Systemic Inflammation Accelerates Age-related Disintegration of Cognitive Control Networks

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Introduction

Systemic Inflammation and Aging

- Peripheral inflammation is an immune response essential to protect the body against pathogens.
- However, **sustained low-level inflammation** even after an acute response is detrimental to long-term health, including brain health (Nathan & Ding, 2010).
- Aging is accompanied by low-grade chronic inflammation, called inflammaging, which increases the vulnerability of inflammatory events as we age (Franceschi et al., 2018; Holmes, 2013).

Impacts on Cognitive Control Networks

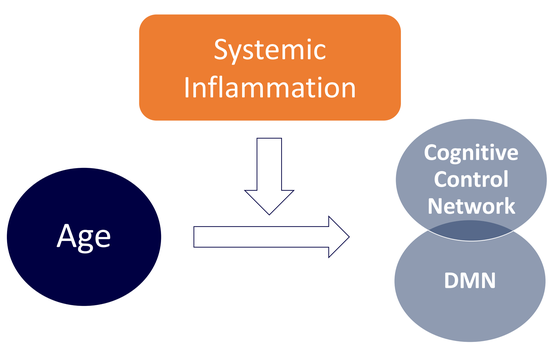
- Cognitive control function is one of the heavily affected cognitive abilities in regard to normal aging and its brain networks are also affected by aging (Grady et al., 2011; Ng et al., 2016).

Less connectivity within cingulo-opercular network (CON)
Less segregation between task-related networks and default mode network (DMN)

- Few studies have examined how systemic inflammation impacts the brain's functional networks, especially relating to cognitive control (Kraynak et al., 2018).
- However, there are no studies directly exploring the effects of systemic inflammation on age-related changes to cognitive control networks.

Hypothesis

Higher levels of systemic inflammation in older adults will accelerate the effects of age on functional networks of the brain related to cognitive control.



Methods

Participants

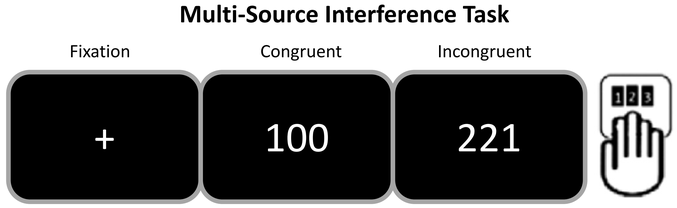
86 healthy older adults (mean age= 70.8, SD= 6.3) participating in the Korean Social Life, Health, and Aging Project (KSHAP) without psychiatric or neurological diseases, traumatic brain injury, or loss of consciousness.

Systemic Inflammation : Salivary C-Reactive Protein (CRP)

- Analyzed via indirect sandwich ELISA (Salimetrics C-Reactive Protein ELISA kit, State College PA) with sensitivity of 10pg/mL
- The values were log transformed for analysis. (mean CRP= 1656.83 pg/mL)

Functional connectivity during Cognitive control task

Multi-Source Interference Task



- The MSIT is a validated fMRI task designed to evaluate interference resolution and activate the cognitive/attention network within individuals (Bush and Shin, 2006)
- Subjects are instructed to identify the number that is different from the other two numbers via button-press regardless of its position.

fMRI Acquisition & Analysis

- EPI using 3T Siemens Trio scanner with the following parameters : TE/TR=30/2250, voxel= 3x3x3, gap=1mm, FA=79, FOV=240mm², straight axial
- With the CONN toolbox, seed-to-voxel connectivity was analyzed at task state using ROIs based on regions previously known to activate during MSIT

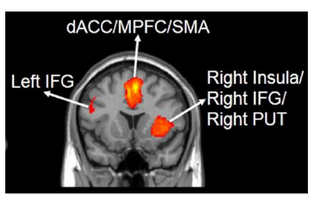


Fig1. Selected ROIs (Deng et al., 2018)

Statistical Analysis

- Moderation model (PROCESS macro for SPSS)
- Sex, education, and BMI were controlled for as covariates.

Results

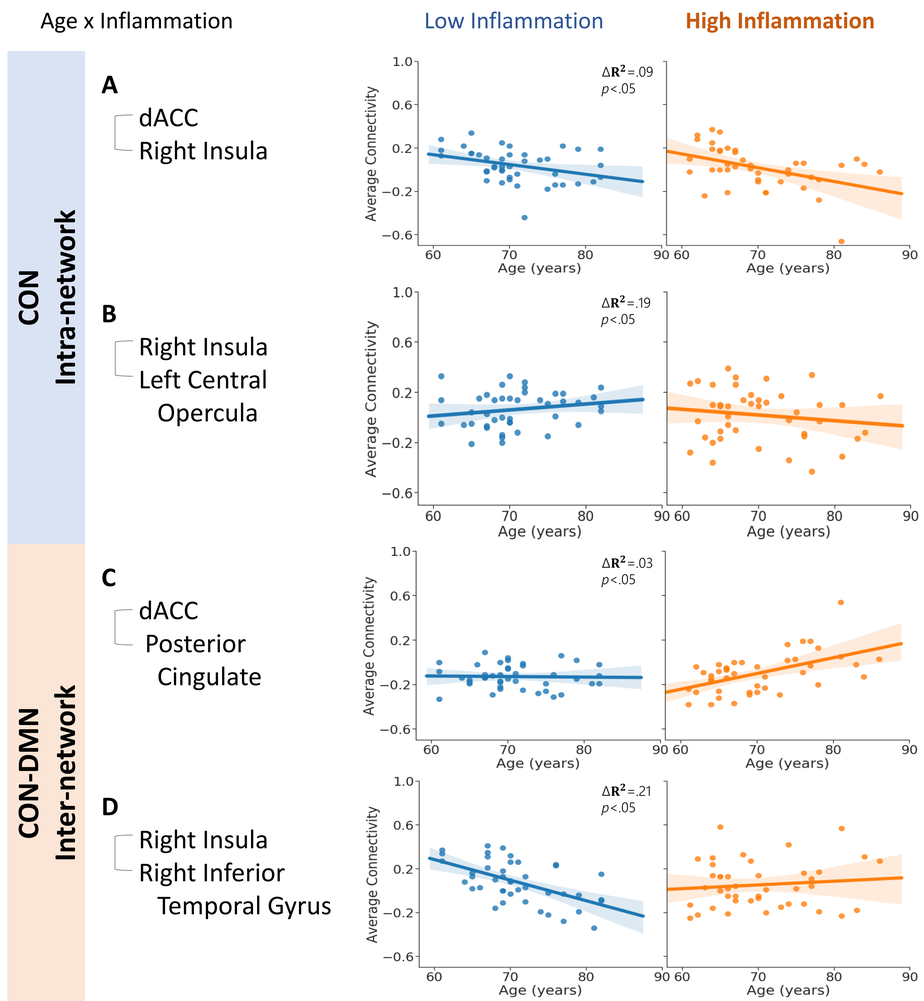


Fig 2. Moderating effects of inflammation levels in age-related changes in connectivity between seed regions dACC (A,C) and right insula (B, D) with other regions (height uncorrected p<.001, cluster FDR-corrected p<.05)

Discussion

- Older adults with higher levels of systemic inflammation showed augmented age-related decrease in connectivity within CON and decrease in segregation between CON and DMN.
- This study supports the importance of systemic inflammation as a risk factor that may aggravate age-related changes in the functional brain.

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