INTRODUCTION AND PURPOSE

- The thalamus is a critical node in networks supporting cognitive functions, including memory and executive functions as well as attention and information processing speed [1].
- Thalamic involvement in MS has been reported by both pathologic and imaging studies.
- A few MRI studies have shown thalamic atrophy in pediatric MS patients with MS.
- The thalamus is an extremely complex structure, organized in nuclear groups with specific functions and connections with cortical and subcortical areas.
- The study of the whole thalamus could be inadequate to explain deficits of specific cognitive functions.
- Integration of DTI tractography with high-resolution T1 structural anatomical imaging has allowed a connectivity-based parcellation of the thalamic subregions and tracing their connections with the cortex.

OBJECTIVES

- To apply connectivity-based segmentation to define the distribution of regional thalamic damage in pediatric MS patients and correlate MRI abnormalities and atrophy in pediatric MS patients.
- To assess the role of abnormalities of thalamic connectivity defined regions (CDR) and their cortical connections for cognitive impairment in pediatric MS patients.

METHODS

- 44 right-handed pediatric MS patients and 26 age- and sex-matched healthy controls (HCs) were enrolled.
- Neurocognitive examination:
  - Clinical evaluation.
  - EDSS score rating.
- Neurophysiological assessment:
  - Expanded Neuropsychological Battery for Children, standardized and validated for Italian pediatric MS [2].
  - Assesses for each of cognitive domains (attention, verbal memory, spatial memory) and verbal (fluency) and a global Z-score of cognitive function (obtained by averaging Z-scores of all tests) were calculated.

MRI Acquisition (3 T systems):
- Parallel acquisition SE EPI with SENSE (acceleration factor=2) and diffusion gradients applied in 30 non-collinear directions. Two optimised b factors were used for acquiring diffusion weighted images (b=0 and b=900 s/mm²).
- Dual-echo TSE.
- 3D TI-weighted fast-filed echo scan.

Conventional MRI analysis:
- Mean/Standard Deviation of T2 hypointensities and T1 hypointense lesion volumes (LV).
- Quantification of normalized brain (NVI), white matter (WMV) and gray matter (GMV) volumes (SEIAX).

Table 3 shows the main demographic and clinical characteristics of the enrolled study subjects.

| Subject | Age (years) | Gender | Sex | Disability | Education | Occupation | Employment | Economic Status | Health Status | Comorbidities | H&Y | EDSS | EDSS SD | CDR FA | EDSS CDR FA | EDSS CDR FA SD | EDSS CDR FA P | EDSS CDR FA CI |
|---------|-------------|--------|-----|------------|-----------|------------|------------|----------------|---------------|--------------|------|-------|----------|--------|--------------|----------------|----------------|----------------|----------------|
| Mean    | 16.5 (9.1) | Male   | 57% | 3.1 (0.8)  | 9.4 (1.4) | 0.8 (0.5)  | 0.25 (0.5) | 0.18 (0.5)    | 0.10 (0.15)   | 0.03 (0.5)   | 0.03 | 0.03 | 0.04    | 0.04  | 0.03       | 0.03 (0.02)    | 0.03 (0.02)    | 0.03 (0.02)    | 0.03 (0.02)    |
| SD      | 4.6 (1.2)  |        |     | 0.9 (0.3)  | 1.2 (0.6) | 0.3 (0.2)  | 0.2 (0.3)  | 0.1 (0.2)     | 0.1 (0.15)    | 0.0 (0.0)    | 0.07 | 0.07 | 0.03    | 0.04  | 0.03       | 0.03 (0.02)    | 0.03 (0.02)    | 0.03 (0.02)    | 0.03 (0.02)    |

Table 3. MRI parameters of thalamic and cortical regions.

RESULTS

Table 2. DTI metrics of left and right thalamic CDRs.

<table>
<thead>
<tr>
<th>Region</th>
<th>Left thalamus</th>
<th>Right thalamus</th>
<th>p value</th>
<th>Left thalamus</th>
<th>Right thalamus</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA</td>
<td>0.44 (0.02)</td>
<td>0.45 (0.02)</td>
<td>0.03</td>
<td>0.43 (0.01)</td>
<td>0.41 (0.02)</td>
<td>0.12</td>
</tr>
<tr>
<td>MD</td>
<td>0.77 (0.02)</td>
<td>0.76 (0.01)</td>
<td>0.01</td>
<td>0.77 (0.02)</td>
<td>0.75 (0.01)</td>
<td>0.001</td>
</tr>
<tr>
<td>T2-T1</td>
<td>0.46 (0.03)</td>
<td>0.46 (0.03)</td>
<td>0.13</td>
<td>0.47 (0.03)</td>
<td>0.47 (0.03)</td>
<td>0.007</td>
</tr>
<tr>
<td>PVT-T1</td>
<td>0.43 (0.02)</td>
<td>0.43 (0.02)</td>
<td>0.05</td>
<td>0.44 (0.02)</td>
<td>0.44 (0.02)</td>
<td>0.001</td>
</tr>
<tr>
<td>PP-T1</td>
<td>0.77 (0.04)</td>
<td>0.76 (0.04)</td>
<td>0.15</td>
<td>0.75 (0.04)</td>
<td>0.75 (0.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>T-4-T1</td>
<td>0.49 (0.02)</td>
<td>0.49 (0.02)</td>
<td>0.01</td>
<td>0.49 (0.02)</td>
<td>0.49 (0.02)</td>
<td>0.001</td>
</tr>
<tr>
<td>O-4-T1</td>
<td>0.50 (0.01)</td>
<td>0.50 (0.01)</td>
<td>0.004</td>
<td>0.51 (0.01)</td>
<td>0.51 (0.01)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 3. MRI metrics of left and right thalamic cortico-thalamic tracks.

CONCLUSIONS

- Similarity to what has been described in adults, both regions of increased and decreased thalamic FA were detected in pediatric MS patients, which might reflect a complex interplay between GM (increased FA) and WM (decreased FA) damage at the level of this structure.
- Damage to specific thalamic-cortical connections in addition to regional thalamic damage explained patients’ global cognitive profile as well as impairment at specific cognitive tests, suggesting that cognitive impairment in pediatric MS is likely due to a cortico-thalamic subcortical lesion.

REFERENCES


DISCLOSURES

- This study was supported by the Italian Ministry of Health and the Italian Ministry of Education, University, and Research.
- The authors have no potential conflicts of interest to disclose.

- The authors have no potential conflicts of interest to disclose.