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Basal Ganglia Mechanisms Underlying Precision Grip Force Control

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Abstract

The classic grasping network has been well studied but thus far the focus has been on cortical regions in the control of grasping. Sub-cortically, specific nuclei of the basal ganglia have been shown to be important in different aspects of precision grip force control but these findings have not been well integrated. In this review we outline the evidence to support the hypothesis that key basal ganglia nuclei are involved in parameterizing specific properties of precision grip force. We review literature from different areas of human and animal work that converges to build a case for basal ganglia involvement in the control of precision gripping. Following on from literature showing anatomical connectivity between the basal ganglia nuclei and key nodes in the cortical grasping network, we suggest a conceptual framework for how the basal ganglia could function within the grasping network, particularly as it relates to the control of precision grip force.

Keywords

grasping; network; gripping; sub-cortical; imaging

1. Introduction

The ability to grip an object is an important skill in everyday life impacting such actions as writing, grooming, and holding a drink. The ability to skillfully manipulate objects around the environment is not possible unless appropriate forces are developed and then adjusted to the demands of the object being gripped and the task at hand. The consequences of a poor grip in healthy adults can range from mild (e.g. sloppy handwriting) to serious (e.g. spilling hot coffee). The brain circuitry that underlies the control of gripping an object is not yet fully understood.

The ability to grip is itself part of a larger construct of grasping, which includes reaching toward an object and pre-shaping the hand appropriately depending on the visual properties of the

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object (Cattaneo et al., 2005; Jeannerod et al., 1995; Santello and Soechting, 1998; Wang and Stelmach, 1998). While there are many ways to reach out to an object or hold it, the act of exerting force against the object is a common action across all grasping tasks. Control of grip force during grasping differs from other aspects of grasping and movement because it is defined by the interaction of the hand with the object. Thus, precision grip control requires precise and fine manipulation of the forces applied to an object. The forces developed are, at least initially, based on the visual properties of the object and prior experience, and thus the visuomotor transformation process plays an important part in precision grip force control.

Standard neuroscience teaching often defines the visuomotor transformations required for reaching and grasping an object as involving two different pathways from the primary visual cortex to the premotor areas (Figure 1): a dorsolateral circuit consisting of the anterior intraparietal (AIP) area connected to the rostral part of the ventral premotor cortex (PMv; area F5), and a dorsomedial circuit consisting of the anterior portion of the occipito-parietal sulcus (area V6A) and the caudal dorsal premotor cortex (PMd; area F2). Within this classification, it is the dorsolateral circuit which has been linked to the grasping and manipulation of prehension, whereas the dorsomedial circuit has been linked to the reaching component of grasping. However, within the grasping circuit, the role of subcortical structures, particularly the basal ganglia, in such a classification has not been well defined. In a recent review entitled “The Neuroscience of Grasping”, Castiello (2005) argued that the classic grasping circuit is overly simplistic and does not include other regions such as cerebellar and subcortical areas. In this review, we focus on recent evidence to support the role of the basal ganglia in precision gripping.

The basal ganglia (BG) are a set of interconnected subcortical nuclei in a circuit composed of excitatory and inhibitory neurotransmitters that are hypothesized to regulate cognitive, limbic, and sensorimotor processes (Alexander et al., 1990; Bhatia and Marsden, 1994; DeLong and Wichmann, 2007; Parent and Hazrati, 1995; Utter and Basso, 2008). The five principle nuclei of the basal ganglia are the putamen, caudate nucleus, globus pallidus, substantia nigra, and subthalamic nucleus (STN) (Figure 2). They have major projections to the thalamus, cerebral cortex, and certain brain stem nuclei, and receive major input from several regions including the cerebral cortex, thalamus, and cerebellum. Over the past several decades, models of basal ganglia circuitry have been developed in animals that describe how neurotransmitters change the inhibitory and excitatory properties of specific basal ganglia nuclei (Alexander et al. 1986). The role of the basal ganglia in the control of limb movements has also been well documented (Anderson and Turner, 1991; Mushiake and Strick, 1995; Turner et al., 2003; Vaillancourt et al., 2004b). However, there is emerging evidence from work in healthy individuals, as well as in individuals with diseases affecting the basal ganglia, that the basal ganglia also play an important role in the control of precision grip force. Indeed, it has been suggested that a pallidothalamic pathway directly innervates the hand representation in primary motor cortex (Holsapple et al., 1991; Nambu et al., 1988) suggesting that the basal ganglia can directly influence the hand representation of the primary motor cortex.

