

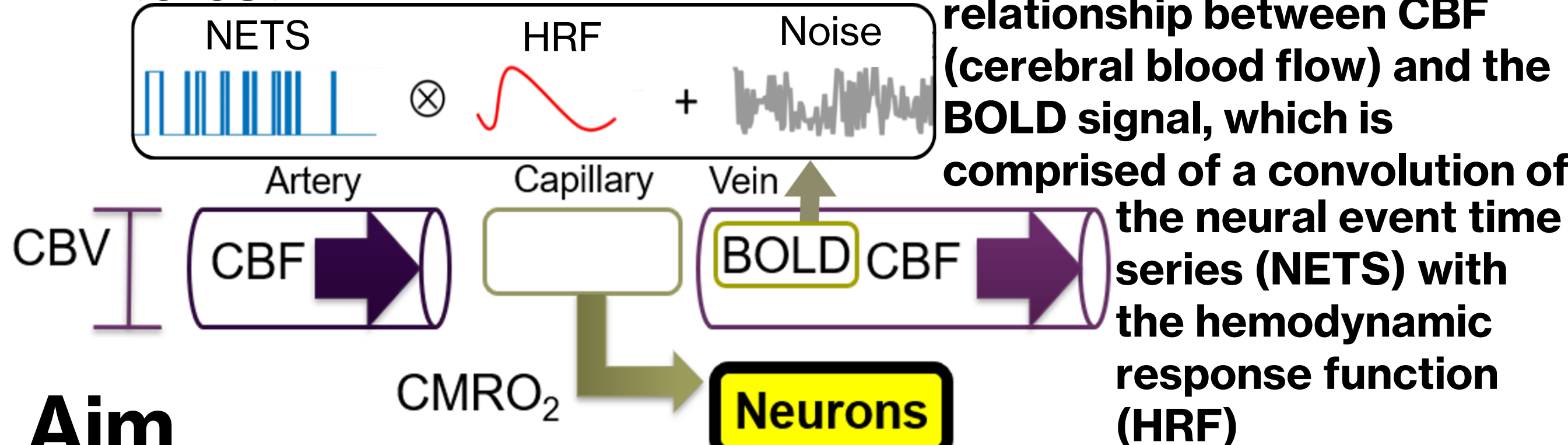
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Introduction

The BOLD signal reflects neural activity and vascular responses, which can confound interpretation of underlying brain function.

- The blood-oxygen-level-dependent (BOLD) signal measured with functional magnetic resonance imaging (fMRI) reflects both underlying neural activity and the hemodynamic response which accompanies it
- The hemodynamic response varies between people, thus confounding the neural activity that is often of primary interest



Aim

Validate neural event time series-based functional connectivity

- Assess functional connectivity (FC) using common method (Pearson correlation for linear correlation) and less-common method (mutual information (MI) for linear and non-linear correlation).
- Pearson correlation & MI applied to BOLD are compared to MI applied to the neural event time series (NETS)

