Biological Systems and the Development of Self-Regulation: Integrating Behavior, Genetics, and Psychophysiology

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ABSTRACT: Self-regulation is the ability to control inner states or responses with respect to thoughts, emotions, attention, and performance. As such, it is a critical aspect of development and fundamental to personality and behavioral adjustment. In this review, we focus on attentional, cognitive, and emotional control as we discuss the genetic mechanisms and brain mechanisms that contribute to individual differences in self-regulation. We conclude with a discussion of the implications for deviations in the development of this complex construct and suggestions for future research.

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What explains the remarkable variation between children in how well they adapt to their ever changing environments? In part, the answer lies in *self-regulation*, a critical aspect of development in infancy, early childhood, and beyond. A set of developing regulatory processes appears to be fundamental to individual differences in personality development and behavioral adjustment[1–3] and includes biological components such as physiology, neurobiology, and genes, and situational components such as parenting, environment, and experience.[4,5] As such, self-regulation can be examined at many different levels and can have multiple definitions.[6] This necessarily makes self-regulation a complex construct and developmentalists have typically simplified the study of self-regulation by focusing only on one or two of these conceptual levels at a time, such as the regulation of emotion.[2,7]

There is general agreement, however, that self-regulation operates at the physiological, attentional, emotional, cognitive, and behavioral levels.[1,8,9] In this review, we define self-regulation as the ability to control inner states or responses with respect to thoughts, emotions, attention, and performance.[6] Thus, our conceptualization of self-regulation could be described as cognitive control and emotion control. Within this conceptualization, we highlight attentional control as the mechanism for early developing self-regulation in both the cognitive and emotional domains.[10–12] As such, we go beyond the typical focus on relationships between either cognitive functioning or attentional control and consequential emotion regulation[5,7] and provide a more dynamic view of self-regulatory processes.[11]

Our focus in this review is on the biological components of developing self-regulation, as the situational and contextual components have been reviewed elsewhere.[6,7] We begin by highlighting the psychobiological framework that we use in conceptualizing regulatory processes. Then we discuss biological mechanisms of self-regulation associated with the development of specific cognitive and emotion behaviors. Because of our focus on psychobiology, we next examine genetic and brain mechanisms of self-regulation processes by integrating the functions associated with central nervous system and autonomic nervous system networks that are prominent in attentional control. Our position in this review is that psychophysiological processes of attention, cognition, and emotion act as intermediaries between gene expression and complex psychological behaviors.[13] This position highlights our interests in individual differences in the development of self-regulation, as well as in the general maturation of self-regulatory processes. The individual differences framework encompasses not only wide-ranging boundaries of normal development of self-regulation, but also clinical implications for when the development of various components of self-regulation goes awry. Children who experience difficulties in the development of self-regulation skills may present with disruptive social behavior problems or other difficulties associated with peer interactions or school readiness.[1,7,8] Thus, we next include a brief section on clinical implications for deviations in development. We conclude with a summary of key directions for future research on the development of self-regulation.

Self-regulation includes a host of biological mechanisms, including serotonin and dopamine neurotransmitter system genes and central and peripheral nervous system connectivity and activation involving prefrontal cortical and limbic regions of the brain. As the methods for detecting reliable differences in children at the level of DNA and neural activity continue to advance, researchers who study the development of self-regulation will need to turn away from the current trend of examining simple and direct effects and turn toward tests of comprehensive theories of biology-environment interplay. We offer this

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review as a first step in that process by considering both genetic and psychophysiological aspects of self-regulatory behaviors in early development.

PSYCHOBIOLOGICAL FRAMEWORK FOR EMERGING SELF-REGULATION

We view self-regulation within a psychobiological theoretical framework, thus focusing on physiological and genetic, as well as behavioral, indices of cognition and emotion.

Development of Attention Regulatory Behaviors

With this psychobiological approach, we highlight the temperament-based attentional control associated with Posner's Executive Attention System and the frontal lobe architecture of the anterior cingulate cortex (ACC) as critical for development of self-regulation.[3,14,15] Temperament refers to biologically based individual differences in emotional reactivity and the emergence of regulation of that reactivity beginning late in the first year of life.[16] Rothbart et al[17,18] propose that early regulation of temperamental distress is facilitated by the development of the Executive Attention System and resultant improvements in attentional control. According to Rothbart and colleagues, attentional control is associated with mechanisms for resolving conflict among thoughts, feelings, and responses.[9] Thus, attentional control is important for the development of self-regulation,[12] and this may be especially true for children who are emotionally or behaviorally reactive, such as children who are behaviorally inhibited or aggressive.[1,19]

