Analysis of Time-Delayed Effective Connectivity for Normal Cognition and MCI under Motion Detection Tasks: an EEG Study

Boxin Sun[1], Jinxian Deng[1], Alina B. Renli[2], Voyko Kavcic[3,6], Jian Ren[1], Bruno Giordani[4,6], Rong Zhang[5], and Tongtong Li[1,6*]

[1] Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI, USA
[2] Department of Neuroscience, Michigan State University, East Lansing, MI, USA,
[3] Institute of Gerontology, Wayne State University, Detroit, MI, USA
[4] Departments of Psychiatry, University of Michigan, Ann Arbor, MI, USA
[5] Departments of Neurology and Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA
[6] Michigan Alzheimer's Disease Research Center, Ann Arbor, MI, USA

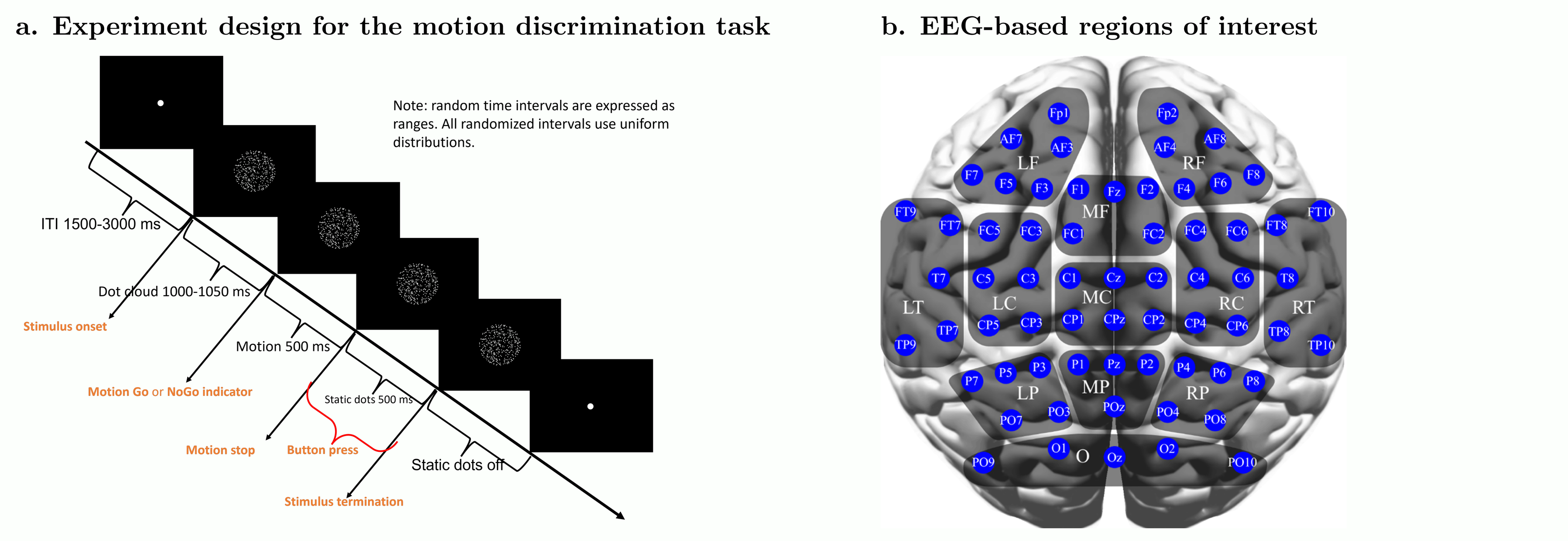
Background

Existing work suggests that Alzheimer's Disease (AD) pathology can affect the direction and intensity of information signaling among functional brain regions. In this EEG–based study, we aim to explore the impact of cognitive impairment on directed information transfer in the brain network by investigating time-delayed effective connectivity of normal cognition (NC) participants and patients with mild cognitive impairment (MCI).

EEG Data Description and Preprocessing

Our research focuses on task-based EEG (64-channel). The current dataset includes 56 consensus-diagnosed, community-dwelling African Americans (aged 60-90 years, 28 normal controls (NC) and 28 MCI patients). Participants who reported a recent change in memory on a screening questionnaire were recruited into the study through the Wayne State Institute of Gerontology and Michigan Alzheimer's Disease Research Center. Participants received two (eye-closed) resting state electroencephalograms (rs-EEG) between which they engaged in a visual motion direction discrimination task. The experiment design is shown in Figure 1.