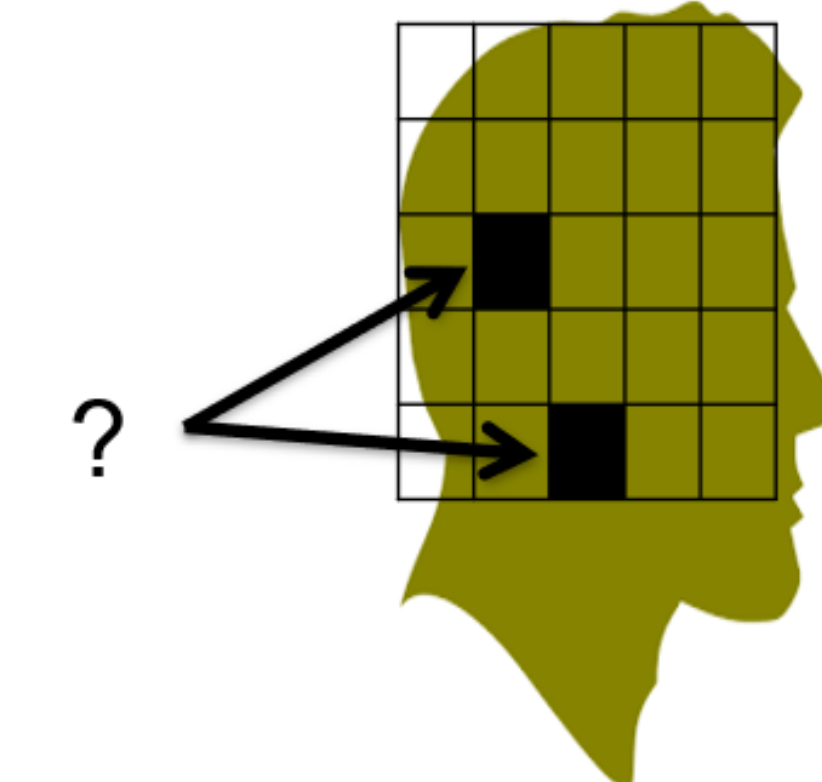


Fig 2: Functional connectivity describes dynamic relationship in brain activity between spatially distinct brain regions over time

Methods

Demonstrate neural event time series ability to identify FC differences between groups with healthy and less-healthy vascular function

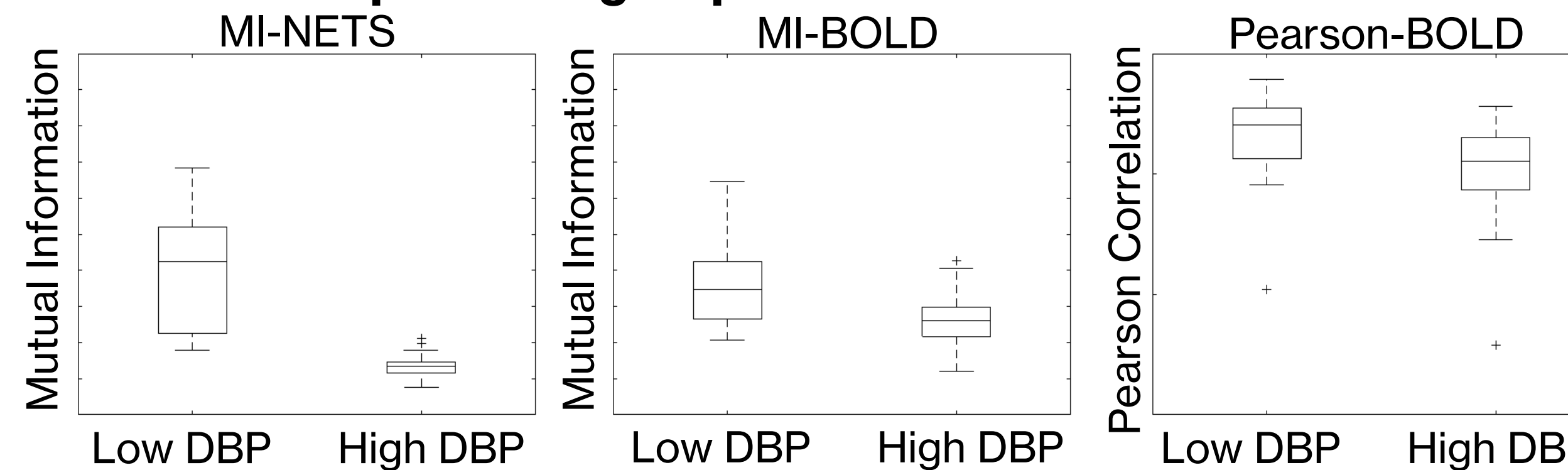
- A machine learning-based deconvolution method is used to remove the hemodynamic response function (HRF) from BOLD signal and estimate the neural event time series (NETS).
- FC is assessed using Pearson correlation applied to the BOLD signal (Pearson-BOLD) and MI applied to both the BOLD signal (MI-BOLD) and NETS (MI-NETS).
- The dataset consists of fMRI scans from 30 participants with healthy diastolic blood pressure ("low DBP") and high diastolic blood pressure ("high DBP") from the Bogalusa Heart Study.
- Regions activated during the Stroop task, along with an additional uninvolved control region, are identified for each participant.
- Group-wise statistical analyses are performed to identify FC differences between low and high DBP groups.
- MI captures both linear and non-linear correlations, whereas Pearson correlation is limited to linear relationships.
- Both MI and Pearson correlation have previously been applied in BOLD-based FC analysis.

