Tracking ongoing cognition in individuals using brief, whole-brain functional connectivity patterns

Javier Gonzalez-Castillo^{a,1,2}, Colin W. Hoy^{a,b,1}, Daniel A. Handwerker^a, Meghan E. Robinson^{a,c}, Laura C. Buchanan^a, Ziad S. Saad^d, and Peter A. Bandettini^{a,e}

^aSection on Functional Imaging Methods, Laboratory of Brain and Cognition, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892; ^bHelen Wills Neuroscience Institute, University of California, Berkeley, CA 94720; ^cVeterans Affairs Boston Healthcare System, Boston, MA 02130; ^dStatistical and Scientific Computing Core, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892; and ^eFunctional MRI Facility, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892

Edited by Russell A. Poldrack, University of Texas at Austin, Austin, TX, and accepted by the Editorial Board June 1, 2015 (received for review January 21, 2015)

Functional connectivity (FC) patterns in functional MRI exhibit dynamic behavior on the scale of seconds, with rich spatiotemporal structure and limited sets of whole-brain, quasi-stable FC configurations (FC states) recurring across time and subjects. Based on previous evidence linking various aspects of cognition to group-level, minute-to-minute FC changes in localized connections, we hypothesized that whole-brain FC states may reflect the global, orchestrated dynamics of cognitive processing on the scale of seconds. To test this hypothesis, subjects were continuously scanned as they engaged in and transitioned between mental states dictated by tasks. FC states computed within windows as short as 22.5 s permitted robust tracking of cognition in single subjects with near perfect accuracy. Accuracy dropped markedly for subjects with the lowest task performance. Spatially restricting FC information decreased accuracy at short time scales, emphasizing the distributed nature of whole-brain FC dynamics, beyond univariate magnitude changes, as valuable markers of cognition.

fMRI | connectivity dynamics | functional connectivity states | cognitive states | classification

Resting state functional MRI (rs-fMRI) focuses on spatial patterns of blood oxygenation level dependent (BOLD) signal fluctuations recorded in the absence of externally driven tasks or stimulation. These patterns, known as functional connectivity (FC) patterns, are usually computed on the basis of an entire scan (often >6 min). Their cognitive significance (1) and long term reproducibility (2) are well established, and preliminary data suggest that they have potential clinical value (3). However, recent studies have shown that FC patterns are highly dynamic at shorter temporal scales (4) (i.e., tens of seconds), adding yet another challenge to developing fMRI-based protocols with sufficient single-subject specificity and sensitivity to inform clinical decisions.

FC patterns computed with 1- to 2-min portions of a scan can vary substantially around a mean FC pattern obtained using complete 6- to 20-min scans. This dynamic behavior has been observed in awake and sleeping humans (5–8), as well as in anesthetized animals (9, 10). Several studies involving simultaneous fMRI and electrophysiological recordings have suggested that FC dynamics may be driven by neurophysiological sources rather than noise (6, 11, 12). Furthermore, FC dynamics exhibit rich spatiotemporal structure. Connections between higher order cognitive regions are more variable than those between primary sensory-motor regions (13–15), and a limited set of whole-brain, quasi-stable FC configurations—known as FC states—reliably recur both within and across subjects at rest (13, 16).

Given that cognition is supported by highly dynamic brain processes, it has been hypothesized that FC states may reflect changes in ongoing cognitive states during rest (13). Initial task-based studies have been able to differentiate between a limited set of mental tasks (17, 18) and arousal levels (19) on the basis of localized changes in FC at the scale of 45 s to 2 min. However, all these studies examined only a reduced set of predefined connections expected to best differentiate states of interest. In doing so,

these studies neglect the highly distributed and parallel nature of cognitive processing (20, 21) and consciousness itself (22), thus only partially validating the cognitive significance of FC states as originally defined: quasi-stable, global representations of FC across the whole brain.

