Spectral Diversity in Default Mode Network Connectivity Reflects Behavioral State

Michael M. Craig, Anne E. Manktelow, Barbara J. Sahakian, David K. Menon, and Emmanuel A. Stamatakis

Abstract

Default mode network (DMN) functional connectivity is thought to occur primarily in low frequencies (<0.1 Hz), resulting in most studies removing high frequencies during data preprocessing. In contrast, subtractive task analyses include high frequencies, as these are thought to be task relevant. An emerging line of research explores resting fMRI data at higher-frequency bands, examining the possibility that functional connectivity is a multiband phenomenon. Furthermore, recent studies suggest DMN involvement in cognitive processing; however, without a systematic investigation of DMN connectivity during tasks, its functional contribution to cognition cannot be fully understood. We bridged these concurrent lines of research by examining the contribution of high frequencies in the relationship between DMN and dorsal attention network at rest and during task execution. Our findings revealed that the inclusion of high frequencies alters between network connectivity, resulting in reduced anticorrelation and increased positive connectivity between DMN and dorsal attention network. Critically, increased positive connectivity was observed only during tasks, suggesting an important role for high-frequency fluctuations in functional integration. Moreover, within-DMN connectivity during task execution correlated with RT only when high frequencies were included. These results show that DMN does not simply deactivate during task execution and suggest active recruitment while performing cognitively demanding paradigms.

INTRODUCTION

Large-scale brain networks form a complex system of connections capable of supporting a wide range of behaviors. Using fMRI, multiple brain networks have been consistently identified using a variety of statistical techniques (Smith et al., 2009; Damoiseaux et al., 2006). Many of these networks have substantial overlap with brain areas important to various tasks, suggesting the collective activity of the network mediates exteroceptive attention (Dosenbach et al., 2007). The default mode network (DMN), despite initial studies suggesting it deactivates during externally driven tasks (Mazoyer et al., 2001; Shulman et al., 1997), has recently been shown to play a crucial role in a variety of introspective and attentionally demanding tasks (Vatansever, Menon, Manktelow, Sahakian, & Stamatakis, 2015a, 2016; Buckner & Carroll, 2006). This includes introspective attentional processes such as autobiographical memory, prospective memory, moral judgment, and theory of mind (Spreng, Sepulcre, Turner, Stevens, & Schacter, 2013; Andrews-Hanna, 2012; Spreng & Grady, 2010; Buckner, Andrews-Hanna, & Schacter, 2008), as well as attentionally demanding executive function tasks (Vatansever, Menon, Manktelow, Sahakian, & Stamatakis, 2015b).

A recurrent element in brain network studies is that network fluctuation is maximally observed at low frequencies; therefore, most researchers bandpass filter their data before statistical analysis, typically retaining frequencies above ~0.01 Hz and below ~0.1 Hz (Murphy, Birn, & Bandettini, 2013; Fox et al., 2005; Fransson, 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Biswal, Yetkin, Haughton, & Hyde, 1995). Although it is true that most statistical power is contained within these low frequencies, recent work has shown that higher frequencies (those above 0.1 Hz) also contain non-noise signal (Kalcher et al., 2014). High-pass filtering is relatively uncontroversial, as it removes low-frequency drifts due to scanner noise. However, low-pass filtering has been shown to be problematic in that it decreases sensitivity to task-related activations without increasing specificity (Della-Maggiore, Chau, Peres-Neto, & McIntosh, 2002; Skudlarski, Constable, & Gore, 1999) and induces spurious autocorrelation in resting-state studies (Davey, Grayden, Egan, & Johnston, 2013). Furthermore, recent work has found that many artifactual signals have spectral peaks within the low frequencies used to identify large-scale networks or are aliased into these frequencies by the low sampling rate of fMRI (Van Dijk et al., 2010; Birn, Smith, Jones, & Bandettini, 2008). Recently, these problems have been dealt with through novel denoising statistical techniques like the anatomical CompCor (aCompCor; Chai, Castañon, Ongür, & Whitfield-Gabrieli, 2012; Behzadi, Restom, Liu, & Liu, 2007), in which principle components from noise ROIs and movement parameters and their first derivatives are removed.
There is a small but growing body of literature focused on understanding high-frequency contributions to functional connectivity measures (De Domenico, Sasai, & Arenas, 2016; Lewis, Setsompop, Rosen, & Polimeni, 2016; Chen & Glover, 2015; Gohel & Biswal, 2015; Kalcher et al., 2014; Boyacioglu, Beckmann, & Barth, 2013; Niazy, Xie, Miller, Beckmann, & Smith, 2011; Wu et al., 2008). A recent study by Chen and Glover (2015) collected resting-state data at different echo times (TEs) to examine the relative contributions of BOLD and non-BOLD components to resting-state connectivity at different timescales. Their study focused on connectivity in DMN and the executive control network (a subnetwork of the dorsal attention network [DAN]) and found altered spatial patterns at different frequency bands. Notably, they found that some participants showed anticorrelations between DMN and executive control network only in low frequencies. These connections became positive when sampled between 0.2 and 0.4 Hz, suggesting that anticorrelations between DMN and DAN, as initially described by Fox et al. (2005) and Fransson (2005), may be frequency dependent. Furthermore, studies comparing network connectivity between resting state and tasks tend to retain high frequencies, with the assumption that behaviorally relevant signals are in the higher ranges (Cole, Takuya, Bassett, & Schultz, 2016; Schultz & Cole, 2016; Cole, Bassett, Power, Braver, & Petersen, 2014). This is due to the fact that univariate analyses of task-based fMRI data typically employ high-pass filters. Although this is a sensible intuition, a direct investigation of bandpass and high-pass filtered datasets and the effect of filtering on DMN connectivity during tasks has not yet been performed.