Figure 1. Experiment design and EEG-based brain regions



ROI Regions: Right frontal—RF, Medium frontal—MF, Left frontal—LF, Left temporal—LT, Left central—LC, Medial central—MC, Right central—RC, Right temporal—RT, Left parietal—LP, Medial parietal—MP, Right parietal—RP, occipital—Occ.

ROI Selection and Data Preprocessing

- As shown in Figure 1(b), a total of 12 EEG-defined brain regions of interest (ROI) were selected for further analysis. Since effective connectivity is directional, this implies that there are a total of $\mathbf{12 \times 11 = 132}$ possible region pairs.
- We calculated the current source density (CSD) or the Laplacian (second spatial derivative) of the scalp voltage from the EEG signal for all the ROIs.

Method: Causalized Convergent Cross Mapping (cCCM)

CCM and Causalized CCM

Consider two dynamically coupled variables X and Y which share the same attractor manifold $\mathbf{M}$. Let $\mathbf{X}^n = [X_1, X_2, \cdots, X_n]$ and $\mathbf{Y}^n = [Y_1, Y_2, \cdots, Y_n]$ be the time series consisting of samples of X and Y, respectively.

1. Construct the shadow manifolds with respect to $\mathbf{X}^n$ and $\mathbf{Y}^n$.
$$\mathbf{M}_x = \{\mathbf{x}_t \mid \mathbf{x}_t = [X_t, X_{t-\tau}, \cdots, X_{t-(E-1)\tau}],\ t = 1 + (E-1)\tau, \cdots, n\} \quad (1)$$
$$\mathbf{M}_y = \{\mathbf{y}_t \mid \mathbf{y}_t = [Y_t, Y_{t-\tau}, \cdots, Y_{t-(E-1)\tau}],\ t = 1 + (E-1)\tau, \cdots, n\} \quad (2)$$
2. For each vector $\mathbf{x}_t$, find its $E+1$ nearest neighbors and denote the time indices (from closest to farthest) of the $E+1$ nearest neighbors of $\mathbf{x}_t$ by $t_1, ...t_{E+1}$.
3. If the two signals X and Y are dynamically coupled, then the nearest neighbors of $\mathbf{x}_t$ in $\mathbf{M}_x$ would be mapped to the nearby points of Y_t on manifold $\mathbf{M}$. The estimated Y_t based on $\mathbf{M}_x$, or say the cross mapping from X to Y, is defined as:
$$\hat{Y}_t|\mathbf{M}_x = \sum_{i=1}^{E+1} w_i Y_{t_i},\ \text{where}\ w_i = \frac{u_i}{\sum_{j=1}^{E+1} u_j},\ \text{with}\ \ u_i = \exp\left\{-\frac{d(\mathbf{x}(t), \mathbf{x}(t_i))}{d(\mathbf{x}(t), \mathbf{x}(t_1))}\right\}, \quad (3)$$
here d denotes the Euclidean distance between two vectors. The cross mapping from Y to X can be defined in a similar way. As n increases, it is expected that $\hat{X}_t|\mathbf{M}_y$ and $\hat{Y}_t|\mathbf{M}_x$ would converge to X_t and Y_t, respectively.
4. The cross mapping correlations are defined as
$$\rho_{CCM}(X \to Y) = \rho(\mathbf{Y}^n, \hat{\mathbf{Y}}^n) \quad \text{and} \quad \rho_{CCM}(Y \to X) = \rho(\mathbf{X}^n, \hat{\mathbf{X}}^n) \quad (4)$$
where ρ denotes the Pearson correlation.
5. If $\rho_{CCM}(X \to Y) > \rho_{CCM}(Y \to X)$ and converges faster than $\rho_{CCM}(Y \to X)$, then we say that the causal effect of X on Y is stronger than that in the reverse.

Causalized CCM (cCCM) If we limit the search of all the nearest neighbors in $\mathbf{M}_x$ to $t_i < t$, that is, we only use the current and previous values of X and the past values of Y to predict the current value Y_t, and operate in the same way for the other direction, then CCM is converted to Causalized-CCM. The corresponding cross mapping correlation, or the cCCM causation, is denoted as ρ_{cCCM}.