The Executive Attention System exhibits initial developmental changes around 10 months of age.[17,20,21] This is also the same time frame for initial developmental changes in cognitive control behaviors (withholding a dominant response in order to perform a nondominant response, such as searching for a toy in a new location after seeing it hidden there rather than looking back to the original hiding sight.[22,23] and emotion control or regulation strategies (such as self-comforting or self-distraction).[12,20,24,25] The proposal that attentional control may be associated with both cognitive control and emotion regulation is prominent in the developmental literature.[5,20,26–32] Despite all the speculation, however, there are no known studies designed to explore the interrelated development of the dynamic associations among attentional, cognitive, and emotion control. This dynamic relationship is portrayed in Figure 1. Although our focus here is on the critical influence of attentional control on the development of cognitive control and emotion control, it is likely that cognition and emotion likewise influence the development of attentional control to some extent.

After initial developmental change around 10 months, attentional control associated with the Executive Attention System then increases rapidly during the toddler and preschool years and is the basis of the temperament construct that Rothbart and colleagues call *effortful control*.[3,9,15,16,33,34] Effortful control refers to the child's volitional use of executive attention and involves the abilities of inhibitory control, detection of errors, and planfulness. For example, effortful control is involved when a child must wait before touching an attractive toy or when a child must whisper when something exciting is happening.[35] Thus, effortful control reflects the influence of temperament on behavior.[3] A series of longitudinal and cross-sectional studies have demonstrated initial development of effortful control around 27 to 30 months of age.[33,35,36] There appears to be much improvement in effortful control of behavior between the ages of 3 and 4 years of age,[15,37–39] with conspicuous improvements through age 7.[40,41]

Thus, controlled attentional abilities and resultant effortful control skills associated with the Executive Attention System demonstrate vast improvement from infancy through the end of early childhood. At the same time, stable individual differences emerge. For instance, by middle childhood, it is possible to predict a quarter of the variance in attention regulation from prior attention regulation, even when the data are based on different observers at each assessment.[42] Because of its stability and its involvement in the selection, coordination, and storage of information, effortful control may play a prominent role in the development of a broad range of behaviors and

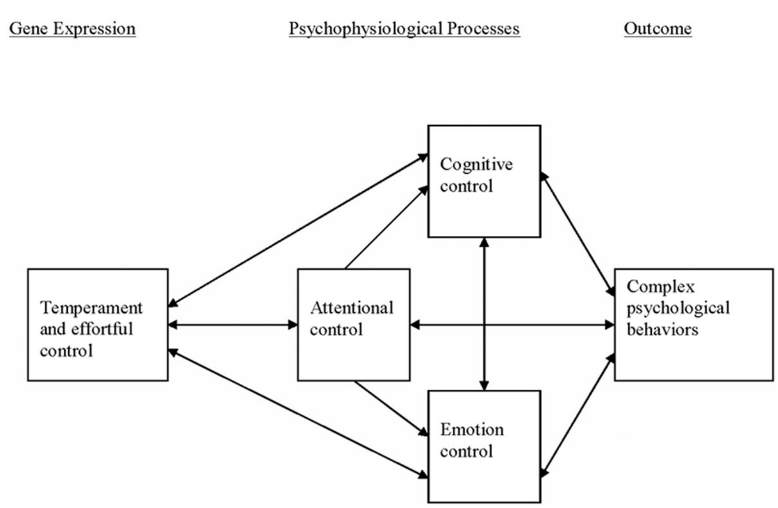

Figure 1. Dynamic interplay among behavior, genetics, and psychophysiology with respect to self-regulation.

cognitions, including personality and a number of psychopathologies.[3,43]

Development of Cognitive Regulatory Behaviors

We are very specific in the cognitive construct that we conceptualize as most associated with self-regulation and that construct is working memory.[10] In the conceptualization of working memory of Engle et al,[44] there is a limited-capacity, domain-free controlled attention component that is comparable to the construct of executive attention as defined in Posner's Executive Attention System. The attentional component is able to maintain short-term memory representations on-line in the presence of interference or response competition. Thus, this executive attention component is not needed for all cognitive processing, but is called into action in circumstances that require inhibition of prepotent responses, error monitoring and correction, and decision making and planning.[45,46] Engle and colleague refer to individual differences in executive attention as *working memory capacity*.[44,46] This capacity is associated with a wide variety of cognitive abilities.[44] For example, preschool children with high and low working memory capacity differ in performance on attentional control tasks[47] and may be at risk of attention deficit disorder.[45] Researchers have begun to demonstrate associations between attentional control characteristics and cognitive regulatory tasks involving working memory and inhibitory control in preschool children,[28,36,47–49] as well as in the neural network modeling of cognitive tasks in infants.[50] It is clear that from early in life, attentional control and working memory not only are coupled with each other, but also underlie many other aspects of cognitive performance associated with school readiness.[27,47]