In the following study, we used a continuous, multitask paradigm to study the relationship between ongoing cognition and dynamic changes in FC patterns derived from BOLD measurements at different temporal scales. We use the term “ongoing cognition” to refer to brain activity that is the result of experimentally constrained cognitive processes, in contrast to resting state, which includes unconstrained ongoing cognition of an unknown, internally driven nature (23). Although giving subjects freedom to transition between states at will may better reflect the self-directed nature of cognition during rest, such an experimental design would lack ground truth regarding the timing and nature of cognitive states, thus precluding detailed evaluation of their relationship with FC states. Consequently, our experimental design uses tasks to control these variables and monitor subject performance via behavioral responses. This framework provides the basis for rigorously testing the degree to which FC states reflect ongoing cognition at short temporal scales and, in that manner, informs the interpretation of BOLD connectivity dynamics during both task and rest.

Significance

Recently, it was shown that functional connectivity patterns exhibit complex spatiotemporal dynamics at the scale of tens of seconds. Of particular interest is the observation of a limited set of quasi-stable, whole-brain, recurring configurations—commonly referred to as functional connectivity states (FC states)—hypothesized to reflect the continuous flux of cognitive processes. Here, to test this hypothesis, subjects were continuously scanned as they engaged in and transitioned between mental states dictated by tasks. We demonstrate that there is a strong relationship between FC states and ongoing cognition that permits accurate tracking of mental states in individual subjects. We also demonstrate how informative changes in connectivity are not restricted solely to those regions with sustained elevations in activity during task performance.

Author contributions: J.G.-C., C.W.H., D.A.H., M.E.R., and P.A.B. designed research; J.G.-C., C.W.H., M.E.R., and L.C.B. performed research; Z.S.S. contributed new reagents/analytic tools; J.G.-C., C.W.H., D.A.H., M.E.R., and L.C.B. analyzed data; and J.G.-C., C.W.H., D.A.H., Z.S.S., and P.A.B. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission. R.A.P. is a Guest Editor invited by the Editorial Board.

Data deposition: The MRI data have been deposited in Xnat Central, <https://central.xnat.org> (project ID: FCStateClassif).

¹J.G.-C. and C.W.H. contributed equally to this work.

²To whom correspondence should be addressed. Email: javier.gonzalez-castillo@nih.gov.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1501242112/-DCSupplemental.

Fig. 1. Experimental paradigm and summary of analysis for multitask scans.

Participants were scanned continuously for ~25 min as they engaged and transitioned between four mental tasks: two-back working memory (memory), numerical computations (math), visual attention (video), and rest. Subjects engaged in each task for two non-consecutive 3 min periods (Fig. 1). Responses and response times were obtained for the three active tasks. For each of 20 subjects, whole-brain FC patterns were computed for nonoverlapping windows of different durations (range 180 s to 22.5 s) and used to generate time lines of FC states. In this manuscript, the word FC state refers to a vector populated with connectivity values (i.e., Fisher's transform of the Pearson's correlation value) computed using only the portion of the data inside a given window. Because the Pearson's correlation removes the means and divides by the SDs of the input time series, windowed connectivity matrices computed this way are less prone to bias by shifts in activity levels across task blocks. Finally, these FC state time lines were then compared with mental state time lines defined by the timing of the experimental paradigm (see Fig. S1 for a detailed depiction of the analysis). We show that the structure imposed by these task-related demands, or ongoing cognition, can be recovered from short-term FC state dynamics at the single-subject level on the scale of tens of seconds with near perfect accuracy.

Results

Behavioral. Table 1 shows across-subject average values for percentage of correct responses ($P_{Correct}$), percentage of trials when a response was required but none was given ($P_{Missing}$), and reaction time (RT) for all task blocks. On average, subjects performed much better on the math and memory tasks ($P_{Correct} > 90\%$; $P_{Missing} < 20\%$) than they did on the video task ($P_{Correct} \approx 67\%$; $P_{Missing} \approx 30\%$). RTs were on average quite similar across blocks of the same task. Individualized measures of $P_{Correct}$, RT, and $P_{Missing}$ are reported in Fig. S2. This figure also shows the difference across same-task blocks for each of the metrics (i.e., $\Delta P_{Correct}$, ΔRT , and $\Delta P_{Missing}$), which informs us about performance consistency across the whole scan. Subjects S05, S12, and S14 had the worst overall performance in terms of $P_{Correct}$ (Fig. S2A) and $P_{Missing}$ (Fig. S2E), being the only ones with $P_{Missing} > 25\%$ and $P_{Correct} < 80\%$. They were also among those with the highest RTs (Fig. S2C), ΔRT (Fig. S2D), and $\Delta P_{Missing}$ (Fig. S2F). One of them in particular, S12, showed the highest levels of discrepancy for all three metrics, perhaps signaling an intermittent loss of concentration/awareness during the scan. Importantly for our discussion, these three subjects

also had markedly degraded performance in terms of FC state-based classification (Figs. 2 and 3).

