoughts about the present. Another subsystem anchored in the medial temporal lobe has been associated with memory-based construction of future scenarios. The posterior cingulate and anterior medial prefrontal cortices may function as a DMN "core" because they co-activate and are functionally connected with both subsystems (Andrews-Hanna et al., 2010b).

The study of brain activity in an awake, task-free ("resting") state, in which daydreaming is a predominant activity, has recently emerged as an approach to understanding functional networks (Buckner et al., 2013). Brain areas with correlated oscillations, typically based on time series over 5–10 minute resting state fMRI (rs-fMRI) scans, are said to have functional connectivity (FC). This approach has revealed that the spatial organization of networks during rs-fMRI is surprisingly similar to that during unconscious states (e.g. sleep, anesthesia) (Horovitz et al., 2008; Vincent et al., 2007). However, network FC strength may vary for different cognitive states (Shirer et al., 2012) and consciousness levels (Vanhaudenhuyse et al., 2010). Therefore, in the awake resting state, how FC patterns reflect ongoing daydreaming,

Abbreviations: amPFC, anterior medial prefrontal cortex; DDF, daydreaming frequency; DMN, default mode network; dmPFC, dorsomedial prefrontal cortex; FC, functional connectivity; FCV, functional connectivity variability; MTL, medial temporal lobe; PCC, posterior cingulate cortex; rs-fMRI, resting state functional magnetic resonance imaging.

☆ This work was performed at Toronto Western Research Institute, University Health Network.

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versus neurophysiological operations that are independent of consciousness, remains unknown.

Conventional FC analysis, which assumes static connectivity over several minutes, may not capture dynamic thoughts spontaneously jumping from topic to topic. Recent studies demonstrated that FC fluctuates across shorter time-windows (e.g. 30–60 s) during rs-fMRI, with regions that are correlated with one another during some periods being uncorrelated and/or anticorrelated during other periods (Allen et al., 2014; Chang and Glover, 2010; Handwerker et al., 2012). Such dynamic FC fluctuations occur in anesthetized animals (Hutchison et al., 2013b; Majeed et al., 2011) and therefore cannot be explained purely by mind-wandering. However, fluctuating FC of specific networks might reflect daydreaming.

Here we propose that dynamic FC based on FC variability (FCV) between the DMN core and subsystems, across time-windows on the order of seconds, reflects mind-wandering. We previously demonstrated that individual tendencies to mind-wander away from painful stimulation are unrelated to the tendency to daydream (Kucyi et al., 2013). We showed that spontaneous FCV between the periaqueductal gray and medial prefrontal cortex was significantly correlated with individual differences in the tendency to mind-wander away from pain, but did not investigate the brain dynamics of general tendencies to daydream or fluctuations in mind-wandering states within individuals. The current study builds on and differs from our previous work as follows: First, we linked DMN FC and FCV with inter-individual differences in general tendencies to daydream. Then, we used thought probes during fMRI with painful stimulation to link the same metrics with intra-individual fluctuations in degree of mind-wandering (Fig. 1). Our unique paradigm enabled us to dissociate the components of spontaneous brain dynamics that relate to the general tendency to daydream across individuals versus the fluctuating state of daydreaming within an individual. We hypothesized that static DMN FC reflects largely unconscious brain operations related to the general tendency to daydream regardless of cognitive state, whereas dynamic DMN FCV reflects mind-wandering events.

Materials and methods

Participants

Fifty-one right-handed healthy volunteers (26 females, 25 males; mean age ± SD = 25.02 ± 2.68) participated in the study, as reported in a separate analysis (Kucyi et al., 2013). All of these subjects were included in resting state analyses, whereas only fifty were included in task fMRI analyses because one subject did not complete the task fMRI. Exclusion criteria included any history of neurological, psychiatric, or chronic illness, regular pain in the last six months, and medication use (besides birth control). Informed written consent was obtained for procedures approved by the University Health Network REB.

Assessment of daydreaming

We used two approaches to assess daydreaming. First, subjects completed the daydreaming frequency scale (DDF) of the Imaginal Processes Inventory (Singer and Antrobus, 1972) prior to MRI scanning on a different day. This provided a single overall measure for each subject of their propensity to daydream and allowed us to evaluate individual differences in brain connectivity related to individual propensity to daydream. DDF scores were normally distributed ($p = 0.78$, 1-sample Kolmogorov–Smirnov). Second, we used a thought probe method to determine when subjects were mind-wandering throughout an fMRI scan that included sensory stimulation (see below). This allowed us to evaluate connectivity dynamics related to intra-individual fluctuations in their state of mind-wandering (Fig. 1). To test whether the general tendency to daydream was dissociated from mind-wandering state during sensory stimulation, we calculated Pearson's correlation coefficient for DDF versus mean frequency of mind-wandering reports across the scans involving thought probes (two-tailed).

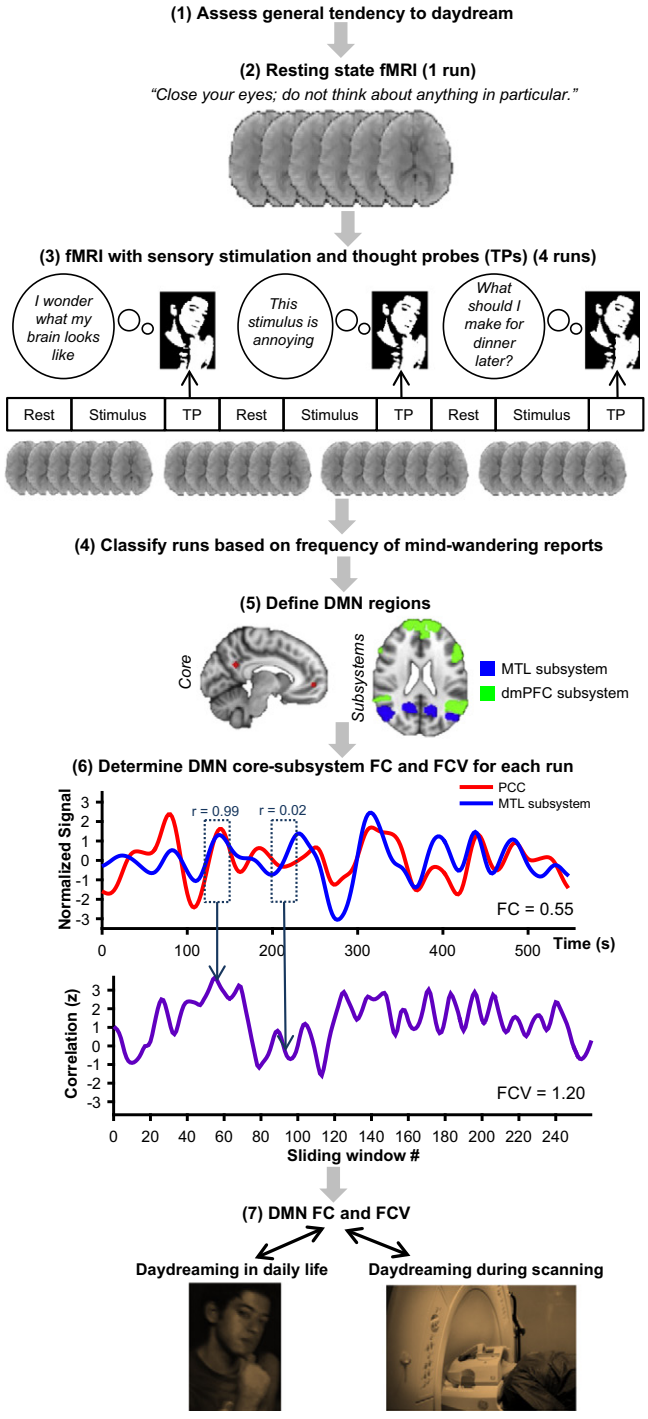

Fig. 1. Overview of the study's design and analyses. Subjects were assessed with a questionnaire for their general tendency to daydream (daydream frequency, DDF). They then underwent one run of resting state fMRI and four runs of fMRI coupled with sensory stimulation and thought probes. The runs with stimulation were classified based on frequency of mind-wandering reports. Regions of the default mode network (DMN) core and subsystems were defined. For each DMN core–subsystem pair, static functional connectivity (FC) and dynamic FC (based on FC variability (FCV)) was calculated within each run. A single-subject example is shown for fluctuations in the time series, and sliding window correlation series, for the posterior cingulate cortex (PCC) and medial temporal lobe (MTL) subsystem. The FC and FCV values were correlated with scores on the daydreaming frequency questionnaire and with intra-individual variability in run-to-run mind-wandering frequency during scanning.