The current study fills this gap in the literature by presenting novel evidence of higher-frequency DMN connectivity and its relationship to behavior. Data from resting state, a finger opposition task (blocked design), and a stop signal task (SST; event-related design) were temporally preprocessed in two different ways, one using bandpass filtering (0.009 < f < 0.08) and one using high-pass filtering (0.09 < f < 0.25). These tasks were selected to investigate how temporal filtering affects DMN connectivity during both block and event-related task designs. We hypothesized that the inclusion of high frequencies would alter connectivity patterns between DMN and DAN across behavioral state. Furthermore, we hypothesized that retaining high-frequency fluctuations in the DMN would be associated with task performance.

**METHODS**

**Participants**

This study was approved by the Cambridgeshire 2 research ethics committee (LREC 08/H0308/2/46), and all participants gave written informed consent before testing. All participants were right-handed, had no history of psychiatric or neurological disease, had no history of drug or alcohol abuse, had no contraindication to MRI scanning or severe claustrophobia, and were not taking medications that affect their physical or cognitive performance. Additional exclusion criteria required a score above 70 on the National Adult Reading Test and a score above 23 on the Mini Mental State Examination. Twenty-two healthy participants were included in the study (19–57 years old, M = 35.0, SD = 11.2, 9 women and 13 men). Participants had average scores of 117.1 (SD = 5.76) on the National Adult Reading Test and 29.33 (SD = 0.85) on the Mini Mental State Examination.

**Paradigm Specifications**

**Resting State**

Participants underwent a 5-min resting-state scan where they were instructed to stay still and keep their eyes closed.

**Motor Task**

The motor task is a boxcar design, self-paced finger opposition paradigm with five alternating 30-sec blocks of task and fixation (5 min total). Participants were instructed to touch their fingers with their right thumb, moving sequentially from the index to the little finger. They continued this process throughout the entire duration of the task block. The task block was initiated by participants seeing the word “move” on the screen, whereas fixation blocks started with participants seeing the word “rest.”

**Stop Signal Task**

The SST is an event-related fMRI paradigm and has previously been described by Rubia et al. (Rubia, Smith, Taylor, & Brammer, 2007; Rubia, Smith, Brammer, & Taylor, 2003). Briefly, an arrow is displayed on a computer screen (white on black background) that is facing either left or right. Participants are instructed to respond with their right index or middle fingers, depending on the arrow direction (go trials). This task has a total of 240 trials, including 200 go trials and 40 stop trials. There were a minimum of three and a maximum of seven go trials between each stop trial. The stimulus duration for go trials was 1000 msec, whereas the stop trial stimulus duration was a minimum of 100 msec and maximum of 300 msec. In a subset of trials, the arrow is followed by another arrow pointing upwards (stop trials), indicating the participant should stop themselves from pressing a button. For the first stop trial, the interval between onset of the go trial and onset of the stop trial (i.e., stop signal delay [SSD]) was 150 msec. Stopping difficulty is manipulated across trials by a tracking algorithm described by Rubia et al. (2003) that is designed to alter the time interval between go and stop signals, so that each participant succeeds in 50% of the stop trials.
Successful inhibition resulted in the SSD to increase by 50 msec, whereas unsuccessful inhibition resulted in SSD decreasing by 50 msec. This ensures that each participant is working at the edge of their ability, resulting in a comparable level of difficulty between participants. Of the four conditions included in this task (go success, go failure, stop success, stop failure), only go success trials were considered in this study. This is because we are interested in measuring task-related activity generally, not neural activity specific to stop inhibition. One participant was removed from the SST because of excessive head motion during scanning, leaving 21 participants in this group.

