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

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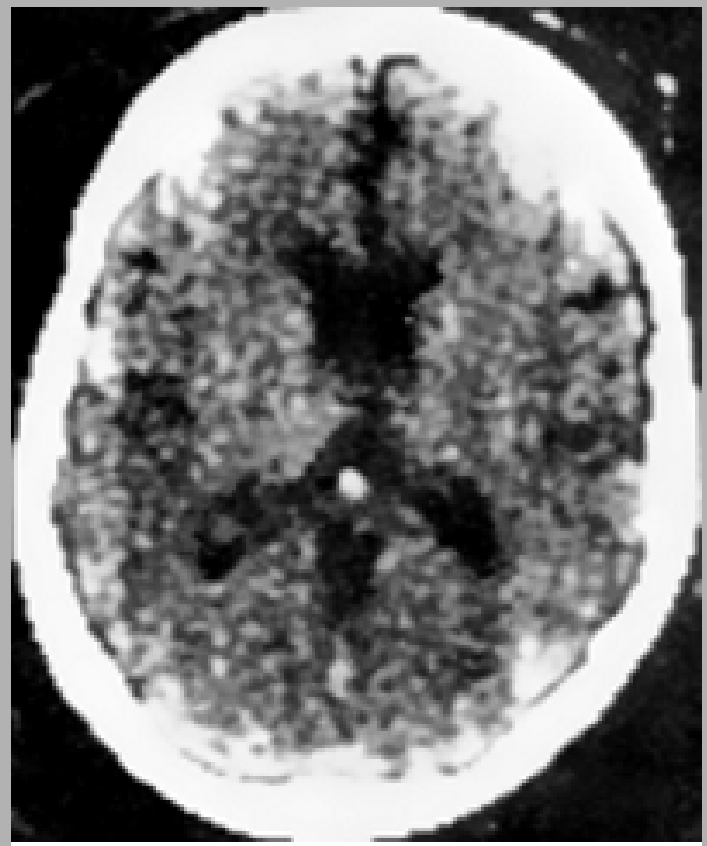
Background: atrophy

- **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**



'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)

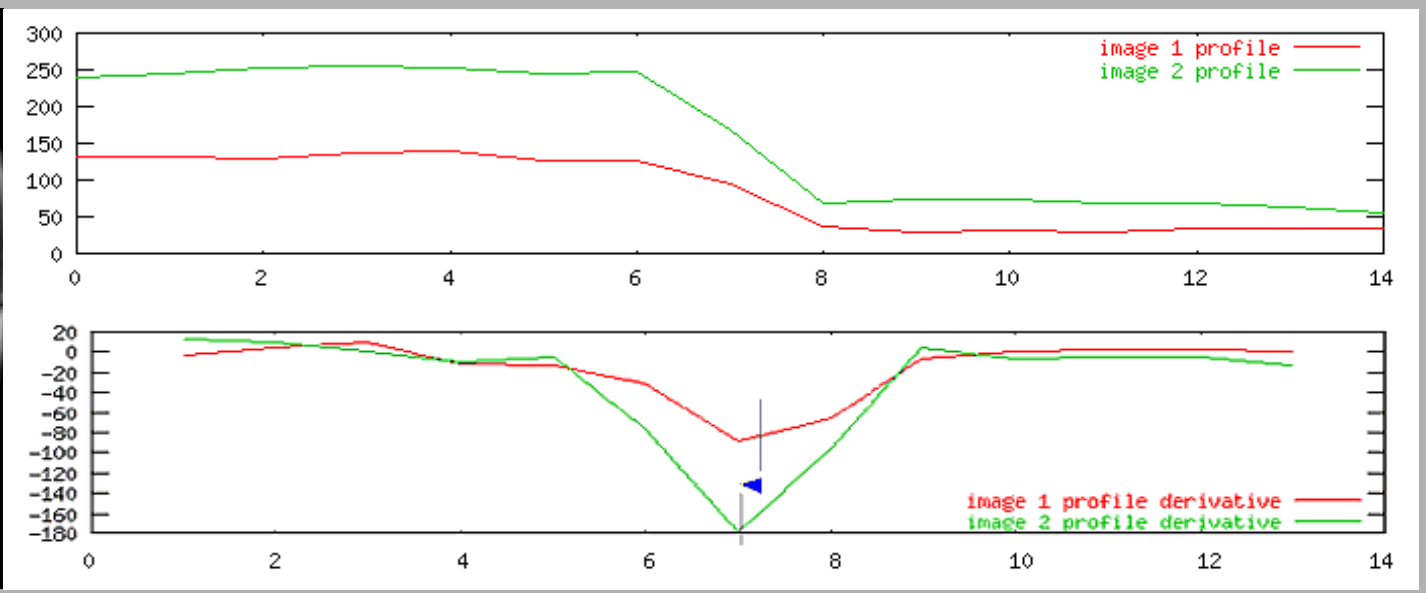
Data analysis MRS

- **LC-Model 6.0-1 (Stephen Provencher)**
- **Absolute and ratio-based (/Cr) Quantification for : NAA, Cho, Cr, H_2O**

