Large-Scale Brain Systems and Subcortical Relationships: Practical Applications

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This article describes an interactive paradigm for understanding brain functioning. This model requires both explicit and implicit learning processes. This paradigm is illustrated through the interpretation of practical examples of behavior. Applications of current neuropsychological tests are presented within this interactive paradigm. The development of new neuropsychological tests is presented, as derived from experimental test paradigms that evaluate implicit learning processes.

Key words: cognitive control systems, interactive test paradigms, implicit learning, neuropsychological testing

INTRODUCTION

The first three articles in this series discussed the structure, organization, development, and functions of large-scale brain systems (LSBS). This final article provides integration of this information and adds guidelines through the practical application of neuropsychological testing. The functional architecture of the brain evolved and developed to serve the needs of interactive behavior (Cisek & Kalaska, 2010). Because this principle and process were strongly conserved during phylogeny, we also proposed a paradigm shift for neuropsychological evaluation. When we simply observe people and what

they do and when we apply rating scales to quantify these observations, we are essentially making observations within an ethological and ecologically valid framework; we are watching others within their natural habitat, or "niche." This habitat might be the classroom, the playground, the work place, the shopping mall, etc.—any place at all where the essence of life readily emerges, even when observing a behavior suggests that person does not "fit into that niche" very well. However, because past behavior usually predicts future behavior, we are gathering useful information (Isquith, Roth, Kenworthy, & Gioia, 2014). We are always doing something, and even when at rest, considerable activity is observed within the default mode network as it "thinks," either in a self-reflective way, about other people, or about the external world. Regardless of self-referential, social/interpersonal, or other "object"

thought content, aspects of this process necessarily include "actions" (Sandrone, 2012; Whitfield-Gabrieli & Ford, 2012).

The traditional neuropsychological testing paradigm, based upon serial order processing, does not reflect the *interactions* in which we normally engage. Within this artificial model, first we perceive, then we "think," and finally, we respond. We are not indicting this paradigm because this model is useful for understanding certain aspects of problem solving. However, according to Bargh (1999) and others cited previously in this series of manuscripts, as much as 95% of behavior is implicit and automatic and occurs outside of conscious cognitive awareness. Therefore, it is critical to complement the traditional serial-order-processing paradigm with a model of interactive behavior that can be evaluated through formal neuropsychological evaluation. Interaction is driven by neurobiologically situated brain–behavior relationships. Without expanding upon the current paradigm, neuropsychological assessment remains incomplete. During the course of the day, we quickly alternate our functioning by engaging in automatic, routine behavior with episodes of conscious cognitive control to adjust to dynamically changing situational demands (Evans, 2008; Restivo & Franklin, 2010). Most neuropsychological testing tasks focus on the component of thinking without paying attention to any implicit processes. Therefore, the considerable amount of information that is being "missed" needs to be incorporated into the formal evaluation process (Strauss, Sherman, & Spreen, 2006). In a sense, what we observe people do within the day-to-day environment is a "mirror image" that mimics the processes that occur *internally, within the brain*. Just as people change or switch from doing one thing to another, the brain is managing this behavior through its dynamically changing patterns of functional connectivity (Cole et al., 2013). This process is described in the next section.

## INTERACTION: MOVEMENT, THINKING, AND LARGE-SCALE BRAIN NETWORKS

The needs of interactive behavior require continuous neural processing. This neural processing occurs within LSBS, which develop slowly in human beings (Menon, 2010, 2013). These networks have "small-world" properties (as described in Part II of this series) to support segregated and distributed information processing dynamically and rapidly, while reusing aspects of "hubs" to quickly meet changing task demands (Cole et al., 2013). This maximizes efficiency and minimizes the biologic "energy costs" of the processes necessary for adapting to similar yet different task demands depending upon context (Bassett & Bullmore, 2006). These networks

