# Table S8 *Brain PET*

**Associations between putative brain PET biomarkers and clinical measures of disease severity, in longitudinal studies included in the systemic review of biomarkers for disease progression in Alzheimer’s disease**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | |  |  | **Association of change in ligand binding with change in:** | | |
| **PET ligand** | **Region in which change in binding measured** | **Reference**  **(first author, year)** | **n at baseline** | **Number of scans** | **Time between first and last scan (years)** | **MMSE** | **ADAS-cog** | **CDR-SB** |
| FDG | Frontal cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Mielke, 19942 | 25 | 2 | 1.1 | R = 0.4◘ |  |  |
| Occipital cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Mielke, 19942 | 25 | 2 | 1.1 | R = 0.44\* |  |  |
| Parietal cortex | Engler, 20061 | 16 | 2 | 1.9 | R = 0.59\* |  |  |
| Temporal cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Temporoparietal cortex | Mielke, 19942 | 25 | 2 | 1.1 | R = 0.49\* |  |  |
| Striatum | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Subcortical white matter | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Cerebellum cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Pons | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Entire cerebrum | Mielke, 19942 | 25 | 2 | 1.1 | R = 0.38 |  |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | |  |  | **Association of change in ligand binding with change in:** | | |
| **PET ligand** | **Region in which change in binding measured** | **Reference**  **(first author, year)** | **n at baseline** | **Number of scans** | **Time between first and last scan (years)** | **MMSE** | **ADAS-cog** | **CDR-SB** |
| FDG  (continued) | Left cingulate | Mega, 20053 | 12 | 2 | 0.2 | R = 0.70\* |  |  |
| Metabolic rate† | Mielke, 19942 | 25 | 2 | 1.1 | R = 0.28 |  |  |
| PET score‡ | Herholz, 20114 | 35 | 4 | 2.0 |  |  |  |
| Statistical region-of-interest§ | Chen, 20105 | 69 | 2 | 1.0 | R? = 0.23◘ | R? = 0.59 | R? = 0.25\* |
| PiB | Frontal cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Occipital cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Parietal cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Temporal cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Striatum | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Subcortical white matter | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Cerebellum cortex | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Pons | Engler, 20061 | 16 | 2 | 1.9 | NSA |  |  |
| Neocortical Aβ burden (\bar{x} \!\,)• | Villemagne, 20116 | 35 | 3 | 3.3 | NSA |  |  |

**Key**

† The ‘metabolic rate’ equals the mean regional cerebral glucose metabolism in regions typically affected by Alzheimer’s disease (temporoparietal and frontal association cortex) divided by the mean regional cerebral glucose metabolism in unaffected regions (cerebellum, brainstem, lentiform nucleus, primary visual and sensorimotor cortex).

‡ PET score = log2 [(ADtsum/11089) + 1]. AD t-sum indicates the severity of the metabolic decrease in brain areas that are typically affected by Alzheimer’s disease (multimodal association cortices mostly located in the temporal and parietal lobes), including an adjustment for age.

§ This study examined the change in the regional cerebral metabolic rate for glucose in a pre-defined statistical region-of-interest. This included voxels consistently associated with decline as determined by the application of statistical parametric mapping (SPM) to a training data set.

• Neocortial Aβ burden was expressed as the average standardised uptake values (SUVR) of the area-weighted mean (i.e. averaged across both hemispheres) of frontal, superior parietal, lateral temporal, lateral occipital, and anterior and posterior cingulated regions.

\bar{x} \!\, Where this symbol is show then the value given is the average of left and right hemispheric structures. If not shown then it is unclear from the text whether the value represents an average or a total (left and right hemispheric structures combined) value.

**PET ligands**

FDG [18F]-2-fluoro-2-deoxyglucose

PiB [11C]Pittsburgh compound B

Superscript numbers correspond to the list of references

**Correlations**

Pearson’s correlation coefficient R

Correlation coefficient unspecified R?

NSA No significant association No symbol: P not significant, but actual value not stated

POS Significant positive association ◘ P ≥ 0.05

NEG Significant negative association (\*) P significant, but actual value not stated

SIG Significant association direction not stated \* P < 0.05

\*\* P < 0.01

\*\*\* P < 0.001

**Clinical Rating Scales**

ADAS-cog Alzheimer’s Disease Assessment Scale – cognitive subscale7

CDR-SB The Washington University Clinical Dementia Rating Sum-of-Boxes score8

MMSE Mini-Mental State Examination9

**References**

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