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Executive Function and Psychopathology: A Neurodevelopmental Perspective

Philip David Zelazo

Institute of Child Development, University of Minnesota, Minneapolis, Minnesota 55455-0345, USA; email: zelazo@umn.edu

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Abstract

Executive function (EF) skills are neurocognitive skills that support the reflective, top-down coordination and control of other brain functions, and there is neural and behavioral evidence for a continuum from more “cool” EF skills activated in emotionally neutral contexts to more “hot” EF skills needed for the reversal of motivationally significant tendencies. Difficulties in EF are transdiagnostic indicators of atypical development. A neurodevelopmental model traces the pathway from adverse childhood experiences and stress to disruption of the development of neural systems supporting reflection and EF skills to an increased risk for general features of psychopathology. Research indicates that EF skills can be cultivated through scaffolded training and are a promising target for therapeutic and preventive intervention. Intervention efficacy can be enhanced by mitigating disruptive bottom-up influences such as stress, training both hot and cool EF skills, and adding a reflective, metacognitive component to promote far transfer of trained skills.

Contents

INTRODUCTION

Executive function (EF) skills are a set of neurocognitive skills that support the conscious, top-down control of thought, action, and emotion; are necessary for deliberate reasoning, intentional action, emotion regulation, and complex social functioning; and allow for self-regulated learning and adaptation to changing circumstances (Diamond 2013, Zelazo 2015). Early-appearing difficulties with EF are a prominent feature of a wide range of clinical conditions with childhood or youth onset, including learning disabilities (e.g., Toll et al. 2011), attention-deficit/hyperactivity disorder (ADHD) (e.g., Petrovic & Castellanos 2016), conduct disorder (CD) (e.g., Rubia 2011), autism spectrum disorder (ASD) (e.g., O'Hearn et al. 2008), obsessive–compulsive disorder (OCD) (e.g., Pietrefesa & Evans 2007), depression (e.g., Nelson et al. 2018), and anxiety (e.g., Shi et al. 2019). The ubiquity of EF difficulties across disorders suggests that the disruption of EF development may be a common consequence of many different kinds of developmental perturbation (e.g., genetic/environmental/epigenetic, cognitive/emotional/social), although different types of perturbation may lead to different clusters of symptoms, and different aspects of EF may be implicated in different disorders or within a single disorder. For this reason, the presence of EF difficulties can usefully be considered a transdiagnostic indicator of atypical development in general (e.g., Beauchaine & Cicchetti 2019, Sonuga-Barke et al. 2016).

This article addresses why EF skills play such a central role in the etiology of psychopathology. Dimensional approaches to the structure of psychopathology (e.g., Krueger 1999) have found considerable support for a bifactor model—a hierarchical model consisting of a general factor (p), which accounts for substantial (>50%) variance among symptoms and reflects impairments common across clinical categories, and at least two lower-order factors, such as internalizing and externalizing (e.g., Caspi et al. 2014, Lahey et al. 2017). The general p factor accounts for psychopathological comorbidity from early childhood into adolescence (e.g., Martel et al. 2017), and there is evidence that it is associated with high levels of disinhibition/impulsivity, delay discounting, neuroticism, and hopelessness and with low levels of response inhibition, performance IQ, and agreeableness (Castellanos-Ryan et al. 2016). Results from longitudinal research indicate stability of the p factor between ages 7 and 15 years (Murray et al. 2016) as well as both the strengthening of the general p factor (increasing comorbidity) and "p differentiation," suggesting a general risk that develops into more specific forms of psychopathology, between 2 and 14 years (McElroy et al. 2018).

