Neuropsychologia 99 (2017) 199–206

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

# Amygdala functional connectivity is associated with locus of control in the context of cognitive aging

Ping Ren[a], Mia Anthony[a], Benjamin P. Chapman[b,c], Kathi Heffner[a,b], Feng Lin[a,b,d,*]

[a] School of Nursing, University of Rochester Medical Center, Rochester, NY, USA
[b] Department of Psychiatry, University of Rochester Medical Center, Rochester, NY, USA
[c] Depart of Public Health Science, University of Rochester Medical Center, Rochester, NY, USA
[d] Department of Brain and Cognitive Science, University of Rochester, Rochester, NY, USA

ARTICLE INFO

*Keywords:*
Locus of control
Personality
Mild cognitive impairment
Resting state fMRI
Functional connectivity

ABSTRACT

Locus of control (LOC) measures the extent to which individuals perceive control over their lives. Those with a more "internal" LOC feel self-sufficient and able to determine important aspects of their own future, while those with a more "external" LOC feel that their lives are governed by events beyond their control. Reduced internal LOC and increased external LOC have been found in cognitive disorders, but the neural substrates of these control perceptions are yet unknown. In the present study, we explored the relationship between amygdala functional connectivity and LOC in 18 amnestic mild cognitive impairment (MCI) and age-, sex-, and education-matched, 22 cognitively healthy controls (HC). Participants completed cognitive challenge tasks (Stroop Word Color task and Dual 1-back) for 20 min, and underwent resting-state functional magnetic resonance imaging immediately before and after the tasks. We found significantly lower internal LOC and higher external LOC in the MCI group than the HC group. Compared to HC, MCI group showed significantly stronger positive associations between internal LOC and baseline right amygdala connections (including right middle frontal gyrus and anterior cingulate cortex), and stronger negative associations between internal LOC and change of these right amygdala connections. Across all participants, external LOC explained the relationships between associations of another set of right amygdala connections (including middle cingulate cortex and right superior frontal gyrus), both at baseline and for change, and performance in the cognitive challenge tasks. Our findings indicate that the right amygdala networks might be critical in understanding the neural mechanisms underlying LOC's role in cognitive aging.

## 1. Introduction

Locus of control (LOC) reflects the extent to which individuals see internal or external factors as influencing their desired outcomes. Internal LOC is defined as the belief in one's own skills and capabilities in controlling life, while external LOC is the perception of inevitable environmental constraints or powerful others as controls over one's life (Lachman, 1986). Numerous studies have contributed to distinguishing the two types of LOC and their distinct outcomes (Rashid, 2016). For example, higher internal LOC has been associated with better life outcomes, including better memory performance (Lachman, 2006), less disability (Gruber-Baldini et al., 2009), greater mental health and well-being (Johnson et al., 2009), and positively perceived health status (Berglund et al., 2014). Meanwhile, external LOC has been associated with more negative outcomes, such as high risk for anxiety and poor mobility in older adults (Beekman et al., 1998; Sartori et al., 2012). Aging seems to particularly affect internal LOC but not external LOC, and lower internal LOC in older adults is related to more memory problems and physical disabilities (Lachman, 2006). Conversely, compared with young adults, older adults often present higher external LOC (Lachman, 1986). These findings indicate that aging is closely related to change of LOC, which can affect health outcomes in old age (Caplan and Schooler, 2003; Fauth et al., 2007; Infurna et al., 2011; Krause and Shaw, 2000). Given the dissociated trajectories and impacts of internal vs. external LOC, addressing LOC may provide a pathway for maintaining successful aging.

