# Understanding Neuropsychopathology in the Twenty-first Century: Current Status, Clinical Application, and Future Directions

Leonard F. Koziol
Private Practice, Park Ridge, Illinois

Deborah E. Budding
Private Practice, Manhattan Beach, California

James B. Hale
University of Victoria

Koziol, L. F., Budding, D. A., & Hale, J. B. (in press). Understanding neuropsychopathology in the twenty-first century: Current status, clinical application, and future directions. In L. A. Reddy, A. S. Weissman, & J. B. Hale, (Eds.), *Neuropsychological assessment and intervention for emotional and behavior disordered youth: A step-by-step evidence-based approach.* Washington, DC: American Psychological Association.

## *Shifting Perspectives: From Categorical to Dimensional Approaches*

Many childhood psychopathology textbooks and associated coursework focus on overt symptoms and behavior in order to describe different disorders and to evaluate their empirically-based treatments. However, in this book authors attempt to move beyond this reductionist simplicity to include discussion of the interrelated brain structures, functions, and systems governing human behavior that when impaired lead to psychopathology. The term *neuropsychopathology* is used to make clear our perspective that psychopathology has, for far too long, been governed by categorical disorder definitions that require counting of informant-reported symptoms and arbitrary thresholds for identification. While categorical labels may be useful for political or economic reasons, they perpetuate misinformation and misunderstanding that suggests a false dichotomy between what is "normal" and what is "abnormal" in the manifestation of brain-behavior relationships. The "neuro" focus provides us with the impetus to understand the etiology, manifestation, variability, and outcomes observed among children with psychopathological disorders.

We all have characteristics or *personalities* that explain who we are, how we think, and what we do. However, personalities should not be seen as conceptually or functionally distinct from psychopathology. When does an introvert become withdrawn, an individualist become antisocial, or a visionary become psychotic? These are fine lines to draw indeed, especially given that intra-individual differences can be more important in understanding and helping children than inter-individual ones. Neuropsychological theory and research explains why adaptive and maladaptive characteristics often exist in the same individuals, suggesting these characteristics represent multiple *dimensions* of psychosocial functioning. Interdependent and multi-determined, these dimensions represent interrelated brain-based systems that range on a continuum from normal to impaired.

Careful neuropsychological evaluation and clinical elucidation are needed in order to incorporate a dimensional perspective that will help us understand and serve individuals affected by neuropsychopathology. This dimensional approach recognizes that phenotypic presentation for any given individual is highly variable and dependent on both genetic endowment and environmental determinants. Neuropsychological and neuroimaging research has revealed the brain to be much more plastic than was ever anticipated, and this fact leads us to conclude that the clinical presentation of any

individual is highly malleable and modifiable. This plasticity is not unidirectional, however, as impaired brain functioning can be made better with proper intervention, while normal brain functioning can become problematic if exposed to deleterious environmental circumstances. Those who receive intensive neuropsychological training and supervised experience are most likely to recognize the biological bases of the cognitive, academic, behavioral, and psychosocial diversity governing a child's function in the natural environment, and can thus help to reach a more advanced understanding of neuropsychopathology.

To understand these biological dimensions of psychopathology, this chapter presents a tiered model of brain function that emphasizes cortical, basal ganglia, and cerebellar interactions (Koziol & Budding, 2009), similar to what Hale et al. term the superior-inferior axis of interpretation (Hale et al., 2009). Neuroscience research has confirmed the reciprocal nature of a brain system in which higher-order cognitive control and automatic behavior coexist and interact to achieve optimal environmental adaptation. We illustrate how this knowledge helps explain a wide variety of behaviors and functions along a continuum from normal adjustment to psychopathology. We conclude by discussing some of the future implications for neuropsychological assessment and treatment that naturally follows from an understanding and application of this model.

*Replacing Cortico-centric Models of Behavior*

Neuropsychological evaluation of childhood disorders has historically been based on a cortico-centric model of behavior, assuming that all relevant brain-behavior relationships are rooted in the highly developed and specialized cortical regions. However, the last 25 years of brain research has demonstrated that this cortico-centric model is overly reductionist, inaccurate in its assumptions, and ultimately clinically misleading. Similarly, neuropsychological assessment has historically focused on higher-order cognitive functions (Lezak & Loring, 2004), with most instruments focusing on conscious cognitive control for accessing brain functions through the "dorsolateral channel" (Ardila, 2008). In contrast, the medial and orbital frontal systems, involved in motivation, affect regulation, social judgment, and adaptive behavior, are more difficult to directly evaluate using neuropsychological tests (Zald & Andreotti, 2010).

Due to this focus on evaluating relatively narrow aspects of cognition, neuropsychology has largely ignored brain-related functions such as motivation and affect regulation, in addition to myriad other behaviors not under conscious control. All too frequently, neuropsychological test profiles without obvious cognitive deficits are dismissed as inconsequential, incorrectly leading to clinicians suggesting childrens' psychosocial problems can be attributed to poorly understood or even mysterious "psychological factors" that are presumed to be solely environmentally determined. Recent advances in our understanding of the biological bases of psychopathology has led to development of neuropsychological measures that assess socioemotional perception or regulation (NEPSY-II Affect Recognition, Theory of Mind), and motivational influences on behavior (e.g., Balloon Analogue Risk Task; Iowa Gambling Task), so recognition of cortical influences on behavior have extended beyond the dorsolateral-dorsal cingulate areas to include the orbital and associated ventral cingulate regions (see Miller & Cummings, 2007).

