Brain Spectroscopic Imaging, Morphometry, and Cognition in Recovering Alcoholics and Active Heavy Drinkers

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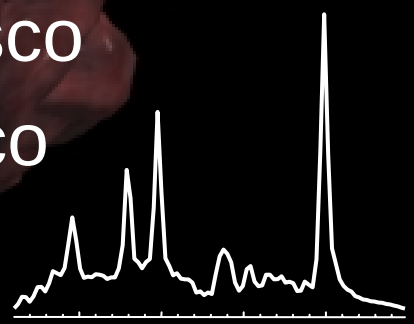


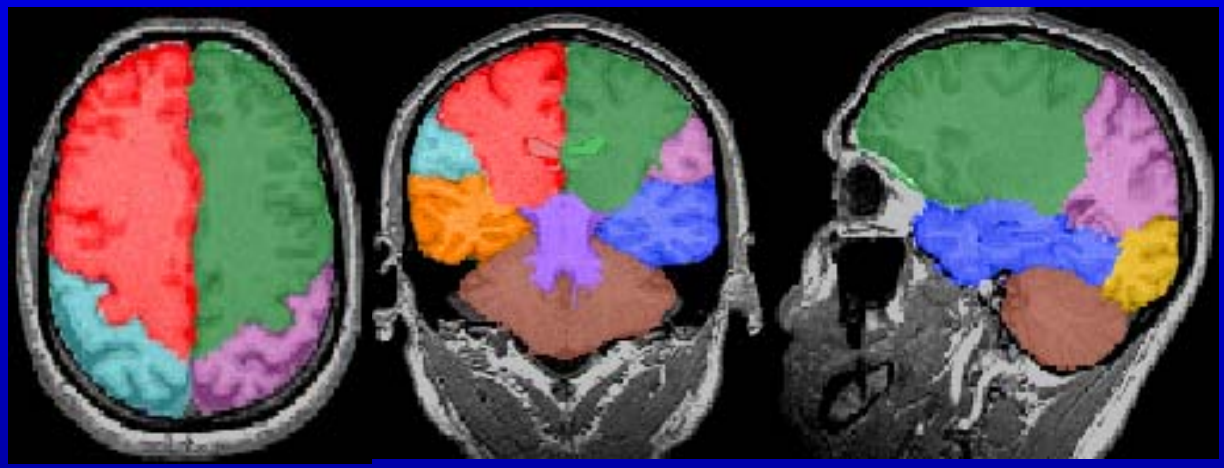
Outline

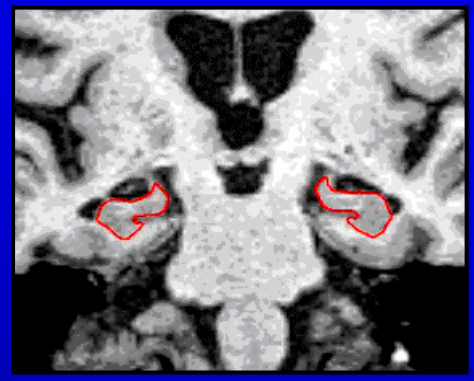
- Part 1: Chronic Heavy Drinkers
  - Detectable brain injury?
    - MRI, MRSI
    - Neuropsychology
  - Functional significance?

- Part 2: Recovering Alcoholics
  - Brain injury
  - Brain changes during abstinence and relapse
    - Functional significance?
    - Time course?

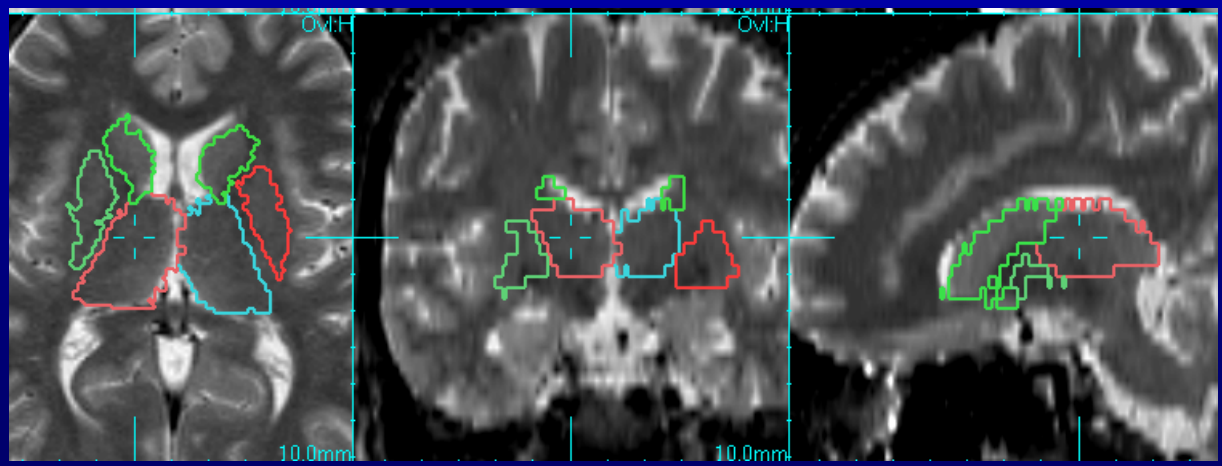
Automated MR Image Analysis I

voluming by non-linear warping to reference brain

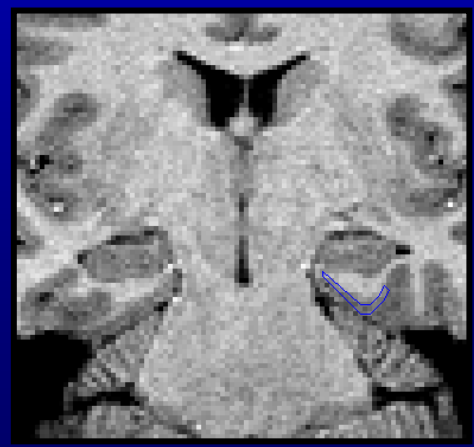




hippocampal SNT



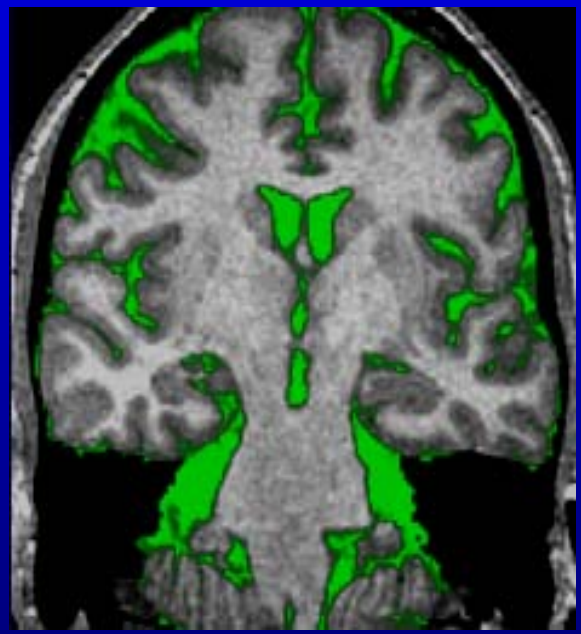
Identification of subcortical nuclei



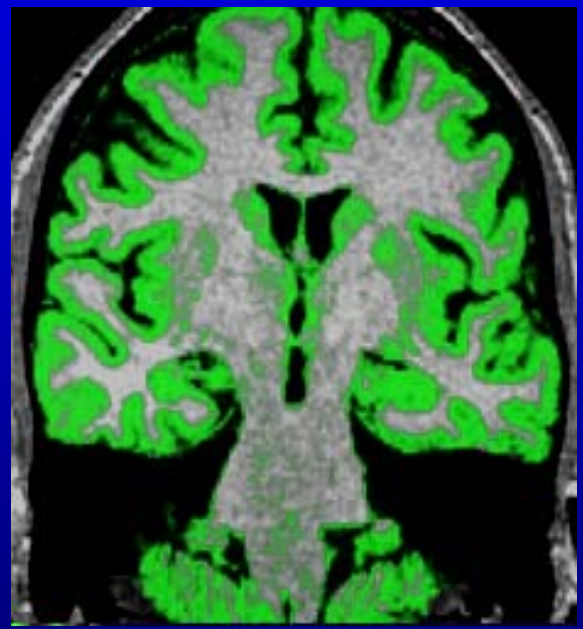
manual ERC

Automated MR Image Analysis II

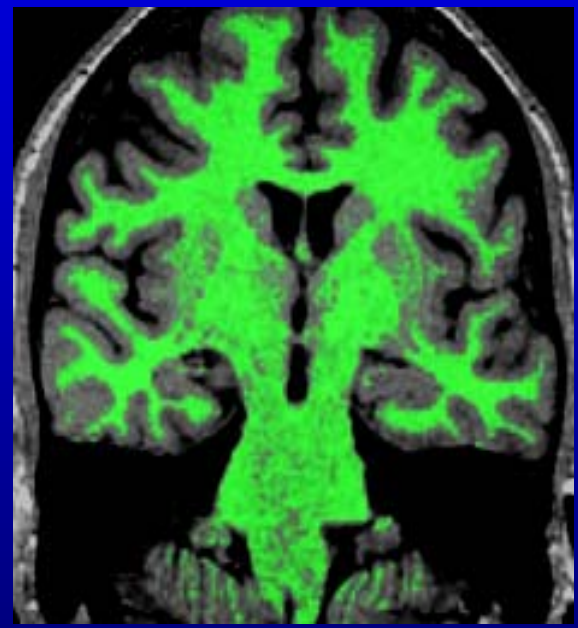
Identification of tissue types by probabilistic image segmentation



