UK PARKINSON'S Excellence Network

What drugs might affect the interpretation of DaTSCAN?

Appraised by Kevin Galbraith, 9 February 2016

Update due 2019

Clinical question

In the diagnosis of Parkinson's and parkinsonism, what drugs might affect the interpretation of DaTSCAN?

Background

DaTSCAN is used to detect or exclude dopaminergic degeneration by imaging the dopamine transporter in patients with parkinsonian conditions. Some drugs can have a significant influence on the visual interpretation and/or quantification of DaTSCANs.[1]

Clinical bottom line

1. A number of medications and illicit drugs can interfere with the interpretation of a DaTSCAN. A table below lists some that might often be encountered in clinical practice.

2. The evidence underpinning summaries of such interactions is limited to (i) a guideline that has not clearly followed current procedural guidance, and (ii) a narrative review which constitutes expert opinion (level 5 evidence). The list of interactions derived from these two articles was supplemented for this CAT with those noted by the manufacturer of DaTSCAN (General Electric).

3. This CAT cannot therefore be regarded as a reliable guide to drug interactions that might affect interpretation of DaTSCAN. It does however highlight the need for a rigorously conducted synthesis of primary scientific research in this area

Search terms

(Ioflupane OR FP-CIT OR DaTSCAN OR DaTscan OR DaT-SPECT OR dopaminergic imaging) AND (medication$ OR drug$) AND (interaction$ OR binding OR contraindication$)

Search strategy

Ovid Medline, adapted for Embase and Cochrane Library from 1996 to February 2016. This yielded one relevant narrative review.[1] Hand searching of bibliographies located a guideline from 2010. The guideline[2] is summarised and critically appraised below.

Evidence

A guideline published in 2010 by the European Association of Nuclear Medicine Neuroimaging Committee (ENC) provided procedural recommendations for the use of DaTSCAN, including medications and drugs of abuse that should be avoided prior to the investigation.

Darcourt J, Booij J, Tatsch K, Varrone A, Vander Borght T, Kapucu ÖL, et al. EANM procedure guidelines for brain neurotransmission SPECT using 123I-labelled dopamine transporter ligands, version 2. European journal of nuclear medicine and molecular imaging. 2010;37(2):443-50

Summary

The stated aim of the guideline was to: "assist nuclear medicine practitioners when making recommendations, performing, interpreting, and reporting the results of clinical DAT-SPECT studies using 123I-labelled radiopharmaceuticals." The work was guided by the views of several listed national societies: the Task Group Neuro-Nuclear-Medicine of the German Society of Nuclear Medicine, the 'Kompetenznetz-Parkinson' sponsored by the German Federal Ministry of Education, and the Task Group of Neuro-Nuclear Medicine of the French Society of Nuclear Medicine. The guideline included a table reproduced from the narrative review also located in the literature search:[1]

Medications and drugs of abuse which may significantly influence the visual and quantitative analysis of [123I]FP-CIT SPECT studies

Drug class	Drug name	Comments
Cocaine		May decrease striatal [123I] FP-CIT binding
Amphetamines	d-amphetamine, methamphetamine, methylphenidate	May decrease striatal [123I] FP-CIT binding
CNS stimulants	Phentermine or ephedrines	May decrease striatal [123I] FP-CIT binding; influences are likely when used as tablets
Modafinil		May decrease striatal [123I] FP-CIT binding
Antidepressants	Mazindol, bupropion, radafaxine	May decrease striatal [123I] FP-CIT binding
Adrenergic agonists	Phenylephrine or norepinephrine	May increase striatal [123I] FP-CIT binding; influences are likely when infused at high doses
Anticholinergic drugs		Benztropine may decrease striatal binding ratios; other anticholinergics may increase these ratios which will likely not affect visual assessments
Opioids	Fentanyl	May decrease striatal [123I] FP-CIT binding
Anaesthetics	Ketamine, PCP, isoflurane	May decrease striatal [123I] FP-CIT binding; of interest particularly for animal SPECT studies, although ketamine and PCP are sometimes used illicitly

Some additional interactions were described:

- Smoking may interfere with DAT availability, though the effect would likely be too small to lead to misinterpretation.[3]

- Antiparkinsonian medications (such as levopoda, dopamine agonists, NMDA receptor blockers, MAO-B inhibitors and COMT inhibitors taken in standard doses) "do not markedly affect DAT binding and therefore do not need to be withdrawn prior to DAT SPECT."[4] Caution is advised in intra-individual follow-up studies, since downregulation of DAT expression by levodopa cannot be excluded.[5]

A critical appraisal of the guideline was carried out using the AGREE II instrument.[6] Points were noted and scores calculated (between zero and 100%) for each domain as follows:

- **Scope and purpose:** The aims of the guideline were clearly stated, there was clarity regarding the particular aspects of DaTSCAN procedure to be addressed, and the applications of the guideline were very specific. **Score 94%**.

