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Functional correlates of instrumental activities of daily living in mild Alzheimer's disease

Neelesh K. Nadkarni[a,b,c,*], Naama Levy-Cooperman[a,c], Sandra E. Black[a,b,c,d,**]

[a] L. C. Campbell Cognitive Neurology Research Unit, Neuroscience Research Program, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
[b] Division of Neurology, Department of Medicine, Toronto, Ontario, Canada
[c] Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada
[d] The Rotman Research Institute, Baycrest Centre for Geriatric Care, Toronto, Ontario, Canada

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Abstract

Instrumental activities of daily living (IADL) includes the integration of task-initiation, -planning, and -performance. Little is known on the cerebral perfusion correlates of these subcomponents of IADL in Alzheimer's disease (AD). In 121 AD patients, cerebral perfusion, using single-photon emission computed tomography, in 13 bilateral regions of interest (ROI) and the perfusion correlates of IADL subcomponents, rated on the Disability Assessment in Dementia scale, were explored. Significant correlations were observed between IADL initiation and multiple bilateral prefrontal-striatal-anterior cingulate ROI ($p < 0.01$), IADL planning and right occipital ROI ($p < 0.05$), and IADL performance and right parietal ROI ($p < 0.05$). Multiple regression, accounting for age, cognitive impairment, and depression severity, revealed significant relationship between right basal ganglia perfusion and IADL-initiation ($R = 0.6$, $R^2 = 0.39$, $F(4,117) = 17.8$, SE = 1.56; $p < 0.001$) and right occipital perfusion and IADL-planning ($R = 0.6$, $R^2 = 0.34$, $F(4,117) = 19.5$, SE = 1.47; $p < 0.001$). In AD, perfusion correlates of these subcomponents may be linked to the heterogenous cognitive processes involved in IADL.

Keywords: Alzheimer's disease; Cerebral perfusion; Instrumental activities of daily living

1. Introduction

Dementia in Alzheimer's disease (AD) and other disorders is commonly defined by the presence of memory impairment and a decline in 1 other cognitive domain severe enough to impede an individual's functional ability in everyday life (APA, 1994). The progressive decline in activities of daily living during the course of the disease usually follows a hierarchical pattern of loss of functional routines. During the early stages of AD, patients have difficulty with complex instrumental activities of daily living (IADL), such as managing finances, going on an outing, shopping, and preparing meals. This loss of IADL performance is eventually followed by a decline in self-care activities of daily living such as eating, dressing, and bathing (Gauthier et al., 1997; Lehfeld and Erzigkeit, 2000; Mitnitski et al., 1999).

IADL is a multidimensional construct that reflects many different components. It has been suggested that breaking down these components of IADL into subcomponents at every step of an activity rather than the global task performance allows for more robust assessment of functional ability in dementia (Beck and Frank, 1997). Functional rating scales such as the Disability in Dementia scale have been devised incorporating the motivational and cognitive aspects of every task such as ability to initiate an activity, ability to correctly plan the involved sequences, and then effectively perform the sequences for an appropriate execution of the task (Gelinas et al., 1999). Functional status has

* Corresponding author at: A421, L. C. Campbell Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON, Canada M4N 3M5. Tel: +1 416 480 4551.
E-mail address: neelesh.nadkarni@utoronto.ca (N.K. Nadkarni).
** Alternate corresponding author at: A421, L. C. Campbell Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON, Canada M4N 3M5. Tel: +1 416 480 4551.
E-mail address: sandra.black@sunnybrook.ca (S.E. Black).

