MRI Volumetric Studies in Alcoholism and Psychopathy: A Focus to the Medial Temporal Lobe Structures

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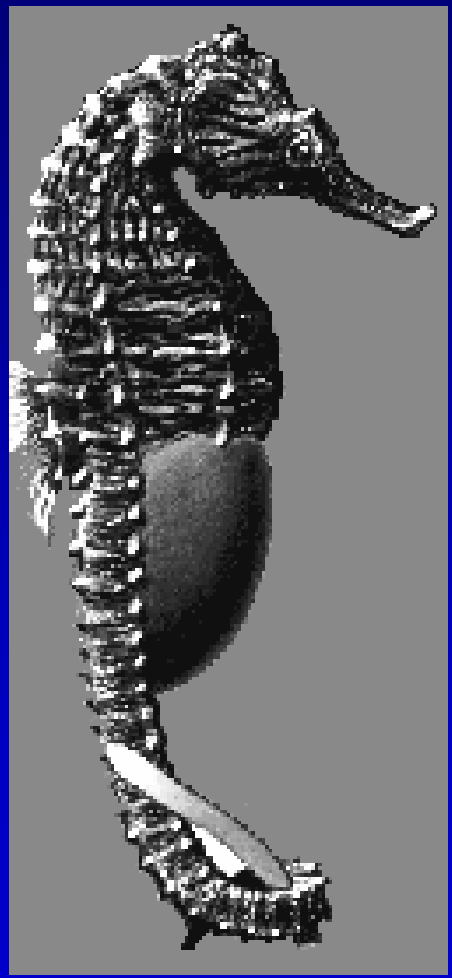
Motivation for MRI Volumetry of Hippocampus in Alcoholics

