# #1531 Contributions of covert self-driven cognition to resting stat dynamic functional connectivity

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## INTRODUCTION

Brain functional connectivity (FC), as measured with fMRI, is not stationary. Although it is well accepted that task engagement alters FC, when it comes to dynamic FC changes (dFC) during rest, there is no consensus about its origin or significance (Figure 1.A). Some argue that rest dFC reflects fluctuations in on-going cognition, or is a manifestation of intrinsic brain maintenance mechanisms, which could have predictive clinical value. Conversely, others have concluded that rest dFC is mostly the result of sampling variability, head motion or fluctuating sleep states.

HYPOTHESIS (Figure 1.B). It has been reported that when subjects are asked to rest, they engage in a sucession of self-paced cognitive processes. Most common ones include: inner speech, music sensation, episodic memory, periods of hightened somatosensory sensation, thinking about the self and arithmetics [1].

1) IF a relationship between those mental processes and dFC exists,

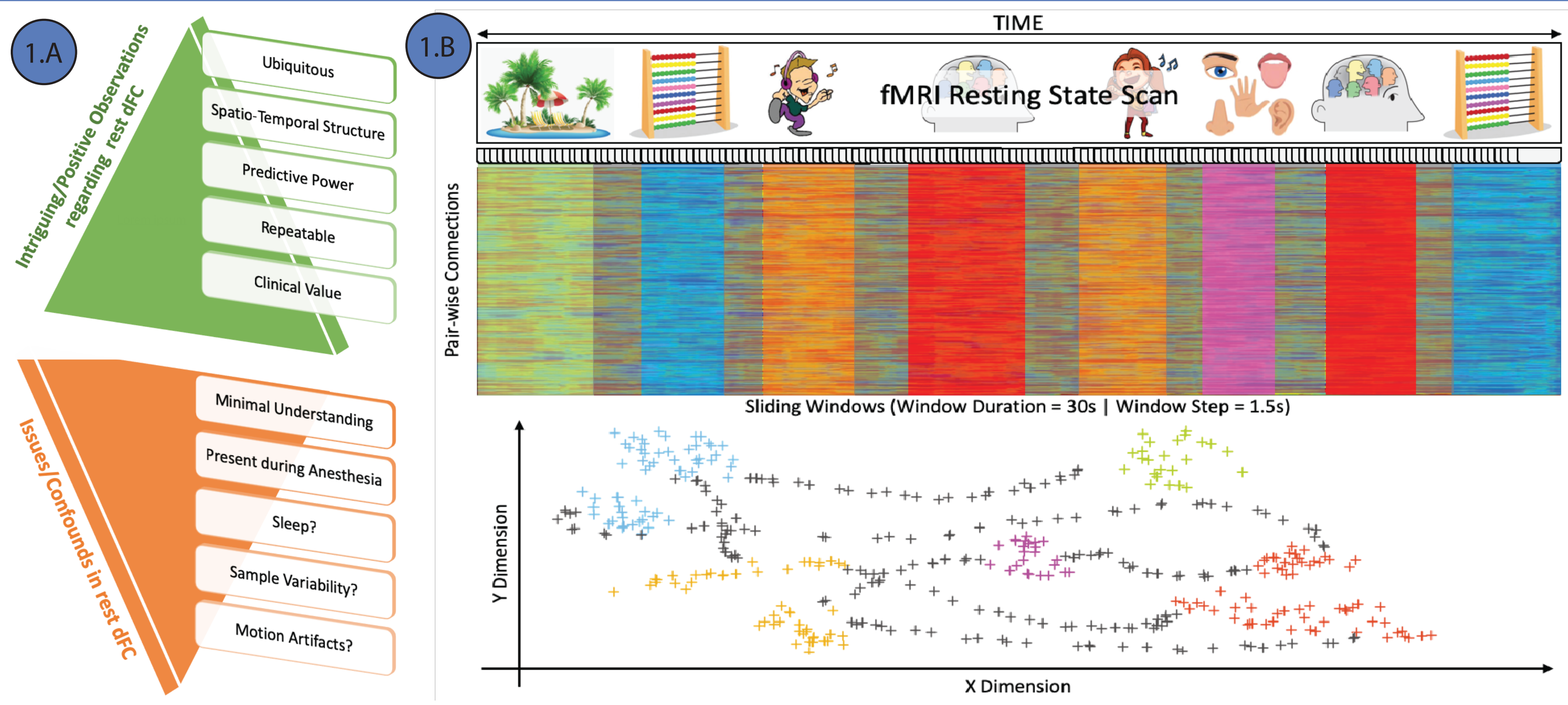
AND

2) dFC patterns could be visualized in a low dimensional space,

THEN