FC-Based Classification. Fig. 2 shows group-level, FC-based classification results in terms of the adjusted rand index (ARI). The ARI is a clustering validation metric that quantifies the level of agreement between a data-driven clustering (e.g., FC states + k -means) and existing knowledge of the underlying structure of the data (i.e., window groupings based on mental tasks) while also correcting for chance (24). Interpretation of the ARI is well established in the literature (25): $ARI < 0.65$ signals poor recovery of the underlying group structure of the data; $0.65 < ARI < 0.8$ indicates moderate recovery; $0.8 < ARI < 0.9$ indicates good recovery; and $0.9 < ARI < 1.0$ indicates excellent recovery. Group-level ARI results are reported in Fig. 2 in terms of the median (white dot), 25–75% percentiles (gray box), and most extreme data points not considered outliers (dotted whiskers). In addition, outliers are marked with a (+) symbol in Fig. 2. For window length (WL) ≥ 30 s, the median ARI equals 1, signaling that we were able to perfectly group windows based on whole-brain FC snapshots. For WL = 22.5 s, the median ARI decreases slightly, but it is still within the excellent recovery range (green). Finally, only five subjects were marked as outliers with classification accuracies well below the rest of the group. Subjects S03 and S08 were outliers only for one of the various WLs, yet their ARI remained within the good recovery zone. Conversely, subjects S05, S12, and S14 were outliers for several WLs, and their ARI dropped in the moderate (subject S05) or poor recovery zone (subjects S12 and S14).

Fig. 3 shows classification results for six representative subjects at all WLs in the form of “classification staffs” (results for all 14 additional subjects can be found in Figs. S3 and S4). In each “staff,” the x axis corresponds to time (in units of windows), and the y axis to FC states. Each time window is represented by a color-coded bar and a dot. The color of the bar signals the imposed mental state (gray, rest; blue, memory; green, math; yellow, video). The location of the dot on the y axis signals the FC state to which that window was assigned. Agreements between groupings based on mental state and FC state are marked with black dots, and errors are marked with red dots. In addition, for each subject, we report two measures of classification success (classification accuracy and ARI) to the right of the staff. $P_{Correct}$, RT, and $P_{Missing}$ for each task block and subject are reported in Table S1.

Fig. 3A shows results for subject S01, a representative non-outlier subject. No classification errors occurred for this subject. Fig. 3B–F shows results for the five outliers reported above. Fig. 3B shows results for subject S03, outlier at WL = 30 s, due to two errors (first rest and seventh video windows). These two errors at WL = 30 s were sufficient to push the ARI down to the good recovery zone although accuracy remained above 95%. Two additional errors occurred for this subject at windows at the edge of task blocks (transition windows) for WL = 22.5 s. Fig. 3D shows results for subject S08, outlier at WL = 60 s, due to a single misclassification (last rest window). One more error occurred on the same rest window for WL = 30 s.

Fig. 3C shows results for subject S05, outlier for WL = 60 s, 45 s, 30 s, and 22.5 s. For all these windows, the ARI fell within the moderate recovery range. All but one misclassification involved grouping of rest and memory windows together (red line). This subject had the largest $P_{Missing}$ for the memory task (along with

Table 1. Average behavioral measures across all subjects

	Memory-B1	Memory-B2	Math-B1	Math-B2	Video-B1	Video-B2
$P_{Correct}$, %	91.92 $\pm$ 7.20	93.25 $\pm$ 6.65	95.69 $\pm$ 4.64	91.11 $\pm$ 9.30	66.25 $\pm$ 18.18	67.19 $\pm$ 21.92
$P_{Missing}$, %	12.75 $\pm$ 15.85	18.33 $\pm$ 24.27	0.83 $\pm$ 1.82	2.50 $\pm$ 4.84	30.62 $\pm$ 16.95	31.25 $\pm$ 21.65
RT, s	0.94 $\pm$ 0.37	1.05 $\pm$ 0.58	2.31 $\pm$ 0.45	2.55 $\pm$ 0.51	1.39 $\pm$ 0.17	1.37 $\pm$ 0.22

B, block.