- Hippocampal structures involved in learning, memory and conditioning

Hippocampal Atrophy

- Alzheimer’s disease
- Frontotemporal dementia
- Epilepsy
- Schizophrenia

Hippocampus

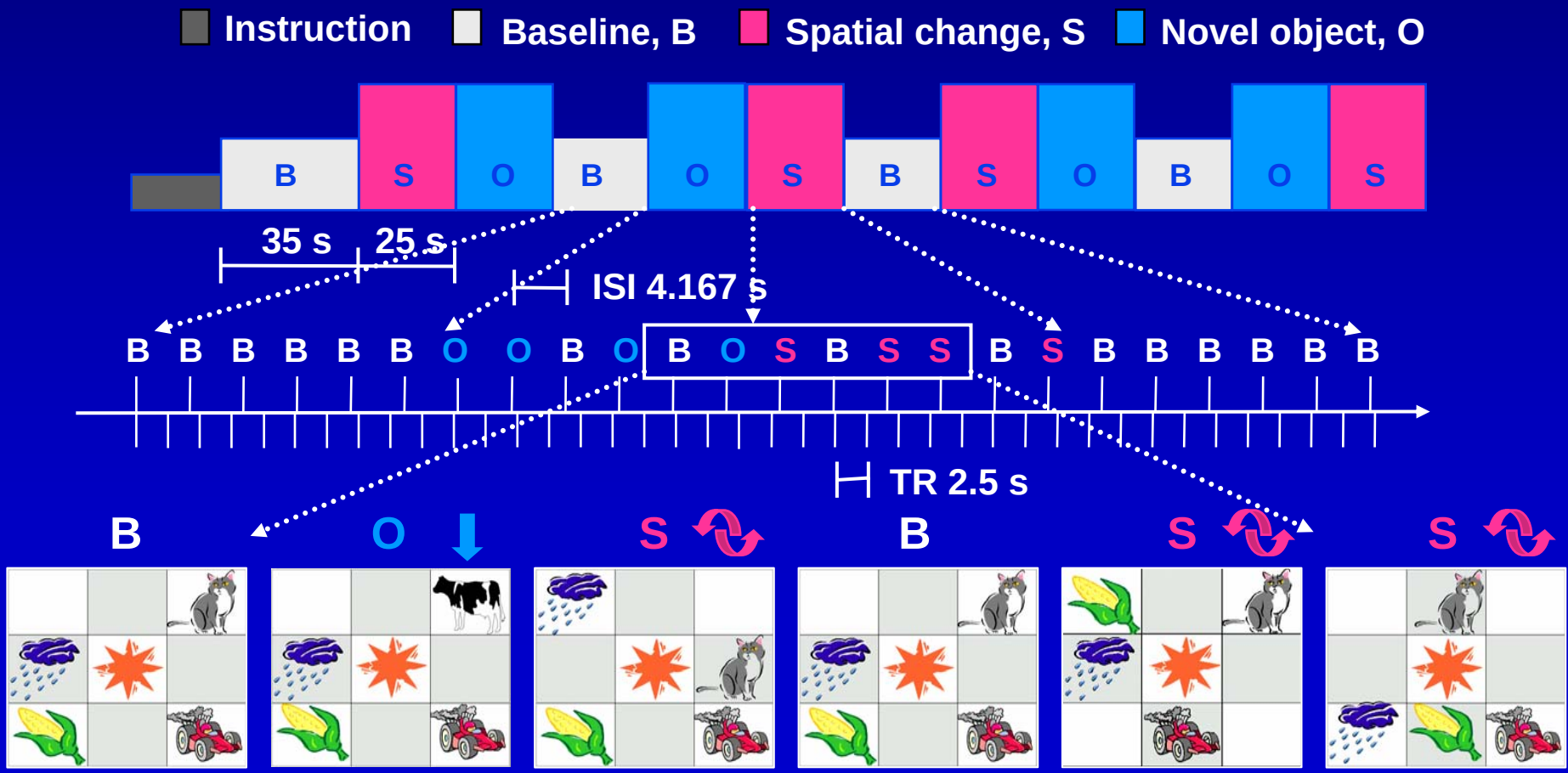


Hippocampus

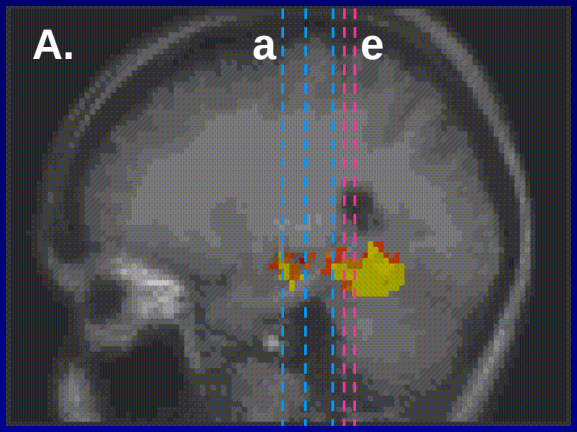
- Usually less than 4 cm longitudinal axis
- Anterior and posterior parts of the hippocampus may have different functions and connections inside the medial temporal lobe and to other brain regions

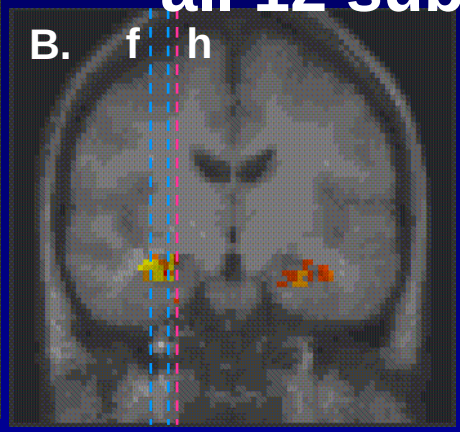
The Visuospatial Activation Task

- Baseline (B): 5 familiar objects in the same spatial order
- Spatial change (S): familiar objects in new spatial arrangements
- Novel object (O): a novel object among the 4 familiar objects
- Instruction: carefully follow the pictures and their arrangement



The MTL Activation Areas, data averaged over all 12 subjects



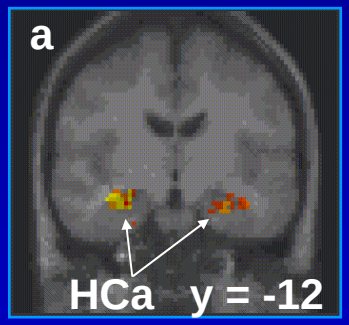


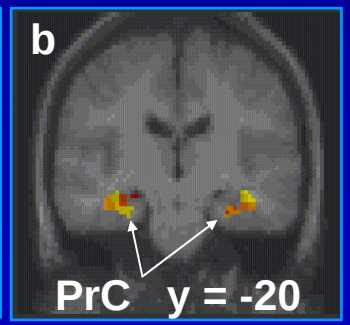
The sagittal image (A): slice positions of the coronal views (a-e).

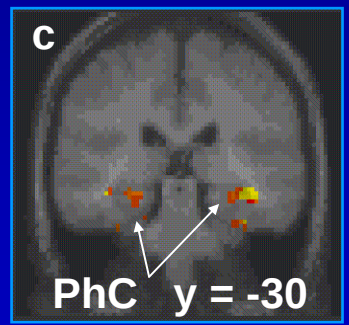
The coronal image (B): slice positions of the sagittal views (f-h).

