Atrophy of the Posterior Subiculum Is Associated with Memory Impairment, Tau- and Ab Pathology in Non-Demented Individuals
Hippocampal atrophy is key feature in many neurodegenerative diseases

However several diseases display volume decline in the same range
Shape analysis of the hippocampus. A step to recognize different diseases?

AD

BvFTD

SD
Selective measurement of hippocampal subfields is another approach.

Hippocampal subfield volumetry in mild cognitive impairment, Alzheimer's disease and semantic dementia

Renaud La Joie, Audrey Perrotin, Vincent de La Sayette, Stéphanie Egret, Loïc Doeuvre, Serge Belliard, Francis Eustache, Béatrice Desgranges, Gaël Chételat
Subfields measurements is usually not considering anterior vs. posterior volumetric differences within one field (which we may find in shape analysis).
But the anterior & posterior part of the same subfield may be parts of different brain networks.
Deficits in episodic memory & scene processing which are symptoms associated with Alzheimer’s disease is potentially more dependent on brain systems connected to the posterior hippocampus.
Atrophy of the Posterior Subiculum Is Associated with Memory Impairment, Tau- and Aβ Pathology in Non-demented Individuals

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Subdivision of the subiculum

From Freesufer 5.3
Participants from The Swedish Biofinder Study

http://biofinder.se/

**TABLE 1** | Demographical data.

<table>
<thead>
<tr>
<th></th>
<th>ALL</th>
<th>CN</th>
<th>SCD</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>656</td>
<td>302</td>
<td>183</td>
<td>171</td>
</tr>
<tr>
<td>F/M</td>
<td>352 (306)</td>
<td>182/120</td>
<td>100/83</td>
<td>102/69</td>
</tr>
<tr>
<td>Age</td>
<td>72.2 (5.5)</td>
<td>73.7 (5.0)</td>
<td>70.5 (5.7)*</td>
<td>71.3 (5.3)*</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.4 (1.6)</td>
<td>29 (0.9)</td>
<td>28.5 (1.4)*</td>
<td>27 (1.8)**</td>
</tr>
<tr>
<td>Memory score, errors</td>
<td>3.6 (2.8)</td>
<td>2 (2)</td>
<td>3.4 (2)*</td>
<td>7 (2)**</td>
</tr>
<tr>
<td>CSF Aβ42</td>
<td>618 (216)</td>
<td>667 (102)</td>
<td>630 (222)</td>
<td>510 (218)**</td>
</tr>
<tr>
<td>CSF P-tau</td>
<td>58 (24)</td>
<td>54 (19)</td>
<td>57 (25)</td>
<td>67 (29)**</td>
</tr>
<tr>
<td>Left HC</td>
<td>3753 (612)</td>
<td>3884 (520)</td>
<td>3826 (595)</td>
<td>3441 (674)**</td>
</tr>
<tr>
<td>Right HC</td>
<td>3815 (604)</td>
<td>3929 (548)</td>
<td>3893 (679)</td>
<td>3546 (647)**</td>
</tr>
<tr>
<td>Aβ42 −/+</td>
<td>398/258</td>
<td>220/62</td>
<td>114/69</td>
<td>64/107</td>
</tr>
<tr>
<td>P-tau−/+</td>
<td>324/332</td>
<td>160/142</td>
<td>101/82</td>
<td>63/108</td>
</tr>
<tr>
<td>APOE4</td>
<td>401/252</td>
<td>216/55</td>
<td>108/73</td>
<td>77/94</td>
</tr>
</tbody>
</table>

SCD was defined as being referred to a memory clinic due to cognitive complaints but not showing signs of objective cognitive impairment in the neuropsychological battery.
CSF analysis

CSF followed the Alzheimer’s Association Flow Chart for CSF biomarkers.

CSF total tau (T-tau), and Aβ42 were analyzed by EUROIMMUN (Ei) enzyme-linked immunosorbent assays (ELISAs) (EUROIMMUN AG, Lübeck, Germany).

Tau phosphorylated at Thr181 (P-tau) were analyzed with INNOTEST (IT) ELISAs (Fujirebio Europe, Ghent, Belgium).
MRI

T1-weighted images were obtained on a single 3 tesla MR scanner (Trio, Siemens, Germany). Volumetric analysis was performed on T1-weighted 3D MP-RAGE image.

Hippocampal subfield segmentation in Freesufer 5.3 (http://surfer.nmr.mgh.harvard.edu/)
n=398 high- compared with n=258 low levels of $\text{A}\beta_{42}$ in cerebral spinal fluid (CSF)

Cutoff $\leq 527$ nanogram/liter (ng/l)

(left) (right)
Correlation with phosphor tau (p-tau) in CSF in all included subjects n=656
Subjective cognitive decline n=183

Cutoff ≤52 ng/l
Mild cognitive impairment n=171
Delayed recall of 10-items (ADAS-cog)

All participants n=656

Control & SCD n=473
In conclusion, AD pathologies and mild memory dysfunction are mainly associated with atrophy of the posterior parts of the subicular subfields of the hippocampus in non-demented individuals.

In light of these findings we suggest that segmentation of the HC subfields may benefit from considering the volume of the different anterior-posterior subsections of each subfield.
Thickness correlation with posterior vs. anterior subiculum (left hemisphere) 302 ctl
H70 Left hemisphere n=630 non-demented participants, age of 70-years of age.

H70-study
Resting-state network dysfunction in Alzheimer’s disease: A systematic review and meta-analysis

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BA23 och 31

Scatterplot of multiple variables against lh_BA23_31_ThickAvg
L_total_subiculum_1_2_3_4
L_total_subiculum_7_8_9_10
1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0
lh_BA23_31_ThickAvg
100 150 200 250 300 350 400 450 500

Scatterplot of multiple variables against rh_BA23_31_ThickAvg
R_total_subiculum_1_2_3_4
R_total_subiculum_7_8_9_10
1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8
rh_BA23_31_ThickAvg
50 100 150 200 250 300 350 400 450 500

H70 all
Decline in MMSE baseline – 4 year in 100 SCD
Thanks to:

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In particularly to:

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and Svenska Hjärnfonden.
15 patients semantic dementia – the anterior 40%