Hippocampal Connectivity in Aging: The Impact on Purpose in Life

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Abstract

Alterations in the hippocampus are a significant marker of brain aging. This study examined the age differences in resting hippocampal functional connectivity (HP-FC), which measures the synchronized activity between the hippocampus and other brain regions during rest. We then explored how age-related differences in HP-FC are associated with alterations in various dimensions of psychological well-being over a 10-year period, including autonomy, environmental mastery, personal growth, positive relationships with others, purpose in life, and self-acceptance. Utilizing resting-state fMRI data from 120 participants in the 3rd follow-up of the Midlife in the U.S. (MIDUS) study ($Mean_{age}$ = 65.65, SD_{age} = 9.23, age range = 48-95), we assessed the association between age and HP-FC across 330 brain regions of interest (ROIs), controlling for sex, education level, and head motion. Our analysis identified an age-related decline in HP-FC with 15 ROIs (FDR corrected, $p < .05$), all located in the left hemisphere, including the superior temporal gyrus, postcentral gyrus, inferior parietal lobule, precentral gyrus, insular gyrus, and superior parietal lobule. Further analysis revealed a negative correlation between HP-FC in these 15 regions and the difference score (MIDUS 2 - MIDUS 3) for purpose in life, indicating that higher HP-FC is associated with a smaller decline in purpose in life over time. This correlation was not observed for the other aspects of psychological well-being. Mediation analysis suggested an indirect effect, where decreased HP-FC due to aging was associated with greater decline in purpose in life over time. These findings indicate that reductions in HP-FC may not only reflect neurological changes with aging but also contribute to a diminished sense of purpose in life as people age, highlighting the importance of maintaining HP-FC for well-being in older adults. Future research should investigate the long-term progression of HP-FC and elucidate how purpose in life both influences and is influenced by these changes.

Background

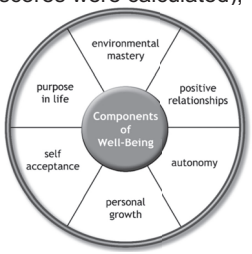
- Brain aging is a significant marker of the aging process (Shephard, 1997).
- Structural and functional properties of hippocampus are impacted by the aging process (Damoiseaux et al., 2016;Fraser et al., 2015).
- Individuals with a comparatively smaller hippocampus tend to have lower subjective well-being (Van 't Ent et al., 2017).
- Psychological well-being is vulnerable to aging, especially purpose in life and personal growth (Ryff et al., 2016).
- The Midlife in the U.S. (MIDUS) study collected resting functional Magnetic Resonance Imaging (fMRI) data across a more extensive and older age spectrum than is customarily studied.
- Psychological well-being data collected across different waves were used to assess changes in psychological well-being during aging.

Implication

- Aging indirectly impacts purpose in life through a decline in HP-FC, highlighting brain health as a crucial factor in the aging process.
- This study supports previous findings that a stronger purpose in life is associated with brain features indicative of better health (Nair et al., 2024; Stacey et al., in preparation).
- The research lays the groundwork for exploring the long-term impact of HP-FC changes on purpose in life.

Method

- Neuroscience Data from the Midlife in the United States (MIDUS) study's third follow-up (N = 120; $Mean_{age}$ = 65.65, SD_{age} = 9.23, age range = 48-95) were used.
- Psychological well-being was measured at MIDUS 2 and MIDUS 3 (differences scores were calculated); Resting fMRI data (8 mins; 240 TRs).



Resting fMRI preprocessing:
Remove the first 4 time points; Slice timing;
Volume registration and motion correction; Bias field correction;
Realign (coregistration, and normalization);
Regress out nuisance (white matter, CSF, head motion and derivatives);
Temporal bandpass filter (0.01–0.1 Hz); Censor time points (Euclidean norm);
Smoothing.
Brain parcellation (Schaefer, 2018; Tian et al., 2020; included 300 cortical and 32 subcortical regions).

- Data analysis:
  - Regression: HP-FC with ROI X ← Age + Sex + Race + Education + Head motion
  - Regression: Psychological well-being ← Average HP-FC + Sex + Race + Education + Head motion
  - Mediation: Age → Average HP-FC → Psychological well-being

Results

- Age demonstrated negative associations with HP-FC across 15 ROIs (FDR corrected, $p < .05$; Fig 1).
- The ROIs with HP-FC that negatively associated with age included: superior temporal gyrus, postcentral gyrus, inferior parietal lobule, precentral gyrus, insular gyrus, and superior parietal lobule. All located in the **left hemisphere** and primarily distributed within the **somatosensory area**.
- The average HP-FC from the 15 ROIs, is negatively associated with the decrease in purpose in life across the 10-year period (as indicated by the difference score, MIDUS 2 - MIDUS 3), but not with the other aspects.
- The average HP-FC mediated the relationship between age and the decline of purpose in life (see Fig. 2). Age was negatively associated with hippocampal functional connectivity (HP-FC), and lower HP-FC was, in turn, associated with a greater decline in purpose in life.

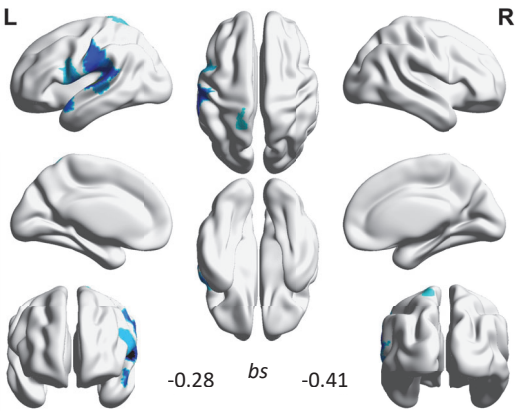
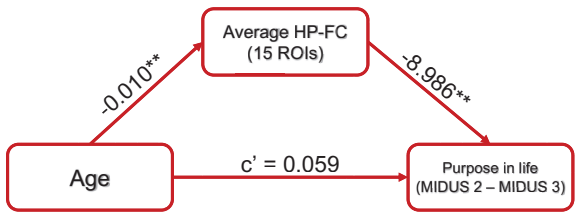


Fig. 1 The association between age and AMYG-FC



Indirect effect = 0.089, p = .001

Fig. 2 Mediation role of HIP-FC