



# Functional Neural Correlates of Cognitive Frailty Transition and Mobility Changes in Older Adults: A 12-Month Prospective Study



Jingyi WU, MSc 1; Jinyu CHEN 1; Juncen WU 1; Anthony PH Lo 1; Chun Liang HSU, PhD 1\*

Department of Rehabilitation Sciences, Faculty of Health and Social Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China

## Introduction

- Cognitive Frailty (CF)** is characterized by mild cognitive impairment (MCI) and physical frailty<sup>1,2</sup>.
- Previous studies demonstrated potential convertibility of cognitive frailty<sup>3-7</sup>.
- Default mode network (DMN), dorsal attention network (DAN), and the sensorimotor network (SMN) play crucial roles in aging, physical frailty, and MCI<sup>8-10</sup>.
- The underlying neural mechanisms of its conversion remain poorly understood.
- Aim: to characterize neuroimaging features and clinical outcomes associated with both conversion from cognitive frailty and its persistence.**
- Key Words: cognitive frailty, fMRI, conversion, mobility**

## Methods

- Study Design:** 12-month longitudinal exploratory study.
- Participants:** 15 cognitively frail older adults and 21 non-cognitively frail older adults.
- Cognitive Frailty:** Montreal Cognitive Assessment score 18-25/30 and Short Physical Performance Battery < 10/12 at baseline and endpoint.
- Conversion from CF to healthier states may involve:** (1) converting from CF to MCI; (2) converting from CF to physical frailty; and (3) converting from CF to non-MCI and non-physical frailty (as exhibited in those defined as individuals without CF).
- Executive Function:** Trail Making Test (A and B) and Stroop Test (I, II, and III)
- Mobility:** Timed-Up and Go test (TUG)
- Brain Function:** functional network connectivity was quantified with resting state fMRI data, including intra- and inter- network connectivity of DMN, DAN, and SMN.
- Statistical Analysis:** (1) two way repeated ANOVAs were used to determine differences in MoCA and SPPB from baseline to 12 months across the three groups. (2) MANOVA were constructed to indicate the differences in functional connectivity within the left DMN and between DMN-DAN, DMN-SMN, and DAN-SMN among three groups. (3) MANOVA were constructed to detect the differences in clinical measurements (i.e., executive function and mobility).

## Results

Table 1. Study Participant Characteristics

| Groups          | Cognitively frail converters |             | Individuals with Persistent CF |              | Individuals without CF |              |
|-----------------|------------------------------|-------------|--------------------------------|--------------|------------------------|--------------|
|                 | Mean (SD)                    | (n=7)       | Mean (SD)                      | (n=8)        | Mean (SD)              | (n=19)       |
| Age             | Baseline                     | 73.71 ± 1.6 | 12-Month                       | 75.62 ± 3.02 | Baseline               | 73.84 ± 2.85 |
| Sex (M/F)       | 2/5                          | -           | 2/6                            | -            | 9/10                   | -            |
| Education (yrs) | 11 ± 6.24                    | -           | 10.12 ± 4.58                   | -            | 13.42 ± 3.34           | -            |