Data analysis MRI

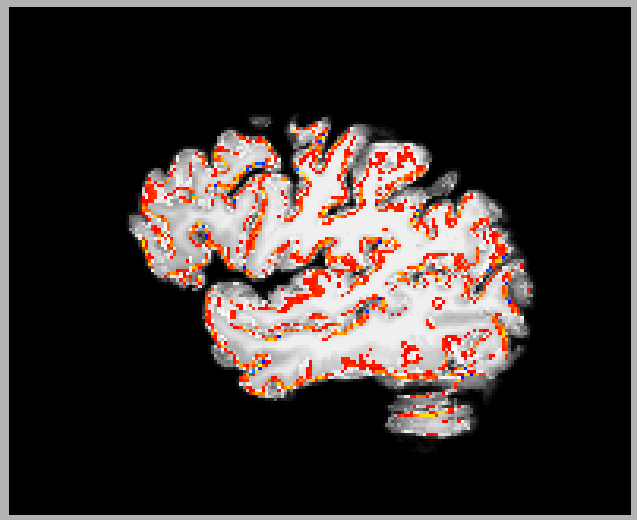
Morphometric detection of cerebral edge motion by SIENA (part of FSL-*www.fmrib.ox.ac.uk/fsl*)

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

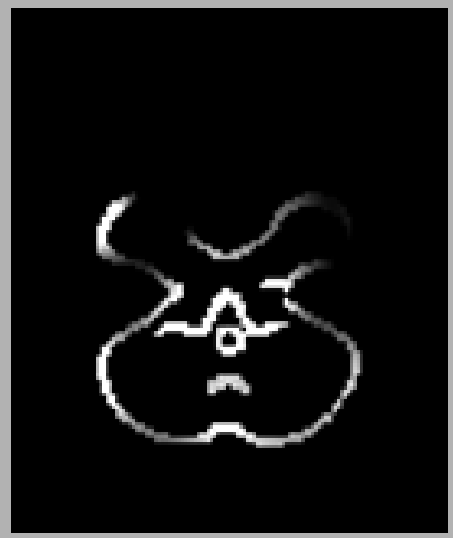


Data analysis MRI

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