It is now also clear that these cortical regions include afferent and efferent pathways with the basal ganglia and cerebellum, structures traditionally thought to be only co-processors of movement. Advances in neuropsychopathology now reveal how brain structures interact to play essential roles not only in cognition, but also in social, affective, and motivational behavior (Koziol & Budding, 2009; Schmahmann, 2004; Hirata, Tanaka, Zeng, Hozumi, & Arai, 2006; Stocco, Lebiere, & Anderson, 2010). These brain regions contribute not only to conscious cognitive control – often referred to as executive function – but also thinking and behavior beyond conscious awareness. Failure to recognize these

important tenets of behavior contributes to a naive and woefully incomplete understanding of brain functioning and psychopathology.

Volitional behavior is grossly overestimated in the human experience. Estimates suggest as much as 95% of a person's daily behavior lies outside the realm of conscious cognitive awareness (Bargh, 1997; Bargh & Chartrand, 1999), which essentially means much of our behavior is automatic and routinized. As these automatic behaviors need modification in response to changing environmental conditions (e.g., dropping the soap when showering), we need to exert some degree of conscious cognitive control and self-awareness to adjust our behavior, and then we often again return to automatic, routinized behavior (Hikosaka & Isoda, 2010). Essentially, life consists of considerable automatic or routine behavior alternating with brief episodes of conscious cognitive control, with variations in executive control and internal states having dramatic implications for our understanding of typical behavior and neuropsychopathology (Fox & Raichle,2007).

For example, previous chapters in this book recognize abnormal functioning within the context of broader categories such as internalizing or externalizing psychopathology, but they share a commonality: The manifest behavior is thought to exist largely outside of, or to interfere with, the child's conscious cognitive control. From a dimensional perspective, typical and atypical behaviors are defined in part by whether the child can exert cognitive control over them. In psychopathology, atypical behaviors cannot be turned "on" (e.g., engaged) or "off" (e.g., inhibited) at will. A child with a hand washing compulsion rationally knows his hands are clean and attempts to exert cognitive or executive control to inhibit the behavior, but anxiety builds and the maladaptive compulsion soon overtakes this volitional attempt at suppressing the behavior. We argue here that neuropathological behaviors are largely automatic and fundamental to the individual's level of environmental adaptation, even if dysfunctional in relation to most contexts the behavior is displayed.

Traditional clinical or even neuropsychological models focusing on cognition are unable to provide a meaningful understanding of the simultaneous co-existence of more than one diagnostic condition occurring within the same individual at the same time (Levy, 2010). The answer to perplexing diagnostic pictures lies in a neuropsychopathological model of understanding the typical-atypical dimensional continuum. As a first step, the field needs to develop a scientifically relevant, functionally coherent model of brain-behavior relationships that appropriately incorporates the cortex, basal ganglia, and cerebellum. In addition to the traditional (and now largely outdated) cortico-centric view that interpretation requires only an understanding of the left-right hemisphere and anterior-posterior dimensions, neuropsychology needs to actively consider the brain's vertical organization (Koziol & Budding, 2009) or the superior-inferior axis of interpretation (e.g., Hale et al., 2009).

*A Brief Analysis of the Major Players: The Neocortex, Basal Ganglia, and Cerebellum*

The entire brain, working in concert, essentially generates an interactive *dual-tiered system of cognition and behavior* essential for successful environmental adaptation (Koziol, Budding, & Chidekel, 2010). The neocortex can be divided along two interpretive axes, an anterior (frontal)-posterior (occipital, temporal, parietal) axis, and left-right hemisphere axis. Consistent with Luria's (1973) functional model, the posterior regions of the brain are primarily viewed as sensory information processors, where the highest levels of understanding take place in the occipital-parietal-temporal tertiary cortical regions known as the *Zones of Overlapping* (Luria, 1973). The frontal lobes represent Luria's *Superstructure,* which govern all aspects of volitional behavior related to self (ventral system) and environmental (dorsal system) control. Frontal systems develop the motor programs necessary for successful environmental response (premotor) or routinized (supplementary motor) motor activity. Just as learning novel information requires a shift from novel problem solving during acquisition (right frontal) to routinized understanding (left posterior), so too does learning motor scripts, transferring

unknown motor skills from the premotor to supplementary motor areas for routinized performance or *praxis* (Goldberg, 2001).

Once a skilled behavior or way of responding has been learned, future behaviors requiring the same skill are executed in an expedited manner (Heilman & Rothi, 2003). We no longer have to think about the action to do it well; our brain does the work spontaneously, simply because the task requires activation of a known script (Saling & Phillips, 2007). The sensory-perceptual aspects of these skilled movement formulas are related to inferior parietal lobe functioning, sometimes referred to as *praxicons.* Together, the inferior parietal and supplementary motor regions provide the *cortical* basis of skilled motor movements that are mostly outside the purview of conscious awareness, where inferior (i.e., subcortical) structures and functions play an important role.

Representing the inferior portion of the superior-inferior axis are two vertically organized re-entrant systems that interface the descending cortical system. These are the cortico-basal ganglia system and the cortico-cerebellar system. They are termed re-entrant systems because their circuitries form "loops" or self-regulatory circuits that originate in the cerebral cortex. Serving an important modulatory function, these subcortical regions play a critical role in deciding what information is or is not returned to the cerebral cortex for subsequent modification (Andreasen & Pierson, 2008). This "looped architecture" represents an organizational system central to brain-behavior relationships, and therefore, in a broader context, these circuitries should be central to neuropsychology. Neuropsychology needs to develop procedures and tests for the various functions of the vertically organized brain in order to evaluate cognitive, affective, socio-emotional, and motivational functioning, as is suggested by Hale et al. (2009) to foster accurate disorder identification and efficacious intervention practices.