More recently, efforts have been made to understand the association between neurologic disorders and LOC. In patients with Parkinson's

*Abbreviations:* ACC, anterior cingulate cortex; AD, Alzheimer's disease; FC, functional connectivity; HC, healthy control; IIVRT, intraindividual variability in reaction time; LOC, locus of control; MCC, mid-cingulate cortex; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PFC, prefrontal cortex; RAVLT, Rey's Auditory Verbal Learning Test; RMFG, right middle frontal gyrus; RSFG, right superior frontal gyrus; Rs-fMRI, resting state functional magnetic resonance imaging

* Corresponding author at: School of Nursing, University of Rochester Medical Center, Rochester, NY, USA.
*E-mail address:* vankee_lin@urmc.rochester.edu (F. Lin).

http://dx.doi.org/10.1016/j.neuropsychologia.2017.03.016
Received 18 November 2016; Received in revised form 7 February 2017; Accepted 12 March 2017
Available online 14 March 2017
0028-3932/ 

disease, greater internal LOC is associated with less disability (Gruber-Baldini et al., 2009). Emerging studies also suggest that traits related to LOC may help differentiate individuals at risk for AD from older cognitively normal populations. Conscientiousness, which reflects a sense of personal responsibility similar to internal LOC, and neuroticism, which often indicates vulnerability and helplessness similar to external LOC, have emerged as potent protective and risk factors, respectively, for the incidence of dementia (Duberstein et al., 2011; Low et al., 2013). Higher conscientiousness and lower neuroticism also appear to delay or prevent the onset of significant dementia symptoms in the presence of AD pathology (Terracciano et al., 2013). Similar to cognitive aging literature (Lachman, 2006), within the context of neurological disorders, internal LOC might provide individuals with a sense of agency or influence over their ability to manage declining cognition (e.g., developing effective coping strategies), facilitating adaptation. So far, however, no study has explored the neural mechanism of LOC, especially under cognitive demand in a group with probable AD-associated neurodegeneration. Noticeably, amnestic mild cognitive impairment (MCI), a subtype of MCI with compromised episodic memory, is considered a preclinical phenotype of AD (Eklund et al., 2016). A thorough mechanistic investigation of LOC may aid in the development of effective preventive strategies to address cognitive decline in this group.

The amygdala, a subcortical structure in the fronto-limbic system, may be critical for understanding the neural mechanism of LOC. There are multiple psychological, emotional, or cognitive links to amygdala, such as emotion regulation (Labuschagne et al., 2010; Siegle et al., 2007), neuroticism (Cremers et al., 2011; Lu et al., 2014; Omura et al., 2005), and acute stress regulation (van Marle et al., 2010; van Marle et al., 2009), including in AD patients (Poulin et al., 2011). Moreover, dysfunction of the amygdala has been implicated in personality disorders involving stress reactivity (Meyer-Lindenberg et al., 2009; New et al., 2007), as well as amnestic MCI (Hasselbalch et al., 2008). In addition to the amygdala, accumulated evidence suggests that stronger functional connectivity (FC) between the amygdala and other brain regions, such as prefrontal cortex (PFC), is associated with less social anxiety (Blackford et al., 2014), lower neuroticism scores (Cremers et al., 2010), reduced negative affect (Banks et al., 2007), and better cognitive control (Fine et al., 2001; Ochsner and Gross, 2005). All of these psychosocial, cognitive, and affective factors have been linked to LOC in the literature (Carden et al., 2004; Cooklin et al., 2013). Taken together, we speculate that the amygdala network may be important in understanding the neural substrates of LOC, including those at risk for AD.

In the present study, we compared the internal vs. external LOC in the context of everyday cognition (e.g., handling finance, playing cross-word puzzle) between participants with amnestic MCI and their age-, sex-, and education-matched healthy counterparts (HC) and examined the relevant neural mechanism with resting-state functional magnetic resonance imaging (rs-fMRI). In addition to determining the static neural correlates of LOC, we also employed a cognitive challenge task protocol to examine whether the LOC relevant neural correlates would link to cognitive performance in the cognitive challenge tasks. Of note, previous studies showed that brain networks derived from rs-fMRI can be immediately modulated by short-term cognitive demands seen in the cognitive challenge tasks, (e.g., Van Dijk et al., 2012).