In the review that follows, we first review literature from different areas of human and animal work that converges to build a case for basal ganglia involvement in the control of precision gripping. Then, we review the literature that establishes anatomical connectivity between the basal ganglia nuclei and key nodes in the grasping network and suggest a conceptual framework for how the basal ganglia could function within the grasping network, particularly as it relates to the control of precision grip force.

2. The basal ganglia are involved in the control of precision grip force

A review of the literature from both human and animal work is provided. We first discuss evidence linking the basal ganglia to the control of precision gripping in healthy individuals. Next we examine evidence from lesion studies of the basal ganglia in both animals and humans. Then we review precision gripping deficits in humans with movement disorders affecting the basal ganglia.

2.1. Evidence from neuroimaging in neurologically intact individuals

Transforming visual cues about an object into an appropriate grip force to apply to an object requires both planning to select an appropriate initial grip force, and then careful modulation of the applied grip force following interaction with the object. The basal ganglia are well suited to meeting both of those needs. Advances in neuroimaging techniques have recently allowed investigation of how specific nuclei of the basal ganglia function during precision grip force control. These studies in healthy individuals have suggested that while all BG nuclei show increased activation with precision grip force tasks, the more anteriorly located basal ganglia nuclei (caudate, posterior putamen, anterior putamen, and external portion of the globus pallidus (GPe)) show a scaled blood-oxygenation-level-dependent (BOLD) response in relation to the planning aspects of precision gripping such as selecting which force to apply or predicting an appropriate force level for a given task. In contrast, the more posteriorly located nuclei (STN and internal portion of the globus pallidus (GPi)) show a BOLD response that scales with dynamic parameters of grip force output such as force amplitude and rate of force generation (Figure 3).

Planning to apply precision grip force requires, among other things, predicting how much force would be required to grip the object and selection of an appropriate initial level of force. Specific basal ganglia nuclei have been implicated as being important in each of these planning steps. Vaillancourt et al. (2007) asked subjects to produce precision grip force that was either at a consistent force amplitude level or was deliberately varied by the subject to select different force amplitudes. Using fMRI to examine activation in the basal ganglia, they found increased activation in caudate, putamen, GPe, GPi, and STN. However, only the anterior basal ganglia nuclei (caudate, anterior putamen and GPe) show increased activation related to the selection component of the task whereas activation in the posterior nuclei was specifically involved in the regulation of basic aspects of dynamic force pulse production. Pope and colleagues (2005) used a slightly different task to Vaillancourt et al., but also found a specific role for anterior basal ganglia nuclei in precision grip force control. They used fMRI to examine brain activation during four self-paced pinch grip force tasks that varied in force amplitude and relative timing. They found a clear pattern of activation across all tasks compared to rest that included activation in the basal ganglia. The magnitude of activation in putamen and caudate was highest for the two conditions where the task required switching between two force amplitude levels compared to the two tasks where the timing varied but force amplitude was the same. This switching between different force amplitudes may be analogous to the selection of different force amplitudes.

Memory of previous gripping experiences allows adjustment of force output in a predictive, feed-forward manner (Gordon et al., 1993; Johansson et al., 1992). Prediction therefore is an important element in grip control. Wasson et al. (2007) investigated how predictability influenced both the amplitude and time-varying response of the BOLD signal in the cortex, basal ganglia, and cerebellum during a precision grip force control task. Within the basal ganglia, both putamen and caudate scaled in activation with increases in the predictability of the grip force necessary to achieve the target. Boecker et al. (2005) used positron emission tomography (PET) to examine predictive motor control in a task which required coordinated grip and pull forces. During the task, subjects were required to exert a grip force on an object

which was coordinated with a pull force exerted on that object which acted through the elbow. This task therefore required the subject to predict the consequences on grip of their own pulling behavior and adjust the grip force appropriately. Examining the interaction effect of grip force and pull force while factoring out activity related to grip or pull force alone revealed activation in the ipsilateral posterior cerebellum, the anterior cingulate cortex, the ipsilateral lingual gyrus, and the ipsilateral caudate nucleus. Taken together, these studies offer direct support to the role of anterior basal ganglia nuclei in the planning aspects of grip force control.

