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BRAIN MRI ABNORMALITIES IN KENNEDY'S DISEASE

P. M. Ferraro,[1] F. Agosta,[1] G. Querin,[4] N. Riva,[2] C. Bertolin,[4] E. Da Re,[4] M. Copetti,[5]
G. Comi,[2] A. Falini,[3] G. Sorarù,[4] M. Filippi.[1,2]

[1]Neuroimaging Research Unit, [2]Department of Neurology, Institute of Experimental Neurology, and [3]Department of Neuroradiology and CERMAC, Division of Neuroscience, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; [4]Department of Neurosciences, University of Padova, Padova, Italy; [5]Biostatistics Unit, IRCCS-Ospedale Casa Sollievo della Sofferenza, San Giovanni Rotondo, Foggia, Italy.

INTRODUCTION and OBJECTIVE

✓ Kennedy's Disease (KD) is a rare X-linked neurodegenerative disorder affecting spinal and bulbar lower motor neurons, associated with a trinucleotide (CAG) repeat expansion in the first exon of the androgen receptor (AR) gene.[1]

✓ There is preliminary evidence that KD might be more than a selective disorder of the lower motor neurons, highlighting the possible multisystemic nature of the disease.

✓ Diagnosis of KD might be challenging. Prior studies reported a mean time of 5.5 years from symptoms onset to diagnosis.[2] KD patients are often misdiagnosed as amyotrophic lateral sclerosis (ALS).

✓ Subtle brain Magnetic Resonance Imaging (MRI) structural alterations in KD patients have been reported.[3] However, the extent of central nervous system involvement relative to ALS phenotypes still needs to be clarified.

✓ Aim of our study was to investigate cortical and white matter (WM) alterations in a large sample of KD patients compared to healthy subjects and sporadic ALS patients.

MATERIALS and METHODS

✓ 19 patients with genetically confirmed KD (ALSFRS-r: 42.45 ± 1.54; disease duration: 135 ± 55 months), 17 sporadic non-demented ALS patients (ALSFRS-r: 42.35 ± 3.16; disease duration: 21 ± 20 months) and 21 age and sex matched healthy subjects were enrolled.

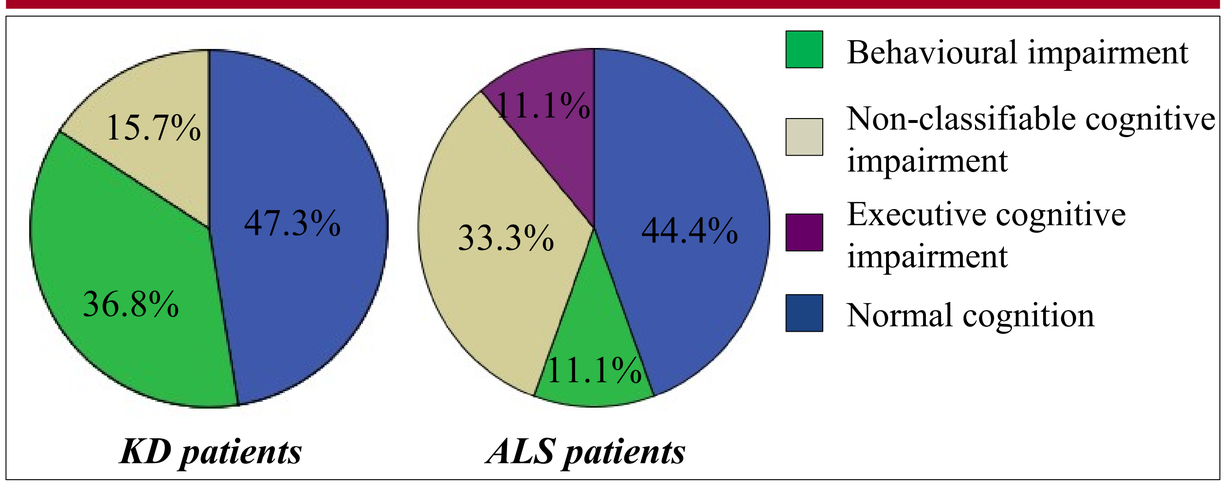
✓ All patients underwent clinical evaluation, neuropsychological assessment, T1-weighted and diffusion tensor (DT) MRI.

✓ A surface-based morphometry analysis was used to assess cortical thickness.

✓ Tract-based spatial statistics was applied to investigate DT MRI metrics of WM tracts.

✓ ANOVA models were used to compare MRI features between groups.