Functional connectivity for temporal windows covering the first instance of a given mental state should concentrate in a small portion of the low dimensional space, distinct from that occupied by windows associated with different mental state. Also, if a subject returns to a previous mental state, FC should return to occupy the same portion of the low dimensional space. Finally, FC for windows spanning the transitions between mental states should form trajectories linking the portions of space associated with the starting and ending mental states.

Here, we present novel analyses suggesting testing this hypothesis. Results suggest that rest dFC is influenced by short periods of spontaneous mental processing, and that the cognitive nature of such mental processes can be inferred blindly from the data.




## METHODS / EXPERIMENTAL DESIGN

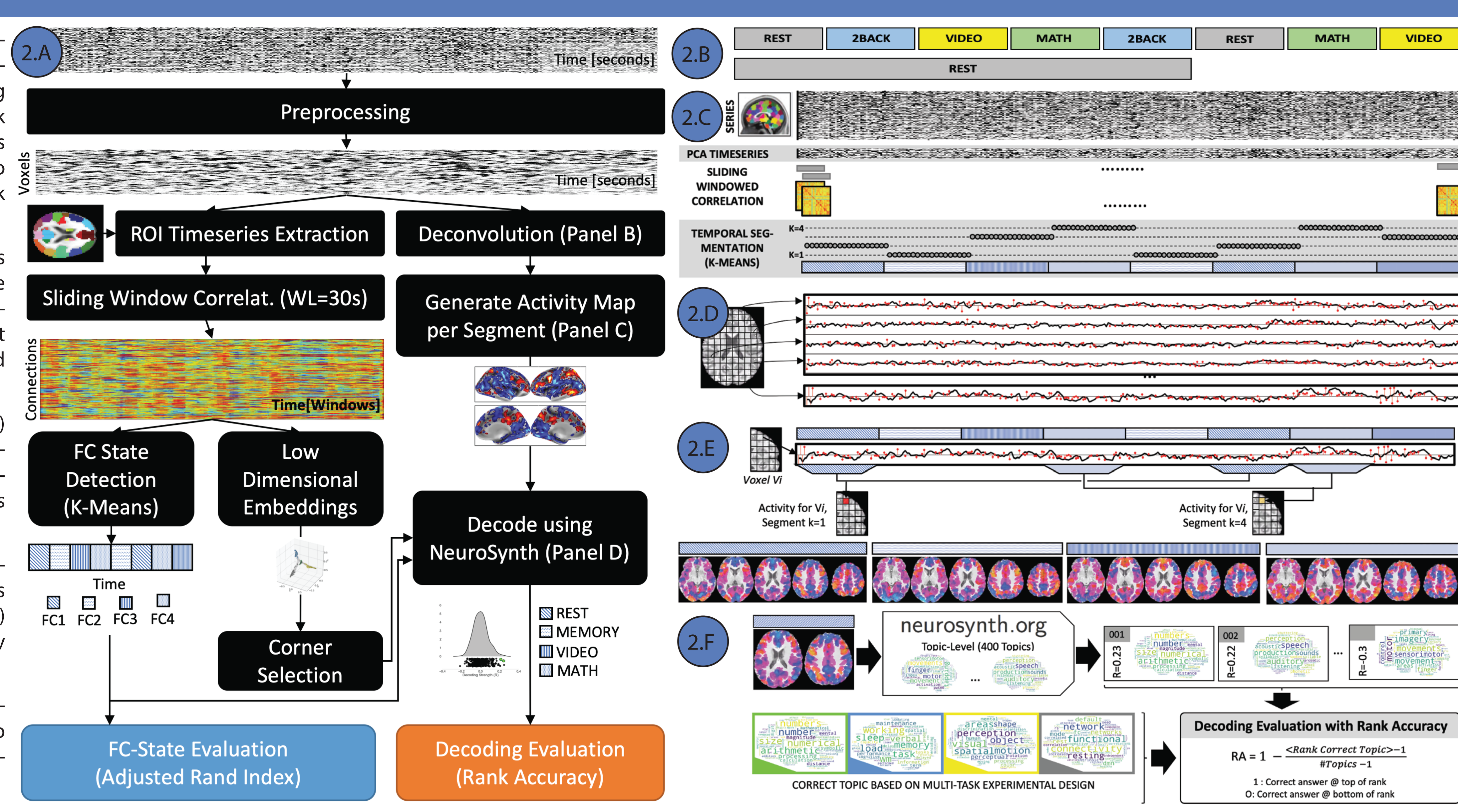
DATA. We worked with two datasets (2.B): multi-task and rest-only. The multi-task dataset consists on 20 subjects scanned continuously for 25 mins as they perform and transition between four different mental states dictated by task demands: 2-back working memory, simple arithmetic, visual attention, and rest. Subjects performed each task during two disjoint three minutes periods [2]. The rest-only dataset consists of 15 mins eyes-open rest scans from the 7T release from the HCP [3]. Rest scans were selected as to minimize motion and sleep artifacts. Analyses were first conducted on the multi-task data to validate interpretation. Then, on rest-only data to test our hypothesis.