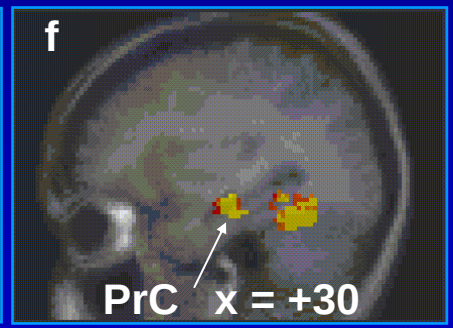
x- and y-letters: the corresponding Talairach coordinate values

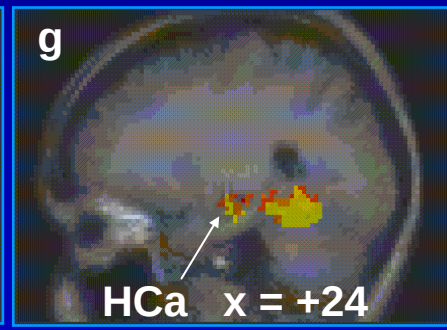
Novel Object *vs* Baseline:



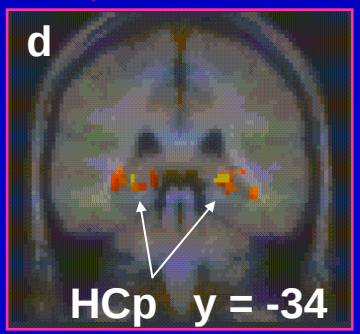


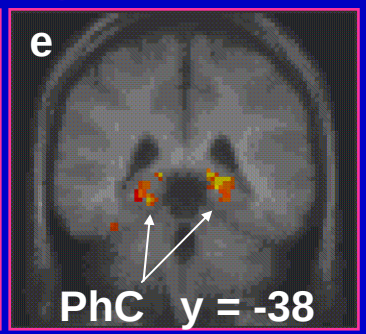


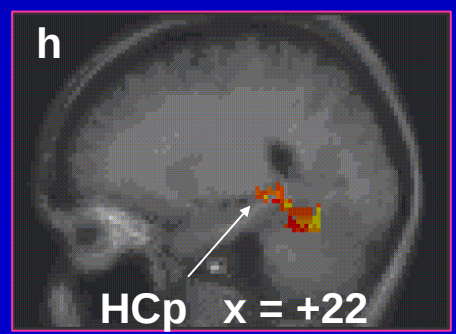




Spatial Change *vs* Baseline







Pihlajamäki et al., *resubmitted*

Recognition of novel object *vs* new spatial arrangements, Conclusions II

- A functional dissociation also exists in the human between
  - PrC encoding of object novelty and HC encoding of new spatial arrangements.

- An anterior (O) –> posterior (S) activation gradient was found inside the HC and PhC
- These findings expand prior knowledge about the distinct roles of human MTL structures

Pihlajamäki et al., Recognition of novel objects and new spatial arrangements of objects differentially activates the MTL subareas in humans, *resubmitted*

Motivation

- One paper at the time from hippocampal volumes in type 1 alcoholism (Sullivan et al. 1995)
- No previous volumetric data from hippocampus and/or type 2 alcoholism

Primary Approach

- To compare the hippocampal volumes of type 1 alcoholics, type 2 alcoholics and controls

Type 1 Alcoholic Subjects

- The type 1 alcoholics were recruited for the study from a local rehabilitation center for alcoholics.
- All the type 1 subjects fulfilled the ICD-10 and the DSM-IV criteria for alcohol abuse or dependence, and met the concept of late-onset type 1 alcoholism as proposed by Cloninger.
- None had committed violent criminal offences or were considered to have violent tendencies. None had signs of antisocial personality disorder according to items of the Structured Clinical Interview for the DSM-IV.

Type 2 Alcoholic Subjects

- The type 2 antisocial alcoholics were recruited for the study from a forensic psychiatric evaluation.
- Fulfilled the ICD-10 and DSM-IV criteria for alcohol abuse or dependence, met the concept of early-onset Cloninger type 2 alcoholism.
- Each subject had a diagnosis of antisocial personality disorder.

Type 2 Alcoholics

Nr.	Age	Being charged for:	Previous violent offences include:
1.	20	Attempted manslaughter	Assault (several)
2.	22	Assault	Attempted arson
3.	23	Murder (×2)	Aggravated assault
4.	24	Aggravated assault (×2)	Aggravated assault, assault towards an officer (×3), assault (×6)
5.	24	Assisting manslaughter	-
6.	25	Attempted murder	-
7.	25	Manslaughter	Armed robbery, aggravated assault (×2), assault towards an officer, assault
8.	25	Manslaughter	Arson
9.	26	Aggravated assault	-
10.	27	Attempted manslaughter	Attempted manslaughter, aggravated assault
11.	30	Armed robbery	Attempted manslaughter, assault (several)
12.	32	Armed robbery	Manslaughter, attempted manslaughter, assault (×3)
13.	33	Armerd robbery, assault	Manslaughter (×2), assault (×2)
14.	33	Murder	Aggravated assault, rape (×2)
15.	33	Manslaughter	Manslaughter, arson, armed robbery (×2)
16.	36	Manslaughter, aggravated assault	Aggravated assault, assault towards an officer (×2), assault
17.	38	Manslaughter (×2)	Manslaughter, aggravated assault, assault (×3), assault towards an officer
18.	45	Armed robbery (×2)	Armed robbery, assault towads an officer, assault (×3)
19.	47	Manslaughter	Attempted manslaughter, assault (×3)