Following the initial selection and prediction of an appropriate grip force, there are many gripping parameters that must be controlled in order for the grip to be successful. These include the rate at which grip force is developed so that there is appropriate coordination of the grip and load forces, the amplitude of applied grip force so that it is scaled appropriately to the weight of the object being lifted, and the duration over which grip force is applied. Specific basal ganglia nuclei have been implicated in the control of each of these parameters. Vaillancourt et al. (2004a) used fMRI during a visually guided precision grip task to investigate brain regions that scaled in activation volume with the rate of change of force development and the duration of force. Subjects produced force at different rates and durations to a target of set amplitude. They found that only activation in the STN and GPi scaled parametrically with the rate of change of force production. In contrast, the putamen and GPe increased in activation with the duration but not the rate of grip force contraction. These findings were subsequently replicated by Prodoehl et al. (2008) and extended to include the control of auditory guided precision grip force control.

In addition to the rate at which grip force is controlled, there must be appropriate coordination between the applied grip force and the load force. Ehrsson and colleagues (2003) examined the coordination of thumb-finger grasp in a grip-load force task using fMRI. They found an extensive distribution of activation which included bilateral putamen when comparing the grip-load force task to the baseline rest condition. They concluded that fronto-parietal areas located in both hemispheres and subcortical motor structures work in concert in the control of skillful manipulatory actions.

Another important parameter in precision grip force that must be controlled is the peak grip force exerted. When attempting to lift an object, the size of the object itself influences the peak grip force exerted on the object such that larger objects are lifted with higher peak grip forces (Gordon et al., 1991). Kinoshita et al. (2000) used positron emission tomography (PET) to examine functional brain areas involved when subjects used a precision grip to lift small objects of different weights. (Note: recording of grip and lift forces were performed in separate experimental sessions to PET scanning in this study). They found that in addition to the primary and secondary sensorimotor cortical areas expected to be activated during a grip and lift task, there was activation in the inferior parietal cortex, contralateral posterior putamen, thalamus and cerebellum. Although activation in the primary motor cortex scaled across all three object weights, activation in the putamen increased only when the heaviest weight was compared to the lowest weight suggesting some scaling of basal ganglia activation with object weight. Spraker et al. (2007) specifically investigated activation scaling in the basal ganglia associated with changes across a large range of grip force amplitudes. They showed that specific nuclei of the basal ganglia and thalamus increased in percent signal change with the amplitude of grip force. Subjects produced pinch grip force to targets ranging from 5% to 80% of their maximum voluntary contraction. Within the basal ganglia they found that the GPi and STN had a positively scaled increase in percent signal change when producing force contractions of increasing force amplitude whereas GPe, putamen, and caudate did not.

In summary, there is evidence in the literature to support the hypothesis that anteriorly located basal ganglia nuclei (caudate, anterior putamen, and GPe) are involved in planning aspects of

precision gripping, whereas posteriorly located nuclei (posterior putamen, GPi and STN) are involved in scaling dynamic parameters of grip force output (e.g. rate and amplitude). Based on the model presented in Figure 3, one might ask the following question: how do planning signals pass to the thalamus if the output nucleus (e.g. GPi) does not specifically regulate planning of grip force output? In addressing this question, it is important to emphasize that even though activation in posterior basal ganglia nuclei does not scale when the planning aspects of grip tasks are manipulated, there is activation present in posterior basal ganglia nuclei (e.g. GPi) when grip force contractions are compared to a resting baseline state (Vaillancourt et al. 2007). By the same token, even though the activation in anterior basal ganglia nuclei does not scale with the rate and amplitude of grip force, there is greater activation in anterior basal ganglia nuclei during a grip force task than at a baseline resting state (Spraker et al. 2007). Thus, as shown in Figure 2, we suggest that neural signals are sent from the basal ganglia to the thalamus via GPi or the substantia nigra pars reticulata (SNpr), and these two output nuclei do not necessarily have to modify the neural signals in the same way as previous basal ganglia structures. Next, we review the findings from studies which have examined behavioral changes following damage to the basal ganglia.