Data Acquisition

MRI data were obtained using a Siemens (Erlangen, Germany) Trio 3T scanner equipped with a 12-channel head matrix transmit–receive coil at the Wolfson Brain Imaging Centre at Addenbrooke’s Hospital in Cambridge, UK. First, participants underwent a high-resolution T1-weighted, magnetization-prepared 180° radio frequency pulses and rapid gradient-echo (MPRAGE) structural scan (repetition time [TR] = 2300 msec, TE = 2.98 msec, TA = 9.14 min, flip angle = 9°, field of view read = 256 mm, voxel size = 1.0 × 1.0 × 1.0 mm, slices per slab = 176). The structural scan was followed by whole-brain EPI for the resting state, motor task, and SST (TR = 2000 msec, TE = 30 msec, flip angle = 78°, field of view read = 192 mm, voxel size = 3.0 × 3.0 × 3.75 mm, volumes = 160, slices per volume = 32). Other tasks were also completed by the participants (n-back, Tower of London, and Rapid Visual Information Processing) and were presented in a randomized order. The motor task always followed the resting-state scan, and randomization of the remaining tasks was used to avoid potential fatigue on any single task. Portions of these data were used in previously published studies to address alternative experimental questions (Vatansever, Manktelow, Sahakian, Menon, & Stamatakis, 2017; Moreno-López, Sahakian, Manktelow, Menon, & Stamatakis, 2016; Vatansever et al., 2015a, 2015b, 2016).

Preprocessing

Preprocessing for resting-state functional data and task functional data followed an identical pipeline described below.

Spatial Preprocessing

Spatial preprocessing for functional and structural images was performed using SPM 8.0 (www.filion.ucl.ac.uk/spm/) and MATLAB version 2008a (www.mathworks.co.uk/products/matlab/). Weissenbacher et al. (2009) performed a comprehensive analysis of preprocessing step order and found the following order to be most optimal: (1) slice timing correction, (2) realignment, (3) spatial normalization, (4) smoothing, and (5) noise signal removal. We deviated slightly from Step 5 in that we used the aCompCor method for removing noise signals (Behzadi et al., 2007). Otherwise, we used the preprocessing step order they defined in their article. For all functional scans, the first five volumes were removed to eliminate saturation effects and achieve steady-state magnetization. Subsequently, functional data were slice-time adjusted and underwent motion correction using SPM realign. High-resolution T1 structural images were coregistered with the mean EPI and segmented into gray matter, white matter, and cerebrospinal fluid masks and were spatially normalized to Montreal Neurological Institute (MNI) space with a resolution of 2 × 2 × 2 mm cubic voxels (Ashburner & Friston, 2005). Transformation parameters were applied to motion corrected functional images that were then smoothed with a 6-mm FWHM Gaussian kernel.

Temporal Filtering

To deal with physiological and movement-related noise, data underwent despecking with a hyperbolic tangent squashing function, followed by the aCompCor technique. aCompCor removes the first five principal components of the signal from white matter and cerebrospinal fluid masks, as well as the motion parameters and their first-order temporal derivatives and a linear detrending term (Behzadi et al., 2007). aCompCor has been shown to effectively remove physiological noise components that would otherwise be aliased in to data sampled at the standard ~2 sec TR. This process was identical for both temporal filtering sets.

Each participants’ preprocessed functional images were then high-pass (0.009 Hz < f < 0.25 Hz) and band-pass filtered (0.009 Hz < f < 0.08 Hz). The value 0.25 Hz was selected as the low-pass filter for the high-pass group because it is the Nyquist frequency for data acquired with a TR of 2. The Nyquist frequency is the highest reliably sampled frequency given the sampling rate of the data (i.e., half the sampling rate). This resulted in two groups of functional images that were identical, except that one was high-pass filtered and the other was bandpass filtered. Temporal filtering was performed using a fast Fourier transform (FFT).

Obtaining Power Spectrum

We calculated the power spectrum at the single-participant level using the FFT implemented with MATLAB version 2008a (www.mathworks.co.uk/products/matlab/). The frequency bands were restricted to signals between 0.009 and 0.25 Hz.

ROI Definition

ROIs were defined as 10-mm spheres and centered at seven regions (Fox et al., 2005). Four of the regions made...
up the DMN and included the posterior cingulate cortex/precuneus (PCC; −6, −52, 40), medial pFC (mPFC; −1, 49, −5), and right (R Ang; 46, −70, 36) and left (L Ang; −46, −70, 36) angular gyri. As is standard in studies examining DMN connectivity, global connectivity of the PCC is reported. The remaining three ROIs made up the task-positive network and were centered in the intraparietal sulcus (IPS; −25, −57, 46), the FEF region of the precentral sulcus (25, −13, 50), and the middle temporal region (MT+; −45, −69, 2). Seed-based connectivity results from the IPS are also reported to show DAN connectivity. Spherical ROIs were created using the MarsBaR toolbox (marsbar.sourceforge.net).