MRI Acquisition

- 1.0 T Impact, or with 1.5 T Magnetom or Vision (Siemens; Erlangen, Germany) using a standard head coil and a tilted T1-weighted coronal 3D gradient echo sequence (MPRAGE: TR 10 ms, TE 4 ms, TI 250 ms, flip angle 12°, FOV 250 mm, matrix 256 × 192, 1 acquisition).

Hippocampal Volumetry

- Tracing of the hippocampi was done by a single tracer, blinded to the clinical data of the study subjects.
- The volumes were manually traced from contiguous coronal 2.0 mm thick images oriented perpendicular to the intercommissural line by using a custom made software for a standard Siemens' work console.

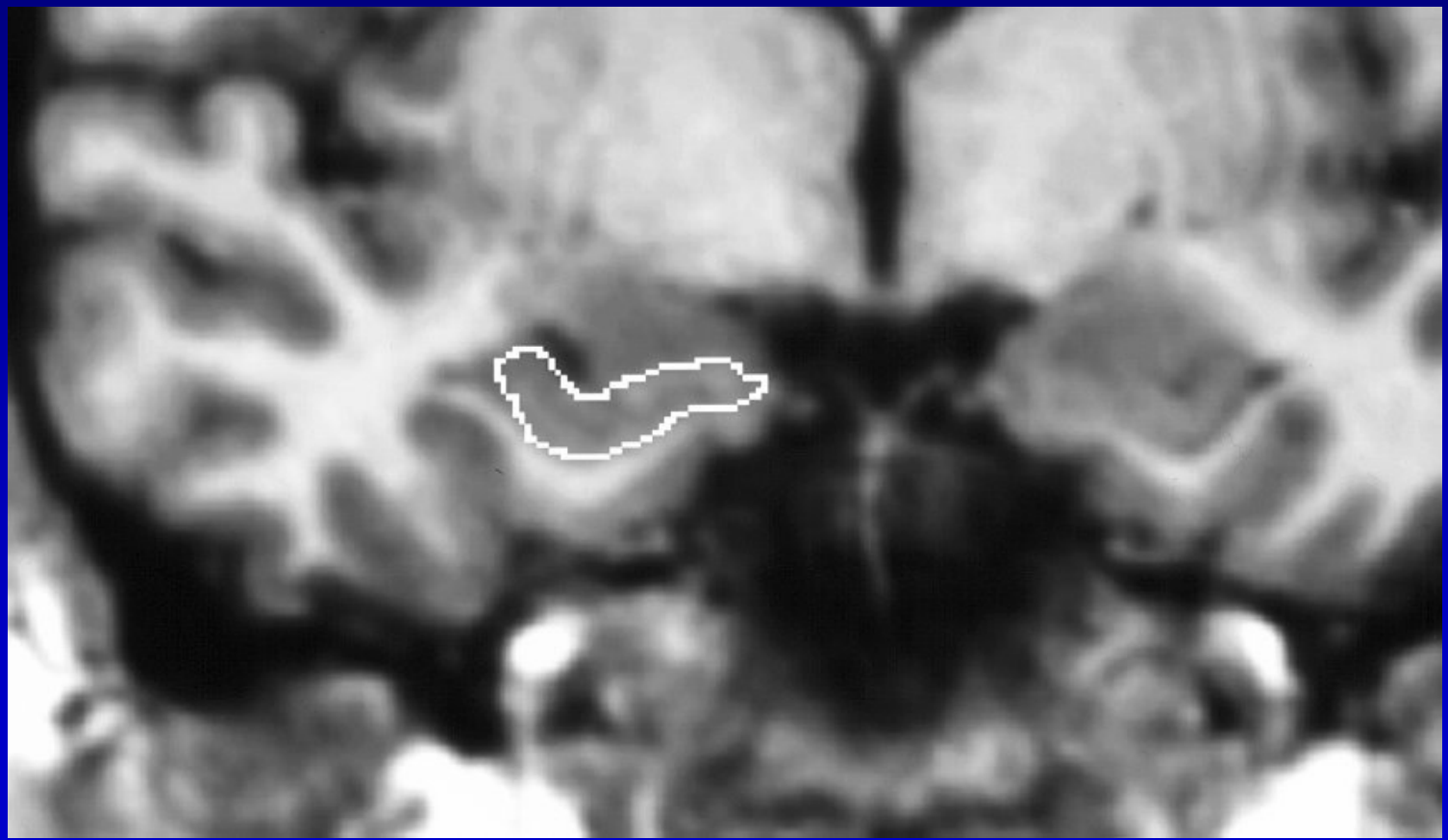
Hippocampal Volumetry

- The hippocampus included the dentate gyrus, the hippocampus proper and the subicular complex.
- The rostral end of the hippocampus, as it first appears below the amygdala, was the anatomical starting point, and the last section was the one in which the crura of the fornices depart from the lateral wall of the lateral ventricles.