Scanning procedures

Scans were conducted with a 3-Tesla GE MRI system fitted with an eight-channel phased-array head coil. A T_1-weighted anatomical scan was first collected with the following acquisition parameters: matrix = 256 × 256; 104 axial slices; 0.78 × 0.78 × 1.5 mm^3 voxels; flip angle = 20°; TE = 3 ms; TR = 7.8 ms; TI = 300 ms. Next, we collected a rs-fMRI scan in which subjects were instructed to "close your eyes; do not try to think about anything in particular; do not fall asleep." This T_2*-weighted echo-planar scan consisted of 277 volumes collected over a 9 min 14 s duration: matrix = 64 × 64; 36 axial slices per volume; 3.125 × 3.125 × 4 mm^3 voxels; interleaved slice acquisition; no gap; flip angle = 90°; TE = 30 ms; TR = 2000 ms. We then acquired 4 T_2*-weighted echo-planar task fMRI scans, each consisting of 266 volumes over 8 min 52 s (other parameters same as for the rs-fMRI scan) that included intermittent thought probes to sample attentional state. Subjects wore MRI-compatible goggles to view displays presented with EPrime v1.1 (Psychology Software Tools, PA, USA).

The task fMRI runs included external stimuli (pain) and experience sampling procedures (Christoff et al., 2009; Stawarczyk et al., 2011b) to probe attention toward versus away from the stimuli, as reported previously (for details, see (Kucyi et al., 2013)). Briefly, stimuli consisted of 50 Hz median nerve transcutaneous electrical nerve stimulation (TENS) (Empi Inc., MN, USA). For each subject, prior to scanning, we determined the current to be used during scanning that produced pain intensity rated as 4–5 on a scale from 0 (no pain) to 10 (most intense pain imaginable). This current level was adjusted between fMRI runs to maintain a pain level of 4–5. The subject was instructed to avoid actively attending either toward or away from pain, to avoid structured thinking such as counting or singing, and to look at a central fixation cross during pain stimulation and rest periods. Each run consisted of a 30 s rest period followed by 10 28 s task trials followed by a 22 s rest period. Each trial consisted of 20 s of painful TENS followed by an attentional state thought probe (TP) during which the subject pressed a button to indicate one of four options shown on a screen as follows: "At the end of this last trial, to what degree were your thoughts/feelings about pain or something else?" "Only pain", "Mostly pain", "Mostly something else", or "Only something else." After all runs, the subject was asked to indicate the degree to which trials where they indicated "something else" was due to external sensory distractions (e.g. scanner noise/discomfort), task-related interferences (e.g. thinking about upcoming thought probe), or mind-wandering (thoughts/feelings completely unrelated to the present sensory environment) (Stawarczyk et al., 2011a, 2011b). Ratings were given for external sensory distractions, task-related interferences and mind-wandering on a Likert scale (1 = never; 7 = always). Subjects were also encouraged to give examples of thoughts/feelings unrelated to the present sensory environment that occurred during scanning.

Data preprocessing

Preprocessing and analyses were carried out with tools in FSL v5.0 (Jenkinson et al., 2012), AFNI (Cox, 1996), MATLAB v7.12.0 (Mathworks Inc., Natick, MA, USA), fMRISTAT (Worsley et al., 2002), and SPSS (Armonk, NY, USA: IBM Corp), and were in line with our previous work (Kucyi et al., 2012, 2013, 2014). The first 4 and first 5 volumes were deleted for resting state and task scans, respectively. For all scans, motion correction (MCFLIRT) as well as linear registration (FLIRT) to T1 image (6 DOF) and standard MNI152 (12 DOF) space were performed. The transformation matrices obtained from these registrations were used in subsequent analyses (see below). To remove physiological and scanner-related noise, aCompCor (Behzadi et al., 2007) was applied. Partial volume maps of white matter (WM) and cerebrospinal fluid (CSF), obtained with FSL's FAST segmentation of T1 images, were registered to fMRI space. These images were then thresholded to retain 198 cm^3 and 20 cm^3 of voxels with the highest probability of being WM and CSF, respectively (Chai et al., 2012). Principal component analysis was applied in fMRISTAT within runs: 1) within the eroded WM volume; and 2) within the eroded CSF volume. The 5 highest variance WM components, 5 highest variance CSF components, and 6 motion parameters obtained with MCFLIRT were then regressed out of the data. Spatial smoothing (6 mm FWHM kernel) and band-pass temporal filter (0.01–0.1 Hz) were then applied. This temporal filter range is typical for resting state fMRI studies, although some studies have shown that functional connectivity at frequencies higher than 0.1 Hz may contain information relevant to cognitive processes (Norman-Haignere et al., 2012; Shirer et al., 2012). We therefore performed a supplementary analysis in which we applied a high-pass temporal filter (0.01 Hz) but no low-pass filter.

For task runs only, a general linear model (GLM) analysis was performed using FSL's FEAT to regress stimulus-/task-related activation out of the data and minimize contributions of externally-driven pain- or thought probe-related activations to FC and FCV estimates (described below). The GLM included two regressors that were convolved with a gamma hemodynamic response function: 1) 20 s pain stimulation periods, and 2) 8 s rating periods. The GLM residuals were used in all analyses of task data. While these residuals may have contained some stimulus-/task-evoked activity not explained by the GLM, our regression procedures ensured that variability in the BOLD signal across trials could not be explained by differences in mean activations evoked by pain or attentional state ratings.

Regions of interest

Regions-of-interest (ROIs) included the DMN core [posterior cingulate cortex (PCC), anterior medial prefrontal cortex (amPFC)] and subsystems [medial temporal lobe (MTL) and dorsomedial prefrontal cortex (dmPFC)]. For the DMN core regions, spherical ROIs (10 mm diameter) were created in MNI152 standard space surrounding coordinates reported by Andrews-Hanna et al. (2010b) for the PCC (xyz = −8, −56, 26) and amPFC (xyz = −6, 52, −2). The two DMN subsystem ROIs were obtained in MNI152 standard space from a data-driven 17-network whole-brain atlas defined based on a clustering approach applied to rs-fMRI and FC in 1000 healthy individuals (Yeo et al., 2011) (Fig. 2) (http://freesurfer.net/fswiki/CorticalParcellation_Yeo2011). The subsystems were selected as networks within the atlas that most closely matched the definitions provided by Andrews-Hanna et al. (2010b). The MTL subsystem bilaterally includes the posterior inferior parietal lobule (pIPL; BA 39), retrosplenial cortex (Rsp; BA 29/39/19), parahippocampal cortex (PHC; BA 20/36/19), and parts of the hippocampal formation (HF; BA 20/36). The dmPFC subsystem bilaterally included the dmPFC (BA 9/32), angular gyrus (AG; BA 39), lateral temporal cortex (BA 21/22) and temporal pole (BA 21).

To confirm and determine the generalizability of our results to other proposed DMN definition schemes, we performed additional analyses (described below) using DMN subsystems from a published rs-fMRI network atlas that was derived from an independent component analysis of data from healthy individuals (Shirer et al., 2012) (http://findlab.stanford.edu/functional_ROIs.html). This atlas includes a "ventral DMN" which partially resembles the MTL subsystem (i.e., includes bilateral pIPL, Rsp, and PHC, and additionally bilateral precuneus, bilateral middle/superior frontal gyrus, and right cerebellar lobe IX) and a spatially distinct "dorsal DMN" that does not resemble either subsystem (includes dmPFC, HF, amPFC, PCC, thalamus, and posterior AG). Since this atlas includes sensory networks that we did not expect to be related to daydreaming, we also used two of these networks (sensorimotor, primary visual) to test the specificity of our findings. The sensorimotor network includes bilaterally the precentral gyrus, postcentral gyrus, ventral thalamus and lobules V and VI of the cerebellum. The primary visual network includes bilaterally the intracalcarine cortex.

