Basal Ganglia 3 (2013) 19–24

Contents lists available at SciVerse ScienceDirect

Basal Ganglia

journal homepage: www.elsevier.com/locate/baga

# The percentage of interneurons in the dorsal striatum of the rat, cat, monkey and human: A critique of the evidence

Dorothy E. Oorschot *

*Department of Anatomy, Otago School of Medical Sciences, and the Brain Health Research Centre, University of Otago, Dunedin, New Zealand*

ARTICLE INFO

*Article history:*
Received 1 October 2012
Accepted 7 November 2012

*Keywords:*
Dorsal striatum
Interneurons
Cholinergic
Parvalbumin
Somatostatin
Calretinin

ABSTRACT

In the published literature on mammals, there are various answers to the question: What percentage of the total population of neurons within the dorsal striatum is represented by interneurons? The percentage of interneurons is reported to be 26% for the human, 23% or 4–6% for the monkey, 5–6% or <3% for the rodent, 4–5% for the cat and 5–10% for the mammal. Based on a critique of the literature, including the use of stereological approaches, caution is needed when citing historical non-stereological data on the percentage of interneurons in the dorsal striatum of the cat, monkey and human. In these species, the vast majority of neurons in the dorsal striatum are spiny projection neurons and a smaller number are interneurons, yet the precise percentage is currently unknown. Hence, in the absence of stereological data on the absolute number of all neuronal subtypes for the cat, monkey and human, it is currently unknown if there is a species difference, or not, for the percentage of interneurons in the dorsal striatum of the human and monkey versus the cat and rat. Modern stereological data indicate that the percentage of interneurons in the rat dorsal striatum is <3%. More specifically, in the Sprague-Dawley rat, 0.8% of all neurons are somatostatin/neuropeptide Y/GABA interneurons, 0.4% are cholinergic interneurons, ~0.6% are GABA/parvalbumin interneurons and 0.5% are GABA/calretinin interneurons. Current stereological data also indicate that the percentage of interneurons in the dorsal striatum is <1% for cholinergic interneurons in the Sprague-Dawley rat and human.



## 1. Introduction

The mammalian dorsal striatum is a major input nucleus of the basal ganglia and is primarily involved with motor and associative functions [1]. The dorsal striatum in rodents is a single nucleus called the caudate-putamen. In higher vertebrates the dorsal striatum is comprised of the caudate nucleus and the putamen, which are partitioned by the internal capsule. Within the dorsal striatum of mammals, the vast majority of neurons are considered to be medium-sized spiny projection neurons [2]. The number of interneurons in the dorsal striatum is thus generally considered to be small. Compared to the striatal spiny projection neurons, the striatal interneurons are aspiny [2]. In spite of a relatively small number of aspiny interneurons, their role(s) are likely to be functionally profound [2].

In the published literature on mammals, there are various answers to the question: What percentage of the total population of neurons within the dorsal striatum is represented by interneurons? A difference in prevalence between species has been indicated by some [3–10] but not by others [11,12]. Species differences could be important, for example, in determining the validity of animal models of human pathology.

The percentage of interneurons in the dorsal striatum is reported to be 26% for the human [4,13,14], 23% or 4–6% for the monkey [3,11,12], 5–6% for the rat and mouse (i.e. rodent [3]) or <3% for the rat [15], 4–5% for the cat [4,16], and 5–10% for the mammal [2,17]. The early evidence for these percentages is summarised by Roberts et al. [4] (see their Table 5), which is included in this current review as Table 1. These reports raise the question: For the percentage of interneurons in the dorsal striatum is there a species difference or not between the human, monkey, cat and rat? A critique of the evidence is discussed in the next sections.

Four major types of aspiny interneurons have been identified within the normal dorsal striatum of mammals [2,10]. These are the large cholinergic interneurons, and the medium-sized GABA/parvalbumin interneurons, GABA/calretinin interneurons, and somatostatin/neuropeptide Y/nitric oxide synthase/GABA interneurons (see Fig. 1). The cholinergic, GABA/parvalbumin, and somatostatin/neuropeptide Y/GABA interneurons innervate the

* Corresponding author at: Department of Anatomy, Otago School of Medical Sciences, University of Otago, P.O. Box 913, Dunedin, New Zealand.
Tel.: +64 3 479 7379; fax: +64 3 479 7254.
*E-mail address:* dorothy.oorschot@anatomy.otago.ac.nz.

2210-5336/$ – see front matter © 2012 Elsevier GmbH. All rights reserved.
http://dx.doi.org/10.1016/j.baga.2012.11.001

**Table 1**
The early evidence cited by Roberts et al. [4] on the percentage of aspiny neurons (i.e. interneurons) in the dorsal striatum of the human, monkey (*Macaca fascicularis*), cat and rat (Sprague-Dawley). Note that this evidence is based on non-stereological data and may be misleading for the human, monkey and cat (see the text for further details). In the Sprague-Dawley rat, the percentage of all the aspiny interneurons is half the value indicated here (i.e. <3%, see Table 2).

| Species | Medium spiny (%) | Medium aspiny (%) | Large aspiny (%) |
|---|---|---|---|
| Human[a] | <76 | >23 | 1 |
| Monkey[b] | 76 | 23 | 1 |
| Cat[c] | 95–96 | 3–4 | 1 |
| Rat[b] | 95–96 | 4–5 | 1 |

[a] Data from Graveland et al. [13].
[b] Data from Graveland and DiFiglia [3].
[c] Data from Kemp and Powell [16].

spiny projection neurons (see reviews by Kawaguchi et al. [2] and Oorschot [18]). Whether the GABA/calretinin neurons innervate the spiny projection neurons remains to be investigated. A critique of the evidence for the percentage of each type of interneuron in the dorsal striatum of the rat, monkey and human is also discussed in the next sections.

