Striatal Dopamine Transporter Spect Quantification: Head-to-Head Comparison Between Two Three-Dimensional Automatic Tools

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Short communication

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Abstract

**Purpose.** Our aim was the head-to-head comparison between two automatic tools for semi-quantification of striatal dopamine transporter (DAT) specific-to-non displaceable (SBR) ratio brain SPECT values in a naturalistic cohort of patients.

**Procedures.** We analyzed consecutive scans from one-hundred and fifty-one outpatients submitted to brain DAT SPECT for a suspected parkinsonism. Images were post-processed using a commercial (Datquant®) and a free (BasGanV2) software. Reading by expert was the gold-standard. A subset of patients with pathological or borderline scan was evaluated with the clinical Unified Parkinson's disease rating scale, motor part (MDS-UPDRS-III).

**Results.** SBR, putamen-to-caudate (P/C) ratio, and both P and C asymmetries were highly correlated between the two software with Pearson’s ‘r’ correlation coefficients ranging from .706 to .887. Correlation coefficients with the MDS-UPDRS III score were higher with caudate than with putamen SBR values with both software, and in general higher with BasGanV2 than with Datquant®. Datquant® correspondence with expert reading was 84.1% (94.0% by additionally considering the P/C ratio as a further index). BasGanV2 correspondence with expert reading was 80.8% (86.1% by additionally considering the P/C ratio).

**Conclusions.** Both Datquant® and BasGanV2 work reasonably well and similarly one another in semi-quantification of DAT SPECT. Both tools have their own strength and pitfalls that must be known in detail by users in order to obtain the best help in visual reading and reporting of DAT SPECT.

Introduction

Dopamine transporter (DAT) brain SPECT is widely used to diagnose parkinsonian disorders. Image reading is currently the recommended way of reporting [1] but semi-quantification with automatic, three-dimensional tools can reliably assist visual reading, especially in doubtful or borderline cases [2]. Several methods have been proposed, some available either free [3] or commercial [4], with results varying mainly depending upon region of interest (ROI) identification method [5]. However, seldom head-to-head comparisons between such tools have been performed [5–6], or attempts have been made to comparatively correlated data with a clinical measure as an ‘external’ reference.

Our aim was to compare a widely distributed commercial and tool with an older free software i) one another, ii) with a clinical motor score, iii) versus reading by experts.

Materials And Methods

One-hundred and fifty-one consecutive patients (87 males, mean age:72.5 ± 9.2, range 46–82) submitted to brain DAT SPECT for suspected degenerative parkinsonism in a clinical setting were enrolled in a single center using a 2-head, parallel-hole, high-resolution collimator camera (Discovery®, G.E.)
Healthcare, Hatfield, Hertfordshire, UK). Patients received intravenously 150–185 M bq I-123 Ioflupane (Datscan®, G.E. Healthcare, as above) and were scanned for 40 min between 3 and 5 hours after injection, according to the European Association of Nuclear Medicine guidelines [1]. Images were reconstructed on the Xeleris® workstation using an Ordered Subset-Expectation Maximization algorithm (10 subset, 10 iterations) with a 0.6 Butterworth filter, and corrected for attenuation with the Chang method (coefficient 0.11 cm$^{-1}$).

Patients were informed that their images could have been used for retrospective research purposes and gave their written consent for usage and publication in an anonymized form. The local ethic committee approved this retrospective data analysis.

Reconstructed images were visually analyzed by two experts independently, blind to clinical information, who agreed to classify 136 (90%) scans. The remaining 10% was resolved by a 3rd expert. At last, there were 79 positive, 56 negative, and 16 borderline scans. Images were then automatically processed by Datquant® (G.E. Healthcare, as above) and by BasGanV2 [3] (freely downloadable from https://www.aimn.it/site/page/gds/gds-5). The two software automatically position three-dimensional ROI and allow to compute specific-to-non displaceable binding ratio (SBR) by normalizing counts on an occipital ROI, and to compare values with a group of control subjects embedded in the software itself. Datquant® automatically reorients images and recognizes the reconstruction procedure adapting control subjects to the one under examination. Moreover, it computes SBR for anterior and posterior putamen separately. On the other hand, BasGanV2 requires manual image re-orientation, does not distinguish anterior and posterior putamen, and performs partial volume effect (PVE) correction.