As with other regulatory abilities, working memory and cognitive regulation demonstrate great changes during infancy and early childhood.[23,47,49,51–54] Cognitive regulatory tasks used in developmental research have known associations with frontal lobe functioning, perhaps part of the brain basis of regulatory behaviors. As infants and toddlers become preschoolers, stable individual difference in cognitive regulation emerge.[55]

Development of Emotion Regulatory Behaviors

Like working memory, emotion-related regulation appears to also be strongly associated with attentional control, and this type of regulation can occur before, during, or after the elicitation of emotion.[56] Regulatory aspects of temperament are driven by individual differences in arousal and reactivity.[15] The construct of effortful control, noted above, represents a behavioral system that emerges in the second year and allocates resources for the voluntary control of arousal and emotion. Rothbart et al[15] suggest that the development of executive attention might underlie the effortful control of emotion, evidenced in the finding that children who show more effortful control also tend to show less anger, fear, and discomfort. The developmental literature supports that association. This is especially true of the work of Kochanska and colleagues, who have proposed that effortful control is crucial to the development of a conscience.[35,38,57]

Just as attentional control and working memory display dramatic developments during infancy and early childhood, so does emotion regulation.[58–60] Developmental changes in emotion regulation are demonstrated as the infant progresses from almost total dependence on caregivers for regulation of emotion state to independent self-regulation of emotions.[58] According to Kopp and colleagues,[2,61,62] early emotion regulation is influenced mainly by innate physiological mechanisms. Beginning around 3 months of age, some voluntary control of arousal is evident, with more purposeful control evident by 12 months, when developing motor skills and communication behaviors allow for intentional interactions with caregivers. During the second year, infants begin to use language skills and better impulse control,[2,61] thus promoting the transition from passive to active methods of emotion regulation.[58] Kopp[2] considers this emotion self-control to fully emerge between 3 and 4 years of age. Rothbart et al[15] have suggested that the changes in self-control occurring between ages 3 and 4 years are related to the Executive Attention System.

It is worth pondering for a moment whether an articulated framework involving attention, cognition, and emotion is necessary, in contrast to a more parsimonious notion of global or general "self-control." As described above, nearly all children show dramatic improvements in regulation of attention, cognition, and emotion from infancy through early childhood. Furthermore, although individual differences are vast, these become fairly stable over time by the end of early childhood. Thus, it is possible to describe children as relatively more or less "regulated" relative to each other and to apply this label across many domains of their functioning. Although this approach to conceptualizing self-regulation is certainly useful, its value is largely descriptive. In our view, it is through the measurement of dynamic biobehavioral mechanisms that we will eventually identify precise mechanisms—mechanisms that probably differ in very important ways for different children, different outcomes, and at different points in development.

SELF-REGULATION AND GENETIC MECHANISMS

Individual differences in executive attention, working memory, and emotion—and the interconnections between them in a system of self-regulation—arise from complex transactions between genetic and nongenetic (environmental) influences. With respect to attention and effortful control, twin and adoption studies have shown the emergence of moderate to substantial heritable variance over early and middle childhood,[62–65] as well as in adulthood.[66] More recent research using a multi-informant behavioral ratings measure (teachers, testers, and observers) of attention span and task persistence suggests a shift in heritable variance from 3 to 8 years of age. Among preschoolers, heritability estimates tend to be modest or highly variable across measures[67,68] but may become more substantial and consistent by the time children complete the transition to formal schooling.[69] At the same time, these recent studies point to maternal warm supportive behavior as a critical part of the development of better attention span and regulation, even after genetic influences have been controlled statistically.

Research on the development of genetic influence on working memory mimics the pattern found for attention and effortful control, with modest and highly variable heritability estimates among younger children[70] and larger more consistent heritability estimates in samples of adolescents and adults.[71,72] That the development of heritability of attention and working memory parallel each other is not surprising given the close links between executive attention and working memory performance at the behavioral (described above) and neural (described below) levels.

