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Original article

A longitudinal follow-up study of the quantification of dopamine transporters with ^{123}I-Ioflupane (DaTscan)

Suivi longitudinal de la quantification des transporteurs de la dopamine avec l'^{123}I-Ioflupane (DaTscan)

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Abstract

Introduction. – The aim of this study was to test a quantification tool to measure the evolution of the functional reserve of dopaminergic transporters, from two consecutive ^{123}I-Ioflupane Datscan.
Methods. – Images of 58 patients who underwent two consecutive ^{123}I-Ioflupane examinations (DaTscan®) in the Nuclear Medicine Department of Toulouse University Hospital from 2002 to 2016 were analysed in this retrospective study. Twenty-four patients had a normal dopaminergic neuronal operation (N group), 34 had a pathological impairment of the dopamine transporters (P group) which 15 did not receive any treatment (PO group) and 16 who received treatment (P1 group). The DaTscan® image quantification was performed with the DaTsofr3D® software, permitting to measure the right and left binding potential (PL) of the caudate nucleus (NC), putamen (PU) and striatum (ST).
Results. – In the N group, the annual mean change of the binding potential (NC, PU, ST) was respectively (−0.03%/year, −0.96%/year, −0.43%/year) and did not significantly differ from the normal physiological decline of −0.66%/year. The annual binding potential mean changes of the P group (−9.6%/year, −13%/year, −11%/year) significantly differed not only from the N group but also from the physiological decline. No significant difference was shown between P0 and P1 groups.
Conclusion. – The DaTsoft3D® quantification software permits to split up two groups according to the evolution of the dopamine transporter density with a significant difference in the binding potential mean annual rate.

Keywords: [123I]FP-CIT SPECT; Quantification; Parkinson's disease; SPECT/CT; Antiparkinson treatment

Résumé

Introduction. – Cette étude évalue une méthode de mesure de la variation au cours du temps de la réserve fonctionnelle en transporteurs dopaminergiques, à partir de deux Datscans à l'^{123}I-Ioflupane consécutifs.
Méthode. – Les images de 58 patients ayant bénéficié de 2 examens à l'^{123}I-Ioflupane (DaTscan®) dans les services de médecine nucléaire de Toulouse de 2002 à 2016 ont été analysées pour cette étude rétrospective de groupes. Vingt-quatre patients avaient un fonctionnement normal des neurones dopaminergiques (groupe N), 34 avaient une atteinte pathologique des transporteurs de la dopamine (groupe P) dont 15 n'avaient pas reçu de traitement (groupe P0) et 16 avaient reçu un traitement (groupe P1). La quantification des images DaTscan a été effectuée avec le logiciel DaTsoft3D®, permettant les mesures des potentiels de liaison (BP) droits et gauches des noyaux caudés (NC), des putamens (PU) et du striatum (ST).

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Résultats. – Pour le groupe N, les variations annuelles moyennes des potentiels de liaison (NC, PU, ST) avaient pour valeurs respectives (−0,03 %/an, −0,96 %/an, −0,43 %/an) ne s'écartant pas de manière significative de la valeur de la décroissance physiologique normale de −0,66 %/an. Les variations annuelles moyennes des potentiels de liaison du groupe P (−9,6 %/an, −13 %/an, −11 %/an) différaient significativement, d'une part, du groupe N, et d'autre part, de la décroissance physiologique. Aucune différence significative n'a été montrée entre les groupes P0 et P1.

Conclusion. – Le logiciel de quantification DaTsoft3D® permet de séparer deux groupes de sujets selon l'évolution de la densité des transporteurs de la dopamine avec une différence des moyennes hautement significative de la variation annuelle des potentiels de liaison.

Mots clés : [123I]FP-CIT SPECT ; Quantification ; Maladie de Parkinson ; SPECT/CT ; Traitement antiparkinsonien

1. Introduction

The search for new neuroprotective treatments against neurodegenerative diseases raises the question of an objective evaluation of the evolution of neuronal loss over time. To objectively control the efficacy of a protective targeted treatment of dopaminergic neurons, the use of one of the dopaminergic neurotransmission specific radiotracers used in nuclear medicine seems to be applicable. There currently exists ^{123}I-Ioflupane for single-photon emission tomography (SPECT) marketed under the brand name DaTscan®, and recently ^{18}F-DOPA for positron emission tomography (PET).

In this retrospective study, we limited ourselves to the SPECT imagery at DaTscan®, which profits from a great number of examinations that have already been carried-out. DaTscan binds specifically to presynaptic dopaminergic neurotransporters (DaT), and could therefore present a basis prove useful in monitoring the evolution of the functional state of neuronal terminations.

DaTscan is currently used in nuclear medicine to aid in the differential diagnosis of Parkinson's syndromes. We must remember that this type of diagnosis is clinical when the symptomatology is typical [1]. Complementary examinations, including nuclear imaging of the central grey nuclei, are useful in case of doubt or atypical clinical presentation and help clinicians in their diagnostic approach. This type of examination makes it possible to determine the presence or absence of the pathological character of the presynaptic slope of the striatal dopaminergic neurotransmission. Interpreting an examination on DaTscan by the nuclear medicine physician is first of all visual. Quantification of images is recommended to assist in interpretation [2].

In this article, we are interested in DaTscan®, not as a diagnostic aid, but as a way to monitor the evolution of dopaminergic neuronal loss over time. We must remember that in healthy subjects there is a physiological decrease in the age of the number of dopaminergic neurons in healthy subjects. This physiological decrease has been estimated at about 6.6% per decade, or 0.66% per year for a linear model [3].

A neurodegenerative disease is characterized by a faster decrease than in the healthy subject. The natural course of the disease is that it progressively worsens, with a gradual escape of current treatments.

Much more than PET imaging, SPECT imaging has limitations in terms of measurement accuracy. In fact, several physical phenomena seriously disrupt the images, and consequently the quantification. These include high statistical noise, limited spatial resolution responsible for blurring in images, and partial volume effect, self-attenuation and Compton scattering.

To these phenomena can be added the approximations made during the quantification, such as the use of an anatomical striatum model or the imprecision of the recalibration of this model on clinical data. In this context, a quantitative evaluation of the functional reserve in dopaminergic neuronal terminations remains a challenge, which has not yet been completely solved. From this point of view, this study will be the means of testing the robustness of the quantification software used, and whether, despite all the imperfections in the data, it is possible to carry out a coherent longitudinal follow-up of a group of subjects.

The main objective of this article was to compare the evolution of dopaminergic neurodegeneration longitudinally, in the same patient, between a group labeled nonpathologic, i.e. free of presynaptic dopaminergic denervation visible in DaTscan, and a pathological group using the DaTsoft3D® software. In a second stage, we will try to analyze whether the current antiparkinsonian treatments, without distinguishing one treatment from another, modify the evolution of the binding potentials measured in DaTscan.

2. Materials and methods

2.1. Patients

Patients were recruited from the image database of the Department of Nuclear Medicine at the University Hospital of Toulouse, during the period between May 2004 and April 2016, 2857 DaTscan. Of these, 59 patients performed consecutively two examinations spaced more than 6 months apart. The evolution of 1 subject appeared irregular. This subject was not included in the study.

The re-examination was justified by either a discrepancy with the clinical examination or the initial diagnostic hypothesis. Patients were referred to us to permit the clinician to make a case either for the diagnosis of Parkinson's disease, which was most often, but also for Lewy body disease or other neurodegenerative pathologies affecting the central grey nuclei.

The initial classification of the subjects divided the patients into 2 groups, with or without an involvement of the dopaminergic pathways: group N and group P, respectively.