process or "code" the salient properties of objects, such as what they look like and feel like, as well as what they are used for, which in essence is their reward value. *All of these properties are represented in the same sensory and motor brain circuits that were activated or recruited when the information about the objects was initially acquired*, which has critical implications as discussed in this section (Martin, 2007; see Cisek & Kalaska, 2005, 2010, for in-depth reviews). In brief review, the ventral attention network (VAN) registers what an object is and what it is used for, which is another way of saying it "codes" its identification and salience, or reward value. The dorsal attention network (DAN) registers where an object is and how to use it—in other words, specifying the proper parameters for action; this provides frontal systems with the necessary information about "how" the behavior should be performed. Therefore, these streams of information processing are critical for "action" control. Salience information "biases" potential behaviors by providing information about reward value associated with the identity of the object. This "biasing" about reward value is essentially a form of anticipation or prediction (Kinsbourne & Jordan, 2009; see Mars, Sallet, Rushworth, & Yeung, 2011, for a comprehensive review). We "know" that when we "interact" with an object ("object" is defined as a person, a thing, a nutrient, or an animal), there will be a certain outcome that has a certain purpose or meaning. Several potential behaviors are available in nearly all circumstances. Choices and decisions are made on the bases of anticipated reward—either obtaining satisfaction or avoiding a negative outcome. However, the point of the matter is that *potential activities, choices, or decisions are represented over large regions of the cerebral cortex. Therefore, decision making is not strictly localized within the prefrontal cortex, nor is it localized within the frontoparietal network (FPN); instead, these functions are localized within the same sensorimotor circuits that were activated when processing the information, when associating that information with reward value, and when programming and executing the associated actions. Behaviors that are adaptive can be generated either implicitly (without conscious thought) or explicitly (deliberately, through cognitive control or thought)*. Behaviors can be released through an automatic environmental "cue" or through a goal-directed plan (Griffiths, Morris, & Balleine, 2014). Current cognitive models posit that the basal ganglia (and specifically the caudate) and the cerebro-cerebellar circuitry systems "train" the prefrontal cortex during the course of development (Antzoulatos & Miller, 2014; Koziol, Budding, & Chidekel, 2012; Koziol & Lutz, 2013). Ramnani has proposed that the cerebellum provides the cerebral cortex with the input necessary for the automation of skilled cognitive operations (Koziol, Budding, Andreasen et al., 2013; Ramnani et al., 2005).

Automaticity and adapting behaviors across similar contexts are achieved through the operations of the cerebro-cerebellar circuitry system (Njiokiktjien, 2010). The learning of new behavior is supported by the reward-based instrumental learning corticobasal ganglia system (Frank, Seeberger, & O'Reilly, 2004). These systems, in combination, allow for a level of functioning characterized by alternating episodes of automatic behavior and cognitive control (Koziol, 2014). Therefore, "cognition" is not separate from sensorimotor control (Cisek & Kalaska, 2005, 2010). The "locus of control" over interactive behavior is a dynamically changing process. We refrain from relying on the term "executive functioning" (EF) in this system of behavioral organization because there is always decision making and problem solving based on multiple options, because the behavior that is either *explicitly* or *implicitly* chosen is based on the

anticipation of "reward value" or predicted outcome, and because behavioral control is a *dynamically changing yet neurobiologically situated* process. However, there is no well-localized homunculus or central executive that "directs" all behavior (Hazy, Frank, & O'Reilly, 2006, 2007). Implicit behavior lying outside of conscious awareness *is adaptive and is not traditionally considered "EF" even though the activity reflects adaptive decision making. When decisions are made explicitly, we prefer to use the term cognitive control.* This interactive paradigm is illustrated in Figure 1 (Cisek & Kalaska, 2010).