The three comparison steps were i) correlation analysis between SBR of the four basal ganglia, the putamen/caudate ratio of each side, the caudate and the putamen asymmetry, as obtained by the two software; ii) correlation analysis between these eight values and the Movement Disorder Society-Unified Parkinson’s Disease Rating scale, motor section (MDS-UPDRS-III) in the subset of patients with a positive or borderline scan on expert reading and an available MDS-UPDRS-III score (49 patients). At the end of diagnostic procedure 33 patients were diagnosed with Parkinson’s disease, 5 with dementia with Lewy bodies, 3 with corticobasal syndrome, 2 with idiopathic REM sleep behavior disorder, 1 with progressive supranuclear palsy, 1 with frontotemporal dementia, 2 with tremor of unknown origin and 2 with unspecified dementia); iii) comparison with reading by experts as the gold-standard. The software output could be negative, positive, or borderline (if falling between 1.64 and 2.17 standard deviation below the average value, adjusted for age). For discrepant cases, the putamen-to-caudate (P/C) ratio was regarded as a further index of normalcy/pathology with reference to specific normal cut-off. The lower P/C limits were 0.79 in the right and 0.77 in the left hemisphere, respectively, for Datquant® [7]; they ranged between 0.763 and 0.815 for BasGanV2, according to age [3]. All correlation analyses were corrected (Bonferroni) for multiple comparisons.

Results
SBR, P/C ratio and asymmetries were significantly correlated between the two software (Table 1) with correlation coefficients ranging from $r = .706$ (left P/C ratio) to $r = .887$ (caudate SBR asymmetry) (Fig. 1).

**TABLE 1a. CORRELATION BETWEEN DATQUANT® AND BASGANV2 SBR, RATIO, AND ASYMMETRIES**

|                  | Right Caudate | Left Caudate | Right Putamen | Left Putamen | Right P/C ratio | Left P/C ratio | Caudate asymmetry | Putamen asymmetry |
|------------------|---------------|--------------|---------------|--------------|-----------------|----------------|------------------|------------------|
| Datquant®/       | $r = .771$    | $r = .752$   | $r = .866$    | $r = .847$   | $r = .793$      | $r = .706$     | $r = .870$       | $r = .783$       |
| BasGanV2         | $p < .0001$   | $p < .0001$  | $p < .0001$   | $p < .0001$  | $p < .0001$     | $p < .0001$    | $p < .0001$     | $p < .0001$     |

**TABLE 1b. CORRELATION BETWEEN MDS-UPDRS-III SCORE AND SBR, RATIO, ASYMMETRIES ACHIEVED WITH DATQUANT® AND BASGANV2**

|                  | Datquant®/    | BasGanV2/    |
|------------------|---------------|--------------|
| MDS-UPDRS-III    | $r = -.414$   | $r = -.523$  |
| $p = .0015$      | $p = .0001$   | $p = .0001$  |
|                  | $p = -.434$   | $p = -.532$  |
| $p = .0009$      | $p = .0001$   | $p = .0001$  |
|                  | $p = -.251$   | $p = -.366$  |
| $p = .0405$      | $p = .0048$   | $p = .0001$  |
|                  | $p = -.282$   | $p = -.447$  |
| $p = .0248$      | $p = .0006$   | $p = .0001$  |
|                  | $r = .027$    | $r = -.361$  |
| $p = .4275$      | $p = .0053$   | $p = .0001$  |
|                  | $r = .095$    | $r = .082$   |
| $p = .2573$      | $p = .2884$   | $p = .0284$  |
|                  | $r = .423$    | $r = .277$   |
| $p = .012$       | $p = .0268$   | $p = .0053$  |
|                  | $r = .201$    | $r = .321$   |
| $p = .0413$      | $p = .0122$   | $p = .0001$  |

In the columns the values of SBR, P/C ratio and asymmetry are reported. Asymmetries are computed without taking into account the side of the more affected hemisphere. See the text for abbreviations. Bold characters show statistically significant correlation (one-tail Pearson’s r) while * denotes those correlations surviving Bonferroni’s correction for multiple comparisons (p = .00625 as first level of statistical significance).

Correlation coefficients with the MDS-UPDRS-III score were higher with caudate than with putamen SBR values with both software, and in general higher with BasGanV2 (Table 1; Fig. 2).

Datquant® semi-quantification correspondence with expert reading was in 127 (84.1%) instances. Discrepancies included twelve patients with a major mismatch, i.e., an altered scan according to experts was normal on Datquant®, eleven patients with a borderline scan according to experts but normal on Datquant®, and one patient with a borderline scan for experts but an altered scan on Datquant®. By considering the P/C ratio as a further index of abnormality, ten out of the twelve patients who were normal on Datquant® scored lower than the established cut-off. This raises the agreement with experts to 137 (90.7%) instances.