METHODS (2.A). First, a dFC matrix [ROI-2-ROI Connections X Temporal Windows] was generated via sliding window correlation analysis (WL=30s). This matrix constitutes the input to both an FC-state detection algorithm (2.C; [2]) and to a non-linear dimensionality reduction algorithm (Laplacian Embeddings [4]). Those two analyses are aimed at segmenting fMRI scans into cognitively homogenous temporal segments (FC states and corner structures in 3D embeddings).

In parallel, voxel-wise timeseries were input to a deconvolution algorithm (SPFM [5]; 2.D) to obtain traces of most prominent events leading to canonical hemodynamic responses in the absence of any information about the nature and timing of the mental processes (or tasks). These traces were then averaged within each cognitively homogenous period to generate an "activity-like" representative per period (2.E).

Finally, those activity-like representations are used as inputs to an open-ended decoding engine (Neurosynth [6]). This engine takes as input activity maps, and generates as outputs rangked lists of topics (2.F). Topics with strong associations (right-tailed outliers) descrive cognitive constructs likely associated with the input map. Decoding accuracy was evaluated with the Rank Accuracy Metric [7].

Although a direct "connectivity-2-cogitive construct" decoding engine would be preferable, such platform does not exist yet. This is why it was necessary to devise a way to generate an activity-like representative per time period, in addition to the already existing FC representative (e.g., the centroid of the k-means step in the FC-State detection).




