The effect of respiration variations on independent component analysis of resting state functional connectivity

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Introduction:
The analysis of functional connectivity in fMRI can be severely affected by cardiac and respiratory fluctuations (1-3).   While some of these artifactual signal changes can be reduced by physiological noise correction routines (4), signal fluctuations induced by slower breath-to-breath changes in the depth and rate of breathing are typically not removed (2). These slower respiration-induced signal changes overlap with many of the regions of the default mode network (DMN), and occur at low frequencies similar to the fluctuations used to infer functional connectivity. This overlap in both space and frequency has been shown to significantly affect seed-ROI or seed-voxel based functional connectivity analysis, particularly in the default mode network (2).   In this study, we investigate the effect of respiration variations on functional connectivity maps derived from independent component analysis (ICA) of resting-state data. Since these respiration-induced fluctuations occur at similar low frequencies and in similar brain regions as the default mode network, we hypothesize that the ICA component typically identified as representing the "default mode network" will have a significant contribution from and correlation with respiration variations.

Methods:
ICA was performed using the MELODIC program from FSL (5) on resting-state data from 10 subjects. The data were taken from a previous study in which a seed-ROI functional connectivity approach demonstrated significant overlap between respiration-induced signal changes and the DMN (Fig 1c,d) (also, see Reference 2). Time series of T2*-weighted echo-planar MR images were acquired on a 3T General Electric (GE) MRI scanner (Waukesha, WI, USA). (Whole brain coverage with 27-28 sagittal 5 mm thick slices, TR: 2s, TE: 30 ms, Flip angle: 90º, FOV: 24 cm, slice thickness: 5 mm, matrix: 64x64, 165 image volumes per time series.) Regions of the default mode network were identified by deactivations during a lexical decision task (Word vs. Non-word). Respiration was measured with a pneumatic belt positioned at the level of the abdomen. An estimate of the respiration volume per unit time (RVT) was obtained as described in (2). Regions with significant RVT-related signal changes were determined by computing the correlation between the RVT time course and resting-state MR time series data.
Components were identified as "default mode network" or "RVT-related" by computing the spatial correlation between each component and a spatial mask derived from either the individual subject or the group deactivations or RVT-related changes. The contribution of respiration in each component was also assessed by computing the correlation coefficient between each component time series and the RVT time course.

Results + Conclusions:
Contrary to our hypothesis, ICA appeared to separate the default mode network and the respiration-related changes in most (14/18) cases (Figs 1e,f), even though the spatial locations of the expected changes (Figs 1a,b) and temporal frequencies of the components (Figs 1g,h) were similar. In some cases, however, the component automatically identified as the default mode network was the same as the component identified as RVT-related. In other cases, there were several components that were similarly correlated with the DMN mask. Furthermore, for most subjects the time series associated with the DMN component was still significantly correlated with the changes in respiration, suggesting that ICA may not completely separate respiration from the default mode network. In all of these cases, an independent measure of the respiration provides valuable information to help distinguish the default mode network from respiration-related signal changes, and to assess the degree of residual respiration related effects.
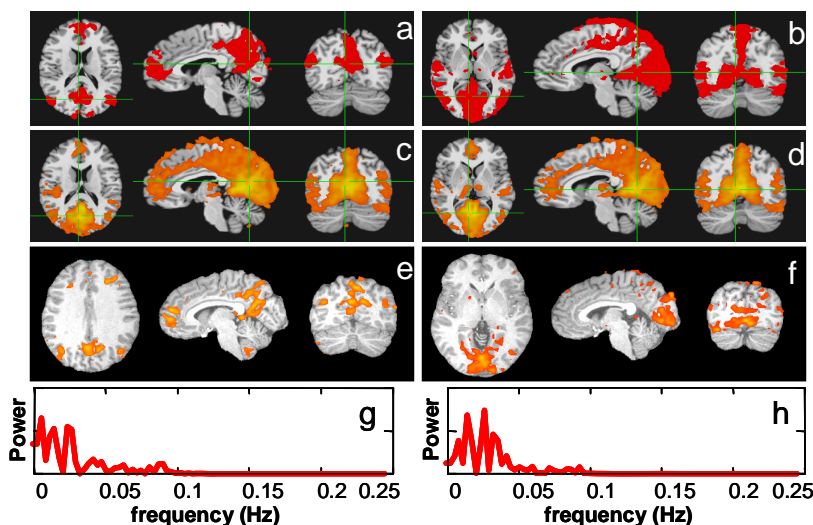
Figure 1: **a**) regions of the default mode network (DMN) that are deactivated during the lexical task (group results) **b**) regions correlated with respiration-volume per time (RVT) changes (group results). **c-d**) regions significantly correlated at rest with a seed region from the posterior cingulate, averaged over the group of subjects (c & d show different views of the same functional connectivity map) **e-f**) two ICA components from one representative subject, identified as **e**) "DMN", and **f**) "RVT-related".   **g-h**) power spectra of the time series associated with components e-f, respectively.

References:
1. R.G. Wise, et al., NeuroImage 21, 2004.
2. R.M. Birn, et al., NeuroImage 31, 2006.
3. T.E. Lund, Magn. Res. Med. 46(3), 2001.
4. G. Glover, et al., Magn. Res. Med. 44(1), 2000.
5. C.F. Beckman, et al., IEEE Trans. Med. Imag. 23, 2004.