

## Spatially coupled functional and vascular networks

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**Target audience:** Researchers studying functional or vascular networks in task-related and resting-state BOLD fMRI data.

**Purpose:** Independent component analysis (ICA) can identify network structure in resting-state fMRI data<sup>1</sup>. However, it is challenging to determine the origin of signal fluctuations in these networks. We apply breath-hold tasks that drive a global BOLD signal increase via the vascular response to hypercapnia. Using ICA, we demonstrate that neural and vascular networks can be identified and isolated.

**Methods:** Six breath-hold fMRI scans were collected in 12 healthy subjects (aged  $32 \pm 6$  years, 5 female) using a 3 T GE HDx scanner and a BOLD-weighted gradient-echo EPI sequence (TR/TE = 2000/35ms; FOV=22.4 cm; 35 slices, resolution =  $3.5 \times 3.5 \times 4 \text{mm}^3$ , 165 volumes, 5.5 minutes). Each scan consisted of six end-exhalation breath-holds (BH) of either 10s, 15s, or 20s duration interleaved with periods of cued paced breathing. In three scans, all breath-holds were identical (*All 10s*, *All 15s*, *All 20s*), and in three scans the length of breath-holds varied (*Avg 12.5s*, *Avg 15.0s*, *Avg 17.5s*). Expired gas content was continuously monitored via a nasal cannula and end-tidal CO<sub>2</sub> time series were extracted. fMRI data were motion corrected (AFNI) and the first 3 volumes removed. A high-resolution T1-weighted structural image was collected and used to register all functional data to MNI template space.

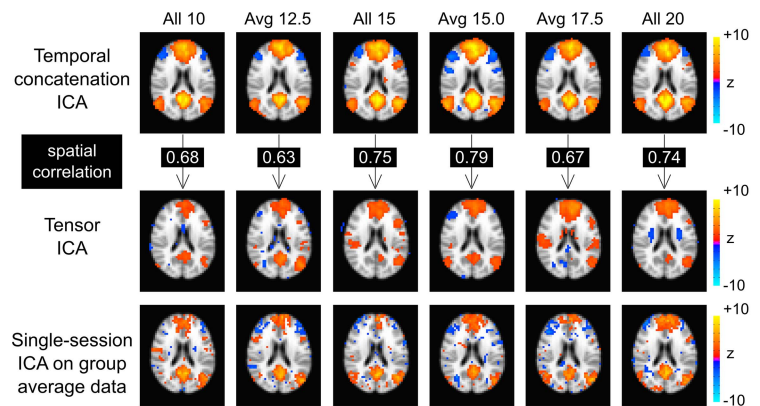
For each breath-hold paradigm, independent component analysis (MELODIC, FSL) was applied on a temporal concatenation of the 12 subjects' data to extract both task-related and intrinsic signal fluctuations. The default mode network was identified using spatial correlation with connectivity networks from the literature<sup>1</sup>. Tensor ICA was applied to the same data to identify task-locked signal networks. Finally, the average dataset (across subjects) was calculated for each of the 6 scan types using AFNI, and single-session ICA was performed on the results. Spatial correlation was used to identify instances of the default mode network in the tensor and single-session ICA results. The component timeseries were compared with the CO<sub>2</sub> data for each scan type and with the timing of the breath-hold paradigm.

**Results:** We identified network maps similar to the default mode network in all ICA results (Fig.1). In the tensor and group-average ICA datasets, we can deduce that this network exhibits activity that is time-locked to the respiratory paradigm and is not due to "intrinsic fluctuations," which should be nulled in these analyses. Additionally, we identified *two* components in the data that are closely related, spatially, to the default mode network from the literature. Fig. 2 illustrates these two components in the *Avg 17.5* data. The upper component exhibits a time series that is well-modeled by the end-tidal CO<sub>2</sub> data convolved with an HRF, demonstrating a strong vascular contribution to this network. The lower component exhibits *negative* BOLD signal changes during the execution of the breath hold challenges and minimal positive CO<sub>2</sub>-related BOLD signal changes, indicating neural deactivation coupled to task performance.

**Discussion:** We show that respiratory challenges deactivate the default mode network, and that these signals can be extracted using independent component analyses. Specifically, the default mode network demonstrates a decrease in BOLD signal during the execution of a respiratory task. This may be linked to neural deactivation during elevated attention to the stimulus or to changes in neural metabolism associated with the specific breathing challenges, but it does not appear strongly associated with the vascular hypercapnia response. In contrast, a second network was identified that also demonstrates strong spatial correlation with the default mode network but is tightly coupled to hypercapnic vascular effects. As the network is spatially similar to the DMN but responds to a global vasodilatory CO<sub>2</sub> stimulus, this suggests that the vasculature is organised into networks similar to function.

**Conclusions:** The breath-hold paradigm may provide a means for probing the relationship between vascular and functional architecture in the brain. Functional networks must be supported by vascular networks, and the results presented demonstrate that a vascular network exists that may support the function of the DMN.

**References:** [1] Smith et al (2009) PNAS Proc Natl Acad Sci USA 106(31):13040-5.



(above) Fig. 1. The default mode network identified in breath-hold ICA results. (below) Fig. 2. Two components are identified as strongly correlated with the default mode network. The time series of the group average data for each component is plotted (blue lines). One component exhibits CO<sub>2</sub>-related signal increases while the other exhibits task-related signal decreases.