Normalization of Hippocampal Volumes with the Intracranial Area

- The intracranial area on a coronal section at the level of the anterior commissure was measured and used for normalization of the volumetric data. For data presentation purposes, the volumes reported herein were normalized to the intracranial area according to the formula: (volume / intracranial area) × 1000

An Example of Lineation of Anterior Hippocampus from a 2 mm thick coronal Slice

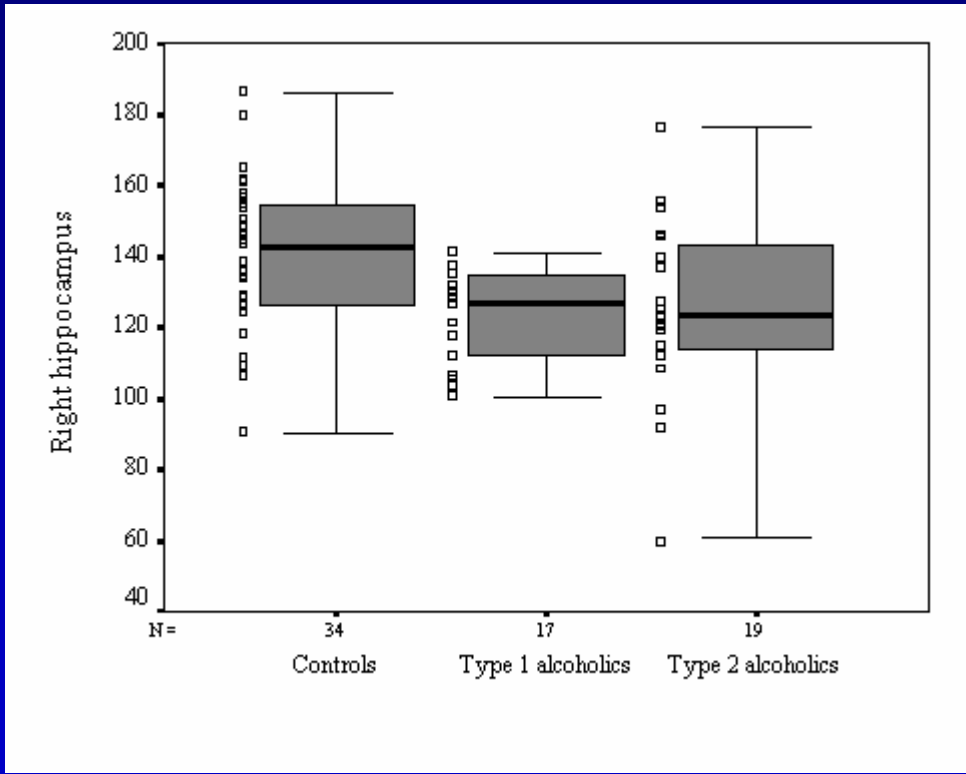


Laakso et al. 2001

Results

- Compared to the controls, the right, but not left hippocampi were significantly smaller in both alcoholic groups.

Individual Normalized Volumes of Right Hippocampi



Laakso et al. 2000

Demographics and the Normalized Hippocampal Volumes

	Controls	Type 1 alcoholism	Type 2 alcoholism
Number	34	17	19
Age (range)	35 ± 12 (22-70)	48 ± 5* (38-58)	30 ± 8 (20-47)
Education	14 ± 2	13 ± 4	9.2 ± 1.4*
WAIS-R IQ	NE	111.0 ± 11.8	91.6 ± 13.2
WAIS-R IQ_{lan}	NE	111.3 ± 10.0	91.6 ± 11.9
WAIS-R IQ_{man}	NE	110.6 ± 12.3	92.8 ± 14.2
Age of onset	-	34 ±6	16 ± 2
HC Right	139 ± 21	122 ± 13 (-11.6%)*	125 ± 26 (-10.2%)*
HC Left	132 ± 19	124 ± 16 (-6.2%)	124 ± 20 (-6.2%)