Knowledge for all behavior and about rewards is derived from sensorimotor *anticipation* (Pezzulo, 2011; Pezzulo & Dindo, 2011; Pezzulo & Rigoli, 2011). This anticipation develops or unfolds through environmental interaction. *Sensorimotor activity is never random* (von Hofsten, 2004, 2007, 2009). Even primitive and transitional
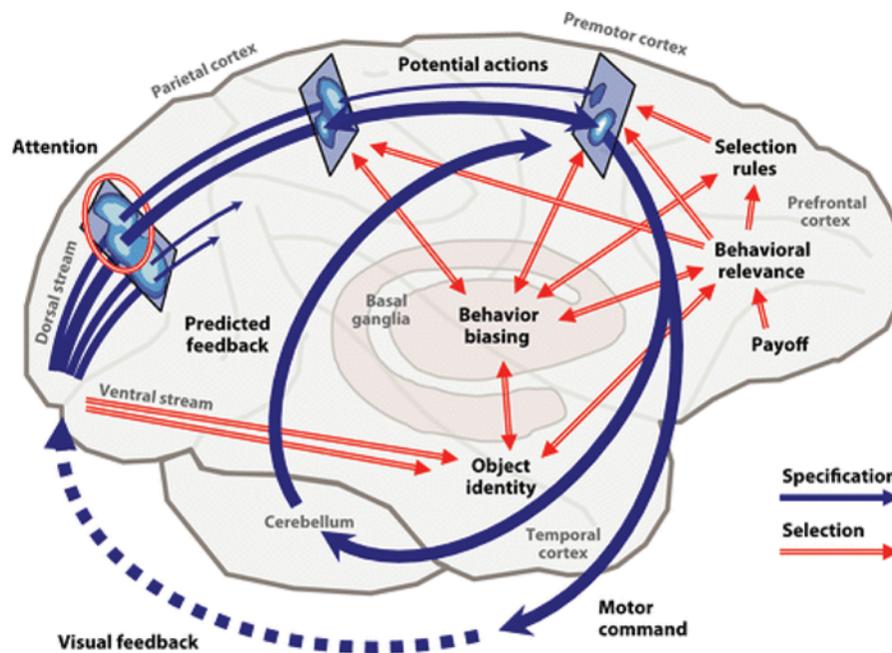
Cisek & Kalaska, 2010.
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FIGURE 1   This diagram represents a sensorimotor interaction paradigm for visually guided movement and illustrates interactions between the cortex, basal ganglia, and cerebellum. The dorsal stream (dorsal attention network), which consists of the parietal cortex and reciprocal connections with the frontal eye fields and premotor regions, is concerned with practical representations or programs for the opportunities for action that situations offer. The dark blue arrows stand for action specification and include all the parameters for the performance of the behavior. This processing originates in the occipital lobes (visual network) and proceeds in a rightward direction through the dorsal pathway. This dorsal pathway registers not only where something is, but also "how to do" something, such as how to grasp, as might be determined by an object's shape, size, and movement. This region plays a critical role in the procedural memory for action concepts. The ventral stream (ventral attention network) serves object identity and reward value. When interacting with the frontoparietal network, this becomes an "action control" network. (All connections are not directly illustrated; see text.) The polygons represent three potential actions (neural populations) along the dorsal route. Competition for action choice or selection is biased by "reward center" input from the basal ganglia to the parietal, temporal, and prefrontal neocortical regions. Reciprocal red arrows represent this evaluative biasing process. Therefore, action choices are represented over large regions of the cerebral cortex and subcortical regions. The action that is selected depends on the behavior with the strongest bias. The cerebellum (blue and dotted blue arrows connecting the cerebellum in this drawing) adjusts behavior on the basis of anticipated or predictive outcome, which is inherent in cerebellar control models. *Source*: Cisek & Kalaska (2010).