Indiviadual edge flow image superimposed on HWT

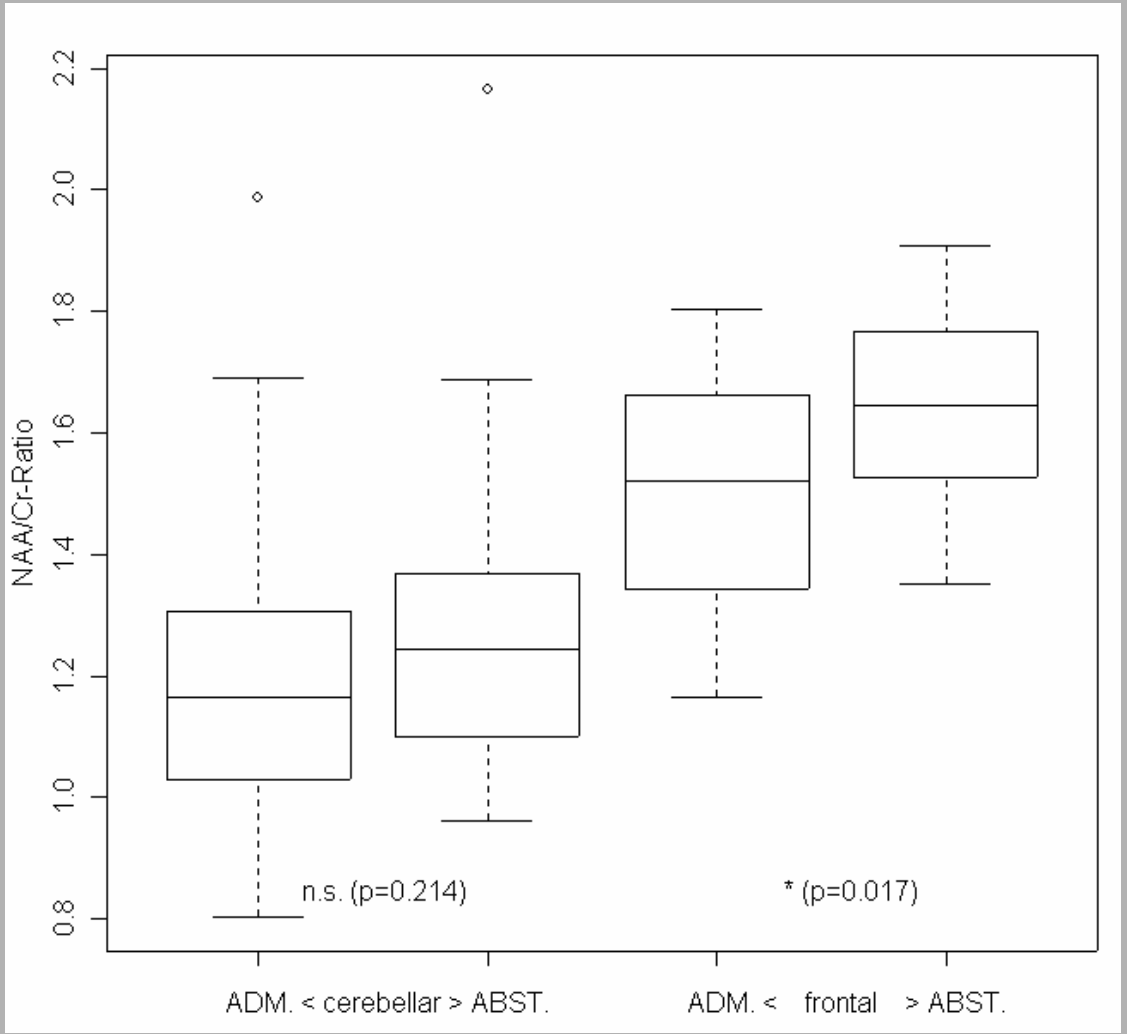


Standardized edge flow image (MNI)

Psychological performance

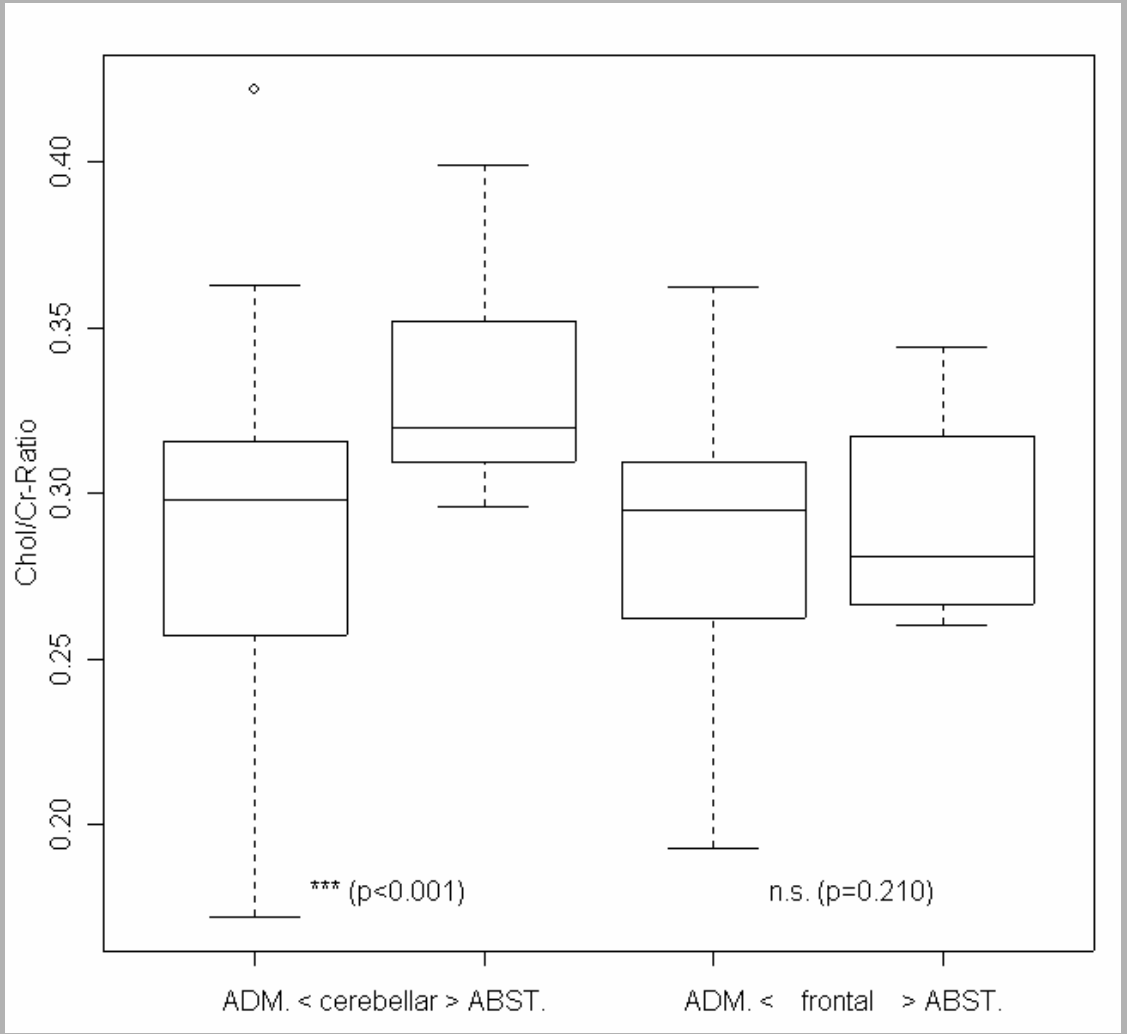
- **Performed in parallel to MRI/MRS**
- **Concentration-Load Test (d2)**
  - **Concentration, coordination**
- **Audio-Visual-Learning Test (AVLT)**
  - **Memory**

