Randomness of motor activity and cognitive performance in people living with HIV

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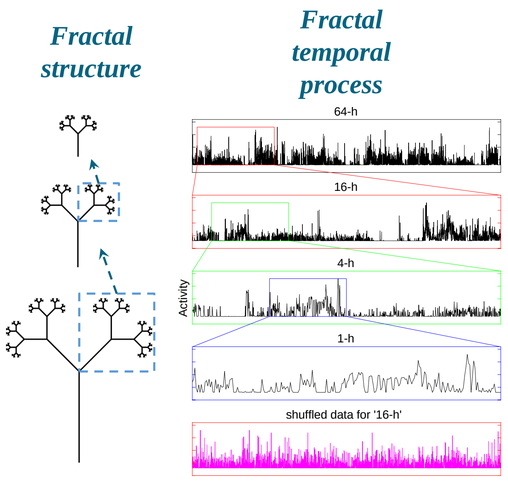
Introduction

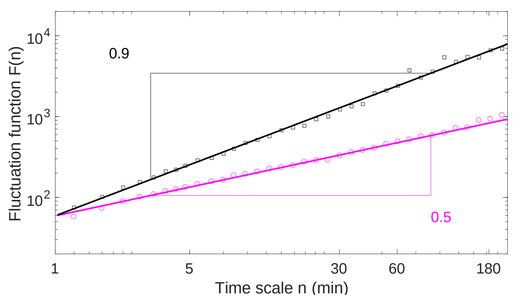
- Healthy physiological control systems exhibit complex behavior [1]
  - Neither random, nor regular
  - Hovering somewhere in between, at a critical point
- This intrinsic complexity renders fractal patterns in physiological outputs
  - Fractal temporal process: self-similar patterns across multiple time scales



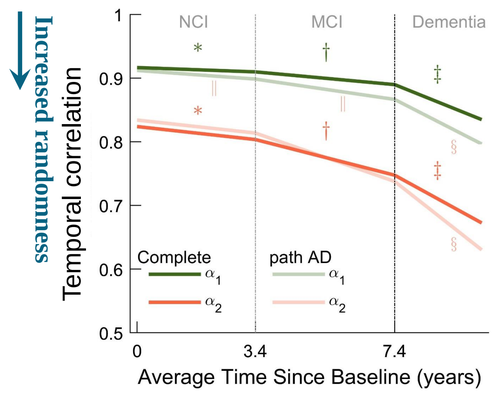
- Detrended fluctuation analysis (DFA) [2]
  - to quantify temporal correlations across multiple time scales
  - Fractal temporal process renders an exponential function form

$$F(n) \sim n^{\alpha}$$

  - ✓ α > 0.5: signals with positive correlations;
  - ✓ α = 0.5: uncorrelated white noise.
  - ✓ $\alpha \sim 1$ → the highest complexity
  - ✓ Reduced α → Reduced temporal correlation (increased randomness)

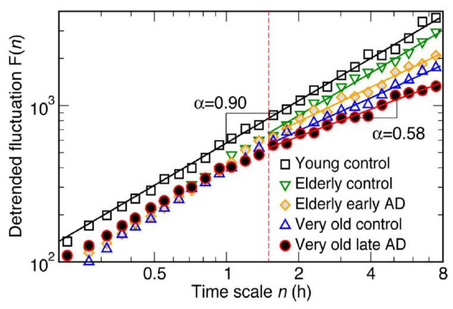


- Motor activity becomes more random during aging
  - Which further speeds up with Alzheimer's progression [3]

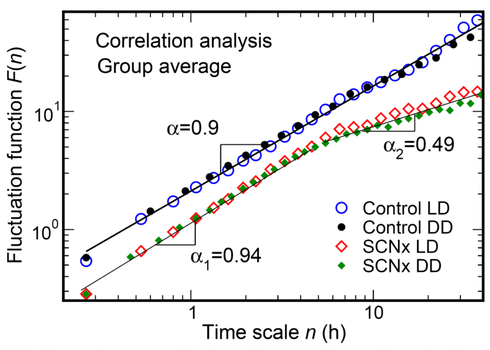


α_1 and α_2 represent the scaling exponents in two timescale regions (<1.5h and 2-10h)
*: Significant decline over time
†: Significant difference in the rate of decline between NCI and MCI
‡: Significant difference in the rate of decline between MCI and dementia stages
§: Significant difference in rate of change between the subset with AD pathology (path AD) and the remained subset (|| for p<0.1)

