[P334] Third ventricle enlargement correlates to different patterns of regional fiber integrity in the corpus callosum of relapsing-remitting and secondary progressive multiple sclerosis patients

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Background: Enlargement of the 3rd ventricle in multiple sclerosis (MS) occurs early and its prognostic value for long-term disease progression has been shown. Complementary corpus callosum (CC) degeneration accompanied by tissue atrophy and fiber degeneration is found most frequently.

Objective: To investigate the impact of regional differences in CC degeneration quantified by DTI (diffusion tensor imaging) on 3rd ventricle expansion in different MS subtypes and healthy subjects.

Methods: For 34 MS patients [16 relapsing-remitting (RR), 18 secondary-progressive (SP)] and 20 age matched control subjects axial EPI DTI datasets and thin-sliced sagittal T1-weighted images were acquired on a 1.5T MRI scanner and post-processed using the MeVisLab© software system. The 3rd ventricle volume (3VV) was quantified and normalized to the intra-cranial cavity volume. The CC was subdivided into 7 segments to evaluate regional fractional anisotropy (FA), mean diffusivity (MD), and whole CC FA and MD results. Segments 1-3 correspond to frontal/prefrontal cortical areas, segments 4 and 5 to sensomotoric areas and segments 6 and 7 to parietal/occipital cortical areas. Clinical parameters included EDSS, disease duration and maximal walking distance. Mean group differences and correlations between the 3VV and DTI based quantitative MR parameters were assessed.

Results: In contrast to healthy controls (0.82 ml) MS patients presented significant higher 3VV (SPMS: 1.90 ml, $p<0.001$; RRMS: 1.34 ml, $p=0.002$) and a significant reduction of FA and increase of MD (both age corrected) in the whole CC (FA/MD in controls: 0.60/0.95 RR: 0.50/1.10 SP: 0.43/1.23, p always < 0.001) and in all CC subregions. Generally, anterior (2) and posterior (7) segments had higher FA and lower MD than the central regions. In RRMS only moderately significant correlations were found between FA / MD and 3VV in segment 2. In contrast, correlations between the 3VV and regional FA and MD were highly significant in the segments 2-4 and segment 7 (only FA) in the SPMS group. Similarly, whole CC DTI indices correlated well to 3VV in SPMS, but not in the RRMS subgroup.

Conclusion: 3rd ventricle enlargement in MS is accompanied by CC degeneration which shows different regional patterns of influence in RRMS and SPMS. In the relapsing-remitting stage DTI results in the anterior CC segments seems to be most sensitive, while in progressive MS, FA and MD in the anterior and the posterior CC segments are involved.

Third ventricle enlargement correlates to different patterns of regional fiber integrity in the Corpus Callosum of Relapsing-Remitting and Secondary Progressive Multiple Sclerosis Patients

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Introduction

Enlargement of the 3rd ventricle in multiple sclerosis (MS) occurs early and its prognostic value for long-term disease progression has been shown [1]. Similarly corpus callosum (CC) degeneration accompanied by tissue atrophy and fiber degeneration is found most frequently, also in early stages of MS [2].

Objective

To investigate the impact of regional differences in CC degeneration quantified by DTI (diffusion tensor imaging) on 3rd. ventricle expansion in different MS subtypes and healthy subjects.

Methods

For 34 MS patients and 20 age matched control subjects (Table 1) axial EPI DTI datasets and thin-sliced sagittal T1-weighted images were acquired on a 1.5T MRI scanner and post-processed using the MeVisLab© software system.

The 3rd. ventricle volume (3VV) was quantified and normalized to the intra-cranial cavity volume. The CC was subdivided into 7 segments to evaluate regional fractional anisotropy (FA), mean diffusivity (MD), and whole CC FA and MD results. Segments 1-3 correspond to frontal/prefrontal cortical areas, segments 4 and 5 to senso-motoric areas and segments 6 and 7 to parietal/occipital cortical areas [3]. All DTI results were corrected for natural aging effects. Clinical parameters included EDSS and disease duration. Mean group differences and correlations between the 3VV and DTI based quantitative MR parameters were assessed.

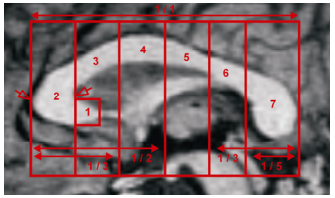

Figure 1: Subdivision of the corpus callosum into 7 segments

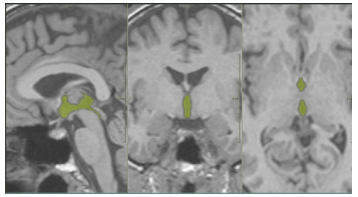

Figure 2: Volumetry of the 3rd. ventricle by semi-automatic segmentation

Results

In contrast to healthy controls MS patients presented significant higher 3VV and a significant reduction of FA and increase of MD (both age corrected) in the whole CC and in all CC sub-regions. Differences between the MS subgroups were significant for 3VV, whole CC FA and MD in CC-section 2. Generally, anterior (2) and posterior (7) segments had higher FA and lower MD than the central regions. In RRMS only moderately significant correlations were found between FA / MD and 3VV in segment 2. In contrast, correlations between the 3VV and regional FA and MD were highly significant in the segments 2-4 and segment 7 (only FA) in the SPMS group. Similarly, whole CC DTI indices correlated well to 3VV in SPMS, but not in the RRMS subgroup.