- **Stakeholder involvement:** The guideline was itself guided by the views of several national societies, though the composition of panels from each were not described. There was no mention of patient involvement. The target users of the guideline were clearly defined, as were the particular aspects of practice that would be informed by the guideline. **Score 39%**.

- **Rigour of development:** There was no description of a systematic search for evidence, nor was there any description of criteria for selection of evidence. The strengths and limitations of the evidence were not addressed. There was no explicit method for formulating the recommendations. Some judgement was evident in weighing up the risk of using drugs with minimal effects on DAT binding. There was no clear strategy to link recommendations with evidence, other than the simple provision of bibliographic references. In terms of external review, several international societies were consulted, but the stage at which this occurred in the guideline development process was unclear. No plan was outlined for updating the guideline. **Score 12.5%**.

- **Clarity of presentation:** Few examples were given from each class of drugs. However, the recommendations logically followed stages of the DaTSCAN procedure. **Score 75%**.

- **Applicability:** There was no attempt to describe facilitators or barriers to application of the guideline, no advice on how it might be put into practice, no attempt to address resource implications, and no audit criteria were offered. **Score zero**.

- **Editorial independence:** No information was given regarding funding or competing interests. **Score 25%**.

- Overall, the guideline was rated as of poor quality, with a score of 2 (where 1 = lowest possible quality, and 7 = highest possible quality). The most important limitation was the lack of systematic search and selection of evidence.

In view of these limitations, the particular interactions described in this guideline were compared with those described in the prescribing information provided by the manufacturer of DaTSCAN, General Electric (3.gehealthcare.co.uk). The 'information for physicians' was as follows:

"No interaction studies have been performed in humans. Ioflupane binds to the dopamine transporter. Medicines that bind to the dopamine transporter with high affinity may therefore interfere with DaTSCAN diagnosis. These include amfetamine, benzatropine, buproprion, cocaine, mazindol, methylphenidate, phentermine and sertraline. Medicines shown during clinical trials not to interfere with DaTSCAN imaging include amantadine, trihexyphenidyl, budipine, levodopa, metoprolol, primidone, propranolol and selegiline. Dopamine agonists and antagonists acting on the postsynaptic dopamine receptors are not expected to interfere with DaTSCAN imaging and can therefore be continued if desired. Medicinal products shown in animal studies not to interfere with DaTSCAN imaging include pergolide."

Of note is the inclusion of sertraline (an antidepressant of the selective serotonin reuptake inhibitor class) among the medicines that bind to the dopamine transporter with high affinity. This was not included in the guideline.

References

1. Booij J, Kemp P. Dopamine transporter imaging with [(123)I]FP-CIT SPECT: potential effects of drugs. European Journal of Nuclear Medicine & Molecular Imaging. 2008;35(2):424-38.

2. Darcourt J, Booij J, Tatsch K, Varrone A, Vander Borght T, Kapucu ÖL, et al. EANM procedure guidelines for brain neurotransmission SPECT using 123I-labelled dopamine transporter ligands, version 2. European journal of nuclear medicine and molecular imaging. 2010;37(2):443-50.

3. Yang YK, Yao WJ, Yeh TL, Lee IH, Chen PS, Lu RB, et al. Decreased dopamine transporter availability in male smokers -- a dual isotope SPECT study. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(1):274-9.

4. Schillaci O, Pierantozzi M, Filippi L, Manni C, Brusa L, Danieli R, et al. The effect of levodopa therapy on dopamine transporter SPECT imaging with(123)I-FP-CIT in patients with Parkinson's disease. European Journal of Nuclear Medicine & Molecular Imaging. 2005;32(12):1452-6.

5. Fahn S, Oakes D, Shoulson I, Kieburtz K, Rudolph A, Lang A, et al. Levodopa and the progression of Parkinson's disease. N Engl J Med. 2004;351(24):2498-508.

6. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. Canadian Medical Association Journal. 2010;182(18):E839-E42.