Fig. 2. Group-level FC state classification results.

subject S14) (Fig. S2E) and had the second worst $P_{Correct}$ for this task (Fig. S2A).

Fig. 3F shows results for subject S14, outlier for WL = 45 s, 30 s, and 22.5 s. At these WLs, all errors but one were related to confusion with the memory task, mostly (26 of 30) with rest windows (red line). Subject S14's ARI for WL = 30 s and 22.5 s lies in the poor recovery zone. Behaviorally, subject S14 had the largest $P_{Missing}$ (tied with subject S05) for the memory task.

Finally, Fig. 3E shows results for subject S12, outlier for all window lengths. Subject S12 had the worst classification of the group, with ARIs in the poor recovery zone for all WLs. According to all three behavioral metrics, this subject was the most inconsistent across blocks and was also among the four worst subjects in terms of task performance. Across all WLs, 70 of 73 misclassifications involved confusion with the video task (red

lines). Subject S12's performance was low and variable during the video blocks, as evidenced by having the lowest $P_{Correct}$, largest $\Delta P_{Missing}$ and $\Delta P_{Correct}$, and second largest $P_{Missing}$ and ΔRT for this task.

FC-Based Classification Accuracy vs. Behavior. Scatter plots of classification accuracy (ARI) versus each of the six behavioral indices are shown in Fig. 4 for WL = 22.5 s. In each plot, subjects are represented as gray circles. A linear fit to the data is shown (dotted line), and correlation values and their significance (P value) are reported. We found significant correlations between ARI and all behavioral metrics for this window length, as well as for WL = 30 s, 45 s, and 60 s. When the three worst performers (subjects S05, S12, and S14) were excluded from this analysis, the correlations were no longer significant although this negative result may be partly due to ceiling effects on the ARI (all remaining subjects had $ARI \geq 0.88$ and 9 of 17 had $ARI = 1$). This observation suggests that large deviations in task performance are required to produce substantial errors in FC classification.

Contribution of Task-Specific Regions to Classification. To determine the overlap between the connectivity changes driving the FC-based classification and the locations of activation-induced changes in BOLD magnitude, we sorted regions of interest (ROIs) according to how well they differentiated the tasks in terms of activation levels (see SI Methods for details). We subsequently attempted FC-based classification using progressively smaller sets of ROIs. In one analysis, we removed the most task-discriminative ROIs first. In a second parallel analysis, we removed ROIs in the opposite order (least task-discriminative first).

Fig. S5A shows activation maps for the contrasts between the three active tasks and rest. Although maps do differ, in all instances, activation foci were present in visual cortex, anterior insula, inferior

Fig. 3. Individual level FC state classification results. (A) Representative nonoutlier subject (S01). (B–F) Outlier subjects for one or more WLs.

task (28) content outperforms activity-based classification, and extend this finding to whole-brain FC patterns. Overall, we show that short-term fluctuations in whole-brain fMRI connectivity patterns can be reliably used to track ongoing cognition, on an individual subject basis, despite the noisy and indirect nature of BOLD signals as a marker of neuronal activity.

Our results extend previous attempts at tracking cognition on the basis of short-term fMRI FC patterns (17–19, 29–31) in several ways: (i) We report higher accuracy for shorter windows, which suggests that FC states follow cognition at much shorter temporal scales than previously reported; (ii) we do so in individual subjects without a priori selection of informative connections or training datasets, which makes this approach suitable for studying a wide range of cognitive states and for single-subject clinical applications; (iii) we demonstrate that FC states are most identifiable when defined as global, whole-brain phenomena; and (iv) we report additional analyses aimed to devise the best methods for tracking cognition using FC states.