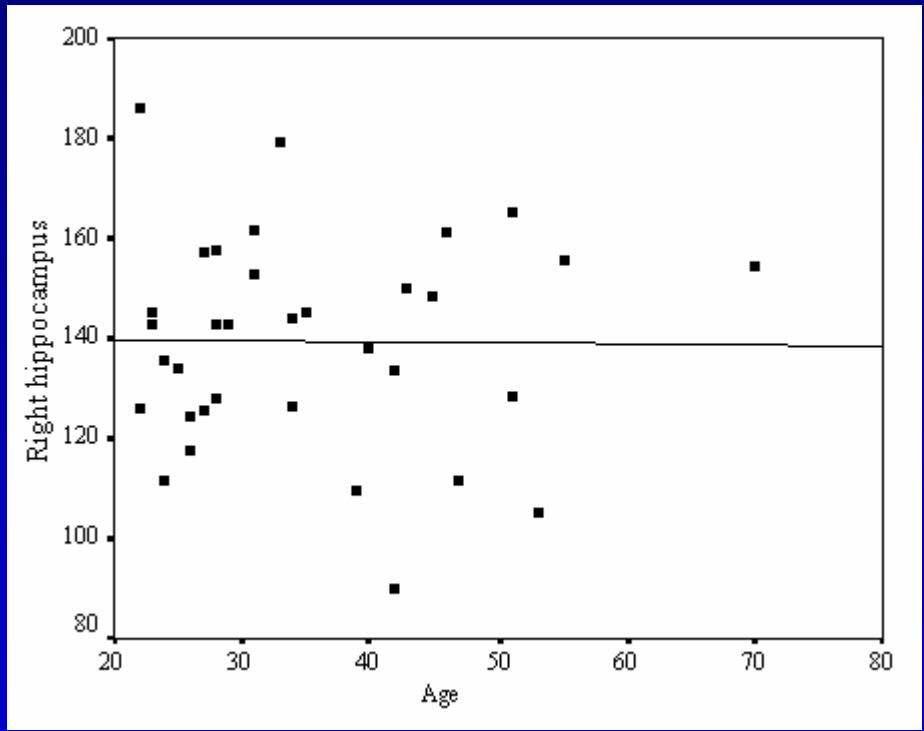
Laakso et al. 2000

* P<0.05: groups significantly different from the controls in the post hoc analysis. In WAIS-R performance, the two alcoholic groups differed significantly from each other (P<0.001 for all scores)

Results

- No correlation between the hippocampal volumes with age in the control subjects
- Tendency towards decreased volumes with aging and also with the duration of alcoholism in the type 1 alcoholic subjects.

Age versus Right Hippocampal Volume in Controls

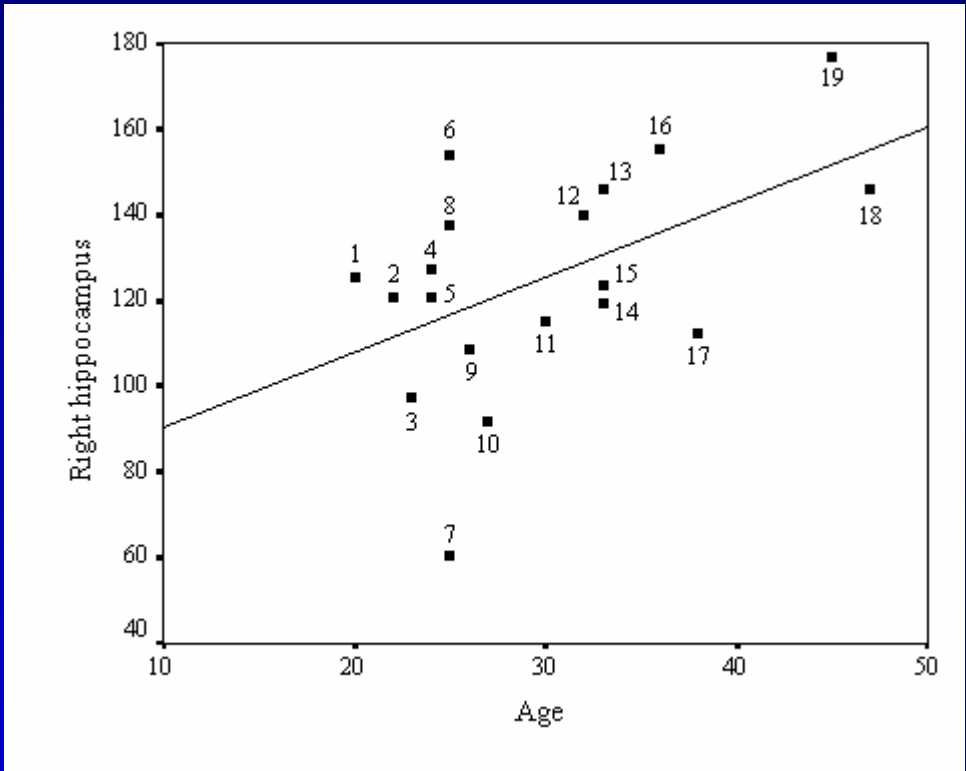


Laakso et al. 2000

Results: Type 2 Alcoholism

- Significant positive correlation between the right hippocampal volume and age in the type 2 alcoholism ($r=0.51$, $p<0.05$).

