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Ventral striatal volume is associated with cognitive decline in older people: a population based MR-study

L.W. de Jong[a,b], Y. Wang[a], L.R. White[c], B. Yu[a], M.A. van Buchem[b], L.J. Launer[a,*]

[a] *Laboratory of Epidemiology, Demography and Biometry, of the National Institutes on Aging (NIH), Bethesda, MD, USA*
[b] *Department of Radiology, Leiden University Medical Center, Leiden, the Netherlands*
[c] *Kuakini Medical Center and Pacific Health Research Institute, Honolulu, HI, USA*

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Abstract

Striatal degeneration may contribute to cognitive impairment in older people. Here, we examine the relation of degeneration of the striatum and substructures to cognitive decline and dementia in subjects with a wide range of cognitive function. Data are from the prospective community-based Honolulu Asia Aging Study of Japanese American men born 1900–1919. Brain magnetic resonance imaging (MRI) (1.5 T) was acquired on a stratified subsample (n = 477) that included four groups defined by cognitive status relative to the scan date: subjects without dementia (n = 347), subjects identified as demented 2–3 years before brain scanning (n = 30), at the time of scanning (n = 58), and 3–5 years after scanning (n = 42). Volumes of the striatum, including the accumbens, putamen, and caudate nucleus were automatically estimated from T1 MR images. Global cognitive function was measured with the cognitive ability screening instrument (CASI), at four examinations spanning an 8-year interval. Trajectories of cognitive decline were estimated for each quartile of striatal volume using mixed models, controlling for demographic variables, measures of cerebro-vascular damage, global brain atrophy, and hippocampal volume. Diagnosis of dementia before, during, and after brain scanning was associated with smaller volumes of n. accumbens and putamen, but not with caudate nucleus volume. Subjects in the lowest quartile of n. accumbens volume, both in the total sample and in the subjects not diagnosed with dementia during the study, had a significantly ($p < 0.0001$) steeper decline in cognitive performance compared with those in the highest quartile. In conclusion, volumes of the n. accumbens and putamen are closely associated with the occurrence of dementia and n. accumbens volume predicts cognitive decline in older people. These associations were found independent of the magnitude of other pivotal markers of cognitive decline, i.e. cerebro-vascular damage and hippocampal volume. The present study suggests a role for the ventral striatum in the development of clinical dementia.
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Keywords: Caudate nucleus; Dementia; MRI; Nucleus accumbens; Putamen; Striatum; Ventral striatum; Volumetry

1. Introduction

The effects on cognition of degenerative changes in the medial temporal lobe have been widely studied. However, other structures atrophy with age as well and may also contribute significantly to late-life cognitive impairment. The striatum is of particular interest because it is part of two systems prone to degeneration in older people, the limbic and the frontostriatal system. The striatum, depicted in Fig. 1, is anatomically divided by the capsula interna into the caudate nucleus, putamen, and nucleus accumbens. The caudate nucleus and putamen are histologically similar and their functions are thought to be congruous with their somato-topographical connections to the neocortex. The caudate nucleus is part of circuits to the dorsolateral prefrontal cortex, lateral orbital prefrontal cortex, and posterior parietal cortex. The putamen is part of circuits with the motor cortex and the somato-sensory cortex (Utter and Basso, 2008). The nucleus accumbens, located ventroanterior, differs histologically and functionally from the caudate nucleus and putamen. Its cells have smaller dimensions and are organized into subnuclei (Brockhaus, 1942). The n. accumbens projects to, and receives input from, several

* Corresponding author. Tel.: +1 301 496 1178; fax: +1 301 496 4006
E-mail address: launerl@mail.nih.gov (L.J. Launer).

