Physiological Component of the BOLD Signal: Influences of Age and Heart Rate Variability Biofeedback Training

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Background and Motivation

There are interactions between autonomic physiological processes (e.g., heart rate and respiration) and neural activity. Most times, physiological effects on brain signal measurements are ignored in studies of brain function, but they may provide useful information about autonomic health. Since Blood Oxygen Level-Dependent (BOLD) fMRI signals capture brain activity via blood flow changes, systemic physiological effects (e.g., low-frequency changes in cardiac rate and and respiratory volume) that impact blood flow can also affect BOLD. These physiological influences on BOLD can be indicative of autonomic and brain vascular health.

Central Question: How does aging affect the interaction between fMRI and systemic physiological signals? And can this relationship be modulated with an intervention?

Datasets

Nathan Kline Institute (NKI) Rockland Sample: n = 399 participants (18 – 85 years). 3T imaging, single-echo fMRI with spatial resolution = 2mm isotropic and TR (temporal sampling) = 1.4 seconds. Cardiac (PPG) and respiration (belt) were acquired at 62.5 Hz sampling rate.

Heart Rate Variability - Emotion Regulation (HRV-ER) Dataset: n = 110 participants (18 – 80 years). 3T imaging, multi-echo fMRI with spatial resolution = 3mm x 3mm x 4mm and TR = 2.4 seconds. Cardiac (PPG), CO2 (capnography signal), respiration (belt) were acquired at 10 kHz and downsampled to 1 kHz. Each participant was scanned before and after 5 weeks of daily heart rate variability (HRV) biofeedback training. HRV measures the variation in time intervals between heartbeats and is a key indicator of autonomic nervous system health. Individuals were assigned to one of two conditions: increasing HRV (Osc+) or decreasing HRV (Osc-).

Signal Processing

Preprocessing Imaging Data:

- T1 MRI: skull-strip and register to MNI152 standard space.
- Functional data: motion and slice time correction; multi-echo independent component analysis to to decompose signal from noise, affine registration to T1; non-linear registration to MNI152 space; spatial blurring to 3mm FWHM; nuisance regression to remove motion and slow scanner drifts; temporal normalization of BOLD signal as percent signal change.

Physiological Data Preprocessing:

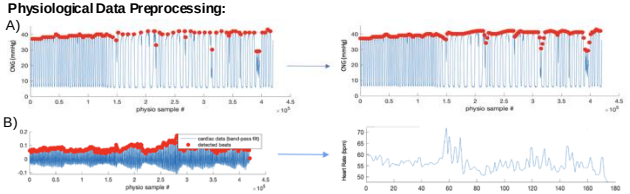

Figure 1. Preprocessing pipeline for physiological data. A) In the HRV-ER dataset only, peaks were extracted from the capnography signal (representing the end of an exhaled breath) to obtain end-tidal CO2. This was interpolated to the fMRI TR (2.4 seconds) and co-aligned with respiratory variation. B) Peaks were extracted from the PPG signal after band pass filtering for easier peak detection. The number of beats was counted in a 6-second sliding window centered at each TR to obtain heart rate, scaled to beats-per-minute.

Physiological Deconvolution:

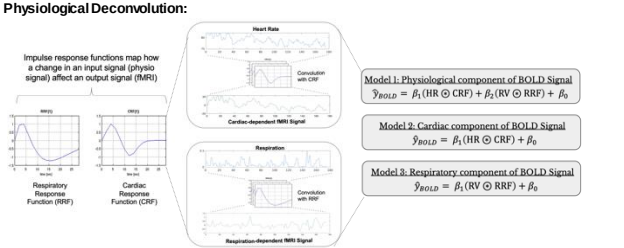

Figure 2. Deconvolving the physiological, cardiac, and respiratory component of the BOLD signal. Participant physiological signals (i.e., heart rate and respiration volume) were convolved with physiological impulse response functions and subsequently input into least squares regression models. This yielded the physiological brain maps, where every voxel captures the degree to which heart rate and respiration impacted the BOLD signal.

