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Three-year changes in leisure activities are associated with concurrent changes in white matter microstructure and perceptual speed in individuals aged 80 years and older

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ABSTRACT

Accumulating evidence suggests that engagement in leisure activities is associated with favorable trajectories of cognitive aging, but little is known about brain changes related to both activities and cognition. White matter microstructure shows experience-dependent plasticity and declines in aging. Therefore, we investigated the role of change in white matter microstructure in the activities-cognition link. We used repeated assessments of engagement, perceptual speed, and white matter microstructure (probed with diffusion tensor imaging) in a population-based sample of individuals over 80 years without dementia ($n = 442$, $M_{age} = 85.1$; $n = 70$ for diffusion tensor imaging; 2 occasions 3 years apart). Using multivariate latent change modeling, we observed positive correlations among changes in predominantly social activities, white matter microstructure, and perceptual speed. Interindividual differences in change in white matter microstructure statistically accounted for the association between change in leisure activities and change in perceptual speed. However, as analyses are based on observational data from 2 measurement occasions, causality remains unclear.

1. Introduction

Among all factors that may influence maintenance or decline of cognitive abilities in aging, leisure activities are of major interest because they are an important part of older individuals' everyday life, a major source of stimulation, and amenable to intervention (Lövdén et al., 2010a; Ngandu et al., 2015; Park et al., 2014). An association between engagement in leisure activities and cognitive performance among healthy older adults is well established (Hertzog et al., 2009; Lindenberger, 2014; Stern, 2009). Little is known, however, about changes in the brain that might underlie this association. The brain's white matter microstructure is modifiable by experience (Fields, 2010; Lövdén et al., 2010b; Reuter-Lorenz and Park, 2014; Scholz et al., 2009; Zatorre et al., 2012) and relates to cognitive functioning in older age (Kievit et al., 2014; Madden et al., 2012; Vernooij et al., 2009). We therefore hypothesized that aging-related change in white matter microstructure is related to both activity engagement and cognition. If so, change white matter microstructure can even more be seen as a candidate factor in explaining why activity engagement might be related to cognition in aging. This should then be reflected in a mediation effect where change in white matter microstructure statistically accounts for the association between change in activities and change in cognition. We investigated these hypotheses using measures of within-person, longitudinal changes in activity, white matter microstructure, and cognition from cohorts older than 80 years.

Several studies that used longitudinal designs have reported that change in engagement in leisure activities is positively associated with change in several cognitive functions in aging; this has been shown for physical activities (Angevaren et al., 2010; Ku et al., 2012; Lindwall et al., 2012; Small et al., 2012; van Gelder et al., 2004), cognitive activities (Bielak et al., 2014; Ghisletta et al., 2006; Hultsch et al., 1999; Mitchell et al., 2012; Small et al., 2012), social activities (Bielak et al., 2014; Brown et al., 2012; Small et al., 2012), and for combined scores of different kinds of leisure activities (Bielak et al., 2007; Lövdén et al., 2005; MacKinnon et al., 2003; but see Bielak et al., 2012).

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Less is known about the association between change in engagement in activities and change in brain structure. To our knowledge, only 1 study has directly investigated the association between leisure activities and white matter microstructure in late adulthood (Gow et al., 2012). However, this study measured white matter microstructure just once, which renders conclusions regarding aging-related changes in white matter microstructure difficult. Using diffusion tensor imaging (DTI), a magnetic resonance (MR) technique that probes white matter microstructure by quantifying the diffusion of water molecules in tissue, Gow et al. (2012) found an association between physical activities at age 70 years and higher fractional anisotropy (FA) at a measurement occasion 3 years later. The FA measure reflects fiber density and coherence within a voxel, and higher FA in a given white matter region potentially indicates more efficient functioning (Fields, 2008). Gow et al. (2012) observed no associations with mean diffusivity (MD), which reflects the sparseness of tissue in a voxel (with higher values indicating a less-dense fiber structure, potentially related to less efficient functioning; Fields, 2008). Although evidence from observational studies is limited, training studies in humans (Lövdén et al., 2010b) as well as studies with animals in enriched environments (reviews: Fields, 2008, 2010, Taubert et al., 2012, Zatorre et al., 2012) suggest an association between changes in activity and changes in white matter microstructure in older age.

White matter microstructural changes are considered a potential correlate of cognitive decline in aging (Andrews-Hanna et al., 2007; Bartzokis, 2004, 2011; Kochunov et al., 2012; O'Sullivan et al., 2001; Salami et al., 2012; Voineskos et al., 2012). Thus, preserved cognitive functioning may be characterized by maintained white matter microstructure (Hedden and Gabrieli, 2005; Nyberg et al., 2012; Voss et al., 2011). To test this assumption, studies need to analyze how within-person changes in white matter microstructure are associated with within-person changes in cognition (Nyberg et al., 2012; Salthouse, 2011). Using data from a subsample of octogenarians and nonagenarians taking part in a population-based study, the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), we recently reported significant mean changes of white matter microstructure (FA and MD) in 6 major white matter tracts over 2.3 years (Lövdén et al., 2014). In addition, we observed interindividual differences in within-person change and an association between change in the microstructure of the corticospinal tract and change in perceptual speed (Lövdén et al., 2014; see also Barrick et al., 2010; Bender and Raz, 2015; Charlton et al., 2010; Ritchie et al., 2015a, 2015b).