Behavioral genetics studies also show moderate amounts of genetic variance in the development of individual differences in negative emotionality (e.g., anger, fear, sadness) throughout childhood, adolescence, and adulthood.[63,73–75] This genetic influence is seen even for forms of fear that are highly conditioned and context or stimulus dependent, such as the strength of fear conditioning underlying the formation of some phobias.[76] As we have noted above, the regulatory aspects of attention and working memory have been implicated in modulation of negative affect, implying separate but interconnected biological systems for affect and cognitive control. This can be seen at the behavioral genetic level of analysis, demonstrated as independent genetic influences for anger versus attention in their links with child conduct problems.[77]

Although behavioral genetic studies are useful for delineating the likelihood of genetic effects, what is needed are studies that identify specific chromosome regions, genes, and single nucleotide polymorphisms (SNPs) that account for these genetic effects. In this regard, much of the research on attention regulation and working memory performance points to polymorphisms in genes involved in the production and utilization of the neurotransmitter dopamine. The most promising candidate genes and regions— based largely on studies of attention-deficit/hyperactivity disorder—include dopamine receptors 4 and 5 as well as a region of the dopamine transporter gene, although the effect sizes are small and findings mixed.[78] Variations in the structure of these genes have been associated with differences in levels of dopamine in the brain. Dopamine operates in many parts of the brain, but of particular relevance to the current review is its role in the prefrontal and frontal cortex. Variation in *DRD4* and *COMT* (a gene involved in metabolizing dopamine) is implicated in better attentional control and working memory performance, as well as stronger neural activation in these frontal regions.[79,80] In addition, although it has been studied in regards to dementia in adulthood, the *APOE* gene (apolipoprotein E) has been implicated in typical variation in adults' working memory performance as well[81,82] and may emerge as a gene that explains variation in working memory performance even in childhood.

There also is a growing literature on genes for negative affect—anger and fear in particular—with *DRD4* implicated in several studies of infants' negative emotional reactivity.[83,84] However, most of the evidence points to a critical role of serotonin neurotransmitter genes. In particular, a transporter gene (*5-HTTLPR*) and a gene involved in the production of an enzyme that constrains serotonin production (*TPH*) are associated with individual differences in anger, fear, anxiety, depression, and trait neuroticism.[85–88] Furthermore, the transporter gene has been implicated in differences in activity in the circuits linking cingulate cortex and the amygdala, the location in the brain where emotions and control of emotions occur.[89]

Although the molecular genetic research on attention, working memory, and emotion has made great strides in the past decade, there are a number of caveats to bear in mind. Often the findings are equivocal, the effects sizes are modest, and very little research has involved children or used longitudinal designs. This is a consequence of studying complex, interacting sets of multiple genetic and nongenetic influences that are involved in the development of an integrated system of self-regulation. In addition, there is an ever-present need for further refinement of methodology, from the level of behavioral assessment to the level of gene structure and function.

SELF-REGULATION AND BRAIN MECHANISMS

At a less molecular level of analysis, recent work in the neuropsychological and psychophysiological literatures has provided the impetus for attentional control as the catalyst for self-regulation. In this section, we note the developmental work on attentional control that has focused on brain imaging measures of the central nervous system, as well as the developmental work that has focused on cardiac measures of autonomic nervous system indices of attentional control. The brain imaging measures tend to conceptualize the ACC as the foundation of attentional control, self-regulation, and autonomic modulation, whereas the cardiac measures focus mainly on the nucleus ambiguus as a key component of attention and self-regulation. After briefly reviewing these literatures, we make note of research that is beginning to integrate these two literatures by highlighting a model that incorporates both of these regulatory systems.

Executive Attention System and the Anterior Cingulate Cortex

Posner and colleagues[90] have proposed that the attentional skills associated with the Executive Attention System and ACC in the frontal cortex serve to regulate both cognitive and emotional processing. The ACC is viewed as having two major sections that process cognitive and emotional information separately, as well as being a source of autonomic nervous system modulation.[91,92] The cognitive section has interconnections with the prefrontal cortex, parietal cortex, and premotor and supplementary motor areas. This portion of the ACC is activated by tasks that involve choice selection from conflicting information, which includes many target detection and working memory tasks.[90,93–95] The emotion section has interconnections with the orbitofrontal cortex, amygdala, and hippocampus, among other brain areas. This portion of the ACC is activated by affect-related tasks, such as the emotional-Stroop[90] and the classic odd-ball task using aversive photos that vary in emotional valence.[96,97] The emotional-Stroop is a variation of the classic color-word Stroop task that is used to assess inhibitory control. In the classic version of the task, words that are the names of colors are printed in incongruent colors of ink. The task is to name the color of the ink, ignoring the actual word. This requires much effort because proficient readers tend to focus on the word, not the color of the ink. The emotional-Stroop uses emotion-laden words, rather than words that are the names of colors. The classic odd-ball task presents an infrequent stimulus, such as a square, among a frequently used stimulus, such as a circle. The task is to count the squares. Aversive photos can be interspersed throughout the stimulus set. Past reports demonstrated that there is suppression of the affective section during cognitive processing and suppression of the cognitive subdivision during affective processing. However, recent studies of adults indicate some level of interaction between the cognition and affective sections of the ACC on Stroop-like or similar conflict tasks.[90,93]