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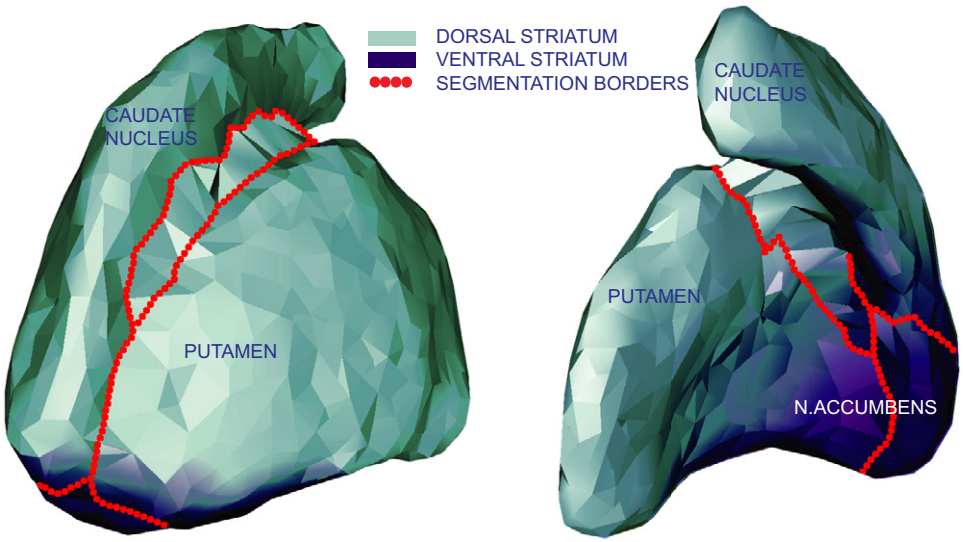

Fig. 1. Anatomical and functional division of striatumPresented is a 3D model of the striatum, based on the segmentation of those voxels that were labeled striatum in > 20% of the segmentation masks. Model was created with GAMEs (Ferrarini et al., 2007) and displayed here for the purpose of explanation.

limbic regions, including the medial temporal lobe and anterior cingulate cortex. Functionally, the ventral striatum (n. accumbens and fundi of the caudate and putamen) participates in processing limbic information and the dorsal striatum (caudate nucleus and putamen) in sensorimotor information (Voorn et al., 2004).

The role of the striatum in cognitive processes has been studied in specific basal ganglia disorders and as part of basal forebrain atrophy in Alzheimer's disease (AD). In Huntington's disease (HD), atrophy of the caudate nucleus is associated with impaired executive functioning (Peinemann et al., 2005), bicaudate ratio with impaired language learning (De Diego-Balaguer et al., 2008), and smaller volumes of the putamen with worse psychomotor function (Jurgens et al., 2008). Apart from classical basal ganglia diseases, in a recent volumetric study it was observed that AD cases had significantly decreased volumes of putamen compared with memory complainers (de Jong et al., 2008). Also, basal forebrain atrophy, including parts of the ventral striatum, was observed as long as 4.5 years before the development of clinical symptoms (Hall et al., 2008; Teipel et al., 2005). Despite the data on striatal volumes in dementia and basal ganglia diseases, little is known about the relation between striatal volume and cognitive decline in older people, varying from cognitively "normal" to impaired. Also not known is whether other predictors of cognitive impairment, such as cerebro-vascular damage, global brain atrophy, or hippocampal volume, mediate this relationship or whether striatal volumes can improve our ability to predict cognitive decline in older people.

Here we examine the relation of striatal volume to dementia and global cognitive function and decline, in the entire spectrum from cognitively healthy to demented older subjects. We account for the presence and extent of several pivotal cerebro-vascular damage parameters, hippocampal volume, and global brain atrophy. Subjects are from the well-characterized population based cohort of the Honolulu-Asia Aging Study (HAAS), who participated in a magnetic resonance imaging (MRI) substudy.

2. Methods

2.1. Subjects and study design

Study subjects were older Japanese–American men, born between 1900 and 1919, who participated in the HAAS, an expansion of the Honolulu-Heart Program. A detailed description of the HAAS can be found elsewhere (White et al., 1996). In short, subjects were examined in 1991-1993 (baseline examination four), and in three follow-up examinations in 1994-1996 (examination five), 1997-1999 (examination six), and 1999-2000 (examination seven). The study was approved by the IRB of the Kuakini Hospital and all respondents signed informed consent forms, except those who were demented, for whom an informed caretaker signed the consent.

2.1.1. Assessment of cognitive function and dementia

During each examination all subjects were evaluated on cognitive performance and dementia cases were ascertained using a multistep procedure described elsewhere (White et al., 1996). Briefly, all subjects were screened with the Cognitive Ability Screening Instrument (CASI), which ranges in score from 0-100 (Teng et al., 1994). If subjects were screened positive, they were further evaluated with neuropsychological tests based on the CERAD battery (Morris et al., 1989), a neurologic examination, a proxy interview, and a diagnostic brain scan. Diagnoses were made in a consen-