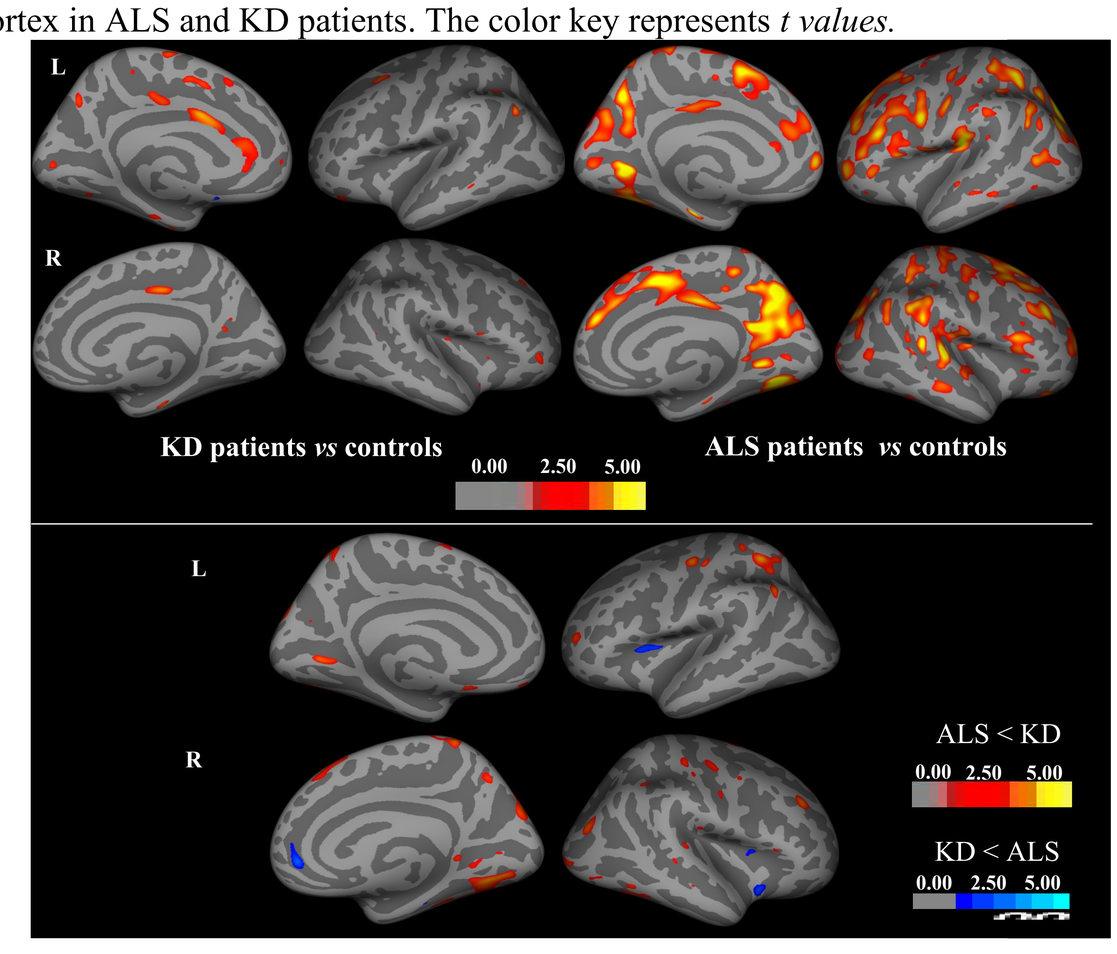
COGNITIVE RESULTS



✓ According to recent criteria,[4] KD patients were characterized by pronounced behavioral symptoms and only subtle cognitive deficits.