CSF



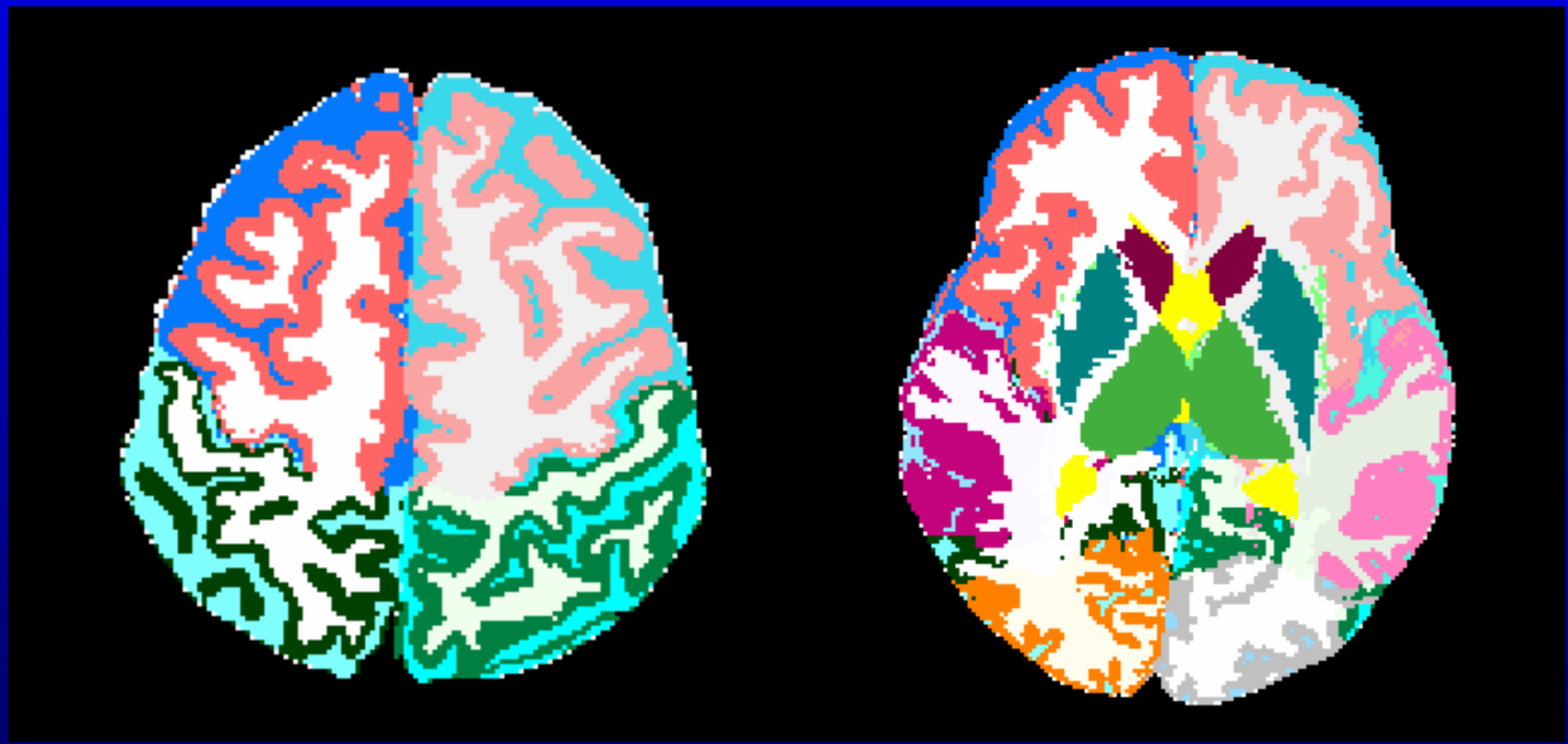
gray matter
GM



white matter
WM

Studholme C, Song E et al. 2002

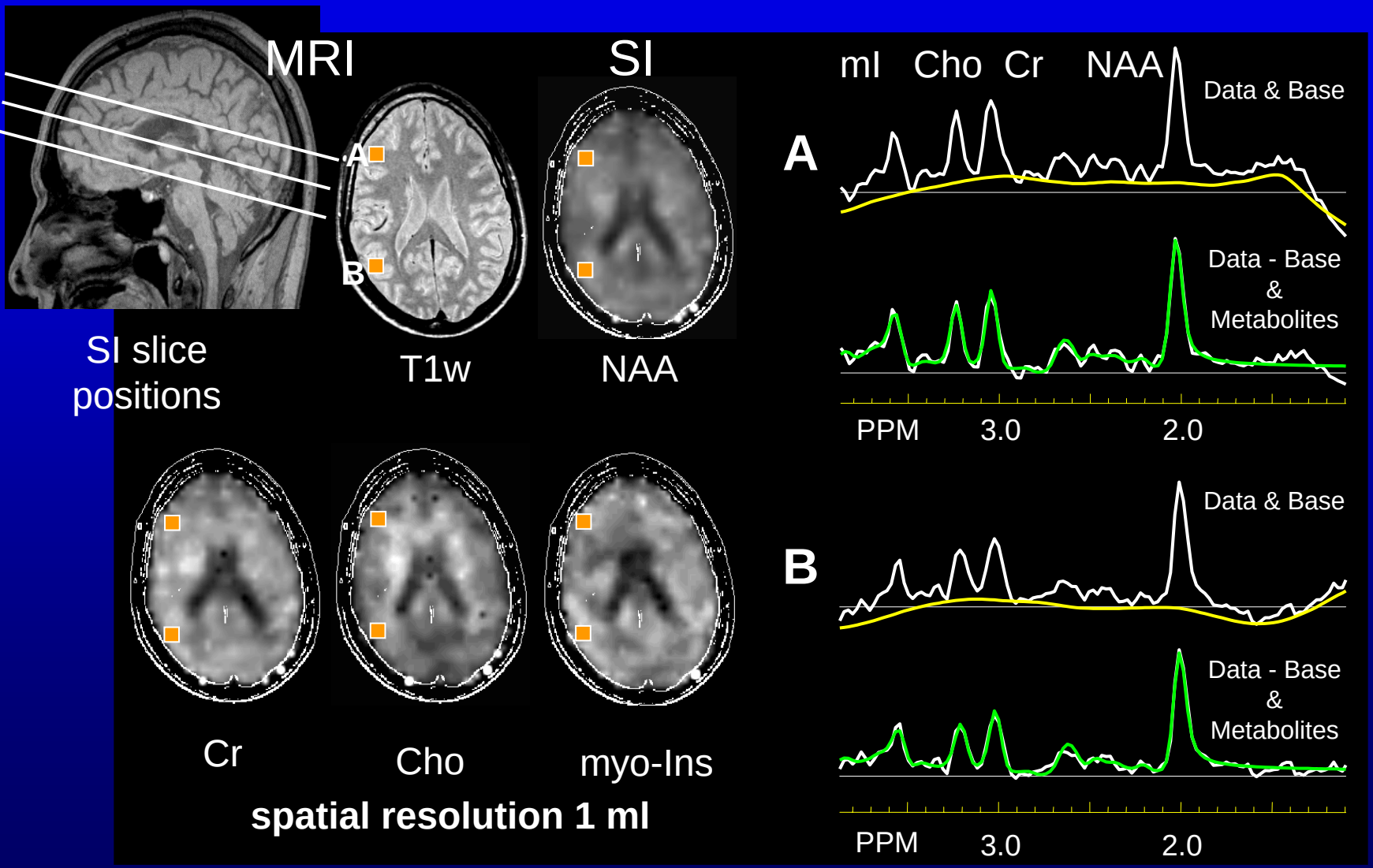
Final Product of Automated Tissue Segmentation



Volumes expressed as % of intracranial volume (ICV)

^{1}H MR Spectroscopic Imaging TE = 25 ms

Metabolite Distribution and Quantitation



Soher B et al. MRI 2000

Demographics 3 Drinking Groups

DEMOGRAPHIC	Light drinkers (LD) n = 27	Heavy drinkers (HD) n = 24	Recovering alcoholics (RA) n = 24
Age [years]	48.2 ± 5.0	48.8 ± 4.4	50.0 ± 7.3
Education [years]	15.8 ± 2.3	14.4 ± 2.3	13.2 ± 2.5
Drinks per month last 3 years	10 ± 11	224 ± 116 *	436 ± 178 *
Drinks per month over lifetime	12 ± 14	191 ± 166	264 ± 139
Lifetime alcohol consumption [kg]	61 ± 49	862 ± 900 *	1436 ± 751 *
Duration heavy drinking [years]	NA	18 ± 9	23.0 ± 8.9
Onset age heavy drinking [years]	NA	25.9 ± 9.6	24.0 ± 9.0
Drinks during 24 hours before MR	0.5 ± 0.7 (n=4)	2.7 ± 3.4 (n=13)	0
Time since last alcohol [hrs]	18 ± 7 (n=4)	14 ± 4 (n=13)	>120
DSM-IV physiol. dependence [%]	0	64	100

* RA > HD, $p<0.01$

Heavy Drinking and Regional Brain Volumes

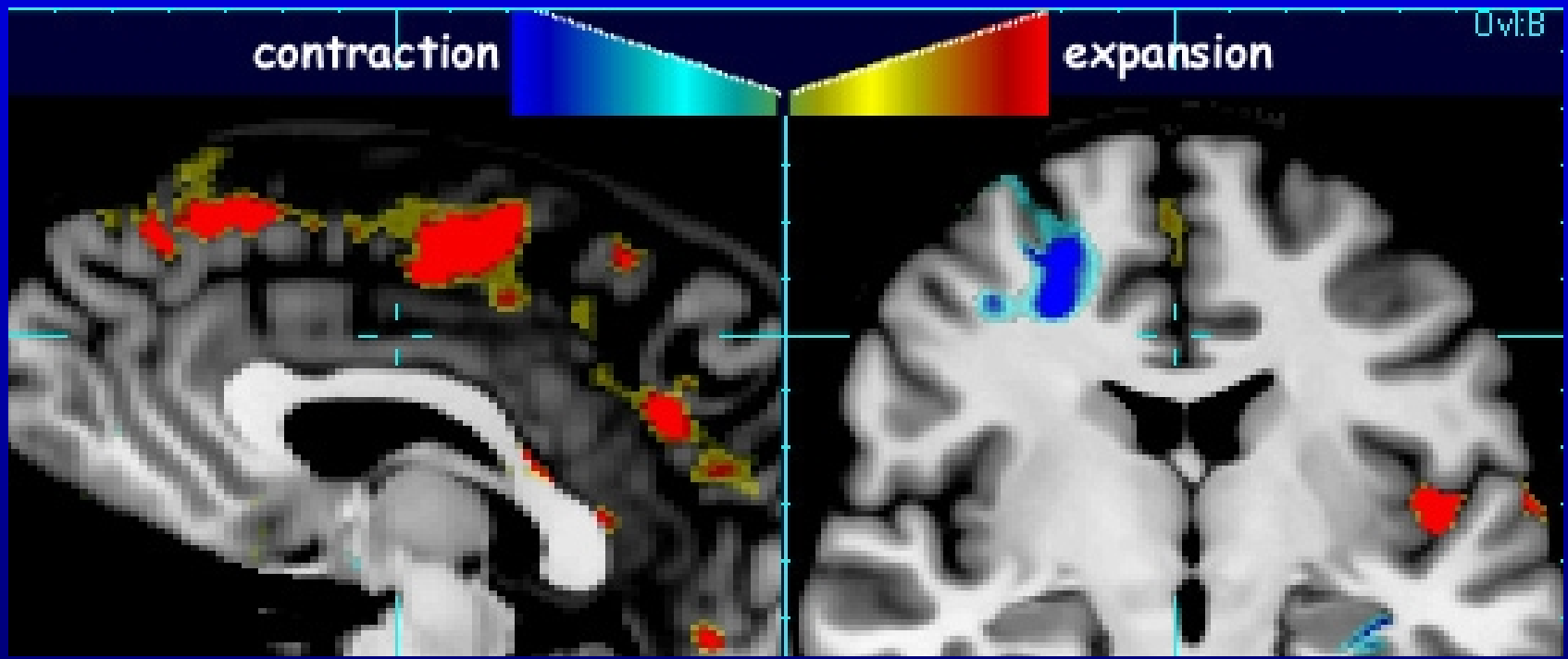
TISSUE	REGION	Light drinkers (LD) n = 26	Heavy drinkers (HD) n = 23	Difference [%]	p
WM	**cerebral**	33.1 ± 2.7	33.3 ± 3.0	+1	n.s.
GM *	**cortical**	34.5 ± 2.7	33.2 ± 2.6 *	-4	0.09
	frontal	14.4 ± 1.3	14.0 ± 1.1 *	-3	n.s.
	parietal	8.1 ± 0.7	7.7 ± 0.7 *	-5	0.04
	temporal	8.9 ± 0.6	8.6 ± 0.7 *	-3	0.08