## RESULTS ON MULTI-TASK DATA

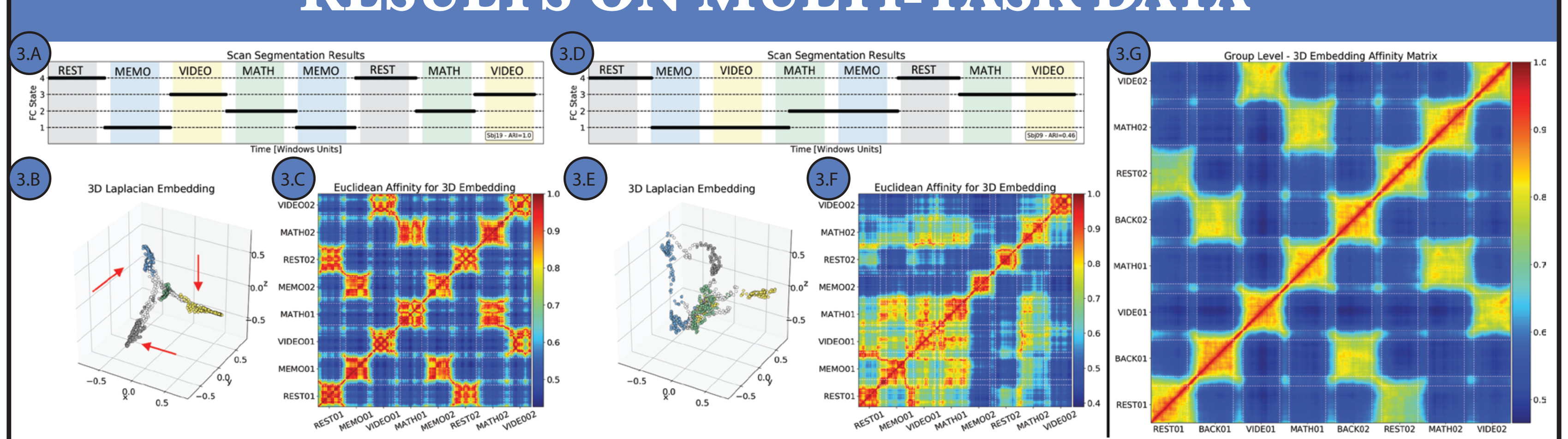



Fig. 3.A hows a FC-state timeline for a case of perfect agreement between FC states and mental states. Fig 3.D shows a subject where recovery was poor. Figs. 3.B & E show 3D visualizations of windowed connectivity for these subjects. In those, each dFC snapshot is represented as a 3D point (grey=rest; green=math; blue=memo; yellow=visual attention; white=more than one task). For subjects whose FC states faithfully reproduced task states (15 out of 20), task homogeneous snapshots cluster together into "spoke" formations (red arrows)—one "spoke" per task—that extent away from the center of the embedding; while transition-snapshots (white dots) form links between spokes going through the center of the embedding. This motif is less clear in instances of poor agreement between FC states and tasks (Fig. 3.E). Fig. 3.C & F show affinity matrices for the embeddings depicted in Fig. 3.B & E. Fig 3.C shows a matrix with clear blocks of high affinity for task homogenous snapshots. This pattern becomes even more apparent when we average affinity matrices of all 15 well behaving subjects.