- We evaluated the time-delayed effective connectivity at different time periods of the motion-detection task across all the possible EEG region pairs using cCCM.

Method (cont.)

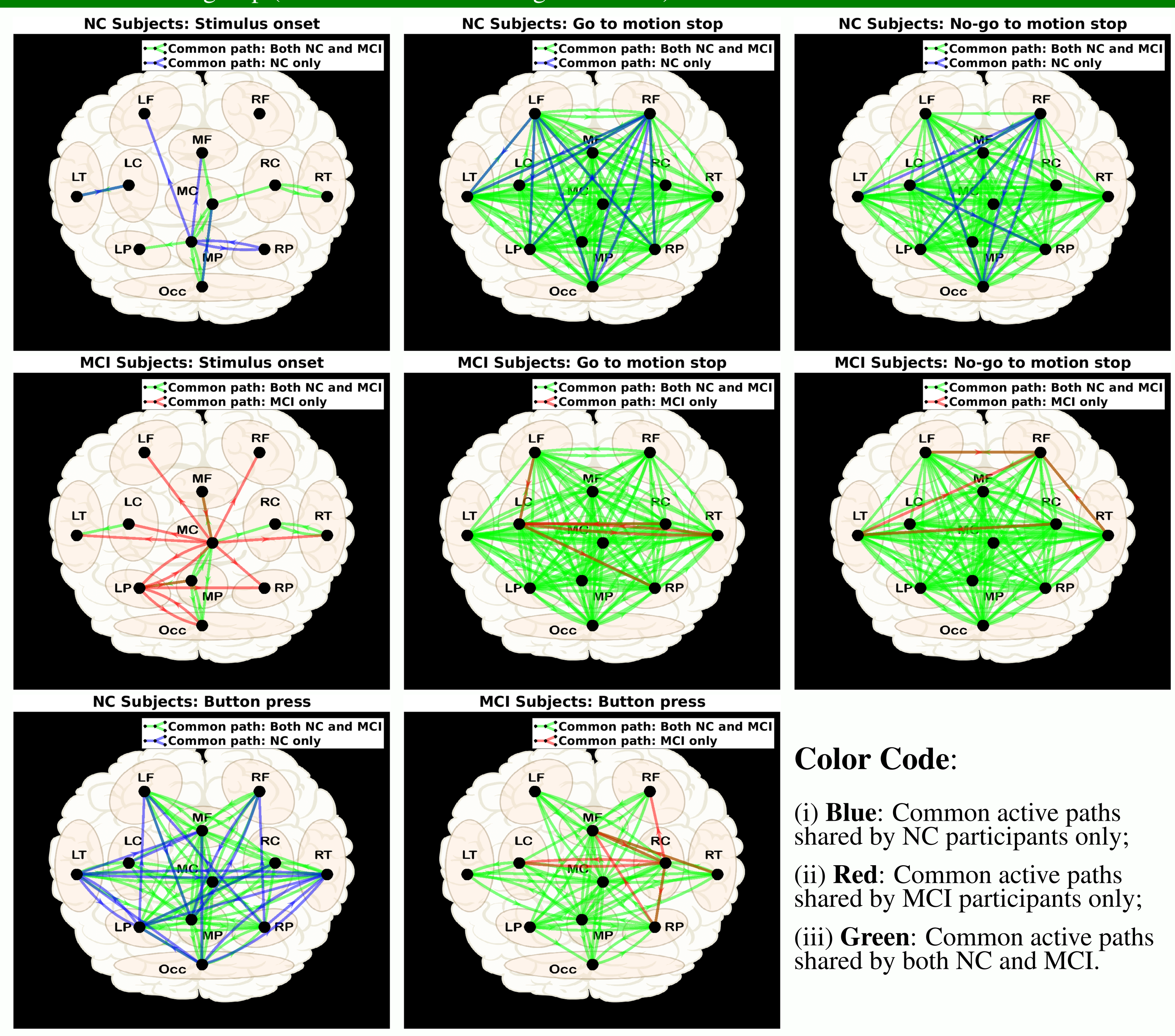
- For each task trial, the successive time periods being examined include: (I) stimulus onset to Go/No-Go indication, (II) Go/No-Go indication to motion-stop, and (III) the button-press period.
- For each subject, we evaluated the time-delayed cCCM values (up to 85 ms) across all the possible region pairs for each time period in each trial, and then identified the peak cCCM value and corresponding delay in the trial. The result is first averaged over all the 40 trials for each subject, and then averaged over all the subjects within the NC or MCI group.
- For both the NC and MCI groups, a path is called a **common active path** if the averaged peak $\boldsymbol{\rho_{cCCM}}$ is greater than or equal to 90% of the global average of peak cCCM value of NC group, and occurs over 70% of the participants within the group.

