MR spectroscopy and MR morphometry of cerebral edge motion: short-term metabolic and morphometric brain changes in abstinent alcohol abusers

Martin Bendszus, Andreas Bartsch

Dept. of Neuroradiology
University of Würzburg, Germany
Background: atrophy

• Reversibility of brain atrophy in chronic alcoholism is well known
  – Sprouting of axons and dendrites?
  – Glial hyperplasia?
  – Rehydration?

• Pronounced at the early stages of sobriety

[Image: Reversible brain atrophy... Carlen et al. Science 1978; 200:1076-8]
Background: metabolism

• Chronic alcoholism vs. controls (n=6):
  – NAA/Cr reduction (6/6)
  – Additional Cho/Cr reduction (2/6)

• Longitudinal changes in sobriety (n=4)
  – No change (1/4)
  – NAA/Cr increase (1/4)
  – Cho/NAA increase (1/4)
  – NAA/Cr and Cho/Cr increase (1/4)

• Different methodology, different localization, small sample size
Purpose

• To evaluate sequential
  – Metabolic (MR-spectroscopy)
  – Morphologic (MR-morphometry)
  – Neuropsychological

changes in recently detoxified chronic alcohol abusers during early sobriety
Patients

- 15 patients
  - 10 male, mean age 42 years
  - above 5 years of primary alcohol dependence (mean: 10 years)
  - At least 5 out of 8 ICD-10 criteria (mean: 6)
  - Mean alcoholic drinks/day: 27
  - Mean drinking days/month: 28
  - Regular monitoring for abstinence
MR-Protocol

• 2 examinations:
  first: day 1-3
  second: day 36-39 after beginning of abstinence
• MRI:
  T2-w, T1-w MPR (isotropic voxel, 1mm³)
• MRS:
  Single voxel PRESS frontal lobe and cerebellum
  (+/- water suppression, 128/20 acq., TE 135 ms)
Data analysis MRS

- LC-Model 6.0-1 (Stephen Provencher)
- Absolute and ratio-based (/Cr)
  Quantification for:
  NAA, Cho, Cr, H₂O
Data analysis MRI

Morphometric detection of cerebral edge motion by SIENA (part of FSL-www.fmrib.ox.ac.uk/fsl)

1. Brain extraction (bet, Steve Smith)
2. Coregistration exam ½, FLIRT
3. Intensity profiles along edges
4. Correlate profile Derivatives
Data analysis MRI

- non-binary dilatation of flow images
- full-affine transform to standard space \((\text{MNI152, flirt, 12 DoF})\)
- (Re-) Masking by standard edge image, Gaussian smoothing \((10\text{mm FWHM})\)

Individual edge flow image superimposed on HWT

Standardized edge flow image (MNI)
Psychological performance

• Performed in parallel to MRI/MRS

• Concentration-Load Test (d2)
  - Concentration, coordination

• Audio-Visual-Learning Test (AVLT)
  - Memory
Results MRS: NAA

- cerebellum
- frontal lobe
Results MRS: Cholin

cerebellum  frontal lobe
Results MRS: Creatin, $H_2O$

No significant change
Results Morphometry

SIENA
Global recovery during abstinence
(1.85 +/- 1.32 %, p<.001, t>5.42, df=14)
Results Morphometry

SIENAL
Local recovery during abstinence
$(p_{corr} < .05, u>4.33, df=14, SnPM)$
Results SIENAL

Regeneration most pronounced
periventricular, perimesencephal, superior
vermis, frontomesial cortex
Psychological performance

Significant improvement (p<.001)
MRS vs. MR-Morphometry

(PBVC, Ps/iChol/CrRC)

s (supratentoriell): $r=0.770$, $p=.001$, $t=4.35$

i (nfratentoriell): $r=0.892$, $p=.000$, $t=7.10$

Not significant
MR-Morphometry vs. function

Significant positive correlation between brain volume increase (%) and d2 test performance improvement

\( p = 0.048, z = 1.98, \tau = 0.42 \)
MRS vs. function: NAA

Significant positive correlation between NAA increase and d2 test performance improvement

\( p=0.026, \ z=2.22, \ \tau=0.47 \)
Discussion

• Marked morphologic and metabolic recovery of brain tissue at early stages of sobriety

• Several levels of morphologic, metabolic and functional recovery which may interact
Discussion Rehydration

• probably not the main determinant
  - Constant absolute water integrals (p>.440)
  - Constant absolute Creatin values (p>.400)
  - Constant Serum Hk & MCV-values (p>.050)
Discussion Morphology

• Brain regeneration most pronounced in periventricular regions
• Repair of glial damage?
• Cholin increase is positively correlated with increase of brain tissue volume (choline: membrane marker)
• Brain volume increase also correlated with functional improvement
Discussion Metabolism

Two levels of regeneration:

A) Cholin increase
   • related to regression of atrophy
   • pronounced in the cerebellum
   • Glial regeneration

B) NAA increase
   • pronounced in the cerebrum
   • related to functional improvement
   • not related to brain volume changes
   • Sprouting of axons / dendrites
   • Restoration of neuronal function
Perspectives

Combined MRS, MRI and neuro-psychological studies offer tool for in-vivo detection of brain regeneration in abstinence

Future challenges MRS:
• absolute quantification of metabolites
• short echo times (glutamate, lipids, inositol, etc.)
• chemical shift imaging
• Multi-channel coils
• larger patient groups
Co-workers

- László Solymosi, Monika Warmuth-Metz, (Würzburg)
- Gerd Wiesbeck, Gerd Weijers, Jobst Böning, (Würzburg)
- Steve Smith, Mark Jenkinson, Peter Bannister, Image Analysis Group, FMRIB, (Oxford)

Contact
bendszus@neuroradiologie.uni-wuerzburg.de