From the perspective of developmental psychopathology (e.g., Cicchetti 1984), which takes a developmental systems view (e.g., Bronfenbrenner 1979, Gottlieb 1992) of the etiology and life course of atypical behavior, a wide range of variables and their interactions influence biological and psychological development and can result in psychopathology. Adversity experienced in childhood is a well-established risk factor for both internalizing problems (e.g., Hoppen & Chalder 2018) and externalizing problems (e.g., Humphreys et al. 2019), and evidence suggests that adversity is associated with a general, nonspecific risk for psychopathology (e.g., Keyes et al. 2012). Moreover, in a cross-sectional study with 2,395 children aged 6–12 years, performance on a battery of EF measures was associated with risk for a latent general psychopathology factor but not specific factors (Martel et al. 2017).

These findings suggest a developmental pathway that leads from (*a*) adverse childhood experiences (ACEs) and other sources of stress to (*b*) the disruption of the development of neural systems supporting EF skills and then to (*c*) an increased risk for general psychopathology, including transdiagnostic features of a wide range of clinical conditions (cf. McLaughlin 2016). The role of EF difficulties in this developmental pathway can be understood as a consequence of (*a*) the fundamental role that EF skills play in learning and adaptation across social and nonsocial contexts, (*b*) the relative plasticity of EF skills over an extended period of time (i.e., from infancy into early adulthood, with periods of greater plasticity occurring in early childhood and the transition to adolescence), and (*c*) the hierarchical nature of both EF skills and the neural systems that support them.

EXECUTIVE FUNCTION SKILLS

Historically, the construct of EF was derived from neuropsychological observations of the consequences of damage to the prefrontal cortex (PFC) (e.g., Luria 1966). Patients with damage to the PFC often show intact basic cognitive skills (e.g., memory, language) together with difficulty regulating those basic skills in a goal-directed, contextually appropriate way. For example, the neurologist Lhermitte (1983) noted that patients with lesions to the PFC may become stimulus bound and respond automatically to objects in a stereotypical fashion—they exhibit utilization behavior. Lhermitte described a patient who had been a nurse before suffering damage to the PFC. During an office interview, Lhermitte displayed a number of medical instruments, such as a sphygmomanometer, a tongue depressor, and a syringe. The patient proceeded to use the instruments on Dr. Lhermitte, going so far as to administer a gluteus maximus injection. Children with ADHD also exhibit high levels of utilization behavior (Archibald et al. 2005).

An important historical influence on current thinking about EF comes from the work of Vygotsky and Luria during the first half of the 20th century. Their research on the self-regulatory role of language in controlling behavior provided a foundation for later work on the importance of rule use (self-directed speech) for EF (e.g., Bunge & Wallis 2008, Zelazo et al. 2003). Luria (1966) also characterized the hierarchical nature of brain function; in his model, the PFC was at the highest level in the hierarchy, exerting top-down control over other brain regions, but also was influenced by these other regions in a reciprocal, bidirectional way. Subsequent research has supported Luria's hierarchical conceptualization and expanded it to include a characterization of hierarchical structure within the PFC. According to several complementary accounts, higher levels in the hierarchy of PFC regions involve more abstract representations, more complex rules, or

NEURAL ACTIVITY ASSOCIATED WITH EXECUTIVE FUNCTION SKILLS

In a neuroimaging study with a sample of healthy adults, researchers used a single paradigm with parametric variations to tax working memory, inhibitory control, and cognitive flexibility (Lemire-Rodger et al. 2019). Results indicated that working memory was more associated with activity in the dorsolateral prefrontal cortex (PFC), lateral parietal cortex, and bilateral insula; inhibitory control was more associated with the right lateral and superior medial PFC, bilateral inferior parietal lobules, and right middle and inferior temporal cortex; and cognitive flexibility was more associated with bilateral activity in the medial PFC, posterior cingulate cortex, precuneus, left inferior parietal lobule, lateral temporal cortex, and right thalamus.

both (e.g., Badre & D'Esposito 2007, Bunge & Zelazo 2006, Christoff & Gabrieli 2000, Munakata et al. 2012). It should be noted, however, that although various PFC regions play key roles in EF skills, they play these roles only as parts of more complex networks (and networks of networks) that also involve regions outside the PFC—including the targets of top-down modulation, such as the striatum, the amygdala, and other parts of the limbic system (e.g., Niendam et al. 2012).

