# Atrophy and aging in Parkinson's: evidence from meta-analysis, patient and population samples

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## Introduction:

Parkinson's disease (PD) is a neurodegenerative disease affecting mainly the motor system[1]. In addition to the well-known degeneration of basal ganglia in PD, heterogeneous patterns of cortical atrophy, i.e. reduced gray matter volume (GMV), have been reported and related to non-motor symptoms (NMS), especially for older ages of onset and advanced disease progression[2-6]. While PD seems to be related to the aging process, little is known about age trajectories in patients with PD. The current study aims at (1) identifying consistent cortical areas of atrophy in PD by conducting systematic coordinate-based meta-analysis (CBMA); (2) validating CBMA results in an independent sample of PD patients; and (3) disentangling age-related from disease-related alterations by comparing PD patients and a large population-based cohort of older adults.

## Methods:

CBMA was performed using activation likelihood estimation (ALE)[7]. 43 whole brain voxel-based morphometry (VBM) studies investigating GMV differences in PD vs healthy controls (HC) or GMV changes with cognitive abilities in PD were included resulting from systematic searches in pubmed/BrainMap plus cross-references from 2004-2017. Significance of ALE maps was set at p<.05 (family-wise error corrected on cluster level). For validation of CBMA results, subjects were recruited from the University Hospital Duesseldorf (UKD) (PD: n=65, 22 f, age: 60.9 ± 9.7 yrs; HC: n=65, 29 f, age: 58.2 ± 9.1 yrs), and a sample of 1000BRAINS from the Research Center Juelich with comparable age and gender distribution was used as the population-based reference (n=831, 381 f; age: 64.6 ± 8.4 yrs)[8]. Structural data from both samples were acquired on 3T Tim-TRIO MR scanners (voxel size: 1mm3). CBMA results served as regions of interests (ROIs) in regional VBM analysis executed using the VBM8 toolbox in SPM 12 with standard settings. For each ROI, group comparisons (PD vs. HC) on GMV were conducted in the UKD sample. For each ROI, correlations of GMV with cognitive test scores (Montreal Cognitive Assessment (MoCa)[9]; Mattis Dementia Rating Scale (MDRS)[10]) were calculated in PD, and with age in all UKD and 1000BRAINS subjects. Interaction effect between disease state (PD/HC) and age was tested for the UKD sample. Results were considered as significant at p<.05.

## Results:

CBMA revealed reduced GMV in PD vs HC in left anterior cingulate cortex (aCC_L) and bilateral intraparietal sulcus (IPS_L, IPS_R). Cognitive performance was positively correlated with GMV of the right hippocampus (Hipp_R). Validating the ROIs via group comparison in the UKD sample showed lower GMV in PD for all ROIs (aCC_L p=.001; IPS_L p=.004; IPS_R p=.038; Hipp_R p=.005). Worse performance in cognitive tests correlated with GMV reduction in PD (MoCa: aCC_L p=.028, Hipp_R p=.021; MDRS: aCC_L p=.009). Age-related atrophy was found in all ROIs in the PD group (aCC_L p=.001; IPS_L p<.001; IPS_R p=.002; Hipp_R p=.001) but only in aCC_L (p=.05) in HC. However, in the large 1000BRAINS sample age-related GMV changes were significant for all ROIs (p<.001). Further, disease*age interaction was significant for all ROIs (aCC_L p< .001; IPS_L p< .001; IPS_R p=.009; Hipp_R p<.001).

## Conclusions:

In the current CBMA, we identified convergent clusters of atrophy in PD, i.e. in left aCC, bilateral IPS and right hippocampus, which could be validated in a local sample of PD patients. GMV reductions in left aCC and right hippocampus were associated with global cognitive decline in PD, supporting previous findings of cortical atrophy related to NMS[3, 4]. Importantly, age-related decreases in GMV were not only present in the PD sample but also within the 1000BRAINS cohort of HC. Thus, structural atrophy within the ROIs does not seem to be specific for PD, but also manifests during normal aging, although to a lesser extent. We showed that disease state is interacting with age, therefore we assume that PD patients might show accelerated aging as compared to HC resulting in cognitive deficits.