reflexes, the earliest observations of purposeful movement, mediated by the brainstem and midbrain regions, are associated with the anticipation of an outcome. Behaviors such as "latching on" and reflexive "sucking cycles" anticipate the outcome of nurturance, a "reward." It is no accident that deficits in these behaviors are strong predictors of future neurodevelopmental abnormalities (Poore & Barlow, 2009). This also implies that the development of higher-level brain systems requires the integrity of "bottom-up" support (Zhong et al., 2014). In fact, structural and functional asymmetries are even observed at the level of the brainstem, which presumably supports these early behaviors (Baizer, 2014). There is a voluminous literature, well beyond the scope of this selected review, that demonstrates the inexorable relationship between motor anomalies and cognitive control deficits (for summary reviews, see Koziol et al., 2012; Shaheen, 2013). The fact that movement is never random is not only evident in typically developing behaviors, but in neurodevelopmental disorders as well. For instance, in attention-deficit hyperactivity disorder (ADHD), the release of primitive and/or transitional reflexes is often observed (Konicarova, Bob, & Raboch, 2013). Nayate and colleagues have proposed that autism spectrum disorders can even be considered movement disorders (Nayate, Bradshaw, & Rinehart, 2005). Children with anxiety disorders exhibit motor impairment upon formal systematic clinical evaluation (Skirbekk, Hansen, Oerbeck, Wentzel-Larsen, & Kristensen, 2012). Parker and Andreasen describe schizophrenia as a disease process that is characterized by poor coordination, or dysmetria, in both motor and cognitive functions (as cited in Koziol, Budding, Andreasen et al., 2013). Chiari malformations, neonatal jaundice, and hypotonia have been linked to both motor and cognitive control deficits (Koziol & Barker, 2013; Koziol, Budding, & Chidekel, 2013). Adaptation is really all about "action control." And inherent in action control is the coupling of ideas, or aspects of ideas, with motor linkages for the purpose of interactive behavior. In aggregate, the rapidly emerging literature is demonstrating that just about any disorder that interferes with daily, interactive, cognitive, emotional, and social behavior is associated with anomalies in movement. In aggregate, the neurobiologically situated substrates of this "synchrony" are the corticobasal ganglia and the cerebro-cerebellar systems. The neural systems and mechanisms that support motor adaptation are not distinct from those that support cognitive and related functions (Keisler & Shadmehr, 2010).

THE DEVELOPMENT OF INTERACTIVE BEHAVIOR—FOUR STEPS

Thinking evolved to develop the ability for anticipation to guide the physical actions necessary for survival. In other words, we "think" in order to control and anticipate the outcomes of what we do; we "think" to control the motor system. Four steps describe the development of this cognitive control system. Motor activity, and control over it, comes first. It is fundamental to survival, development, and adaptation. Second, early exploratory movement leads to cognition. Movement and cognition are coincidental. This is evident in the exploratory behavior of the toddler. A child learns about the world by discovering objects in the environment and learning how to use them. The "value" of these objects represents reward characteristics. All of the properties of objects are learned by interacting with them. So in a way, this interactive "learning" occurs by coincidence. Third, motor activity and cognition coexist. Through this interactive learning process, children start to form simple "intentions" about what they want and what they want to do because they learned about reward contingencies and they use that anticipatory cognition to "control" behavior. At this point, movement and cognition are inexorably linked, so there is no "duality" between movement and cognition. This point cannot be overemphasized; this is a form of "working memory" that guides behavior in the moment, but it is based upon a perception/object–action link. Without this association, there is no need for that behavior. At this early stage in development, behavior is highly dependent on "reward," and this is supported by the developmental anatomical trajectory of LSBS (Menon, 2013). Fourth, these initial activities and cognitions become routine, such as feeding and playing, which are enjoyable, positively rewarding activities. Similarly, other behaviors that are not so pleasurable are resisted. This provides early inferential evidence that the basal ganglia are the critical player in learning what to do and what not to do (Cockburn & Frank, 2011; Nakanishi, Hikida, & Yawata, 2014). At this time, the behaviors that were learned are automatic. Movement, or activity, then rises *above* cognition. These behaviors become routine, and conscious cognitive awareness and explicit control are no longer necessary for those behaviors. Cognition then resides a notch *below* automatic behavior. This four-stage process repeats itself, over and over again, throughout the course of ontogeny, childhood, adolescence, and adulthood, and generates adaptive implicit and explicit decision making and adaptation.

We "step-down" and revert back to "cognition" in learning new activities and in solving problems. This often involves the abstraction of divergent thinking. We "imagine/predict/anticipate" how objects might be used in a way that is different from the way the object was initially intended to be used, and we combine these "predictions" about different objects to meet the stimulus-based properties of problems for which there is no readily available or "routine" solution. We then

use this information, derived from the "off-line" simulation of object use (thinking or imagining), to continue to guide the motor system. *This is exactly why symbolic or imaginative play is so important in young children.* It represents an early manifestation of the development of the cognitive control system. This is also why the absence of this type of play is often predictive of the development of disorders characterized by poor interpersonal skills or a lack of empathy. Adaptive interpersonal skills and empathy are not much more than anticipating what another person will think or feel on the basis of what we say or do, and we use that anticipation to control our behavior when interacting with others. In fact, Vakalopoulos (2013), in a very comprehensive, detailed, and compelling review, described how empathy develops from the motor system.

