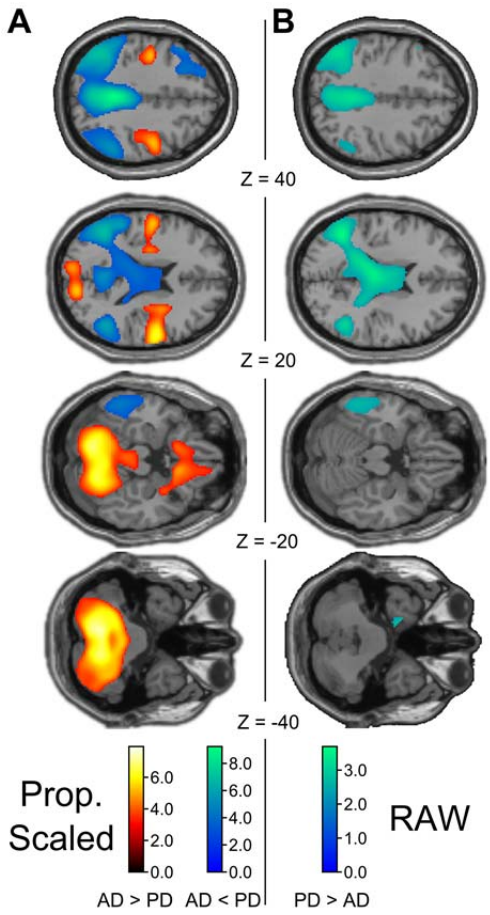
I. Pattern of the direct comparison Alzheimer vs Parkinson (AD vs PD)

Although it is not necessary for the creation of our topological map, we compared the two marginal groups directly. This direct group comparison between PD and AD revealed bilateral occipital hypometabolism in PD, involving the lingual gyrus (Supplemental Figure 1A). To evaluate and visualize the effect of the pre-processing (proportional scaling), we reanalysed the data using raw (not intensity normalized) images. In comparison to the intensity scaled data, the raw data analysis showed no differences in the cerebellum and the postcentral gyrus.

Despite the artificially induced rCMRglc differences in the t-maps of the proportionally scaled data analysis, the scaling reduced within group variance and therefore increases differentiation properties of the resulting metabolic pattern as indicated by stronger T-values (see Supplemental Figure 1).



Supplemental Figure 1: Statistical map of the direct group comparisons AD vs. PD. Direct group comparisons AD vs. PD using different pre-processing/intensity normalization procedures: **Panel A**: global proportionally scaled data **Panel B**: statistical map based on raw intensity values. Proportionally scaled data resulted in artificial spatial differences (e.g. cerebellum) evoked by differences in the normalization factor between groups. However, proportional scaling reduces within group variance and therefore increases differentiation properties of the resulting metabolic pattern (indicated by stronger T-values, see colour bar scaling above). Statistical maps were shown with a threshold of $p_{unc}<0.001$.

