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Clinical, neuropsychological, immunopathological and radiological analysis of progressive multiple sclerosis patients

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Aim

To conduct a multifactorial analysis of patients with progressive forms of multiple sclerosis (PMS) with regard to clinical and neuropsychological presentation, as well as immunopathological and neuroimaging characteristics. Obtained information will be used for the creation of diagnostic algorithms, which may allow for earlier diagnosis of the progressive phase of the disease and in consequence enable to earlier optimize the therapy and consequently contribute to the improvement of the therapeutic effect in these patients. The outcomes of this study may also contribute to the refinement of the methodology of the evaluation of disease progression and assessment of the efficacy of the therapies used in PMS.

Methods

1. **Clinical analysis** – medical history, neurological examination and Expanded Disability Status Scale (EDSS)
2. **Neuropsychological analysis** – BICAMS battery consisting of Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT) and Brief Visuospatial Memory Test Revised (BVMT-R); Verbal Fluency Test (VFT), The Stroop Colour and Word Test (SCWT)
3. **Laboratory analysis** – enzyme linked immunosorbent assay (ELISA) to determine the concentrations of neurofilament light chains (Nf-light), chemokine ligand 13 (CXCL-13) and chitinase-3 like-protein-1 (YKL-40) in serum
4. **Radiological analysis** – volumetric parameters of local brain atrophy assessed on MRI scans with the application of machine learning software; measurements included i.a.: thalamic, cerebellar, hippocampal and corpus callosal volumes

Results

1. Study group characteristics at baseline are presented in **Table 1.**
2. The severity of cognitive impairment (CI) assessed with BICAMS battery at baseline and after follow-up period is shown in **Figure 1.**
3. Mean serum concentrations of the investigated molecular markers in particular disease subtypes at baseline and after follow-up period are presented in **Figure 2.**
4. Mean volumes of the left thalamic volume (LTV), right thalamic volume (RTV) and corpus callosum volume (CCV) are illustrated in **Figure 3.** More MRI measurements are in progress. Exemplary pictures of the volumetric measurements are depicted in **Figures 4., 5.** and **6.**

		TOTAL	SPMS	PPMS
N		50	25	25
Sex	M	15	8	7
	F	35	17	18
Mean age [years]		55.5 ± 8.4	56.3 ± 8.4	54.8 ± 8.6
Mean disease duration [years]		13.5 ± 9.2	19.3 ± 7.8	7.8 ± 6.5
Mean EDSS		5.3 ± 1.1	5.7 ± 0.9	4.8 ± 1.2

Table 1. Study group characteristics at baseline

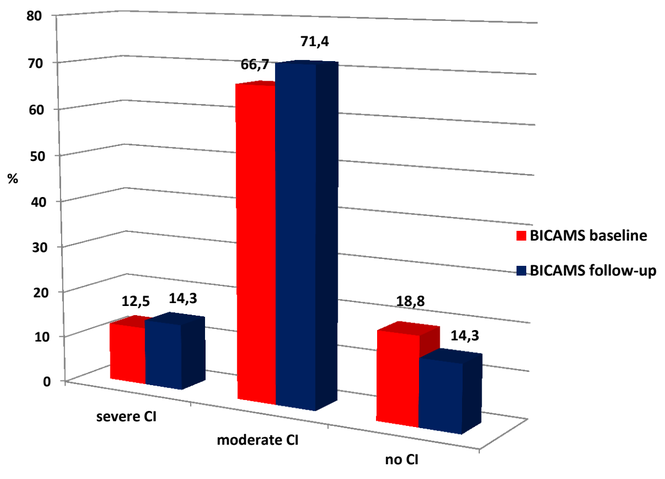

Figure 1. Percentage of cognitive impairment (CI) based on BICAMS battery

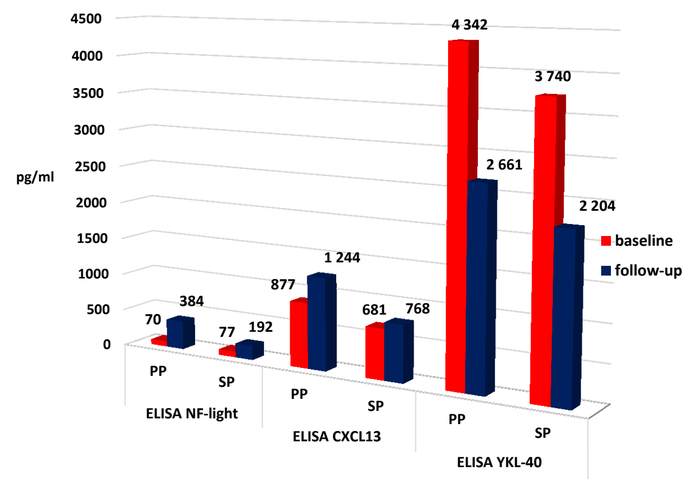

Figure 2. Mean serum concentrations of selected molecular markers at baseline and after follow-up according to PMS subtype

