THE CLASSIFICATION OF PROJECTION NEURONS IN THE RAT GLOBUS PALLIDUS

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The globus pallidus (GP) is a central nucleus of the basal ganglia, projecting to all other basal ganglia nuclei (Bolam *et al.*, 1993; Smith and Bolam, 1989; Bevan *et al.*, 1998; Sato *et al.*, 2000). It plays a crucial role in the function of the basal ganglia as a whole (Gillies *et al.*, 2002; Ashby *et al.*, 1998). Most authors agree that several types of projection neurons exist in the GP (Kita and Kitai, 1991; Nambu and Llinás, 1994, 1997; Cooper and Stanford, 2000). Based on morphological characteristics, these GP projection neurons can be divided into two classes; radial and discoidal (Park *et al.*, 1982). However, there is much less agreement in classifying the variety of electrophysiological neuron characteristics (Kita and Kitai, 1991; Nambu and Llinás, 1994, 1997; Cooper and Stanford, 2000). Neurons may be classified by whether they contain the ramp depolarisation characteristic of a potassium A–current (Cooper and Stanford, 2000). Alternatively, they may be classified by whether they exhibit a post–hyperpolarising response characteristic of the the low threshold calcium current (Nambu and Llinás, 1994, 1997) or whether they have depolarising sag in membrane voltage generated by the anomalous inward rectifier Ih (Cooper and Stanford, 2000). Furthermore neurons can be divided into physiological classes based on whether they are spontaneously active, generate bursts or are quiescent at rest (Kita and Kitai, 1991). The physiological classes of GP neurons will play a crucial role in the computations performed by the pallidum, particularly in the recurrent interactions it has with the subthalamic nucleus and striatum (Kita *et al.*, 1983; Shink *et al.*, 1996; Bevan *et al.*, 1998). We present models of the physiological and morphological characteristics of GP projection neurons. These models not only allow us to make explicit the role of morphology and channel types in the physiological characteristics of GP projection neurons, but also allow us to compare the conflicting views of neuron classes within a structured framework.

By grouping together the physiological properties where there is agreement among authors we identify two main neuron types exhibiting a minimum set of distinct physiological features. We label these type 1 and type 2. A third physiological type is recognised to exist but due to its low frequency of experimental isolation we have insufficient data to explore it. Type 1 neuron characteristics include an anomalous inward rectifier Ih, long action potential duration, and a long lasting after–hyperpolarisation. Type 2 neuron characteristics include an A–type outward current and shorter action potential duration and after–hyperpolarisation. Examples of characteristics that cross these minimal groupings include low threshold calcium spikes which may be classified in either group by various authors and the observations of spontaneous, burst, or quiescent activity.

We construct multicompartmental models using the two classes of morphological types of rat GP projection neuron and the physiological properties of the type 1 and type 2 neuron classes. Using this modelling framework we demonstrate the following:

1. The primary characteristics of the type 1 and type 2 neurons are reproduced with a minimum set of channels confirming the dominance of the anomalous inward rectifier Ih in type 1 and the A current in type 2.

2. Experimentally derived kinetic forms of specific channel types obtained from other areas of the CNS in rat are sufficient to fully characterise the key physiological properties

of the two classes of GP projection neuron.

3. The two physiological classes reside in the same morphological class; that is, type 1 and type 2 neurons have discoidal dendritic fields.

4. Both neuron types can exhibit the bursting and non-bursting firing characteristics. This is determined by the presence and distribution of the low threshold calcium channel.

5. Both type 1 and type 2 neurons are based on channel distributions that may form a continuum encompassing both types. This provides an explanation for the wide variation in projection neuron characteristics experimentally observed.

All simulations were performed in the NEURON simulation environment.

These models make explicit the core features and the underlying mechanisms of the experimentally observed primary neuron types in the rat GP. They also allow us to predict the channel distributions across populations of GP neurons that lead to the variety of neuron characteristics observed. Furthermore, they provide a framework in which to explore the interactions of the GP projection neurons with the subthalamic nucleus, striatum, and entopeduncular nucleus.

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