**ROI-to-Voxel Functional Connectivity**

We calculated ROI-to-voxel (seed-based) connectivity from one ROI for both the DMN (PCC seed) and DAN (IPS seed) for each behavioral condition: (1) resting-state, (2) block motor task, and (3) event-related SST. Each analysis used two sets of the same functional data, with the only difference between the sets being the temporal filtering (high-pass vs. bandpass filtering).

In the SST, functional connectivity was measured for events when participants successfully completed a go trial (go success). Go success trials were used because (a) they occurred more often than the other events (i.e., go failure, stop success, stop failure) and (b) we are interested in the general effects of bandpass filtering on an event-related design, not on stop inhibition specifically.

Both high-pass and bandpass filtered images for resting state, motor task, and SST were entered into the Conn toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). The Conn toolbox is a set of MATLAB scripts for running functional connectivity analyses that utilizes SPM routines. This method computes temporal correlations between an ROI and all other brain voxels using a general linear model approach. Data from any participant moving more than half a voxel (>1.5 mm) during scanning were removed. A total of 22 data sets (for each temporal filtering group, n = 22 high pass and n = 22 bandpass) were included in rest and motor analysis. The SST included 21 data sets (n = 21 high pass, n = 21 bandpass). One participant was excluded from the SST due to excessive head motion during scanning.

Resting state, motor task, and SST ROI-to-voxel parameter estimate (beta coefficient) maps for each ROI in both bandpass and high-pass datasets were calculated for each participant and entered into second level analyses using paired t tests in SPM. Age was entered as a confounding variable in these second level analyses. Results were considered significant at voxel level (p < .001, uncorrected) and cluster level (p < .05, FWE-corrected for multiple comparisons).

**ROI-to-ROI Functional Connectivity**

We also directly compared connectivity between the seven ROIs (four for DMN and three for DAN) in the three behavioral states. We constructed 7 × 7 matrices of Fisher z-transformed bivariate correlation coefficients (Pearson’s r) using the ROIs described above. A hierarchical clustering analysis that places functionally similar ROIs in either DMN or DAN domains was conducted to assess whether any region changed its network membership across behavioral state. All connections between ROIs were FWE-corrected (p < .05) at the ROI and network levels using the network-based statistics toolbox. This method uses nonparametric permutation testing of network intensity to identify which ROI-to-ROI functional connections were statistically significant (Zalesky, Fornito, & Bullmore, 2010).

**Relating DMN Connectivity with RT**

Connectivity within the DMN was measured and correlated with RT in the go success trials for the SST, with the aim of assessing the relationship between DMN connectivity and a measure of behavioral performance at the participant level. This analysis involved averaging the edge strength (Pearson correlation coefficients normalized to z scores using the Fisher transformation) between PCC and the three DMN nodes (mPFC, L Ang, and R Ang). The final value is a measure of network-wide correlations for each participant in the analysis. This step was performed for both high-pass and bandpass filtered sets, resulting in two different groups (high-pass PCC–DMN connectivity, bandpass PCC–DMN connectivity). These values were then correlated (Pearson’s correlation using R studio, https://www.rstudio.com/) with each participant’s RT score. An equivalent analysis was not carried out for the motor task, because performance was not assessed during motor task beyond ascertaining that participants were carrying out the task.

**RESULTS**

**Effects of aCompCor and Temporal Filtering on BOLD Signal**

This study focused on understanding the role of high frequencies in DMN connectivity and their behavioral relevance. Figure 1 (A–J) shows the power spectrum (FFT)
from the average signal obtained from the gray matter mask of one participant used in the analysis. The top row panels (A, B, C) show the raw data, the middle row shows the effects of \textit{aCompCor} preprocessing with a high-pass filter (D, E, F), and the bottom row shows \textit{aCompCor} preprocessing with a bandpass filter (H, I, J). As expected, most of the power is contained within low frequencies (less than 0.08 Hz). However, it is clear that some power is contained within higher frequencies as well, suggesting that potentially relevant activity is removed from functional connectivity analyses that implement bandpass filtering. To control for possible confounds, we used the Nyquist frequency as a low-pass filter in the high-pass set to be sure all the signals analyzed were reliably sampled. The following analyses aim to understand the functional and behavioral role of these high frequencies in relation to DMN connectivity.