The neuropsychological work involving examination of the ACC is accomplished with the functional magnetic resonance imaging (fMRI) brain imaging technique on adult research participants[90] or children in middle childhood.[94] The use of fMRI for research purposes with very young children is difficult, however, because the demands of the testing situation require no movement for long periods of time. Brain electrical activity recorded from the scalp is more conducive to brain imaging research with infants and children.[98]

In developmental research, activity of the ACC is typically inferred using the brain electrical activity technique of event-related potentials (ERPs). ERPs are produced when brain electrical activity is recorded during repeated stimuli presentations. They represent time-locked electrical signals whose waveforms are analyzed for amplitude and latency of wave deflection from the onset of the stimulus.[99] Researchers typically interpret deflections over the medial frontal or frontal midline scalp locations at a specific latency (which varies with development) as reflective of activity in the ACC and self-regulatory mechanisms.[100,101] For example, during infancy, there is an ERP component called the Nc (negative central, latency = 700 ms after stimulus onset) at frontal and central scalp electrodes that increases in amplitude between 4 and 7.5 months during the process of sustained attention.[102] This developmental pattern parallels gains in initial development of the Executive Attention System noted by Rothbart et al[18] Spatial components analysis of infant ERPs locates the cortical source of the Nc at the prefrontal cortex and ACC.[102,103]

Another physiological measure of brain electrical activity is the electroencephalogram (EEG). The EEG signal is continuous and spontaneous but context related, meaning that the signal generated during quiet rest is different from the signal generated during mental activity. The EEG is the spontaneous background signal from which ERPs are extracted. Differences in EEG activity between quiet rest and presentation of stimuli or tasks are assumed to be an indication of cortical functioning at underlying cortical areas. During adult cognitive processing, executive function or cognitive control tasks are most likely to be associated with baseline-to-task changes at frontal scalp electrodes, so that task performance can be tied to the specific patterns of EEG change.[104] This also is true for research with infants and very young children. Only infants with high performance on a cognitive control task exhibit this typical pattern of changes in frontal EEG from baseline to task. Infants with low performance do not demonstrate this pattern.[105] There are similar frontal EEG findings with preschool children.[49] When using EEG, researchers typically are not more specific than global cortical locations when interpreting this form of brain electrical activity during cognitive processing. However, it may be that the frontal EEG activation associated with working memory and target detection tasks could be associated with activity in the ACC.

During emotion processing, greater EEG activation at left frontal scalp locations is typically associated with approach-related emotions and behaviors (reflecting motivation to engage or explore), whereas the same pattern at right frontal locations is typically associated with withdrawal-related emotions and behaviors (reflecting motivation to avoid). Individual differences in emotion control may be inferred from these frontal asymmetry patterns.[106,107] Greater right frontal activation is associated with difficulty in regulating negative arousal, biases toward the experience and display of negative emotion, and withdrawal in the face of threat.[99] Frontal EEG asymmetries may reflect forebrain and limbic sensitivity specific to the amygdala.[19,108] The amygdala is part the emotion network of the Executive Attention System and projects to the ACC.

Vagal Tone and the Nucleus Ambiguus

Just as brain imaging techniques are used to examine attentional control with respect to the central nervous system, cardiac measures allow peripheral measurement of attentional control via the parasympathetic and sympathetic branches of the autonomic nervous system. Porges[109–111] has proposed that the functioning of the parasympathetic branch is critical to both attentional and emotional regulation. Specifically for attentional regulation, there are two distinct patterns of cardiac activity, with phasic heart rate (HR) associated with reactive attention and changes in the variability of the HR (HRV) associated with sustained attention. According to Porges' Polyvagal Theory,[109–111] cardiac vagal tone, a component of parasympathetic control, can be used as an index of physiological self-regulation. Vagal tone can be quantified in at least three ways: as HRV, as the amplitude of respiratory sinus arrhythmia (RSA), or as Porges' specific measure of vagal efferents from nucleus ambiguus (V_{na}) in the medulla. Porges' method applies a time-series analysis to the HR rate pattern to remove rhythms that are slower than those associated with respiration. The result is a measure of variability in the frequency range of spontaneous breathing, a frequency range that varies systematically with development.

