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Proper name retrieval and structural integrity of cerebral cortex in midlife: A cross-sectional study

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ABSTRACT

There is currently little understanding on whether retrieval of proper names differs in midlife compared to young adulthood and if so, whether the age differences in this ability are associated with differences in structural integrity of the cerebral cortex. To answer these questions, we studied retrieval of proper names in 115 cognitively healthy middle-aged persons (49.7, ± 3.2), comparing their performance on a tip-of-the-tongue (TOT) task with that of 68 young persons (25.4, ± 3.5) from the Cam-Can data repository (http://www.mrc-cbu.cam.ac.uk/datasets/camcan/). Grey matter (GM) density and cortical thickness were used as indices of structural integrity of the cerebral cortex. The middle-aged (MA) group experienced more TOTs during proper names retrieval than young adults (YA), ($t = 3.789$, $p < .005$) and had considerably less GM density and cortical thickness across a range of brain areas bilaterally. Small clusters in left BA 45 and right BA 44 (cortical thickness) and in right BA 40 (volumetry) revealed group differences when accounting for TOTs. However, we observed no correlations between MA's TOT scores and GM volumes or cortical thickness of the brain regions typically reported as implicated in retrieval of proper names: left anterior temporal lobe, left insula, and left superior and middle temporal gyri.

1. Introduction

Research on the effects of aging on the brain and cognition in neurologically intact persons has traditionally focused on adults aged 60 years or more, despite the evidence suggesting that neurocognitive decline begins in the early 20s (Salthouse, 2010). Gradual changes in the brain that typically begin in early adulthood include reduction in the brain's overall size and weight, grey and white matter regional volume reduction and integrity deterioration, expansion of cerebral ventricles and sulci, cortical thinning, changes in functional connectivity, myelin integrity, concentration and receptor density of neurotransmitters, accumulation of neurofibrillary tangles, reduced synaptic density, and so forth (Giorgio et al., 2010; Lindenberger, 2014; Marstaller, Williams, Rich, Savage, & Burianova, 2015; Salat et al., 2004; Salthouse, 2009). Some cognitive functions appear to be more resilient to aging than others. For instance, vocabulary and general knowledge may continue to grow past the age of 60, whereas processing speed, memory, executive function and problem solving typically begin to deteriorate in early adulthood (Ackerman, 2008; Salthouse, 2010).

One domain particularly vulnerable to aging is knowledge of proper names. Knowledge of proper names serves an important cognitive function: it helps us to identify an entity despite its different manifestations or different contexts in which it appears, which in turn allows us to structure the world around us (Van Langendonck, 2007). More importantly, proper names allow us to achieve a unique reference even when our knowledge about the entity in question is limited (Burks, 1951). Cognitively healthy elderly persons have difficulties when retrieving proper names, with increased occurrences of tip-of-the-tongue states (Burke, MacKay, Worthley, & Wade, 1991; Cohen & Burke, 1993; Huijbers et al., 2016; James, 2006; Salthouse & Mandell, 2013; Shafto, Burke, Stamatakis, Tam, & Tyler, 2007; Shafto, Stamatakis, Tam, & Tyler, 2009). A tip-of-the-tongue (TOT) state is a metacognitive state in which a person is aware of his/her failure to retrieve the target word accompanied by a strong feeling that the sought for target is within reach. Difficulty in retrieving proper names was also found in persons with neurological conditions, such as Alzheimer's disease (Semenza, Nichelli, & Gamboz, 1996), Parkinson's disease and advanced multiple sclerosis (Semenza, 2009), after language-dominant temporal lobectomy (Tsukiura et al., 2002), and in aphasia due to brain injury

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(Miceli et al., 2000; Semenza & Zettin, 1988, 1989). In contrast to word retrieval deficits caused by brain damage, TOT experiences involve only a temporary inability to recall a specific word. However, even a temporary and only occasional inability to access knowledge of proper names, as in TOT states, is frustrating and indicates that there is something peculiar about proper names that makes them susceptible to forgetting.

Philosophical, linguistic, and neuropsychological theories agree that proper names have a special status in language. The long tradition of philosophical thinking on proper names involves debates regarding the question of how proper names name, i.e. whether they have meaning/sense or whether they are directly referential expressions (e.g. Frege, 1892/1949; Katz, 1977; Kripke, 1980; Mill, 1843; Russell, 1905; Searle, 1958, among others). As a linguistic category, proper names belong to language universals. Unlike verbs, which name events and states (De Almeida & Manouilidou, 2015), and unlike common nouns, which denote categories of objects, proper names refer to unique entities, such as persons, animals, places, buildings, brands, languages, and currencies. Thus, proper names lack the meaning in the sense in which common nouns have meanings. In some languages, they also differ in morpho-syntax and may follow different syntactic rules (Alego, 1973; Longobardi, 2005; Van Langendonck, 2007). Given the peculiar nature of proper names, it is not surprising that they figure differently than other semantic classes in memory (Bartlett, 1932). In general, proper names are more susceptible to forgetting than common nouns (Hanley, 2011; Salthouse & Mandell, 2013; Semenza, 2009; Semenza et al., 1996), even in case of name-occupation homophones (e.g., *Baker-baker*, *Potter-potter*), which cannot be explained by differences in phonological form or frequency of occurrence (Cohen & Burke, 1993).