2.2.Evidence from lesion studies

Animal work has focused on lesioning specific sub cortical regions and examining the behavioral consequences on grip force control. These studies have demonstrated that specific lesions within the basal ganglia have direct consequences on grip force behavior. For example, Dunnett et al. (1998) examined grip strength in rats following unilateral lesioning of the nigrostriatal bundle. In their task, the rat held on to a bar and resisted attempts to be pulled away. The applied force at which the rat released the bar was measured as grip strength. Two weeks after lesioning, the animals showed significantly increased peak grip force on the grip force release task in the contralateral limb compared to control rats. The authors interpreted the increase in grip force following lesion as either being a homologue to the rigidity seen in human Parkinson's disease or as impairment in the ability to release applied force following lesioning. The increase in contralateral limb grip strength following nigrostriatal lesioning was later replicated by Jeyasingham et al. (2001) and the results extended to include increases in grip strength following lesions isolated to the neostriatum. When comparing grip strength changes between rats with nigrostriatal lesions and rats with striatal lesioning, striatal lesioning did not produce as much change in grip strength as nigrostriatal lesioning. These two animal lesion studies provide a direct link between structural changes in the basal ganglia and changes in grip force behavior.

Individuals who have suffered a stroke centered in the BG offer a unique opportunity to study the isolated effects of BG damage on motor control. Specifically related to grip force, one task which is expected to show deficits in individuals with BG lesions is the ability to scale applied grip force to the size of the object. In healthy individuals, the grip force exerted to lift an object normally increases as object size increases (Gordon et al., 1991) suggesting that the programming of grip force is dependent on the integration of visual and tactile information. Dubrowski et al. (2005) examined grip force control in a single case study design of an individual with unilateral basal ganglia damage following ischemic stroke which was centered on the left putamen, but extended to include the anterior internal capsule, the head of the ventral caudate and the GPe. They examined grasping of three objects which differed in size but not mass. They found that, unlike healthy individuals, the individual with chronic stroke produced significantly higher grip forces and was unable to appropriately scale the applied force to the size of the object when using the contralesional hand. In addition, the individual showed an impaired ability to scale the peak rate of grip force production to object size when using the contralesional hand, but not when using the ipsilesional hand. These findings suggest that the

BG nuclei are important in the appropriate scaling of motor output to the demands of the task and in the initial selection of gripping parameters based on visual properties of the object.

2.3.Evidence from studies of patients with movement disorders affecting the basal ganglia

There are many movement disorders which are thought to arise as a result of basal ganglia malfunction. Each of these movement disorders has a widely differing clinical presentation and yet the most common disorders have precision gripping deficits associated with them.

2.3.1. Parkinson's disease—Parkinson's disease (PD) affects basal ganglia functioning due to striatal dopamine depletion. Similar to individuals with focal BG lesions, individuals with PD have been shown to produce higher peak grip forces compared to controls when the load required for the task is unknown (Fellows et al., 1998; Wenzelburger et al., 2002) or even when patients have some a priori knowledge of the upcoming load (Nowak and Hermsdorfer, 2006). In patients with deep brain stimulation (DBS) of the subthalamic nucleus (STN), this excessive grip force has been shown to be either improved (Nowak et al., 2005; Wenzelburger et al., 2002) or worsened (Fellows et al., 2006) when stimulation is turned on.