Best results from prior studies showed classification accuracies around 80% for durations of 60 s or more (17, 19). For shorter windows, when reported, accuracy dropped quickly. Here, we report accuracies well above 80% for windows as short as 22.5 s (Fig. 3), which approaches the upper limit of temporal scales (256 ms to 16 s) for which EEG microstate (32) sequences show scale-free behavior (33). Previous research already had limited success matching temporal sequences of EEG microstates to rs-fMRI networks, despite the contrast between their dynamic and stationary definitions (34–36). In addition to the better conceptual match between microstates and FC states as quasi-stable, global brain phenomena that are in flux over short time periods, our results show that FC states also share the functional utility of microstates in terms of tracking ongoing cognition at behaviorally relevant time scales. These findings suggest that examining these two phenomena in conjunction may help elucidate the relationship between dynamics in fMRI and electrophysiological signals.

The original observation of FC states by Allen et al. (13) relied on whole-brain connectivity data and k -means, a data-mining technique that does not require a preexisting training dataset. However, all attempts at validating the concept of FC states as a correlate of cognition (17–19, 29, 37) have relied upon supervised techniques that required a training dataset and/or some a priori selection of connections based on the mental states under scrutiny, both of which limit the generalizability of those approaches. To our knowledge, ours is the first study to show a strong correlation between FC and mental states without the need of any such priors. Unsupervised approaches such as k -means are preferable because they are independent of mental state and suitable for single-subject applications, but they have their own set of limitations. First, most of them require a priori selection of the number of states (k). We were able to develop robust classification procedures based on the ground truth for k established by the experimental paradigm, but obtaining the correct number of FC states in an unbiased, data-driven manner is an important challenge for the field. Second, unsupervised classification techniques simply group similar objects (e.g., whole-brain FC patterns) into sets. They cannot assign any label or meaning (e.g., mental computations) to the discovered groups. In other words, unsupervised methods can reveal when subjects are engaged in the same mental state, but not what state that is. Fortunately, once proven that FC states consistently represent cognitive states within subjects, one could envision a second step in which detected FC states are compared against dictionaries of FC patterns for which a label does exist. For such a dual-step approach to work, we first need to understand the conditions under which FC states faithfully represent cognitive states, particularly across subjects and for internally, self-induced mental states such as those present in rest. This topic is not directly addressed in this work, but previous studies have demonstrated successful group-level FC-based classification of more loosely controlled cognitive states without sensory stimulation or motor responses (17, 37). Although FC/cognitive state dictionaries are not yet available, equivalent dictionaries for activity-based patterns are being

constructed today (38). We believe that better characterization of across-subject consistency in FC states, combined with parallel efforts to develop such FC-based dictionaries, may provide the means to track ongoing cognition during rest.

Several factors may have contributed to obtaining such high classification results for shorter temporal scales than previously reported. First, data were acquired on a high-field scanner, which translates into better signal-to-noise ratio. Second, an adaptive high-pass filtering scheme was used to avoid spurious fluctuations in correlation values (39). In fact, when such filtering is not in place, classification notably degraded for the shorter windows (Fig. S6D). Third, we used a finer grained parcellation of the brain than previous studies (200 ROIs vs. $\sim$ 100 ROIs). Reanalysis of the data with versions of the Craddock atlas (26) ranging in number of ROIs from 30 to 500 (Fig. S6A) suggests that best results are obtained with a minimum of 200 ROIs. Fourth, we used distinctive tasks in terms of their cognitive load, response patterns, and difficulty, which may have enhanced our ability to discern between cognitive states. Fifth, most previous studies used supervised classification algorithms and evaluated their results using cross-validation across subjects and/or runs. Here, because each subject was analyzed separately with unsupervised methods, an external evaluation metric (ARI) was used to evaluate each subject individually. Differences in the evaluation framework may also contribute to some differences in classification results. Finally, considering whole-brain connectivity patterns as opposed to just a subset of connections may have also provided an additional boost in accuracy for the shortest windows. Results from the “selective exclusion of ROIs” analyses suggest that valuable information for tracking cognition is spatially distributed across the whole brain. Particularly at shorter time windows, removing a limited set of regions/connections can cause a substantial reduction in classification accuracy (Fig. 5, *Bottom Plot*), even if those connections do not show sustained task activations. These findings reemphasize the original definition of FC states as whole-brain phenomena (13, 18) and fit current theories of consciousness that characterize mental states in terms of global access to widely distributed information (40) and highlight the irreducible nature of information integrated across large-scale networks (41).