Some findings indicate that there exists a dedicated area for retrieval of proper names (Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Gorno-Tempini et al., 1998; Shafto et al., 2007), but there is currently no consensus on which area it is. One model promotes the notion of the critical role of the left anterior temporal lobe (ATL) in the retrieval of proper names (Abel et al., 2015; Damasio et al., 1996; Mehta et al., 2016; Tsukiura et al., 2002). Evidence supporting this model comes from a series of studies involving brain-damaged and neurologically intact subjects, using a range of methods, from positron emission tomography (PET), functional magnetic resonance imaging (fMRI), electrocorticography to diffusion tensor imaging. Another model, which is based on PET evidence obtained from six healthy male subjects, argues for an amodal semantic network distributed across the left anterior and posterior extrasylvian temporal cortex (Gorno-Tempini et al., 1998). The model allows a degree of modularity within the network, with some areas being differentially involved in specific types of processing (e.g. faces, words, objects). For example, it was suggested that the anterior middle temporal gyrus (MTG) and superior temporal gyrus (STG) are the areas supporting retrieval of famous persons' names (Gorno-Tempini et al., 1998). A third model, based on f/MRI evidence, suggests that the left insula plays a critical role in retrieval of names and that increased TOT states during proper names retrieval indicate difficulties with phonological access to the mental lexicon (Shafto et al., 2007). The disparate research findings suggest that the fundamental question of neurobiological underpinnings of proper name retrieval has not been entirely resolved.

So far, most research on age-related decline in proper name retrieval has been focused on elderly persons, leaving largely unexplored the question of whether this cognitive ability is already affected in midlife. Given the evidence suggesting that increased age negatively affects proper name retrieval (Burke et al., 1991; James, 2006), in the present study we wanted to determine whether the ability to retrieve proper names would differ in midlife compared to young adulthood and if so, whether these differences would be related to differences in grey matter (GM) density and cortical thickness. We tested for age-differences in cortical thickness in addition to GM density because growing evidence indicates that cortical thinning is also an important index of atrophy in aging (Im et al., 2008; Lemaitre et al., 2010; Panizzon et al., 2009), with global cortical thinning becoming apparent by the third decade of life (Salat et al., 2004). Furthermore, considering previous findings indicating that left ATL, left MTG, STG and left insula support retrieval of proper names (Damasio et al., 1996; Gorno-Tempini et al., 1998; Shafto et al., 2007), we wanted to determine whether GM density and cortical thickness of these specific regions in middle-aged persons would be related to their ability to retrieve proper names. In general, greater GM density and thicker cortex have been associated with better cognitive performance, but associations between reduced density and normal cognition were also found. (For example, a negative correlation between GM density in the caudate nucleus and general intellectual ability in cognitively normal young people was reported by Frangou, Chitins, and Williams (2004).) Magnetic resonance imaging (MRI) allows *in vivo* studying of brain morphometrics, permitting insights into structural brain differences and possible associations between regional volumetric as well as cortical thickness properties and behavioral measures of proper names retrieval.

Thus, we studied retrieval of proper names in a sample of 115 cognitively healthy middle-aged persons (MA) (mean age 49.7, ± 3.2), comparing their performance on a tip-of-the-tongue (TOT) task with that of a group of 68 young adults (YA) (mean age 25.4, ± 3.5). In addition to comparing the two groups' performance on the TOT task, we explored group differences in overall GM density and cortical thickness obtained from MRI data, and tested for possible associations between volumes as well as cortical thickness of the regions that were previously identified as supporting proper names retrieval – left ATL, MTG, STG, and insula – and MA group's performance on the TOT task.

2. Materials and methods

2.1. Participants

Data used in the preparation of this work were obtained from the Cambridge Center for Ageing and Neuroscience (Cam-Can) data repository, available at http://www.mrc-cbu.cam.ac.uk/datasets/camcan/. The study followed the recommendations of the Helsinki Declaration on studies involving human subjects and was approved by the local ethics committee (see Shafto et al., 2014; Taylor et al., 2017 for details on the Cam-Can protocol). Cognitive and structural neuroimaging data were retrieved for 183 cognitively healthy subjects, including 115 middle-aged persons (age range 45–55 years, mean age 49.7, ± 3.2) and 68 young adults (age range 18–30 years, mean age 25.4, ± 3.5). There were no statistically significant differences in gender distribution between the groups (Pearson Chi-Square, $\chi^2 = 0.157$, $p = .692$). However, the original sample was reduced during image preprocessing (Section 2.3) due to removal of the images with an overall covariance below two standard deviations, which left a total of 168 subjects (MA = 102, mean age 49.7 ± 3.3; YA = 66, mean age 25.3 ± 3.5; t (1 6 6) = 46.066, $p < .005$). The sample reduction did not affect the gender distribution pattern (MA: 48 females, 54 males; YA: 29 females, 37 males; Pearson Chi-Square, $\chi^2 = 0.165$, $p = .684$, n.s.). The groups did not differ considerably in the total intracranial volume (t (1 6 6) = −0.054, $p = .95$, n.s.).

2.2. Behavioral data: tip-of-the-tongue task

In the tip-of-the-tongue task, participants were presented with 50 pictures of faces that represented famous people (actors, musicians, politicians, etc.). The task was to name a person upon seeing a picture. The pictures were presented in a pseudorandom order. Before each trial, a fixation cross was presented for 1000 ms, which was followed by a picture that remained on the screen for 500 ms. The task allowed three categories of responses: "know" response, i.e. retrieval of the name, "don't know" response if they did not know who the person on the picture was, and a TOT response, meaning they knew who the