In relation to the control of precision grip force, individuals with PD show increased variability in grip force output when maintaining a consistent grip force compared to healthy individuals (Vaillancourt et al., 2001). While it appears that patients retain the ability to scale grip force according to load (Fellows et al., 1998; Nowak and Hermsdorfer, 2006), individuals with PD show dyscoordination of the temporal coupling between grip and load force (Alberts et al., 1998; Fellows et al., 1998; Ingvarsson et al., 1997; Nowak and Hermsdorfer, 2002). This is particularly evident in more complicated tasks requiring multi-finger coordination. For example, Santello and colleagues (2004) examined the control of multi-digit grasping in PD by changing an object's center of mass either predictably or unpredictably. They found clear differences between controls and individuals with PD in the temporal evolution of fingertip forces as a function of the object's center of mass location. When on medication, PD subjects were able to modulate forces to the object's center of mass location to a greater extent compared to when off medication. Control subjects employed a wider range of forces when the object's center of mass location could be predicted than when it could not be. In contrast, predictability did not enhance overall force modulation in individuals with PD when off medication, suggesting that they did not take advantage of the a priori knowledge of the object's center of mass to plan the next set of grip forces.

A higher than necessary grip force is not unique to individuals with BG lesions or PD. This phenomena is also seen in healthy individuals when cutaneous afferents of the hand are subjected to local anesthesia (Nowak et al., 2001; Witney et al., 2004) and in individuals with peripheral sensory neuropathy (Hermsdorfer et al., 2004; Nowak et al., 2004) suggesting that sensory afferent information from the digits may also play an important role in scaling applied grip force to expected object load. Indeed, individuals with PD have been shown to have deficits in sensory processing (Demirci et al., 1997; Jobst et al., 1997; Klockgether et al., 1995; Schneider et al., 1987) which might be related to their grip force scaling deficits. Higher than expected grip forces and disturbances in grip and load force coordination have also been shown in patients with cerebellar dysfunction (Fellows et al., 2001; Serrien and Wiesendanger, 1999a; Serrien and Wiesendanger, 1999b), and it has been suggested that the integrity of sensorimotor cortical areas, the cerebellum, and the basal ganglia is necessary for the optimal regulation of grasping forces during manipulative tasks (Wiesendanger and Serrien, 2001).

In summary, lesioning the basal ganglia and PD can result in higher grip forces, an impairment in releasing objects, a reduced ability to scale forces, and increased variability in force production. Each of these deficits could be characterized as an alteration in the ability to program and regulate grip force in the face of rigidity. However, while it is true that that the

presence of rigidity could lead to difficulties in releasing objects and could also result in higher grip forces, it is not clear that rigidity per se would cause problems in programming and regulating grip force beyond simply overgripping. In addition, STN DBS has been shown to improve limb rigidity (Shapiro et al., 2007) and yet it can impair grip force control (Fellows et al., 2006). As such, limb rigidity probably does not explain all the gripping impairments seen following focal BG lesions or in PD.

2.3.2. Dystonia—Dystonia describes a movement disorder characterized by abnormal, involuntary sustained twisting movements and abnormal postures of affected body parts (Fahn et al., 1987). Evidence thus far has suggested that dystonia is related to an abnormality in basal ganglia function (Bhatia and Marsden, 1994; Sheehy and Marsden, 1982). Patients with dystonia have been shown to have difficulty in different aspects of precision gripping. Similar to individuals with PD, individuals with focal hand dystonia have been shown to program higher than normal grip forces (Nowak and Hermsdorfer, 2006; Obergren et al., 1996; Serrien et al., 2000). Patients with writer's cramp have also shown an impaired ability to regulate precision grip force in both the symptomatic and asymptomatic hands, although their ability to anticipate an upcoming load perturbation appears to be intact (Serrien et al. 2000).

2.3.3. Huntington's disease—Huntington's disease (HD) is an inherited neurodegenerative disorder of a progressive nature, with known basal ganglia pathology, particularly affecting the striatum. Similar to PD and dystonia, HD is associated with elevated grip force levels (Schwarz et al., 2001; Serrien et al., 2001; Serrien et al., 2002a) and slowness of grip force development (Serrien et al., 2001). Grip and load force coupling is also disturbed in HD, and these disturbances increase with task complexity (Serrien et al., 2002a). Individuals with HD also show increased grip force variability, both in magnitude (Reilmann et al., 2001; Schwarz et al., 2001) and timing relative to the load (Gordon et al., 2000; Schwarz et al., 2001). This increased variability in static grip force has been shown to be correlated with motor measures of clinical impairment (Gordon et al., 2000), and to worsen over a three year follow-up period (Reilmann et al., 2001). When a precision grip is unexpectedly perturbed in patients with HD, they show a significant lag in their response (Fellows et al., 1997; Serrien et al., 2001). This delayed response to loading in HD has been interpreted as being due to attenuated afferent responses by a damaged striatum. Under this hypothesis, the threshold for eliciting a corrected response would be reached significantly later than normal, thus explaining the delayed grip change responses seen in individuals with HD.