V_{na} is associated with the balance between internal homeostasis and adaptation to external demands in the environment.[111,112] The vagus nerve to the heart from the nucleus ambiguus serves an inhibitory function of slowing HR and modulating the effects on the heart of the sympathetic branch of the autonomic nervous system. With the introduction of an external demand, the vagal efferents quickly withdraw or suppress vagal tone (termed withdrawal of the "vagal brake" by Porges[112]) and allow the sympathetic nervous system to increase the HR—an essential step for cognitive or emotional responding.[4] Thus, cardiac vagal tone can be conceptualized as a measure of the efficiency of central and autonomic neural feedback mechanisms,[113] whereby baseline measures are indicative of response potential. As such, higher resting baseline measures of RSA are associated with more efficient attentional processing[114–117] and with more reactive emotional responding.[118] As might be expected, higher levels of baseline RSA, or vagal tone, are associated with the ability to suppress vagal tone during cognitively or emotionally challenging circumstances.[118,119]

Assessing HR is a classic method for measuring attentional control in infants and young children, and in this tradition Richards and Casey[120] have highlighted HR-defined phases of attention. When orienting to a stimulus, there is a large deceleration in HR associated with the orienting reflex. Following this is a brief period of sustained attention involving voluntary, child-controlled information processing during which the HR remains at a slower level and HRV decreases.[120,121] During the effortful sustained attention associated with this decrease in HR, infants and young children cannot be distracted from a stimulus in the center of their field of vision by a stimulus in their peripheral field of vision. As HR returns to prestimulus levels, children may appear to be processing information because they are still looking at a central stimulus target, but they are easily distracted with stimuli at the periphery. Richards and Hunter[122] have speculated that the neural control of HR associated with sustained attention originates from a cardioinhibitory center located in the frontal cortex. We have already noted work from Richards indicating that the ACC may be the part of the brain system associated with HR-defined effortful, controlled attention during infancy.[103,121] Recent fMRI work with adults also has highlighted ACC in regulation of HR during effortful cognitive processing.[91,92]

Measures of autonomic nervous system activity during cognitive processing are widely used in developmental studies. Infants who exhibit decreases in V_{na} during stimulus presentation will habituate more quickly (i.e., efficiently) than infants who do not decrease V_{na} during information processing.[4] For infants and young children alike, changes in HR from baseline to task are associated with better performance on working memory tasks (Bell MA. Individual differences in spatial working memory at 8 months: contributions of electrophysiology and temperament. Under review.).[49] Studies of working memory in adults also show associations between HR/HRV and working memory performance.[114] These findings suggest a link between autonomic nervous system functioning and prefrontal cortical activity.

Turning again to emotion, measures of HRV, RSA, and V_{na} have been linked to emotional reactivity and regulation. Infants with higher HRV are more emotionally expressive and reactive.[24,118,119,124–126] This reactivity typically produces distress and irritability. As regulatory abilities develop, perhaps due to development of the Executive Attention System, the reactivity can lead to concentration when interest is paramount or to more expressive reactivity when other situations take precedent.[20,124] Thus, by middle childhood, V_{na} may be associated even with highly complex self-regulatory skills such as empathy and other aspects of social competence.[127,128] It appears that HRV may be associated with coping behaviors involving attentional control during both infancy and early childhood.[118,129,130] Thus, individual differences in attention, cognition, and the regulation of emotion are correlated with autonomic activity.[20]

Integrative Model of Central Nervous System

As is evident above, there is a large amount of conceptual overlap, as well as duplication of research findings, between studies based on the Executive Attention System proposed by Posner and colleagues and those based on Porges' conceptualization of vagal tone. As a result of this work and research based on other functional networks in the central nervous system, Thayer and Lane[113] have proposed a model whereby a network of central nervous system structures associated with behavior and regulation work together to modulate psychophysiological functioning during cognition, emotion, and attention. Thus, the core brain networks underlying cognitive, emotional, and physiological processes may be one single network.[131] This neurovisceral integration model takes into account recent reports that cognitive tasks that involve response conflict evoke autonomic changes, as well as activate the ACC. The model also is supported by findings that pyramidal neurons of the ACC project directly to subcortical brain areas associated with autonomic control.[91]

Researchers working with adult participants have used fMRI to demonstrate correlations between activity in the ACC and cardiovascular measures.[91,132] There is some speculation that the ACC is the origin for descending efferent commands for cardiovascular functioning in response to environmental demands associated with cognitive and emotional challenges. Likewise, the ACC may be the location where ascending afferent information gets integrated from peripheral autonomic activity during cognitive and emotional events.[132] As noted by Critchley and colleagues,[91] there is a long history of evidence demonstrating the role of the ACC in autonomic nervous system control, but this past work has been overlooked in recent discussions of the ACC.

