Imaging of serotonin and dopamine transporters in the living human brain

Jyrki T. Kuikka¹, Jari Tiihonen², Kim A. Bergström¹, Jari Karhu³, Päivi Hartikainen⁴, Heimo Viinamäki⁵, Esko Länsimies¹, Johannes Lehtonen⁵, Panu Hakola²

¹ Department of Clinical Physiology, Kuopio University Hospital, FIN-70210 Kuopio, Finland
² Department of Forensic Psychiatry, Kuopio University Hospital, FIN-70210 Kuopio, Finland
³ Department of Clinical Neurophysiology, Kuopio University Hospital, FIN-70210 Kuopio, Finland
⁴ Department of Neurology, Kuopio University Hospital, FIN-70210 Kuopio, Finland
⁵ Department of Psychiatry, Kuopio University Hospital, FIN-70210 Kuopio, Finland

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Abstract. Alterations in brain serotonin (5-HT) and dopamine (DA) activity are associated with several neuropsychiatric disorders, but until now it has not been possible to simultaneously visualize or quantify the 5-HT and the DA transporter density in the living human brain. In this paper we report on the imaging of 5-HT and DA transporters in 28 healthy controls with single-photon emission tomography using iodine-123 labelled 2β-carbomethoxy-3β-(4-iodophenyl)tropane ([123I]13-CIT) as the tracer. The [123I]13-CIT distribution showed the most prominent 5-HT activity in the medial frontal cortex, hypothalamus, midbrain and occipital cortex and the greatest DA activity in the basal ganglia. The specific binding of the 5-HT transporters in the medial frontal cortex was 0.377±0.031 and that of the DA transporters in the basal ganglia, 0.916±0.007. Gjedde-Patlak plots indicated two separate components: the first was assumed to represent 5-HT transporters with a slope of 1.29±0.27 h⁻¹ and the second, DA transporters with a slope of 0.30±0.04 h⁻¹. This distinct kinetic pattern and the fact that 5-HT and DA transporters are situated in different parts of the brain provides an opportunity to study in vivo patients suffering from various neuropsychiatric disorders.

Key words: 2β-Carbomethoxy-3β-(4-iodophenyl)tropane – Iodine-123 – Dopamine – Receptor – Serotonin


Introduction

Dysfunction of serotonergic and dopaminergic activity in the central nervous system (CNS) has been reported in several neuropsychiatric disorders. Decreased dopamine (DA) transporter density in the basal ganglia has been observed in Parkinson’s disease [1] and Alzheimer’s disease [2] in post-mortem studies. A large number of studies have shown that decreased 5-hydroxyindoleacetic acid (5-HIAA) levels in spinal fluid are associated with depression and impulsive, suicidal and aggressive behaviour [3, 4]. The anatomical distribution of DA and serotonin (5-HT) receptors has recently been studied in humans by means of positron emission tomography (PET) [5,6]. However, until now it has not been possible to image simultaneously the 5-HT and DA re-uptake sites in the living human brain.

Using an iodine-123 labelled cocaine congener, [123I]β-CIT, it has been possible to image concomitantly summed 5-HT and DA re-uptake sites in the brain of monkeys [7] and humans [8–10] with SPET. We now report on the imaging and semi-quantification of 5-HT and DA transporters in the living human brain.

Materials and methods

Twenty-one healthy male and seven healthy female subjects (aged 19–64 years) were investigated. The study subjects were recruited from the hospital staff and they had no evident neurological disorders. The procedure was approved by the local ethical committee and all subjects gave their informed consent. A dose of 110–185 MBq of [123I]β-CIT (specific activity greater than 1.1×10¹⁴ Bq/mmol) was given intravenously in a dark and quiet room. Radiolabelling, radiochemical purity, radiopharmaceutical safety and dosimetry of [123I]β-CIT have been presented previously [8, 11, 12]. The radiation load to the subjects was on average 4 mSv as given by the effective dose equivalent [12]. The first SPET scan was started 1 h after injection of tracer using a dedicated Siemens MultiSPECT 3 gamma camera with high-resolution collimators. A full 360° rotation was performed (40 views/head, each 40 s) and the total scanning time was 25 min. The imaging resolution was 8–9 mm. The subjects received 20 mg citalopram per os (a specific 5-HT re-uptake inhibitor) immediately after their first imaging. The second SPET scan was performed 2 h and the third scan 21–23 h after injection of tracer. Three male subjects were scanned dynamically (17 scans: 3×2.5 min, 3×5 min, 3×10 min, 4×20 min immediately after injection of tracer and
Fig. 1. Position of three regions of interest. On the left: medial frontal cortex and basal ganglia; on the right: white matter. The slices are 30–37 mm and 58–65 mm above the OM line and represent the 1-h image set. The total slice thickness used in analysis was 7 mm.

Fig. 2. Top: Two consecutive slices (3.5 mm thick) of a healthy female imaged 1 h after injection of tracer. Similar slices are shown of a female patient with major depression (middle) and a female patient with panic disorder (bottom). Note the altered regional 5-HT re-uptake in these patients. The panic patient has abnormally high cortical uptake (especially in the medial frontal cortex, right middle frontal gyrus and occipital cortex) whereas in the depressive patient the cortical activity is significantly reduced. The patient’s left is on the right.