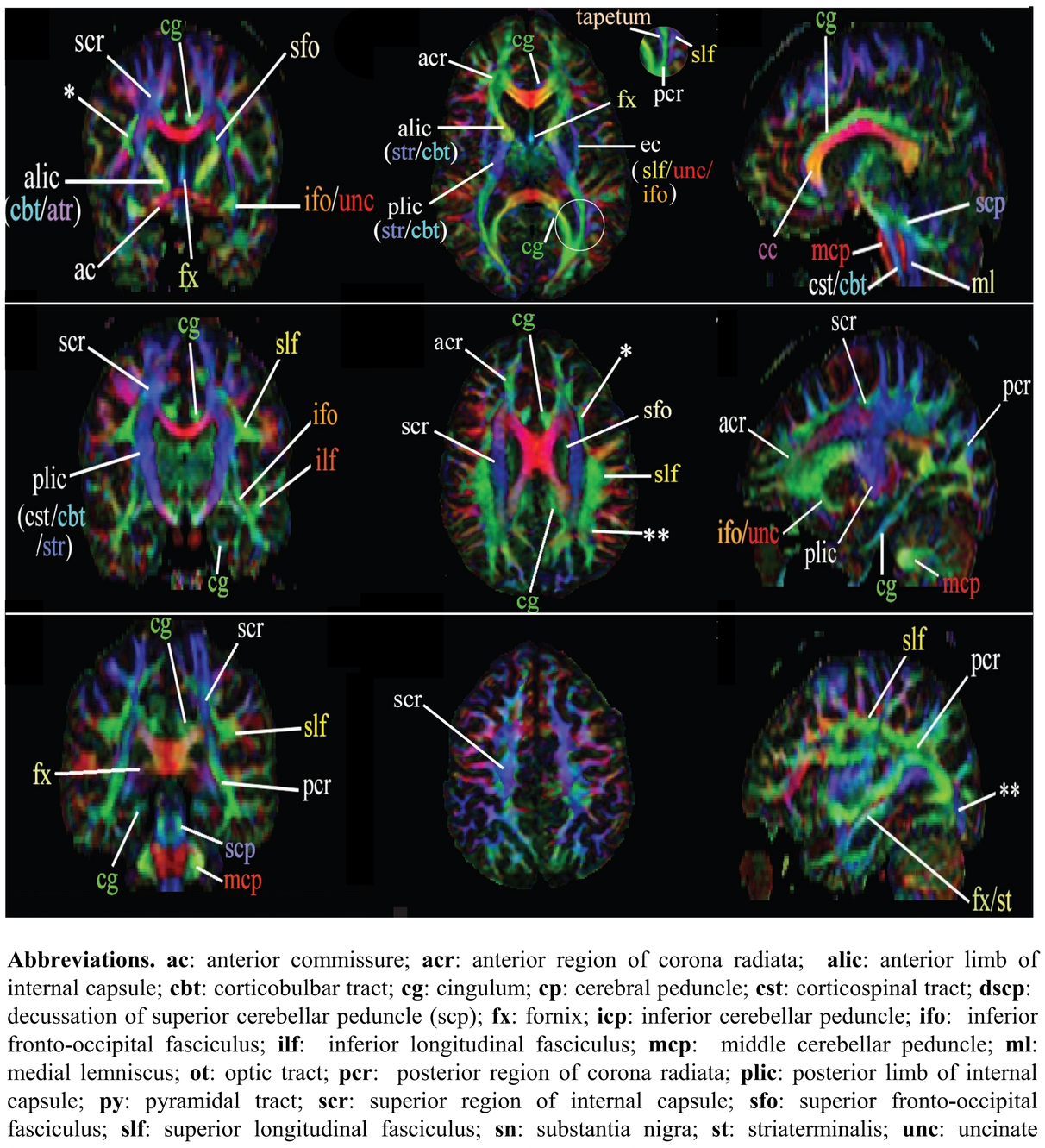
CORTICAL THICKNESS ANALYSIS

Fig.1 Three-dimensional reconstructed MR imaging maps show distribution of the cortical thinning on the inflated surface in the left (L) and right (R) sides of the Cortex in ALS and KD patients. The color key represents *t values*.



TRACT-BASED SPATIAL STATISTICS

Fig.2 DT imaging color maps of WM fibers[5] assessed in patients and controls. On color maps, red, green, and blue represent fibers running along right-left, anterior-posterior, and superior-inferior axes, respectively.



Abbreviations. ac: anterior commissure; **acr**: anterior region of corona radiata; **alic**: anterior limb of internal capsule; **cbt**: corticobulbar tract; **cg**: cingulum; **cp**: cerebral peduncle; **cst**: corticospinal tract; **dscp**: decussation of superior cerebellar peduncle (scp); **fx**: fornix; **icp**: inferior cerebellar peduncle; **ifo**: inferior fronto-occipital fasciculus; **ilf**: inferior longitudinal fasciculus; **mcp**: middle cerebellar peduncle; **ml**: medial lemniscus; **ot**: optic tract; **pcr**: posterior region of corona radiata; **plic**: posterior limb of internal capsule; **py**: pyramidal tract; **scr**: superior region of internal capsule; **sfo**: superior fronto-occipital fasciculus; **slf**: superior longitudinal fasciculus; **sn**: substantia nigra; **st**: striaterminalis; **unc**: uncinate fasciculus; *: short-range association fibers; **: vertical occipital fasciculus.

✓ KD patients showed decreased fractional anisotropy (FA) of the pontine crossing fibers (p= 0.04), right fronto-temporal and fronto-occipital tracts (p= 0.04) relative to controls; they also showed increased mean diffusivity (MD) and radial diffusivity (radD) of the right cingulum (p= 0.05; p= 0.04).

✓ ALS patients showed reduced FA and increased MD of the corticospinal tract (p= 0.01; p= 0.02) and corona radiata bilaterally (p= 0.05; p= 0.02) relative to controls, with an additional involvement of the left superior longitudinal (p= 0.03), frontotemporal and fronto-occipital tracts (p= 0.03).

✓ The involvement of the corticospinal tract (p= 0.01), corpus callosum (p= 0.03; p= 0.01), external capsule bilaterally (p= 0.003; p= 0.002) and left superior longitudinal fasciculus (p= 0.007) was greater in ALS compared to KD patients.

CONCLUSIONS

✓ To date, this is the largest study assessing brain structural changes in KD patients.

✓ Our findings demonstrated subtle cortical abnormalities and the involvement of long-range frontal and limbic connections in patients with KD, probably related to the behavioural abnormalities observed.

✓ The pattern of damage of frontal and limbic WM tracts is similar in KD and ALS patients, while DT MRI measures of the corticospinal tract and corpus callosum are proven to be powerful tools to differentiate ALS from mimic syndromes, including KD.

✓ Our study confirms that MRI might represent a useful tool in the differential diagnosis between motor neuron disease phenotypes.

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