Brain, Behavior, and Immunity 60 (2017) 63–70

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

Full-length Article

Body mass and cognitive decline are indirectly associated via inflammation among aging adults

Kyle Bourassa *, David A. Sbarra

Department of Psychology, University of Arizona, 1503 E. University Blvd., Bldg #68, Rm. 312., Tucson, AZ 85721-0068, United States

ARTICLE INFO

Article history:
Received 16 June 2016
Received in revised form 30 August 2016
Accepted 19 September 2016
Available online 19 September 2016

Keywords:
Inflammation
C-reactive protein
Body mass
Cognition
Executive functioning
Memory

ABSTRACT

Inflammatory models of neurodegeneration suggest that higher circulating levels of inflammation can lead to cognitive decline. Despite established independent associations between greater body mass, increased inflammation, and cognitive decline, no prior research has explored whether markers of systemic inflammation might mediate the association between body mass and changes in cognitive functioning. To test such a model, we used two longitudinal subsamples (*ns* = 9066; 12,561) of aging adults from the English Longitudinal Study of Ageing (ELSA) study, which included two cognitive measures components of memory and executive functioning, as well as measurements of body mass and systemic inflammation, assessed via C-reactive protein (CRP). Greater body mass was indirectly associated with declines in memory and executive functioning over 6 years via relatively higher levels of CRP. Our results suggest that systemic inflammation is one biologically plausible mechanism through which differences in body mass might influence changes in cognitive functioning among aging adults.

1. Introduction

Preserved cognitive functioning is an important marker of quality of life among aging adults (Abrahamson et al., 2013; Nys et al., 2006). Although cognitive decline is linked with aging, the rate of this decline in aging is highly variable (Fillit et al., 2002; Park et al., 2003) and can depend on a variety of individual differences, including exaggerated inflammatory responses (Tegeler et al., 2016; Teunissen et al., 2003; Yaffe et al., 2003) and elevated body mass (Memel et al., 2016), as well as a host of psychosocial and health behavior variables (e.g., social engagement, physical health, physical activity, and depression; Bourassa et al., 2015). With the rate of adults that are 65 years and older rising relative to the overall population in almost all developed countries (Restrepo and Rozental, 1994), understanding what risk factors are associated with cognitive decline is essential for developing interventions to promote successful aging. To explore one potential pathway that might explain risk for cognitive decline among aging adults, we examined the associations among body mass, inflammation, and change in cognition over 6 years in a nationally representative sample of older adults.

1.1. Inflammation and cognitive decline

Inflammation is one biologically-mediated pathway that might explain individual differences in cognitive decline among aging adults. Higher systemic inflammation levels are associated with cognitive decline in normative aging populations (Tegeler et al., 2016; Teunissen et al., 2003; Yaffe et al., 2003), as well as in clinical samples experiencing age-related neurological disorders (Perry et al., 2007). Inflammatory models of neurodegeneration propose that systemic inflammation is negatively associated with cognition via increases in neuro-inflammation. Inflammatory cytokines – including Tumor Necrosis Factor(TNF)α, Interleukin (IL)-1β, and IL-6 – secreted by microglia in the brain likely establish and maintain neuro-inflammation (Glass et al., 2010), which can lead to neuronal apoptosis over the long-term (McCoy and Tansey, 2008; Simi et al., 2007), and inhibit neurogenesis in adults (Ekdahl et al., 2003). Systemic inflammation in the periphery is tied to neuro-inflammation in neurodegenerative disorders (Perry, 2004), as well as in aging populations more generally (Perry, 2010). For example, IL-6 and C-reactive protein (CRP) assessed in the periphery are associated with changes in brain morphology and cognitive decline in midlife (Marsland et al., 2015). As a result, individual differences in systemic inflammation may explain a portion of the variability in cognitive decline among aging adults.

* Corresponding author.
E-mail address: kylebourassa@email.arizona.edu (K. Bourassa).

http://dx.doi.org/10.1016/j.bbi.2016.09.023
0889-1591/

1.2. Body mass, inflammation, and cognition

Body mass is broadly associated with both inflammation (Visser et al., 1999; Wisse, 2004) and cognition (Benito-León et al., 2013; Cournot et al., 2006; Memel et al., 2016). For example, people with higher body mass index scores perform worse than people with body mass in the healthy range across a variety of cognitive tasks (Gunstad et al., 2007). Despite the large literature exploring the association of body mass and cognition for aging adults, there is relatively less research examining the specific biologically-mediated pathways through which body mass might influence cognition. There are several pathways through which body mass might influence changes in cognitive functioning over time. For example, greater adipose tissue and body mass, for example, increase the production of proinflammatory cytokines tied to metabolic syndrome (Wisse, 2004) and greater body mass predicts greater leptin and insulin resistance, insulin dysregulation, and inflammation, all of which are associated with cognitive decline (Considine et al., 1996; Al Hazzouri et al., 2013; Greenwood and Winocur, 2005; Visser et al., 1999; Wisse, 2004). One potential biologically-mediated pathway that could explain the association between higher body mass and cognitive decline is inflammation. Higher body mass is associated with specific markers of systemic inflammation, including IL-6 and CRP (Park et al., 2005), both of which are implicated in inflammatory models of neurodegeneration (Glass et al., 2010). Thus, inflammation is one biologically-mediated pathway that might help explain the link between body mass and subsequent cognitive decline.