Age versus Right Hippocampal Volume in Type 2 Alcoholism



Laakso et al. 2000

Positive Correlation between the Right Hippocampal Volume and Age in the Type 2 Alcoholism: Interpretation

- Unlikely caused by plasticity changes: the hippocampi do not ”grow” in type 2 alcoholism
- The finding may be related with the cross-sectional study design
- Younger type 2 subjects may represent a genetically or developmentally different entity or a more severe psychopathology being ”natural born killers”

Secondary Approach

- More detailed morphometric analysis and correlation with PCL-R scores in type 2 alcoholics

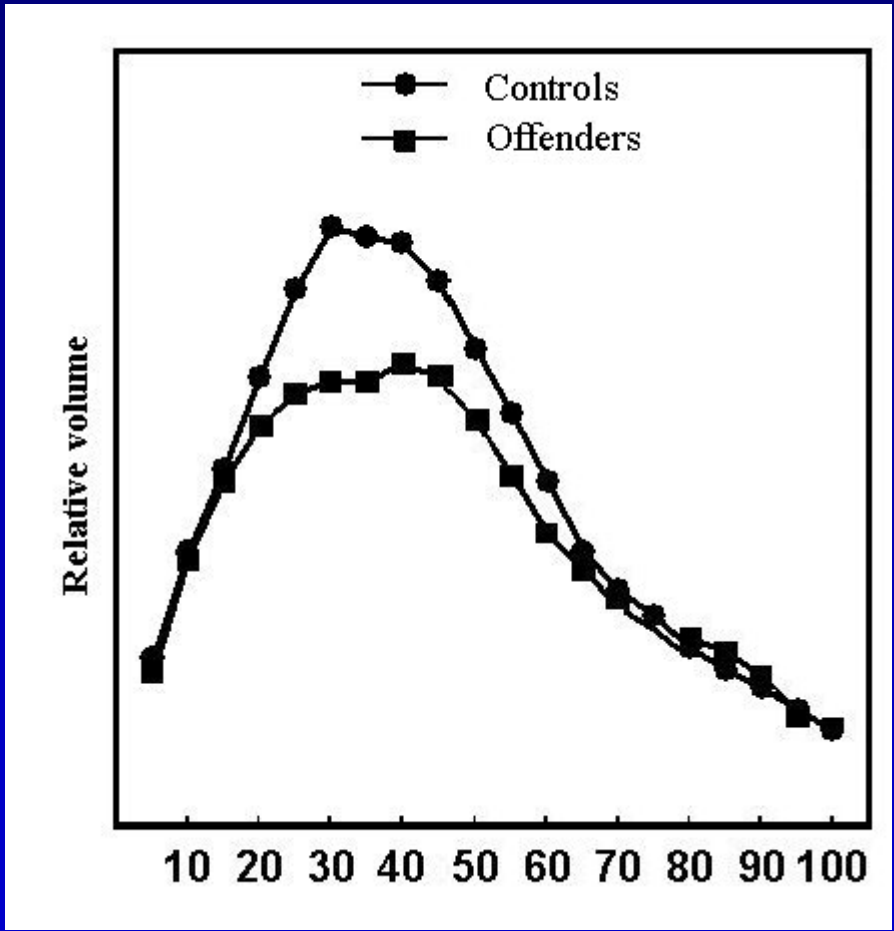
Grading of the Degree of Psychopathy

- The PCL-R is a 20-item measure for the clinical features of prototypical psychopathy based on biological trait theories and behavioral psychology, which indicates interpersonal, affective and behavioral components
- The PCL-R is particularly apt for correlation studies, as it is not only categorical in nature, but in addition provides a dimensional score to the extent of which a given individual is judged to match the prototypical psychopath.

