Transcranial ultrasound (TCS) in sarcoidosis - relation to fatigue, depression and anxiety

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Abstract

The substantia nigra – SN ("black substance") is a brain structure located in the mesencephalon (midbrain) that plays an important role in reward, addiction, and movement; also starter function, motivation, drive.

The nucleus ruber – NR

Functions: Motor coordination (above all shoulder and upper arm but also forearm and hand), arm movements during walking, crawling, baby; movement initiation, muscle tone, body posture; circular rhythm, but "Pompeian"/basic internal adaptation and preparation processes in order to act according to potential or certain unexpected events.

Raphe

Main function is to release serotonin to the rest of the brain.

The area of ventral tegmentum is very important in emotional responsiveness, the feeling of security, and motivation. This area can thus influence the cognitive impairments in humans.

The purpose of this study was to elucidate the interactions between depression, anxiety and fatigue with the mesencephalic structures i.e. substantia nigra (SN) nucleus ruber (NR) and brainstem raphe.

We used:

- Hamilton Depression Scale (HAMD) and Beck Depression Inventory (BDI), to evaluate the feeling of depression in our patients.
- For evaluation of the anxiety we used Hamilton Anxiety Scale, (HAMA) and Fatigue, Fatigue Assessment Scale (FAS).
- We also evaluated the existing steroids therapy in the possible outburst of depression and anxiety.

In this study 40 biopsy positive sarcoidosis patients were analysed (28 female/12 male) mean age 48.0±12 years. Patients recruited for this study are the part of the major cohort of patients. They are all members of the Yugoslav Association of Sarcoidosis (YAS) that counts 1270 patients with different clinical forms of sarcoidosis. Patients voluntarily cooperated in completing the study questionnaires (HAMA, HAMD, BDI, and FAS) before performing transcranial ultrasound. Transcranial sonography was performed in the Clinic of Neurology, Clinical center Belgrade, by experienced neurologist.

Statistical analyses:

- between the groups without and within anxiety according to the HAMA score ≥17, between the groups without and within depression HAMD score ≥17 and BDI score ≥10, and between groups without and with depression FAS ≥22 were done using Fisher’s Exact Test.
- The Discriminant Analyses were done in order to estimate the consistence of TCS impairments with anxiety, depression and fatigue in the analysed group. Canonical Discriminant Function Coefficient (CD) was estimated as ≥0.051. Min. value magnitude as estimated was 0.051. Statistical analyses were done using SPSS version 18, Chicago, Illinois.

Normal findings in transcranial sonography

Photo: Mesencephalic brainstem of a healthy individual with normal, only slightly visible substantia nigra, and normal, highly echogenic brainstem raphe, which has the same echogenicity as the red nuclei.

Transcranial sonography (TCS) images of corresponding midbrain axial sections in three subjects. The butterfly-shaped midbrain was normal, only slightly visible substantia nigra, and normal, highly echogenic brainstem raphe.

Echogenicity of substantia nigra – (SN)

Normal 0.19cm²

0.19-0.24cm² moderate hyperechogenicity

Above 0.24cm² hyperechogenicity

Echogenicity of brainstem raphe: Echogenicity of brainstem raphe is rated semi-quantitatively using the highly echogenic red nuclei or signal intensity of the basal-castrums as reference points. (Grade 1) Brainstem raphe echogenicity should be rated as reduced if it only appears interrupted (or not visible) at both sides of investigation. Hyperechogenicity grade 0 observed to be related to depression.

Echogenicity of red nuclei – (NR)

Normally, the red nuclei can only be discerned on CT by dot-like echo signals at the lateral border of the red nuclei near the SN, and/or the medial border of the red nuclei near the brainstem midline raphe. In case of a signal increase (“hyperchogenicity”), the red nuclei shows high echogenicity at its whole anatomic extension. While reduced echogenicity of red nuclei has not been described as a pathological condition, its hyperchogenicity has been associated with restless legs syndrome (Godau et al., 2008).

Conclusion

TCS revealed the possibility of ultrasound investigations of the ventral tegmentum structures in sarcoidosis.

- Depression, anxiety and fatigue frequently accompany sarcoidosis. Besides other possible reasons related to granulomatous inflammation, the cognitive impairments mentioned above might possibly interrelate with structural changes in these areas of the brain; correlation probably caused by the lack of adaptable forces generated in these areas, to carry on with disabling, chronic disease.
- The most interesting fact that comes out of this study is that the majority of patients (33/40) showed hyperchogenicity of SN and hyperechogenicity of NR (25/40), the findings related to movement disorders i.e. restless legs syndrome.

This study is the very beginning, in the field of sarcoidosis and transcranial sonography. It is done in a small group of 40 volunteer patients and these are the first modest results.