TRANSCRANIAL ULTRASONOGRAPHY IN PARKINSON'S DISEASE AND OTHER MOVEMENT DISORDERS

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ABSTRACT

In recent years, transcranial ultrasonography (TCS) has become widely used for the visualization of the brainstem. With this method, changes of the echotexture – increased echogenicity – of the substantia nigra (SN) in about 90% of patients with Parkinson's disease (PD). In contrast, increased SN echogenicity is rarely found in patients with atypical or symptomatic Parkinsonian syndromes, providing a valuable tool for differential diagnosis.

Interestingly, increased SN echogenicity can also be found in about 8 to 10% of healthy subjects. The studies showed that the ultrasound signal does not change in the course of the disease and this hypercogenicity of the SN is present in the early stages of the disease, also in the presymptomatic patients. So, TCS may represent a biomarker for vulnerability of the nigrostriatal system and this method may even be helpful for the preclinical identification of people at risk for PD.

Key words: Parkinson's disease(PD); transcranial ultrasonography(TCS); hyperechogenicity; substantia nigra(SN)

INTRODUCTION

PD is the second most common movement disorder, with an occurrence of 1-2% in the population aged over 60 years. The diagnosis of PD is based on the clinical finding of bradykinesia combined with rigidity, resting tremor, and postural instability in the later stages. In the early stage in particular, when the symptoms are minor, clinical diagnosis can be difficult because there is not a specific paraclinic test.(10,16)

Over the past 15 years the use of transcranial B-mode sonography to assess brainstem and subcortical brain structures has become an important tool for the diagnosis and differential diagnosis of various movement disorders. The most widely recognised finding for movement disorders has been an increase in echogenicity of SN, who is characteristic for idiopathic PD.(10)

TCS is increasingly applied in the diagnosis of Parkinson's disease (PD) and its differentiation from atypical parkinsonian syndromes.(1-4) An area of increased echogenicity at the anatomical site of the substantia nigra (SN) has been found in more than 90% of PD patients.

Table 1. *Principles of TCS examination (10)*

- Echograf with transducer with the frequency about of de 1,6-2,5 MHz.
- Parameters of ultrasonography: penetration deepth: 14-16 cm, dynamic range-DR: 45-55dB.
- The transducer placed firmly to the temporal bone window at the preauricular site.
- Patient is in a supine position (head up to 60 degree).
- The dimension of hyperecogenicity differs function of the machine used but as convention an area of SN between 0.20 and 0.25 cm2 was assessed as a borderline value.

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- The typical scanning planes of TCS in movement disorders are: midbrain level, cerebellum level, thalamus level, cella-media level.

TCS evaluation of brain structures is realized through the transcranial preauricular acoustic window using a duplex probe with the frequency about 1–4 MHz, trying to obtain the image of the contralateral bone (12). The parameters for examination are ilustrated in table 1.and the principales planes of TCS are explained in fig.1 and fig.2.

- axial scanning plane parallel to the orbitomeatal line
- in the centre of image is the butterfl y-shaped mesencephalic brainstem, which is surrounded by the echogenic basal cisterns
- in this plane can be assessed the echogenicity of the ipsilateral SN, ipsilateral red nucleus (RN), and median midbrain raphe
- is visualised by tilting the ultrasound beam about 10-20° upwards
- in this plane, can be measured the transverse diameter of the third ventricle and of the frontal horn of the contralateral lateral ventricle
- it can be evaluated the echogenicity of the contralateral thalamus, lenticular nucleus and caudate nucleus (normally isoechogenic)

In comparison with conventional neuroimaging methods such as CT and MRI, advantages of TCS are low costs, short investigation times, noninvasiveness, unlimited repeatability, bedside availability and lower dependency on patient's compliance. Disadvantages are dependency on acoustic temporal bone windows, which accounts for missing or only partial accessibility of 10% to 20% of patients (2), and dependency on examiner's skills. Also TCS reveals new and complementary findings about the structure of SN in PD patients (6) because is a neuroimaging method who has the ability to provide data about various brain structures in its B-mode(1,7,11,15). In addition, transcranial color-coded duplex sonography is able to provide information on the intracranial arteries and veins as well, fact that is important in the differential diagnosis with the vascular parkinsonism. (1,7)

APPLICATION OF TCS IN PARKINSON'S DISEASE

Becker et al. in 1995 were the first who report a highly characteristic enlargement of the echogenic signal ("hyperechogenicity") of the SN in idiopathic PD .