Generally, the frontal-striatal-thalamic circuits originate in cortical regions and first project to the excitatory striatum (caudate nucleus, putamen), and then to the inhibitory globus pallidus for modulation, which in turn projects to the thalamus for sensory or motor release, and returns to the cortical area where the circuit first originated, therefore directing attention or generating an activity. These connections consist of the direct and indirect pathways that work in opposition to one another. When the cortex stimulates the direct pathway, behavior is released by inhibiting inhibition. When the cortex activates the indirect pathway, behavior is stopped or inhibited. This circuitry allows the brain to act upon its intentions. An additional "hyperdirect" pathway by-passes the striatum by directly linking the frontal lobes to the subthalamic nucleus; activation of this pathway is the quickest way to stop a behavior. This circuit plays a particularly important role in impulse control (Nambu et al., 2000; Frank, 2006). Accordingly, disturbances within this circuitry result in problems executing behavioral intentions. There are five prototypical frontal-striatal-pallidal-thalamic circuits. These comprise the motor circuit, the occulomotor circuit, the dorsolateral prefrontal circuit, the orbitofrontal circuit, and the medial or anterior cingulate circuit, all named after their cortical points of origin (Alexander, DeLong, & Strick, 1986; Denckla & Reiss, 1997).

These circuits serve very specific functions related to executive control and psychopathology. The dorsolateral circuit is involved in *external* or environmental executive functions such as planning, organization, strategizing, monitoring, evaluating and changing behavior, the orbitofrontal circuit is involved in *internal* or behavioral regulation functions such as impulse control and social judgment and problem solving, and the medial circuit, intimately related to the nucleus accumbens and appetitive behavior, is involved in motivation, error monitoring, and decision making in concert with the other circuits (Hale et al., 2009; Koziol & Budding, 2009). The specific functions of these circuits are segregated, allowing for focused and maintained activity, but this fact does not explain how their functions are integrated in practical behavior. For this integration to occur, there are four basal ganglia integrative networks which allow for behaviors to be modified and learned. However, describing these

networks and their neurochemistry is beyond the scope of this paper (for a detailed review, see Steiner & Tseng, 2010).

This cursory explanation is offered to help readers understand the anatomic underpinnings for circuitry interaction and the occurrence and comorbidity of psychopathology. Recognizing circuit functions can further our understanding of volitional control or intentional behavior. Intention programs can be characterized along four dimensions (Heilman, Valenstein, Rothi, & Watson, 2004):

1) Knowing when to start a behavior;
2) Knowing when not to start a behavior;
3) Knowing when to persist with a behavior;
4) Knowing when to stop a behavior.

It is critical to understand these intention programs because these are the *programs that are disturbed in most neuropsychopathological conditions* described in this volume. However, in order to understand this, it is important to first acknowledge the basal ganglia's role in instrumental learning of adaptive or maladaptive response repertoires.

The basal ganglia help the brain learn according to instrumental learning principles (Yin & Knowlton, 2006). If a behavior serves in the person's best interest, a *combination or sequence* of new movements or a new *motor (praxic) program,* is acquired. The basal ganglia are believed to chunk together and bind the elements of a movement program so that the behavioral sequence can be stored within the supplementary motor area, the motor association cortex responsible for self-directed movement. If a behavior is effective, the basal ganglia respond by a phasic increase (*burst)* in dopamine (DA), which is the brain's most important reward chemical (Frank, 2005) involved in appetitive behavior. However, if the behavior is not effective, the basal ganglia respond by a phasic decrease (*dip*), in dopaminergic activity. This dopaminergic-mediated learning makes it very likely that under similar stimulus conditions, a behavior will be released (if a DA burst occurred) or inhibited (if a DA dip occurred) according to whether the behavior was successful. Success is in part determined physiologically by the nucleus accumbens, the reward structure sensitive to DA input, with DA bursts registered as rewards, and DA dips registered as punishments. This in turn influences the amygdala, which is important in "flight or fight" reactions, further influencing reward-based instrumental learning (Heimer, Van Hoesen, Trimble, & Zahm, 2008; Blackford, Buckholtz, Avery, & Zald, 2010). As a result, it is easy to see how aberrant intention programs develop as a result of abnormal sensitivity to the reward or punishment, and how they lead to psychopathology.

*Cognition, Affect, and Motivation as Motor Analogues*

This conceptualization of frontal-subortical circuit influence allows us to develop cognitive, affective, and motivational analogues to motor functions. In this way, if we understand the most basic principles that govern movement and intention, and the dopaminergic fuel that feeds them, we can better understand other aspects of human behavior and neuropsychopathology. The basal ganglia are not really *movement* structures. Instead, they govern regulation of intention. *What the basal ganglia do for movement, they also do for cognition, emotion, and motivation*. When the motor circuitries are impaired, the resultant disorders of *movement intention* are considered along a dimension of speed (Blumenfeld, 2002), ranging from slow (bradykinesia/hypokinesia) to fast (myoclonus). The same concepts can be applied to cognition and psychosocial functioning. Slowed cognition or bradyphrenia may be characteristic of depression, while fast cognition or hyperphrenia, may be characteristic of racing thoughts and flight of ideas seen in mania. This implies involvement, either hypo- or hyperactivity, of the dorsolateral circuit, which in turn is related to the medial circuit that regulates motivation. Lack of activity would be seen in an amotivational syndrome in which nothing interests the child. Excessive activity in this circuitry would be manifest by increased motivation and energy that also

can be characteristic of manic or hypomanic patients (Mega & Cummings, 2001). Finally, this continuum can be applied to emotional and/or social circuitries mediated by the orbitofrontal-subcortical circuits. Hypoactivity within an affective channel would result in lack of emotional awareness or responsiveness, leading to social detachment or withdrawal. Excessive activity within an emotional circuit would result in hyper-emotional responsiveness, with an associated intense social awareness or even social anxiety resulting, especially if reinforced intention programs are considered maladaptive by others.