- Cross-sectional comparisons showed more random motor activity in people with Alzheimer's disease (AD) at larger time scales [4]

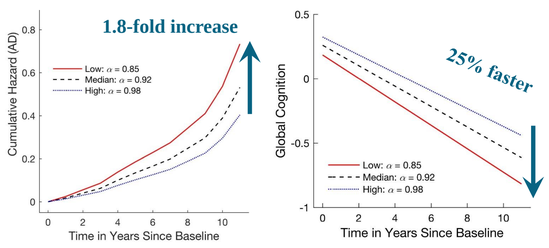


- Animal studies revealed a causal relationship between the randomness in motor activity at larger time scales and circadian intactness [5]



SCN: Suprachiasmatic Nucleus (the central circadian clock)
SCNx: SCN lesion
LD: light dark;
DD: constant dark

- Increased randomness in activity at smaller time scales predicted increased Alzheimer's risk and faster cognitive decline in older adults [6]



Goal

- In middle (or middle-to-older) aged people living with HIV (PLWH)
  - To investigate the randomness of motor activity
  - To examine its relationship with neurocognitive performance

Methods

- **UK Biobank**
  - >0.5 million participants
  - >0.1 million with actigraphy
- **Ascertain of PLWH** [7]
  - HIV serostatus
  - ICD or self-report

Covers 386094 participants

Evidence 1: HIV seropositive
Covers 9690 participants

Evidence 2: Self-report OR ICD-10/9
Covers 437506 participants

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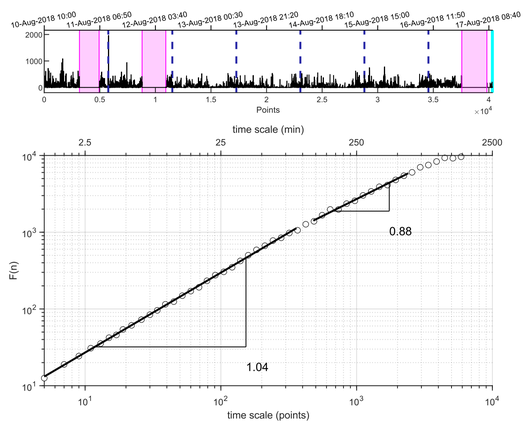
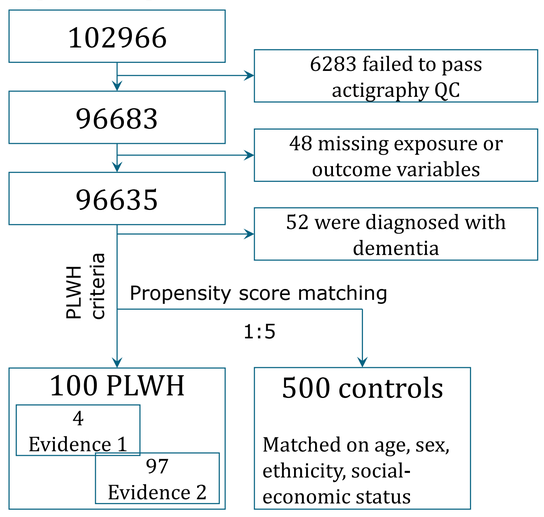
This research has been conducted using the UK Biobank Resource under Application Number 33883.