Results

Our analysis shows that:

1. Delayed effective connectivity is noticeably stronger than its zero-delay counterpart, suggesting the existence of non-zero delays in inter-region information transfer.
2. NC and MCI share common active paths, but each group also has its own unique common active paths. Our results reflect the weakened effective connectivity across certain brain regions as well as the compensatory mechanism of the brain in MCI patients.

Figure 2. Time-delayed effective connectivity analysis: common active paths shared by at least 70% of the participants in NC or MCI group (threshold = 90% of NC global mean).



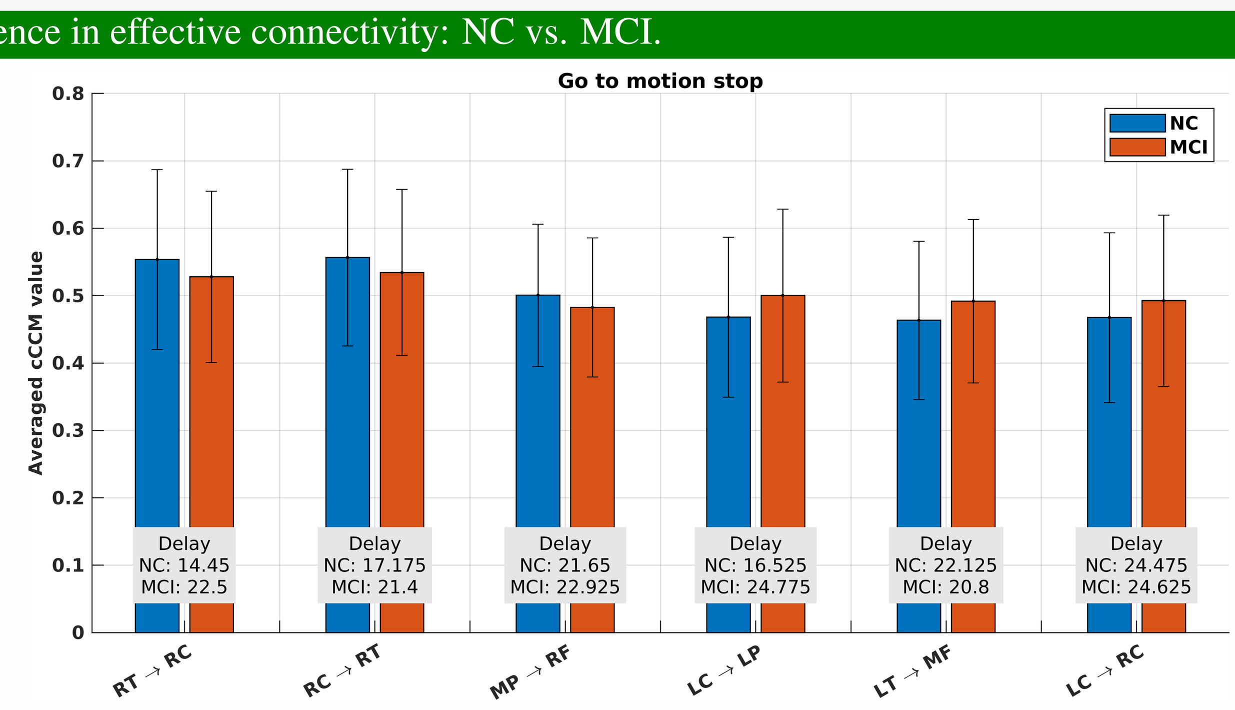
Color Code:

(i) **Blue**: Common active paths shared by NC participants only;

(ii) **Red**: Common active paths shared by MCI participants only;

(iii) **Green**: Common active paths shared by both NC and MCI.

Figure 3. Difference in effective connectivity: NC vs. MCI.



Conclusions

- Our results show that time-delayed effective connectivity analysis may enable identification of possible signaling pathways in the brain and of dissimilarities in pathway usage between NC and MCI.