

Till Burkhardt, Daniel Lüdecke, Lothar Spies, Linus Wittmann, Manfred Westphal, Jörg Flitsch

Hippocampal and cerebellar atrophy in patients with Cushings Disease

Objective

Cushing's disease (CD) may cause atrophy of different regions of the human brain, mostly affecting the hippocampus and the cerebellum. This study evaluates the use of 3-T MRI of newly diagnosed patients with CD to detect atrophic degeneration with voxel-based volumetry

Methods

Subjects with newly diagnosed, untreated CD were included and underwent 3-T MRI. Images were analyzed using a voxelwise statistical test to detect reduction of brain parenchyma. In addition, an atlas-based volumetric study for regions likely to be affected by CD was performed.

Results

Nineteen patients with a mean disease duration of 24 months were included. Tumor markers included adrenocorticotrophic hormone (median 17.5 pmol/L), cortisol (949.4 nmol/L), and dehydroepiandrosterone sulfate (5.4 µmol/L). The following values are expressed as the mean ± SD. The voxelwise statistical test revealed clusters of significantly reduced gray matter in the hippocampus and cerebellum, with volumes of 2.90 ± 0.26 ml (right hippocampus), 2.89 ± 0.28 ml (left hippocampus), 41.95 ± 4.67 ml (right cerebellar hemisphere), and 42.11 ± 4.59 ml (left cerebellar hemisphere). Healthy control volunteers showed volumes of 3.22 ± 0.25 ml for the right hippocampus, 3.23 ± 0.25 ml for the left hippocampus, 50.87 ± 4.23 ml for the right cerebellar hemisphere, and 50.42 ± 3.97 ml for the left cerebellar hemisphere.

Conclusion

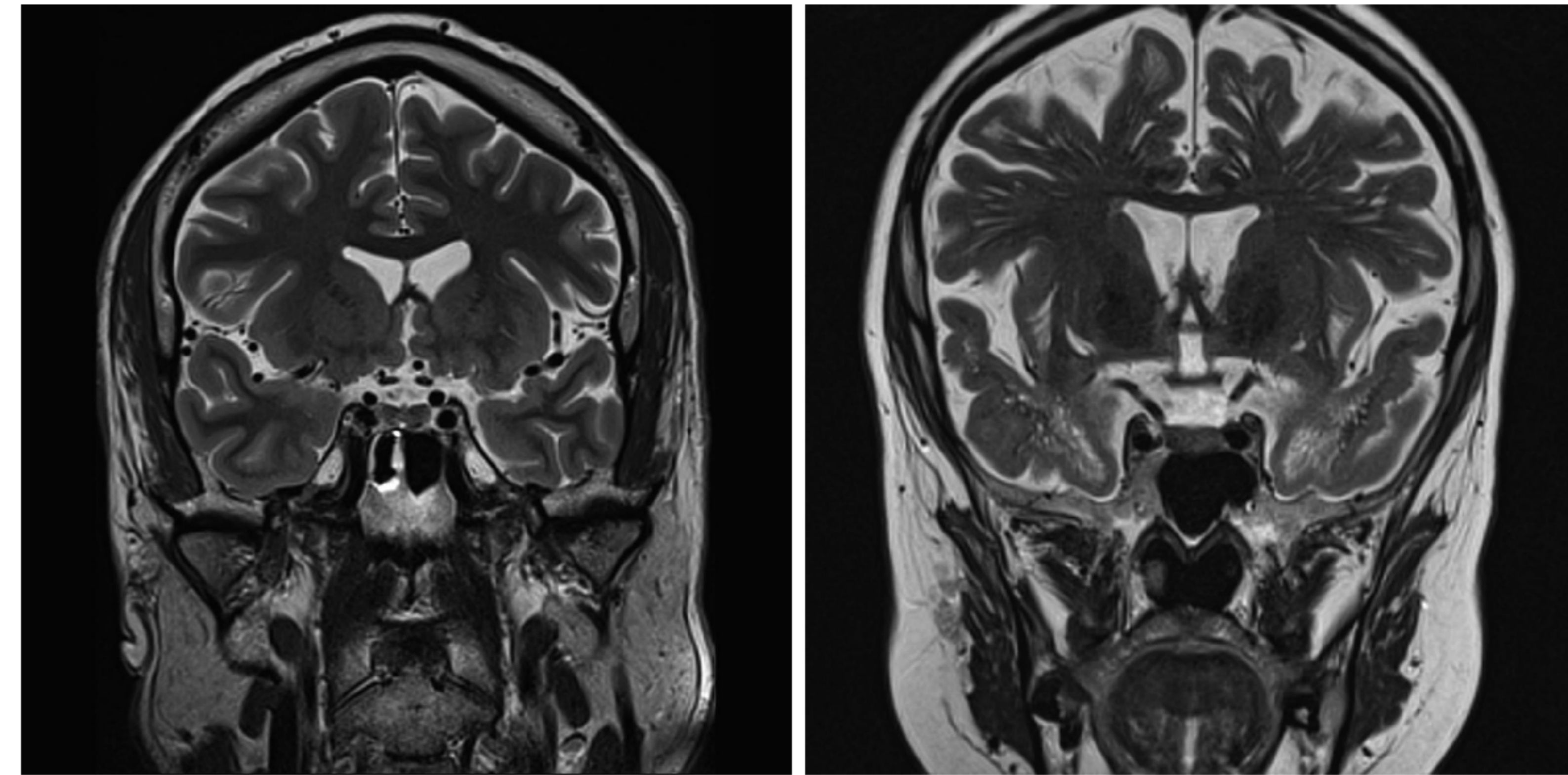
Patients with untreated CD show significant reduction of grey matter in the cerebellum and hippocampus. These changes can be analyzed and objectified with the quantitative voxel-based method described in this study.