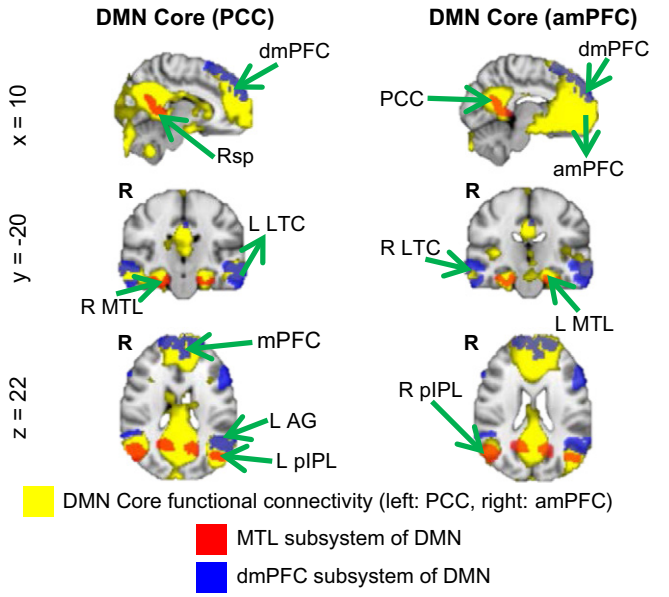

Fig. 2. Group-level (n = 51) maps illustrating whole-brain static resting state functional connectivity of the default mode network (DMN) core regions: posterior cingulate cortex (PCC) and anterior medial prefrontal cortex (amPFC) (FWE-corrected $Z > 2.3$, cluster-based $p < 0.05$). The maps are overlaid with the medial temporal lobe (MTL; red) and dorsomedial prefrontal cortex (dmPFC; blue) subsystems of the DMN defined by Yeo et al. (2011), which show a high degree of spatial overlap with both PCC and amPFC connectivity. AG = angular gyrus; LTC = lateral temporal cortex; Rsp = retrosplenial cortex; pIPL = posterior inferior parietal lobule.

Resting state fMRI analysis

We followed our previously reported procedures for seed-based FC analysis (Kucyi et al., 2012, 2014) to map whole-brain FC of the DMN core regions (PCC, amPFC). The PCC and amPFC seed regions were converted to individual fMRI space using the transformation matrix obtained with FLIRT, and the mean time series across all voxels within each seed were extracted from the preprocessed data. First-level GLMs were then performed in FEAT with FILM prewhitening and the seed time series (done separately for PCC and amPFC) entered as a regressor. The whole-brain positive connectivity maps obtained from this GLM (contrast of parameter estimate images) were then entered into a group-level mixed effects (FLAME 1) analysis in standard MNI152 space (FWE-corrected $Z > 2.3$; cluster-based $p < 0.05$).

We next tested whether FC/FCV between DMN core regions and DMN subsystems were associated with individual differences in DDF. For FC analysis, Fisher-transformed correlations of the PCC and amPFC time series with all other brain voxels were calculated. For the FCV analysis, scans were split into 30 s sliding time-windows, with the onset of each window progressively shifted by 2 s (1 TR) from that of the previous window, resulting in a total of 258 windows. Fisher-transformed correlations were calculated between seed region time series and all other brain voxels within each window. An FCV map was then created by calculating the standard deviation of these correlation values across all windows within each voxel. The FC and FCV maps were transformed to standard MNI152 space using the previously computed transformation matrix. The mean value across all voxels within standard space DMN subsystems of interest was then extracted from each seed FC and FCV map (excluding voxels that overlapped with the seed itself).

We performed four multiple linear regressions (one for each DMN seed–subsystem pair) with DDF entered as dependent variable and both FC and FCV as independent variables. For each seed–subsystem pair, there was no significant correlation between FC and FCV (PCC–MTL: $r = -0.19$, $p = 0.18$; PCC–dmPFC: $r = 0.093$, $p = 0.52$; amPFC–MTL: $r = 0.066$, $p = 0.65$; amPFC–dmPFC: $r = -0.11$, $p = 0.45$), so the FC and FCV metrics may be considered as independent contributors to DDF. A seed–subsystem pair was considered as significantly related to DDF if the multiple regression model including its FC and FCV had a $p < 0.01$ (i.e., results are Bonferonni-corrected for 4 comparisons). For significant seed–subsystem pairs, Pearson's correlation was calculated to delineate the relationship of DDF with FC and FCV. Partial correlations were also performed to determine the unique links of FC versus FCV with DDF. We tested the effect of calculating FCV using 30, 40, 50, and 60 s sliding windows on the correlation with DDF as done previously (Kucyi et al., 2013) (main results are reported for 30 s windows). Effects of motion on FC values can persist despite the performance of preprocessing steps similar to those used here (Power et al., 2012; Van Dijk et al., 2012), so here we used partial correlation to test whether mean motion, calculated as mean absolute displacement of each brain volume compared to the previously acquired volume (Van Dijk et al., 2012), affected any identified significant relationships between DDF and FC/FCV. To determine the specificity of our results, we also correlated DDF with PCC-sensorimotor network and PCC-primary visual network FC and FCV (significance set at $p < 0.05$, two-tailed).

Task fMRI analysis

To ensure that our analysis reasonably captured brain dynamics underlying intra-individual fluctuations in mind-wandering (rather than external sensory distractions or task-related interferences), only subjects who reported a minimum rating of 4 for mind-wandering on the post-scan questionnaire (n = 33) were selected for task fMRI analysis. For 30 of these subjects, 4 runs were included in the analysis, and for the remaining 3 of subjects, only 3 runs were included due to scan acquisition errors (missing trial responses, or missing brain slices). Additional analyses of 17 subjects who reported mind-wandering ratings below 4 were performed to test specificity of results to mind-wandering as opposed to external sensory distractions or task-related interferences (see below). Therefore a total of 50 subjects were included in the task fMRI analyses. Calculations of FC and FCV proceeded as in the resting state analysis for preprocessed data in each task run individually (using 30 s sliding windows to calculate FCV). Each run was classified in terms of degree of ongoing mind-wandering by calculating the percentage of total trials in the run in which a subject reported either “mostly something else” or “only something else.”

We tested whether the links identified in rs-fMRI between DDF and DMN FC/FCV could be reproduced when using independent data from task fMRI to calculate FC/FCV. For the 33 subjects included in the task fMRI analysis, we tested the directed hypothesis that the mean of PCC–MTL subsystem FC values across all task fMRI runs negatively correlates with DDF (as identified in rs-fMRI analysis, described below), with significance set at $p < 0.05$ (one-tailed). We also correlated the mean of the PCC–MTL subsystem FCV values across task fMRI runs with DDF, with significance set at $p < 0.05$ (two-tailed). These analyses were repeated using PCC–ventral DMN FC/FCV.

To perform a group analysis that assesses the link between relative fluctuations in DMN FCV and degree of mind-wandering within individuals, we normalized all values for each variable within a subject by subtracting the mean across all runs out of values in individual runs. As the rs-fMRI analysis revealed a positive correlation between individual differences in PCC–MTL subsystem FCV and DDF, we tested the directed hypothesis that a positive correlation between PCC and MTL subsystem FCV reflects the degree of ongoing mind-wandering. Pearson's correlation was calculated between normalized FCV and mind-wandering scores, using all runs in all subjects. Degrees-of-freedom were adjusted conservatively to reflect the number of constraints introduced by multiple subjects (129 runs − 33 subjects = 96 DOF), and significance was set at $p < 0.05$ (one-tailed). The analysis was repeated for the ventral DMN and using static FC. Furthermore, to explore whether our results were specific to the MTL subsystem/ventral

DMN, we conducted static FC and dynamic FCV analyses for the dmPFC subsystem of the DMN, sensorimotor network, and primary visual network (correlations reported with two-tailed p values).

To test the specificity of identified links between brain activity and mind-wandering, we repeated analyses in 17 subjects who reported mind-wandering ratings of less than 4. We expected that if brain–behavior correlations identified in subjects with mind-wandering ratings of 4 or higher were reflective of mind-wandering rather than other factors, these correlations would be reduced in magnitude in the low mind-wandering subgroup. As in the analysis of high mind-wandering subjects, degrees-of-freedom for the reported p values were adjusted (67 runs − 17 subjects = 50 DOF).

Results

Daydreaming behavior

Individuals included in the rs-fMRI (n = 51) varied in their DDF scores (mean ± SD = 34.3 ± 10.5; range: 14–56). For individuals included in the task fMRI (sensory stimulation coupled with thought probes) analysis (n = 33), the proportion of trials with mind-wandering reports across all 129 runs was 55.1% + 27.4% (mean ± SD). Within individuals, proportions of mind-wandering reports varied from run to run (group average for mean %change across within-subject runs: 19.6 ± 10.2%), indicating that individuals fluctuated in their states of mind-wandering across scanning runs. For subjects included in task fMRI analysis, there was no significant correlation between DDF and mean frequency of mind-wandering reports across task fMRI scans ($r = -0.12$, $p = 0.49$). This confirms that our paradigm of fMRI coupled with painful stimulation dissociated general individual tendencies to daydream from state-related daydreaming, consistent with our previous analysis (Kucyi et al., 2013).

Resting state: connectivity between the DMN core and subsystems

We first sought to confirm that during rs-fMRI in our sample, DMN core regions (PCC, amPFC) were functionally connected with the dmPFC and MTL DMN subsystems, as previously defined (Yeo et al., 2011). Group-level whole-brain static FC analysis revealed that both these DMN core regions were functionally connected bilaterally with the major nodes of both MTL and dmPFC subsystems (Fig. 2), including the pIPL, retrosplenial cortex, parahippocampal cortex, HF, dmPFC, angular gyrus, lateral temporal cortex, and temporal pole.