Investigation of the percentage of interneurons, and the percentage of each type of interneuron, requires quantitative data from stained sections of the dorsal striatum. The limitations of some of the methods that have been used are discussed below.

## 2. A critique of the early evidence for the cat, monkey and human

To obtain quantitative (i.e. stereological) data from sections on the number and percentage of neurons, one must be confident that all of the cells of interest are observable (stained) and can be distinguished from other cell types [19,20]. One must also know the three-dimensional extent of the entire region that contains the neurons (i.e. the dorsal striatum in this instance). This ensures that all of the neurons can be sampled with equal probability and permits the measurement of the absolute number of the specific neurons of interest [19,20]. The use of these stereological principles will now be discussed for the relevant literature.

In the cat, the percentage of 4–5% for all interneurons in the dorsal striatum is derived from Golgi stained sections [16]. A fundamental characteristic of Golgi impregnation is that it outlines only 5–10% of the neurons present in a given structure [21,22]. This limitation restricts considerably its value in regard to the quantitative evaluation of the relative proportion of various neuronal types [21,22]. Such a limitation may be even stricter since it is possible that certain classes of cells are more susceptible

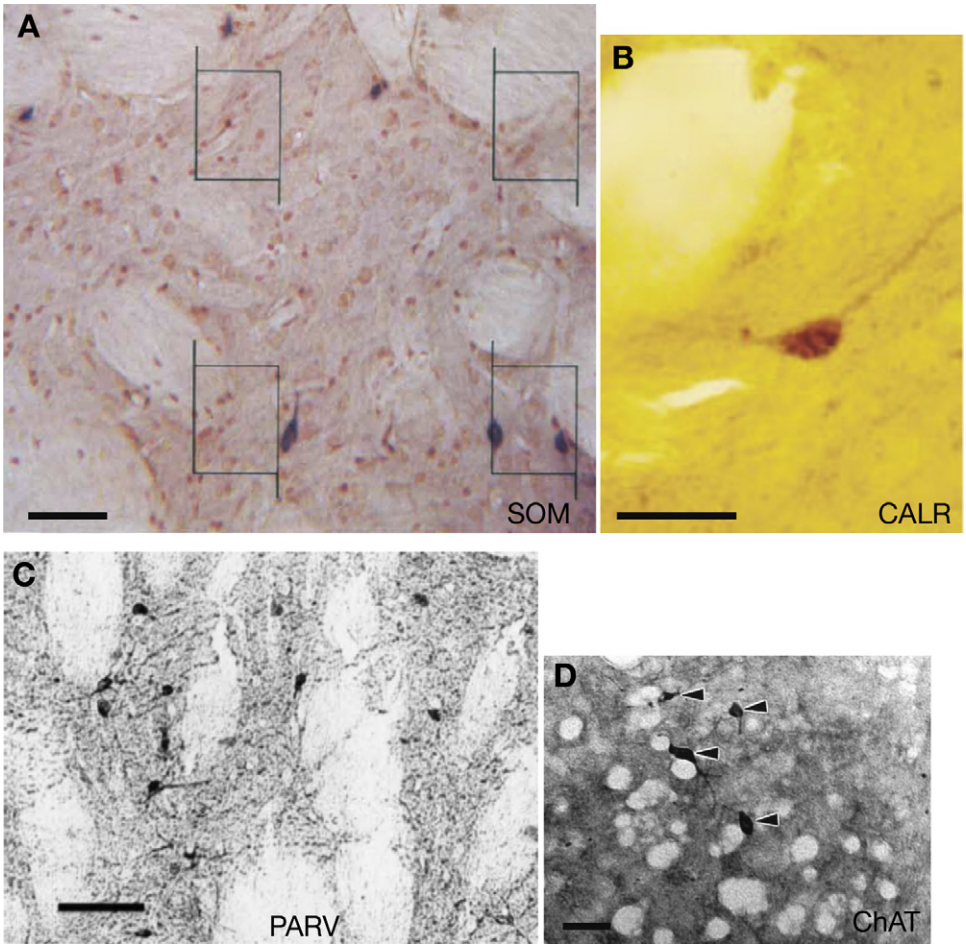


**Fig. 1.** Light micrographs of interneurons in the dorsal striatum of the Sprague Dawley rat. (A) Somatostatin (SOM) interneurons (from Ref. [33]), (B) a calretinin (CALR) interneuron (from Ref. [36]), (C) parvalbumin (PARV) interneurons (from Ref. [35]), and (D) cholinergic (ChAT) interneurons (from Ref. [34]). In (A), the purple interneurons have been in situ hybridised for somatostatin mRNA and the tissue, including the nucleus of the hybridised interneurons, has been counterstained with neutral red. Superimposed on the section are a number of unbiased counting frames that were used to count these somatostatin interneurons using the optical disector method. In (B), a calretinin interneuron has been double-immunostained for calretinin and for bromodeoxyuridine (a nuclear label for detecting recently generated neurons during development). In (C) parvalbumin interneurons have been immunostained for parvalbumin. In (D) cholinergic interneurons (arrowheads) have been immunostained for choline acetyltransferase (ChAT). Scale bars: (A) 50 μm, (B) 25 μm, (C) 100 μm and (D) 45 μm. Used with permission.