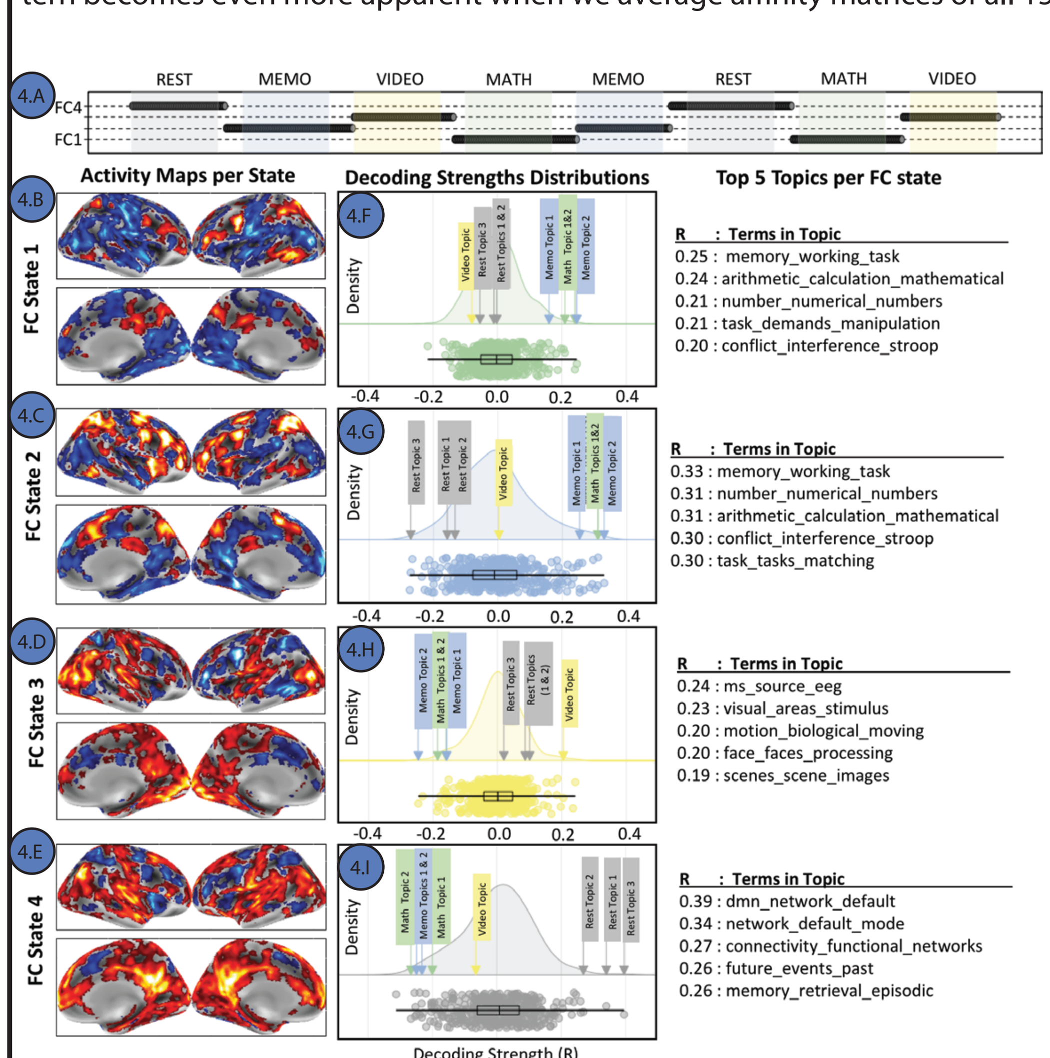



Fig. 4 show decoding results one subject. Panel 4.A shows its FC-State timeline. Panels B-E shows "activity" maps per FC-State. Panels F-I show decoding for each FC-State both as a the top-five table and as cloud plots with the distribution of decoding strength across all 400 topics. For evaluation, correct topics are also clearly marked. For this subject, FC-State 1 spanned periods of MATH and FC-State 2 periods of the MEMO. Activity maps for these two states contain prominent clusters of activity in dorsolateral pre-frontal cortex and parietal regions (4.B & C). Similarly, FC state 3, which overlaps in time with the visual attention task, has prominent areas of activity around the MT/V5 region and other visual regions (4.D). Finally, for FC state 4—which spans rest periods—we observe activity in regions of the default mode network (4.E). As for the actual decoding, for FC states 1 and 2, we observe topics with terms such as "memory", "working", "arithmetic", "calculation" and "numbers" among the top decoding topics (4.F & G). For FC state 3, top topics include the terms "visual", "motion", "biological", "moving" and "scenes" (4.H). Finally, for FC state 4, the three topics that best describe rest appear as the top three decoding terms for this FC state (4.I).