Resting state: static FC and dynamic DMN FC relate to daydreaming frequency

We next tested whether static FC and dynamic FC between DMN core regions and DMN subsystems were associated with individual differences in DDF. We have defined static FC as the correlation between activities from distinct brain regions over an entire time series in a given fMRI scan, whereas dynamic FC (FCV) was defined as the standard deviation of FC across 30 s progressively sliding windows of 2 s increments within a scan (Fig. 1) (Kucyi et al., 2013). To assess the link between DDF and DMN FC/FCV, we performed four multiple linear regressions (one for each seed–subsystem pair) with DDF entered as dependent variable and both FC and FCV as independent variables. This regression approach was motivated by the fact that for each seed–subsystem pair, there was no significant correlation between FC and FCV (see Materials and methods), so both could independently be associated with DDF. Multiple regression revealed that individual differences in DDF were significantly related to the combined variance of FC and FCV for the PCC–MTL subsystem pair ($R^2 = 0.18$, $p = 0.008$) at the Bonferonni-corrected level. In contrast, there was no significant association of DDF with the combined variance of FC and FCV for the PCC–dmPFC subsystem ($R^2 = 0.049$, $p = 0.30$), amPFC–MTL subsystem ($R^2 = 0.011$, $p = 0.76$), or amPFC–dmPFC subsystem ($R^2 = 0.013$, $p = 0.73$) pairs (Table 1).

Most striking was a clear relationship between individual tendencies to daydream, as reflected by DDF scores, and connectivity of the PCC–MTL subsystem of the DMN (Fig. 3). Specifically, DDF scores were negatively correlated with PCC–MTL subsystem static FC ($r = -0.36$, $p = 0.01$) and positively correlated with dynamic PCC–MTL subsystem FCV ($r = 0.30$, $p = .035$). These correlations remained unchanged when controlling for mean head motion (FC: $r = -0.36$, $p = 0.01$; FCV: $r = 0.30$, $p = 0.034$). When controlling for PCC–MTL subsystem FCV, the partial correlation between DDF and FC remained significant ($r = -0.32$, $p = 0.023$). When controlling for PCC–MTL subsystem FC, the partial correlation between DDF and FCV was slightly reduced ($r = 0.25$, $p = 0.08$).

To confirm and determine the generalizability of our results to other proposed DMN definition schemes, we performed additional analyses using DMN subsystems and other networks from a rs-fMRI network atlas that includes the dorsal DMN and ventral DMN as well as sensory networks including the sensorimotor network and primary visual network (see Materials and methods) (Shirer et al., 2012). The PCC–ventral DMN FC/FCV was significantly related to DDF ($R^2 = 0.26$, $p = 0.001$) at the Bonferonni-corrected level (Table 1) whereas the other core–subsystem pairs did not show significant correlations with DDF: PCC–dorsal DMN ($R^2 = 0.12$, $p = 0.052$), amPFC–ventral DMN ($R^2 = 0.012$, $p = 0.75$), and amPFC–dorsal DMN ($R^2 = 0.017$, $p = 0.66$). There were negative, and positive correlations of DDF with PCC–ventral DMN FC ($r = -0.39$, $p = 0.005$; controlling for mean head motion: $r = -0.36$, $p = 0.009$) and FCV ($r = 0.35$, $p = 0.013$; controlling for mean head motion: $r = 0.38$, $p = 0.006$), respectively (Fig. 4). When controlling for PCC–ventral DMN FCV, the correlation between DDF and FC remained significant ($r = -0.36$, $p = 0.01$). When controlling for PCC–ventral DMN FC, the correlation between DDF and FCV remained significant ($r = 0.40$, $p = 0.004$). The correlations of DDF with static FC were not significant for the PCC–sensorimotor network ($r = -0.19$, $p = 0.19$) or for the PCC–primary visual network ($r = -0.11$, $p = 0.45$). Furthermore, DDF was not significantly correlated with dynamic FCV for PCC–primary visual network ($r = 0.25$, $p = 0.08$), although a significant correlation was found for PCC–sensorimotor network ($r = 0.30$, $p = 0.03$) (Fig. S1).

It is not well established how FC dynamics revealed with rs-fMRI sliding-window analyses are affected by window duration used to calculate FCV. We therefore tested whether the relationships we identified between PCC–MTL subsystem and PCC–ventral DMN dynamic FCV with DDF were dependent on the duration of the sliding window. We found that positive correlations with DDF remained significant for PCC–MTL and PCC–ventral DMN FCV using a 40 s (instead of 30 s) sliding window (with and without controlling for FC; Table 2). However, when the sliding window was increased to 50–60 s durations, there was a deterioration of the effects we found using the shorter 30 and 40 s windows (Table 2). When we applied a high-pass but no low-pass temporal filter during preprocessing, the relationships of DDF with static FC remained significant for the PCC–MTL subsystem ($r = -0.35$, $p = 0.01$) and PCC–ventral DMN ($r = -0.36$, $p = 0.009$), but the relationships of DDF with dynamic FCV were no longer significant for the PCC–MTL subsystem ($r = 0.04$, $p = 0.76$) or for the PCC–ventral DMN ($r = 0.02$, $p = 0.88$). This suggests that fluctuations in FC that were relevant to DDF were mainly restricted to frequencies in the 0.01–0.1 Hz range.

DMN FCV tracks ongoing mind-wandering

We next used mind-wandering thought probes during fMRI to test 2 hypotheses: 1) dynamic DMN FCV, but not static FC, correlates with ongoing mind-wandering within individuals, and 2) the link between DMN FC (but not FCV) with DDF identified in the rs-fMRI analysis is reproducible during task fMRI coupled with painful stimulation. We classified the fMRI runs of sensory stimulation coupled with thought

Table 1
Resting state fMRI multiple linear regression results (n = 51) for daydreaming frequency (DDF) entered as dependent variable, and functional connectivity (FC) and FC variability (FCV) entered as independent variables for each default mode network core and subsystem pair tested separately. Pearson's correlation coefficient (*r*) values are also shown for DDF versus FC and FCV individually.

DMN core–subsystem pair	R^2 (relationship of FC and FCV with DDF)	*p*	*r* value: FC vs DDF	*r* value: FCV vs DDF
PCC–MTL	0.18	0.008*	−0.36	0.30
PCC–dmPFC	0.049	0.30	−0.11	0.18
amPFC–MTL	0.011	0.76	−0.03	−0.10
amPFC–dmPFC	0.013	0.73	−0.16	0.01
PCC–ventral DMN	0.26	0.001*	−0.35	0.39
PCC–dorsal DMN	0.12	0.052	−0.27	0.15
amPFC–ventral DMN	0.012	0.75	−0.10	0.04
amPFC–dorsal DMN	0.017	0.66	−0.11	0.07

* $p < 0.01$.

probes based on the frequency of within-run mind-wandering reports. Additionally, we calculated DMN core–subsystem FC and FCV for each run and demeaned FC, FCV, and mind-wandering frequency scores within subjects to eliminate variance related to inter-individual differences (Materials and methods). The most striking finding was that the degree of ongoing mind-wandering within a run, as measured during scanning with thought probes, was correlated with dynamic connectivity (i.e., FCV) of the PCC–MTL subsystem ($r = 0.25$, $p = 0.0063$) (Fig. 5) as well as with PCC–ventral DMN FCV ($r = 0.26$, $p = 0.0052$) in the 33 subjects with high mind-wandering ratings (Fig. 6). However, there were no significant correlations between the degree of ongoing mind-wandering and static connectivity (i.e., FC) of the PCC–MTL subsystem FC ($r = -0.0034$, $p = 0.49$) or PCC–ventral DMN FC ($r = 0.15$, $p = 0.076$) (Fig. 5). In the 17 subjects with low mind-wandering ratings (see Materials and methods), the correlations were reduced in magnitude for ongoing thoughts unrelated to the sensory stimulus being delivered versus the FCV of the PCC–MTL subsystem ($r = 0.16$, $p = 0.13$) and versus the FCV of the PCC-ventral DMN ($r = 0.18$, $p = 0.10$) (Fig. S2). This suggests that FCV–behavior relationships were largely driven by mind-wandering rather than external sensory distractions or task-related interferences.