The Effects of High-frequency Fluctuations in Network Dynamics

Functional connectivity between the PCC ROI and all other voxels in the brain during rest (Figure 2A), motor task (Figure 2B), and SST (Figure 2C) was used to measure DMN functional connectivity in both high-pass and bandpass sets. Across all three states, both temporal filtering sets show similar positive functional connectivity with DMN regions, including posterior cingulate/precuneus, mPFC, angular gyrus, and medial-temporal lobe structures. However, a qualitative difference was observed between temporal filtering groups when examining anticorrelations between DMN and DAN. Both sets...
showed anticorrelations in anterior regions of the DAN; however, the bandpass group showed greater anti correlations with posterior DAN, most notably in bilateral inferior parietal cortex. This effect holds across all three behavioral states but is most prominent in the SST. Functional connectivity between IPS and all other brain voxels was also measured for each behavioral state (Figure 3A–C). Connectivity between IPS and other DAN regions, including dorsolateral pFC, ACC, and right IPS, was observed. Again, we found a qualitative increase in anticorrelations with DMN in bandpass filtered data compared with high-pass filtered data while participants performed a task.

**Differences in Functional Connectivity between High-pass and Bandpass Sets**

To examine whether the differences in functional connectivity between temporal filtering sets observed in the PCC were statistically significant, we used paired t tests to compare connectivity maps for each condition (Figure 4A–C). We also measured functional connectivity from IPS to all other voxels to determine whether this effect is observed in a putatively DAN (Figure 5A–C). For the high-pass > bandpass contrast, highlighted regions (in blue) represent a lower magnitude of anticorrelation in the high-pass group compared with the bandpass group. For the bandpass > high-pass contrast, highlighted regions (in red) represent a greater magnitude in correlation in the bandpass group compared with the high-pass group. All results are significant at voxel level $p < .001$ (cluster $p < .05$ FWE-corrected).

At rest, the PCC showed less anticorrelation in high pass compared with bandpass in many regions of the DAN (Figure 4A). These include bilateral insula, pre-motor cortex and inferior parietal cortex, middle frontal gyrus, superior frontal gyrus, right SMA, and several cerebellar regions. The PCC showed greater connectivity with DMN regions in the bandpass > high-pass contrast, most notably the precuneus, mPFC, bilateral angular gyrus, and middle temporal gyrus. For the motor task (Figure 4B), the PCC followed the same pattern as rest, with greater anticorrelation in the bandpass set for high-pass > bandpass and greater correlation in the bandpass group in the bandpass > high-pass contrast. Greater anticorrelation in bandpass filtered data was observed in the bilateral insula, supramarginal gyrus, right SMA, and right inferior frontal gyrus (IFG). The bandpass > high-pass contrast showed greater correlation between PCC and bilateral angular gyrus, mPFC, PCC, right IFG, and right inferior temporal gyrus (ITG) for bandpass filtered data. In the SST (Figure 4C), reduced anticorrelation was observed in the high-pass group compared with the bandpass group in bilateral middle frontal gyrus, inferior parietal cortex, superior frontal gyrus, right middle temporal gyrus, left insula, and right and left inferior occipital cortex. Increased correlation was seen in the band-pass group in the bandpass > high-pass group in DMN regions, including left angular gyrus, bilateral PCC, mPFC, and IFG.

The IPS was less anticorrelated with several DMN regions in the high-pass set (Figure 5A), including mPFC and right angular gyrus. There was also less anticorrelation with bilateral superior temporal gyrus and several motor regions, including right SMA and right precentral gyrus. The IPS showed greater correlation with DAN regions in the bandpass set for the bandpass > high-pass contrast. Regions include the left inferior occipital cortex, left inferior parietal gyrus, left inferior frontal cortex (IFG), left inferior parietal cortex, right precentral gyrus, and right cerebellar crus II. For the motor task, the IPS (Figure 5B) showed less anticorrelation in the high-pass set with DMN regions, including the mPFC, PCC, and right angular gyrus. In the bandpass > high-pass contrast, greater correlation is seen in the bandpass group between IPS and left middle temporal gyrus, right IFG, bilateral superior frontal gyrus, left ACC, and left superior occipital cortex. In the SST, the IPS (Figure 5C) reduced connectivity in the high-pass group in the high-pass > bandpass contrast in several DMN regions, including bilateral mPFC,

![Figure 3. Whole-brain connectivity analysis using IPS as a seed region. The first and third columns show high-pass filtered data, and the second and fourth columns show bandpass filtered data. (A) IPS connectivity during resting state. (B) IPS connectivity during the motor task. (C) IPS connectivity during the SST. Red maps are positive correlations (t values), and blue maps are anticorrelations. Numbers below the axial slices are MNI z coordinates.](http://direct.mit.edu/jocn/article-pdf/30/4/526/1787358/jocn_a_01213.pdf)
precuneus, PCC, parahippocampal gyrus, and right ITG.
For the bandpass > high-pass contrast, IPS showed
greater correlation in the bandpass group in DAN re-
gions, including left IFG, posterior ITG, superior pari-
tal gyrus, middle frontal gyrus, IFG, and right precentral
gyrus.