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also been shown to be an important determinant of the quality of life, mood, and behavior in patients with AD (Albert et al., 1996). Investigating functional performance in relation to clinical profiles can provide insight into functional ability in AD. Several studies have revealed a relationship between functional impairment and cognitive and behavioral symptoms in patients with AD that are thought to reflect frontal dysfunction (Boyle et al., 2003; Cahn-Weiner et al., 2003; Lechowski et al., 2003; Levy et al., 1996; Lopez et al., 1997; Senanarong et al., 2005; Tekin et al., 2001). Robust relationships have also been reported between functional losses in AD and neuropathological hallmarks such as neuritic plaques and neurofibrillary tangle counts in orbitofrontal, medial temporal, occipital, and anterior cingulate regions (Bobinski et al., 1997; Marshall et al., 2006; Roth et al., 1966). Certain neuroimaging markers such as hippocampal volumes have also been reported to be associated with functional ability in heterogeneous sample of community-dwelling elderly (Cahn-Weiner et al., 2007; Farias et al., 2004). Another study reported that the presence of medial temporal lobe atrophy was associated with loss of IADL (Henon et al., 1998). However, there is very little information on the association between impairment in functional ability and *in vivo* functional brain changes such as cerebral perfusion in AD. Salmon et al. (2005) studied the relationship between cerebral metabolism and 4 cognitive and functional scales used to assess severity of AD (Salmon et al., 2005). One of the scales used in this study assessed IADL ability in patients with AD. The authors reported that the total IADL score negatively correlated with regional glucose metabolism in the right parieto-temporal cortex (Salmon et al., 2005). Two studies reported significant associations between functional ability and bilateral temporoparietal regions. Ott et al. (2000) studied the relationship of driving ability to regional perfusion in mild to moderate AD and found that driving score was associated with right frontal and occipital and bilateral temporoparietal perfusion (Ott et al., 2000). Nobili et al. (2001) reported that hypoperfusion in bilateral temporo-parietal regions was predictive of loss of basic self-care activities such as bathing, dressing, and eating (Nobili et al., 2001). These studies suggest that temporo-parietal regions are associated with IADL ability in AD. Whether such regional associations with functional ability differ when the components of IADL are studied is not known.

The main objective of this study, therefore, was to explore the correlation between perfusion in these specific brain regions and overall IADL ability as well as the individual components of IADL ability, namely initiation, preparation or planning, and action or performance, in patients with mild AD. In doing so, we also compared cerebral perfusion and hence, baseline characteristics, in patients with mild AD to that of normal elderly, to examine whether the perfusion in our mild AD sample group was indeed significantly lower and whether the perfusion in our AD sample was typically that of a mild AD population (Bartenstein et al., 1997; Talbot et al., 1998). We hypothesized that overall IADL ability would correlate bilaterally with regions specialized for visuo-spatial function, ie, the lateral temporal, parietal, and occipital regions. However, the correlations between perfusion and subcomponents of IADL would reveal that initiation of IADL, which are dependent on motivation and executive function abilities, would correlate with bilateral frontosubcortical perfusion whereas preparation and performance of IADL, which is dependent on visuo-spatial and perceptual abilities, would correlate with bilateral parieto-occipital perfusion.

2. Methods

2.1. Study participants

Perfusion and functional data of 121 patients with AD and 40 age-matched normal control subjects (NC) was drawn from the Sunnybrook Dementia Study, which is a prospective cohort of community-dwelling healthy elderly control subjects and patients with dementia recruited from a cognitive-neurology clinic at a university hospital. Patients between the ages of 60 and 90 years, who met the National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorder Association (NINDS-ADRDA) diagnostic criteria for probable AD (McKhann et al., 1984) and had a Mini Mental State Examination (MMSE) $\geq$18, were included in this substudy. Presence of associated conditions such as major depressive disorder or unrelated disorders, such as arthritis, can affect functional ability adversely and, therefore, was exclusionary. The data for this study were obtained from the initial neuroimaging and functional assessment, which followed shortly after the patient's first assessment in the memory clinic.

2.2. Regional cerebral perfusion determination

Single photon emission computed tomography (SPECT) is a widely used clinical neuroimaging tool that provides a map of regional cerebral blood flow (rCBF), which can be used as a surrogate measure of neuroanatomical-function in AD. Typically, a radioactive tracer such as Tc99m-ethyl-cysteinate-dimer (^{99m}Tc-ECD) is injected intravenously, which rapidly distributes in the brain in accordance with rCBF. The tracer is believed to be taken up by neurons in accordance with blood flow, so that a regional uptake reflects the functional integrity of the specific region in the resting state. The distribution of the tracer provides a rCBF map.

SPECT imaging was performed using a triple-head gamma camera (Prism 3000XP; Phillips Medical Systems Inc, Cleveland, OH) after injection of 20 mCi of technetium-99m ethyl cysteinate dimer. Each view comprised a 128 $\times$ 128 pixel image with typically a 9.7 mm full-width at half-maximum reconstructed image resolution. Reconstructed images, performed using a ramp-filtered back-pro-