There were significant negative correlations between DDF and mean PCC–MTL subsystem FC across task fMRI runs ($r = -0.32$, $p = 0.035$) and mean PCC–ventral DMN FC across task fMRI runs ($r = -0.34$, $p = 0.028$) (Fig. 5). Therefore, the links between DDF and FC remained regardless of the subject's cognitive state (resting versus painful stimulation). However, there were no significant correlations between DDF and mean PCC–MTL subsystem FCV across task fMRI runs ($r = -0.21$, $p = 0.24$) (Fig. 5) or mean PCC–ventral DMN FCV across task fMRI runs ($r = -0.18$, $p = 0.32$) (Fig. 6).

We also tested whether FC and FCV of the PCC with other networks correlated with the degree of ongoing mind-wandering. Correlations were as follows: dmPFC subsystem of the DMN (FC: $r = -0.19$, $p = 0.065$; FCV: $r = 0.21$, $p = 0.035$), sensorimotor network (FC: $r = 0.15$, $p = 0.16$; FCV: $r = 0.22$, $p = 0.03$), and primary visual network (FC: $r = 0.056$, $p = 0.59$; FCV: $r = 0.19$, $p = 0.066$).

Discussion

We have demonstrated that dynamic DMN connectivity fluctuations track spontaneous mind-wandering in awake humans, suggesting that resting state brain activity fluctuations are not completely independent of consciousness. We found that individual differences in daydreaming in daily life were associated with both static and dynamic aspects of DMN functional connectivity in a task-free, stimuli-independent state. Importantly, we dissociated the general tendency to daydream (DDF, likely a personality trait) from ongoing daydreaming (representing a current cognitive state) and revealed that intra-individual fluctuations in mind-wandering were associated with dynamic, but not static aspects of DMN functional configurations. These findings were specific to connectivity between the PCC and DMN subsystems involved in future-oriented thought that include the MTL, Rsp and pIPL. Importantly, our study demonstrates that dynamic FCV, based on time windows in the order of seconds, can uncover information about spontaneous

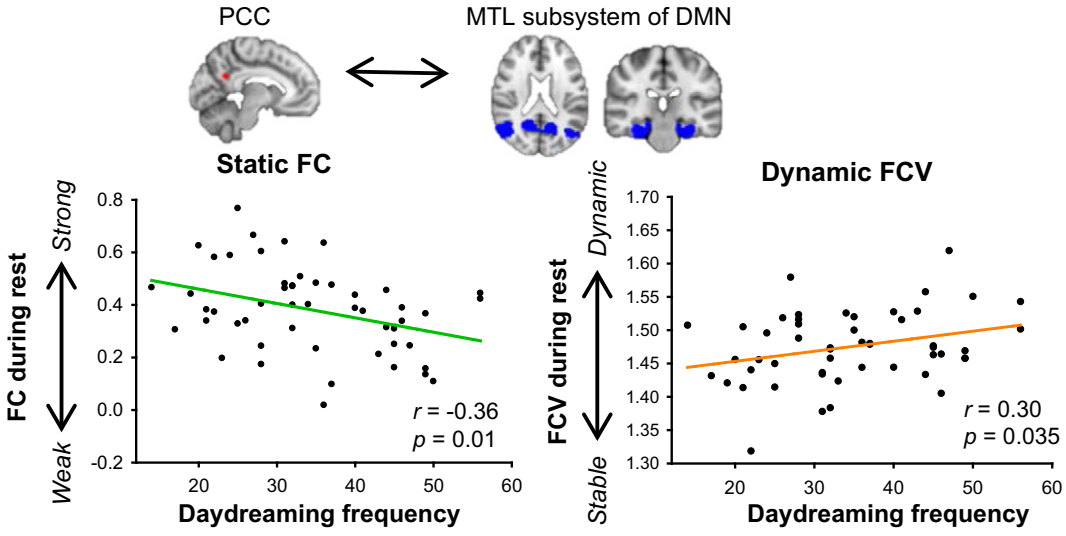

Fig. 3. Static FC and dynamic resting state functional connectivity (FC) relate to individual differences in daydreaming frequency (n = 51). Significant negative correlation between individual differences in PCC–MTL subsystem static FC and daydreaming frequency ($r = -0.36$, 2-tailed $p = 0.01$) (left), and significant positive correlation between dynamic PCC–MTL subsystem FC variability (FCV) and daydreaming frequency ($r = 0.30$, 2-tailed $p = 0.035$) (right). MTL = medial temporal lobe; PCC = posterior cingulate cortex.

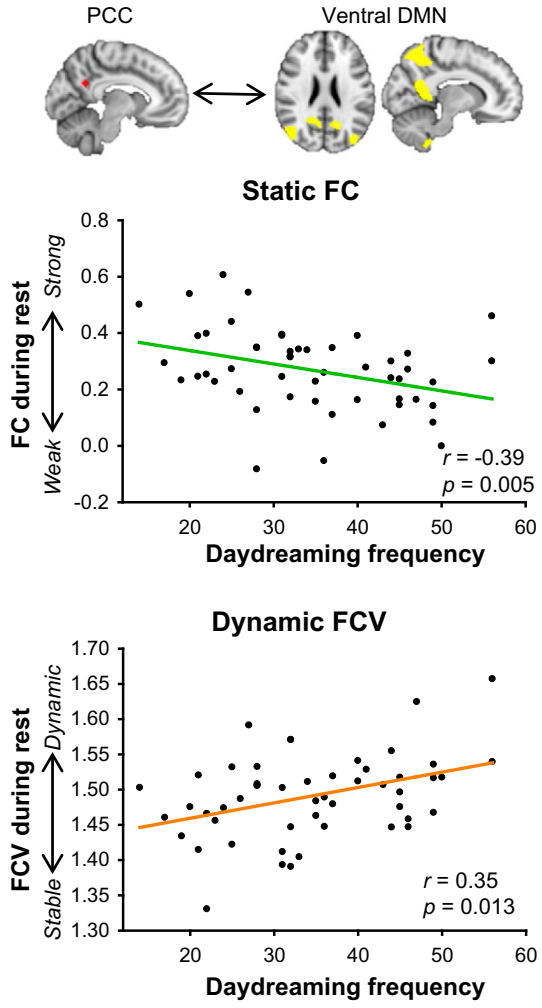

Fig. 4. Analysis of the dorsal/ventral DMN subsystems confirms that static FC and dynamic resting state functional connectivity (FC) relate to individual differences in daydreaming frequency (n = 51). Significant negative correlation between individual differences in PCC–ventral DMN FC and daydreaming frequency ($r = -0.39$, two-tailed $p = 0.005$) (top), and significant positive correlation between PCC–ventral DMN FC variability (FCV) and daydreaming frequency ($r = 0.35$, two-tailed $p = 0.013$) (bottom). DMN = default mode network; PCC = posterior cingulate cortex.

cognition not captured by the more conventional approach of analyzing static FC over several minutes. This may arise from the dynamic nature of "stream of consciousness" thoughts and feelings that fluctuate from second to second.

Since the introduction of rs-fMRI (Biswal et al., 1995), static FC analysis has predominated as the standard approach to understanding functional brain connectivity. In recent years, however, dynamic FC analysis has gained popularity despite unresolved issues regarding methodology and interpretation (Hutchison et al., 2013a). Sliding time-window FC fluctuations may arise in part from stochastic noise (Handwerker et al., 2012). However, computational models (Deco and Corbetta, 2011) and empirical data from simultaneous EEG-fMRI (Chang et al., 2013; Tagliazucchi et al., 2012) as well as fMRI coupled with local field potential recordings (Thompson et al., 2013) strongly suggest a neural basis of dynamic FC. While the behavioral relevance of dynamic FC is currently poorly characterized, here we show that both inter-individual variability and intra-individual variability in behavior are linked with spontaneous FC fluctuations.

Notably, previous studies have shown that inter-individual differences in spontaneous cognition during rs-fMRI, as reported immediately after scanning, are associated with variability in static DMN FC (Andrews-Hanna et al., 2010a; Doucet et al., 2012). However, it is possible that individuals with a greater general tendency to daydream were mind-wandering more frequently during these scans (Mason et al., 2007), and that these FC differences reflect unconscious, intrinsic brain organization, perhaps related to personality or previous experiences rather than the ongoing cognition. Our study differs from this previous work in that we assessed variable states of mind-wandering within individuals, and we analyzed dynamic in addition to static FC. Our combined analyses of rs-fMRI and fMRI coupled with thought probes suggest that static PCC–MTL subsystem/ventral DMN FC may reflect intrinsic individual differences in functional brain organization independent of cognitive state. Therefore, the relationship between FC and DDF remains regardless of the contents of the ongoing cognition. On the other hand, dynamic FCV between the same regions may reflect ongoing daydreaming. If this is the case, the correlation between DDF and FCV at rest, but not during sensory stimulation, may be explained by high DDF individuals mind-wandering the most intensely and/or frequently during the resting state. This is supported by the fact that the degree of ongoing mind-wandering, but not DDF, correlated with FCV during sensory stimulation. As our sensory stimulation paradigm dissociated the trait of DDF from the state of mind-wandering, our findings provide a unique window into the relationship between spontaneous brain dynamics and cognition. However, further studies of mind-wandering away from other sensory events besides pain would be needed to determine whether our results are specific to mind-wandering away from pain or not.