Task-related Internetwork Positive Connections
Are Dependent on the Inclusion of
High-frequency Fluctuations

To directly measure the effect of behavioral task and high
frequencies on network reconfiguration, we measured
functional connectivity between seven previously defined ROIs representing regions of the DMN (PCC, mPFC, L Ang, R Ang) and DAN (IPS, FEF, MT; Fox et al., 2005). Our results show that within-network connectivity is relatively stable regardless of temporal filtering used; however, between-network positive connectivity is reliant on the inclusion of high frequencies in the data. These results are represented as chord diagrams in Figure 6A–F.

First, using a hierarchical clustering algorithm, we show that nodes from both DMN and DAN were reliably
allocated to their respective networks for each behavioral task in both temporal filtering sets, suggesting within-network connectivity is relatively stable across behavioral task and temporal filtering set. Second, anticorrelations between networks exist for both temporal filtering sets but are much more prominent in the bandpass set, complementing our ROI-to-voxel results from the previous section. These anticorrelations also increase during task state for both temporal filtering sets. However, a positive, long-range connection between mPFC in the DMN and MT+ in the DAN is revealed only when high frequencies are included in the data. Crucially, this connection does not exist during resting state and persists during both tasks, suggesting it is related to task engagement and not present due to high-frequency noise, as that would likely be uniformly present across all three behavioral states. It is also not likely to have originated from residual motion-related artifacts, as those tend to result in increased short-range and bilateral connections and decreased long-range, anterior–posterior connections (Murphy et al., 2013; Power, Barnes, Snyder, Schlaggar, & Petersen, 2012). We additionally examined connectivity during the fixation block of the motor task and found no internetwork positive connectivity (data not shown).

**Inclusion of High Frequencies Reveals Task-related DMN Connectivity**

In addition to examining network reconfiguration in the context of a task, we were also interested in assessing the influence of high frequencies in DMN on task-related behavioral measures. To this end, we correlated connectivity within the DMN (edge correlation strength of PCC to other DMN nodes) with RT in go success trials in the SST for both high-pass and bandpass filtered datasets. This analysis revealed a significant relationship with RT in the high-pass group ($R^2 = .19$, $r = -.43$, $p = .046$; Figure 7A) but not the bandpass group ($R^2 = .084$, $r = -.29$, $p = .2$; Figure 7B), signifying that, as within-DMN connectivity increased, RT was faster. This could suggest that task-related connectivity exists exclusively in high-frequency fluctuations in the DMN and that bandpass filtering removes these behaviorally relevant signals.

**DISCUSSION**

Several recent studies have focused on measuring the role of high frequencies in functional connectivity during resting-state scanning (De Domenico et al., 2016; Lewis et al., 2016; Chen & Glover, 2015; Gohel & Biswal, 2015; Kalcher et al., 2014; Boyacioglu et al., 2013; Niazy et al., 2011; Wu et al., 2008). At the same time, increasing evidence is suggesting that the DMN is not a “task-negative” network but plays an active role in mediating a variety of cognitive processes (Vatansever et al., 2015a, 2015b, 2016; Crittenden, Mitchell, & Duncan, 2015; Spreng et al., 2014; Seghier & Price, 2012; Spreng, 2012). In an effort to bridge these two emerging lines of evidence, the aim of this study was to identify whether inclusion of high-frequency fluctuations in fMRI data alter DMN connectivity patterns and whether these alterations are task relevant. To this end, we used fMRI data from three behavioral states (resting state, motor task, SST) processed with
either a bandpass (0.009 Hz < f < 0.08 Hz) or high-pass
(0.009 Hz < f < 0.25 Hz) filter. DMN connectivity was
measured and compared for each behavioral state and
both filtering sets using ROI-to-voxel and ROI-to-ROI con-
nectivity. Using PCC as a seed region, we found that anti-
correlations between PCC and posterior regions of the
DAN were significantly reduced when high-frequency
fluctuations were included, an effect observed across all
three behavioral states, though was most prominent in
the event-related SST. We also observed the inverse effect
when measuring connectivity from IPS, a region of the
DAN. Complementing our ROI-to-voxel result, we mea-
sured connectivity between DMN and DAN ROIs and ob-
served stronger anticorrelations in the bandpass group
across all three behavioral states, suggesting that
between-network anticorrelations primarily fluctuate in
low frequencies. Furthermore, we found that when high
frequencies are included in the data, positive connectivity
is observed between the mPFC and MT+. Critically, this
connection is only seen when participants are engaged in
a task and not during resting state. Our final analysis ex-
tended our initial findings to examine the behavioral
relevance of within-DMN connectivity for individual par-
ticipants. Here we found that greater within-DMN posi-
tive connectivity predicted faster RTs in the high-pass set,
but not the bandpass set. This shows that behaviorally
relevant signals contained within the DMN exist at high
frequencies, which are often removed in functional con-
nectivity analyses attempting to establish the DMN’s role
in behavior.

