Identification of the key role of white matter in the pathogenesis of Huntington's Disease

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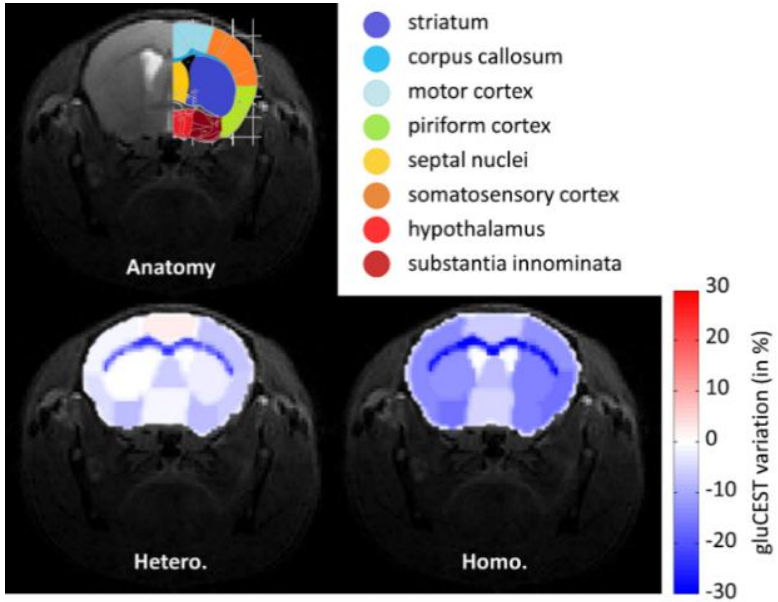
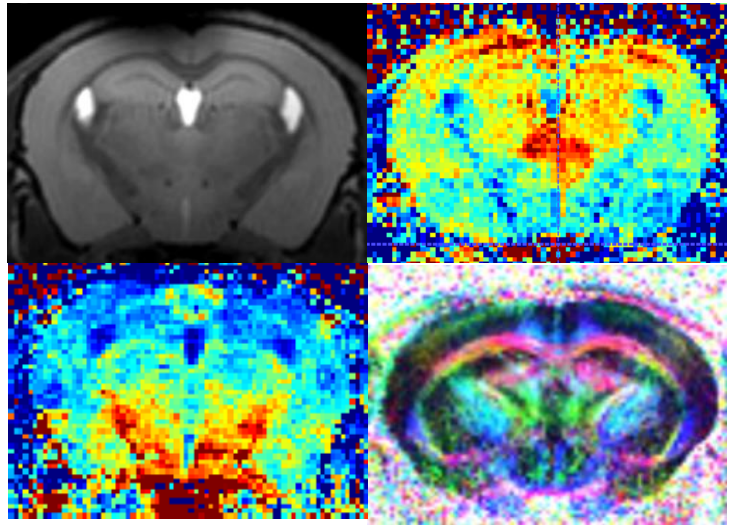
Introduction

- **White matter in HD:**
  - Early atrophy
  - Oligodendrocytes deficiency
  - Impaired synapses