Many studies demonstrated SN hyperechogenicity in 91% to 100% of PD patients, which is marked in 73% to 79% and moderate in 20% to 25% of cases (2,3). This finding is highly characteristic for idiopathic PD and the cause of hyperechogenicity of the SN is not known.In animal and postmortem has been shown a increased tissue iron

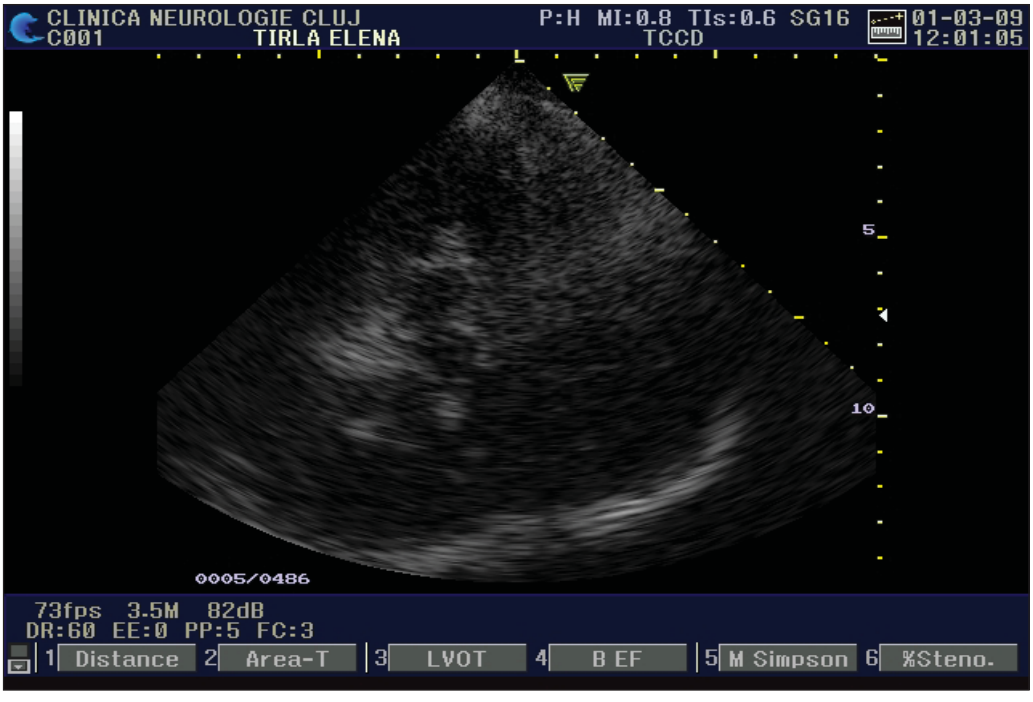

FIGURE 1. *The mesencephalic plane*

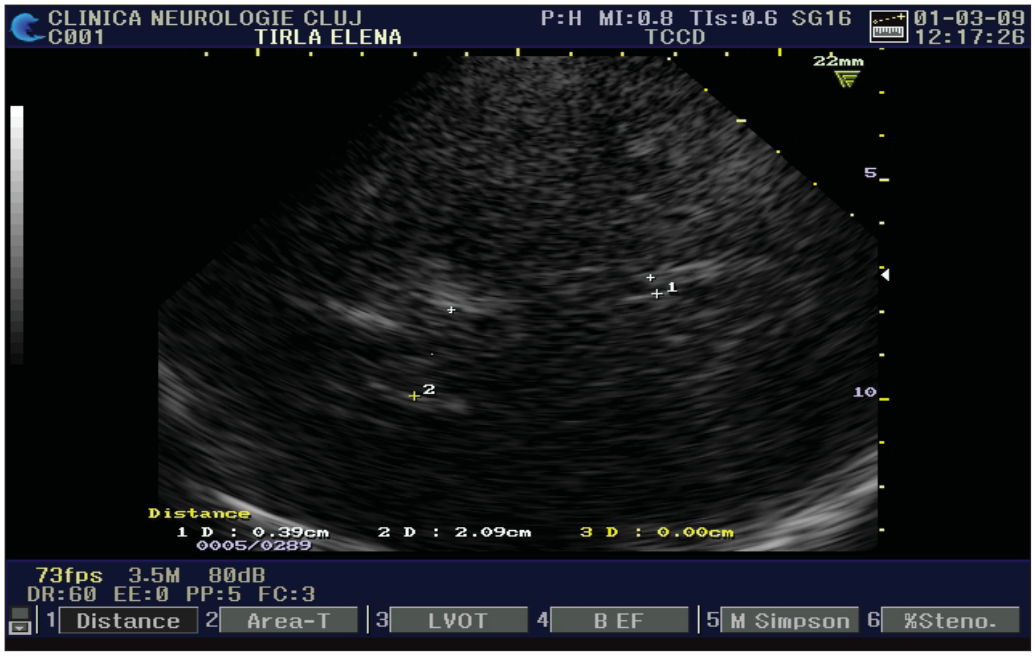

FIGURE 2.*The plane for the evaluation of basal ganglia and ventricles*

concentration associated with an increased area of echogenicity of the SN. For that reason, , is thought that the hyperecogenicity reflect increased amounts of iron, bound to proteins other than ferritin, in the SN. (1, 3,6,7)