## 2. Methods

### 2.1. Participants

Forty participants (22 HC and 18 MCI) completed the study. Participants with amnestic MCI were recruited from university-affiliated memory clinics using the clinical diagnosis of “mild cognitive impairment due to Alzheimer's disease” (Albert et al., 2011). All participants had deficits in memory based on a comprehensive neuropsychological battery, but intact basic activities of daily living and absence of dementia using NINCDS-ADRDA criteria per assessments. Participants had to be stable on Alzheimer's disease medication (i.e., memantine or cholinesterase inhibitors) for 3 months prior to enrollment. Age-, sex-, and education-matched HC participants without self-reported history of dementia or MCI were recruited from the community (e.g., senior centers). In addition, participants from both groups were required to have capacity to give consent based on the research team's assessment, have adequate visual and auditory acuity for testing, be ≥60 years of age, English-speaking, and community-dwelling. Exclusion criteria included presence of severe cardiovascular disease (e.g., chronic heart failure), severe inflammatory disease (e.g., irritable bowel syndrome), severe uncontrollable psychiatric disorders (e.g., major depression), and MRI contraindications (e.g., pacemaker, claustrophobia). The two groups significantly differed in their global cognition (measured using Montreal Cognitive Assessment, MOCA) and episodic memory (measured using delayed recall from the Rey's Auditory Verbal Learning Test, RAVLT) (see Table 1). The study was approved by the university's research subject review board.

**Table 1**
Demographics and clinical characteristics of MCI and HC group.

| | HC (n = 22) | MCI (n = 18) | $t$ or $\chi^2$ test (p value), df |
|---|---|---|---|
| Age, M (SD) | 71.23 (9.61) | 74.44 (10.60) | −1.01 (.32), 38 |
| Years of education, M (SD) | 15.64 (2.50) | 15.39 (2.87) | .29 (.77), 38 |
| Male, n (%) | 8 (36.4) | 8 (44.4) | .27 (.60), 1 |
| Memantine/cholinesterase inhibitor | – | 3 (16.7) | – |
| MOCA, M (SD) | 26.14 (2.67) | 24.17 (2.55) | 2.35 (.024), 38 |
| Delayed recall, M (SD) | 9.24 (2.7) | 5.78 (4.66) | 2.78 (.010), 37 |
| Internal LOC, M (SD) | 5.33 (.52) | 4.64 (.96) | 2.87 (.007), 38 |
| External LOC, M (SD) | 2.09 (.72) | 2.95 (.82) | −3.54 (.001), 38 |
| IIVRT, M (SD) | .31 (.06) | .39 (.06) | −4.11 (< .001), 37 |

Note. HC, healthy control; MCI, mild cognitive impairment; MOCA: Montreal Cognitive Assessment; LOC, locus of control; IIVRT, intra-individual variability in reaction time; LOC, locus of control.

### 2.2. Design and procedure

The present study was cross-sectional, consisting of two sessions within a two-week window. The first session entailed psychological interviews. The second session included a 20-min series of cognitive tasks and two rs-fMRI scans immediately before and after the tasks. The cognitive tasks included two commonly used computerized tasks: Stroop Color Word (inhibitory control) and Dual 1-back task (working memory). For the Stroop task, participants were shown serial colored words on the screen, and asked to judge the color of the word regardless of the meaning of the word as quickly and accurately as possible. For the Dual 1-back task, participants were shown an English letter on the screen, and asked to judge if the current stimulus matched the letter and position of the previous one as quickly and accurately as possible. For both tasks, feedback was displayed after participant responded to an individual trial. Reaction time (RT) and accuracy from the two tasks were recorded for further analysis. Each of the tasks lasted 10 min, and the order of the two tasks was randomized across participants. Instructions and practice were provided before each of the formal tasks.

### 2.3. Measures

#### 2.3.1. LOC assessment

LOC was assessed with the Personality in Intellectual Aging Contexts (PIC) Inventory Control Scales-short form (Lachman, 1986).