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Large-Scale Brain Systems and Subcortical Relationships: The Vertically Organized Brain

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This article reviews the vertical organization of the brain. The cortico-basal ganglia and the cerebro-cerebellar circuitry systems are described as fundamental to cognitive and behavioral control. The basal ganglia anticipate and guide implicitly learned behaviors on the basis of experienced reward outcomes. The cerebellar-cortical network anticipates sensorimotor outcomes, allowing behaviors to be adapted across changing settings and across contexts. These vertically organized systems, operating together, represent the underpinning of cognitive control. The medial temporal lobe system, and its development, is also reviewed in order to better understand how brain systems interact for both implicit and explicit cognitive control.

Key words: basal ganglia, cerebellar-cortical network, medial temporal lobe system, vertically organized brain systems

INTRODUCTION

Part I of this series discussed the structure and function of large-scale brain systems (LSBS). Part II described the "small-world" organization of these systems and an overview of LSBS development. This third article is a selective review of how and why LSBS are related to the structure and functions of the basal ganglia and cerebellum, which have been referred to as the "vertical organization" of the brain (Divac & Öberg, 1992; Koziol & Budding,

2009). These cortical-basal ganglia and cerebro-cerebellar learning systems are the phylogenetically older, yet critical underpinnings for our ability to serve the needs of interacting within a dynamically changing environment, and therefore, by "definition," they play notable roles in executive functioning (EF). However, because successful adaptation also includes problem solving dependent upon perceptions and experiences retained within declarative memory systems (anchored within LSBS), we further include brief mention of the development of the medial temporal-lobe memory system (MTL), which allows access to memories and their manipulation for the purpose of developing new goal-directed behaviors. Finally, for the sake of brevity, we broadly summarize the procedural memory system, which makes a unique contribution to

translating ideas into action. However, this system is actually the "missing link" in clinical neuropsychology's understanding of "working memory" and "executive function." Working memory can no longer be understood as an inferential cognitive mechanism that operates only blatantly or *explicitly*; instead, this construct requires significant modification to include the neuroscientific principle that perceptions and ideas are directly linked with *implicit action* (Dew & Cabeza, 2011). This linkage depends upon interactions between LSBS, the basal ganglia, and the cerebellum. Part IV of this series will integrate these functions and processes by describing how these "multiple memory" systems interact to significantly modify clinical neuropsychology's constructs of attention, learning, and EF and how the functions of LSBS might be assessed through neuropsychological evaluation.

MULTIPLE MEMORY SYSTEMS

The idea that the brain can be described in terms of multiple memory systems is not new (Squire, 1987). At least with respect to understanding humans, ever since it was observed that H. M. (who demonstrated profound anterograde amnesia after bilateral surgical hippocampal removal) was capable of learning a variety of skills and procedures, the discovery of and dissociations between different memory systems were slowly investigated and became a generally accepted reality (Banich & Compton, 2011). There is abundant evidence about how different skills are initially acquired through different learning and memory systems. Most investigations have studied the differences between these systems and have not addressed the issue of how these systems interact. Doya (1999) was arguably the first individual who proposed that the computations of the cerebral cortex, the basal ganglia, and the cerebellum—all making distinct contributions to learning and memory—actually operate within a unified framework, in an integrated way. The integration of these learning systems establishes the global architecture for both *reactive* and *predictive* action selection, or "behavior." Ashby and colleagues are more recent pioneers in investigations of how learning systems interact to generate one common representation for "automatic behaviors" (Ashby & Crossley, 2012). Understanding how multiple learning and memory systems interact is fundamental to the paradigm proposed in Part I of this series, which specifically emphasizes that the brain evolved to meet the needs of interactive behavior. Adaptation is ongoing and is characterized by "automatic," implicit cognitions and behaviors that alternate with episodes of higher-order cognitive control (Evans, 2008; Restivo & Frankland, 2010; Toates, 2005, 2006). In this regard, it has been estimated that perhaps 95% of human behavior

is automatic (Bargh, 1997; Bargh, & Chartrand, 1999; Lakoff & Johnson, 1999). The elegance, flawlessness, adaptability, and quickness characteristic of these adaptive behaviors is quite remarkable (Saling & Phillips, 2007). Similarly, while automatic behaviors are observed throughout the phylogenetic hierarchy, nature's oldest solutions for generating adaptive behaviors *never emphasized sophisticated cognition or conscious cognitive control*, and evolution has also preserved those mechanisms that are effective, nearly all of which have been preserved in humans (Ito, 1997).