Recall that intention programs fall into the four categories described above. Difficulty with movement initiation easily translates to an inability to concentrate in order to start a cognitive activity when there is a disturbance within a dorsolateral circuit. For example, difficulty with retrieval of words as demonstrated on a word list learning task or generating words on a fluency task could translate into limited or inexact social communication during conversation. However, if exaggerated, pressed speech as seen in hypomania may result. Translating this conceptualization to emotional circuitry, this type of impairment might result in difficulty generating an adaptive emotional response to a given social situation (e.g., blunted or exaggerated response). For impairment in the motivational circuitry, there would be a lack of motivation or interest in an activity (e.g., anhedonia), or conversely an excessive interest leading to gregarious, disinhibited, or attention-seeking behavior.

Knowing when to start or not start a movement is relevant to our understanding of dyskinesias. For the motor circuit, behavioral impersistence or repetitive avolitional behaviors such as tics or compulsions fall in this category. Behavioral impersistence can be seen cognitively when people cannot maintain an idea or train of thought, which we describe as “distractibility,” and this is seen socially or interpersonally when relationships with others are described as “superficial.” In a cognitive circuit, disinhibition might be manifest by blurting-out ideas or statements. It might also be manifest as the intrusion of irrelevant ideation or intrusive thoughts often observed in Obsessive Compulsive Disorder. Not knowing when to stop a behavior is also known as perseveration. In a cognitive circuit, this is manifest by repetitive ideation, or thinking about the same thing over and over again. In an affective circuit, affective dyskinesia would look like sudden or exaggerated changes in mood, and even irritability because of difficulty terminating an emotional reaction or “letting go” of a situation. In a motivational circuit, this might be manifest by a waxing and waning of interest levels in activity.

Our purpose here is not to examine every imaginable behavior or to force every behavior into the processes of frontal-basal ganglia systems. Rather, the point is to understand that motor behavior has cognitive, affective, and motivational predispositions and analogues. Understanding the dimensional and reciprocal nature of the frontostriatal circuit system can help clinicians develop a more nuanced understanding of the complex behavioral presentations observed during practice. This purpose provides an understanding that what the basal ganglia does for movement, it also does for numerous other adaptive processes. Instead of attributing maladaptive behaviors to “psychological” factors, this dimensional approach provides the impetus to further our diagnostic skills and refine treatment strategies, which should lead to better adaptive outcomes for children with neuropsychopathology. For further reading on the variety of cognitive, motivational, and affective/emotional outcomes that result from disturbances in intention programs, please consult Bradshaw (2001), Koziol and Budding (2009), and Lichter and Cummings (2001).

*The Cortico-Cerebellar Circuit: Inferior Does Not Suggest Inconsequential*

While traditionally understood as a co-processor of movement, the past 15 years of neuroscience research have made it increasing clear that the cerebellum plays a significant role in cognitive, affective, and motivational behavior (Schmahmann, 2004; Ackermann, 2008; Ito, 2008). The cerebellum’s relationship to the cortex is in principle similar or parallel to that of the basal ganglia – what it does for movement it also does for cognition and other functions. The cortico-cerebellar circuit

begins with cortical areas sending projection fibers to the pons, which in turn sends this afferent information to the cerebellum. After the cerebellum modifies the input, changing its quality, it sends the new, refined message back to the cortex via the thalamus. Reminiscent of the frontal-striatal circuitry, different frontal areas send information to different cerebellar regions, so this circuitry is also segregated accordingly.

Although the following represents an oversimiplified description for the purpose of brevity, a working model of this structure differentiates cerebellar functions along an anterior-posterior and a lateral-medial gradient. Sensorimotor functions are generally mapped in anterior regions of the cerebellum. Cognitive and affective functions are represented within the posterior regions or hemispheres of the cerebellum. The medial vermis of the cerebellum is involved in autonomic and affective regulation. The lateral cerebellar hemispheres are involved in the regulation of executive functions, visuospatial, linguistic, and learning and memory functions, including procedural learning and memory (Stoodley & Schmahmann, 2010; Njiokiktjien, 2010).

The cerebellum generates the appropriate amplification of behavior and it regulates a behavior's rate, rhythm, and force. While the cortex consciously decides "what" to do, and the basal ganglia's intention programs decide "when" to do things, the cerebellum tells the brain "how" to get things done in the most efficient manner. It adjusts the *quality* of movement or activity. Anterior cerebellar damage can lead to dysmetria, characterized by movements that have become erratic in size and direction or amplitude (Houk & Mugnaini, 2003). This is exemplified in intention tremor. In a reaching behavior, the patient often overshoots or undershoots the object. A cognitive analogue of this disturbance might lead to a child going "round and around" in his thinking (Schmahmann, Weilburg, & Sherman, 2007), which leads to undershooting and overshooting the "target" or point of a conversation, with the result being circumstantial speech with excessive verbiage. Another example of the cerebellum's role in force amplification function would be inappropriate prosody (Boutsen & Christman, 2002; Ackermann, 2008). An emotional analog, a very common developmental problem, consists of an uncontrollable temper outburst, in which emotion is expressed much more strongly than is warranted by the circumstances (Koziol, Budding, & Chidekel, 2011).