The integration of multiple systems into a neurovisceral model allows the conceptualization of self-regulation as a unitary construct with multiple levels, rather than as a construct with multiple definitions. As we begin to consider the interconnections among physiological, attentional, cognitive, and emotional regulation, we can begin to examine a more dynamic view of normal development of self-regulation. We also can begin to understand more fully the behavioral, genetic, and psychophysiological implications for deviations in this developmental progression.

One of the greatest challenges to understanding individual differences in self-regulation will be distinguishing between variation arising from universal mechanisms versus multiple qualitatively distinct mechanisms. Nearly all the research and theory on biological influences on regulation either assumes or asserts that the relevant processes operate in more or less the same way for all children. This assumption is rarely tested, yet it is just as plausible (and testable) to propose that individual differences in self-regulation stem from heterogeneous processes, operating in distinctive ways for different subgroups of individuals. If true, the real task for developmental scientists will lie in the identification of which subgroups of children show which biobehavioral self-regulation processes. For example, control of attention may powerfully drive emotion control for some, whereas cognitive control may be the essential causal factor driving emotion control for others. Thus, future theoretical and empirical endeavors will need to address not only the *dynamics* of biobehavioral self-regulation, but the *heterogeneity* of these dynamic processes.

CLINICAL IMPLICATIONS FOR DEVIATIONS IN THE DEVELOPMENT OF SELF-REGULATION

A changing capacity to exercise cognitive control of thoughts, emotions, and behaviors is one of the most profound changes from infancy through early childhood. For a healthy child in a supportive home environment, these abilities develop rapidly into a complex and adaptive system of self-regulation that he or she can take with him or her from one environment to another. For other children, however, limitations in or constraints to self-regulation loom as key factors in the development of a wide range of emotional and behavioral problems.

The development of early self-regulatory skills has implications for adjustment in many areas of functioning. For example, self-regulation is a critical aspect of school readiness,[27] as well as significant for later school adjustment and achievement.[28,133] Understanding self-regulatory processes in typically developing infants and young children is critical because it will allow the generation of hypotheses about the foundations for the development of extremes in self-regulation and associated complexities in cognitive processing.[134] For example, not much attention has been given to the *development* of the cognitive control ability of working memory, despite evidence that knowledge about the development of this self-regulatory ability is crucial for understanding academic performance. For instance, in one study of preschool children, working memory predicted emerging mathematic skills.[135] Likewise in another study, children with poor working memory performance at age 5 scored poorly on reading assessments at age 8.[136] In still another study of 7-year-old children, working memory was associated with English and mathematics achievement.[137] Clearly, there is a need to examine problems with the development of this regulatory ability.

Gathercole and Alloway[138] have proposed a method for diagnosing working memory impairments, as well as techniques to support learning in children with these impairments. Working memory is impaired if a child falls 1 SD below the mean on typical forwards and backwards digit span tasks or a standardized battery, such as the Working Memory Test Battery for Children.[139] Children with working memory deficits may exhibit three characteristic problems in the classroom. They may forget the teacher's instructions, they may fail to keep their place in a complex task, and they may fail to simultaneously process and store information. Gathercole and Alloway also offer suggestions for enhancing learning in children with these classroom problems. For example, frequent repetition of instructions may assist a child in remembering the task at hand. Teachers might also ask the child to repeat back the instructions. As of now, there is no accepted method of directly remediating working memory, so supporting learning in the classroom by a simple modification of teaching techniques should help minimize problems that will result form working memory deficits.[138]

Another deficit in self-regulation that results in problems in the classroom is attention-deficit/hyperactivity disorder (ADHD). Recent proposals in the developmental literature include the assertion that the predominantly inattentive type of ADHD (without hyperactivity) is the result of a problem in the cognitive control of working memory.[45,138] ADHD might be the result of the child's inability to hold information active in memory and use that information to guide behavior.[45,138,140] The neural systems implicated in self-regulatory problems associated with ADHD may be involved in *both* cognitive and emotional control.[141] Because of the mutual influence of cognitive control and affective control in very early development, early temperament may yield predispositions to difficulty in either cognitive or emotion control, and, thus, different types of temperamental tendencies may lead to the development of ADHD.[141]