			Control group Mean ± SD	RRMS Mean ± SD	SPMS Mean ± SD	Correlations between 3. ventricle volume and DTI indices in CC	
						RRMS	SPMS
3. ventricle volume / ml			0.86±0.46	1.38±0.56 ◆◆,◆	1.90±0.82 ◆◆,◆		
FA in whole CC			0.61±0.05	0.51±0.10 ◆◆,◆	0.43±0.10 ◆◆,◆	r=-0.332 p=0.227	r=-0.688** p=0.002
MD in whole CC			0.94±0.08	1.09±0.17 ◆◆	1.23±0.25 ◆◆	r=0.484 p=0.067	r=0.599** p=0.009
		CC-section					
FA	anterior	2	0.73±0.06	0.60±0.11 ◆◆	0.53±0.13 ◆◆	r= -0.535* p=0.040	r=-0.556* p=0.014
		3	0.59±0.06	0.44±0.10 ◆◆	0.41±0.10 ◆◆	r=-0.239 p=0.391	r=-0.627** p=0.005
		4	0.61±0.06	0.48±0.11 ◆◆	0.45±0.09 ◆◆	r=-0.030 p=0.915	r=-0.587* p=0.010
		5	0.52±0.08	0.45±0.12 ◆	0.39±0.11 ◆◆	r=-0.286 p=0.301	r=-0.377 p=0.123
	posterior	6	0.53±0.12	0.40±0.12 ◆◆	0.36±0.13 ◆◆	r=-0.408 p=0.131	r=-0.423 p=0.080
		7	0.79±0.02	0.66±0.15 ◆◆	0.56±0.16 ◆◆	r=-0.399 p=0.141	r=-0.618** p=0.006
MD	anterior	2	0.84±0.08	0.96±0.14 ◆◆	1.13±0.28 ◆◆,◆	r=0.614* p=0.015	r=0.566* p=0.014
		3	0.93±0.10	1.14±0.21 ◆◆	1.31±0.33 ◆◆	r=0.450 p=0.092	r=0.635** p=0.005
		4	0.90±0.09	1.08±0.19 ◆◆	1.22±0.26 ◆◆	r=0.316 p=0.252	r=0.663** p=0.003
	posterior	5	1.07±0.13	1.18±0.29	1.32±0.29 ◆◆	r=0.407 p=0.132	r=0.519 p=0.027
		6	1.08±0.16	1.26±0.20 ◆◆	1.35±0.30 ◆◆	r=0.408 p=0.131	r=0.421 p=0.082
		7	0.79±0.04	0.97±0.21 ◆◆	1.05±0.23 ◆◆	r=0.349 p=0.203	r=0.247 p=0.323

group difference MS to control group (by Student's t-test)
◆◆: highly significant, p≤0.010
◆: significant, p≤0.05

group difference SPMS to RRMS (by Student's t-test)
◆: significant, p≤0.05

Correlation analysis: two sided Pearson's correlation, r: coefficient of correlation, p: significance; ** highly significant (p<0.010), * significant (p<0.050)

Table 1: Clinical data of patients with Multiple Sclerosis (MS) and healthy controls

(Mean±SD) [range]	All patients (N=34; m/f: 13/21)	RRMS (N: 16; m/f: 6/10)	SPMS (N: 18; m/f: 7/11)	Healthy Controls (N: 20; m/f: 8/12)
Age / years	41.2± 11.1 [19-67]	35.1±8.3 [22 - 50]	46.3±10.7 [19-67]	41.3±13.0 [23-70]
EDSS	4.2±1.5 [2.0 –7.0]	3.2±1.4 [2.0 –6.5]	5.0±1.1 [3.0 –7.0]	
Disease duration / years	8.9±8.6 [0 –28]	4.1±6.7 [0 –23]	12.9±8.1 [3 –28]	

Mean: arithmetic mean value; **SD** : standard deviation; **Range**: Min – Max range

SPMS: secondary progressive MS; **RRMS**: relapsing-remitting MS

Conclusion:

3rd. ventricle enlargement in MS is paralleled by CC degeneration which shows different regional patterns of influence in RRMS and SPMS. Although the elevation of 3VV and the decrease / increase of FA / MD in the whole CC and in the CC sub-sections are significant in the MS patients compared to healthy controls, the correlations between the ventricle volume and the DTI indices are prominent only in the SPMS group in the whole CC and in the anterior and posterior regions. In the relapsing-remitting stage we found only moderate correlations between FA / MD and 3VV in the genu of the CC. Thus, although 3rd. ventricle expansion and CC degeneration are both early disease symptoms in MS, the processes seem to base on different degeneration pathes in RRMS (periventricular lesion activity vs. pure interhemispheric fiber degeneration). In SPMS chronic CC lesion load may be more dominant, yielding direct correlations between CC fiber degeneration and 3VV.

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