THE VERTICAL ORGANIZATION OF THE BRAIN, LARGE-SCALE BRAIN SYSTEMS, AND MEMORY SYSTEMS

The vertebrate brain is characterized by two vertically organized systems. First, the cortico-striatal-pallidal-thalamo-cortico system, or basal ganglia system, was described well more than 25 years ago (Alexander, DeLong, & Strick, 1986). An extremely vast body of research literature has accumulated and describes this as an instrumental learning system that primarily operates implicitly (Doll & Frank, 2009; Steiner & Tseng, 2010). Second, cerebro-cerebellar circuitry is the foundation for an anticipatory control system that primarily serves automaticity functions by predicting sensorimotor outcomes, which allows for rapid behavioral adjustment, automatically, through bypassing slowly operating sensory cortical feedback mechanisms (Imamizu, 2010; Shadmehr, 2010; Shadmehr, Smith, & Krakauer, 2010). The functions of this network operate outside of conscious cognitive awareness (Ito, 2005). The MTL, which is essentially a *recognition memory system,* operates along the cortico-thalamic-hippocampal axis, or CTH network (Miller, 2008); in Doya's nomenclature (Doya, 1999), this is analogous to an *unsupervised* learning system. This memory system is not vertically organized, it allows for cortically based information retention, and its primary function allows sensory-perceptual experiences to persist within the neocortex (Squire, 2004). *The MTL is the only memory system directly assessed in neuropsychological evaluation.* However, all three systems require coordinated interactions to generate and apply "EF," which is required for ongoing interactive behavior (Houk et al., 2007; Koziol, Budding, & Chidekel, 2010). Routine behaviors allow us to exploit the predictable features of the world, but because of dynamic, changing interactions with the environment, most routine behaviors alternate with cognitive control episodes; this requires both reactive and predictive selections of behavior. We cannot have "EF" without the bottom-up support of vertically organized brain systems, and we cannot have "EF" without episodes of "top-down" cortical

control (Koziol, 2014). However, one unifying principle of brain function is that all representations of perceptions, cognitions, and behaviors are retained within the same circuits of "functional connectivity" that were activated when these experiences were initially encountered (Cisek & Kalaska, 2010). This fact, well accepted within neuroscience, provides many clues about how the brain functions in a unified way for the purpose of ongoing adaptation.

THE BASAL GANGLIA SYSTEM: SOLVING THE "SELECTION PROBLEM"

It was previously thought that vertically organized brain systems were only coprocessors of movement. However, it is now known that this viewpoint is unequivocally untrue (Arsalidou, Duerden, & Taylor, 2013; Koziol et al, 2013). Instead, what these systems "do" for movement, they also do for cognition, emotion, and motivation. These systems are essentially modulators of all cortical functioning. For the sake of brevity, this article assumes that all clinical practitioners are familiar with corticobasal ganglia structures and network connections that support functional interactions. This system is also sometimes incompletely referred to as the corticostriatal system. (The unfamiliar reader is referred to Koziol & Budding, 2009, and Utter and Basso, 2008, for reviews of the functional neuroanatomy of the direct, indirect, hyperdirect, and striosomal pathways; for a review of basal ganglia integrative networks, see Haber, 2011). Figure 1 illustrates the segregated prototypical topographical organization of cortical-basal ganglia circuitry. However, this figure might imply that because the basal ganglia are involved in modulating such a wide range of functions within the networks of the LSBS, it is tempting to conclude that the basal ganglia subsume multiple and even diverse roles.