***** Correlates with average monthly drinks over lifetime ($r < -0.44$, $p < 0.04$)

With n = 70 each group: regional GM loss ~4%, p<0.003

regional WM loss ~2%, p<0.05

Deformation Morphometry in Heavy Drinkers - Correlation with WCST errors (n=42)



Significant ($p<0.01$) contractions (blue) and expansions (red) correlate with WCST total errors; overlaid on the average spatially normalized MRI.

Heavy Drinking and Metabolites

METAB	TISSUE	REGION	Light drinkers (LD) n = 27	Heavy drinkers (HD) n = 24	Difference [%]	p
NAA	WM	frontal [a]	31.4 ± 3.8	29.6 ± 3.1	-6	0.07
Cr	GM	parietal [b]	20.2 ± 2.3	21.9 ± 3.3	+8	0.03
		temporal	22.0 ± 2.7	24.2 ± 3.2	+10	0.01
mI	GM	parietal [b]	17.8 ± 2.7	20.0 ± 3.7	+12	0.01
		temporal	17.8 ± 3.1	20.0 ± 3.9	+12	0.04
	WM	occipital	17.2 ± 2.2	18.9 ± 2.8	+10	0.02

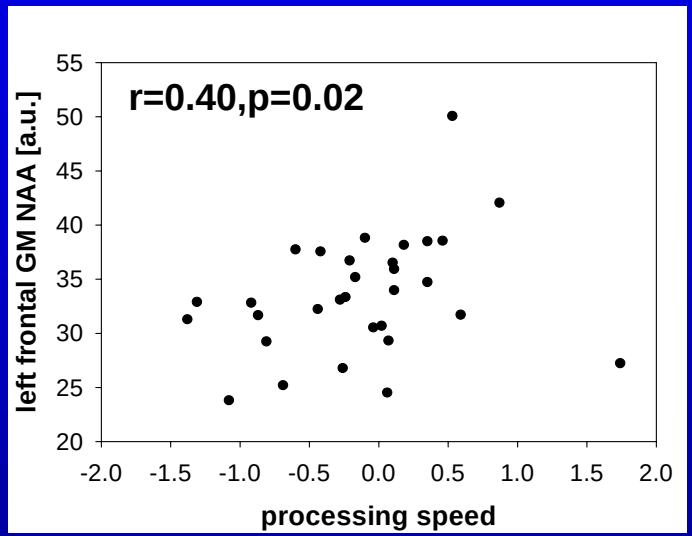
[a] 7 female HD vs. 17 female LD: -13%, p=0.06

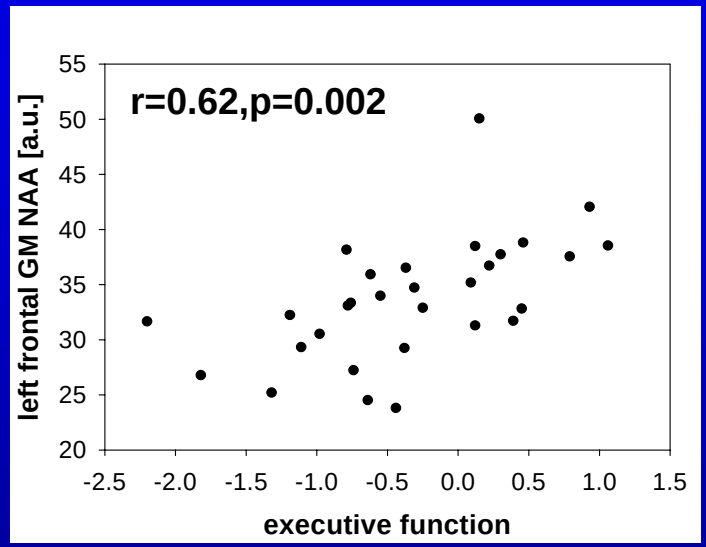
[b] increases with greater current and lifetime drinking quantities

Meyerhoff et al., ACER 2004

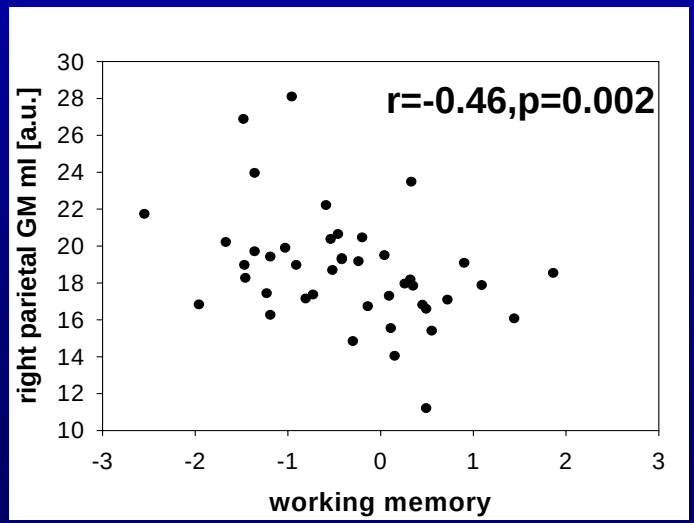
Metabolite Levels vs. Cognition in HD
(Spearman)

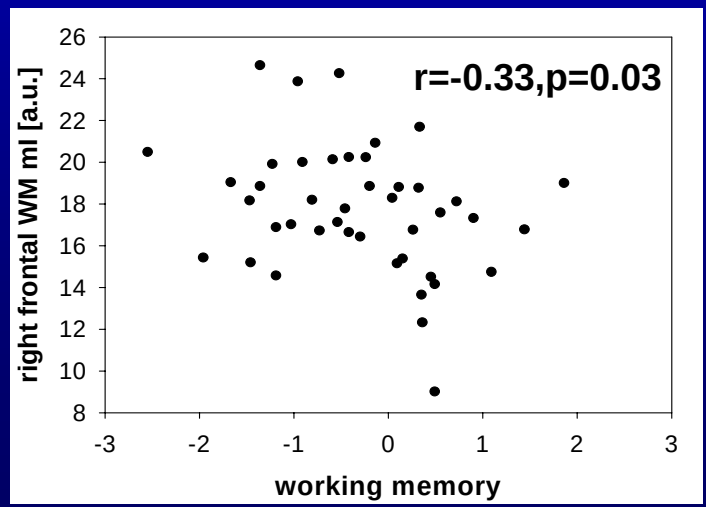
frontal GM NAA vs. z-scores for proc speed, executive





mIno vs. z-scores for working memory





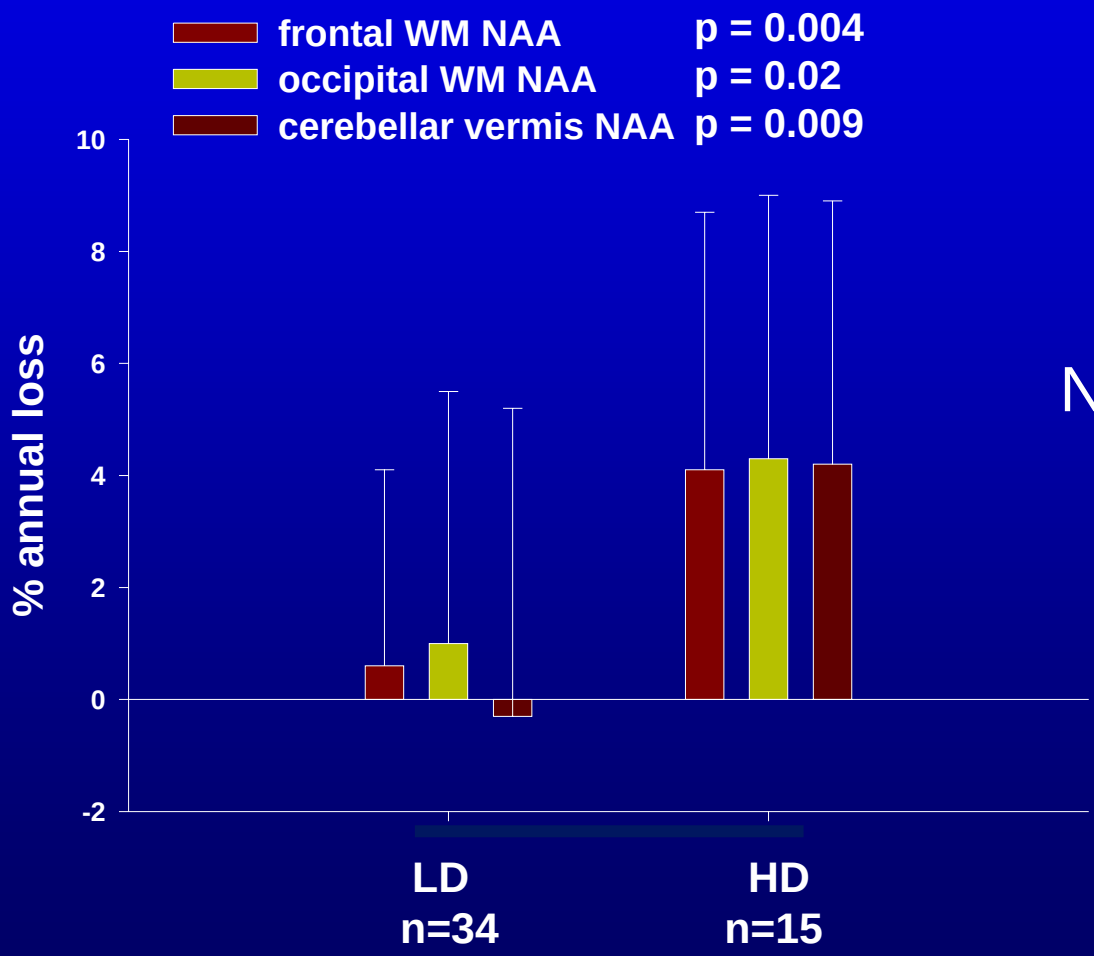
Annual Brain Volume Loss in HD over 2 Years (from difference MRI = BSI)