Our finding of a negative correlation between DDF and static DMN FC may seem counterintuitive if the DMN is thought of as a network whose integrated function supports mind-wandering. Andrews-Hanna et al. (2010a) reported a positive correlation between static FC within the DMN's MTL subsystem and the percentage of time that participants spent thinking about the past and future during a resting state scan, seemingly in contrast to our results. We are unaware of any previous studies linking DDF with resting state DMN FC. However, some studies may be in line with our results. Doucet et al. (2012) found lower within-DMN FC in individuals with greater visual mental imagery and inner language thoughts during resting state scans. Gordon et al. (2014) reported a negative correlation between within-DMN FC and trait-level inattention, a measure of inability to focus on a task at hand that may be related to DDF. Furthermore, if a general tendency to daydream is comparable to a state of sleepiness/dreaming as has been suggested (Fox et al., 2013), studies of sleep support our findings as they have shown that within-DMN FC decreases in the transition from

Table 2
Effect of sliding window duration used to calculate resting state FCV on the correlation of daydreaming frequency (DDF) with PCC–MTL subsystem and PCC–ventral DMN FCV (n = 51).

		Correlation between DDF and FCV							
		30 s windows		40 s windows		50 s windows		60 s windows	
		r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
PCC–MTL subsystem	Without controlling for FC	0.30	0.035	0.30	0.031	0.13	0.35	0.18	0.21
	Controlling for FC	0.25	0.08	0.30	0.036	0.17	0.23	0.23	0.11
PCC–ventral DMN	Without controlling for FC	0.35	0.013	0.39	0.005	0.21	0.13	0.30	0.031
	Controlling for FC	0.40	0.004	0.44	0.002	0.27	0.057	0.40	0.004

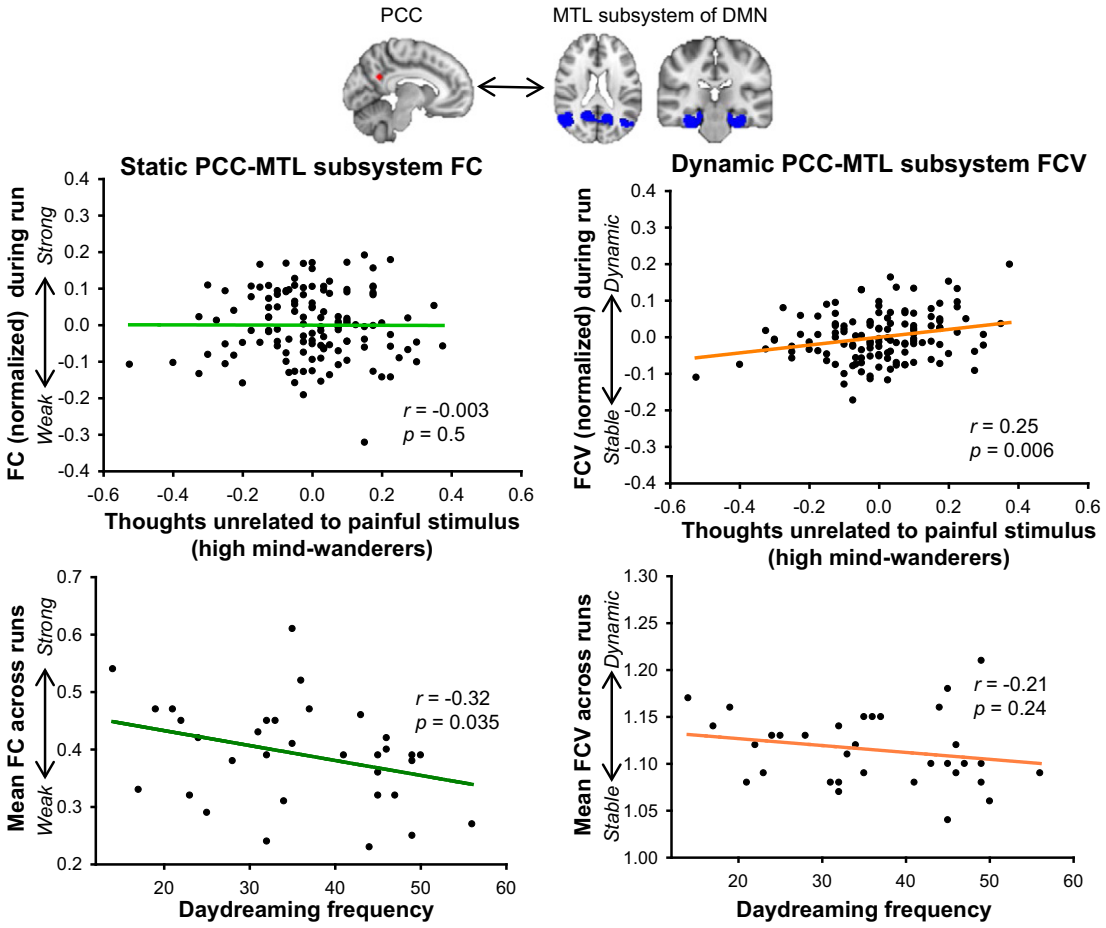

Fig. 5. Results from fMRI coupled with sensory stimulation and thought probes. (Top) Dynamic functional connectivity variability (FCV), but not static functional connectivity (FC), between PCC and MTL subsystem reflects intra-individual ongoing mind-wandering (respectively, $r = 0.25$, 1-tailed $p = 0.0063$ and $r = -0.003$, 1-tailed $p = 0.49$). Individuals were scanned four times with concurrent thought probes to indicate their degree of ongoing mind-wandering (frequency of mind-wandering reports within a run). Each point on each plot illustrates data from an individual scan (total of 129 scans across 33 subjects). Values for each variable were normalized within a subject by subtracting the mean across all runs out of values in individual runs. (Bottom) Mean static FC, but not dynamic FCV across task runs, significantly correlates with inter-individual differences in daydreaming frequency (respectively, $r = -0.32$, 1-tailed $p = 0.035$ and $r = -0.21$, 2-tailed $p = 0.24$).

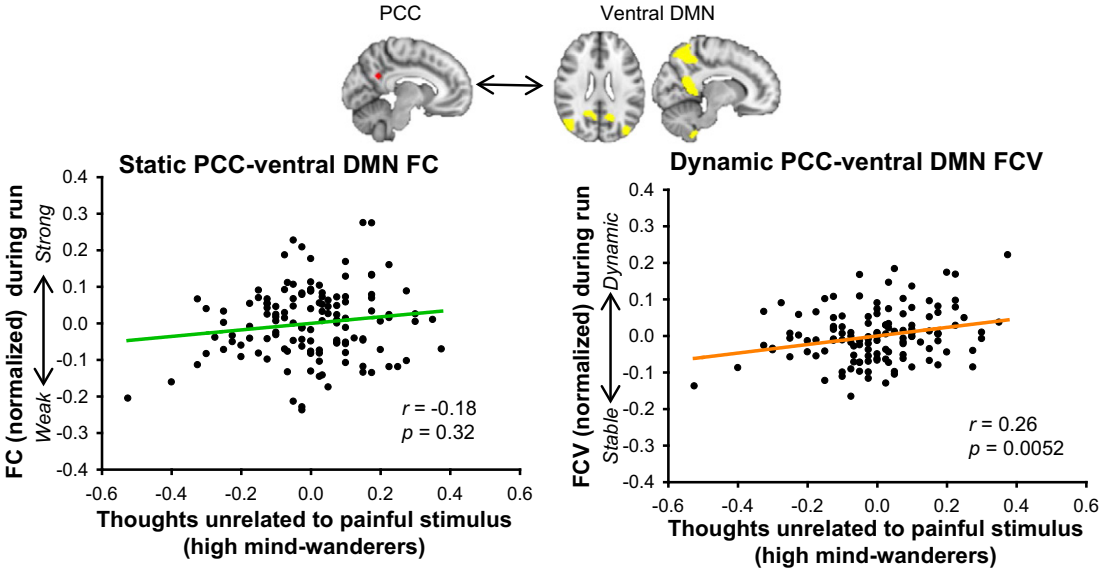

Fig. 6. Analysis of the dorsal/ventral DMN subsystems confirms link between ongoing mind-wandering and FCV from fMRI coupled with sensory stimulation and thought probes. Dynamic functional connectivity variability (FCV), but not static functional connectivity (FC), between PCC and MTL subsystem significantly correlates with intra-individual ongoing mind-wandering (respectively, $r = 0.26$, one-tailed $p = 0.0052$ and $r = 0.15$, one-tailed $p = 0.076$). Individuals were scanned four times with concurrent thought probes to indicate their degree of ongoing mind-wandering (frequency of mind-wandering reports within a run). Each point on each plot illustrates data from an individual scan (total of 129 scans across 33 subjects). Values for each variable were normalized within a subject by subtracting the mean across all runs out of values in individual runs.

wakefulness to sleep (Chow et al., 2013; Samann et al., 2011), sleep deprivation reduces within-DMN FC (Bosch et al., 2013), and daytime sleepiness is negatively correlated with within-DMN FC (Ward et al., 2013).