Today, EF skills are known to depend on increasingly well-understood neural circuits involving brain regions in the PFC and other areas (e.g., Cole et al. 2013, Duncan 2013), and they are typically measured behaviorally as three skills: inhibitory control, working memory, and cognitive flexibility (Miyake et al. 2000). Inhibitory control involves deliberately suppressing attention (or other responses) to something (e.g., ignoring a distraction or stopping an impulsive utterance). Working memory involves keeping information in mind and, usually, manipulating it in some way (e.g., keeping two numbers in mind and subtracting one from the other). Cognitive flexibility involves thinking about a single stimulus in multiple ways—for example, when considering someone else's perspective on a situation. Recent neuroimaging results reveal that these three neurocognitive skills activate partially overlapping regions of the brain, with common areas of activation across tasks that include frontoparietal control and dorsal attention networks (e.g., Cole et al. 2013, Duncan 2013) (see the sidebar titled Neural Activity Associated with Executive Function Skills). These networks develop through differentiation into adulthood, showing changes in between-network connectivity, depending on the type of network (Gu et al. 2015). More specialized, lower-order networks (e.g., sensorimotor networks) show decreases in between-network connectivity with age, whereas higher-order networks involving the PFC show increases.

There is also considerable behavioral and neural evidence that EF skills vary along a continuum from "hot EF" to "cool EF" (Zelazo & Müller 2002). Whereas cool EF refers to EF skills assessed in relatively emotionally neutral contexts and relies more on neural networks involving lateral parts of the PFC, hot EF refers to EF skills that are needed in situations that are motivationally significant and relies more on neural networks involving ventral and medial parts of the PFC. Lesion studies, neuroimaging studies, and research using transcranial direct stimulation point to the importance of the hot–cool continuum in EF (e.g., Bechara et al. 1994, Fonseca et al. 2012, Manes et al. 2002, Nejati et al. 2018).

As typically measured (i.e., using relatively arbitrary or decontextualized tasks in a laboratory or clinic), inhibitory control, working memory, and cognitive flexibility can all be considered aspects of cool EF. An example is the dimensional change card sort (DCCS) (see the sidebar titled The Dimensional Change Card Sort: A Measure of Executive Function Skills), a rule use task that requires all three EF skills in early childhood but that, increasingly with age, serves primarily as a measure of cognitive flexibility (i.e., as inhibitory control and working memory develop, these demands become trivial). Tasks such as the DCCS and measures of inhibitory control and

THE DIMENSIONAL CHANGE CARD SORT: A MEASURE OF EXECUTIVE FUNCTION SKILLS

The dimensional change card sort (DCCS) (Frye et al. 1995, Zelazo 2006, Zelazo et al. 2013) is a rule use task: Participants are shown two bivalent, bidimensional target cards (e.g., depicting a blue rabbit and a red boat) and are told to match a series of test cards (e.g., red rabbits and blue boats) to these target cards first according to one dimension (e.g., color) and then according to the other (e.g., shape) (see **Figure 1**). Regardless of which dimension is presented first, 3-year-olds typically perseverate, continuing to sort cards by the first dimension. Five-year-olds typically switch. Three-year-olds who perseverate fail to reflect before acting, and they show a classic failure of executive function skills—a dissociation between knowing and doing (Zelazo et al. 1996). For example, when children who are supposed to be sorting by shape are asked, "Where do the boats go in the shape game? And where do the rabbits go?" they answer correctly. However, when told to sort the cards by these rules ("Okay, good, now play the shape game: Where does this rabbit go?"), they perseverate, sorting the red rabbit by color. This dissociation reveals the importance of distinctions among levels of conscious reflection on rules.

