Respiration modulates rhythmic resting-state activity

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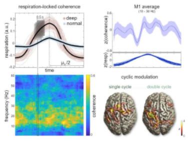
Introduction

Respiration-brain coupling

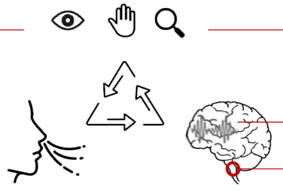
performance varies with respiration phase

Zelano et al., 2016
Schulz et al., 2016
Perl et al., 2019

… so does neural communication



Kluger & Gross, 2020



brain states determine perception, action, cognition

cortical oscillations mark brain states

Thut et al., 2012

medullar control of breathing rhythm (pre-BötC)

Del Negro et al., 2018

respiration ⟷ brain states

Methods

Data

- 2 x 5min resting-state MEG and respiratory data from N = 28 volunteers
- T1 anatomies (MPRAGE) co-registered to MNI

Measures of phase-amplitude coupling

- Morlet wavelet transform on single-sensor time courses yielded global field power (GFP)
- head motion correction Stolk et al., 2013
- Hilbert transform of respiration time course and computation of normalised modulation index (MI) using random shifts
- phase-triggered average (PTA) quantifies GFP over respiration phase (centred around peak inspiration)

Source-level analyses

- LCMV beamformer for source localisation
- non-negative matrix factorisation (NMF) on freq x voxel matrices yielded spatial and spectral distributions of 18 anatomical components
- cluster-permutation tests for significance of frequencies
- hierarchical clustering further reduced 18 NMF components to 7 clusters of nodes

Modulation of global field power over the respiration cycle

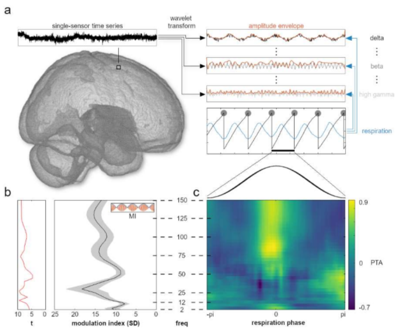


Fig. 1 | a, Exemplary schematic of our analysis approach showing the wavelet transform of time series data from each sensor. Global field power was computed on the time course of all 268 channels for further analyses of the modulation index (MI) and phase-triggered average (PTA). We computed modulation indices for each sensor, frequency, and participant before localising voxelwise time series in source space. **b**, Mean normalised MI (± SEM) over the entire frequency spectrum (right) and corresponding t-values from the cluster permutation test (left). Random shifts of respiration phase were employed to correct for low-frequency bias and to express MI in units of standard deviation (SD) of a surrogate distribution (leading to normalised MI). **c**, Mean PTAs across the respiratory cycle over the entire frequency spectrum. PTAs were computed by averaging frequency-specific amplitude envelopes time-locked to peak inhalation.

Results

Network of respiration-modulated brain oscillations

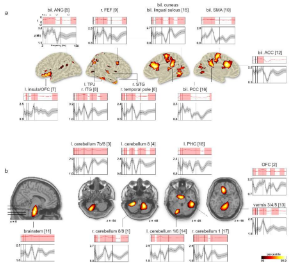


Fig. 2 | a, Cortical components plotted on an inflated brain surface. Bottom graphs illustrate each component's normalised MI course across frequencies. Upper graphs show t-value spectra from cluster permutation tests (significant frequencies shaded). Horizontal red line marks the significance threshold of each component. Spatial maps were thresholded at the 99th percentile. Colour bar indicates corresponding p-values. **b**, Subcortical components plotted on transverse and sagittal slices of the MNI brain. Same format as **a**.

Spectral characteristics of component clusters

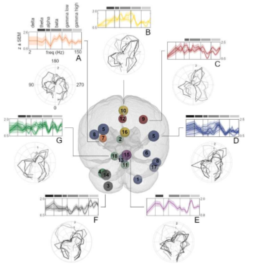


Fig. 3 | Hind view illustrates the distribution of component clusters A-G. Spheres mark peak locations of components. Top curve plots depict normalised MI of individual components within the cluster (M ± SEM) over log-transformed frequencies. Horizontal bars show frequency bands in which at least one component showed significant modulation. Polar plots illustrate temporal modulation of RMBOs of frequency bands averaged within clusters as a function of respiration.

Mapping RMBO components to canonical neural networks

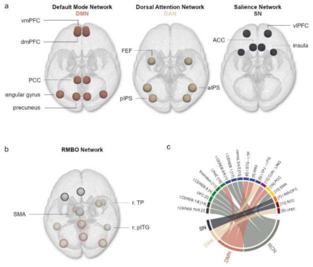


Fig. 4 | a, Top-view stylised illustrations of neural nodes composing the DMN, DAN, and SN. **b**, Cortical brain areas showing significant RMBOs, colour-coded according to their correspondence to networks shown in **a**. **c**, Direct mapping of all 16 clustered NMF components to the resting state networks and the respiratory control network (RCN) gained from the literature.

Discussion

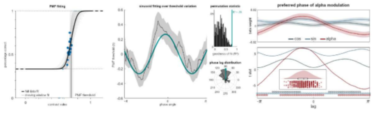
Summary

- respiration-modulated brain oscillations (RMBOs) span a widespread network of cortical and subcortical brain areas
- instead of a uniform modulation pattern across brain areas and frequencies, respiratory modulation signatures differ between brain areas in their spectro-temporal profiles
- sources of these modulatory effects correspond to nodes of canonical networks in control of resting state activity and respiratory function
- one key mechanism is cross-frequency coupling: slow respiratory rhythms drive slow neural oscillations which are subsequently translated into faster cortical rhythms
- natural fluctuations in arterial CO_2 during normal breathing significantly influence oscillatory power Driver et al., 2016
- interplay of arterial CO_2, pH, and adenosine, which reduces excitability during hypercapnia Ito et al., 2003

Outlook

Active sensing, respiration, and behaviour

- respiration has been suggested as an overarching 'clock' mechanism organising neural excitability throughout the brain Ito et al., 2014
- with cortical excitability fluctuating over the respiration cycle, information sampling during states of high excitability optimises efficient communication between brain areas
- in temporally coordinating the breathing act and internal brain dynamics (i.e., heightened excitability), the sampling of bottom-up sensory information can be aligned with top-down predictive streams Corcoran et al., 2018



Kluger et al., in preparation