II. Patterns of PC_{mot} and PC_{cog} in comparison to patterns in PD as summarized by Peng et al. (2014)

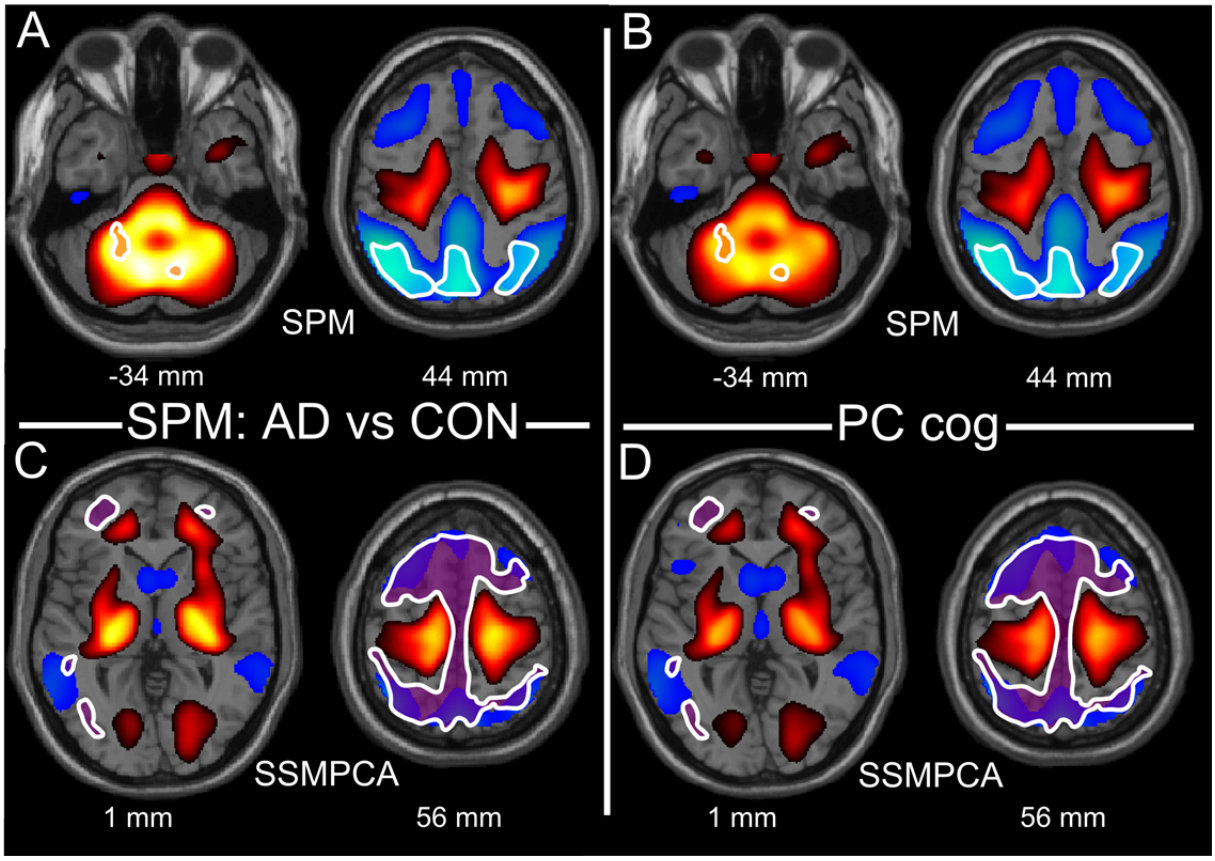
In our study, we use a voxel-based approach without predefined regions of interest and additionally included clinical scores (MMSE and UPDRS III) to detect motor and cognition related patterns. We then applied a statistical method to disentangle the individual metabolic pattern into both a cognition and a motor related component. The patterns we achieved are shown within our paper in Fig. 4.

Furthermore, to visualize similarities and differences to previously reported motor and cognitive patterns in non-demented PD patients, we have overlaid the motor and cognitive patterns by contour plots of the motor and cognition-related patterns traced from figures presented in a review by Peng et al. *(1)*. However, clinical characteristics of our patient groups (e.g. inclusion of demented patients), sample sizes and the three methods applied (SPM, SSMPCA and our reconstructed PC patterns) differ significantly and make it difficult to compare the patterns directly. We summarized the results and interpretations in the following two sections (II a. and II b.) and figures (Supplemental Figure 2a and 2b).

In conclusion, taken into account clinical and methodic differences, our results essentially resample previous findings and extend them by covering different dementia syndromes.

II a. Cognitive pattern (PC_{cog}) in relation to previous work

The cognitive pattern (PC_{cog}) is widely in accordance with previously reported cognitive related covariance patterns *(1,2)*. Anyhow, we found cerebral regions with relatively stronger rCMRglc increases in our study (cerebellum, thalamus and SMA) as compared to Peng et al. (shown in Fig. 4A and Supplemental Figure 2a). This discrepancy can be explained by the proportionally scaling preprocessing step, reducing within group variances but also causing artificial, non-pathological blobs in the visualized patterns and with the missing group references as already mentioned above (Supplemental Figure 1). This scaling effect is probably stronger in our setup, because we have focused on groups (MCI, AD, PDD, DLB) with patients suffering from relevant cognitive deficits, whereas Peng et al. only described metabolic patterns in non-demented PD patients.