The cerebellum also serves an essential timing function with respect to certain types of learning, such as classical conditioning. Damage to the cerebellum interferes with the ability to learn to make the appropriate *anticipatory* response at the correct time interval. This function is particularly relevant for psychopathologies such as Panic Disorder and phobias, which can be understood as manifestations of abnormal classical conditioning. The cerebellum also plays a critical role in procedural learning (Molinari, Restuccia, & Leggio, 2009), adapting motor functioning to improve performance across situations. In other words, the cerebellum follows the truism that "practice makes perfect", leading to quicker and more precise action following repetition and practice. This efficiency of action is consistent with current research suggesting the cerebellum's role in development of progressive, short-cut, anticipatory control models (Bellebaum & Daum, 2007; Imamizu & Kawato, 2009). In essence, a cerebellar internal "model" of what the brain would like to do is based on its performance of multiple previous episodes during which it has already performed that behavior, and practice leads to increasingly accurate predictions to inform successive behavioral executions , allowing for quick, efficicient performance (Houk et al., 2007). Automaticity is achieved and the behavior can be generalized across different situations. These processes of procedural learning and adaptation allow the brain to store the most efficient representations of the *praxicons and innervatory motor patterns* described above, but they may lead to inappropriate repertoires in children who experience psychopathology.

A case in point is what has become known as Cerebellar Cognitive Affective Syndrome (CCAS), a constellation of cognitive, affective, and behavioral abnormalities associated with cerebellar lesions (Schmahmann & Sherman, 1997), especially to the vermis and paravermian regions (Schmahmann et al., 2007). Virtually indistinguishable from primary psychopathology, CCAS leads to executive, attention,

working memory, cognitive set shifting, perseveration, spatial processing, and language use or fluency deficits. Emotional dysregulation in the form of aberrant behavior modulation or personality style can lead to flattening of affect and social withdrawal at one of the continuum to socially inappropriate flippant and humorous comments on the opposite end.

*A Dual-Tiered Model of Brain Functioning*

Human beings adapt to their environments through interaction with the world around them. This process of adaptation is not dependent solely upon cortical functions (Panksepp, Moskal, Panksepp, & Kroes, 2002; Cisek & Kalaska, 2010), but subcortical ones as well (Koziol & Budding, 2009). Stimulus-based responding is composed of intrinsic behaviors and behaviors that result from learned associations that allows for automatic responding in familiar, routine situations. The behaviors governed by this system allow for exploitation of the environment's predictable features. This is no small advantage, since many of these routine, automatic behaviors are both elegant and efficient. Because these behaviors do not require higher-order thinking and control, they conserve cognitive and precious higher-order control resources which are required in novel circumstances (Saling & Phillips, 2007; Bruya, 2010). Moreover, this system acts in the "best interest" of the organism as a whole and therefore should be considered as part of the brain's "executive control" system (Ardila, 2008; Miller, 2008).

The environment is not always so predictable, however, and thus cannot be trusted to consistently provide us with stimulus-based cues for responding. Novel or unfamiliar circumstances do not possess the "triggers" to evoke effective stimulus-based behaviors. This issue likely generated considerable evolutionary pressure to develop a system of higher-order executive control over behavior. Our higher-order control system allows for novel problem-solving and provides flexibility for interacting with changing and unpredictable environments. This system allows us to develop adaptive responses in circumstances for which there are no predetermined or known solutions to problems. It facilitates problem-solving by requiring us to assess and discover the stimulus-based characteristics of the novel problem so that we may anticipate an adaptive solution (Badre, 2008; Somerville & Casey, 2010). The solution is developed through adapting a new motor sequence to manage the issue, which ultimately will lead to more refined, sophisticated, and eventually routine behaviors. This system allows us to establish new associations and behaviors that with appropriate repetition can become *overlearned,* routine or "automatic," and can share all of the advantages enjoyed by innate adaptive behaviors. In short, this system can generate adaptive procedural learning.

We need both systems to successfully adapt to the environment. A system based only upon routine, automatic behavior would allow no flexibility for adjusting to novelty, which is not only critical for learning, but psychosocial functioning as well. A system based only upon higher-order cognitive control would not allow us to automate new behaviors, causing us to endure an eternal "Groundhog Day" in which we would be left devoting precious cognitive resources to figuring out every circumstance as if it were completely novel. These two systems must co-exist and interact with each other; we cannot function with appropriate executive autonomy unless we have the ability to make responses to novel situations familiar and automatic. A dual-tiered system of behavioral control allows us to function autonomously in the absence of external strictures and support. As a result, psychopathology can be due to frontal or subcortical dysfunction, and these structures and functions are reciprocally related to environmental determinants of behavior. As we learned in our introductory psychology courses, psychopathology is not due to nature or nuture, it is due to both.

In addition to the frontal, basal ganglia, and cerebellar influences on behavior, we must also consider new perspectives on hemispheric functioning that also follow a novelty-routinization gradient (Goldberg, 2001). Instead of the inaccurate "verbal" versus "non-verbal" dichotomy of the left and right cerebral hemispheres (Macneilage, Rogers, & Vallortigara, 2009), it is important to recognize that the

right hemisphere largely manages novelty and the left hemisphere manages routine information (Podell, Lovell, & Goldberg, 2001). The left hemisphere's role in language thus actually represents a specialized instance of routinization related to the categorization inherent in language functions (Goldberg & Costa, 1981), but novel aspects of language, such as indirect or multiple meanings, metaphor, sarcasm, humor, idiom, and even complex syntax require right hemisphere functions (Bryan & Hale, 2001). This applies to visual perception as well, with novel faces processed by the right hemisphere, while well-known faces processed by the left (Hale & Fiorello, 2004).

