Hypothalamic atrophy correlates with onset of disease-defining symptoms in patients with ALS

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Piguet et al., *Ann Neurol* 2010
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- Hypothalamic alterations have been recently described in an ALS animal model (Vercruysse et al., *Brain* 2016)
Objective / Cohorts

- To investigate structural alterations in the hypothalamus and correlate the hypothalamic volume with functional measures (metabolic indices, disease progression)

Cohort (monocentric data from Ulm, Germany)

- sALS (N=251)
- fALS (N=19)
- healthy controls (N=112)
MRI-based segmentation of the hypothalamus
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Gabery et al., *Acta Neuropathol* 2010
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Makris et al., *Neuroimage* 2016
MRI-based segmentation of the hypothalamus
Data analysis

- Data were shuffled prior to the analysis.
- Both raters were blinded to any clinical demographic or genetic information.
- Inter and intra-rater reliability has been demonstrated (CV<4%, ICC>0.9).
- Quantified volumes were corrected for:
  - Intracranial volume.
  - Gender.
  - Age.
Results: Hypothalamic atrophy

→ Atrophy of the hypothalamus in ALS patients
Correlations with ALSFRS-R / DTI-Staging

→ no significant correlations
Correlations with BMI

→ significant correlation with BMI
Correlations with age at disease onset

→ hypothalamic atrophy predicts age at disease onset
Hypothalamic atrophy prior to disease-defining symptoms?

Mutation carrier cohort (monocentric data from Ulm, Germany)

presymptomatic ALS mutation carriers (N=32)
Atrophy of the hypothalamus also in presymptomatic ALS mutation carriers

Results: Hypothalamic volume in presymptomatic ALS mutation carriers

$N = 251$
$N = 112$
$N = 19$
$N = 32$

$\rightarrow$ Atrophy of the hypothalamus also in presymptomatic ALS mutation carriers
The hypothalamus is substantially atrophied in manifest ALS patients (sporadic + genetic forms) and presymptomatic ALS mutation carriers. The volume loss occurs before motor symptoms.

BMI is correlated with hypothalamic volume in ALS. Hypothalamic volume is uncorrelated with clinical data. Age at onset is predicted by the hypothalamic volume.

**Prospective:** Functional tests of the hypothalamus?
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Hans-Jürgen Huppertz (Zürich)
Angela Rosenbohm (Ulm)
Gabriele Nagel (Ulm)
Patrick Weydt (Ulm/Bonn)
Åsa Petersén (Lund)
Albert C. Ludolph (Ulm)
Jan Kassubek (Ulm) and Luc Dupuis (Strasbourg)

“Hypothalamic atrophy is related to age at onset in amyotrophic lateral sclerosis”, JNNP (in press)