Nevertheless, numerous repeated, replicated investigations of the basal ganglia's neuroanatomic structure, perhaps beginning with Redgrave and colleagues (Redgrave, Prescott, & Gurney, 1999), clearly imply a unified, integrative functional role (Cockburn & Frank, 2011). The cortex functions according to a principle of
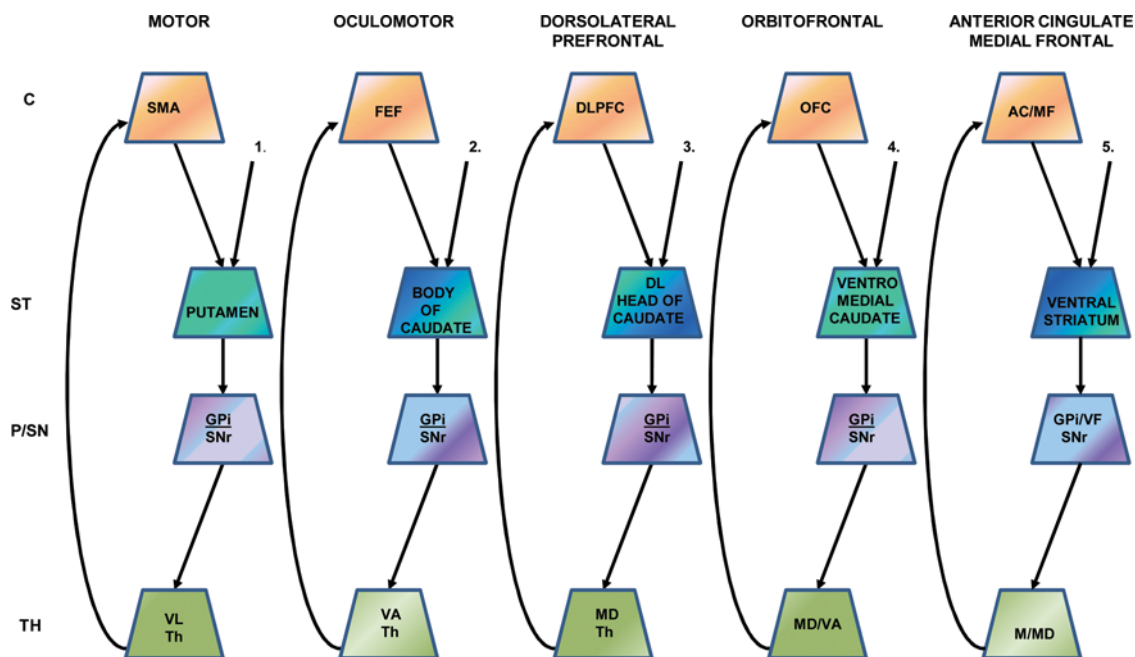

FIGURE 1   Simplified illustration of circuits connecting the cortex, basal ganglia, and thalamus; summary of the prototypical circuits of the basal ganglia. The five prototypical circuits of the basal ganglia: (1) inputs from the anterior cingulate area, motor cortex, and somatosensory cortex, involved in the sensory-motor network; (2) inputs from the dorsolateral prefrontal cortex and posterior parietal cortex, involved in the frontoparietal network and dorsal attentional networks; (3) inputs from the posterior parietal cortex and arcuate premotor area, involved in the frontoparietal network; (4) inputs from the superior and inferior temporal cortices and anterior cingulate area, involved in the ventral attentional, limbic, and default networks; and (5) inputs from the medial temporal lobe/hippocampal region and superior and inferior temporal cortices, involved in the limbic, ventral attentional, and default networks. Although at the cortical level, there is little "cross-talk" between large-scale brain networks, integrative networks are present within the basal ganglia (see text). Cerebro-cerebellar and basal ganglia-cerebellar connections are not illustrated. C = cerebral cortex; ST = striatum; P/SN = pallidum/substantia nigra complex; TH = thalamus; SMA = supplementary motor area; FEF = frontal frontal eye fields; DLPFC = dorsolateral prefrontal cortex; OFC = orbitofrontal cortex; AC/MF = anterior cingulate/medial frontal cortex; GPi = globus pallidus internal segment; SNr = substantia nigra pars reticulata complex; VLTh = ventrolateral thalamus; VATh = ventral anterior thalamus; MDTh = medial dorsal thalamus; MD/VA = medial dorsal and ventral anterior thalamus; M/MD = medial and medial dorsal thalamus.

excitation, and an adaptive system that is constantly "excited" cannot operate effectively without appropriate inhibitory controls (Miller, 2008). An "excited" brain would be attracted to *everything*; we are constantly bombarded by far too many internal and external stimuli and activity choices to be able to function adaptively. Broadly speaking, the basal ganglia are a massive inhibitory system that dynamically and adaptively select, or gate, and update the flow of information originating from points of origin or "hubs" within LSBS through cortical-striatal-pallidal-thalamic-cortical loops. The basal ganglia are uniquely positioned and connected as a type of "relay station." Within this topographically organized group of basal ganglia nuclei, projections from numerous cortical structures converge. (A review of basal ganglia integrative networks is complex in detail and beyond the scope of this article; see Haber, 2011, for a critical presentation).

HOW DO THE BASAL GANGLIA "DO" WHAT THEY "DO"?