Across individuals and populations, mind-wandering is known to be predominantly future-focused and is thought to function in routine autobiographical planning (Baird et al., 2011; Stawarczyk et al., 2011a). Activation of the MTL subsystem of the DMN has been linked with future-oriented thought based on memory (Andrews-Hanna et al., 2010b), and FC within the MTL subsystem has been associated with individual differences in frequency of past/future-oriented thoughts during rs-fMRI (Andrews-Hanna et al., 2010a). Furthermore, direct electrophysiological recordings in humans undergoing brain surgery have revealed increased theta band phase locking between the Rsp and MTL during autobiographical retrieval (Foster et al., 2013). Our findings extend upon this work, implicating connectivity of the MTL subsystem to daydreaming. We also found PCC FC and FCV with the ventral DMN, which includes not only the MTL subsystem regions but also other non-DMN regions (e.g. precuneus and prefrontal regions that were not found to be functionally connected with either PCC or amPFC in our group-level analysis), to be even more strongly related with DDF and ongoing mind-wandering than PCC–MTL subsystem interactions. Furthermore, PCC FCV with sensory networks (sensorimotor and primary visual networks) was found to positively correlate with DDF and with ongoing mind-wandering. This raises the intriguing possibility that the PCC, as a major hub within the brain as a whole (Hagmann et al., 2008), dynamically coordinates the interactions between DMN subsystems and other networks to maintain or suppress attention to stimulus-independent thoughts versus the external environment. A recent magnetoencephalography study of dynamic FC demonstrated that the PCC, compared to other brain regions, functions most frequently in cross-network interactions and engages with nodes of non-DMN networks when those nodes disengage from their corresponding networks (de Pasquale et al., 2012). Future work is needed to uncover the potential relevance of these ms-scale inter-network interactions to spontaneous cognition.

Interpretation of the positive direction of the correlations that we identified between dynamic FCV and daydreaming may be informed by considering studies linking regional brain variability with behavioral performance (Garrett et al., 2011, 2013; Misic et al., 2010). Posteromedial cortical regions, including the PCC, show the greatest increase in brain variability during development (Misic et al., 2010), possibly reflective of increased capacity for higher order cognitive processes that are engaged during daydreaming. Regions within the DMN show decreasing variability in activity during performance of tasks with greater difficulty (Garrett et al., 2013) when mind-wandering would be expected to be minimized. This may be analogous to a state of stable DMN FC, which our data indicate is associated with lower ongoing mind-wandering.

Our fMRI study did not afford us the temporal resolution to investigate dynamic FC underlying single spontaneous cognitive events. Instead, we calculated FCV across 30 s sliding time-windows within scans and linked this with an overall state of mind-wandering indexed by multiple thought probes. This approach was motivated by our previous finding of a link between FCV and individual differences in pain-related cognition (Kucyi et al., 2013), which suggested that FCV is a behaviorally-relevant metric as confirmed and extended upon here. Our paradigm of sensory stimulation coupled with thought probes was not suitable for examining transient changes in FCV during mind-wandering events, as stimuli were only 20 s in duration and we could not determine precisely when attention shifted from a stimulus to a stimulus-independent cognition. Future studies with thought probes during a task-/stimulus-free state may enable further insights into the neural network dynamics of spontaneous cognition.

While there is no ideal sliding window duration for dynamic FC analysis, previous studies have mostly used 30–60 s windows because these durations are short enough to capture interesting transient events but long enough to avoid issues such as poor sampling for correlation analysis and decreased fMRI signal-to-noise when using few data points to analyze FC (Hutchison et al., 2013a). We present our main FCV results with 30 s sliding windows to capture the dynamics of spontaneous cognition, and were motivated by the finding that only 30 s of whole-brain FC patterns are sufficient to identify subject-driven cognitive states with significant accuracy (Shirer et al., 2012). The correlations between DMN FCV and DDF tended to decrease in magnitude when using 50–60 s window durations, suggesting that variability across longer windows does not adequately capture the dynamics of spontaneous cognition. Our findings of no significant correlations between FC and FCV for the region–network pairs that we analyzed, coupled with dissociated relationships with behavior for FC versus FCV, suggest that FCV analysis is sensitive to different aspects of brain network activity than FC.

In conclusion, our results demonstrate that that dynamic DMN connectivity fluctuations track ongoing daydreaming and highlight the relevance of rich temporal information in fMRI network connectivity data to behavior. While dynamic FC during rs-fMRI in part reflects endogenous, intrinsic brain function unrelated to current cognition, variable functional configurations within at least some brain networks do reflect ongoing conscious processes. The involvement of spontaneous cognition in dynamic FC fluctuations should thus be considered when interpreting the results of all studies of brain activity during states that involve mind-wandering — a ubiquitous, defining human experience.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2014.06.044.

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References

Allen, E.A., Damaraju, E., Plis, S.M., Erhardt, E.B., Eichele, T., Calhoun, V.D., 2014. Tracking whole-brain connectivity dynamics in the resting state. Cereb. Cortex 24, 663–676.
Andrews-Hanna, J.R., Reidler, J.S., Huang, C., Buckner, R.L., 2010a. Evidence for the default network's role in spontaneous cognition. J. Neurophysiol. 104, 322–335.
Andrews-Hanna, J.R., Reidler, J.S., Sepulcre, J., Poulin, R., Buckner, R.L., 2010b. Functional–anatomic fractionation of the brain's default network. Neuron 65, 550–562.
Baird, B., Smallwood, J., Schooler, J.W., 2011. Back to the future: autobiographical planning and the functionality of mind-wandering. Conscious. Cogn. 20, 1604–1611.
Behzadi, Y., Restom, K., Liau, J., Liu, T.T., 2007. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. NeuroImage 37, 90–101.
Biswal, B., Yetkin, F.Z., Haughton, V.M., Hyde, J.S., 1995. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn. Reson. Med. 34, 537–541.
Bosch, O.G., Rihm, J.S., Scheidegger, M., Landolt, H.P., Stampfli, P., Brakowski, J., Esposito, F., Rasch, B., Seifritz, E., 2013. Sleep deprivation increases dorsal nexus connectivity to the dorsolateral prefrontal cortex in humans. Proc. Natl. Acad. Sci. U. S. A. 110, 19597–19602.
Buckner, R.L., Krienen, F.M., Yeo, B.T., 2013. Opportunities and limitations of intrinsic functional connectivity MRI. Nat. Neurosci. 16, 832–837.
Chai, X.J., Castanon, A.N., Ongur, D., Whitfield-Gabrieli, S., 2012. Anticorrelations in resting state networks without global signal regression. NeuroImage 59, 1420–1428.
Chang, C., Glover, G.H., 2010. Time-frequency dynamics of resting-state brain connectivity measured with fMRI. NeuroImage 50, 81.
Chang, C., Liu, Z., Chen, M.C., Liu, X., Duyn, J.H., 2013. EEG correlates of time-varying BOLD functional connectivity. NeuroImage 72, 227–236.
Chow, H.M., Horovitz, S.G., Carr, W.S., Picchioni, D., Coddington, N., Fukunaga, M., Xu, Y., Balkin, T.J., Duyn, J.H., Braun, A.R., 2013. Rhythmic alternating patterns of brain activity distinguish rapid eye movement sleep from other states of consciousness. Proc. Natl. Acad. Sci. U. S. A. 110, 10300–10305.
Christoff, K., Gordon, A.M., Smallwood, J., Smith, R., Schooler, J.W., 2009. Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. Proc. Natl. Acad. Sci. U. S. A. 106, 8719–8724.
Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29, 162–173.