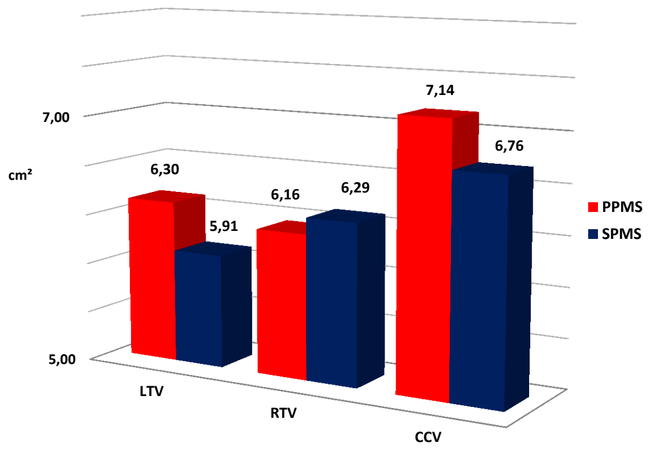

Figure 3. Mean volumes of selected brain structures

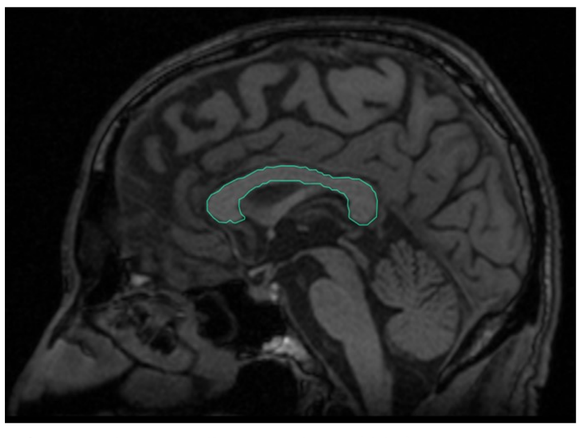

Figure 4. Corpus callosum volume (CCV)

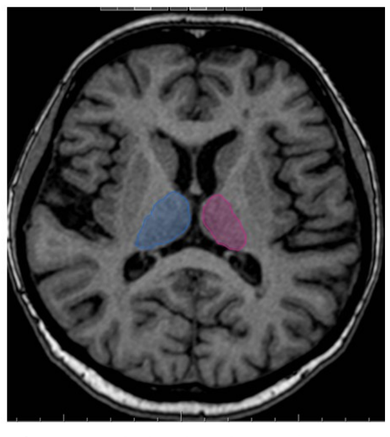

Figure 5. Thalamic volumes (LTV, RTV)

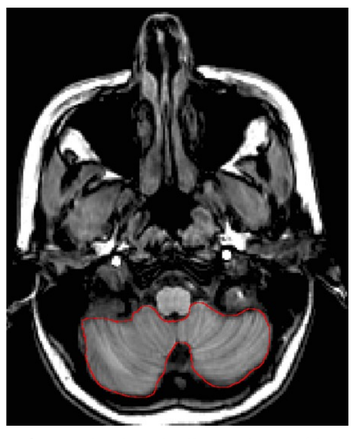

Figure 6. Cerebellar volume (CV)

Publications

1. Review article entitled **„Symbol Digit Modalities Test in progressive multiple sclerosis”**, with doctoral candidate's first authorship, *Multiple Sclerosis and Related Disorderes*, IF=4.808 (under review)
2. Article entitled **„A loop that matters - an unusual case of Bow Hunter's Syndrome”**, with doctoral candidate's first authorship, published in *Brain Sciences*, IF=3.706
3. Next articles in progress, including 2 original articles summarazing the acquired data, will be send for review in the forthcoming months

Conclusions

1. The presented group of people with PMS included 25 SPMS and 25 PPMS patients. The group consisted of patients with advanced neurological disability (mean EDSS 5.3 ± 1.1), mean age was higher in SPMS subgroup, the disease duration was longer in SPMS subgroup. Number of patients evaluated after follow-up period: 30.
2. The serum concentrations of examined molecules was ….higher in PPMS subgroup compared to SPMS subgroup. According to the current scientific knowledge, serum concentrations of these biomarkers are significantly higher in MS than in healthy subjects and are associated with the activity of pathological processes in the disease (1-3).
3. The most common cognitive deficit in the group, was the impairment of processing speed measured with SDMT and was diagnosed in 62,5% of examined patients. Non-verbal memory impairment was found in 47,9% of the participants as measured with BVMT-R. Verbal memory was impaired in 25% of the patients, as assessed with CVLT. In general, more SPMS patients had cognitive deficits than PPMS ones. However, in PPMS patients, severe generalized cognitive deficits were found more often than in SPMS ones. Progression of the deficits was noted. These findings are concordant with the current understanding of cognitive dysfunction in MS (4-5). In the next stage of the project, outcomes of VFT and SCWT scales will be summarized.
4. There were no significant differences in the mean thalamic volumes and corpus callosum volumes between the PMS subtypes. The available literature underlines the importance of brain atrophy measurements in the assessement of MS activity (6-7). However the dynamics of atrophic processes seems to be the most important factor, thus follow-up measurements are crucial for further conclusions. More brain structures will be measured in the forthcoming months.

References

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