*Implications for Neuropsychological Assessment and Intervention*

Understanding neuropsychopathology requires a comprehensive approach that considers the brain, behavior, and environment simultaneously in an attempt to determine an individual's developmental and adaptive status. A neuropsychological evaluation is in essence a special instance of adaptation within a novelty-familiarity principle. In real life, most situations require alternating episodes of automatic behaviors and higher-order control, as described above. This should represent a fundamental underlying principle for neuropsychological test interpretation as well. Essentially, the neuropsychologist must use the evaluation process to explore the anterior-posterior, left-right, and superior-inferior axes in an attempt to uncover the imbalance that results in maladaptive behavior pattern (Hale et al., 2009). Unfortunately, a detailed description of interpretive methodologies is beyond the scope of this paper. Aspects of this interpretive process have been described elsewhere (Hale & Fiorello, 2004; Koziol & Budding, 2011).

Neuropsychological assessment of cortico-basal ganglia and cortico-cerebellar circuits is essential practice for understanding neuropsychopathology, but the common finding of comorbidity among disorders may cause concern to readers. Although this topic requires a chapter of its own, co-morbidity is a special circumstance of interrelated symptoms due to progressive involvement of the various cortico-striatal circuits, as well as the principles of instrumental learning and classical conditioning mediated by cortico-striatal and cortico-cerebellar circuits. Conceptualizing brain functioning as requiring efficient learning interactions between cortex, basal ganglia, and cerebellum is essential for understanding typical behavior and adaptation. With this basic understanding, we can begin to understand features psychopathology and comorbidity in a pragmatic way, since each brain region contributes different learning characteristics and confers different regulatory characteristics on cognition, emotion, and behavior (Doya, 2000; Doya, 1999).

The dual-tiered model of brain function described in this chapter explains general adaptation, psychopathologies and their co-morbidities. This model has implications for the development of neuropsychological testing procedures, as well as implications for developing clinical interventions and treatment strategies. With this dual-tiered framework in mind, intervention would appear to be based on maximizing frontal-subcortical and left-right hemisphere influences on behavior so the child responds in an adaptive fashion depending on each set of environmental circumstances. The principles described herein suggest that too much higher order control, or too little, can lead to psychopathology (Hale et al., 2009). Similarly, an imbalance between cortical and subcortical influences on behavior can lead to maladaptive behavioral patterns in which novel problem solving predominates and does not allow for routinized behavior to occur (too much cortical influence), while too much routinized behavior does not allow for flexible, adaptive responding when new or incongruent information presented (too much subcortical influence) (Koziol & Budding, 2009).

In essence, appropriate intervention would be designed to maximize a child's ability to appropriately alternate between automatic behaviors and those that require higher-order control. Although psychotropic medication can used to target cortical and/or subcortical systems, there are other treatment options to consider. Cognitive-behavioral therapy techniques that examine faulty

executive control of behavior may be useful, and can help clients understand propensities to engage in disinhibited or restricted maladaptive behavioral repertoires, while "practicing" behaviors that lead to appropriate automaticity in routine conditions. Behavior management paradigms can be used to address the properties of the instrumental (basal ganglia) and procedural (cerebellar) learning systems previously described. Even techniques such as desensitization could help individuals regulate conditioned responding. As a result, combining cognitive, behavioral, and/or medication approaches may be optimal as this would ensure maladaptive conscious control and automatic behavior patterns are both addressed. What is critical is that psychosocial well-being requires learning adaptive patterns while reducing or extinguishing maladaptive ones in an attempt to achieve balance between the volitional and automatic systems.

*Conclusions and Future Directions*

Understanding neuropsychopathology requires recognition that traditional neuropsychological assessment has generally focused on higher-order cognitive control, and seldom included direct assessment of instrumental learning, conditioning, and the ability to develop automaticity. Better assessment strategies and tools are needed in order to address these functions so that our evaluations will enable us to better understand how children either succeed or fail in response to environmental demands. In essence, we need to move beyond simply trying to establish stable measures of psychological traits (Hale et al., 2009), and instead consider state measures that can examine cortico-basal ganglia and cortico-cerebellar circuit function. There are numerous experimental methodologies which assess the functions of the basal ganglia and cerebellum that can be applied for these clinical purposes (Koziol & Budding, 2009).

Conceptualizing function in this way would allow not only for more individualized assessment for understanding the continuum or dimensions of normal functioning and psychopathology, it would also offer increased options for developing interventions and more effectively measuring treatment efficacy. The lack of clear, neuroanatomically-based theoretical underpinnings guiding most interventions impedes our ability to fully assess, understand, and improve their effectiveness. To overcome this intervention quagmire, systematic research examining the vertical organization of the brain can lead to greater understanding of the dimensional approach to neuropsychopathological disorders, which will in turn lead to greater sensitivity and specificity of diagnostic measures, and targeted interventions that will ultimately lead to greater treatment efficacy.

References

Ackermann, H. (2008). Cerebellar contributions to speech production and speech perception: psycholinguistic and neurobiological perspectives. *Trends Neurosci, 31,* 265-272.

Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annu.Rev.Neurosci., 9,* 357-381.

Andreasen, N. C. & Pierson, R. (2008). The Role of the Cerebellum in Schizophrenia. *Biol.Psychiatry*.