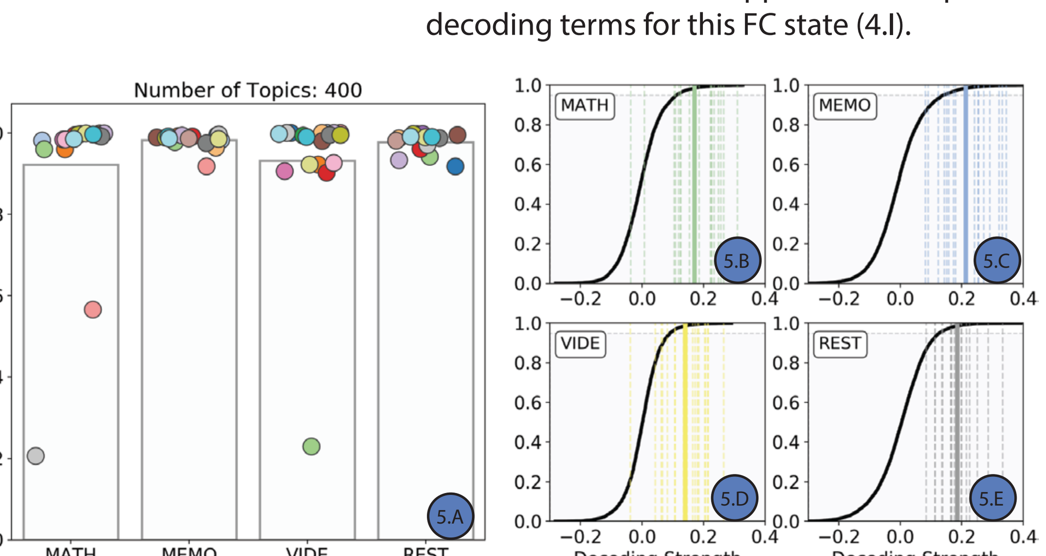



Fig. 5 shows group-level task decoding results. Panel 5.A show rank accuracy values for all task segments and subjects as colored dots, and across-subject mean rank accuracy per task as grey bars. Mean rank accuracy was above 0.8 for all tasks for most subjects. In all instances, mean rank accuracy was significantly higher than chance (p<0.05). Panels 5.B-E show average cumulative distributions of decoding strength for the different tasks (black curves). In addition, individual decoding strength for correct topics are depicted as dashed colored lines. A colored continuous bold line marks the mean correct decoding strength across all subjects. In all instances, except for VIDEO using the 50-topics set (panel 3.E), the mean decoding strength for correct topics fell to the right of 95% of the cumulative distribution of decoding strengths (shaded region).