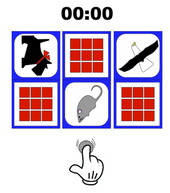
- **Data and signal analysis**
  - Continuous actigraphy lasting for ~7 days
  - DFA was applied to examine the temporal correlations
  - The scaling exponent was fitted within two regions:
    - a_1 for time scales ≤ 1.5h
    - a_2 for time scales ≥ 2h (up to 10 hour)

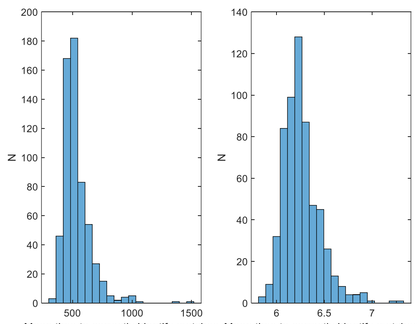


- **Numbers of available participants**

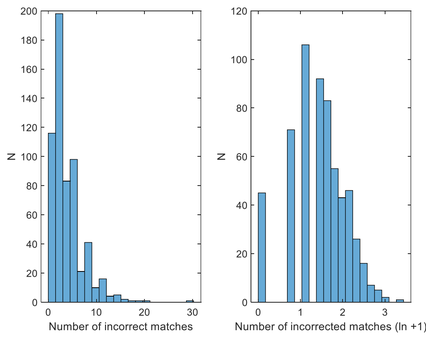


- **Cognitive tests**
  - Reaction time test
  - Range:
    - 50-2000 ms
    - median 527 ms
  - For information processing speed



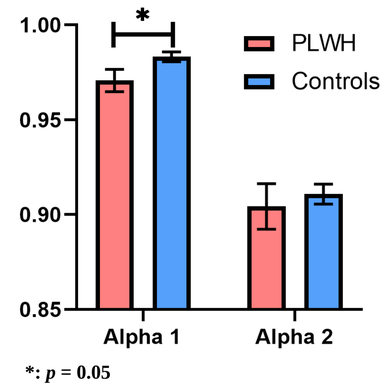


  - Pairs matching test
  - Range:
    - 0-146
    - median 3
  - For visual episodic memory

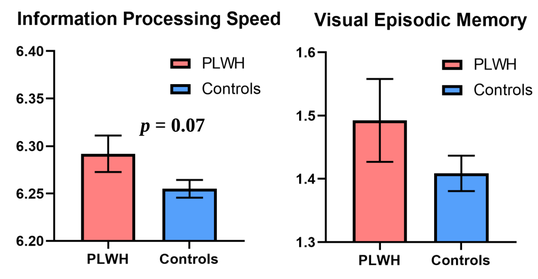


Results

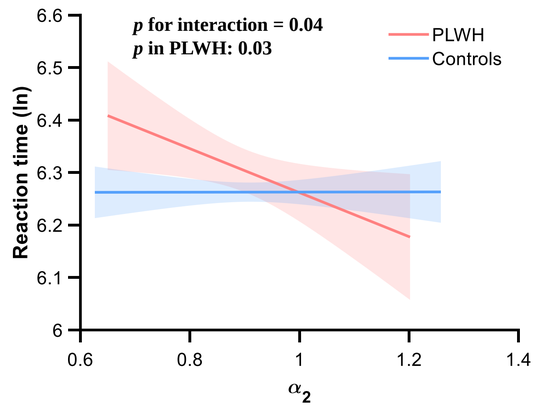
- PLWH had a reduced a_1 but a similar a_2 compared to controls



- PLWH demonstrated a trend of reduction in information processing speed, but similar visual episodic memory compared to controls



- a_2 was positively associated with information processing speed (i.e., negatively associated with reaction time) in PLWH but not in controls



Discussion

- Middle or middle-to-older aged PLWH may have compromised executive function
- They also have increased randomness in their motor activity at smaller time scales
- Increased randomness at larger time scales (i.e., circadian dysregulation) links to lower executive function in PLWH
- Further studies should examine whether drivers of aging (e.g., inflammation, immune activation) and consequent multimorbidity in PLWH underlie the observed association in PLWH

References

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CFAR Harvard University Center for AIDS Research — *Developmental Award To PL:* P30AI060354-21
HARC Healthy Aging Research Center — *Pilot Award To PL:* R33AG067069-01