All of the frontal cortices, posterior sensory cortices, the hippocampus, the amygdala, and basal forebrain reward circuitry systems send projections through the basal ganglia. These projections define the basal ganglia's neuroanatomic position for selecting and integrating information from all the possibilities, or "candidates," of perceptions, cognitions, and motor activities or "actions" that are represented within the cortex. This system selects the most adaptive actions to execute, while they inhibit or suppress the attending to, or execution of, competing perceptions, thoughts, and behaviors. So how do the basal ganglia decide what to choose to attend to or what to do? This is a key question that is critical to understanding the execution of implicit behavior and explicit cognitive control. The most important clue for answering this question is found by investigating the reward-based, reinforcement, or instrumental learning characteristics of the basal ganglia system.

THE DECISION MAKING OF THE BASAL GANGLIA: THE AUTOMATIC RELEASE OF BEHAVIOR AND COGNITIVE CONTROL

Whenever a stimulus is represented (which can be imagined or concretely perceived) within *sensory* cortices, this generates "candidate actions," or behavioral choices and possibilities, within the *premotor* cortex. This is because all of the essential properties of objects, their relevance, location, what they are used for, and how they are used are represented in the same ventral attention network, dorsal attention network, and sensorimotor (SM)

circuits that were recruited or activated when the information about those "objects" was initially acquired (Cisek & Kalaska, 2010). Some of these associated behaviors generate positive outcomes; other behaviors generate negative outcomes. The neural systems governing these behaviors are based on outcomes that are associated with the dopaminergic (reward) and noradrenergic (arousal) systems. The neural systems governing these behaviors that are strongly and repeatedly coactivated are strengthened. Based on environmental stimulus context and generalizability, the basal ganglia release actions that have a high probability of generating positive outcomes and avoiding the selection of those behaviors associated with negative outcomes. Activation through the *direct pathway* always generates a positive outcome; activation through the *indirect pathway* always leads to a negative outcome (Nakanishi, Hikida, & Yawata, 2014). Therefore, the basal ganglia system learns what it should do as well as what it should not do. In novel situations, the frontoparietal network anticipates "reward probabilities" by relying on expectations based on previous experiences. Therefore, *there is always a perception and/or idea–action linkage.* The entire system is based on anticipatory control. It is a system that has been taught to believe, both implicitly and explicitly, that "if I do this, then that should happen." Therefore, this "system" can quickly release "automatic" or implicit behaviors, without conscious cognitive control. Persuasive, extensive neuroscientific investigations demonstrate that under a wide variety of conditions, actions are initiated even though we are unconscious of the goals to be attained or their motivating affect on our behavior (Custers & Aarts, 2010; Thach, 2014). *Simply put, all decision making is not under the control of the prefrontal cortex.* In new, unfamiliar situations, the prefrontal cortices anticipate probabilities, or a "best guess" about outcomes originating from previous perception/idea–action linkages. It serves to "link" or integrate aspects of "knowledge" with "chunks" of previous actions to generate a *new or crude behavioral representation*, which is then *refined by the SM network system* (Dolan & Dayan, 2013; Haber, 2011; Oberauer, Souza, Druey, & Gade, 2013; Paul & Ashby, 2013).

WHAT IS "REWARD"?

Another key feature in understanding this anticipatory control system concerns the conceptualization of "reward." The "reward signal" of the brain is very broadly defined and features a hierarchical organization, ranging from concrete and tangible to abstract rewards. Reward that is not tangibly experienced is a concept referred to as "fictive reward" (Lohrenz, McCabe, Camerer, & Montague, 2007). The reward system is

commonly activated with monetary reward, when cooperating with other people socially, when experiencing a compliment or a criticism, in conforming to the advice of expert opinions, and even in doing something nice for another person or making a charitable contribution (Hunt & Behrens, 2011). It is also activated when experiencing a sense of relief after completing a project or passing/failing an examination, etc. Understanding the reward system in this broad way expands the role of neuropsychology by including applications to "personality functioning." So "reward," ranging from anxiety and negativism to a sense of excitement, pleasure, or simple relief, drives much of what we decide to do, either explicitly or implicitly. However, without considering this hierarchically and abstractly organized system, the unified operation of the basal ganglia and aspects of people's individual differences can never be adequately understood.