## RESULTS ON REST-ONLY DATA

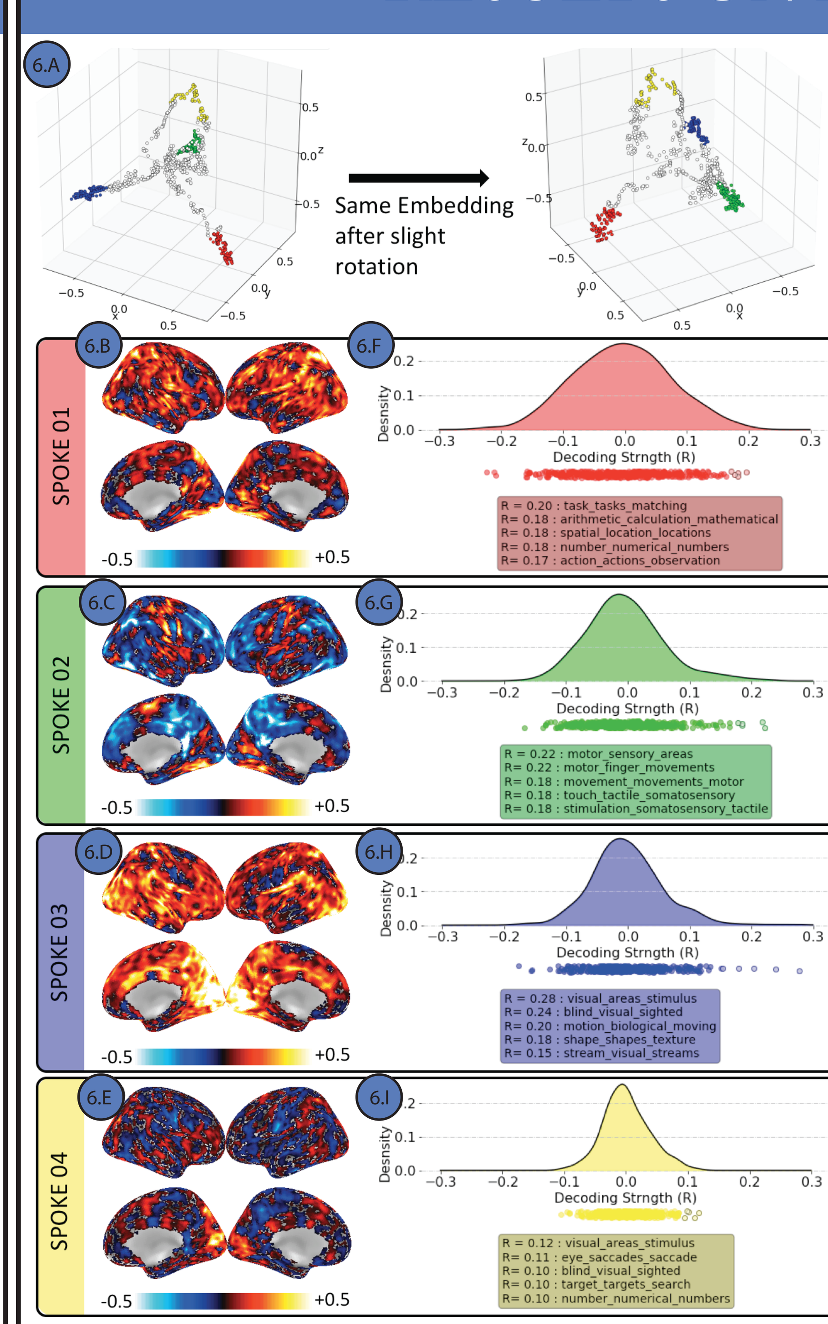
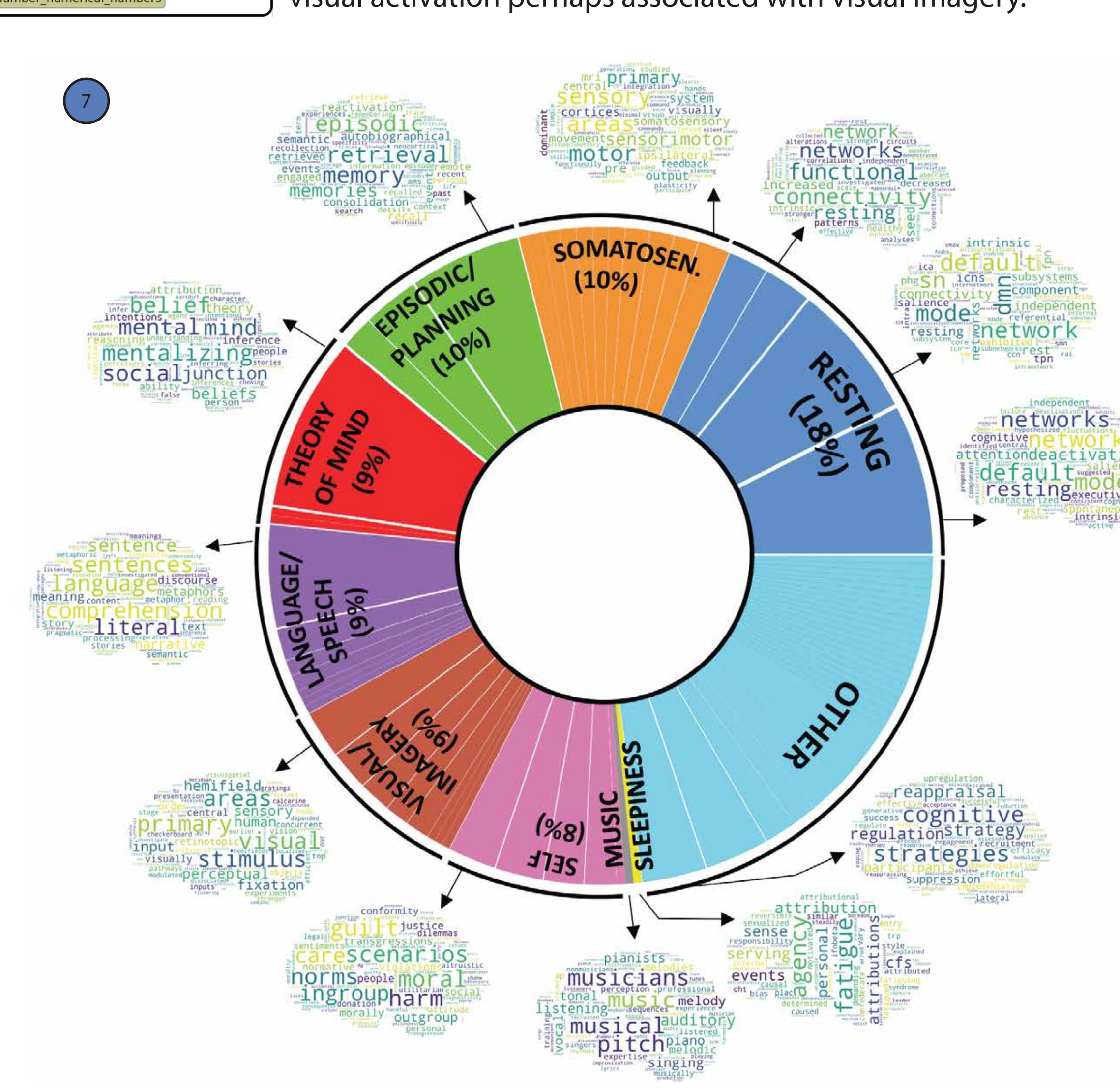