MEASURE	HD n = 16	LD n = 30	p
Annual rate of whole brain tissue loss (absolute volume)	0.28 ± 0.40 (4 ± 5 ml)	0.08 ± 0.26 (1 ± 3 ml)	0.04
Annual rate of ventricular volume gain (absolute volume)	0.06 ± 0.08 (1 ± 2 ml)	0.03 ± 0.07	n.s.
Annual rate of sulcal volume gain (absolute volume)	0.22 ± 0.36 (3 ± 5 ml)	0.05 ± 0.22	0.04

as % of intracranial volume

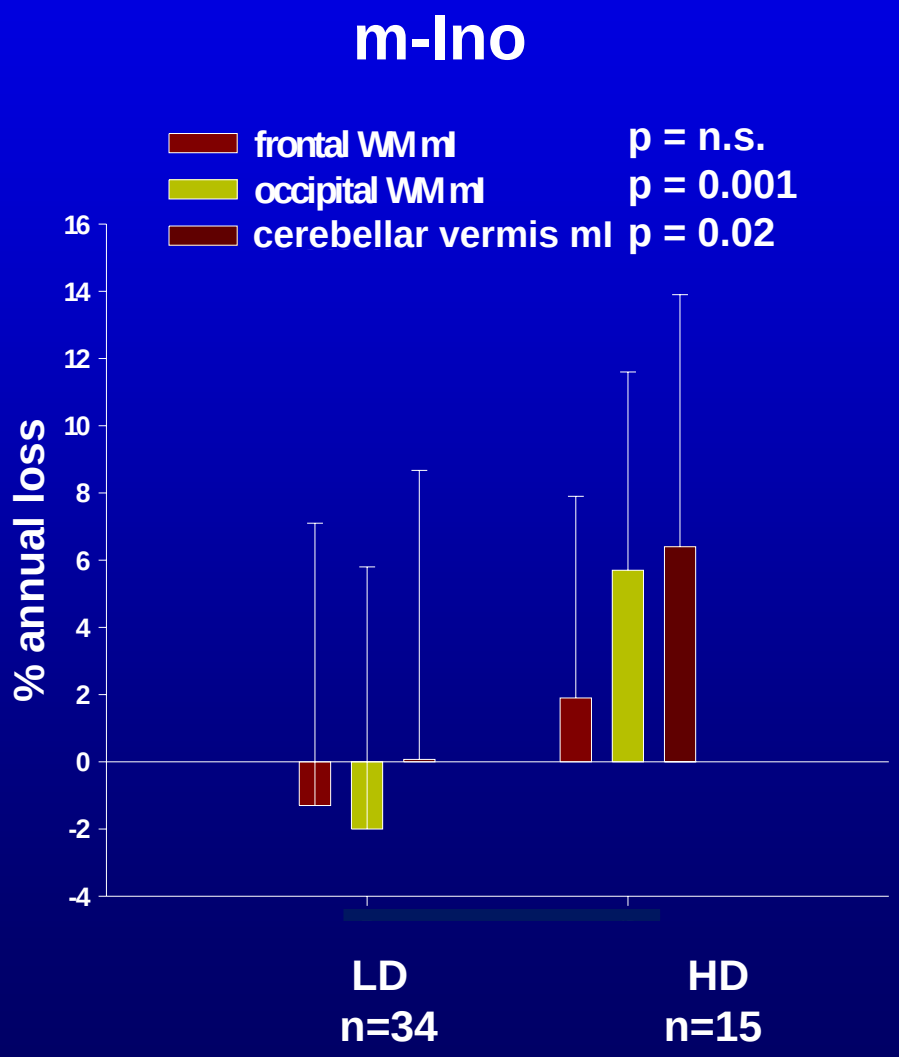
No significant regional volume loss over 2 years.

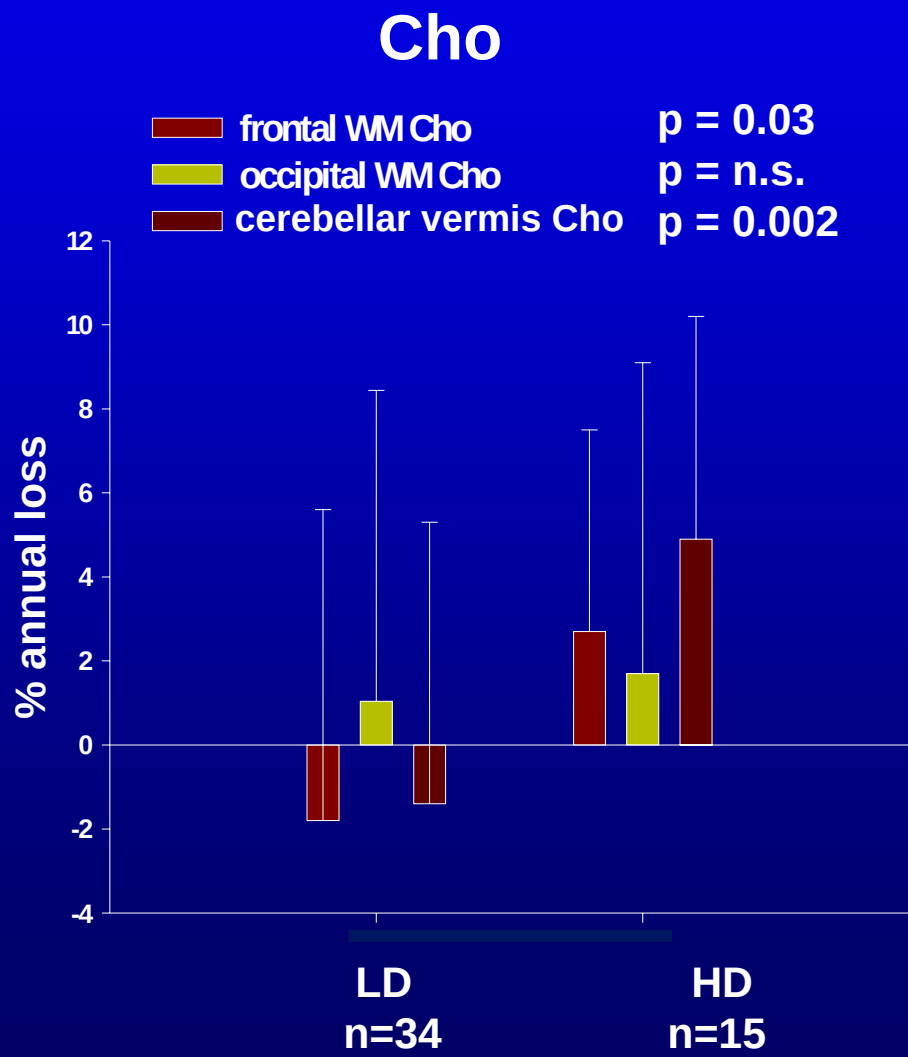
Annual Rate of NAA Loss in HD over 2 Years



~ 4%
NAA loss/year!

Annual Rates of m-Ino and Cho Loss in HD over 2 Years





! Chronic active heavy drinking is associated with clinically significant brain injury !

- Cross-sectional studies
  - dose-dependent lobar GM volume loss
  - frontal WM NAA loss, with female HD > male HD
    ⇒ axonal injury
  - dose-dependent Cr and mI increases in parietal and temporal GM
    ⇒ osmotic changes? gliosis?
  - metabolite alterations and frontal WM loss correlate with cognitive impairment in HD
- Preliminary longitudinal studies over 2 years
  - ongoing whole brain tissue loss
  - ongoing loss of NAA, Cho and mI, mainly in frontal WM and cerebellar vermis
    ⇒ active axonal injury, demyelination

Part 2: Recovering Alcoholics

- Hypotheses
  - **Chronic alcohol consumption damages neurons and glia in specific brain regions. Damage associated with neurocognitive impairment.**
  - **Recovery from alcoholism associated with axonal/dendritic regeneration, glial changes, and cognitive improvements**
- Methods, x-sectional and longitudinal
  - Alcoholics in treatment (1 week, 1 mo, 6-9 mo)
  - Structural and metabolic MR at 1.5T
  - Neuropsychological testing

Demographics

DEMOGRAPHIC	Light drinkers (LD)	Recovering alcoholics (RA)
N	27	24
Age [years]	48.2 ± 5.0	50.0 ± 7.3
Education [years]	15.8 ± 2.3	13.2 ± 2.5
Drinks per month last 3 years	10 ± 11	436 ± 178
Drinks per month over lifetime	12 ± 14	264 ± 139
Lifetime alcohol consumption [kg]	61 ± 49	1436 ± 751
Duration heavy drinking [years]	NA	23.0 ± 8.9
Onset age heavy drinking [years]	NA	24.0 ± 9.0
Time since last alcohol [hrs]	18 ± 7 (n=4)	>120

RA: DSM-IV dependence on alcohol only, no history of significant other drug use, psychiatric, or neurologic disorder

Brain Tissue Loss [% ICV]

1-Week-Abstinent Alcoholics vs. Controls

Tissue type / brain region		Difference [%] 24 RA – 26 LD	p
White Matter	frontal	-6	0.02*
	parietal	-5	0.03*
Gray Matter	frontal	-4	0.05*
	parietal	-8	<0.001*
	temporal	-7	0.003
Thalamus		-6	0.02
Hippocampi (n=11,15)		-12	0.02*
Sulcal CSF	frontal	+20	<0.001*
	parietal	+16	0.003*
	occipital	+22	0.03
	temporal	+14	0.02

* a priori hx

Compare: In HD, ~4% regional GM loss

^{1}H MRSI Metabolites I
1-Week-Abstinent Alcoholics vs. Controls

metabolite	region		difference [%] 25 RA – 20 LD	p
NAA	GM	frontal	-9	0.002*
		parietal	-6	0.02
		temporal	-11	0.007
	WM	frontal	-11	<0.001*
		parietal	-10	0.002
		temporal	-8	0.01
		occipital	-9	0.008
	Thalamus		-8	0.01*
	Caudate		-19	0.02
	Lenticul. Nucl.		-9	0.02
	Brainstem		-7	0.08*
	Cerebellum		-6	0.03*

* a priori hx

Compare: In HD, 6% frontal WM NAA loss.