In a study, blinding the sonographer to the clinical diagnosis of 42 PD patients and 35 controls, it was obtained a positive predictive value of 85.7% and a negative predictive value of 82.9% in the diagnosis of PD solely by interpreting the results of TCS, indicating that TCS is a valuable additional tool in the diagnosis of PD. (5)

No differences of SN echogenicity were found between different clinical subtypes of idiopathic PD (2). Median SN echogenic size was larger contralateral to the clinically more affected side. (2)

The echosignal is not associated with disease severity, as assessed with the Hoehn and Yahr staging or the UPDRS, or as visualised with presynaptic functional striatal neuroimaging and the size of increased echogenicity of the SN does not change with disease progression as shown by 5 years of follow-up; (7,10). SN hyperechogenicity in PD can therefore be regarded as a marker featuring the predisposition for the disease, rather than as a severity marker. (10,14)

Marked SN hyperechogenicity is also detected in about 9% (8% to 14%) of normal subjects of all ages. (2,6,8) Moreover, patients with SN hyperechogenicity but without prediagnosed PD developed more often and more severe extrapyramidal symptoms when neuroleptic therapy had to be applied because of other disorders. (2) These clinical observations substantiate the functional relevance of SN hyperechogenicity in healthy adults.

These findings indicate SN hyperechogenicity as an early marker for nigrostriatal impairment. In future, TCS could be used either to screen for a population at risk or for screening of a population at risk to detect individuals in preclinical disease stages.(10,14)

Recommendation

In adult subjects without neurologic symptoms, the TCS finding of at least unilaterally marked SN hyperechogenicity, indicates a subclinical functional impairment of the nigrostriatal dopaminergic system (level B, class II and class III evidence). (7)

APPLICATION OF TCS IN OTHER MOVEMENT DISORDERS

The diagnosis of PD is a challenge because several other disorders can resemble the idiopathic PD. These extrapiramidal disorders can be divided into secondary parkinsonian syndromes (PS) or atypical PS.

ATYPICAL PARKINSONIAN SYNDROMES

Although more than half of the dopaminergic neurons at the subtantia nigra (SN) have already degenerated when the first motor symptoms of PD occur, in early stages it is often difficult to differentiate between idiopathic PD and atypical parkinsonian.

Atypical PS includes neurodegenerative disorders in which the extrapiramidal syndrome is associated with other features, such as gaze palsy, autonomic symptoms, little or no responsiveness to levodopa, and a more rapid progression of disease than usually found in idiopathic PD. (10,16)

In a TCS study, SN hyperechogenicity was found to discriminate idiopathic PD from multiple-system atrophy and progressive supranuclear palsy in more than 90% of case. (3) Another TCS study on a larger sample of PD patients and patients with clinically possible or probable multiple-system atrophy or progressive supranuclear palsy showed that discrimination between PD and multiple-system atrophy/progressive supranuclear palsy was best when findings of SN echogenicity and LN echogenicity were combined, with a positive predictive value of 90% in differentiation of this pathologies. (4,16)

LN hyperechogenicity is observed in 72% to 82% ofpatients with multiple-system atrophy and progressive supranuclear palsy, but only in 10% to 25% of PD patients. (1,3,4) Bilateral marked SN hyperechogenicity is detected in about 90% of patients with corticobasal degeneration and is the main finding differentiating corticobasal degeneration from progressive supranuclear palsy. (7,9) In addition, third-ventricle dilation exceeding 10 mm was found in progressive supranuclear palsy but not in corticobasal degeneration. (9)

Recommendation

In adult subjects with parkinsonian syndrome with onset age more then 40 years, the TCS finding of at least unilateral marked SN hyperechogenicity in combination with normal LN echogenicity discriminates idiopathic PD from multiple-system atrophy and progressive supranuclear palsy with a positive predictive value of more than 90% (level C, class III and class IV evidence). (7)

The TCS finding of bilateral marked SN hyperechogenicity discriminates corticobasal degeneration from progressive supranuclear palsy with a positive predictive value of more than 90%, especially if combined with third-ventricle width less then10 mm (level U, limited class III evidence).(7)

SECONDARY PARKINSONIAN SYNDROMES

Secondary PS includes symptoms of bradykinesia, rigidity, tremor, that are induced by other causes than degeneration of the nigrostriatal system (tumours, hydrocephalus). (10) Common causes of secondary PS can be shown by structural neuroimaging techniques, such as cranial CT or MRI, which can show the cause of movement disorders (vascular or post-traumatic parkinsonism, hydrocephalus) or metabolic disorders (Wilson's disease or Fahr's disease). Also, some symptoms of parkinsonism can be present in some situations that have no distinct structural alterations, such as depression or essential tremor.(10)