Results MRS: NAA



cerebellum ***frontal lobe***

Results MRS: Cholin



cerebellum ***frontal lobe***

Results MRS: Creatin, H_20

No significant change

Results Morphometry

SIENA

Global recovery

during abstinence

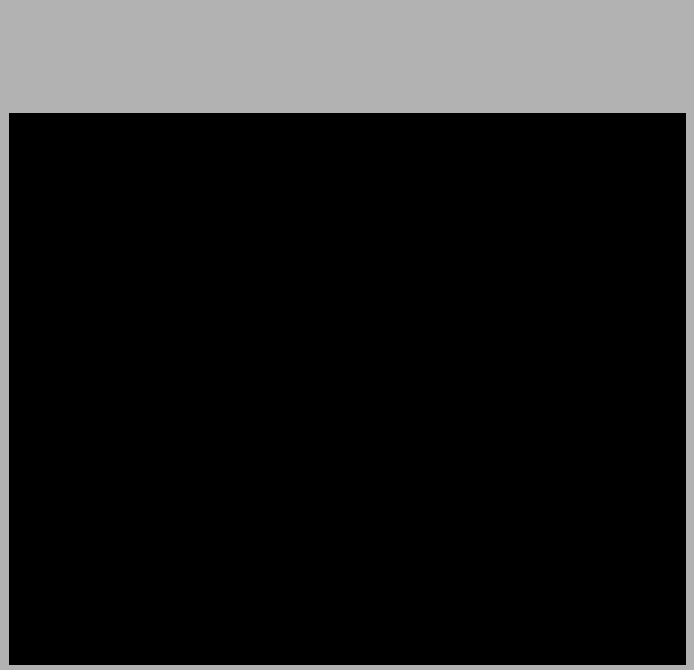
(1,85 +/- 1,32 %, p<.001,

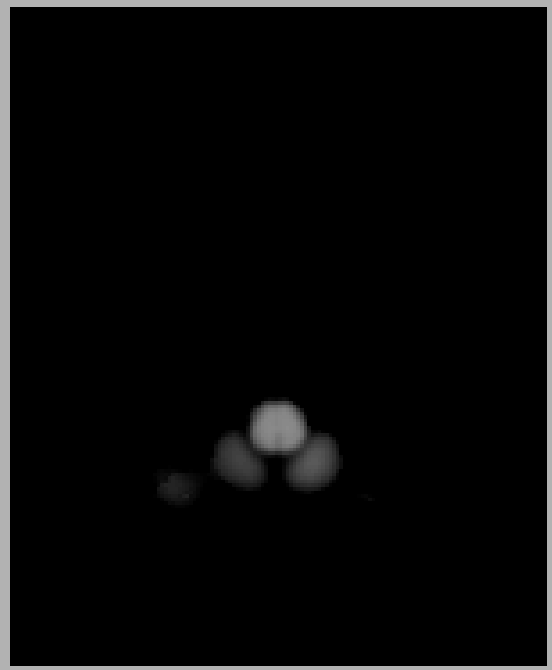
t>5.42, df=14)