Many studies and reviews have demonstrated that because of its instrumental learning properties, the basal ganglia are necessary for certain types of *category learning* (Ashby & Ennis, 2006; Seger, 2006, 2008, 2009). For example, categorizing certain objects as edible, classifying aspects of the environment as safe or dangerous, and classifying a person as a friend or enemy are fundamental skills for survival, and in this way, they are "executive functions." Discrimination learning is a type of categorization, and the studies of Seger, Ashby, and others have established the adequacy and sufficiency of the caudate nucleus for visual discrimination learning, without hippocampal involvement. Therefore, all "judgments" do not appear to be mediated by the MTL or by the frontal cortices. Furthermore, these "executive decisions" are made automatically (Seger & Cincotta, 2005, 2006). These issues are critically important because during development, cortical-basal ganglia connections predominate (Menon, 2013). Although every child's history is characterized by a period of "infantile amnesia" (to be discussed in the section on the MTL), these data imply that considerable adaptive learning occurs well outside of conscious awareness. Figure 2 depicts the basic basal ganglia pathways involved in the instrumental learning of behavior.

THE CEREBRO-CEREBELLAR SYSTEM

The cerebellum is detached from the neocortex and lies within the posterior fossa, just below the occipital lobes. However, it is linked to the cerebral cortex through specific circuits, most of which are believed to originate in "hub" regions within the cortex and basal ganglia (R. Buckner, personal communication, April 3, 2014). Although Hwang and colleagues have demonstrated that both hub and nonhub cortical regions project to
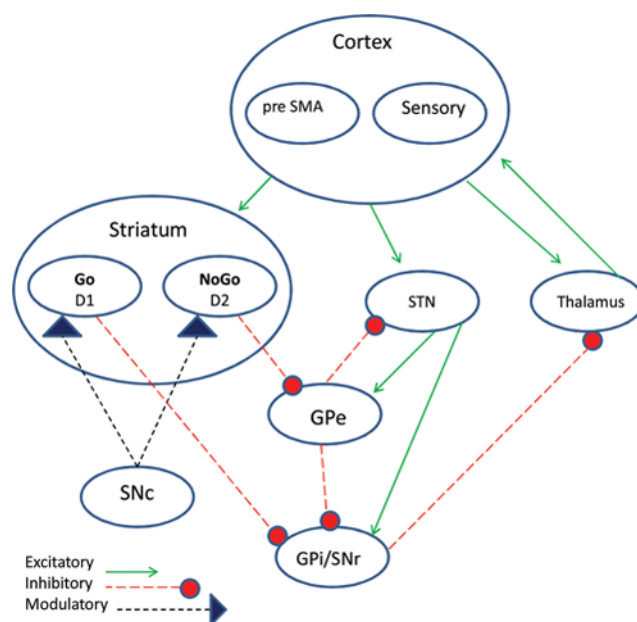

FIGURE 2 Simplified illustration of the basal ganglia circuit. SMA = supplementary motor area; GPi = globus pallidus internal segment; SNr = substantia nigra pars reticulata complex; STN = subthalamic nucleus; SNc = substantia nigra pars compacta; GPe = globus pallidus externa.

the basal ganglia and cerebellum, lesioning connections to functional hubs drastically reduces the efficiency of functional brain networks (Hwang, Hallquist, & Luna, 2012). Without these hub region connections to the cerebellum, long-range transmission of information occurs significantly more slowly, which has potential implications for understanding vague, elusive neuropsychological constructs such as "processing speed."

Cerebro-cerebellar circuits originate within the cortex; they project to the pons, then on to the cerebellar cortex, and from there, to the deep nuclei of the cerebellum. The feedback limbs of these circuits project onto the thalamus and then back to the point of origin within the cerebral cortex. The circuits are segregated and are dedicated in function, or independent from each other; the cerebellum is topographically and modularly organized as well. The anterior lobes of the cerebellum modulate the quality of movement; posterior lobes of the cerebellum are involved in learning new sensorimotor activities and in cognition. The cerebellum is linked to prefrontal and posterior association cortices, to paralimbic regions of the cortex, and with motor regions (Blakemore & Sirigu, 2003; Schmahmann, 1996b). This pattern of circuitry linkage allows the cerebellum to modify or adjust the information received from the cortex and to return this neural message after it has been modified. In other words, while operating together with the cerebral cortex, as an *ensemble,* the cerebellum "decides" what information is or is not

returned to the neocortex, thereby regulating the strength and quality of neural signals (Andreasen & Pierson, 2008). A simplified version of this prototypical circuitry is illustrated in Figure 3.