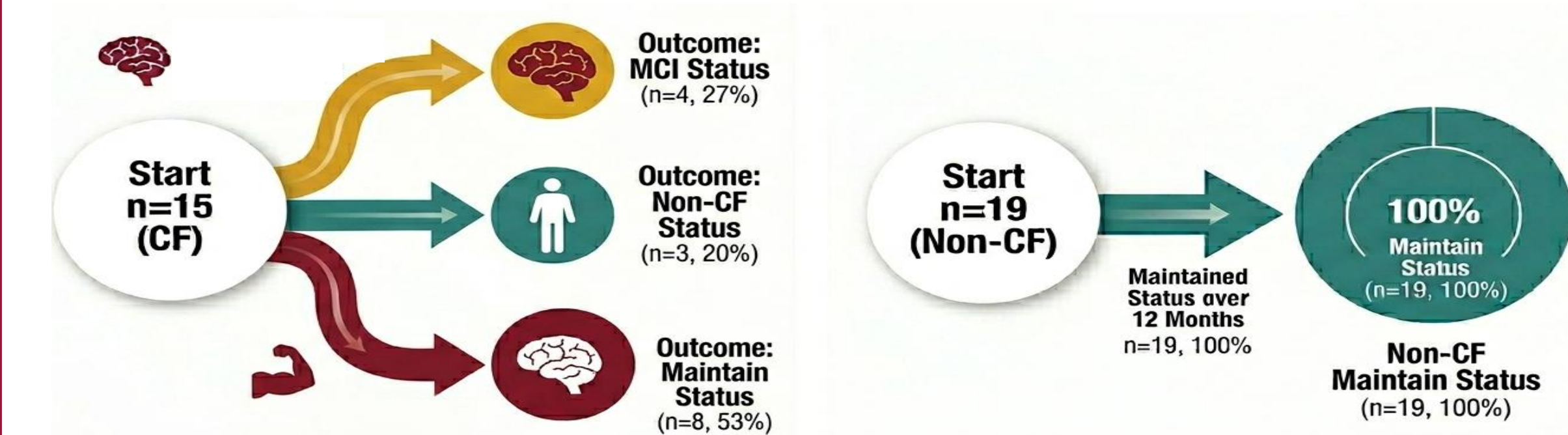


Figure 1. Conversion of Healthy Status over 12-month in Older Adults

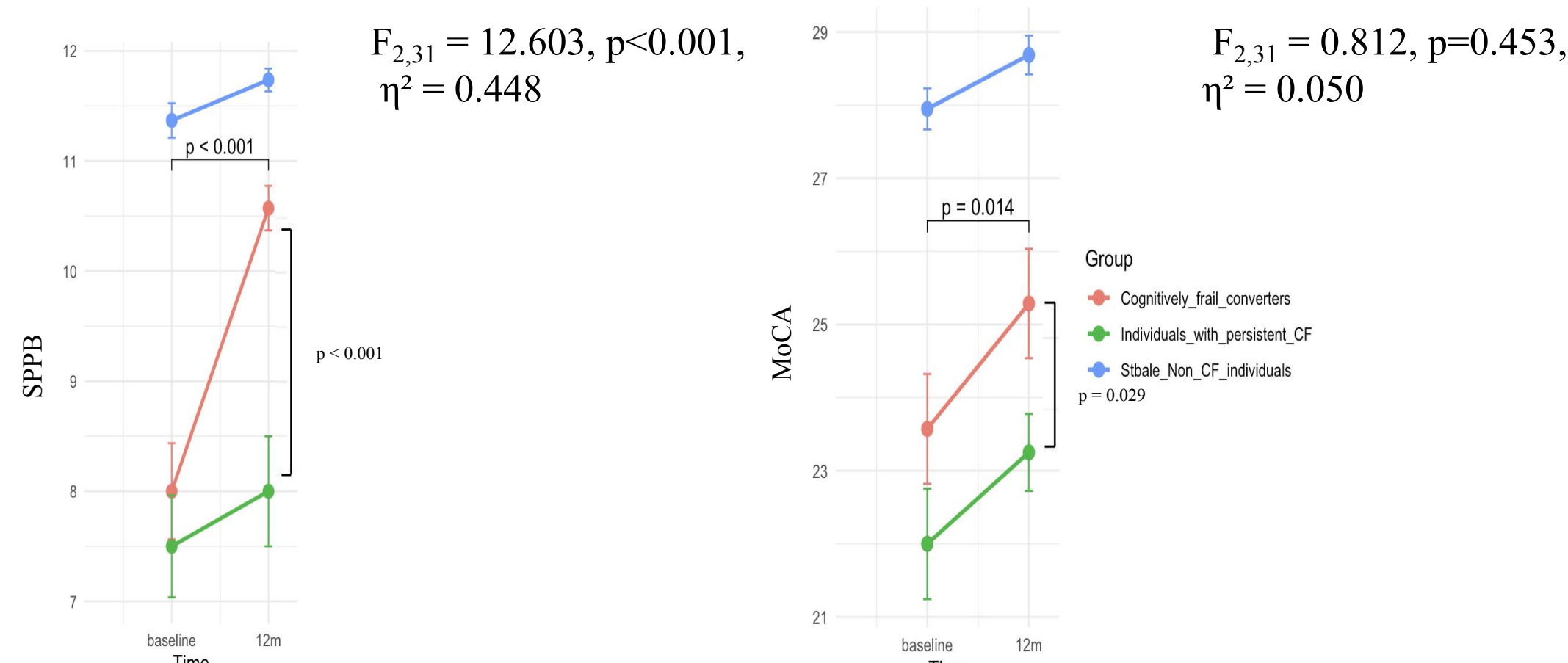


Figure 2. MoCA and SPPB score among the three groups

Table 2. Mobility and executive function among the three groups

| Groups              | Cognitively frail converters |                          |                           | Individuals with Persistent CF |                           |                          | Individuals without CF |                    |                 |
|---------------------|------------------------------|--------------------------|---------------------------|--------------------------------|---------------------------|--------------------------|------------------------|--------------------|-----------------|
|                     | Baseline Mean (SD)           | 12-Month Mean (SD)       | Δ Adjusted Mean (SE)      | Baseline Mean (SD)             | 12-Month Mean (SD)        | Δ Adjusted Mean          | Baseline Mean (SD)     | 12-Month Mean (SD) | Δ Adjusted Mean |
| TUG                 | 10.72 ± 1.52 <sup>b</sup>    | 9.96 ± 1.08 <sup>a</sup> | -0.26 ± 0.46 <sup>a</sup> | 11.98 ± 2.13 <sup>c</sup>      | 13.36 ± 2.50 <sup>c</sup> | 2.47 ± 0.50 <sup>c</sup> | 8.24 ± 1.6             | 8.16 ± 0.96        | -0.72 ± 0.32    |
| TMT B-A             | 102.34 ± 62.14 <sup>b</sup>  | 77.38 ± 55.83            | -24.96 ± 53.24            | 87.92 ± 46.91 <sup>c</sup>     | 107.54 ± 59.58            | 19.62 ± 37.59            | 45.56 ± 18.46          | 58.43 ± 45.54      | 12.87 ± 41.19   |