Hippocampal Profiles

- To evaluate the distribution of volume loss within the hippocampi, sagittal profiles of the hippocampi were created.
- Each profile was formed from each measured slice, displayed on the *y*-axis, and the length (number of slices) on the *x*-axis.
- Because of slightly different number of slices between individuals, the volumes were transformed into standard space for the purposes of the statistical analysis.
- The volume profile was computed by linear interpolation for a relative length of 100%, and the subvolumes were computed for 5% intervals, i.e. the number of slices was transformed to 20 for each subject

Right Hippocampal Profiles in Controls and Offenders



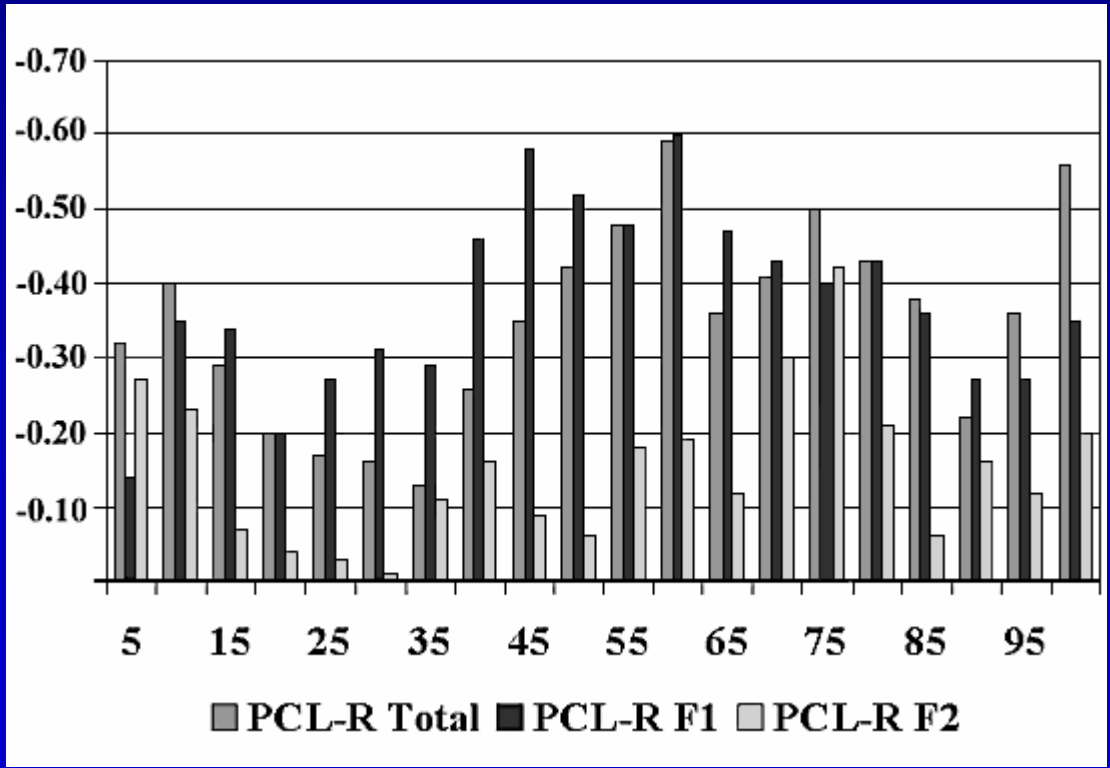
Laakso et al. 2001

Are Hippocampal Subareas Correlated with the Degree of Psychopathy?

Results

- Strong negative correlations, up to -0.79, were observed, among the study subjects, between the psychopathy scores and the posterior half of the hippocampi bilaterally.

Correlations between the PCL-R Scores and the Right Hippocampal Volumes



Conclusions

- The results of the present study support the view that lesions of the dorsal hippocampus impair acquisition of conditioned fear.
- Data provide biological evidence that the type 2 characteristics might represent a primarily antisocial personality disorder than alcoholism itself.
- Conventional MRI indicated in the characterization of alcoholism and psychopathy

Original Publications

- Laakso MP, Vaurio O, Savolainen L, Repo E, Soininen H, Aronen HJ, Tiihonen J. A volumetric MRI study of the hippocampus in type 1 and 2 alcoholics. Behav Brain Res 2000;109:177-186
- Laakso M, Frisoni GB, Könönen M, Mikkonen M, Beltramello A, Geroldi C, Bianchetti A, Trabucchi M, Soininen H, Aronen HJ. Hippocampus and entorhinal cortex in frontotemporal dementia and Alzheimer´s disease: a morphometric MRI study. Biol Psychiat 2000;47:1056-1063
- Pihlajamäki M, Tanila H, Hänninen T, Könönen M, Laakso M, Partanen K, Soininen H, Aronen HJ. Verbal fluency activates the left medial temporal lobe: an fMRI study. Ann Neurol 2000;47:470-476
- Laakso MP, Vaurio O, Koivisto E, Savolainen L, Eronen M, Aronen HJ, Hakola P, Repo E, Soininen H, Tiihonen J. Psychopathy and the posterior hippocampus. Behav Brain Res 2001;118:187-193
- Pihlajamäki M, Tanila H, Könönen M, Hänninen T, Hämäläinen A, Soininen H, Aronen HJ. Recognition of novel objects and new spatial arrangement of objects differentially activates the medial temporal subareas in humans. Resubmitted to Eur J Neuroscience.

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