Unlike the regionally specialized neuronal organization of the cerebral cortex, the internal structure of the cerebellum is uniform (Houk & Mugnaini, 2003). The uniformity of neural composition implies the cerebellum performs only one operation (Eccles, Ito, & Szenthagothai, 1967). A very considerable body of information has accumulated in support of this proposal (Koziol, et al., 2013; Schmahmann, 1996a, 2001). According to Ito (1984, 1997, 2005), different regions of the cerebellar cortex form modules, which he termed "microcomplexes." Each module processes the information provided by its inputs in the same way. Different regions of the cerebellum mediate different functions, depending on their inputs and outputs (Schmahmann, 1996b; Stoodley & Schmahmann, 2009). In other words, there is a repeating modular organization within the cerebellum. Each module receives inputs from a specific hub region. This reflects a repeating functional organization, which is to say that the cerebellum generally performs a common function whether in support of movement or cognition, etc. However, a very important feature to understand is that the LSBS of the neocortex function together along with the cerebellum, as an ensemble (Smaers, Steele, Case, & Amunts, 2013; Smaers, Steele, & Zilles, 2011). This point has absolutely critical implications for understanding neurodevelopment. The neocortex and the cerebellum, while operating as a unit, tend to "keep pace" with each other during the course of infancy, childhood, and early adolescence (Buckner & Krienan, 2013). In fact, the cerebro-cerebellar system,

with the cerebellum and cortex developing in an interactive way, establishes a critical aspect of the framework for the development of cognitive control.

WHAT DOES THE CEREBELLUM DO?

Therefore, at the risk of oversimplification, the cerebellum can be considered a "metasystem" that adjusts the operations of cortically based processes. Working in concert with the cerebral cortex, it optimizes the expression or performance of whatever behavior the brain decides to choose. It performs this operation on the basis of a uniform infrastructure that is primarily composed of different types of excitatory and inhibitory neurons. Perhaps this process can best be understood by considering movement as an initial example and then applying these principles to other cortically based functions.

When motor tasks are initially being acquired, the cerebellum and large regions of the cerebral cortex, including the frontostriatal system, are involved. The frontal system involvement is believed to exert the cognitive control, "programming," or EF guidance necessary to learn the task in question. However, as the task is practiced and becomes more familiar, there is a transition from controlled to automatic processing. This transition is facilitated by the cerebellum *copying the content of cortical working memory*, which contains the sequences of movement and sensory characteristics necessary to perform the task. When learning any new behavior, direct cortical sensory feedback is required for proper execution (Ito, 2012). However, this sensorimotor feedback operates very slowly; it is inevitably delayed by a variety of factors, including the time required for the motor commands to be transmitted from the cortex to the muscles and the time required for the brain to process the sensory information it receives from the moving body part (Imamizu, 2010). The cerebellum functions as a *predictor* (Molinari, Restuccia, & Leggio, 2009). As a behavior is practiced, the cerebellum (because it constantly copies the content of working memory) anticipates what that sensorimotor feedback will be and uses this information to control the behavior. This enables the brain to execute the movement with increasing precision, without depending on feedback from the moving body part. The cerebellum learns through practice to perform operations faster and more accurately. Rapid, smooth, effortless, yet precise movements are supported by the cerebellar infrastructure that calculates motor commands necessary to execute intended movements and *predict or anticipate* sensorimotor feedback from motor commands or intentions before movements are executed (Ito, 2008). These neural mechanisms, called "internal cerebellar control models," are initially developed from the cerebellum
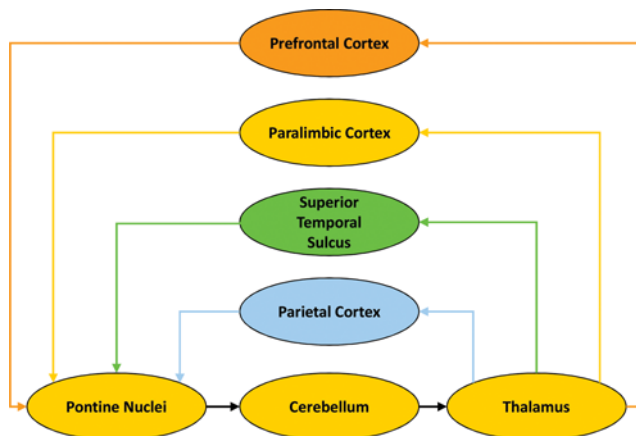

FIGURE 3 Simplified illustration of connections between the cerebral cortex and the cerebellum. *Source:* Koziol, Budding, & Chidekel (2010). © 2010 Springer Science + Business Media. Reproduced by permission of Springer Science + Business Media. Permission to reuse must be obtained from the rightsholder.

"knowing" the content of working memory, which helps explain why almost every task recruits cerebellar activation (Ito, 2012). These control models allow us to engage in behaviors in real time because they allow conscious cortical sensorimotor control, or sensorimotor feedback, to be bypassed.