Results

Neural event time series provides distinct functional connectivity information compared to the BOLD signal.

	N	Age	Sex (%male)	Race (%African American)
High DBP	30	56.89 ± 4.80	53%	30%
Low DBP	30	53.91 ± 4.73	23%	7%

Table 1: Demographic information for the participants in each diastolic blood pressure group.



- Pearson correlation can produce positive and negative values, so the absolute value was used so strong correlation in either direction are interpreted equally.
- Higher FC is expected in the healthy DBP group because elevated mid-life DBP has been associated with poorer cognitive function in later life.
- MI-NETS shows highest separation between groups with no overlap between interquartile ranges, and overlap occurring only in the whiskers.



Fig 3: Stroop task. The participant is asked to select the color of the word, not read the word. Top (congruent), the correct answer is red. Bottom (incongruent), the correct answer is blue.

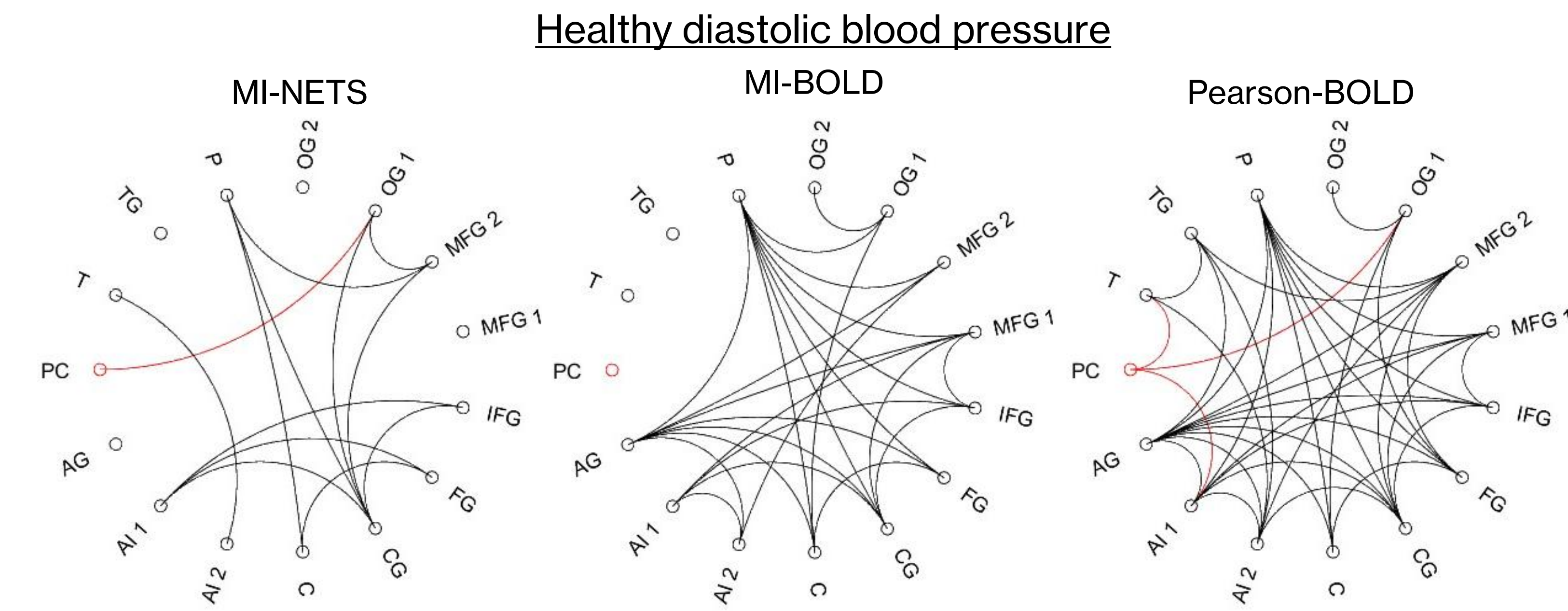
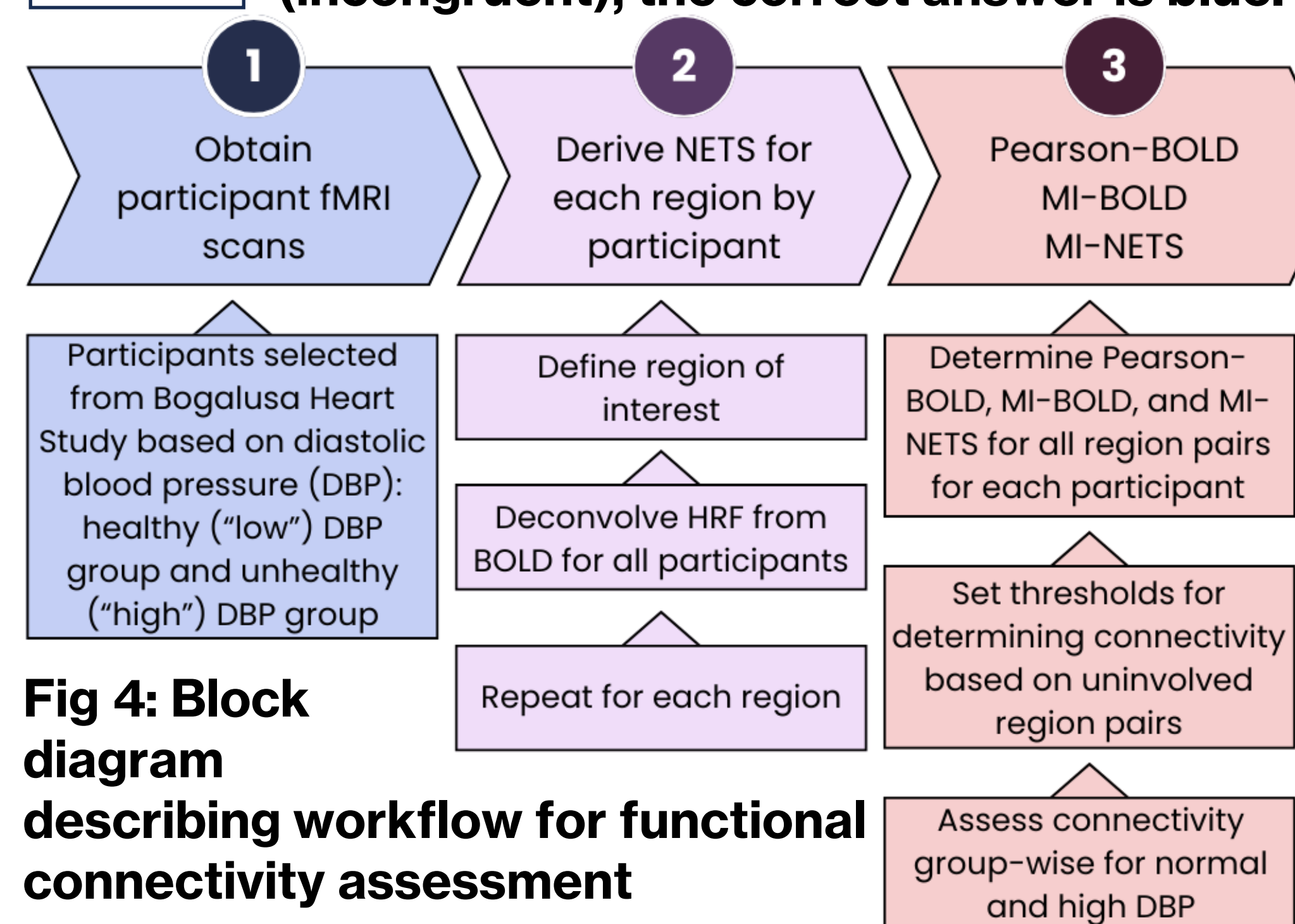


Fig 6: Connectograms for healthy DBP group. The red circle represents the piriform cortex, an uninvolved region in the Stroop task. MI-NETS produces many unique edges that are not present in either BOLD analysis.

