Background

- Multiple clinical, genetic, histological and neuroimaging studies suggest overlap between essential tremor (ET) and Parkinson's disease (PD) [1].
- Mild parkinsonian features (rest tremor, bradykinesia, rigidity) can be observed in some ET patients.
- DaTscan (GE Healthcare, Princeton, N.J.), or I23-Ioflupane SPECT, has been recommended as a tool to image dopaminergic (DAT) and to assist in differentiating between ET and PD in clinically uncertain cases.
- Mild presynaptic dopaminergic deficit in ET patients was reported by some studies utilizing DAT imaging [2]; although the majority of previous studies revealed no difference in DAT imaging between ET and healthy controls [3].
- This study was designed to analyze demographic, clinical and DAT imaging data in patients with ET with or without parkinsonian features.

Methods

- 20 patients with ET with and without parkinsonian features, and 11 healthy volunteers were enrolled.
- All study subjects were examined by a movement disorders neurologist and divided into 4 groups:
  1. Healthy controls, HC (no tremor or parkinsonian features),
  2. ET (no parkinsonian features),
  3. ET with parkinsonian features, ET-p (1 parkinsonian feature or 2 subtle parkinsonian features, no identifiable PD),
  4. ET with concomitant PD, ET+PD (2 or more specific parkinsonian features when clinical presentation meets diagnostic criteria for PD).
- DaTscan imaging was performed at the NorthShore University HealthSystem, Evanston, IL – quantitative DaTscan image analysis.
- Severity of PD in patients with ET+PD was graded according to TETRAS (The Essential Tremor Rating Assessment Scale).
- Severity of PD was graded according to MDS UPDRS (Movement Disorders Society Unified Parkinson’s Disease Rating Scale).
- Posterior putamen, Anterior Putamen, Posterior Putamen, Striatum, and Subthalamus. Quantitative image analysis was performed by a radiologist (Dr. Wu) blinded to the study subjects’ clinical data and to the results of visual image interpretation.
- Statistical analysis was performed using a semi-automated software DaTQUANT, quantitative measurements of striatal binding ratios (SBR) were obtained in the following volume of Interests (VOIs): Caudate, Putamen, Anterior Putamen, Posterior Putamen, Striatum and Subthalamus. Quantitative image analysis was performed by a radiologist (Dr. Wu) blinded to the study subjects’ clinical data and to the results of visual image interpretation.

Results

- 36 ET subjects had slightly higher SBRs than HCs in all VOIs except caudate nucleus where SBRs were equal or even lower in HC (p-value 0.96 / 0.74 for right / left side) (Box 2a). Putamen-to-Caudate ratio was also slightly higher in ET than in HC (p-value 0.29 / 0.04 for right / left side) (Box 2b).
- Among all ET patients, SBRs were slightly lower in ET-p group in all VOIs except caudate nucleus where SBRs were equal or even lower in HC (p-value 0.96 / 0.74 for right / left side) (Box 2a).
- Putamen-to-Caudate ratio was also slightly higher in ET than in HC (p-value 0.29 / 0.04 for right / left side) (Box 2b).

Discussion

- Subpopulation of patients with ET and parkinsonian symptoms includes patients with a combination of ET and PD (ET+PD) and ET with parkinsonian features but without evidence of presynaptic dopaminergic deficit (ET-p).
- DAT imaging in ET+PD group is not different from pure PD patients with predominant and asymmetric dopaminergic deficit in posterior putamen followed by involvement of other VOIs in striatum as disease progresses.
- Parkinsonian features in ET patients do not seem to be related to underlying dopaminergic deficit as measured by DAT imaging. On the other hand, motor symptoms in PD usually manifest only after loss of about 50% of dopamine-containing neurons in the substantia nigra that would reflect in abnormal DAT imaging. Therefore, pathophysiology of parkinsonian features in ET might be different from PD.

Conclusions

- Pathophysiology of parkinsonian features in ET is unclear and might be different from pathophysiology of PD.
- Dopaminergic hypofunction in caudate nucleus might be implicated in pathophysiology of ET and especially ET with parkinsonian features; however, this hypothesis requires further investigation.

References


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