^{1}H MRSI Metabolites II
1-Week-Abstinent Alcoholics vs. Controls

metabolite	region		difference [%] 25 RA – 20 LD	p
Cho	GM	frontal	-7	0.07*
		parietal	-8	0.02
	WM	frontal	-12	0.004*
		parietal	-9	0.02
		occipital	-9	0.01
	Thalamus		-13	0.01*

* a priori hx

Compare: In HD, no Cho changes, ~10% GM mI and Cr increases

Neuropsychology

1-Week-Abstinent Alcoholics

- Very limited testing (BVMT, Digit Span + Symbol)
- Mildly impaired visuospatial learning
- Impaired cognition correlates stronger with regional NAA losses than regional brain tissue volume losses

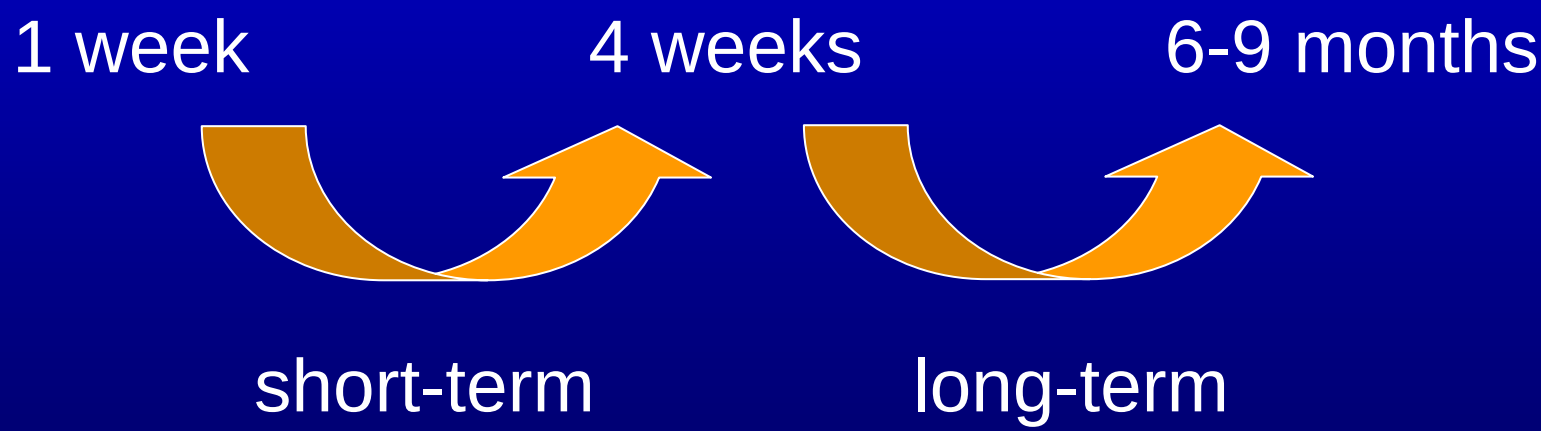
Chronic Alcohol-Induced Brain Injury in 1-Week-Abstinent Alcoholics - Conclusions

- Brain shrinkage and metabolite abnormalities widespread and dose-related
- Neuronal/axonal injury, demyelination (lipid abnormalities), consistent with neuropath lit
- Impaired cognition, associated with abnormal brain MR measures, primarily NAA

⇒ Objective MRS measures as surrogates for CNS injury

- Compared to active HD, RA had greater alcoholism severity, more atrophy, more widespread metabolite damage, more and greater cognitive impairments

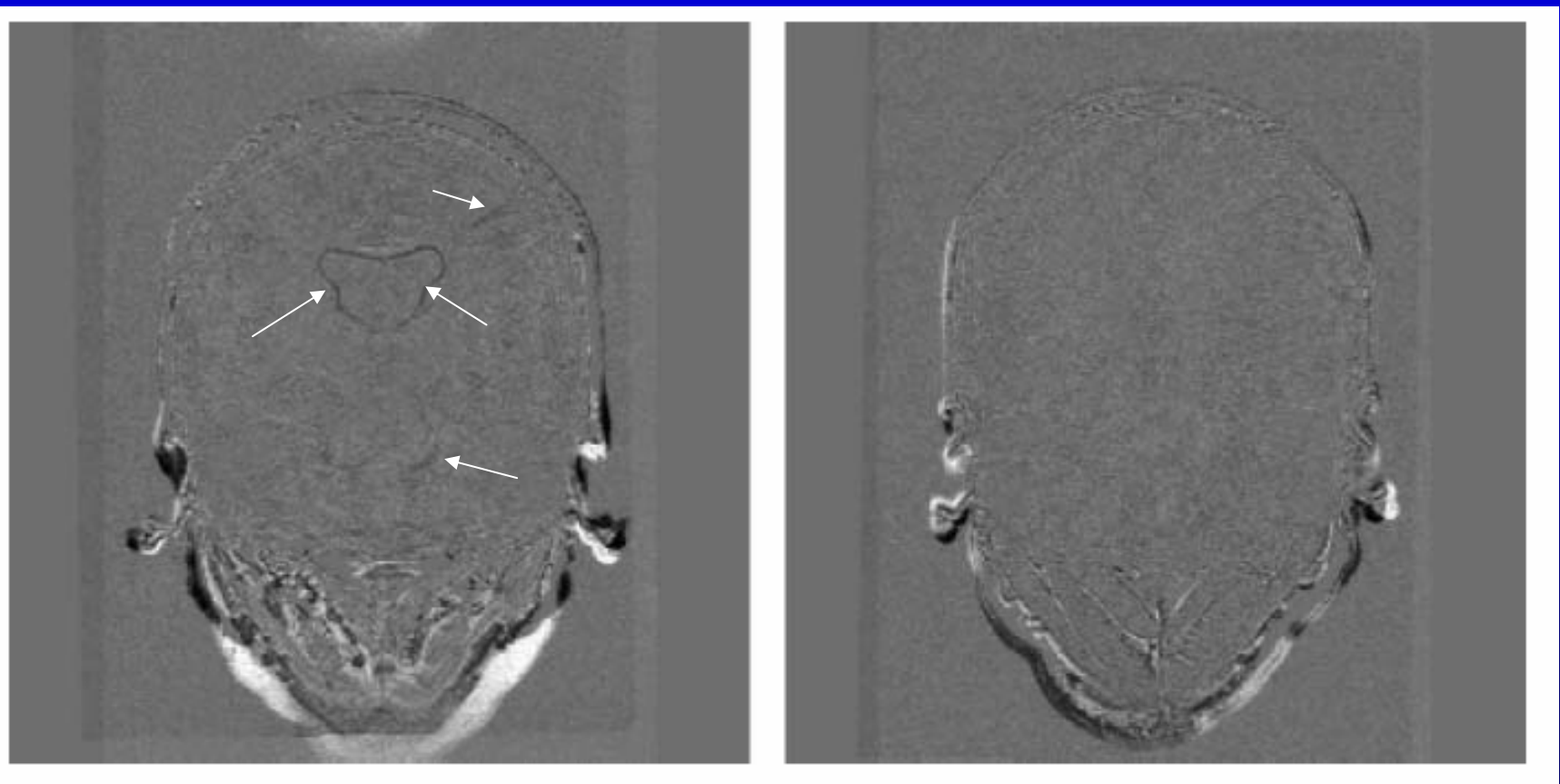
Longitudinal Studies in Recovering Alcoholics



Short-Term Neurostructural Recovery (Boundary Shift Integral BSI)

Recovering alcoholic 3 weeks
ventricular volume decrease

Light social drinker 2 years



BSI: Freeborough and Fox 1997

Whole Brain Volume Recovery over 3 Weeks of Sobriety (from BSI)

	Recovering Alcoholics N = 20	**Light Drinkers** (over 2 years) N = 10	**p**
monthly rate of whole brain tissue gain (absolute volume)	+1.1 ± 0.8 (+12 ± 10 ml)	-0.01 ± 0.01	0.0001
monthly rate of ventricular volume loss (absolute volume)	0.2 ± 0.2 (2 ± 2 ml)	0.00 ± 0.00	0.002
monthly rate of sulcal volume loss (absolute volume)	0.9 ± 0.6 (10 ± 8 ml)	0.01 ± 0.01	0.0001

as % of intracranial volume

see also poster presentation

Regional Brain Volume Recovery in Short-Term Abstinent Alcoholics - Lobes (n=22)

Tissue/Brain Region		gain [%] 4 weeks – 1 week	p
Gray Matter	cortical	1.5 ± 5.3	0.14
	frontal	1.4 ± 4.1	0.09*
	temporal	1.8 ± 5.4	0.09
White Matter	cerebral	**1.4 ± 3.4**	**0.04***
	frontal	**1.8 ± 3.4**	**0.01***
	occipital	**2.0 ± 3.2**	**0.007**
CSF	sulcal	**-2.2 ± 9.3**	**0.03***
	frontal	**-1.7 ± 8.9**	**0.03***
	parietal	-1.6 ± 9.4	0.06
	temporal	-2.4 ± 12.4	0.06
	occipital	-3.1 ± 16.1	0.08
	ventricular	**-5.8 ± 6.3**	**0.0002***

* a priori hx

Regional Brain Volume Recovery in Short-Term Abstinent Alcoholics – non-lobar (n=22)

Brain Region	gain [%] 4 weeks – 1 week	p
Thalamus	0.7 ± 1.0	0.004
Caudate	1.8 ± 1.8	<0.001
Brainstem	0.9 ± 2.1	0.04
Cerebellum	0.8 ± 2.0	0.04*
right hippocampus (n=11)	4.0	0.03*
l + r entorhinal cortices (n=4)	3.0	0.04

* a priori hx

Functional Relevance of Brain Volumes

- **4-weeks-abstinent alcoholics** (n=26)

  - Parietal, temporal, total WM volumes correlate with

    visuospatial learning $r > 0.46$, $p < 0.02$

  - Frontal CSF volumes inversely correlate with

    executive skills
    general intelligence
    visuospatial learning
    visuospatial skills

    } $r < -0.38$, $p > 0.05$

Brain Metabolite Recovery in Short-Term Abstinent Alcoholics (n=20)

Metabolite	Region	Tissue	gain [%] 4 weeks – 1 week	p
NAA	frontal	GM	+2	0.06
		WM	**+5**	**0.02***
Cho	frontal	GM	+8	0.02
		WM	**+15**	**0.001***
	parietal	GM	+10	0.03
m-Ino	frontal	GM	+5	0.08
		WM	**+10**	**0.008***
	cerebellar vermis		-7	0.02