Ardila, A. (2008). On the evolutionary origins of executive functions. *Brain Cogn, 68,* 92-99.

Badre, D. (2008). Cognitive control, hierarchy, and the rostro-caudal organization of the frontal lobes. *Trends in Cognitive Sciences, 12,* 193-200.

Bargh, J. A. (1997). The automaticity of everyday life. *The automaticity of everyday life, 10,* 1-61.

Bargh, J. A. & Chartrand, T. L. (1999). The unbearable automaticity of being. *American Psychologist, 54,* 462-479.

Bellebaum, C. & Daum, I. (2007). Cerebellar involvement in executive control. *Cerebellum., 6,* 184-192.

Blackford, J. U., Buckholtz, J. W., Avery, S. N., & Zald, D. H. (2010). A unique role for the human amygdala in novelty detection. *Neuroimage, 50,* 1188-1193.

Blumenfeld, H. (2002). *Neuroanatomy through clinical cases*. Sinauer Associates.

Boutsen, F. R. & Christman, S. S. (2002). Prosody in apraxia of speech. *Semin.Speech Lang, 23,* 245-256.

Bradshaw, J. L. (2001). *Developmental disorders of the frontostriatal system: Neuropsychological, neuropsychiatric and evolutionary perspectives*. Philadelphia: Taylor & Francis, Inc.

Bruya, B. (2010). *Effortless attention : a new perspective in the cognitive science of attention and action*. Cambridge, Mass.: The MIT Press.

Bryan, K. L. & Hale, J. B. (2001). Differential effects of left and right cerebral vascular accidents on language competency. *J Int.Neuropsychol.Soc., 7,* 655-664.

Cisek, P. & Kalaska, J. F. (2010). Neural mechanisms for interacting with a world full of action choices. *Annu.Rev Neurosci, 33,* 269-298.

Denckla, M. B. & Reiss, A. L. (1997). Prefrontal-subcortical circuits in developmental disorders. In N.A.Krasnegor, G. R. Lyon, & P. S. Goldman-Rakic (Eds.), *Development of the prefrontal cortex: Evolution, neurobiology, and behavior* (pp. 283-294). Baltimore: P. H. Brookes.

Doll, B. B. & Frank, M. J. (2009). The basal ganglia in reward and decision making: computational models and empirical studies. *Handbook of Reward and Decision Making,* 399.

Doya, K. (1999). What are the computations of the cerebellum, the basal ganglia and the cerebral cortex? *Neural Netw., 12,* 961-974.

Doya, K. (2000). Complementary roles of basal ganglia and cerebellum in learning and motor control. *Curr.Opin.Neurobiol., 10,* 732-739.

Frank, M. J. (2005). Dynamic dopamine modulation in the basal ganglia: a neurocomputational account of cognitive deficits in medicated and nonmedicated Parkinsonism. *J.Cogn Neurosci., 17,* 51-72.

Frank, M. J. (2006). Hold your horses: a dynamic computational role for the subthalamic nucleus in decision making. *Neural Netw., 19,* 1120-1136.

Goldberg, E. (2001). *The executive brain*. Oxford: Oxford University Press.

Goldberg, E. & Costa, L. D. (1981). Hemisphere differences in the acquisition and use of descriptive systems. *Brain and language, 14,* 144-173.

Hale, J. B. & Fiorello, C. A. (2004). *School neuropsychology: A practitioner's handbook*. New York: Guildford Press.

Hale, J. B., Reddy, L. A., Wilcox, G., McLaughlin, A., Hain, L., Stern, A. et al. (2009). Assessment and intervention for children with ADHD and other frontal-striatal circuit disorders. In D.C.Miller (Ed.),

*Best practices in school neuropsychology: Guidelines for effective practice, assessment and evidence-based interventions* (pp. 225-279). Hoboken,N.J.: John Wiley & Sons.

Heilman, K. M. & Rothi, L. J. G. (2003). Apraxia. In K.M.Heilman & E. Valenstein (Eds.), *Clinical Neuropsychology* (Fourth ed., pp. 215-235). New York: Oxford University Press.

Heilman, K. M., Valenstein, E., Rothi, L. J. G., & Watson, R. T. (2004). Intentional Motor Disorders and the Apraxias. *Neurology in Clinical Practice: Principles of diagnosis and management,* 117.

Heimer, L., Van Hoesen, G. W., Trimble, M., & Zahm, D. S. (2008). *Anatomy of Neuropsychiatry: The New Anatomy of the Basal Forebrain and its Implications for Neuropsychiatric Illness*. San Diego, CA: Academic Press.

Hikosaka, O. & Isoda, M. (2010). Switching from automatic to controlled behavior: cortico-basal ganglia mechanisms. *Trends in Cognitive Sciences, 14,* 154-161.

Hirata, K., Tanaka, H., Zeng, X. H., Hozumi, A., & Arai, M. (2006). The role of the basal ganglia and cerebellum in cognitive impairment: a study using event-related potentials. *Suppl Clin.Neurophysiol., 59,* 49-55.

Houk, J. C., Bastianen, C., Fansler, D., Fishbach, A., Fraser, D., Reber, P. J. et al. (2007). Action selection and refinement in subcortical loops through basal ganglia and cerebellum. *Philos.Trans.R.Soc.Lond B Biol.Sci., 362,* 1573-1583.

Houk, J. C. & Mugnaini, E. (2003). Cerebellum. In L.Squire, F. E. Bloom, S. K. McConnell, J. L. Roberts, N. C. Spitzer, & M. J. Zigmond (Eds.), *Fundamental Neuroscience* (pp. 841-872). San Diego: Academic Press.

