Neuroscience and Biobehavioral Reviews 71 (2016) 313–322

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

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

Subcortical contributions to large-scale network communication

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ARTICLE INFO

Article history:
Received 30 December 2015
Accepted 29 August 2016
Available online 31 August 2016

Keywords:
Basal ganglia
Connectivity
Dopamine
Hub
Integration
Striatum
Thalamus

ABSTRACT

Higher brain function requires integration of distributed neuronal activity across large-scale brain networks. Recent scientific advances at the interface of subcortical brain anatomy and network science have highlighted the possible contribution of subcortical structures to large-scale network communication. We begin our review by examining neuroanatomical literature suggesting that diverse neural systems converge within the architecture of the basal ganglia and thalamus. These findings dovetail with those of recent network analyses that have demonstrated that the basal ganglia and thalamus belong to an ensemble of highly interconnected network hubs. A synthesis of these findings suggests a new view of the subcortex, in which the basal ganglia and thalamus form part of a core circuit that supports large-scale integration of functionally diverse neural signals. Finally, we close with an overview of some of the major opportunities and challenges facing subcortical-inclusive descriptions of large-scale network communication in the human brain.

Contents

Abbreviations: BG, basal ganglia; CBG, cortico-basal ganglia-thalamic; MRI, magnetic resonance imaging; STN, subthalamic nucleus.

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http://dx.doi.org/10.1016/j.neubiorev.2016.08.036
0149-7634/

1. Introduction

Concepts of functional localization and specialization have shaped modern perspectives of neuroscience. These principles view the brain as a complex multi-scale system composed of neural sub-systems that are responsible for executing specialized neural computations and cognitive operations. Extensive evidence for the concept of functional specialization has been observed across multiple scales of spatial description from neuronal circuits through to large-scale neural systems, firmly cementing this principle in theoretical accounts of brain organization.

However, the recent emergence of sophisticated methods for the acquisition and analysis of neuroanatomical data have led to an increasing recognition that functional specialization does not occur in isolation. Instead, higher brain function also requires integration of distributed neuronal activity across specialized brain systems (Tononi et al., 1994; Mesulam, 1998; Sporns, 2013).[1] Indeed, accumulating evidence suggests that integration across distributed neural systems supports diverse cognitive processes including language (Friederici and Gierhan, 2013), visual recognition (Behrmann and Plaut, 2013), emotion (Pessoa, 2012), cognitive control (Power and Petersen, 2013) and learning (Bassett et al., 2011; Bassett et al., 2015). The overall picture emerging from this work is that a dynamic and coordinated balance between functional integration and segregation is essential for the operation of distributed brain networks underlying cognition and adaptive behaviour (Tononi et al., 1994; Fox and Friston, 2012; Sporns, 2013).

Grounding the theoretical principle of functional integration in a neuroanatomical framework has been of major neuroscientific interest over the past thirty years. Fundamental insights into cortical organization have been gained from detailed examination of tract-tracing data in experimental vertebrate organisms and neuroimaging data in humans. This body of work has demonstrated that the vertebrate brain is organized into a complex hierarchical network in which specialized neural communities communicate via putative transmodal convergence zones (Damasio, 1989; Mesulam, 1998; Sepulcre et al., 2012; Bell and Shine, 2015; Braga and Leech, 2015) and network *hub* regions (for review, see van den Heuvel and Sporns, 2013b) (see Glossary).

Despite insights into *cortical* substrates underpinning systems-level integration in the brain, the subcortex has been underrepresented in prior descriptions of whole-brain anatomical connectivity (Pessoa, 2014). This omission may in part reflect a pervasive 'corticocentric' view of higher brain function, in which the neocortex is considered the key structure for higher function, while deep gray-matter structures are assumed to simply subserve cortical demands (Parvizi, 2009). Contrary to this viewpoint however, cortico-subcortical circuits are linked to a diverse range of limbic, cognitive and motor control functions (Chudasama and Robbins, 2006; Pennartz et al., 2009). Furthermore, extensive reciprocal and non-reciprocal circuits connect the cortex with the basal ganglia (BG), thalamus, cerebellum and brainstem (Alexander et al., 1986; Shepard and Grillner, 2010). Thus, from both an anatomical and functional standpoint, a complete and accurate description of brain structure and function necessarily requires consideration of the extensive cortico-subcortical architecture.

In this *Review*, we examine recent evidence suggesting that subcortical macrocircuits connecting the BG, thalamus and cortex are involved in large-scale functional integration. We begin by examining findings from anatomical work revealing that the BG and thalamus support the convergence of afferent information arriving from cortical, subcortical and neuromodulatory systems. Following this, we discuss complementary results from recent literature that has adopted an explicit network perspective to examine structural brain organization. In synthesizing these findings, we arrive at a new view of the subcortex in which large-scale communication and information integration is a key computational priority. Finally, we conclude with an overview of the opportunities and challenges facing subcortical-inclusive descriptions of large-scale network communication in the human brain.

2.1. Integration in basal ganglia & thalamic circuits

Interactions between the cortex and BG support goal-directed behaviours, including decision-making, motor control, action selection, learning, and habit formation (Graybiel et al., 1994; Houk and Wise, 1995; Pennartz et al., 2009). These interactions take place throughout large-scale anatomical loops that link the cortex, BG and thalamus (Alexander et al., 1986), and are essential for vertebrate forebrain function.

2.1.1. Cortical–basal ganglia loop architecture

Projections from the cortex terminate in the striatum, the major BG input structure. BG output is then channeled back to cortex via the thalamus; thereby completing the cortical–basal ganglia–thalamic (CBG) 'loop' architecture (Fig. 1a). CBG circuits are organized according to a general functional topography, whereby limbic cortex projects to the ventral striatum, associative cortex projects to the ventromedial caudate, and motor cortex projects to the dorsolateral striatum (Alexander et al., 1986). This functional topography is also maintained in extra-striatal BG nuclei (i.e. pallidum and subthalamic nucleus) and thalamus, suggesting that a general topographic organization is preserved at all stations of the CBG loop (Alexander et al., 1986). The discovery of functional topography throughout the CBG loop architecture led to the segregated loop model, which proposed that functionally specialized information remains segregated throughout parallel 'closed' CBG streams (limbic, associative and motor channels, respectively) (Alexander and Crutcher, 1990; Hoover and Strick, 1993).

Although the segregated loop model has proven a useful heuristic for understanding BG function, accumulating evidence over the past two decades suggests that BG and thalamic nuclei are not merely relay stations for propagating signals throughout isolated macrocircuits. Instead, CBG architecture represents a complex dual organizational system, supporting both segregated and integrative information processing across functional channels (see Haber, 2010). In the following section, we review recent work highlighting

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[1] The principles of functional integration and segregation scale with brain organization. For instance, functional integration can be understood at the synaptic and cellular level through the temporal and spatial summation of incoming synaptic inputs. Equally, functional integration may be understood at the *systems*-level through 'binding' of multimodal information (Mesulam, 1998) and communication across large-scale neural communities (Sporns, 2013). In this article, we examine functional integration and segregation at the systems-level. Although this discussion invariably requires consideration of mechanisms on the scale of cells and microcircuits, our primary focus will be on macroscopic neural *systems*.