* a priori hx

Neuropsychological Recovery in Short-Term Abstinent Alcoholics (n=28)

measure	1 week	4 weeks	p	score type
Visuospatial learning [a]	38.1 ± 13.0	47.5 ±11.2	<0.0001	T
Aural attention/ concentration [b]	9.0 ± 3.0	10.3 ± 3.5	0.0008	scale
Visuomotor scanning speed, incidental learning [c]	7.6 ± 2.5	9.0 ± 2.8	0.001	scale
BDI (depressive symptoms)	17.5 ± 10.8	9.4 ± 8.4	<0.0001	raw
STAI-Trait	48.4 ± 14.4	43.9 ± 10.6	0.002	raw
CIWA (withdrawal symptoms)	3.5 ± 4.6	0.32 ± 0.95	0.0003	raw

[a] BVMT-R [b] Digit Span [c] Digit Symbol

Functional Relevance of Metabolite Levels

- **In 4-weeks-abstinent alcoholics** (n=22)
  - Higher parietal WM NAA correlated with
    auditory verbal memory — $r = 0.58$, $p = 0.03$
  - Higher cerebellar vermis NAA correlated with
    visuomotor scanning speed
    incidental learning — $r > 0.52$, $p < 0.04$
  - Cho and myo-Ino in multiple brain regions inversely correlated with
    auditory-verbal learning
    visuospatial abilities
    general intelligence
    } $r < -0.42$, $p < 0.04$

Functional Relevance of Short-Term Brain Metabolite Recovery

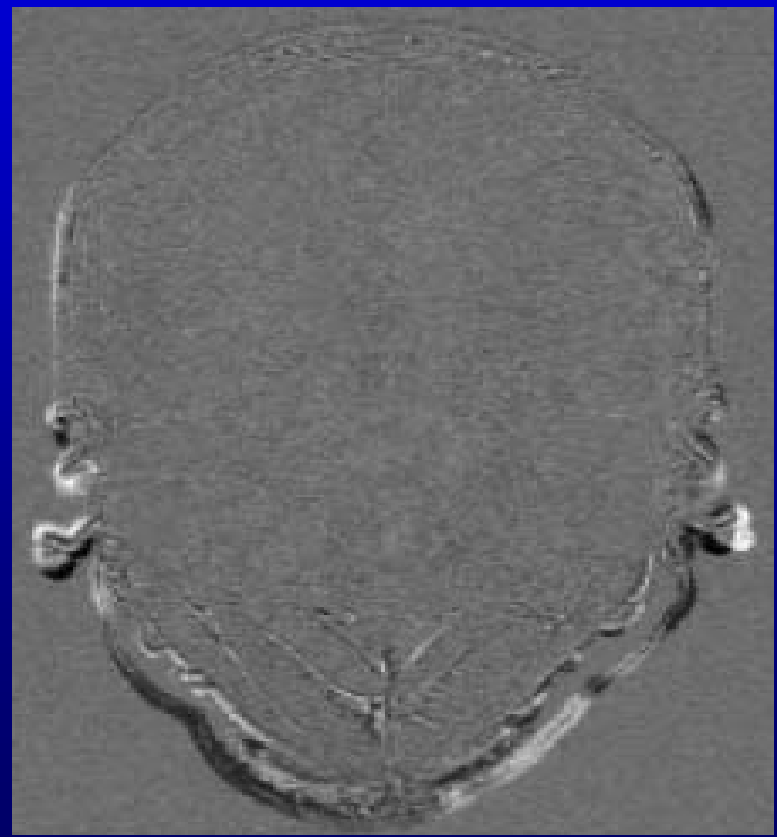
- **Over 4 weeks of sobriety** (n=13)
  - increases of cerebellar vermis NAA correlated with improvement of visuospatial learning and memory

$r = 0.73$, $p = 0.04$

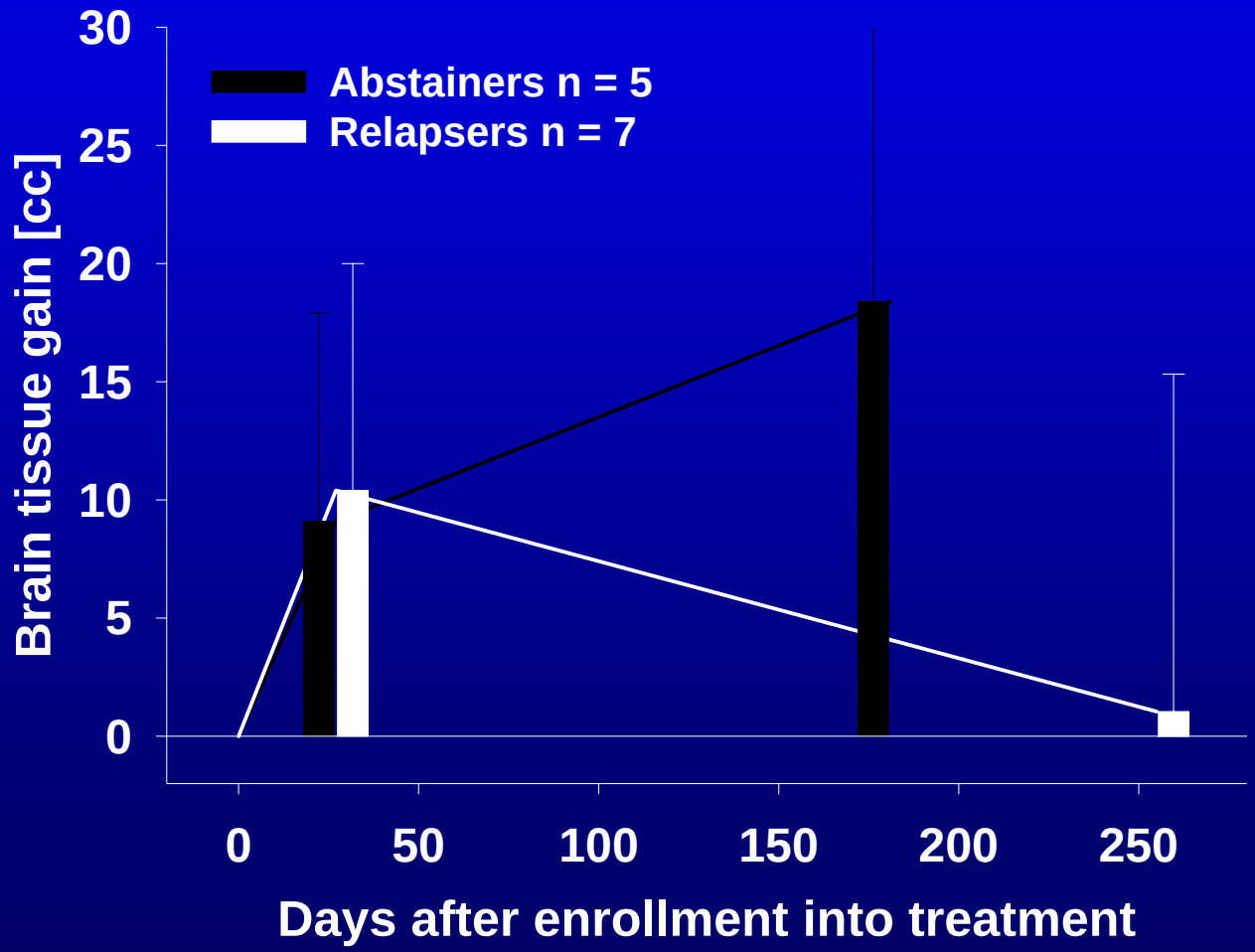
Long-Term Neurostructural Recovery (Boundary Shift Integral BSI)

Recovering alcoholic 8 months
ventricular and sulcal volume decreases

Light social drinker 2 years



Long-Term Structural Change in Recovering Alcoholics (whole brain tissue gain from BSI)



Long-Term Regional Brain Volume Recovery in Abstainers and Relapsers

6-9 Months vs. 1 Month Abstinent Alcoholics

Tissue/Brain Region		Abstainers [% gain] (n = 9 vs. 26)	p Abstainers	Relapsers [% gain] (n=9 vs. 26)	p Relapsers
Gray Matter	cortical	-1.5	n.s.	-0.2	0.04
	frontal	-1.7		-0.1	0.04
	parietal	-1.2		-1.8	0.03
	temporal	-1.0		-0.1	0.04
White Matter	cerebral	**+6.0**	**0.02**	-4.6	n.s.
	frontal	**+6.0**	**0.01**	-6.2	
	parietal	**+4.6**	**0.01**	-3.4	0.05
CSF	sulcal	**-6.2**	**0.03**	+3.6	0.01
	frontal	-4.8	n.s.	+7.3	0.01
	parietal	-3.8		-10.0	0.03
	temporal	-9.5		+10.5	0.01
	occipital	-9.0		-10.0	0.03
	ventricular	**-10.6**	**0.0001**	-2.9	0.02

Regional Brain Volumes
Long-term Abstainers vs. Controls [%ICV]