Data Analysis:

A) Amplitude of Physiological Component

B) Temporal Dynamics of Physiological Component

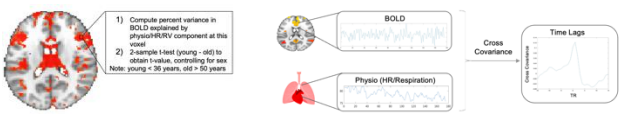

Figure 3. Data analysis to compare the physiological component of the BOLD signal on a whole-brain level across participants. A) Percent variance in the BOLD signal explained by the physiological component was taken by dividing the variance in the of the BOLD physiological component by the total temporal variance of the BOLD signal. Two-sample t-tests for this physiological component at every voxel were computed between the old and young group as well as between the heart rate variability biofeedback training conditions, controlled for sex. B) Computed temporal cross-correlation between physio (HR or RV) and BOLD signals averaged within 4 cortical regions of interest defined by the Schaefer 100 cortical parcellations atlas. This gives information about the temporal dynamics of physiological propagation into brain fMRI signals.

Modulation of BOLD physiological amplitude by age and biofeedback intervention

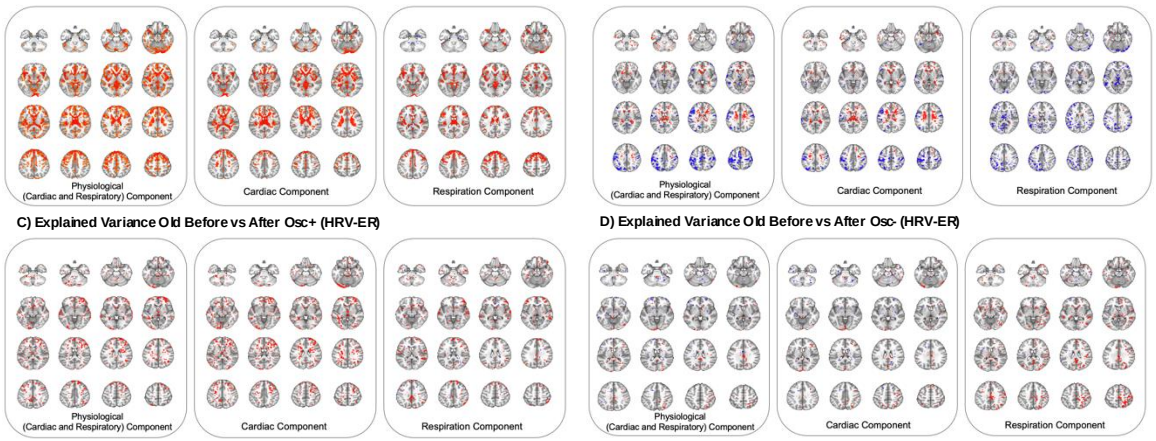

Figure 4. Comparison of BOLD physiological variance between the indicated conditions. A) t-values thresholded above 3.0, indicating regions where explained variance in young adult group are greater than old adult group. All highlighted regions survive threshold-free cluster enhancement (tfce) correction with 5000 permutations ($p < 0.05$). B) t-values thresholded above 2.0, indicating regions where explained variance in young adult group are greater than old adult group (red) or vice versa (blue). Red clusters achieve $p = 0.063$ significance using cluster-based thresholding corrected for multiple comparisons by using the null distribution of the max with 5000 permutations. C) t-values thresholded above 2.0, indicating regions where explained variance in old adult group after HRV biofeedback Osc+ was higher than before (red). With cluster-based thresholding corrected for multiple comparisons by using the null distribution of the max with 5000 permutations, red clusters achieve $p = 0.08$ significance. D) t-values thresholded above 2.0, indicating regions where explained variance in old adult group after HRV biofeedback Osc- was higher than before (red) or lower than before (blue). No trending or significant regions exist after FWE correction.