2.3.4. Gilles de la Tourette syndrome—Gilles de la Tourette syndrome (TS) is an inherited neuropsychiatric disorder with onset in childhood, characterized by the presence of multiple physical tics and at least one vocal tic. The pathophysiology of TS has been linked to BG and thalamocortical circuit dysfunction (Singer, 1997). Individuals with TS have been shown to overscale their motor output during unimanual and bimanual grip and lift tasks compared to controls, and to have more difficulty coordinating grip and load forces during bimanual grip and lift tasks than during unimanual tasks (Serrien et al., 2002b). Functional MRI during a grip and lift task in individuals with TS showed underactivation in the basal ganglia and thalamus compared to controls (Serrien et al., 2002b).

In summary, basal ganglia dysfunction associated with Parkinson's disease, Huntington's disease, dystonia and Gilles de la Tourette syndrome is associated with specific grip force deficits. The common deficit in the presence of basal ganglia dysfunction across both animal and human studies is an overproduction of grip force which is consistent with a role of specific nuclei of the basal ganglia in the parameterization of grip force (Figure 3).

3. Conceptual framework for how the basal ganglia function within the classic grasping circuit

The control of grasping requires precise coordination of fingertip forces (Blakemore et al., 1998; Flanagan and Wing, 1997; Johansson and Westling, 1984; Johansson and Westling, 1988; Wing et al., 1997). The motor commands for grasp and object manipulation must be finely matched to the properties of the object and the goal of the task. Specific nuclei of the basal ganglia may assist the cortex in the planning and parameterization of grip force, via the thalamus. Such parameters would include grip force amplitude and rate of grip force development (Figure 3).

There appears to be two anatomically segregated parieto-frontal circuits which control reaching and grasping: a dorsolateral circuit controlling the grasp component, consisting of an anterior intraparietal (AIP) area connected to the rostral part of the ventral premotor cortex (PMv), and a dorsomedial circuit controlling the reaching component, consisting of the anterior portion of the occipito-parietal sulcus (area V6A) and the caudal dorsal premotor cortex (PMd) (Galletti et al., 2003; Tanne-Gariepy et al., 2002). Application of force to an object falls under the “grasp” part of this network (i.e. the dorsolateral circuit). However, it should be noted that there may not be a strict dichotomy between circuitry controlling the reach and grasp components. In an analysis of the changes in effective connectivity in the occipito-parieto-frontal network during a visually guided reach and grasp task, Grol et al. (2007) suggest that contributions to the dorsolateral and dorsomedial circuits are a function of the degree of on-line control required by the task related in part to the object size and width. Using dynamic causal modeling, they showed that during the prehension of small objects, effective connectivity of the dorsolateral circuit was increased whereas grasping large objects increased inter-regional coupling within the dorsomedial circuit.

The output nuclei of the basal ganglia have shown clear anatomical connectivity with the two key nodes in the dorsolateral circuit controlling grasping, namely the anterior intraparietal area (AIP) and the ventral premotor cortex (PMv) (Figure 4). AIP contains neurons that respond to three dimensional shape, size, and orientation of an object (Murata et al., 2000) and this region may be involved in the reactive online adjustment of grip force during object manipulation (Dafotakis et al., 2008). Consistent activation has been shown in area AIP in humans using fMRI when performing visually guided grasping (Frey et al., 2005), and disruption of AIP in monkeys by injection of muscimol leads to deficits in hand preshaping (Gallese et al., 1994). Area AIP in monkeys has been shown to be selectively and reciprocally connected to area F5, the rostral part of PMv (Ghosh and Gattera, 1995; Lewis and Van Essen, 2000; Luppino et al., 1999; Matelli et al., 1986; Petrides and Pandya, 1984; Tanne-Gariepy et al., 2002), while PMv has been shown to be connected to the primary motor cortex (Martino and Strick, 1987; Tokuno and Tanji, 1993). Reversible inactivation of neurons in the rostral part of area F5 in monkeys, the homologue of human PMv, produces impairments in hand shaping preceding grasping, and impaired scaling of hand posture to object size and shape (Fogassi et al., 2001). In humans, PMv has also been linked to the predictive scaling of precision grip force (Dafotakis et al., 2008).