Cluster topography

Parametric map (color map) for $p < 5e-7$ superimposed to a template in MNI space indicating areas of reduced GM. VBM was performed for all voxel belonging to the parenchymal mask (blue). (A) cross hair points to the location in the left cerebellum of the hottest voxel of the parametric map, which has a t score of 8.14. MNI coordinates are -28, -76, and -54 mm. (B) cross hair points to the location in the right limbic system (MNI coordinates: 26, 2, -18) of the second hottest voxel with a t score of 8.12.

1a: Cerebellar clusters. Cross hair center; MNI coordinates: -28, -76, -54; T score = 8.14 (hottest voxel)

1b: Hippocampal clusters. Cross hair center; MNI coordinates: 26, 2, -18; T score = 8.12 (second hottest voxel)



healthy control 42 years and CD case, 20 y
T2-weighted images for better illustration of cerebral atrophy in this case

	Controls	CD	P value
group size	40	19	
Gender (m/f)	(26/14)	(3/16)	
Age (mean +/- std) [years]	63 +/- 12	45 +/- 13	<0.0001 (two tailed)
TIV (mean +/- std) [ml]	1424 +/- 113	1352 +/- 124	0.03 (two tailed)
HVR (mean +/- std) [ml]	3.22 +/- 0.42	3.06 +/- 0.37	0.08 (one tailed)
HVR ad (mean +/- std) [ml]	3.22 +/- 0.25	2.90 +/- 0.26	<0.0001 (one tailed)
HVL (mean +/- std) [ml]	3.23 +/- 0.43	3.12 +/- 0.31	0.12 (one tailed)
HVL ad (mean +/- std) [ml]	3.23 +/- 0.25	2.89 +/- 0.28	<0.0001 (one tailed)
CVR (mean +/- std) [ml]	50.87 +/- 6.24	44.98 +/- 5.93	0.0005 (one tailed)
CVR ad (mean +/- std) [ml]	50.87 +/- 4.23	41.95 +/- 4.67	<0.0001 (one tailed)
CVL (mean +/- std) [ml]	50.42 +/- 5.87	45.00 +/- 6.06	0.0009 (one tailed)
CVL ad (mean +/- std) [ml]	50.42 +/- 3.97	42.11 +/- 4.59	<0.0001 (one tailed)

Cluster volumes

TIV=total intracranial volume; HVR=hippocampal volume right; HVL=hippocampal volume left; CVR=cerebellar volume right; CVL=cerebellar volume left

All volumes were adjusted to the mean TIV (1424 ml) and mean age (63 yrs) of the control group using bilinear regression.

*one-tailed two sample t test