Additional analyses were conducted to understand what drives the classification. First, to ensure that across-task changes in activation levels or signal variability were not responsible, we attempted classification based on average signal levels and SDs of ROI representative time series. Second, we phase-randomized each ROI time series before computing FC states to ensure that time-varying relationships were needed for accurate classification. Third, we also randomized FC state features (i.e., scrambled the strength of individual connections) to ensure classification was not driven simply by overall across-task changes in connectivity levels. For all these analyses, the ARI dropped into the poor recovery zone for all WLs in all subjects, except for intensity-based classification with WL = 180 s, for which the ARI fell into the moderate recovery zone but was still well below FC-based classification rates (Fig. S7 B, C, E, and F). Finally, to determine whether univariate task activations were necessary for classification, we regressed out the task effects as a nuisance variable in preprocessing and found that the ARI remained excellent (Fig. S7D). These control analyses suggest that classification is driven by orchestrated changes in connectivity across tasks for all window lengths, especially for WL < 180 s, and that first-order activations were neither necessary nor sufficient for robust classification at short time scales.

Additionally, a series of analyses were conducted to evaluate our preprocessing pipeline (Fig. S6). Our results suggest using a finer-grained atlas (more smaller ROIs is better than fewer larger ROIs), a conservative approach to discarding variance (keeping 97.5% of variance produced the best results), and k -means over hierarchical clustering. Most importantly, these results suggest that methodological decisions can influence the strength of measured relationships between FC and mental states, meaning that

caution should be exercised when interpreting results in situations with no ground truth (e.g., resting state).

The brain is an inherently dynamic and distributed system. Although valuable information can be obtained by studying its stable characteristics (e.g., anatomical or stationary rs-fMRI networks), a full understanding will require exploration of its dynamic behavior at different spatial and temporal scales. The strong correspondence between FC states and mental states reported here suggests that the detailed study of FC states may provide novel insights into system-level behaviors of the human brain. Moreover, the rich structure in these dynamics (e.g., number of states, dwell-time, etc.) may be a more sensitive marker for mental conditions than metrics about stable characteristics of the brain (16). Preliminary research has already revealed differences in dwell time between controls and both Alzheimer's disease patients (42) and schizophrenia (43). In two recent reviews on resting state dynamics (4, 16), it was acknowledged that a better understanding of the relationship between BOLD dynamics and behavior was still needed. The work summarized here represents an important step in that direction by showing how fluctuations in FC states, when computed appropriately, are directly related to ongoing cognition

in individual subjects. We believe that future research on FC states in more experimental conditions and populations will help reveal the most cognitively and clinically meaningful ways to observe, describe, and quantify the dynamics of FC states.

Methods

Twenty-two participants were scanned continuously as they engaged in and transitioned between four mental tasks after giving informed consent in compliance with a protocol approved by the Institutional Review Board of the National Institute of Mental Health in Bethesda, MD. After data pre-processing, whole-brain FC patterns (based on Pearson's correlation matrices) were computed for nonoverlapping windows of different durations and used to generate time lines of FC states. These FC-state time lines were then compared with mental-state time lines defined by the timing of the experimental paradigm. Detailed methods are provided in *SI Methods*.

ACKNOWLEDGMENTS. This research was possible thanks to the support of the National Institute of Mental Health Intramural Research Program. Portions of this study used the high-performance computational capabilities of the Biowulf Linux cluster at the National Institutes of Health, Bethesda, MD (biowulf.nih.gov). This study is part of NIH clinical protocol number NCT00001360 and protocol ID 93-M-0170.