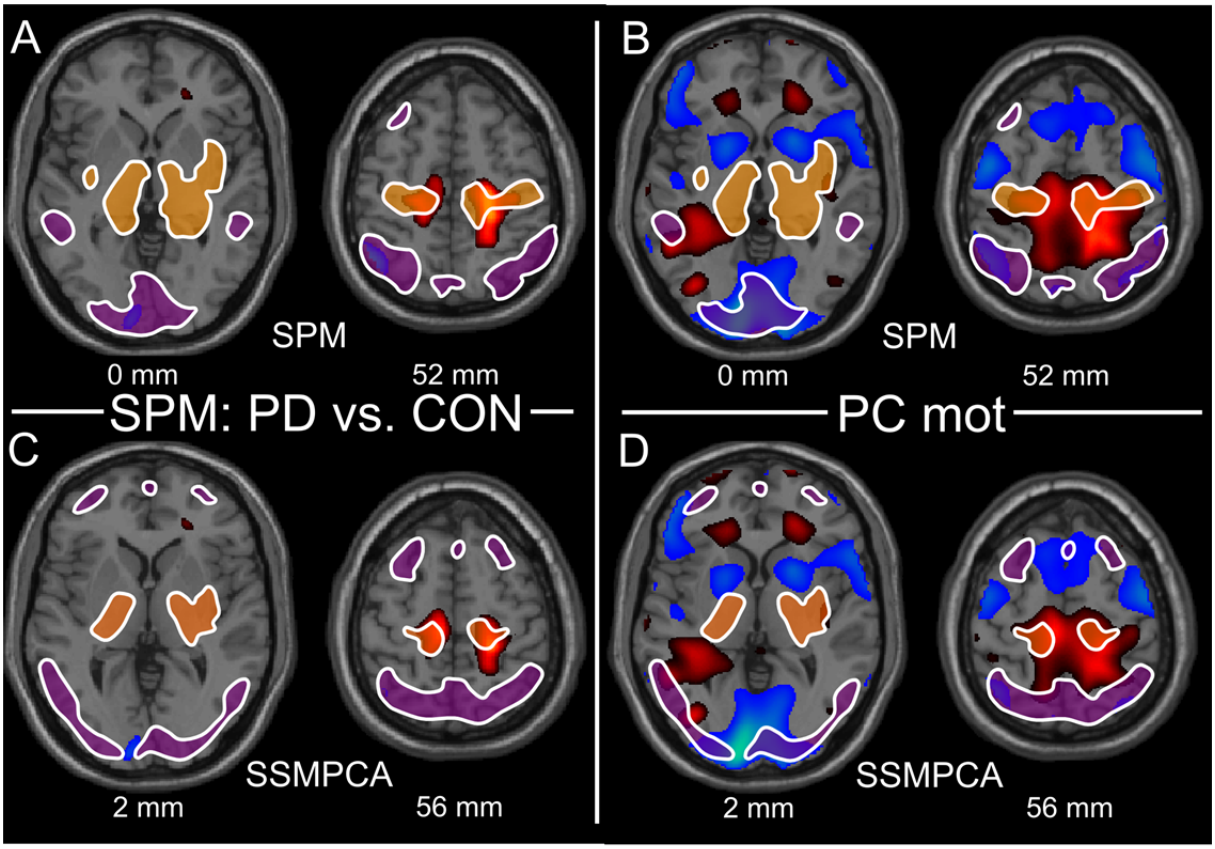
Supplemental Figure 2a: PC_{cog} pattern in the context of previous work. White contours were delineated from the correlation analysis with scores on the California verbal learning test (CVLT) as presented in a review by Peng et al. *(1)*.

Panel A, B: Brain regions with significant cognitive correlations as identified by SPM regression analysis of resting-state FDG PET scans in non-demented patients with Parkinson's disease (PD), overlaid on our dementia related pattern PC_{cog}.

Panel C, D: Parkinson's disease-related cognitive pattern (PDCP) as identified by SSMPCA spatial covariance analysis of resting-state FDG, also overlaid on our dementia related pattern SPM comparison AD vs CON (Panel C) and PC_{cog} (Panel D).

II b. Motor pattern (PC_{mot}) in relation to previous work

The PC_{mot} pattern in our study is widely comparable with the PD related patterns observed in previous studies *(1,3)*. However, we did not find the thalamic region as much involved in our reconstructed pattern and not in our PD comparison with the control group (shown in Fig. 4B and Supplemental Figure 2a: PCcog pattern in the context of previous work 2b). One important reason for this divergence might be the non-existing reference group in our PC_{mot} pattern, delineating only a direction in the image space without the group references (PD and CON) and the orthogonality assumption introduced by the PCA decomposition, which attributed thalamic changes to the PC_{cog} pattern (Supplemental Figure 2a: PCcog pattern in the context of previous work 2b). Furthermore, clinical motor disturbances and group sizes differ in both studies which can explain the differences in the SPM based results.



Suppl. Fig 2b: PC_{mot} pattern in the context of previous work. White contours were delineated from the PD vs. CON group comparisons as presented in a review article by Peng et al. *(1)*.

Panel A, B: Brain regions with significant metabolic abnormalities as identified by the SPM analysis of resting-state FDG PET scans in patients with Parkinson's disease (PD) and controls (CON), overlaid onto our motor pattern (PC_{mot}).

Panel C, D: Parkinson's disease-related pattern (PDRP) identified by SSMPCA spatial covariance analysis of resting-state FDG PET scans in patients with Parkinson's disease (PD) and controls (CON) overlaid onto our SPM comparison PD vs CON (Panel C) and our motor pattern PC_{mot} (Panel D).

References:

1. Peng S, Eidelberg D, Ma Y. Brain network markers of abnormal cerebral glucose metabolism and blood flow in Parkinson's disease. *Neurosci Bull*. 2014;30:823-837.

2. Huang C, Mattis P, Tang C, Perrine K, Carbon M, Eidelberg D. Metabolic brain networks associated with cognitive function in Parkinson's disease. *NeuroImage*. 2007;34:714-723.

3. Ma Y, Tang C, Spetsieris PG, Dhawan V, Eidelberg D. Abnormal metabolic network activity in Parkinson's disease: test-retest reproducibility. *J Cereb Blood Flow Metab*. 2007;27:597-605.