It is thus reasonable to expect that change in activity engagement is related to both change in the brain's white matter microstructure and change in perceptual speed. If changes in all 3 variables are correlated with each other, it seems theoretically plausible that white matter microstructure would also statistically account for the association between activity engagement and perceptual speed. Importantly, because we are interested in change with aging, all 3 variables in the model are estimates of intraindividual change over time. Note that a mediation effect must still not imply a causal effect as long as the data that are used are observational (without intervention or experimental manipulation). Rather, it can only provide estimates that describe the data if the assumption of a causal effect was true (Baron and Kenny, 1986; Lindenberger and Pötter, 1998). Although a mediation effect does not confirm any causal role, absence of a mediation effect implies that a causal role is improbable. In other words, mediation models "provide an opportunity for implications of particular hypotheses of causal relations to be disconfirmed" (Salthouse, 2011). Thus, if we would not find a mediation effect of change in white matter microstructure, we would not maintain that white matter microstructure is likely to be an important neural underpinning of activity-related variance in perceptual speed. There are alternative ways to specify the relations among these variables that may also be plausible. For instance, maintained white matter microstructure could predict continued activity, mediated by preserved perceptual speed. Here, we were mainly interested in the role of white matter microstructure. Therefore, we fitted a model that proposes that change in white matter microstructure mediates an association between change in leisure activities and change in perceptual speed. This model is plausible in light of the previously reported links change in leisure activities and change in cognition (Ghisletta et al., 2006; Lövdén et al., 2005; Small et al., 2012) and between change in white matter microstructure and change in cognition (Bender et al., 2015; Lövdén et al., 2014; Ritchie et al., 2015a).

We investigate the associations among change in leisure activity engagement, perceptual speed, and white matter microstructure, using questionnaire data, cognitive measurements, and DTI assessments at 2 assessments in participants older than 80 years from SNAC-K. As a measure of cognitive ability, we focus on perceptual speed, based on the following considerations: First, reduced perceptual speed is regarded as a powerful indicator of cognitive decline in aging (Finkel et al., 2007, Lindenberger et al., 1993, Salthouse, 1996, 2000). Second, change in perceptual speed relates to change in leisure activity engagement in a number of longitudinal studies (Aartsen et al., 2002; Angevaren et al., 2010; Bielak et al., 2007, 2014; Ghisletta et al., 2006; Lövdén et al., 2005; MacKinnon et al., 2003; Wilson et al., 2012; but see Bielak et al., 2012). Third, perceptual speed is related to white matter microstructure, in both cross-sectional analyses (Laukka et al., 2013b; Lövdén et al., 2014; Penke et al., 2010, 2012; Ritchie et al., 2015a) and longitudinal analyses (Lövdén et al., 2014, but see Ritchie et al., 2015a). The activities our participants were asked to report were clustered according to their degree of being mentally demanding, physically demanding, or social/interactive. A different sample of older individuals from the same population rated each activity on these dimensions (see also Arbuckle et al., 1994; Christensen and Mackinnon, 1993; Karp et al., 2006; Salthouse et al., 2002). As a measure of white matter microstructure, we focus on FA and MD in the corticospinal tract because we had previously found that only changes in this tract are significantly associated with changes in perceptual speed in the current sample (Lövdén et al., 2014). As white matter hyperintensities (WMHs) are related to both microstructural changes (Maniega et al., 2015; Vernooij et al., 2008) and perceptual speed (Longstreth et al., 2005; Ritchie et al., 2015b; Vernooij et al., 2009), we also controlled for global WMH volume in additional analyses.

2. Methods

2.1. Sample

The sample was derived from the population-based longitudinal SNAC-K in the following way. In the SNAC-K study, 3363 individuals in narrow age groups (60, 66, 72, 78, 81, 84, 87, 90, 93, 96, and 99+ years) participated in a baseline assessment of their medical, psychological, and social status comprising clinical examinations, cognitive tests, interviews, and questionnaires. A first follow-up was completed approximately 3 years later, a second follow-up roughly 6 years later. For the purpose of this study, we used only data from the first and second follow-up, henceforth referred to as time 1 and time 2. This is due to the fact that only for these occasions, data from identical DTI protocols are available. The first follow-up included only cohorts aged 81 years and older, therefore is the age range in this study restricted to this age range.

At time 1, $n = 764$ participants were cognitively tested, $n = 112$ of them underwent DTI yielding acceptable image quality. After