Within-network Correlations and Between-network
Anticorrelations Are Most Prominent in
Low-frequency Fluctuations

Our results confirm and expand upon previous observa-
tions that anticorrelations are present between DMN and
DAN in low frequencies (Keller et al., 2015; Fox et al.,
2005; Fransson, 2005). We show that PCC anticorrela-
tions are stronger in the bandpass set compared with
the high-pass set. Conversely, anticorrelations between
IPS and regions of the DMN were also stronger in the
bandpass set. Importantly, we see this effect during all
three behavioral states. These results show anticorrela-
tions are greater at low frequencies when using seed re-
regions from different networks, suggesting that this result
is not specific to DMN regions.

We also observed greater within-DMN connectivity in
the bandpass set compared with the high-pass set. It
has been suggested that anticorrelations serve to segre-
gate neuronal processes that subserve opposite goals or
competing representations (Fox et al., 2005). This rela-
tionship between DMN and DAN has been extensively
explored, with many groups suggesting a dynamic set
of processes wherein DMN is involved in internally di-
rected, self-generated cognition and DAN involved in ex-
ternally directed cognition (Andrews-Hanna, Smallwood,
& Spreng, 2014). Further work has shown that DAN is
actually composed of multiple subnetworks, including
the DAN, cingulo-opercular network, and frontoparietal
control network (Power et al., 2011). The DAN in par-
ticular has been shown to have an anticorrelated or anti-
phase relationship with DMN, whereas the frontoparietal
control network is thought to play a mediating role be-
tween networks (Spreng et al., 2013). Importantly, the
majority of studies focusing on the relationship between
DMN and various DANs have applied bandpass filtering
in the preprocessing stage, thus removing high frequen-
cies from the statistical analysis. These anticorrelations
have therefore been defined primarily in low frequencies.
A likely interpretation could be that anticorrelations exist
disproportionately at low frequencies and that bandpass
filtering allows for a sharper focus on this phenomenon.
This is supported by significant evidence suggesting that
anticorrelations are present in large-scale networks inde-
pendent of preprocessing techniques or experimental
groups (Spreng, Stevens, Viviano, & Schacter, 2016; Chai
et al., 2012).
Task-related Internetwork Connectivity Is a High-frequency Phenomenon

In addition to finding that anticorrelations are behaviorally relevant and exist primarily in low frequencies, we provide two pieces of complementary evidence that suggest the DMN contains task-related activity at frequencies higher than what are typically analyzed in functional connectivity studies. First, we show that when directly comparing connectivity profiles between high-pass and bandpass sets, a positive connection is observed between MT+ and mPFC only during tasks, not during rest. This connection is unlikely to have originated from noise, as one would expect noise to be uniform across all three fMRI datasets. Furthermore, it is not likely to be related to head motion because motion-related artifacts have been shown to increase short-range and bilateral connectivity and decrease long-range and anterior–posterior connectivity (Murphy et al., 2013; Power et al., 2012). The positive connection we observe is both long range and anterior–posterior. Second, we found that within-DMN connectivity reliably correlated with RT only in the high-pass set. Previous studies have retained high frequencies when comparing task-related connectivity with resting state (Cole et al., 2014, 2016; Schultz & Cole, 2016; He, 2013); however, to our knowledge, this is the first demonstration that the DMN displays task-related connectivity only when high frequencies are included in the analysis. These results should be seen as a first step to elucidating network connectivity at higher-frequency bands than usually considered as well as an investigation into the relationship between high-frequency connectivity and behavior. Further research with larger sample sizes and faster TRs (TR ≤ 0.5 sec) is necessary to draw more definitive conclusions.