Modulation of BOLD physiological dynamics by age and biofeedback intervention

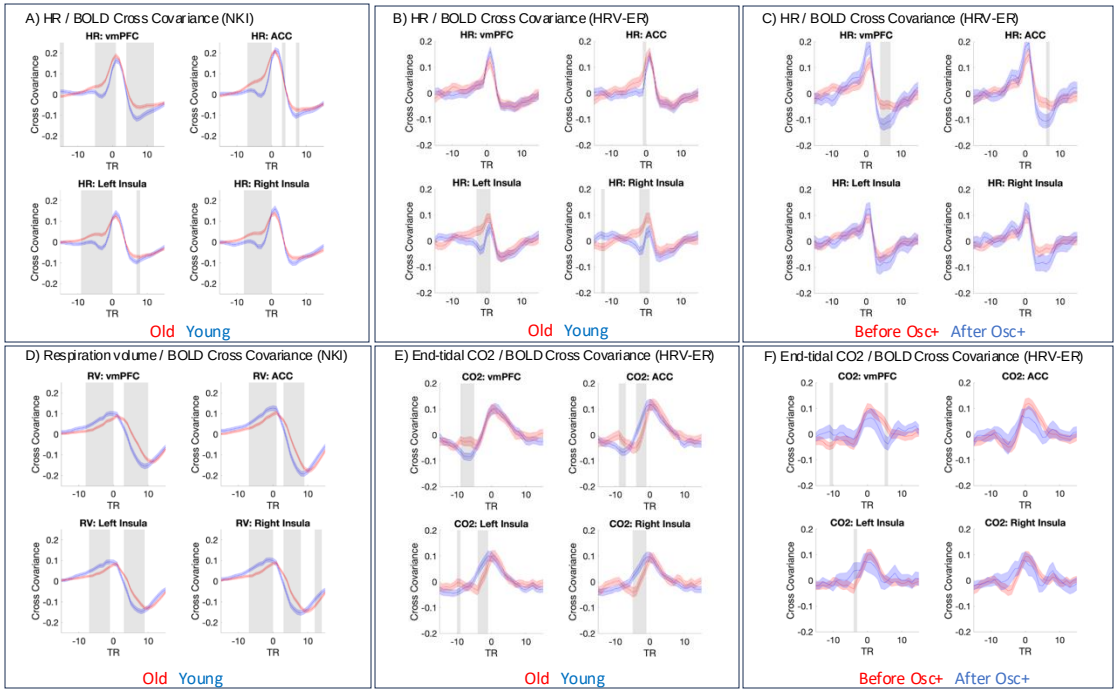

Figure 5. Cross covariance analysis HR/BOLD cross covariance computed between old and young adults in the A) NKI Dataset and the B) HRV-ER dataset with regions of significant difference highlighted. C) In the HRV-ER dataset, HRV/ER cross covariance in the older adult group computed before and after Osc+ demonstrates that HRV biofeedback partially reverses some of the old vs young differences. Respiration/BOLD cross covariance computed between old and young adults in the D) NKI Dataset and the E) HRV-ER dataset with regions of significant difference highlighted. F) In the HRV-ER dataset, HRV/ER cross covariance in the older adult group computed before and after Osc+ demonstrates that HRV biofeedback partially reverses some of the old vs young differences.

Conclusions

The physiological component of the BOLD signal is attenuated in older adults compared to young adults, particularly in the "Central Autonomic Network" which consists of areas like the VMPFC, ACC, and Insula. The temporal dynamics in which physiological signals propagate into the brain also appear to be different in older adults compared to younger adults, although the effect is different in heart rate and respiration. HRV biofeedback training seems to reverse some of the effects seen in the aging brain, making the physiological component of the BOLD signal look more youthful.

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