BACKGROUND

Parkinson disease (PD) is a progressive neurological disorder characterized by alterations in specific areas of the central nervous system such as neuronal loss in the substantia nigra and reduction of dopamine release in the striatum. Early diagnosis of PD remains a challenge due to the characteristic metabolic dysregulation of PD may enable novel biomarkers discovery for early diagnosis.

Recently, we found that a group of circulating amino acid-derived biogenic amines, defined as trace amines (TAs) or elusive amines, underlie early disease-related changes1. TAs (in red in Fig. 1 and Fig. 2) include β-phenylethylamine (β-PEA), tyramine (TYRA), 3,4-dihydroxyphenylalanine (DOPA), octopamine (OCT), synerpine (SYN), and tryptamine (TRY).

They are synthesized in monoaminergic neurons from precursor aromatic amino acids (in blue). L-tyrosine (LTYR), L-phenylalanine (PHE) and L-tryptophan (TRP) by the aromatic-L-amino acid decarboxylase (AADC) together with catecholamines and methanephrine (MTN) (in green). They act as neurotransmitters via specific trace amine–associated receptors (TAARs), and indirectly act as neuromodulators at catecholaminergic synapses. 2-3 Although the role of TAs in the physiology of the nervous system is still largely elusive, their crosstalk with the catecholaminergic system together with the discovery of TAARs have called attention on their possible pathophysiological relevance in CNS diseases.

OBJECTIVE

- To confirm whether circulating TAs and catecholamines and indolamines were altered in PD patients at different stages of the disease
- To assess whether they could behave as biomarkers in early and/or late-stage of PD.

PARTICIPANTS

48 PD patients were enrolled according to UK PDS Brain Bank criteria by movement disorders team at Neurology Clinic at University of Trieste, Italy. • 21 untreated de novo patients (DN group) with movement abnormality manifestations in less than 2 years; • 27 in treatment patients (PD group) with a disease duration of less than 5 years; 10 age-matched healthy subjects (H group) were included in the study for comparison.

Plasma samples were collected, after fasting period and at the same time of day, in heparinized tubes and promptly stored at −80°C.

ACKNOWLEDGMENTS

The study was partially supported by grant from the Michael J. Fox Foundation for Parkinson disease. We gratefully acknowledge the contribution of the late Prof. Gilberto Pizzolato (University of Trieste) to the study design and patients recruitment.

METHODS

Sample Preparation

<table>
<thead>
<tr>
<th>Trace amines and</th>
<th>Plasma sample</th>
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<tr>
<td><strong>SPE Extraction using Biotage VOCULTAV PFCr 25g/test</strong></td>
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<tr>
<td>Pre-treatment: 300µL of plasma + 50µL labeled IS + 300µL NH4 acetate 50mM, pH 4.5</td>
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<tr>
<td>Centrifugation 10min at 13000 rpm</td>
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<tr>
<td>Equilibration: 50µL, NH4 acetate 50mM, pH 4.5</td>
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<tr>
<td>Loading: 300µL of pre-treated sample</td>
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<tr>
<td>Washing: 300µL of MBDH H2O (2 times)</td>
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<tr>
<td>Elution: 80µL + 80µL MBDH containing 5% FA (v/v)</td>
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<tr>
<td>Evaporation under N2 at 37°C</td>
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<tr>
<td>Reconstitution 50µL of water with 0.1% FA</td>
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Statistical Analysis

Univariate and multivariate data analysis were applied for exploratory data analysis. Group comparison was performed by chi-square test, Kruskal-Wallis test followed by Dunn’s multiple comparisons test and Projection to Latent Structures-Discriminant Analysis (PLS-DA). Significance levels were set to α=0.05. In the box plots horizontal lines represent median value, boxes represent interquartile range, and whiskers represent minimum-maximum values.

RESULTS

Increased levels of TYRA, TRP and MTN together with lower levels of NE were found in PD, whereas higher levels of β-PEA were observed in healthy subjects. **: P < 0.001, ***: P < 0.001; P < 0.001; *: P < 0.01, *: P < 0.01; P < 0.005.

CONCLUSIONS

- Parkinson disease is characterized by profound changes in the amimeric and indolic neurotransmitters.
- The amines pattern achieved effective characterization of DN and PD patients versus healthy subjects.
- TYRA can be considered as a promising putative marker for assessing the disease at an early stage for diagnosis of DN from healthy subjects.
- TYRA and TRP can be considered as promising putative markers for the progression of the disease.
- Larger studies are needed to confirm these preliminary results.

REFERENCES


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