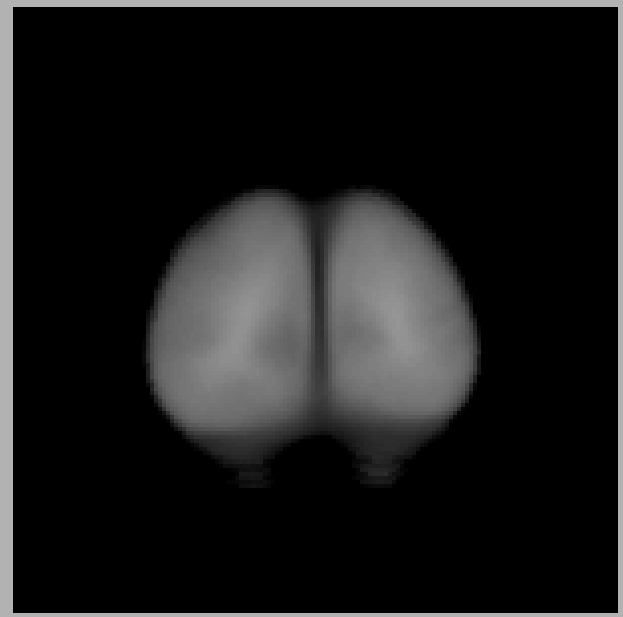
Results Morphometry

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

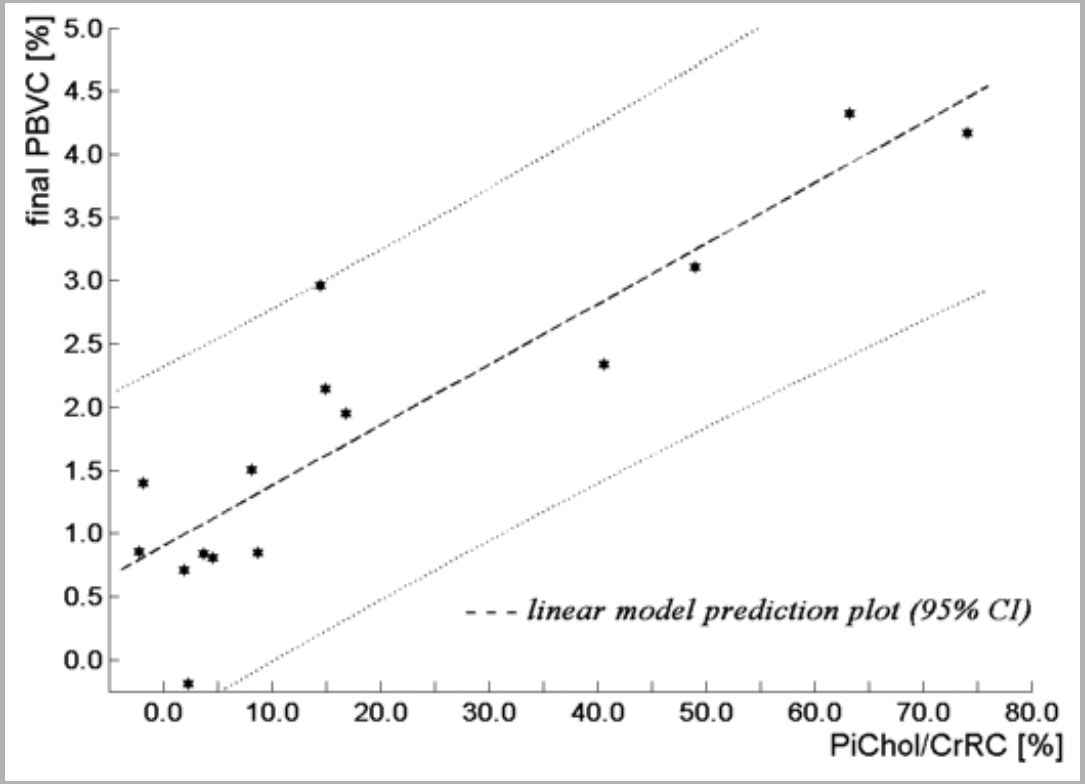
(PBVC, Ps/iChol/CrRC)

(PBVC, PS/NAA/CrRC)

Not significant

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

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



MR-Morphometry vs. function

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

(p=.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**
  (Martin et al. 1995, Parks et al. 2002, Bendszus et al. 2002)
- **Several levels of morphologic, metabolic and functional recovery which may interact**

Discussion Rehydration

- **probably not the main determinant**
  - **Constant abolute 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, inositols, 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)*

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