- Smith SM, et al. (2009) Correspondence of the brain's functional architecture during activation and rest. *Proc Natl Acad Sci USA* 106(31):13040–13045.
- Chou YH, Panych LP, Dickey CC, Petrella JR, Chen NK (2012) Investigation of long-term reproducibility of intrinsic connectivity network mapping: A resting-state fMRI study. *AJNR Am J Neuroradiol* 33(5):833–838.
- Castellanos FX, Di Martino A, Craddock RC, Mehta AD, Milham MP (2013) Clinical applications of the functional connectome. *Neuroimage* 80:527–540.
- Hutchison RM, et al. (2013) Dynamic functional connectivity: Promise, issues, and interpretations. *Neuroimage* 80:360–378.
- Chang C, Glover GH (2010) Time-frequency dynamics of resting-state brain connectivity measured with fMRI. *Neuroimage* 50(1):81–98.
- 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(December):339.
- Smith SM, et al. (2012) Temporally-independent functional modes of spontaneous brain activity. *Proc Natl Acad Sci USA* 109(8):3131–3136.
- Handwerker DA, Roopchansingh V, Gonzalez-Castillo J, Bandettini PA (2012) Periodic changes in fMRI connectivity. *Neuroimage* 63(3):1712–1719.
- Hutchison RM, Womelsdorf T, Gati JS, Everling S, Menon RS (2013) Resting-state networks show dynamic functional connectivity in awake humans and anesthetized macaques. *Hum Brain Mapp* 34(9):2154–2177.
- Keilholz SD, Magnuson ME, Pan W-J, Willis M, Thompson GJ (2013) Dynamic properties of functional connectivity in the rodent. *Brain Connect* 3(1):31–40.
- Chang C, Liu Z, Chen MC, Liu X, Duyn JH (2013) EEG correlates of time-varying BOLD functional connectivity. *Neuroimage* 72:227–236.
- Thompson GJ, et al. (2013) Neural correlates of time-varying functional connectivity in the rat. *Neuroimage* 83:826–836.
- Allen EA, et al. (2014) Tracking whole-brain connectivity dynamics in the resting state. *Cereb Cortex* 24(3):663–676.
- Bassett DS, et al. (2013) Robust detection of dynamic community structure in networks. *Chaos* 23(1):013142.
- Gonzalez-Castillo J, et al. (2014) The spatial structure of resting state connectivity stability on the scale of minutes. *Front Neurosci* 8(June):138.
- Calhoun VD, Miller R, Pearlson G, Adali T (2014) The chronnectome: Time-varying connectivity networks as the next frontier in fMRI data discovery. *Neuron* 84(2):262–274.
- Shirer WR, Ryali S, Rykhlevskaia E, Menon V, Greicius MD (2012) Decoding subject-driven cognitive states with whole-brain connectivity patterns. *Cereb Cortex* 22(1):158–165.
- Richiardi J, Eryilmaz H, Schwartz S, Vuilleumier P, Van De Ville D (2011) Decoding brain states from fMRI connectivity graphs. *Neuroimage* 56(2):616–626.
- Tagliazucchi E, et al. (2012) Automatic sleep staging using fMRI functional connectivity data. *Neuroimage* 63(1):63–72.
- Mesulam MM (1998) From sensation to cognition. *Brain* 121(Pt 6):1013–1052.
- Gonzalez-Castillo J, et al. (2012) Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis. *Proc Natl Acad Sci USA* 109(14):5487–5492.
- Tononi G (2010) Information integration: Its relevance to brain function and consciousness. *Arch Ital Biol* 148(3):299–322.
- Delamillieure P, et al. (2010) The resting state questionnaire: An introspective questionnaire for evaluation of inner experience during the conscious resting state. *Brain Res Bull* 81(6):565–573.
- Hubert L, Arabie P (1985) Comparing partitions. *J Classif* 2(1):193–218.
- Steinley D (2004) Properties of the Hubert-Arabie adjusted Rand index. *Psychol Methods* 9(3):386–396.
- Craddock RC, James GA, Holtzheimer PE, 3rd, Hu XP, Mayberg HS (2012) A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Hum Brain Mapp* 33(8):1914–1928.