Imamizu, H. & Kawato, M. (2009). Brain mechanisms for predictive control by switching internal models: implications for higher-order cognitive functions. *Psychol.Res, 73,* 527-544.

Ito, M. (2008). Control of mental activities by internal models in the cerebellum. *Nat.Rev.Neurosci., 9,* 304-313.

Koziol, L. F. & Budding, D. E. (2009). *Subcortical structures and cognition : Implications for neuropsychological assessment*. New York: Springer.

Koziol, L. F. & Budding, D. E. (2011). Pediatric neuropsychological testing: Theoretical models of test selection and interpretation. In A.S.Davis (Ed.), *Handbook of Pediatric Neuropsychology* (pp. 443-456). New York: Springer.

Koziol, L. F., Budding, D. E., & Chidekel, D. (2010). Adaptation, Expertise, and Giftedness: Towards an Understanding of Cortical, Subcortical, and Cerebellar Network Contributions. *The Cerebellum,* 1-31.

Koziol, L. F., Budding, D. E., & Chidekel, D. (2011). Sensory Integration, Sensory Processing, and Sensory Modulation Disorders: Putative Functional Neuroanatomic Underpinnings. *Cerebellum*.

Levy, F. (2010). Internalizing versus externalizing comorbidity: neural circuit hypothesis. *Australian and New Zealand Journal of Psychiatry, 44,* 399-409.

Lezak, M. D. & Loring, D. W. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Lichter, D. G. & Cummings, J. L. (2001). *Frontal-subcortical circuits in psychiatric and neurological disorders*. The Guilford Press.

Luria, A. R. (1973). The working brain (B. Haigh, trans.). *New York: Basic*.

Macneilage, P. F., Rogers, L. J., & Vallortigara, G. (2009). Origins of the left & right brain. *Sci.Am., 301,* 60-67.

Mega, M. S. & Cummings, J. L. (2001). Frontal subcortical circuits: anatomy and function. *The frontal lobes and neuropsychiatric illness.Washington, DC: American Psychiatric Publishing,* 15-32.

Miller, R. (2008). *A theory of the basal ganglia and their disorders*. Boca Raton: CRC Press.

Molinari, M., Restuccia, D., & Leggio, M. G. (2009). State estimation, response prediction, and cerebellar sensory processing for behavioral control. *Cerebellum., 8,* 399-402.

Nambu, A., Tokuno, H., Hamada, I., Kita, H., Imanishi, M., Akazawa, T. et al. (2000). Excitatory cortical inputs to pallidal neurons via the subthalamic nucleus in the monkey. *Journal of Neurophysiology, 84,* 289-300.

Njiokiktjien, C. (2010). Developmental dyspraxias: assessment and differential diagnosis. In D.Riva & C. Njiokiktjien (Eds.), *Brain lesion localization and developmental functions* (pp. 157-186). Montrouge, France: John Libbey Eurotext.

Panksepp, J., Moskal, J. R., Panksepp, J. B., & Kroes, R. A. (2002). Comparative approaches in evolutionary psychology: molecular neuroscience meets the mind. *Neuro.Endocrinol.Lett., 23 Suppl 4,* 105-115.

Park, J. W., Kim, Y. H., Jang, S. H., Chang, W. H., Park, C. H., & Kim, S. T. (2010). Dynamic changes in the cortico-subcortical network during early motor learning. *NeuroRehabilitation., 26,* 95-103.

Podell, K., Lovell, M., & Goldberg, E. (2001). Lateralization of frontal lobe functions. In S.P.Salloway, P. F. Malloy, & J. D. Duffy (Eds.), *The Frontal Lobes and Neuropsychiatric Illness* (pp. 83-100). Washington, D.C.: American Psychiatric Publishing.

Saling, L. L. & Phillips, J. G. (2007). Automatic behaviour: efficient not mindless. *Brain Res.Bull., 73,* 1-20.

Schmahmann, J. D. (2004). Disorders of the cerebellum: ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. *J.Neuropsychiatry Clin.Neurosci, 16,* 367-378.

Schmahmann, J. D. & Sherman, J. C. (1997). Cerebellar cognitive affective syndrome. *Int.Rev.Neurobiol., 41,* 433-440.

Schmahmann, J. D., Weilburg, J. B., & Sherman, J. C. (2007). The neuropsychiatry of the cerebellum - insights from the clinic. *Cerebellum., 6,* 254-267.

Somerville, L. H. & Casey, B. J. (2010). Developmental neurobiology of cognitive control and motivational systems. *Current opinion in neurobiology, 20,* 236-241.

STEINER, H. & TSENG, K. Y. (2010). *Handbook of basal ganglia structure and function*. Amsterdam: Elsevier/Academic Press.

Stocco, A., Lebiere, C., & Anderson, J. R. (2010). Conditional routing of information to the cortex: A model of the basal ganglia's role in cognitive coordination. *Psychological review, 117,* 541.

Stoodley, C. J. & Schmahmann, J. D. (2010). Evidence for topographic organization in the cerebellum of motor control versus cognitive and affective processing. *Cortex, 46,* 831-844.

Yin, H. H. & Knowlton, B. J. (2006). The role of the basal ganglia in habit formation. *Nature Reviews Neuroscience, 7,* 464-476.

Zald, D. H. & Andreotti, C. (2010). Neuropsychological Assessment of the Orbital and Ventromedial Prefrontal Cortex. *Neuropsychologia, 48,* 3377-3391.