Figure 6 summarizes results of these analyses for one representative rest-only subject. For each subject, we found the x most distal windows in the embedding (in terms of Euclidean distance), with x being equal to the number of FC-states. Next, for each distal end, we selected all windows sitting within a given distance d from it (d = average inter-snapshot distance for all task-homogenous windows in the multi-task dataset). This procedure allowed us to automatically identify sets of spatially contiguous snapshots sitting near the distal ends of the embeddings.

Panel 6.A shows the 3D embedding with the identified spokes for this subject. Each spoke has a different color. Panels 6.B-E show activity maps associated with the windows in each spoke structure. Activity maps are clearly differentiable across clusters. The map for Spoke01 shows activity in lateral parietal and frontal regions. The map for Spoke02 has activity mostly focused on sensory motor regions. The map for Spoke03 presents strong activity in occipital, limbic and insular regions. And, finally, the map for Spoke04 shows activity primarily concentrated in the calcarine region. Panels 6.F-I shows corresponding decoding results. Distributions are similar to those found in the multi-task dataset, namely unimodal "gaussian-like" with a long right tail containing topics with a strong association with the input activity maps. Additionally, top topics are associated with distinct cognitive domains. For example. Spoke01 contains topic associated with numeric mental activity (e.g., "arithmetic_calculation_mathematical" and "number_numerical_numbers"). Spoke02 seems to encompass periods of strong somatosensory activity, as indicated by the terms "motor_sensory_areas", "motor_finger_movements", "movement_movements_motor", etc. Finally, Spoke03 and Spoke04 point to scan segments dominated by strong visual activation perhaps associated with visual imagery.

Across all subjects, out of the 400 available topics, only 78 topics became positive outliers (defined as topics with a decoding strength greater than the third quantile plus 1.5 times the interquartile range) for one or more spokes. The list of most commonly outliers includes topics clearly associated with pure rest (topics 13, 337, 233, 215), thinking about the past or future (topics 309 and 188), theory of mind (topic 269), language/inner speech (topic 214), self-evaluation (topics 159 and 369), mental computations (topics 113 and 376), and visual activity (topic 110). Those all correspond to cognitive domains previously reported as describing the types of mental processes subjects commonly engage with during rest [1]. Finally, Fig 7 provides a summary view of all topics marked as positive outliers for spoke-like structures in pure rest scans. Topics are grouped into the above-mentioned cognitive domains describing resting mental activities. Approximately 75% of topics fall within one of these categories: resting (17.87%), somatosensory (9.89%), episodic/planning (9.51%), theory of mind (9.13%), language/speech (9.13%), visual/imagery (9.13%), self (8.37%), music (0.4%) and sleepiness (0.4%).




## CONCLUSIONS

1) Dynamic functional connectivity during rest is, to some extent, a manifestation of covert self-paced cognition.
2) Sparse Paradigm Free Mapping and Laplacian Embeddings can be used to probe dynamic FC during task and rest.
3) Several different behaviorally relevant whole-brain FC configurations may occur during a single rest scan even when subjects are continuously awake and displayed minimal motion.
4) The cognitive correlates of these FC configurations can be decoded using existing open-ended decoding engines.
5) Data-driven estimates of covert cognition agree with previous reports of most common "resting" mental processes.

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