- Zilverstand A, Sorger B, Zimmermann J, Kaas A, Goebel R (2014) Windowed correlation: A suitable tool for providing dynamic fMRI-based functional connectivity neurofeedback on task difficulty. *PLoS ONE* 9(1):e85929.
- Pantazatos SP, Talati A, Pavlidis P, Hirsch J (2012) Decoding unattended fearful faces with whole-brain correlations: An approach to identify condition-dependent large-scale functional connectivity. *PLoS Comput Biol* 8(3):e1002441.
- Cribben I, Haraldsdottir R, Atlas LY, Wager TD, Lindquist MA (2012) Dynamic connectivity regression: Determining state-related changes in brain connectivity. *Neuroimage* 61(4):907–920.
- Heinze J, Wenzel MA, Haynes JD (2012) Visuomotor functional network topology predicts upcoming tasks. *J Neurosci* 32(29):9960–9968.
- Schlegel A, et al. (2013) Network structure and dynamics of the mental workspace. *Proc Natl Acad Sci USA* 110(40):16277–16282.
- Lehmann D, Strik WK, Henggele B, Koenig T, Koukkou M (1998) Brain electric microstates and momentary conscious mind states as building blocks of spontaneous thinking: I. Visual imagery and abstract thoughts. *Int J Psychophysiol* 29(1):1–11.
- Van de Ville D, Britz J, Michel CM (2010) EEG microstate sequences in healthy humans at rest reveal scale-free dynamics. *Proc Natl Acad Sci USA* 107(42):18179–18184.
- Britz J, Van De Ville D, Michel CM (2010) BOLD correlates of EEG topography reveal rapid resting-state network dynamics. *Neuroimage* 52(4):1162–1170.
- Yuan H, Zotev V, Phillips R, Drevets WC, Bodurka J (2012) Spatiotemporal dynamics of the brain at rest: Exploring EEG microstates as electrophysiological signatures of BOLD resting state networks. *Neuroimage* 60(4):2062–2072.
- Musso F, Brinkmeyer J, Mobascher A, Warbrick T, Winterer G (2010) Spontaneous brain activity and EEG microstates: A novel EEG/fMRI analysis approach to explore resting-state networks. *Neuroimage* 52(4):1149–1161.
- Milazzo AC, et al. (2014) Identification of mood-relevant brain connections using a continuous, subject-driven rumination paradigm. *Cereb Cortex* 2014:bhu255.
- Yarkoni T, Poldrack RA, Nichols TE, Van Essen DC, Wager TD (2011) Large-scale automated synthesis of human functional neuroimaging data. *Nat Methods* 8(8):665–670.
- Leonardi N, Van De Ville D (2015) On spurious and real fluctuations of dynamic functional connectivity during rest. *Neuroimage* 104:430–436.
- Baars BJ (2002) The conscious access hypothesis: Origins and recent evidence. *Trends Cogn Sci* 6(1):47–52.
- Tononi G, Edelman GM (1998) Consciousness and complexity. *Science* 282(5395):1846–1851.
- Jones DT, et al. (2012) Non-stationarity in the “resting brain's” modular architecture. *PLoS ONE* 7(6):e39731.
- Damaraju E, et al. (2014) Dynamic functional connectivity analysis reveals transient states of dysconnectivity in schizophrenia. *Neuroimage Clin* 5(July):298–308.
- Cox RW (1996) AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res* 29(3):162–173.
- Glover GH, Li TQ, Ress D (2000) Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. *Magn Reson Med* 44(1):162–167.
- Birn RM, Diamond JB, Smith MA, Bandettini PA (2006) Separating respiratory variation-related fluctuations from neuronal activity-related fluctuations in fMRI. *Neuroimage* 31(4):1536–1548.
- Chang C, Cunningham JP, Glover GH (2009) Influence of heart rate on the BOLD signal: The cardiac response function. *Neuroimage* 44(3):857–869.
- Jo HJ, Saad ZS, Simmons WK, Milbury LA, Cox RW (2010) Mapping sources of correlation in resting state fMRI, with artifact detection and removal. *Neuroimage* 52(2):571–582.
- Gonzalez-Castillo J, et al. (2013) Effects of image contrast on functional MRI image registration. *Neuroimage* 67:163–174.