| Stroop Interference | 55.29 ± 23.45                | 51.47 ± 14.64            | -3.23 ± 5.70              | 64.23 ± 27.91                  | 54.61 ± 22.81             | -6.32 ± 5.44             | 48.02 ± 27.50          | 44.27 ± 26.63      | -5.36 ± 3.50    |

<sup>a</sup>p: cognitively frail converters compared to individuals with persistent CF; <sup>b</sup>p: cognitively frail converters compared to individuals without CF; <sup>c</sup>p: individuals with persistent CF compared to individuals without CF

## Conclusions

- Cognitive frailty convertibility may be underpinned by alterations in connectivity between DAN-SMN, potentially reflecting an adaptive and flexible neural reorganization among individuals resilient to mobility impairment.
- Persistent CF may be due to disrupted connectivity within and between the DMN, leading to decline in mobility.

## References

<sup>1</sup>Kelaiditi E et al., 2013, <sup>2</sup>Bu Z et al., 2021, <sup>3</sup>Ahmad et al., 2018, <sup>4</sup>Nari et al., 2021, <sup>5</sup>Suprawesta et al., 2024, <sup>6</sup>Chong et al., 2015, <sup>7</sup>Wang et al., 2024, <sup>8</sup>Esposito et al. 2018, <sup>9</sup>Agcaoglu et al. 2015, <sup>10</sup>Lammers et al. 2020

## Acknowledgements

This work was supported by PolyU (grant No. P0043317). CLH is the Kuok Group Young Scholar in Aging and Neuroimaging.