de Pasquale, F., Della Penna, S., Snyder, A.Z., Marzetti, L., Pizzella, V., Romani, G.L., Corbetta, M., 2012. A cortical core for dynamic integration of functional networks in the resting human brain. Neuron 74, 753–764.
Deco, G., Corbetta, M., 2011. The dynamical balance of the brain at rest. Neuroscientist 17, 107–123.
Doucet, G., Naveau, M., Petit, L., Zago, L., Crivello, F., Jobard, G., Delcroix, N., Mellet, E., Tzourio-Mazoyer, N., Mazoyer, B., Joliot, M., 2012. Patterns of hemodynamic low-frequency oscillations in the brain are modulated by the nature of free thought during rest. NeuroImage 59, 3194–3200.
Foster, B.L., Kaveh, A., Dastjerdi, M., Miller, K.J., Parvizi, J., 2013. Human retrosplenial cortex displays transient theta phase locking with medial temporal cortex prior to activation during autobiographical memory retrieval. J. Neurosci. 33, 10439–10446.
Fox, K.C., Nijeboer, S., Solomonova, E., Domhoff, G.W., Christoff, K., 2013. Dreaming as mind wandering: evidence from functional neuroimaging and first-person content reports. Front. Hum. Neurosci. 7, 412.
Garrett, D.D., Kovacevic, N., McIntosh, A.R., Grady, C.L., 2011. The importance of being variable. J. Neurosci. 31, 4496–4503.
Garrett, D.D., McIntosh, A.R., Grady, C.L., 2013, June 7. Brain signal variability is parametrically modifiable. Cereb. Cortex [Epub ahead of print].
Gordon, E.M., Breeden, A.L., Bean, S.E., Vaidya, C.J., 2014. Working memory-related changes in functional connectivity persist beyond task disengagement. Hum. Brain Mapp. 35, 1004–1017.
Hagmann, P., Cammoun, L., Gigandet, X., Meuli, R., Honey, C.J., Wedeen, V.J., Sporns, O., 2008. Mapping the structural core of human cerebral cortex. PLoS Biol. 6, e159.
Handwerker, D.A., Roopchansingh, V., Gonzalez-Castillo, J., Bandettini, P.A., 2012. Periodic changes in fMRI connectivity. NeuroImage 63, 1712–1719.
Horovitz, S.G., Fukunaga, M., de Zwart, J.A., van Gelderen, P., Fulton, S.C., Balkin, T.J., Duyn, J.H., 2008. Low frequency BOLD fluctuations during resting wakefulness and light sleep: a simultaneous EEG-fMRI study. Hum. Brain Mapp. 29, 671–682.
Hutchison, R.M., Womelsdorf, T., Allen, E.A., Bandettini, P.A., Calhoun, V.D., Corbetta, M., Della Penna, S., Duyn, J.H., Glover, G.H., Gonzalez-Castillo, J., Handwerker, D.A., Keilholz, S., Kiviniemi, V., Leopold, D.A., de Pasquale, F., Sporns, O., Walter, M., Chang, C., 2013a. Dynamic functional connectivity: promise, issues, and interpretations. NeuroImage 80, 360–378.
Hutchison, R.M., Womelsdorf, T., Gati, J.S., Everling, S., Menon, R.S., 2013b. Resting-state networks show dynamic functional connectivity in awake humans and anesthetized macaques. Hum. Brain Mapp. 34, 2154–2177.
Jenkinson, M., Beckmann, C.F., Behrens, T.E., Woolrich, M.W., Smith, S.M., 2012. FSL. NeuroImage 62, 782–790.
Killingsworth, M.A., Gilbert, D.T., 2010. A wandering mind is an unhappy mind. Science 330, 932.
Kucyi, A., Hodaie, M., Davis, K.D., 2012. Lateralization in intrinsic functional connectivity of the temporoparietal junction with salience- and attention-related brain networks. J. Neurophysiol. 108, 3382–3392.
Kucyi, A., Salomons, T.V., Davis, K.D., 2013. Mind wandering away from pain dynamically engages antinociceptive and default mode brain networks. Proc. Natl. Acad. Sci. U. S. A. 110, 18692–18697.
Kucyi, A., Moayedi, M., Weissman-Fogel, I., Goldberg, M.B., Freeman, B.V., Tenenbaum, H.C., Davis, K.D., 2014. Enhanced medial prefrontal-default mode network functional connectivity in chronic pain and its association with pain rumination. J. Neurosci. 34, 3969–3975.
Majeed, W., Magnuson, M., Hasenkamp, W., Schwarb, H., Schumacher, E.H., Barsalou, L., Keilholz, S.D., 2011. Spatiotemporal dynamics of low frequency BOLD fluctuations in rats and humans. NeuroImage 54, 1140–1150.
Mason, M.F., Norton, M.I., Van Horn, J.D., Wegner, D.M., Grafton, S.T., Macrae, C.N., 2007. Wandering minds: the default network and stimulus-independent thought. Science 315, 393–395.
Misic, B., Mills, T., Taylor, M.J., McIntosh, A.R., 2010. Brain noise is task dependent and region specific. J. Neurophysiol. 104, 2667–2676.
Norman-Haignere, S.V., McCarthy, G., Chun, M.M., Turk-Browne, N.B., 2012. Category-selective background connectivity in ventral visual cortex. Cereb. Cortex 22, 391–402.
Power, J.D., Barnes, K.A., Snyder, A.Z., Schlaggar, B.L., Petersen, S.E., 2012. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. NeuroImage 59, 2142–2154.
Raichle, M.E., Snyder, A.Z., 2007. A default mode of brain function: a brief history of an evolving idea. NeuroImage 37, 1083–1090 (discussion 1097–1089).
Samann, P.G., Wehrle, R., Hoehn, D., Spoormaker, V.I., Peters, H., Tully, C., Holsboer, F., Czisch, M., 2011. Development of the brain's default mode network from wakefulness to slow wave sleep. Cereb. Cortex 21, 2082–2093.
Shirer, W.R., Ryali, S., Rykhlevskaia, E., Menon, V., Greicius, M.D., 2012. Decoding subject-driven cognitive states with whole-brain connectivity patterns. Cereb. Cortex 22, 158–165.
Singer, J.L., Antrobus, J.S. (Eds.), 1972. The Function and Nature of Imagery. Academic Press, New York.
Stawarczyk, D., Majerus, S., Maj, M., Van der Linden, M., D'Argembeau, A., 2011a. Mind-wandering: phenomenology and function as assessed with a novel experience sampling method. Acta Psychol. (Amst) 136, 370–381.
Stawarczyk, D., Majerus, S., Maquet, P., D'Argembeau, A., 2011b. Neural correlates of ongoing conscious experience: both task-unrelatedness and stimulus-independence are related to default network activity. PLoS One 6, e16997.
Tagliazucchi, E., von Wegner, F., Morzelewski, A., Brodbeck, V., Laufs, H., 2012. Dynamic BOLD functional connectivity in humans and its electrophysiological correlates. Front. Hum. Neurosci. 6, 339.
Thompson, G.J., Merritt, M.D., Pan, W.J., Magnuson, M.E., Grooms, J.K., Jaeger, D., Keilholz, S.D., 2013. Neural correlates of time-varying functional connectivity in the rat. NeuroImage 83C, 826–836.
Van Dijk, K.R., Sabuncu, M.R., Buckner, R.L., 2012. The influence of head motion on intrinsic functional connectivity MRI. NeuroImage 59, 431–438.
Vanhaudenhuyse, A., Noirhomme, Q., Tshibanda, L.J., Bruno, M.A., Boveroux, P., Schnakers, C., Soddu, A., Perlbarg, V., Ledoux, D., Brichant, J.F., Moonen, G., Maquet, P., Greicius, M.D., Laureys, S., Boly, M., 2010. Default network connectivity reflects the level of consciousness in non-communicative brain-damaged patients. Brain 133, 161–171.
Vincent, J.L., Patel, G.H., Fox, M.D., Snyder, A.Z., Baker, J.T., Van Essen, D.C., Zempel, J.M., Snyder, L.H., Corbetta, M., Raichle, M.E., 2007. Intrinsic functional architecture in the anaesthetized monkey brain. Nature 447, 83–86.
Ward, A.M., McLaren, D.G., Schultz, A.P., Chhatwal, J., Boot, B.P., Hedden, T., Sperling, R.A., 2013. Daytime sleepiness is associated with decreased default mode network connectivity in both young and cognitively intact elderly subjects. Sleep 36, 1609–1615.
Worsley, K.J., Liao, C.H., Aston, J., Petre, V., Duncan, G.H., Morales, F., Evans, A.C., 2002. A general statistical analysis for fMRI data. NeuroImage 15, 1–15.
Yeo, B.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zollei, L., Polimeni, J.R., Fischl, B., Liu, H., Buckner, R.L., 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J. Neurophysiol. 106, 1125–1165.