1.3. Present study

Despite established associations among body mass, systemic inflammation, and cognitive decline, no prior research has examined the extent to which systemic inflammation might account for the association of individual differences in body mass and changes in cognitive decline among aging adults. The present study aimed to explore this possibility in two subsamples of aging adults (*ns* = 9066; 12,561) drawn from the longitudinal English Longitudinal Study of Ageing (ELSA). We hypothesized that body mass would be indirectly associated with change in two areas of cognitive functioning – memory and executive functioning – via systemic inflammation levels, as indexed by circulating CRP. More specifically, we predicted that higher body mass would positively predict change in CRP, which in turn would predict greater cognitive decline across the 6 years.

2. Method

2.1. Participants

The English Longitudinal Study of Ageing (ELSA) currently has seven waves of data collected every two years from 1998–2013 (Marmot et al., 2015), which included cognitive measures in Waves 1–6. These waves were supplemented by home visits by a nurse every other wave (Waves 0, 2, 4) during which blood samples were collected and analyzed. ELSA was designed to collect information on a representative sample of people in England over the age of 50, and details regarding the selection, eligibility, and recruitment of participants, participant demographics, and study methodology are reported in more detail in the ELSA Technical Report and User Guide (Marmot et al., 2015).

For the present study, 29,808 unique participants had data across at least one of the waves. Fig. 1 outlines the specific data collected at each of the waves used in the current study. Following standard practices, we excluded participants from the current study that had CRP scores above 10 mg/L, which likely reflects acute infection or an obvious source of inflammation (see Pearson et al., 2003). Participants were excluded from the sample in a stepwise fashion beginning with Wave 0, then Waves 2, and 4. This resulted in excluding 552, 428, and 348 participants due to high CRP scores from waves 0, 2, and 4, respectively. From the remaining 28,408 eligible participants, two subsamples were created by selecting and excluding participants who were assessed on the variables of interest during at least one of the relevant times points, as shown in Fig. 2. For subsample 1 (assessing Waves 0–4), we included participants with assessments at Waves 0, 1, 2, and 4[1], whereas for subsample 2 (assessing Waves 2–5) we included participants assessed at Waves 2, 4, and 5. This resulted in a final sample of 9066 people for subsample 1 and 12,561 people for subsample 2 out of the original ELSA participants[2]. Of these participants, 6354 people completed all the relevant waves of assessment used in the two subsamples (Waves 0–2, 4, and 5), and were included in both subsamples, as none of the measured variables overlapped between the two subsamples at a given wave of assessment. These two subsamples were selected to allow for analysis of change over time in both CRP and cognition—which required a six year time period due to the data collection timeline—and because it allowed us to test whether the effects observed in one subsample would replicate in a second subsample.

2.2. Measures

2.2.1. Demographic covariates

Demographic variables included self-reported age and gender.

2.2.2. Cognition

Cognition was assessed using three tasks—immediate word recall, delayed word recall, and verbal fluency—assessed by a trained interviewers using a standardized process in participants' home. These three measures were used to create two broad constructs for cognitive functioning, memory and executive functioning, similar to prior investigations using similar cognitive measures (Bourassa et al., 2015).

2.2.2.1. Memory function. Memory function was assessed using immediate and delayed word recall task from the Ten-Word Delayed Recall Test. Ten words were presented and participants attempted to recall the words immediately, then again five minutes later, and the two scores were averaged. Similar assessments have been used extensively to measure immediate and delayed memory performance (Green et al., 2011; Hoskins et al., 2010).

2.2.2.2. Executive function. Executive function was assessed using a category fluency task. Participants were asked to name as many animals correctly as possible during a one-minute period. The measure is sensitive to alterations in executive functions in patients with frontal lobe damage (Stuss et al., 1998) and has been used widely in neuropsychological batteries to differentiate between healthy age-related memory change and clinically significant impairments (Haugrud et al., 2011).

[1] In subsample 1, we also then excluded participants without at least one valid CRP score, as this was necessary to reach valid covariance coverage due to high levels of missingness at Wave 0 compared to waves 1, 2 and 4.

[2] We note that the specific waves that we selected from cognitive measures from were adjusted from subsample 1 to subsample 2. The cognitive measures of interest were not collected at Wave 0 and our measure of executive functioning was not collected at Wave 6. As a result, we included cognitive measures spanning Waves 1–4 for subsample 1 and waves 2–5 for subsample 2 to account for these differences and retain the same amount of time between measurements. As a result, the measurement of CRP was completed 2 years and 4 years after the measurement of body mass for subsample 1 and 2, respectively.