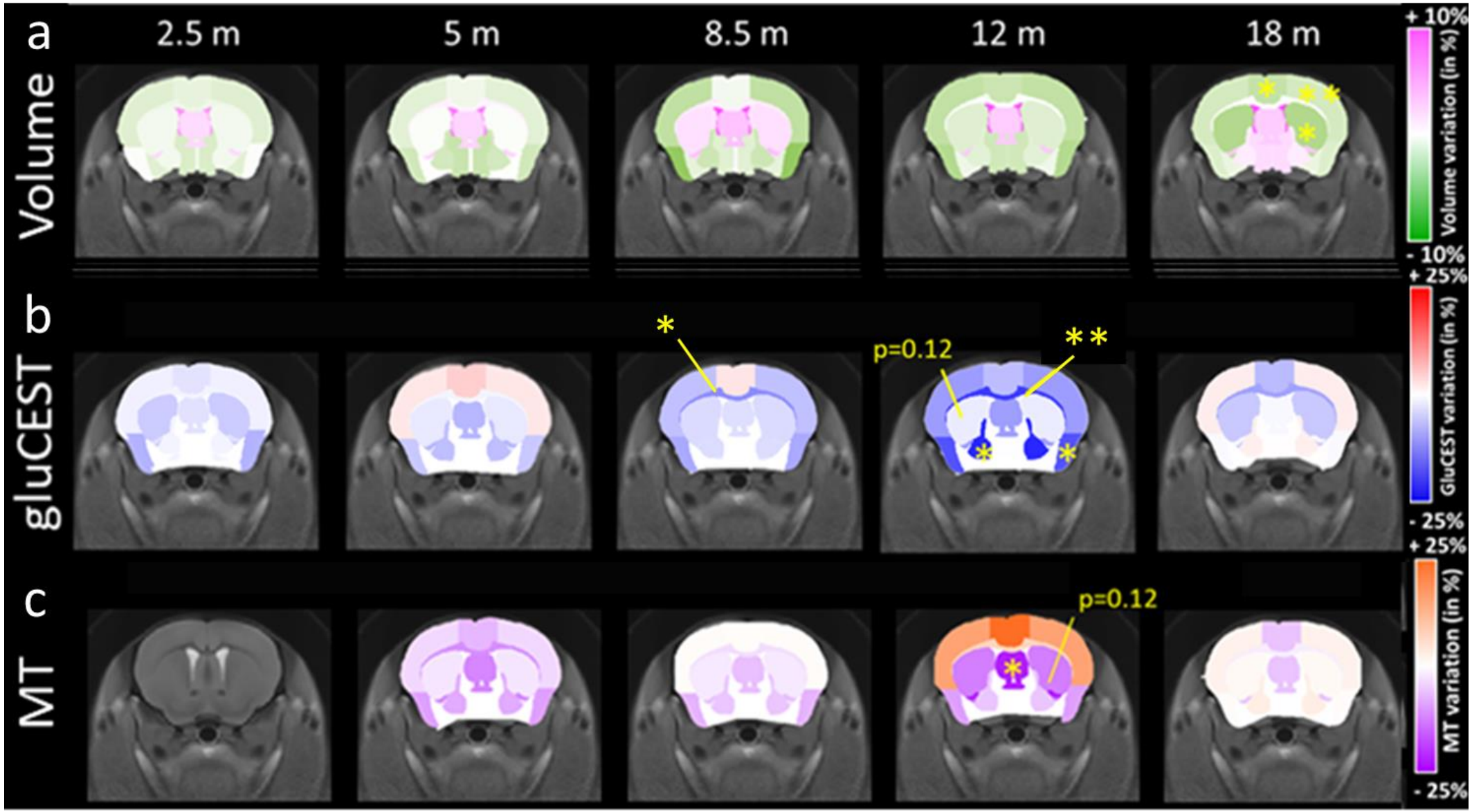
- **White matter preclinical imaging:**
  - Early atrophy, altered diffusion
  - Reduced oligodendrocytes activity, demyelination
  - gluCEST defect in CC of CAG140 mice at 12 m (Pépin et al. 2016)



- **Imaging at 11.7T Bruker MRI with cryoprobe:**
  - Anatomic imaging (a)
  - gluCEST (b) (t_{sat}=1 s, B_1=5 µT, δ=[-5:0,5:5] ppm)
  - Magnetization transfer (c) (t_{sat}=1 s, B_1=10 µT, δ=[-16;16] ppm)
  - Diffusion Tensor Imaging (d)