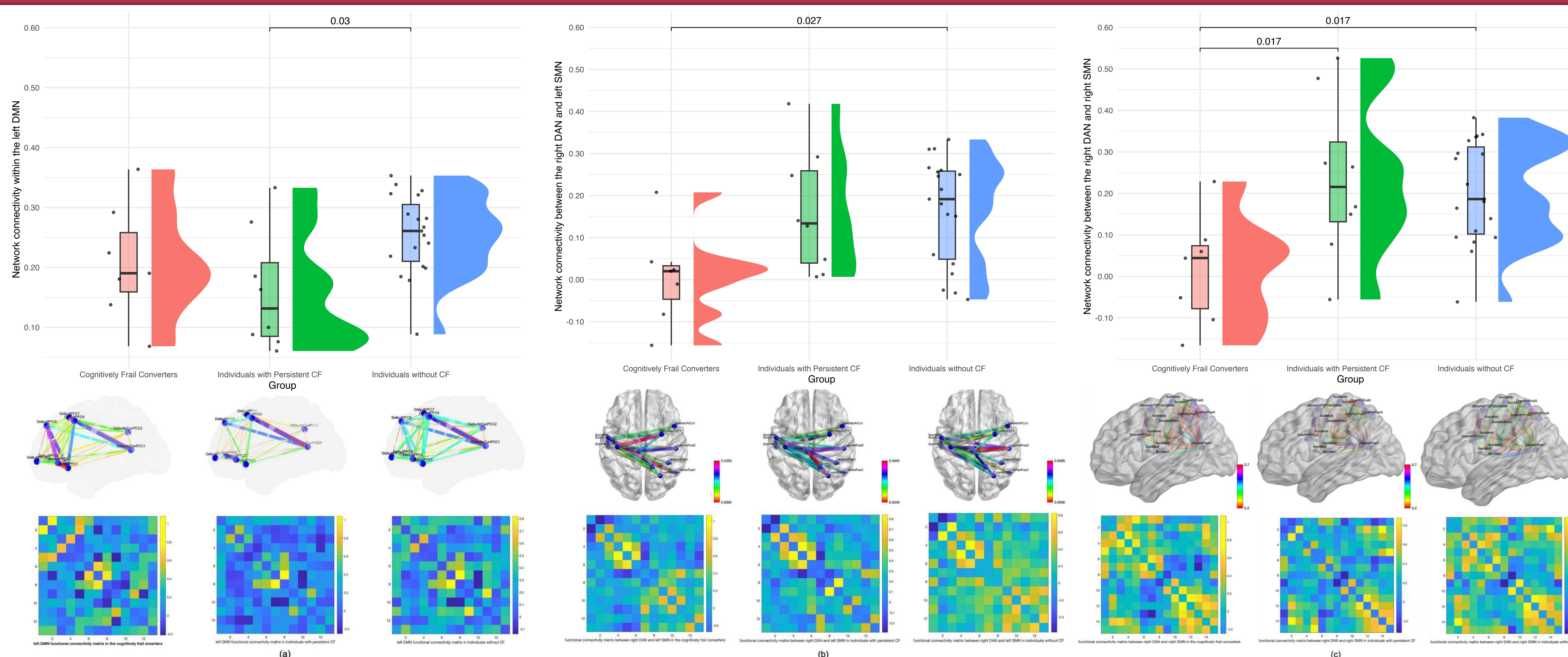


Figure 3. Baseline differences in network level functional connectivity among the three groups. (a) within the left DMN; (b) between right DAN and left DMN; (c) between the right DAN and right SMN. CF: cognitive frailty; DMN: default mode network; DAN: dorsal attentional network; SMN: sensorimotor network.

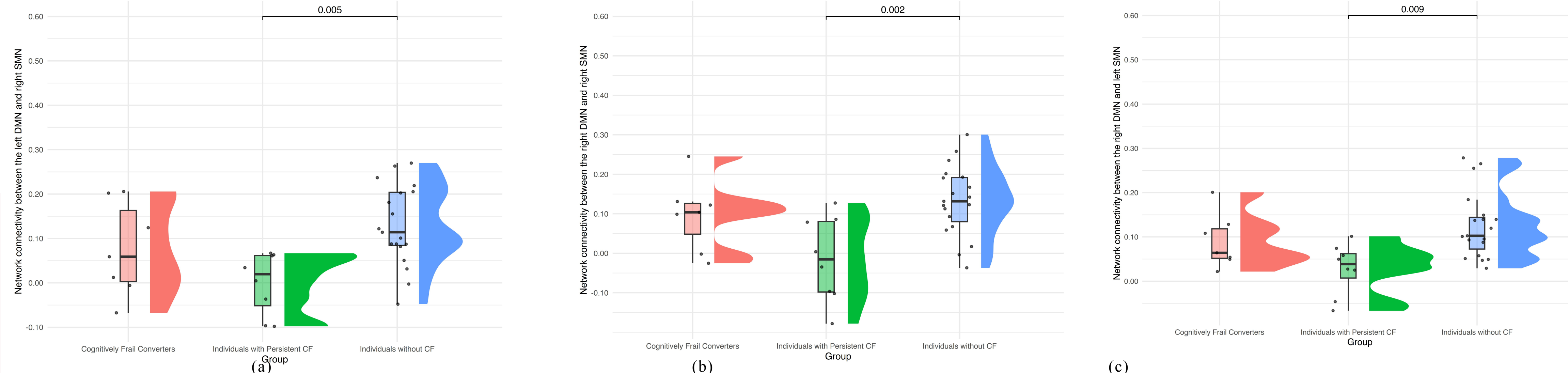


Figure 4. Baseline differences in network level functional connectivity among the three groups. (a) between left DMN and right SMN; (b) between the right DMN and right SMN; (c) between the right DMN and left SMN; CF: cognitive frailty; DMN: default mode network; SMN: sensorimotor network.