THE INTERACTIVE PARADIGM: USING TRADITIONAL NEUROPSYCHOLOGICAL TESTS IN NEW WAYS

As reviewed by Griffiths and colleagues (2014), the ability to learn contingencies between actions and outcomes within a dynamically changing environment is critical for flexible, adaptive behavior. Goal-directed behaviors adapt to changes in action-outcome or sensorimotor contingencies (the cerebro-cerebellar system) and to changes in the reward value of the outcome (the corticobasal ganglia system). We prefer the term "cognitive control system" over "EF" because there is always a distributed network of brain regions, including aspects of LSBS, the basal ganglia, and the cerebellum involved in behavioral control (Nowrangi, Be, Lyketsos, Rao, & Munro, 2014). The term "EF" has traditionally been considered as the function of the prefrontal cortex (Barkley, 2001), but "EF" is a term with no readily agreed-upon definition; similarly, it is clear that we are featuring a system that goes well beyond the prefrontal cortex, and for that matter, even beyond the FPN. The term "cognitive control" is clear; it is defined as control over the interactive motor system for the purpose of adaptation, and as we described, this "control" involves LSBS and interactions with the basal ganglia and cerebellum. The behavioral product can be developed either *explicitly or implicitly*. The FPN need not be involved in adaptive behavior. What remains critical involves the *linkage* between perceptions or aspects of ideas with "chunks" of motor activity. This linkage is exactly what is missing from descriptions of "EF," which ordinarily includes artificial constructs such as "working memory," "inhibition," "shifting," and "planning." In our view, the "work" of "working memory" involves *ideational–action coupling*. That said, how can neuropsychological tests be applied to these processes?

THE REY COMPLEX FIGURE TEST

Usually, whenever a patient draws the Rey Complex Figure Test (RCFT; Meyers & Meyers, 1995) with a disorganized copying approach or with poor "planning," a poor incidental recall 3 min later is the likely result. It is tempting to jump to the conclusion of "visual-spatial" or "visual-motor integration" deficits. But what do those terms mean? We believe that most of the time, except in cases of known parietal-lobe lesions (the parietal lobes specify the parameters for FPN action), the problem lies elsewhere, likely within the linkage between perception/ideation and motor activity. We can say the patient has no "strategy" for completing the task, but this word does not capture the perception–action concept. Therefore, we "walk the patient through" the task. We literally demonstrate adaptive task performance. We draw the RCFT for the patient as we "label" every design element, using common names and descriptors, as the patient actively *observes* the drawing. We then have the patient copy the figure in this *new way*. In a small pilot-study sample size, we have demonstrated significantly improved copy-phase drawing, typically well-retained incidental recall, and even retained 1-hr-delayed, 24-hr, and 48-hr recall. What have we done by violating test administration standards?

We have provided "working-memory" support; we have done the "work" of "working memory" for the patient by *establishing perception/ideational linkages*. This occurred when we labeled every stimulus element (perception/ideation) along with the observation of drawing (action linking). Why is this important? Images evoke *actions*. Aspects of this "coupling" depend on the integrity of the cerebellum (Christensen et al., 2014). We *disproved* the "visual-spatial" deficit hypothesis, and demonstrated that "working-memory" skills, or behavioral sequences, can be taught to improve task performance, with academic, educational implications that unfortunately go well beyond the scope of this article. We have provided useful clinical information with practical implications, while avoiding the pathology of "visual-motor integration" problems that are poorly understood because they have no universally agreed-upon meaning and have no practical treatment value. We applied what occurs in "real-life" situations to a neuropsychological test and made the results meaningful. For example, this might provide a key as to why a child has difficulty learning the procedure of multiple-digit subtraction when the numerical placement of certain numbers within the subtrahend are of greater quantity than certain numbers within the minuend (see Part III in this series). Labeling or "tagging" number identification (perception) with the sequential procedure (action) can provide the necessary linkage to learn this computational process.