Connections to the dorsolateral circuit from the basal ganglia come through both PMv and AIP (Figure 4). PMv is the target of output from both the dentate and the internal segment of the globus pallidus (GPi) via the thalamus (Hoover and Strick, 1993; Middleton and Strick, 2000), and AIP is the target of both basal ganglia and cerebellar output via the thalamus (Clower et al., 2005). Specifically, AIP receives a broadly distributed as well as a focal projection from the dentate nucleus of the cerebellum which forms an output channel via the thalamus to AIP. Within the basal ganglia, AIP receives a projection, via the thalamus, from neurons located in the caudal two thirds of the substantia nigra pars reticulata (Clower et al.,

2005). Therefore, as well as output connections to the motor cortex (Akkal et al., 2007; Clower et al., 2005; Hoover and Strick, 1999; Middleton and Strick, 2000), prefrontal cortex (Middleton and Strick, 1994; Middleton and Strick, 2002), and temporal lobe (Middleton and Strick, 1996), the output of the basal ganglia clearly targets the parietal lobe.

AIP has been shown to be the target of output from SNpr via the thalamus (Clower et al., 2005) whereas PMv has been shown to be the target of output from GPi (Hoover and Strick, 1993). Of the two basal ganglia output nuclei which have targeted output to key nodes in the grasping network, SNpr has been implicated more in the control of saccadic eye movements (Hikosaka and Wurtz, 1983) whereas GPi has been more implicated in the control of limb movements (Horak and Anderson, 1984). Based on this, and the anatomical connection between GPi and PMv, we suggest that basal ganglia output through the GPi is ideally suited to directly influence grasping by helping in the planning and parameterization of grip force.

In addition to the coordination and parameterization of gripping forces, successful grasping also relies on integrating sensory information about the object to maintain appropriate grasp. The basal ganglia have been heavily implicated in the process of sensorimotor integration (Abbruzzese and Berardelli 2003; Boecker et al. 1999; Kaji and Murase 2001; Maschke et al. 2003; Murase et al. 2006; Nagy et al. 2005). Tunik and colleagues (2005) used transcranial magnetic stimulation to induce virtual lesions of AIP and found profound effects on grasping. They suggested AIP could be conceived of as a node responsible for integrating the efference copy of a motor command with incoming sensory input, either for detecting or correcting errors between the signals.

In addition to the importance of sensorimotor integration during grasping, inappropriate grip responses must also be inhibited. The basal ganglia have been implicated in the inhibition of undesirable motor programs (Mink, 1996). Inhibition of inappropriate responses must happen rapidly given the potentially disastrous consequences of a premature release of grip force. Take for example a situation in which a container holding a hot drink starts to break. The initial response to drop it in order to prevent a burn of the hand must be delayed until the arm is far enough away from the body to prevent injury to other parts of the body. The subthalamic nucleus has been implicated in suppressing an initiated go response in a stop signal response inhibition task (Aron and Poldrack, 2006). It has been suggested that stop signal inhibition could be implemented via a hyperdirect pathway between the inferior frontal cortex and the STN (Aron et al., 2007). A hyperdirect pathway between the STN and one of the main nodes in the grasping network would be extremely useful, although this possibility has not yet been explored.