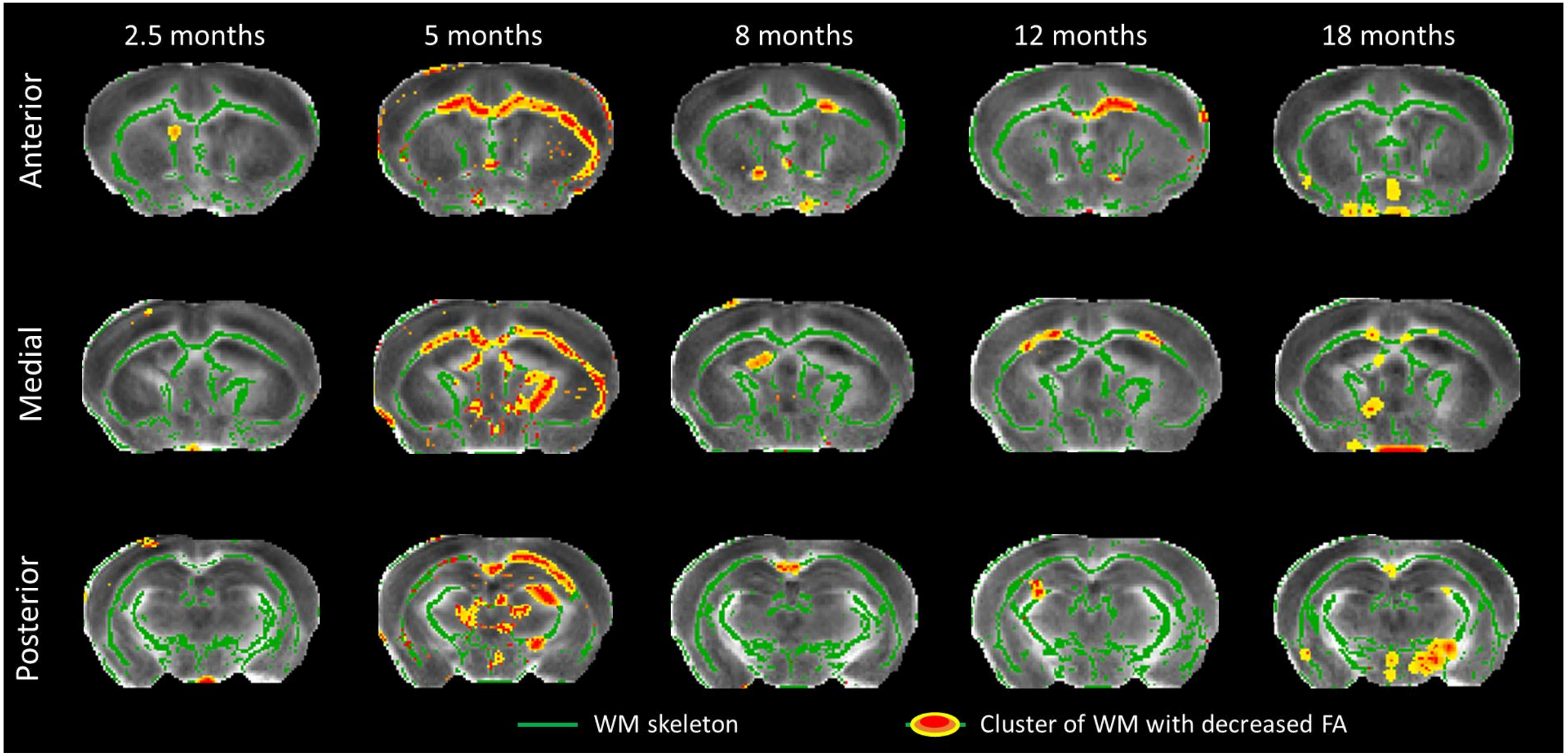


Results

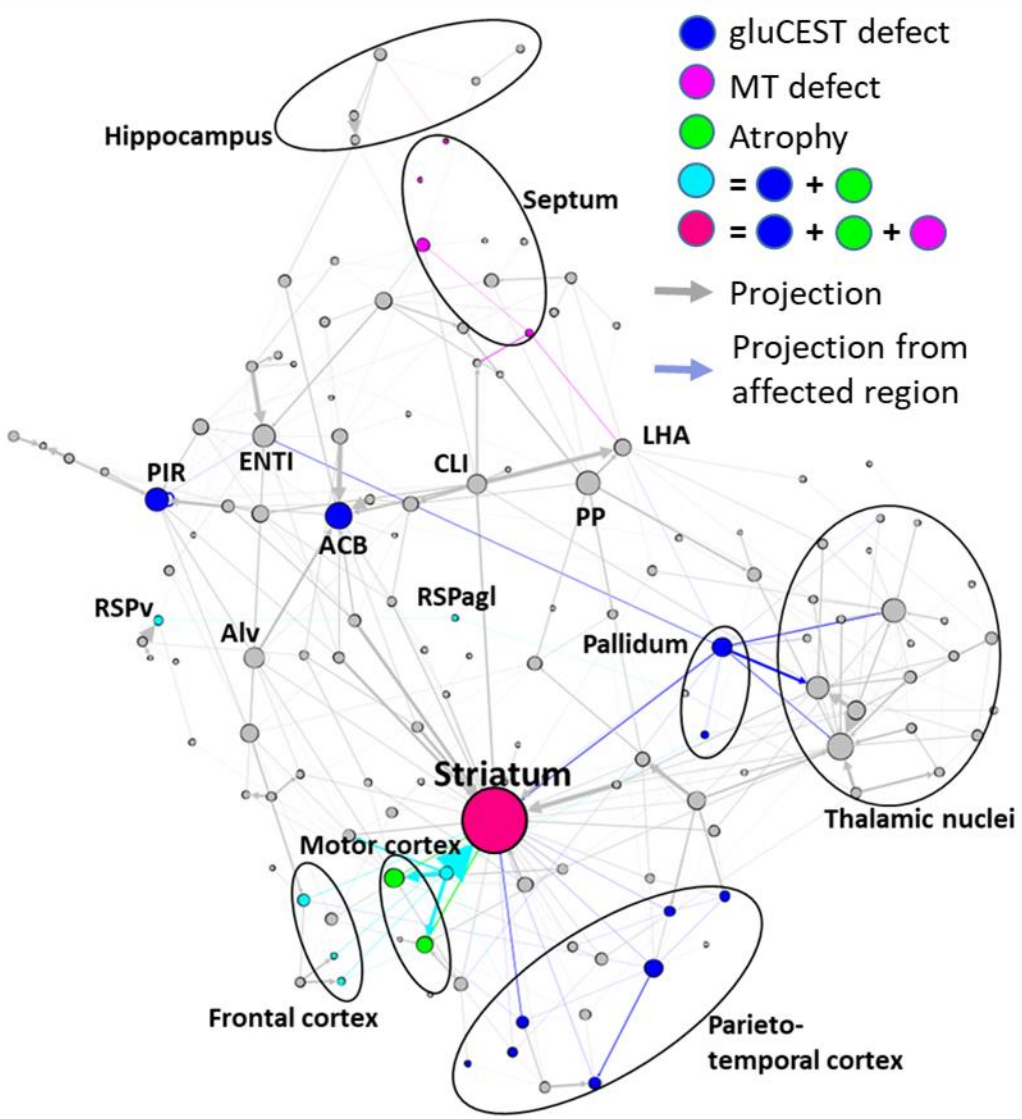

a
Volume
2.5 m
5 m
8.5 m
12 m
18 m
+ 10%
Volume variation (in %)
- 10%
b
gluCEST
*
p=0.12
**
+ 25%
GluCEST variation (in %)
- 25%
c
MT
p=0.12
+ 25%
MT variation (in %)
- 25%

Results

Fractional Anisotropy



Discussion



- **Physical connectivity graph**
  - Arrows: Normalized projection densities (from Oh et al. 2014)
  - Nodes: size represents importance in the network
- **Network**
  - High-degree nodes form a network
  - Centrality of the striatum
- **Overlaying our results**
  - Striatum is vulnerable in CAG140
  - High degree regions surrounding striatum are affected in CAG140
- **Pivotal role of white matter**
  - Cortico-striatal connections
  - Evidences of vulnerability in HD
  - Transfer to clinic