BasGanV2 semi-quantification correspondence with expert reading was in 122 (80.8%) instances. Discrepancies included only two major disagreements, in which BasGanV2 gave normal SBR despite abnormal expert reading, or vice versa. The majority of disagreement concerned normal expert reading
with BasGanV2 borderline results (20 instances). The remaining seven discrepancies included a combination of positive by experts/BasGanV2 borderline (3 instances), borderline by experts/BasGanV2 positive (3 instances), and borderline by experts/BasGanV2 negative (1 instance). If we consider the P/C ratio as a further index of abnormality, the only false negative scan showed an abnormally low P/C ratio, 5 out of 20 normal scans for experts but borderline with BasGanV2 had indeed normal P/C ratios, and two more abnormal cases for experts with borderline values on BasGanV2 had indeed pathological P/C ratio values, raising correspondence with experts to 130 (86.1%).

Finally, in four instances (2.6%) the two software were concordantly against the expert reading, including two negative cases for the experts but borderline for the two software, one borderline case but positive for the two software, and one positive case but negative for the two software.

Discussion

We have shown that two software for DAT SPECT semi-quantification are highly correlated one another both in absolute SBR and derived P/C ratio and asymmetry values. Highest correlation values were reached for the caudate asymmetry and the putamen SBR. These results highlight the strong similarities between the two tools.

The correlation coefficients with the MDS-UPDRS-III (motor) score was generally significant with both tools but they were higher with BasGanV2 than with Datquant® and, with both tools, more at the caudate than at the putamen level. Correlation between this clinical score and basal ganglia was reported to be similar for caudate and putamen [8], higher for the caudate [9], or the putamen [10], likely depending on the semi-quantification tool and on the patient population. Although the nigro-putaminal impairment should be ideally better correlated to a clinical motor score, the identification of caudate nucleus by automatic software could be more accurate than the putamen because of the very low putamen uptake in severely ill patients. Moreover, the BasGanV2 software includes PVE correction while Datquant® does not, which may explain the better correlation achieved with the former.

Correspondence with expert reading was good (> 80% for both software) especially if the P/C ratio was taken into account in those cases showing discrepancies between experts and software, raising the correspondence with experts of 5.3% and 6.6% for BasGanV2 and Datquant®, respectively (thus to 86.1% and 90.7%). Thus, correspondence with experts was generally slightly higher with Datquant® than with BasGanV2. Indeed, we noted that half of discrepancies with Datquant® derives from false negative cases due to the mis-positioning of the background ROI that sometimes fell partially outside the brain. This should be implemented in a version 2, either improving the automatic positioning or leaving the possibility of ROI hand correction. On the other hand, we noted that the majority of issues with BasGanV2 comes from a high number of borderline cases in instances read as negative by the experts. This might be due to factors, such as differences in collimators and reconstruction parameters as well as in control composition, that are fixed in the software and cannot be customized, as instead happens for Datquant®. As a final remark, we choose to consider reading by expert as the gold standard but the
experts may be sometimes wrong (likely in 4 cases in this study), and actually it has been shown that the semi-quantitative analysis can increase accuracy [2]. If we admitted that those 4 cases were wrong by the experts, then a ‘correct’ reading would raise to 88.7% and 93.3% for BasGanV2 and Datquant®, respectively.

In conclusion, both Datquant® and BasGanV2 work reasonably well and similarly in semi-quantification of DAT SPECT. Both tools have their own strength and pitfalls that must be known in detail by users in order to obtain the best help in visual reading and reporting DAT SPECT.

Declarations

Funding:

this research has received no funding.

Conflicts of interest/Competing interest:

Silvia Morbelli and Flavio Nobili have received fees from G.E. Healthcare for teaching lessons on Amyloid PET. Flavio Nobili participated in development and implementation of BasGanV2 software.

Ethics approval, Consent to participate and Consent for publication:

statements included in the main text

Availability of data and material (data transparency):

original data are available on motivated request

Acknowledgment:

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Authors’ Contribution:

All authors were involved in the collection of the data, analyses and revision of the text; SM and FN were involved in study conception and design and in manuscript writing.
Code availability (software application or custom code):

Datquant® is a CE registered software with number CE 0459.

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Figure 1

Plot of linear correlation between the SBR of the caudate nucleus (a) and of the putamen (b) as achieved with Datquant® (x-axis) and BasGanV2 (y-axis) in 151 subjects. Intercept equation, R2, r, and p values are embedded in the Figures.
Figure 2

Plot of linear correlation between MDS-UPDRS-III score (x-axis) and the SBR of the caudate and putamen nuclei as achieved with Datquant® (a, b) and BasGanV2 (c, d) in 49 patients with parkinsonian syndromes. Intercept equation, R², r, and p values are embedded in the Figures.