Early temperamental predispositions and resulting difficulties in self-regulation are implicated in other behavior difficulties as well. For example, behavioral inhibition in young children is a temperament trait characterized by wariness to the unfamiliar.[142] Behavioral inhibition is associated with social withdrawal or extreme shyness, is relatively stable across infancy and childhood,[143] and has been associated with anxiety disorders in adulthood.[144,145] Difficulty with attentional regulation, high resting heart rate (HR), and right frontal electroencephalogram (EEG) activation patterns indicative of withdrawal-type emotions are examples of regulatory difficulties experienced by inhibited children.[19] Children with disruptive, aggressive behavior problems likewise may exhibit problems in physiological regulation. Disruptive toddlers exhibit less of a decrease in respiratory sinus arrhythmia (RSA) during challenging tasks than children with no behavior problems.[146] More importantly, children with little decrease in RSA as toddlers continue to display disruptive behavior problems as preschoolers, even if they are able to suppress RSA during a challenge as preschoolers, indicating that early physiological regulation has far-reaching effects on development.[8]

What does clinical science have to gain from incorporating a biobehavioral perspective of self-regulation into its work with behaviorally, emotionally, and cognitively disordered children? The payoff is in the great potential of the methods and theories we have reviewed for identifying articulated and precise mechanisms in the brain—defined mechanisms that allow clinicians to go beyond general notions of "capacity for self-control." For example, clinical scientists and clinicians want to know whether children show improvements following treatment. Typically, this question is answered by examining change on the outcome of interest for the average or typical child. However, within any population of children with a particular disorder, there usually is wide variation in how much progress those children show following intervention. With more precisely specified mechanisms in place, changes in mediating biological mechanisms can be examined as well, in addition to exploring potentially distinct patterns of change across children and multiple treatment options. Thus, it may be possible one day to see which dynamic biobehavioral processes show the greatest improvements for specific treatments and specific subgroups of children. Ultimately, this precision will allow for more tailor-made treatments that will be most effective for identifiable subgroups of children.

FUTURE RESEARCH

Our goal in this review has been to demonstrate that the development of self-regulation is complex and includes a host of biological mechanisms, including serotonin and dopamine neurotransmitter system genes, central and peripheral nervous system connectivity, and activation involving prefrontal cortical and limbic regions of the brain. Although there is great interest in the construct of self-regulation,[6] much of the current research has failed to examine the dynamic interplay among these different levels of analysis, focusing instead on simple relationships between factors. Therefore, we offer several suggestions for future research.

First and foremost, the dynamic processes associated with self-regulation development should be the focus in future work.[147] Although a similar argument could be made for any aspect of development, we have demonstrated in this review that the study of biological influences may be especially critical to the understanding of self-regulation. The examination of dynamic biological processes of self-regulation will require a combination of short-term and long-term longitudinal studies, as well as dynamical approaches applied to the analysis of real-time information processing and behavior at various points in development. Such approaches are most readily applied in research on psychophysiology and behavior and could be conducted within behavioral genetic designs.

Second, much of the work on biological influences on self-regulation focuses exclusively on the relationships between attentional control and emotion regulation. However, because cognitive and emotion processes are dynamically linked, the study of self-regulation is best conceptualized by work that examines relationships between cognition and emotion with respect to attentional control.[10,11] For example, this could be accomplished with the inclusion of behavioral measures of working memory within studies of attention and emotion—although there are other cognitive processes that also would be relevant, such as conflict monitoring.

Third, although we did not focus in this review on situational and socialization influences on the development of self-regulation, contextual factors cannot be ignored. The caregiving environment in particular has a major impact on the development of self-regulation in childhood and should be considered in any study of developing regulatory abilities.[58,147] Because these socializing influences may have their most important influence as they operate and co-occur in real time with child behavior, methodologies that incorporate direct behavioral observations of caregiver-child transactions, as well as the more standard questionnaire and interview approaches, will need to be used.

Finally, recent work by Rothbart and colleagues and Posner suggests that the Executive Attention System, so critical to burgeoning self-regulatory abilities, can benefit from specific training activities that result in changes in brain electrophysiology.[148] Self-regulation is crucial for school readiness and learning,[27] and these new findings clearly suggest that basic biological mechanisms associated with the effortful control of attention are modifiable—a long-held contention in theories of self-regulation, but one that rarely is demonstrated. This exciting finding represents the type of work that can be done when a more dynamic approach that is sensitive to the importance of the environment is used to conceptualize the development of self-regulation.

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