This review has focused exclusively on the role of the basal ganglia in precision gripping. However, the contribution of other subcortical brain regions to the control of precision gripping should not be ignored. As discussed earlier in the review, the cerebellum is one region which may also assist in the regulation of grasping forces during manipulative tasks. It has been suggested that one possible role of the cerebellum may be related to the anticipatory and reactive aspects of disturbances in grip behavior (Serrien and Wiesendanger, 1999b). What the potential division of labor is between the basal ganglia and cerebellum remains unclear. One possibility is that activation in different neural pathways is associated with different classes of movement (e.g. internally versus externally guided movement generation), or specific task demands. Addressing how the cerebellum and basal ganglia function together to assist in the control of different aspects of precision gripping is an area rich for future exploration.

Although we have focused on precision gripping in this review, different handgrip configurations should not be ignored. The power grip for instance provides an important function during many everyday tasks. Different task requirements exist for different grip

configurations: a power grip requires grasp stability during the production of high force levels whereas a precision grip is useful for the careful manipulation of small objects. Single cell recordings in non human primates has suggested that different grip configurations are controlled by different neural mechanisms (Lemon, 1993). Recent work by Kuhtz-Buschbeck et al. (2008) in humans examined cortical and sub-cortical brain activation during precision and power gripping using light force loads both with and without visual feedback present. Of the brain regions found to be active during the gripping tasks (which included primary sensorimotor cortex, dorsolateral premotor cortex, SMA and cerebellum), no region was specifically more activated during the precision gripping task than during the power gripping task. There was a relative increase in task related activation in the contralateral primary motor cortex and ipsilateral cerebellar hemisphere during the power grip relative to the precision grip. Basal ganglia activation was present during the precision and power gripping tasks performed without visual feedback, and activation was located within the ipsilateral globus pallidus and the contralateral putamen. Based on the study by Kuhtz-Buschbeck and colleagues, we would anticipate that the framework presented in Figure 4 would also exist for power grip tasks. Whether the planning and parameterization model presented in Figure 3 would also exist for power grip tasks remains to be determined.

In conclusion, the literature reviewed suggests that the basal ganglia are involved in the control of precision gripping. Specific basal ganglia nuclei have been shown to be actively involved in the planning and parameterizing of different aspects of grip force with anterior nuclei regulating planning aspects of grip force control and posterior nuclei regulating specific dynamic parameters of grip force. Additionally, deficits in grip force control are a known consequence of pathology involving the basal ganglia, and there is a clear anatomical link between the output nuclei of the basal ganglia and specific nodes of the cortical grasping network. We therefore suggest that the established cortical grasping network be expanded to include the basal ganglia.

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Figure 1.

The classic reaching and grasping network showing cortical regions involved in grasping and reaching. The dorsomedial circuit (blue) connects area V3A in the visual cortex, area V6A in the parietal-occipital sulcus, and the dorsal premotor cortex (PMd). The dorsolateral circuit (red) connects area V3A, the anterior intraparietal area (AIP), and the ventral premotor cortex (PMv).

Figure 2. Basal ganglia circuitry and their relationship to the cortex and thalamus. Excitatory connections are shown in red, inhibitory connections in blue (modified from DeLong and Wichmann (2007)).

	Planning		Parameterization	
	Prediction Selection		Amplitude	Rate
Caudate	X	X		
A. Putamen	X	X		
GPe		X		
P. Putamen			X*	
GPI			X	X
STN			X	X

Wasson et al. (2007) Vaillancourt et al. (2007) *Kinoshita et al. (2000) Vaillancourt et al. (2004a)
 Boecker et al. (2005) Pope et al. (2005) Spraker et al. (2007) Prodoehl et al. (2008)

Figure 3.

A summary of studies which have shown specific grip force processes and the basal ganglia nuclei that have reported BOLD activation that scales when the grip force process is manipulated. It is important to point out that all basal ganglia nuclei are generally active during grip force tasks, but that specific nuclei have BOLD activation that scales with specific neural processes. While SNpr is not included in this summary, this does not mean that SNpr is not involved in precision grip control. Due to the technical difficulties inherent in separating BOLD signal changes in different portions of the substantia nigra, there has not yet been any strong evidence to support scaling of the BOLD signal in SNpr with different grip force processes, although this evidence may emerge as imaging and processing technology advances.

Figure 4. Schematic diagram of the anatomical connectivity between output nuclei of the basal ganglia and key nodes in the cortical grasping network thought to control precision gripping.