THE TRAIL-MAKING TESTS

It has become routine to administer the Trail-Making Tests (TMT; Army Individual Test Battery, 1944). These traditional tests do a good job of evaluating explicit processing, even as a basic index of "processing speed." But how can we make what we observed possibly relevant to the implicit processing required in interactive behavior? Can performance on the TMT be used to generate a deeper understanding of constructs such as "working memory," "processing speed," "implicit learning," and correlating test performance with practical behavior? We advocate an important addition to the administration format to investigate these "constructs."

When we administer "Trails A and B," we assume that all participants "know" the numeric and alphabetic sequences. Our thinking tends to stop right there. However, understanding the potential diagnostic power that can be unleashed by administering these "simple" tests is situated in our knowledge about the rule-governed processes of *sequences*. Noticing the perceptual/ideational components of these tests is obvious. However, in thinking things through a bit further, it becomes clear that another aspect of the numerical and alphabetical sequences concerns their ordering. Every number is assigned a certain quantity; every letter is associated with a certain sound; these are the perceptual/ideational features of Trails A and B. However, the numeric and alphabetic ordering has a set, fixed, unchangeable pattern, sequence, or predictable action—1 is the stimulus for 2; 2 serves as the stimulus for 3; A is the stimulus for B; B is the stimulus for C, etc. These sequences are directly *linked to action* and are so routine that they are inexorably robust. In the interest of manuscript space considerations, only TMT-B will be considered here.

Whenever a person cannot complete TMT-B within the time of a normal control participant, given the assumptions inherent in the test, we are compelled to ask why this "slowness"—or even errors—occurs. We firmly believe poor performance occurs because of the lack of "work" in "working memory." Successful performance, characterized by 1-A-2-B-3-C-4-D, etc., requires a certain process. This process consists of literally *breaking* the established numeric and alphabetic linkages (sometimes referred to as inhibition) and taking an aspect of the perception and *directly linking* that perception of the number and letter with a *new action sequence*. At first, this requires the cognitive guidance of the content of "working memory." But the task goes beyond that idea because the perceptions of numbers and letters must now be coupled with new but related "chunks" of action for the establishment of a novel, rule-governed sequence. Again, in a small sample of participants, we have determined that normal control participants can actually reduce performance time with repeated administration for five trials. This reflects task acquisition, or the achievement of automaticity. However, in neurodevelopmental disorders, when performance is initially slow and characterized by continuing slow speed, errors, and even different and multiple inconsistent errors on five consecutive trials, a problem has clearly emerged. The new perception–action coupling is not established. So, what does this measure? It assesses a "working-memory" failure on the "action" side of the "working-memory" equation. It reflects an inability to quickly establish new perceptual/ideational–action links, exactly what is required for quick, efficient, flexible adaptation. Of course, the VAN is likely recruited to identify numbers and letters; the DAN is recruited to orient the frontal eye fields. But the task is not learned, old action links are not easily or completely (flexibly) decoupled, new "chunks" of action are not coupled, and slowly operating processes of the FPN, likely experienced as effortful episodes of "concentration," do not become independent of conscious, explicit cognitive input across five consecutive trials; slowly operating *sensorimotor feedback* remains necessary for task completion; there is no automation, which is exactly what we want to measure within an interactive test paradigm that mimics habit formation or very broadly defined procedural learning. It also demonstrates the critical importance of speed as it relates to cognitive control or lack thereof. The "flexible hub" of the FPN cannot recruit the activities of aspects of other "hubs" efficiently. Field trials are in progress to determine how these TMT findings translate to the acquisition of routine behaviors such as "automatic" tasks of dressing/undressing, personal hygiene habits, and establishing routines of putting things in proper places, the same way every time, which are behaviors that actually support organizational abilities.

In other words, we are proposing a redefinition of "working memory." Current "working-memory" subtests are blatantly explicit; they assess essentially "declarative" immediate recall types of content such as digits forward and backward and subtests such as Letter-Number Sequencing on the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV; Wechsler, 2003). Within an interactive paradigm, "working-memory" tasks should consist of perception–action codes, merging these with more abstract ideas and thoughts and coupling or linking these with action execution. This is the essence of cognitive control as we interact within a dynamically changing world with unpredictable task demands. Neurocognitive evidence already demonstrates that perception/action codes and motor linkages share the same retrieval mechanisms and that intact perception–action coupling depends on the integrity of the cerebellum (Ashby & Crossley, 2012;

Christensen et al., 2014; Dew & Cabeza, 2011; Keisler & Shadmehr, 2010; Oberauer, Souza, Druey, & Gade, 2013).