Several recent studies have shown that activity in large-scale networks is not restricted to frequencies below 0.1 Hz. A previous study used a high sampling frequency (TR = 645 msec) to measure functional networks across five frequency bands at rest (Gohel & Biswal, 2015). They were able to identify well-established networks, including the DMN and several DANs in high-frequency bands. They also observed significant interhemispheric connectivity across all frequency bands, suggesting functional integration between brain regions is a multiband phenomenon. Concurrently, recent work has shown the DMN to be involved in a variety of cognitive tasks involving both internally and externally directed attentional processes (Vatansever et al., 2015a, 2015b, 2016, 2017; Spreng et al., 2013, 2014). In this context, our work expands upon both lines of research by finding task-related activity in the DMN in high frequencies. This work may also find application in the field of mind-wandering and unconstrained cognition. Likely because of its role in internally directed attention, the DMN has frequently been implicated in mind-wandering; however, a recent meta-analysis showed that several studies have reported connectivity between non-DMN regions during mind-wandering (Fox, Spreng, Ellamil, Andrews-Hanna, & Christoff, 2015). Another recent study used a novel experience sampling method to show that DAN activity increased when participants reported controlling their attention, whereas DMN activity increased when participants reported a state of internal mentation (Van Galster, D’Argembeau, Salmon, Peters, & Majerus, 2017). These studies show that what has come to be known as resting state is a dynamic state where internetwork connectivity likely plays an important role; therefore, mind-wandering and studies examining unconstrained cognition should consider preserving high-frequency fluctuations in their data.

There are many remaining questions regarding high-frequency fluctuations and the DMN. This study is limited in that it only measures connectivity using a priori defined sets of ROIs. One approach could be to examine whether different subregions of the DMN communicate with other networks at different frequencies (Bzdok et al., 2015; Leech, Kamourieh, Beckmann, & Sharp, 2011). The use of data-driven approaches or multivariate analyses could extend this work. One such study by Crittenden et al. (2015) used multivoxel pattern analysis to show that DMN encodes task-relevant information during performance of a task-switching behavioral paradigm. Although it was not the focus of the study, it should be mentioned that a low-frequency bandpass filter was not applied to the data before statistical analysis. Dynamic connectivity methods are another important extension of this work. A recent study by Dixon et al. (2017) presents a comprehensive analysis of DMN–DAN interactions across time, as well as between different cognitive states and DMN subsystems (Dixon et al., 2017). Using dynamic functional connectivity to investigate the ever changing nature of the relationship between DMN and DAN, the authors show that anticorrelation between these networks is transient rather than persistent and that anticorrelation is most prominent with core DMN regions like the PCC, mPFC, and angular gyri. Therefore, another interesting extension of our work could be the investigation of high-frequency connectivity in different DMN subsystems.

Previous work looking to measure high frequencies in fMRI during resting state have used frequency bands originally defined by electrophysiology studies (Penttonen & Buzsáki, 2003) that argue frequency bands oscillate following a natural logarithmic function. The current study did not use this definition of frequency bands because we were limited by the TR of 2 sec, meaning we could only reliably measure oscillations slower than the Nyquist frequency of 0.25 Hz. Future studies should use novel MR acquisition protocols, including multiplex and multiband EPI sequences (Boubela, Kalcher, Nasel, & Moser, 2014; Kalcher et al., 2014; Boubela et al., 2013; Feinberg et al., 2010; Arkinson et al., 2006), that allow for faster TRs and thus higher Nyquist frequencies to further define the role of high frequencies during rest and task-based functional...
connectivity. Using these acquisition protocols would also reduce the potential impact of physiological and motion-related artifacts. A potential area of controversy in the functional connectivity literature that applies to the current study is the use of denoising pipelines. We acknowledge that there are a variety of potential denoising methods that can influence functional connectivity results, including manual denoising using independent component analysis (e.g., fsl_regfilt) and automated denoising methods that implement PCA (Kay, Rokem, Winawer, Dougherty, & Wandell, 2013) or ICA (Salimi-Khorshidi et al., 2014). We chose to use aCompCor because it has been shown to sufficiently remove noise when studying network interactions (Chai et al., 2012). However, a replication of these findings by researchers using alternative denoising pipelines is probably warranted before definitive conclusions on this matter are drawn.

There are two main conclusions that can be drawn from this study. First, we found that the inclusion of high frequencies in functional connectivity analyses results in differences in between network interactions. Second, this high-frequency activity appears to be important particularly when examining connectivity during task performance. This is supported by two sets of results, both of which delineate the role of high frequencies in the DMN. First, we found differences in connectivity patterns while participants perform an attentionally demanding task, and second, DMN connectivity correlated with RT only when high frequencies are included. These results suggest that functional connectivity studies should also include high frequencies, especially when examining DMN connectivity during task execution.

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Reprint requests should be sent to Michael M. Craig, Division of Anaesthesia and Department of Clinical Neurosciences, School of Clinical Medicine, University of Cambridge, Box 93, Addenbrooke’s Hospital, Hills Road, Cambridge CB2 0QQ, United Kingdom, or via e-mail: mmc57@cam.ac.uk.

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