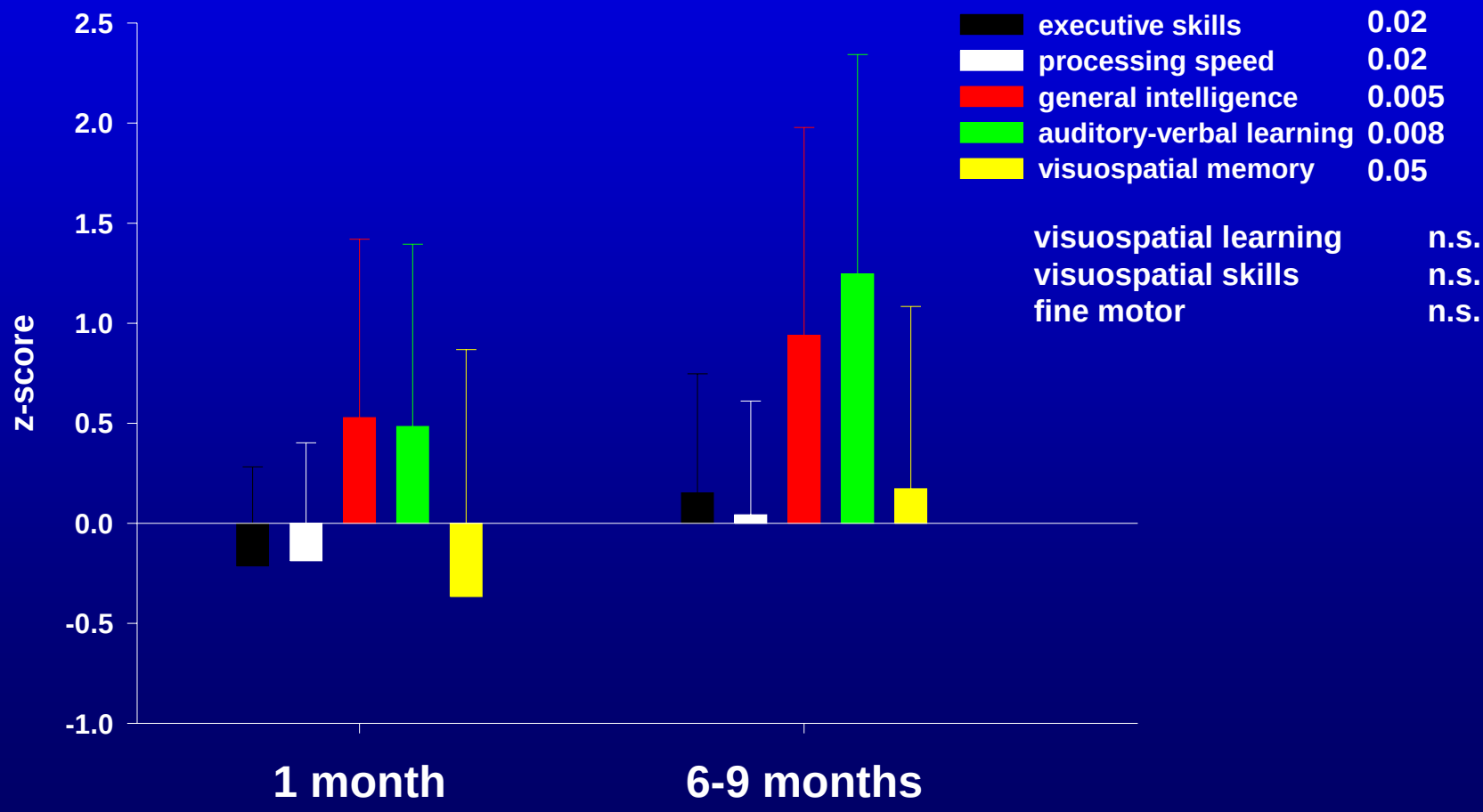
brain region		difference [%] 9 RA – 18 LD	p
Gray Matter	**cortical**	-4.7	0.06
	parietal	**-6.4**	**0.03**
	temporal	-6.4	n.s.
White Matter	**cerebral**	+0.2	n.s.
	frontal	-1.0	
	parietal	-0.2	
	temporal	+1.0	
CSF	**sulcal**	**+8.9**	**0.03**
	frontal	**+13.0**	**0.02**
	parietal	**+14.0**	**0.03**
	ventricular	-1.2	n.s

^{1}H MRSI Metabolites
Long-term Abstainers vs. Controls

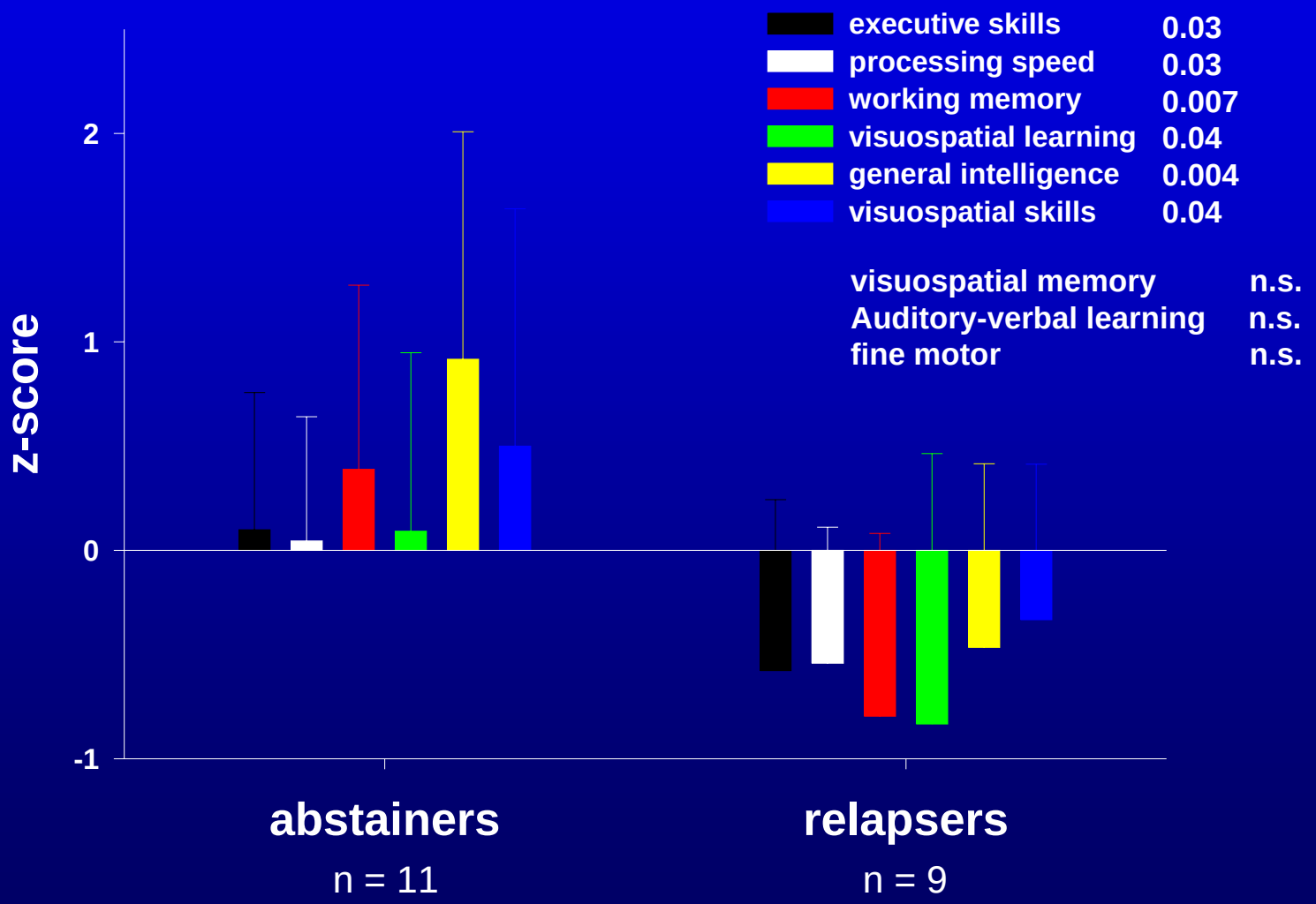
metabolite	region		difference [%] 9 RA – 20 LD	p
NAA	GM	frontal	-8	0.02
		temporal	-9	0.04
	WM	frontal	-11	0.008
		parietal	-9	0.02
		temporal	-14	0.005
		occipital	-7	0.05
	Thalamus		-8	0.03

No significant Cho or mI abnormalities remain after 6-9 months.

Long-Term Neuropsychological Recovery in Abstainers (n=12)



Neuropsychological Performance in Long-Term Abstainers vs. Relapsers



Longitudinal MR Changes in Recovering Alcoholics - Summary

MRI

- Over 4 weeks:
  - WM ↑
  - sCSF ↓
  - GM ↗
- Over 6-9 months:
  - WM ↑, normal
  - sCSF ↓
  - vCSF ↓, normal
  - GM ↗, low

MRSI

- Over 4 weeks:
  - Fro WM NAA ↑
  - Fro WM mI ↑
  - Fro Cho ↑
- Over 6-9 months:
  - NAA ↗ , low
  - Cho ↑, normal
  - mI ↑, normal

After only 4 weeks of sobriety, the brain recovers measurably from alcohol-induced brain injury

- MR changes consistent with WM volume recovery, axonal repair, remyelination, and astrocytosis
- Improvements in visuospatial and incidental learning, visuomotor speed, attention/concentration
- Cognitive recovery associated with regional NAA increases, but not with structural improvements.

- CT, neuropathology show greater tissue density

  ⇒ remyelination, fiber regeneration (protein synthesis)

- Most studies may not capture the full extent of brain injury

Brain recovery slows down between 1 mo and 6-9 mo of sobriety. Relapse stops brain improvements.

- lobar WM volumes continue to recover;
  no significant lobar GM volume recovery
- persistent and widespread lobar and thal NAA deficits;
  Cho and mI normalize
- normalization of executive function, processing speed, and auditory-verbal learning;
  residual visuospatial impairment

Long-Term Recovery from Chronic Alcohol-Induced Brain Injury - Conclusions

- Most recovery during first weeks of sobriety
- WM tissue recovers faster than GM tissue:
  WM volume increases, remyelination, astrocytosis
- Persistent GM volume deficits
- Persistent neuronal/axonal damage
- Cognition mostly normalized despite persistent structural and neuronal abnormalities.

⇒ Importance of astrocytes in brain function!

⇒ The brain during long-term abstinence may compensate functionally for persistent biological injury.

Team Efforts

- **Recruitment, NP, Assessment** — Timothy Durazzo, PhD
- **MR studies** — Stefan Gazdzinski, PhD
- **MRI analyses** — Colin Studholme, PhD; Valerie Cardenas, PhD; Enmin Song, PhD
- **Clinical support** — Frank Ezekiel, BA; Peter Banys, MD; David Pating, MD; Donald Tusel, MD; Johannes Rothlind, PhD
- **Participation** — SADH and Kaiser Permanente study volunteers