All existing neuropsychological tests, potential modifications, and/or reinterpretations of these tests obviously cannot be covered in this manuscript. However, a few brief, additional ideas can be proposed. For example, facial recognition tasks take on new significance in view of our knowledge about the VAN. The ultimate usefulness of these sensitive tasks might very well be in assessing the integrity of aspects of the salience network. Why? We are social creatures living in a social, interactive world. Assessing salience as it relates to social cognition expands the role of neuropsychological assessment by including personality functioning. Although it is generally accepted knowledge that facial identification/recognition is processed within the fusiform gyrus of the temporal lobe, the temporal lobes send direct projections to the caudate nucleus of the basal ganglia, which we have emphasized as a reward-based, instrumental learning system. Specifying "reward value" is broadly defined to include meaning. And in social interactions, *meaning is affect. Facial expressions convey affect.* This is a form of categorization that we have already identified as *visual discrimination, which is basal ganglia-determined learning.* Coupling social salience with reward anticipation might prove to be critical in understanding a child's interpersonal behavior. Unfortunately, the vast literature on the neurobiology of social cognition goes beyond the scope of this article. (The interested reader is referred to http://www.scn. ucla.edu). Similarly, tests such as Arrows from the NEPSY I & II (Korkman, Kirk, & Kemp, 1998, 2007) and Judgment of Line Orientation from the Benton series (1983; Benton, Hamsher, Varney, & Spreen, 1994) can perhaps be reinterpreted as potential indicators of the integrity of the DAN under frontal eye field control and/or a neurodevelopmental inability to inhibit saccadic eye reflexes; this could implicate the frontal eye field (DAN)–cerebellar circuitry ensemble (Ito, 2011) instead of routinely attributing performance to "visual-spatial" functional integrity. It has been recently documented that contrary to previous theory, the parietal lobes, which provide input to the prefrontal lobes and frontal eye fields for the orientation of attention, *also play a critical role in protecting working memory from distracting influences* (Jacob & Nieder, 2014). This has obvious implications for our understanding of the role of the parietal lobes in the control of attention, thinking, and movement. It is widely known that attention is frequently shifting from one place to another and that the activity in visual regions is anything but stable (Treue, 2001). The purpose of this series of articles is to stimulate thinking about how test paradigms might be applied to the operations of LSBS. We are establishing a neuroscientific framework for the reader to explore for the possible updating of clinical neuropsychological practice.

ASSESSING THE REWARD SYSTEM

Perhaps the most widely known test for evaluating reward systems is the Iowa Gambling Task (Bechara, Damasio, Damasio, & Anderson, 1994). We have reservations about the usefulness of this procedure for a number of reasons: The task might be cognitively mediated; it is introduced as a "betting" game; and the task has no commercially available counterpart for use with children. We prefer bypassing all of these issues by using a task that is very frequently used successfully in experimental studies of reward preferences of normal control participants, patients with known basal ganglia instrumental learning system pathology, and neuropsychiatric populations, including adolescents and older school-aged children diagnosed with ADHD (Frank, Samanta, Moustafa, & Sherman, 2007; Frank, Santamaria, O'Reilly, & Willcutt, 2007; Frank, Scheres, & Sherman, 2007; Frank et al., 2004). In many of these studies, reward preferences have been manipulated according to medication status. The primary task employed to evaluate reward characteristics is the Probabilistic Category Learning task. This task offers positive and/or negative reinforcement, but only for certain percentages of time, while bypassing cognitive control processes. It is very similar to the Knowlton Weather Prediction Task (Knowlton, Squire, & Gluck, 1994), although instead of using recognizable objects as stimuli, abstract shapes are substituted to avoid cognitive mediation. However, given our knowledge of LSBS, their connections with basal ganglia and cerebellar systems, the importance of reward and salience for motivation, amotivational syndromes without depression, and even the current controversies over symptom validity testing, we see no alternative other than to obtain objective identification and characterization of reward preferences. This is not only critical to treatment planning, but evaluating reward systems would again place neuropsychological assessment within the realm of evaluating personality functioning. Similarly, because certain medications that manipulate reward preferences in amotivational populations require close monitoring for dosage effectiveness and eliminating untoward side effects, this would represent a valuable contribution to the field of behavioral health by providing a medication monitoring mechanism.