working memory can be rendered relatively hot when they are used in motivationally significant contexts. However, what makes EF hot and engages neural networks involving the more ventral and medial regions of PFC is not affective salience per se (Allan & Lonigan 2014) but rather the specific requirement of flexibly reappraising whether to approach or avoid a salient stimulus (e.g., Rolls 2004). Many measures that require the modification of the value of specific stimulus–reward associations have been found to depend on neural systems connecting the ventral and medial PFC with mesolimbic regions including the amygdala and striatum (Happaney et al. 2004). Examples include measures of reversal learning (in which a rewarded approach–avoidance discrimination must be reversed), delay of gratification and delay discounting (in which the value of an immediate reward must be reconsidered relative to a larger delayed reward), and extinction (when a previously rewarded stimulus is no longer rewarded and must now be avoided). A task that appears to require both hot and cool EF skills is the Iowa Gambling Task (IGT) (Bechara et al. 1994), in which the options that at first appear advantageous (higher rewards) are revealed gradually to be disadvantageous (higher rewards but even higher losses), and vice versa. Cool EF skills (e.g., working memory) also play a role in the IGT (e.g., Manes et al. 2002), and in general, given that cool EF skills engage and modulate hot EF skills, relatively complex hot EF tasks, such as the IGT, or the less-is-more task (Carlson et al. 2005), may activate both hot and cool EF processes (e.g., Moriguchi & Shinahara 2019). Finally, hot EF is also involved in deliberate emotion regulation, which involves intentionally modulating approach–avoidance reactions, including through reflection and cool EF processes, as seen in decentering, psychological distancing, and related metacognitive practices (e.g., Bernstein et al. 2015, Kross et al. 2011, Travers-Hill et al. 2017).

Hot and cool EF both play fundamental roles in deliberate learning, intentional action, emotion regulation, and social functioning (for review, see, e.g., Zelazo 2015), and individual differences in EF skills measured behaviorally in childhood predict a wide range of developmental outcomes, including school performance and social competence in adolescence (e.g., Mischel et al. 1989); college grade point average and graduation (McClelland et al. 2013); and physical health, socioeconomic status (SES), drug-related problems, and criminal convictions in adulthood (Moffitt et al. 2011). The predictive power of EF is often greater than that of IQ, and long-term predictions are seen even when controlling for IQ and childhood SES (e.g., Duckworth & Seligman 2005). It is not surprising, therefore, that the atypical development of these skills can lead to widespread and pervasive challenges to brain growth and healthy adaptation. Evidence

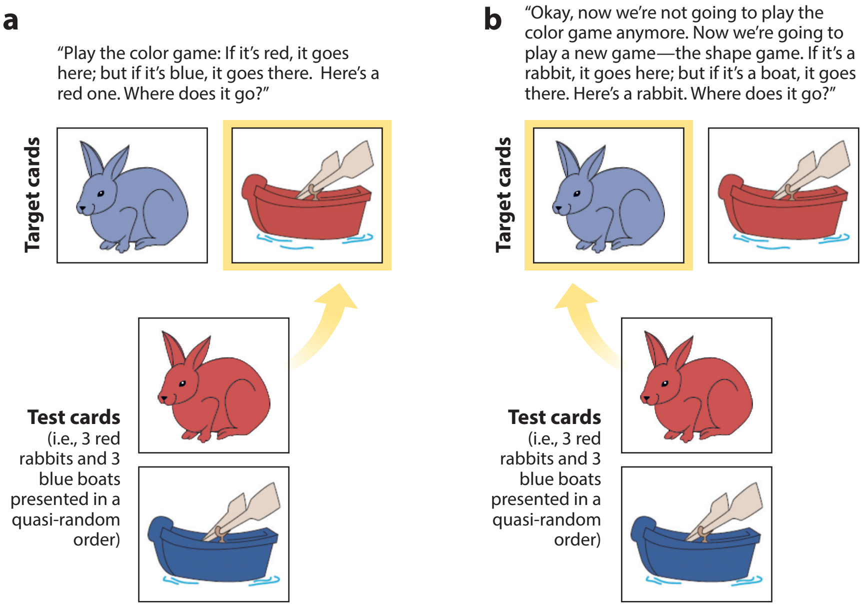

Figure 1

Sample target and test cards in the standard version of the dimensional change card sort (DCCS). Figure adapted with permission from Zelazo (2006).