Another simple example, which can easily be applied to neuropsychological assessment, is the neurologist's finger-to-nose test. Why does this "test" work? Simply put, you do not ordinarily "see" your nose and certainly not when your eyes are closed! When extending an arm and asked to touch your nose, there are only four possible outcomes. You successfully touch your nose, which reveals the construct of the cerebellar control model. The successful outcome was based upon the *prediction or anticipation* of the location of your nose. If you "miss" the nose by overshooting or by undershooting (two other outcomes), the control model has *anticipated* or *predicted* incorrectly. Perhaps the model is absent because of cerebellar structural impairment so that the movement is solely controlled by the premotor cortex, which has been unable to receive an efficient representation of the behavior from the cerebellum. The fourth outcome, dysmetria, is observed by jerky, uncoordinated movements that are *no longer adapting to the changing requirements of the moment as the individual attempts to reach the nose.* And what the cerebellum does for movement, it also does for thought; the cerebellum allows us to think just as effortlessly and automatically as we move. It allows for the anticipation of thought outcomes and therefore supports planned behavior, or "EF." In this regard, certain cerebellar modules process information that is of a purely abstract nature (Balsters & Ramnani, 2008; Ito, 2008; Koziol et al., 2013).

In this regard, one "cognitive" example is in order. Imagine learning to subtract arithmetic problems with multiple-digit numbers. Whenever the subtrahend is of a larger value than the minuend, a specific process of regrouping or borrowing and carrying of numbers is required. This specific sequence of operations must be applied in the same sequence, in the same way, every time. This "cognitive sequence" is actually a motor program. At first, this procedure is usually learned through the cognitive guidance of working memory. The cerebellum, by copying this working-memory content, constructs a control model. When this sequence is acquired, it becomes independent of the cognitive control of working memory. After learning, the cerebellum immediately recognizes the configuration of numerical values and immediately "knows" the sequence that needs application, automatically and effortlessly, without giving the matter a second thought. It adapts to the changing "library" of the cortical content of the numbers automatically, because the control model bypasses time-consuming thought by instantly anticipating, or predicting, the operation that needs

application. And this process is typically outside of our conscious awareness; we simply recruit the process, effortlessly. Similarly, this process of learning and understanding, generating automaticity and adaption, can easily be applied to functional competence from simple addition to complicated mathematical operations. In a seminal article, Schmahmann and colleagues described how these behaviors can be translated to neuropsychiatric analogues with illustrative examples of cognitive and emotional dysregulation (Schmahmann, Weilburg, & Sherman, 2007).

So, just as we are usually unaware that we are moving, so we are often unaware that we are thinking. This is because the operations of the cerebellum are outside of conscious cognitive control and awareness. To achieve optimal cognitive/behavioral performance, this process includes the learning of actions that depend on adaptation to environmental change (Njiokiktjien, 2010). In other words, it allows for the transfer of an automated action to the same action within similar yet different circumstances, while projecting the most efficient representation of that activity to the cortex, where the program is retained (Galea, Vazquez, Pasricha, de Xivry, & Celnik, 2011). So the cortex retains what the cerebellum learns. Therefore, instead of thinking of the cerebellum as a coprocessor of movement, it is best to think of the cerebellum as a coprocessor of LSBS. There is unequivocal evidence that demonstrates that the cerebellum supports action–observation learning and *action–perception linkage* or coupling, which are critical to executive, cognitive control processes (Christensen et al., 2014; Schmahmann & Sherman, 1998). In all these ways, it plays a critical role in serving the needs of interactive behavior.

THE MEDIAL TEMPORAL-LOBE SYSTEM: SEMANTIC AND EPISODIC MEMORY

Inherent in all problem solving, or in adapting to the ambiguity of novelty, we must *identify or discover the stimulus-based properties of the problem.* To accomplish this, we typically rely on the facts we know and/or the experiences we have had. The retention of much of this information is mediated by the MTL system. It was initially believed that the functional immaturity of the association areas of the cortex was the primary limiting factor in the development of memory in childhood (Bachevalier, Malkova, & Beauregard, 1996). However, it is now very well accepted that understanding the development of semantic and episodic memory is complex and multifaceted. For one, the neurobiology of certain types of category learning implicates structures outside of the MTL system. Category learning is present relatively early in development and implicates adaptive learning outside of conscious awareness that is not directly associated with the MTL hippocampal system.

Furthermore, independent of the cortical-basal learning system, the MTL system has its own developmental trajectory.