## Disorders of the Nervous System:

Parkinson's Disease and Movement Disorders [1]

## Imaging Methods:

Anatomical MRI

## Lifespan Development:

Aging [2]

**Keywords:**

Aging
Degenerative Disease
Meta- Analysis
Movement Disorder
Other - Voxel-based morphometry

[1|2]Indicates the priority used for review

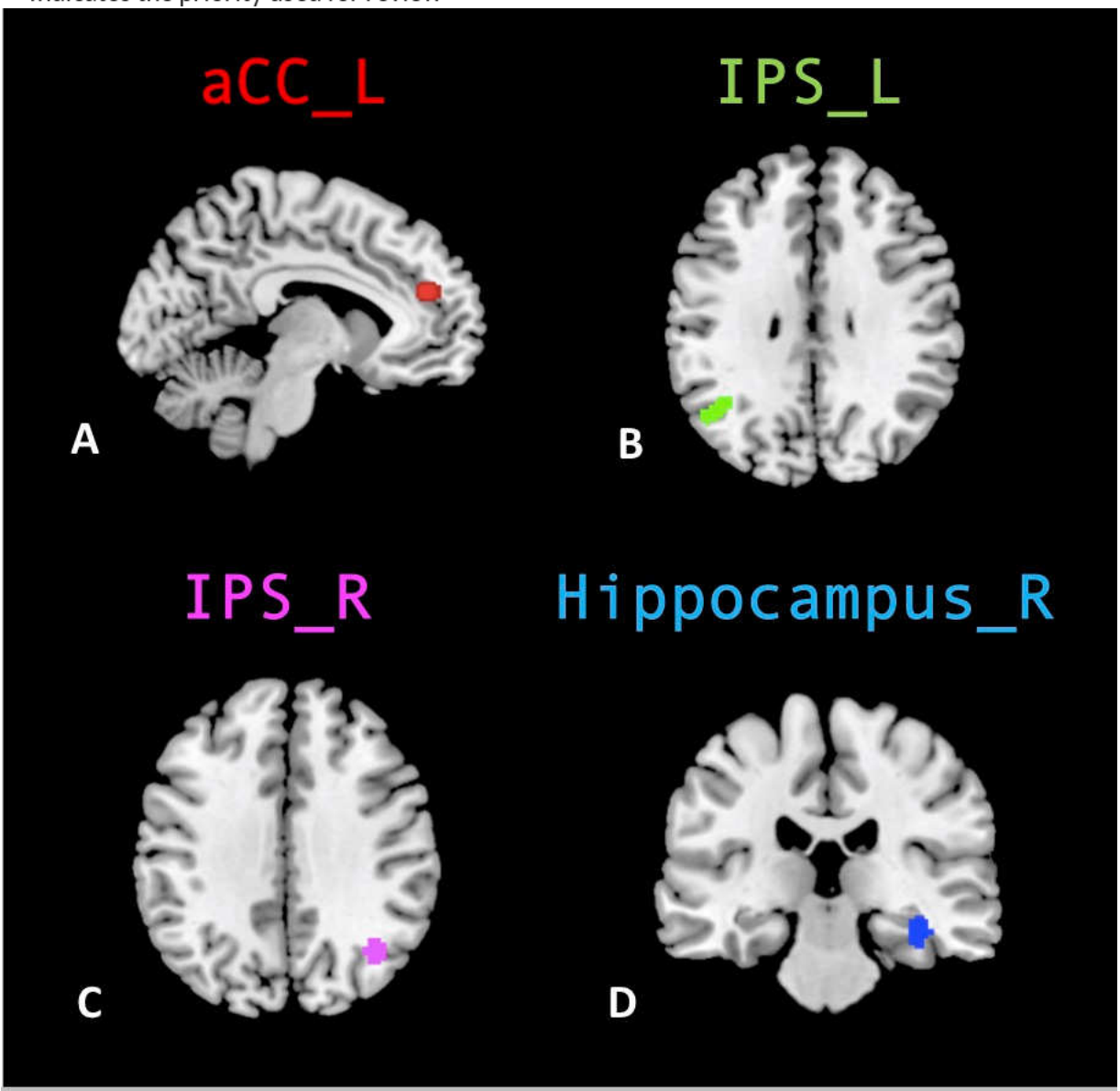


**Figure 1:** Regions of significant convergent GMV reduction in PD resulting from CBMA

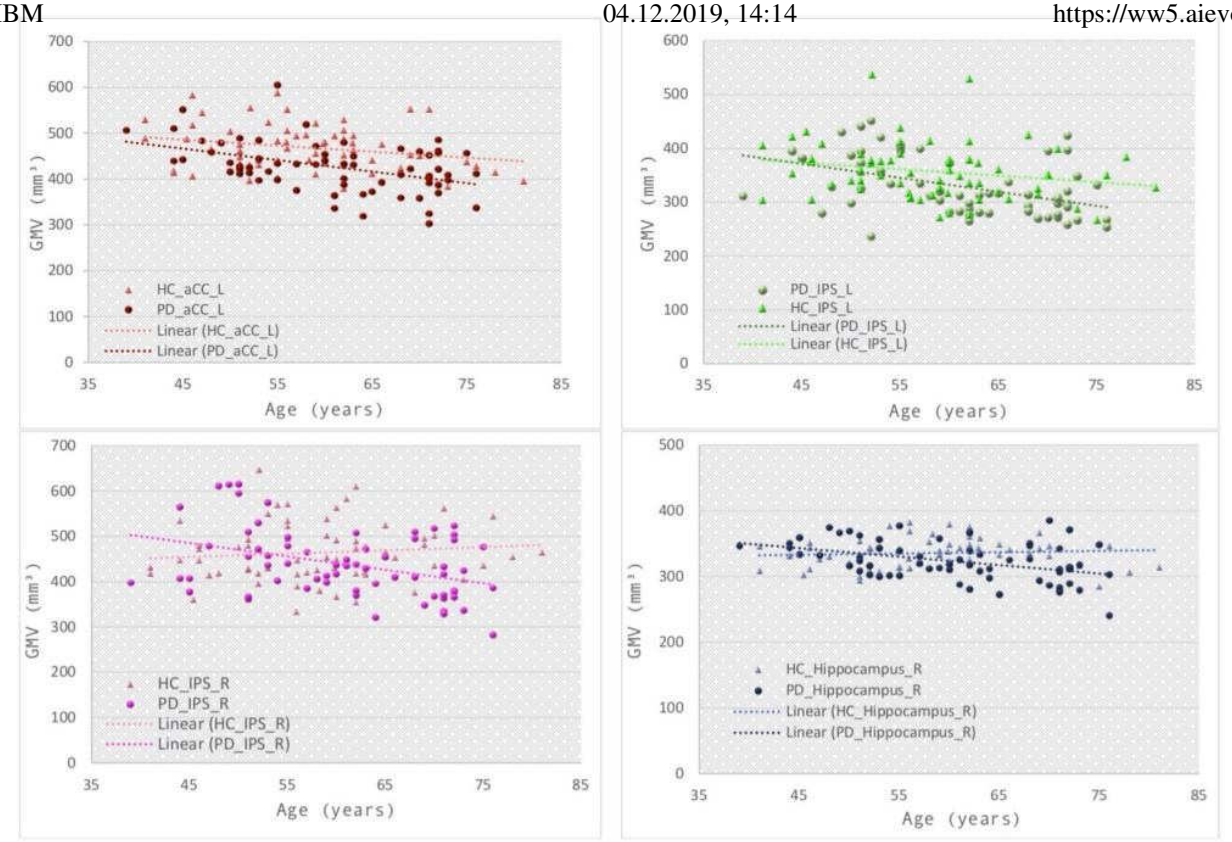


**Figure 2:** Age-related GMV reduction in PD and HC from the UKD sample

**My abstract is being submitted as a Software Demonstration.**

No

**Please indicate below if your study was a "resting state" or "task-activation" study.**

Other

**Healthy subjects only or patients (note that patient studies may also involve healthy subjects):**

Patients

**Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.**

Yes

**Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.**

Not applicable

**Please indicate which methods were used in your research:**

Structural MRI

**For human MRI, what field strength scanner do you use?**

3.0T

### Which processing packages did you use for your study?

SPM

### Provide references using author date format

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