THE CEREBELLUM

Traditional neuropsychological testing has never included a measure of the integrity of the cerebellum. This is likely

because until relatively recently, the cerebellum was considered only a coprocessor of movement. As described in Part III of this series, the cerebellum is a coprocessor of the cortex! The cerebellum and cortex work together as an ensemble (Smaers, Steele, Case, & Amunts, 2013; Smaers, Steele, & Zilles, 2011). The easiest way to incorporate a screening measure of cerebellar integrity is to employ the neurologist's finger-to-nose test. However, the operations of the cerebellum include the ability to adapt behavior across similar contexts, while numerous studies have demonstrated the role of the cerebellum in anticipatory thinking and object–action linkage (Christensen et al., 2014; Imamizu & Kawato, 2012; Ito, 2008; Koziol , Budding, Andreasen et al., 2013). Therefore, it would also be useful to add tasks that require cerebellar input for automation and adaptation as the learned task becomes independent of cognitive control/ the "cortical content of working memory." The Pursuit Rotor Task has proven to be useful in activating motor, sensorimotor, and certain cognitive modules of the cerebellum in a procedural learning task. This task has recently been computerized as described by Dean and colleagues (2014; the task is available through Life Science Associates in New York). It requires a participant to follow a moving target around a rectangular track, using a computer mouse held in the preferred hand. Multiple 20-inch trials are administered, with 5-inch intervals between trials, and blocks of trials can be administered between the administration of other tasks, so that multiple samples of the procedural learning and adaptation to the task can be obtained. Because the cortex retains what the cerebellum learns (see Part III of this series), a task of this type would provide information about cerebellar–cortical information transfer, which is critical to interactive adaptation. Impaired performance has been associated with both procedural learning and cognitive pathology.

SUMMARY

The patient, diligent reader who has read all four articles in this series has come a long way in assimilating and modifying their knowledge about brain-behavior relationships. Many of the ideas and concepts introduced are new; the wealth of information presented might not even be understood upon initial reading, in which case this series might serve as reference material. Some readers might question how the interactive paradigm, based upon "action" or movement, might apply to "exceptional" cases, such as the congenitally blind; others might wonder how congenital deafness might impact upon the orientation and efficiency of attention; readers might question how cognition develops in neurodevelopmental disorders characterized by significant movement impairment, and whether or not

this might differ from the cognition of a typically developing child, adolescent, or adult who always possessed movement capacities and then lost the ability to move because of an acquired disease process. Space limitations did not allow for coverage of these "exceptional" cases. However, the interactive model summarized here applies to all these cases, and has been described previously (the interested reader is referred to Koziol, 2014). Some of the methodologies presented admittedly violate tradition and might appear quite surprising. However, we have attempted to present an update on functional neuroanatomy in order to establish a firm foundation to be used as an anchor point for evidence-based neuropsychological test interpretation. We have expanded upon the traditional neuropsychological test paradigm, not because we are rogue, but because neuroscience is advancing exponentially and because the gap between neuroscience and neuropsychology must be filled, integrated, and closed. We do not indict current neuropsychological practices. We reinforce traditional constructs, modify others, and provide the practitioner with guidelines. We hope we stimulated independent thinking. The reader might wonder how the introduction of new administration procedures and new tests might increase the time necessary to conduct a neuropsychological evaluation. However, we also believe that the skilled clinician might reflect upon current practices and find certain current tests unnecessary because they are based upon an a-theoretical instead of a demonstrable evidence-based framework. Our overall goal is to move the field forward, hopefully in the spirit of the late John F. Kennedy who once stated, "Change is the law of life. And those who look only to the past or present are certain to miss the future" (1963).

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