Essential tremor

Tremor is the principal symptom in this entity who is considereted the most common movement disorder and clinically, it may be sometimes difficult to distinguish between essential tremor and tremor-dominant PD, particularly in early stages of the disease. In patients with essential tremor, typically a normal SN echogenicity is found. Other TCS findings did not discriminate between these entities.(7)

Vascular parkinsonism

The vascular parkinsonism (VP) patients have like principal extrapiramidal symptomatology gait difficulty at a older onset age than those of the idiopathic PD patients. Usually the patients have vascular risk factors and sometimes a history of stroke. The symptoms are usually symmetric (83.3%) and predominant in the lower limbs, and they have a poor response to levodopa therapy . Sometimes it is still difficult to make a correct diagnosis based only on clinical manifestations and TCS examination can be helpfull in this direction.(13)

In a study , there was no significant difference in SN hyperechogenicity between the VP patients and healthy controls, whereas SN hyperechogenicity was markedly increased in the IPD patients. The small vascular lesions that bring about vascular parkinsonism are not visible with TCS B-mode

imaging. (10) In addition, the hemodynamics of the intracranial large arteries by TCS can disclose other information with vascular abnormality (66.7%) and generalized increased flow resistance, which may indicate stenosis or occlusion of the distal parts of these arteries. Contrary to the VP patients, only 5% of IPD patients had a vascular abnormality.(13)

Dystonia

TCS is usefull al so in the diagnosis of dystonia. The studies show that more than 75% of patients with cervical or upper-limb dystonia display LN hyperechogenicity, being most pronounced in the medial part representing the globus pallidus internus (7) and the patients with facial dystonia present LN hyperechogenicity only in 31% of cases. (7)

In practice, the presence at TCS of LN hyperechogenicity can be useful to support diagnosis of idiopathic dystonia in differentiation from tardive or psychogenic dystonia.

Wilson disease

In Wilson's disease, the TCS examination can revealed LN hyperechogenicity who is caused by copper accumulation. Some patients with Wilson's disease also might present SN hyperechogenicity, hyperechogenic lesions of thalamus and dilation of third and lateral ventricles. LN echogenic sizes and ventricle widths are correlated with disease severity. (7) It was observed that in some cases of neurologically asymptomatic patients with normal MRI, the TCS revealed LN hyperechogenicity, fact who suggests that TCS can detect copper accumulation in basal ganglia already in preclinical disease stages.

OTHER DISEASES

Restless legs syndrome is frequent neurological disorder characterised by a compulsive urge to move the legs or other body parts at rest. (10) The studies showed that TCS scans reveals decreased echogenicity of the SN in more than 90% of patients with idiopathic restless legs syndrome and 60% of patients with symptomatic restless legs syndrome.(10)

In some metabolic diseases such as Fahr's disease TCS might found abnormal hyperechogenicity from calcification in the basal ganglia and this finding can be seen earlier with ultrasound than with from usual imagistic cerebrals techniques (CT, RMN). (7,10)

Patients with depression associated with motor slowing can be distinguished from patients with idiopathic PD because only PD is generally associated with hyperechogenicity of the SN. Depression can be a premotor sign of PD and the patient with depression is at risk to develop PD. Another finding at TCS in depression is the low echogenicity of the midbrain raphe: low echogenicity of the raphe is a common finding in 50–70% of patients with unipolar depression (13,10).

CONCLUSIONS

In the recent years, many research groups have studied the relevance of TCS in movement disorders pathology. TCS examination offers new informations and therapeuthiques perspectives in PD because the TCS findings can provide a early recognition and differential diagnosis of this entity with the possibility of a neuroprotective therapy.

TCS reveals characteristic changes in several neurodegenerative disorders, such as abnormal hyperechogenicity of SN in PD (more the 90% of patients) and of lenticular nucleus in dystonia, Wilson's disease and atypical Parkinsonian disorders. The finding of marked SN hyperechogenicity in combination with normal lenticular-nucleus echogenicity discriminates idiopathic PD from multiple-system atrophy and progressive supranuclear palsy with a positive predictive value of more than 90%. In healthy adults, the TCS finding of marked SN hyperechogenicity indicates a subclinical functional impairment of the nigrostriatal dopaminergic system. TCS is a quick, noninvasive and rapide method and might provide new and complementary findings about various brain structures.

Therefore, TCS can be seen as an useful and future tool for routine diagnosis in movement disorders pathology . The method has a great potential to be more widely used and to become one of the most importante investigations in the neuroimagery of extrapiramidal disorders.

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