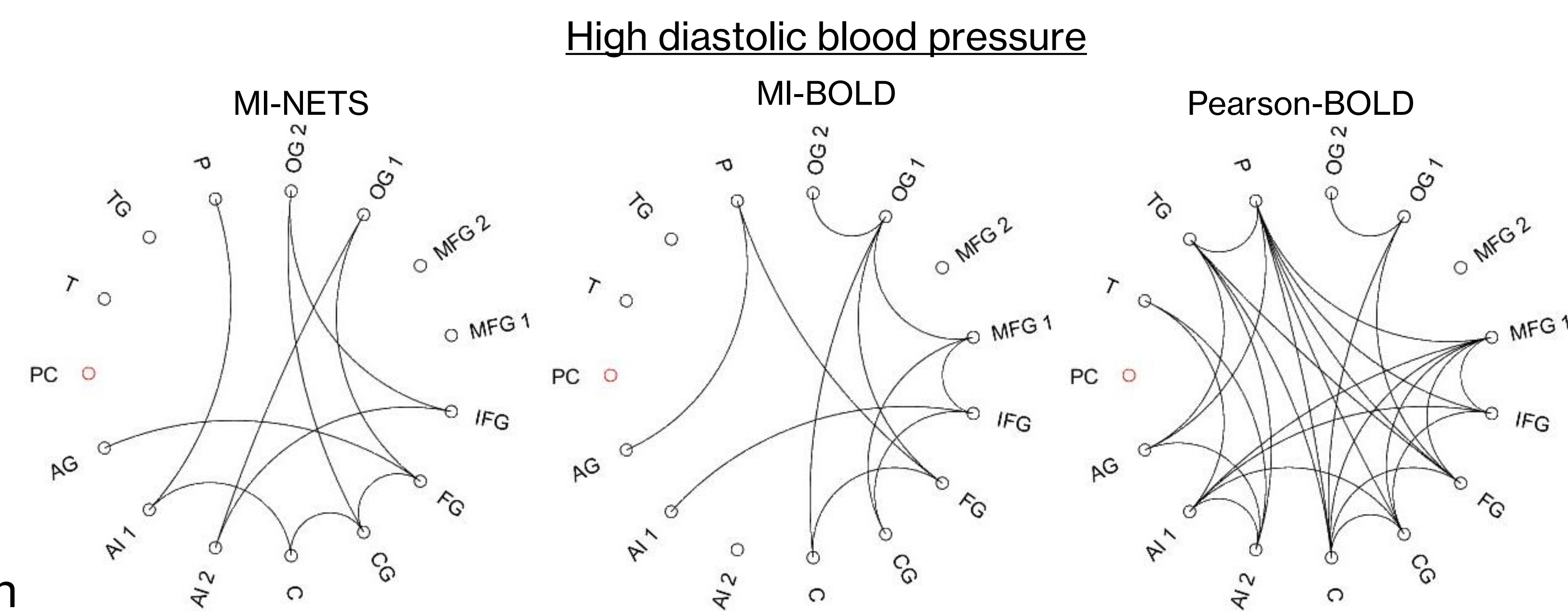


Fig 7: Connectograms for high DBP group. The red circle represents the piriform cortex, an uninvolved region in the Stroop task. MI-NETS produces unique edges not present in BOLD-based analyses.

- An edge was included in each connectogram when the robust Cohen's d exceeded 0.8, corresponding to a "very large" effect size.
- The low DBP group exhibited more edges than the high DBP group across all metrics, indicating better FC in the low DBP group.
- Compared with Pearson-BOLD and MI-BOLD, MI-NETS identified 8 unique edges in the high DBP group and 3 unique edges in the low DBP group, suggesting that NETS-based analysis captures information not present in the BOLD signal alone.

Conclusion

Neural event time series-based FC is a promising approach to calculating functional connectivity

- MI can be applied to the NETS to identify FC between brain regions.
- NETS-based analysis yields information that differs from connectivity estimates derived directly from the BOLD signal.
- MI-NETS may improve FC analysis when used in populations with known vascular confounds, such as high blood pressure.
- Future work will extend this framework to additional vascular confounds and cardiovascular risk factors.