Acknowledgements

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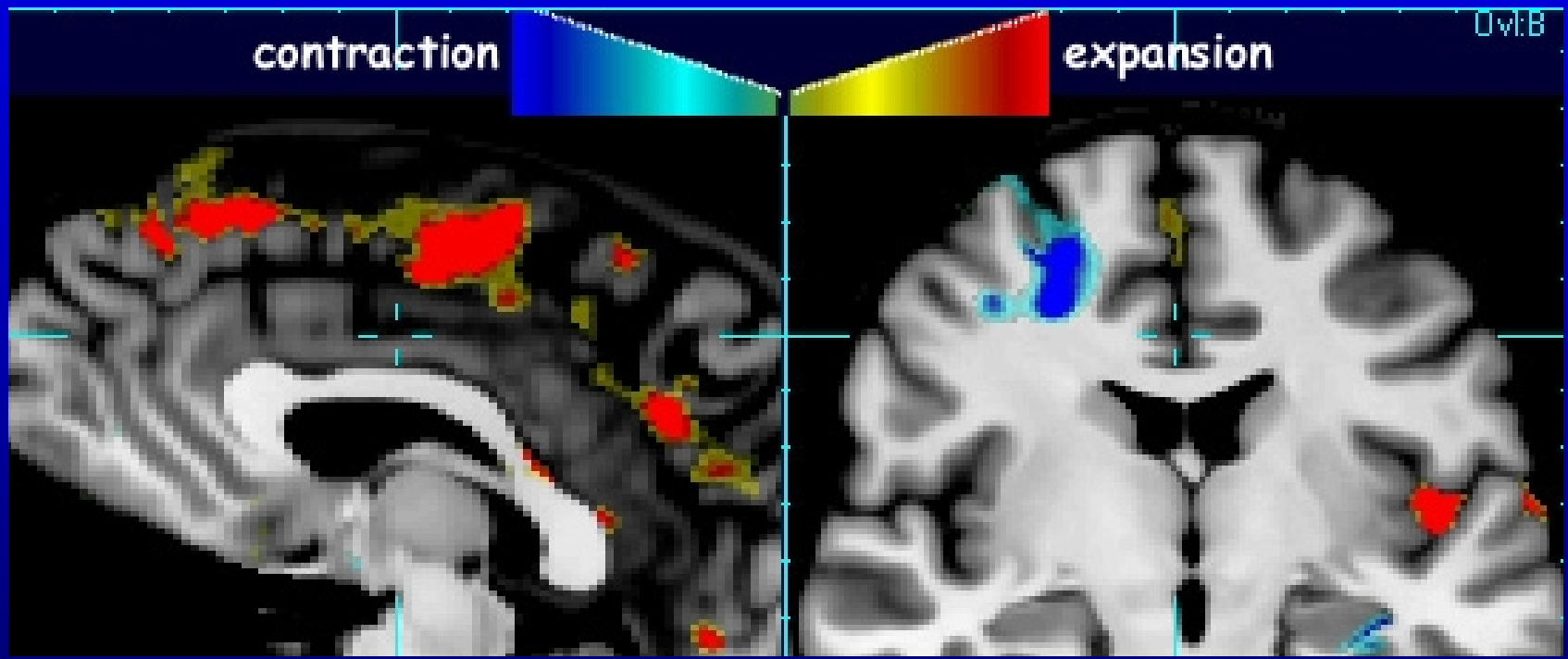
☺ YOU 


NEED CASH
FOR ALCOHOL
RESEARCH

Deformation Morphometry in Heavy Drinkers - Correlation with WCST errors (n=42)



Significant ($p<0.01$) contractions (blue) and expansions (red) correlate with WCST total errors; overlaid on the average spatially normalized MRI.

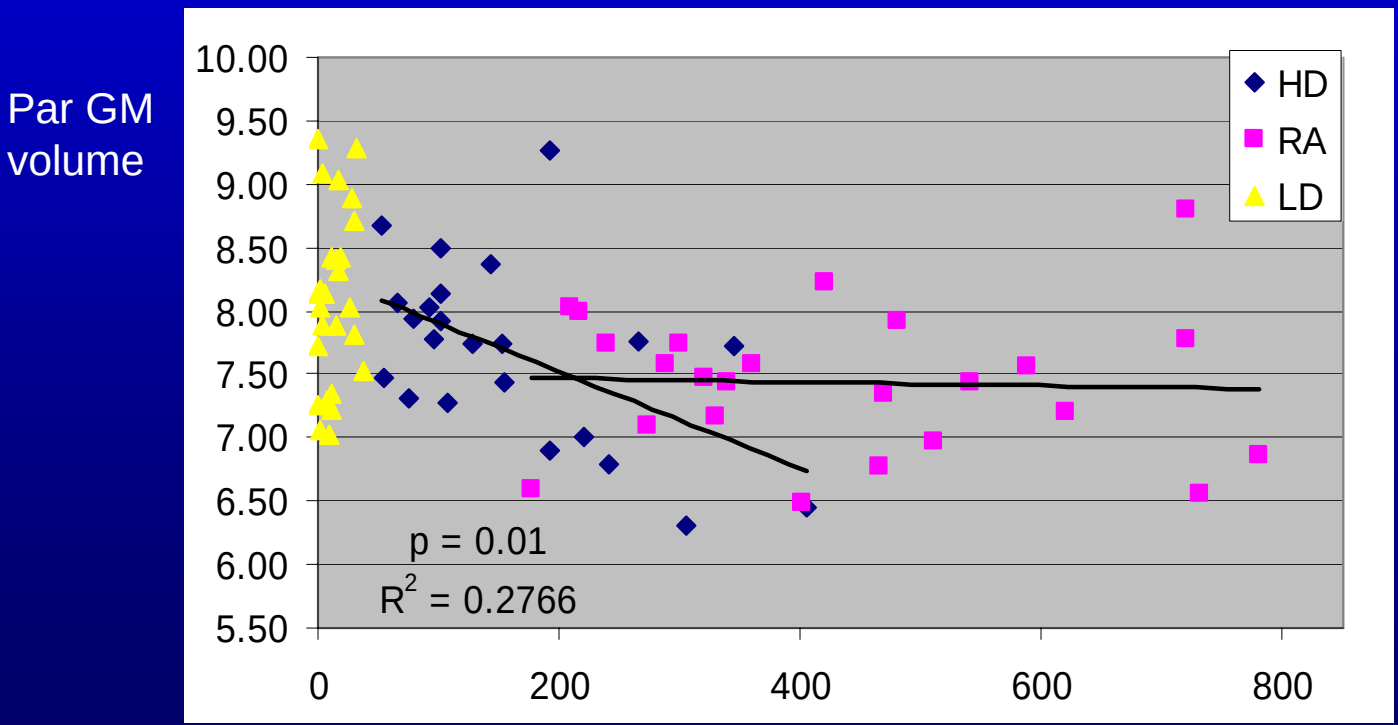
Demographics 3 Drinking Groups

DEMOGRAPHIC	Light drinkers (LD) n = 27	Heavy drinkers (HD) n = 24	Recovering alcoholics (RA) n = 24
Age [years]	48.2 ± 5.0	48.8 ± 4.4	50.0 ± 7.3
Education [years]	15.8 ± 2.3	14.4 ± 2.3	13.2 ± 2.5
Drinks per month last 3 years	10 ± 11	224 ± 116 *	436 ± 178 *
Drinks per month over lifetime	12 ± 14	191 ± 166	264 ± 139
Lifetime alcohol consumption [kg]	61 ± 49	862 ± 900 *	1436 ± 751 *
Duration heavy drinking [years]	NA	18 ± 9	23.0 ± 8.9
Onset age heavy drinking [years]	NA	25.9 ± 9.6	24.0 ± 9.0
Drinks during 24 hours before MR	0.5 ± 0.7 (n=4)	2.7 ± 3.4 (n=13)	0
Time since last alcohol [hrs]	18 ± 7 (n=4)	14 ± 4 (n=13)	>120
DSM-IV physiol. dependence [%]	0	64	100

* RA > HD, $p<0.01$

Chronic Heavy Drinkers vs. Recovering Alcoholics

- RA have greater alcoholism severity, more atrophy, more widespread metabolite damage, more and greater cognitive impairments



Alcohol-Induced Brain Injury
Neuropathology, Histology

- localized loss of neurons and their axons, superior frontal cortex (= gray matter, GM)
- widespread shrinkage of neuronal cell bodies, in frontal, cingulate, and motor cortices
- reduced synaptic branching and dendritic pruning
- loss of white matter, demyelination

Harper, Kril et al. 1992-2001

Are clinical in-vivo MR methods sensitive to such degeneration or its effects?

Alcohol-Induced Brain Injury
General Structural Neuroimaging Findings

- enlarged ventricles and sulci
- brain tissue loss, especially frontal
- smaller size and other abnormalities of subcortical structures, pons, hippocampus, and cerebellum
- dose-response relationship
- unclear if magnitude of injury similar in men and women
- smaller tissue volumes in older alcoholics

Alcohol-Induced Brain Injury
cross-sectional single volume ^{1}H MRS studies

- less NAA in frontal lobe, cerebellum, basal ganglia, and thalami of recovering alcoholics

  Fein and Meyerhoff, NIAAA 1994; Furuya et al. ISMRM 1994; Fuyimoto et al. ISMRM 1996; Jagannathan et al. MRI 1996; Seitz et al. Alc Clin Exp Res 1999; Schweinsburg et al. Alc Clin Exp Res 2001; Parks et al. Alc Clin Exp Res 2002.

- higher m-Ino in white matter and thalamus of recovering alcoholics

  Schweinsburg et al. Alc Clin Exp Res 2000

- less Cho in cerebellum of recovering alcoholics

  Martin et al. Alc Clin Exp Res 1995, Parks et al. Alc Clin Exp Res 2002

Weeks to months into abstinence: neuronal/axonal damage, gliosis, altered lipid metabolism

^{1}H MRSI Metabolites
1-Week-Abstinent Alcoholics vs. Controls

metabolite	region		LD n=20	RA at 1 week n=25	difference [%]	p
NAA	GM	frontal	33.3 ± 3.3	30.2 ± 3.4	-9	0.002*
		parietal	32.3 ± 3.4	30.5 ± 2.6	-6	0.02
		temporal	27.0 ± 3.2	24.1 ± 3.8	-11	0.007
	WM	frontal	32.5 ± 3.7	29.0 ± 2.9	-11	0.0006*
		parietal	31.4 ± 3.7	28.3 ± 3.1	-10	0.002
		temporal	28.7 ± 3.6	26.4 ± 2.7	-8	0.014
		occipital	32.6 ± 3.8	29.6 ± 3.3	-9	0.008
	Thalamus		37.3 ± 4.2	34.4 ± 4.2	-8	0.01*
	Caudate		32.7 ± 8.9	26.4 ± 4.9	-19	0.02*
	Lenticul. Nucl.		31.8 ± 5.2	28.8 ± 3.7	-9	0.02*
	Brainstem		35.3 ± 5.1	32.8 ± 5.7	-7	0.08*
	Cerebellum		36.0 ± 3.0	33.8 ± 3.9	-6	0.03*
Cho	GM	frontal	6.0 ± 0.7	5.6 ± 0.8	-7	0.07
		parietal	5.0 ± 0.6	4.6 ± 0.5	-8	0.02
	WM	frontal	6.1 ± 0.6	5.4 ± 0.9	-12	0.004
		parietal	5.2 ± 0.5	4.7 ± 0.8	-9	0.02
		occipital	4.6 ± 0.5	4.2 ± 0.6	-9	0.01
	Thalamus		7.2 ± 0.9	6.3 ± 1.1	-13	0.01

No significant mI or Cr group differences.

* a priori hx

Social Gatherings

Alcoholism?

So, how many “standard drinks” are this, Charlie?!