Although study of the development of the MTL system is in its infancy, semantic information (knowledge of the world) and episodic memory (memory for personally experienced past events) depend upon different but closely interacting systems (Prince, Tsukiura, & Cabeza, 2007). The period of infantile amnesia refers to the phenomenon in which very few events from the first 2 years of life are consciously recalled by adults. However, even infants are capable of demonstrating semantic recognition memory skills (Raj & Bell, 2010). This recognition is usually associated with, or observed as, *a perception–action experience*. How this type of recognition might be related to corticobasal ganglia recognition/classification has not been considered or systematically investigated. In fact, it can be argued that reward-based classification is irrelevant to episodic and autobiographical memory and that this dissociation reveals the adaptive, economical organization of brain function. Memory systems operate on a "need-to-know" basis.

Episodic memory includes attributing a memory episode to its source or origin of information. This requires a binding process that encodes relationships among and between stimuli and experiences, or "knowing" that certain features of a memory episode belong together. Development of this system is a slow, protracted process that is somewhat but not solely dependent upon allocentric spatial memory skills. Rudimentary skills are evident at 18 months old and abilities are much improved by the age of 2 years and gradually improve through 7 years of age (Ribordy, Jabes, Banta Lavenex, & Lavenex, 2013). However, during this period of childhood, there are very few autobiographical memories that can be recalled later in life—a phenomenon known as childhood amnesia. Kwok, Shallice, and Macaluso (2012) identified process-specific dissociations of retrieval processes for objects (recruiting the hippocampus), temporal organization (the precuneus), and spatial location (frontal-parietal cortices). So semantic, episodic, and autobiographical recall are dependent upon distinct retrieval mechanisms that interact and can be dissociated. At least aspects of "*automatic recognition*" are likely governed by cortical-basal ganglia reward classification. Similarly, the hippocampal formation, essential for processing all of these aspects of *declarative information*, is characterized by distinct circuits, all developing at different times and rates, which culminate in the emergence of reliable episodic memories as all hippocampal circuits reach full maturation during late adolescence/early adulthood (Ghetti & Bunge, 2012; Lavenex & Lavenex, 2013; Pathman, Larkina, Burch, & Bauer, 2013). So, why is this relevant? Good

judgment, good decision making, and good cognitive control are partly explained by a slowly developing MTL system, despite the fact that ventral and dorsal pathways are integrated early within the framework of LSBS.

THE PROCEDURAL MEMORY SYSTEM

If our understanding of how the MTL system develops is in its infancy, then our knowledge of the procedural memory system remains within the period of gestation. The declarative and procedural memory systems are dissociated; they act independently of each other. However, procedural knowledge, through the process of self-referential thinking, which is inherent within the default mode network, can lead to the development of declarative knowledge (Pezzulo, 2011; Pezzulo & Dindo, 2011; Pezzulo & Rigoli, 2011). As a general rule, performance on declarative memory tasks improves at a faster rate in comparison with performance on procedural memory tasks (Lum, Gelgec, & Conti-Ramsden, 2010). Therefore, even though neuroimaging techniques identify the SM network as active early during infancy, the fact remains that multiple memory systems reach functional maturity at different points in development. However, if we reflect upon what we observe during infancy and childhood, we are reminded that *the primary purpose of child development is to acquire increasing control over the motor system*, which is believed to be stable and mature during the ages of 10 to 12 years (Njiokiktjien, 2010; Welsh, Pennington, Groisser, 1991). All *action* is dependent upon this system, and different developmental tasks, based upon perception–action linkages, are required at different ages. This system is also critically dependent upon the basal ganglia circuitry system for the "chunking" together of various action sequences. Because developmental tasks follow such a slow trajectory as related to the cognitive control system, our ability to investigate this system might also be dependent upon task variability and complexity, with *behavioral action sequences retained within a slowly maturing cortex.* What remains important is our understanding of *perception–action linkages* and the interaction of LSBS with basal ganglia and cerebellar systems, which will be discussed in Part IV of this series of manuscripts.

SUMMARY

This article focused on the vertical organization of the brain. The functions of the corticostriatal and cerebro-cerebellar systems were described, albeit in an extremely simplified way. Categorization, the MTL, and procedural memory systems were also selectively

summarized. The purpose of this discussion was to establish the foundational background for understanding a systems approach to functional neuroanatomy. This is critically important because it leads to a modified conceptualization of constructs such as attention, learning, and memory, which ultimately drive cognitive control. This lays the groundwork for the interpretation of neuropsychological tests within an interactive paradigm.

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