from young children indicates that whereas poor hot EF is more strongly associated with problem behaviors in school (e.g., inattentive and overactive behavior), cool EF is more strongly associated with academic outcomes, including math and reading (e.g., Brock et al. 2009, Willoughby et al. 2011). Groppe & Elsner (2014) examined 1,657 children aged 6–11 years and found that cool but not hot EF was related to fluid intelligence. In contrast, other research found hot but not cool EF to be related to emotional intelligence (Checa & Fernández-Berrocal 2019). Both hot and cool EF are related to key aspects of social cognition, such as theory of mind (ToM) (e.g., Carlson et al. 2004, Frye et al. 1995), but evidence indicates that hot EF relates more strongly than cool EF to emotion-related social cognition, such as ToM stories involving affect (Wilson et al. 2018) and ToM mental state/emotion recognition (Reading the Mind in the Eyes Test) (Kouklari et al. 2019).

The development of EF skills appears to involve the experience-dependent functional specialization of EF skills and the neural networks that underlie them (Johnson 2011). Initial confirmatory factor analysis of adults' performance on a wide range of cool EF measures suggested three correlated latent variables (Miyake et al. 2000), but subsequent research has supported a hierarchical, bifactor model involving a common EF latent variable together with updating (working memory) and shifting (cognitive flexibility) variables (e.g., Friedman & Miyake 2017). In contrast to studies of adults, however, several studies with young children have found that cool EF measures load onto one factor (e.g., Wiebe et al. 2011) or two factors (inhibitory control and working memory; see, e.g., Miller et al. 2012) and appear to become differentiated by middle childhood or adolescence as a bifactor structure emerges involving common EF and multiple specific factors (e.g., Cirino et al. 2018).

In contrast to the slow differentiation within cool EF, differences between hot and cool EF have been observed relatively early in development, at least when hot EF is measured using tasks involving the need to delay approaching a tempting reward (e.g., Brock et al. 2009, Willoughby et al. 2011). For example, studies with children as young as 2 years (e.g., Bernier et al. 2012) have found support for hot and cool factors in children's performance on batteries of EF measures. Willoughby et al. (2011) found support for hot and cool EF factors in a study with over 750 children aged 4–5 years. A recent study with a diverse-SES sample of 1,900 children aged 2–5 years also found support for hot and cool EF factors across multiple direct behavioral assessments of each construct (Montroy et al. 2019). As with cool EF, however, there have been contradictory results (e.g., Allan & Lonigan 2014), probably depending on the hot EF measures used. It is also possible that hot and cool EF become more robustly differentiated as the neural circuitry underlying them is engaged and activated. A pattern of age-related differentiation during childhood and into adolescence has also been found to occur between EF skills and other non-EF cognitive functions, as measured by the NIH Toolbox Cognition Battery (Mungas et al. 2013), and this pattern may reflect use-dependent specialization of neural systems (Johnson 2011).

AN ITERATIVE REPROCESSING MODEL OF EXECUTIVE FUNCTION AND ITS DEVELOPMENT

According to the iterative reprocessing (IR) model (e.g., Cunningham & Zelazo 2007), and as applied specifically to the development of EF skills (Zelazo 2015), EF skills modulate attention and consequently control behavior in corresponding ways, allowing behavior to be more adaptive, planful, and focused during problem solving. In general, detection of uncertainty, or stimulus or response conflict, can interrupt automatic processing and signal the need to proceed deliberately in a top-down, controlled fashion (e.g., Botvinick et al. 2001); it can result in pausing. The IR model proposes that conflict/uncertainty detection triggers reflection, or the active reprocessing of information, which in turn allows individuals to keep information actively in mind and to formulate more complex action-oriented rules that allow for greater cognitive flexibility and inhibitory control. Reflection and the engagement of EF skills in turn result in the downregulation of conflict detection.

The development of EF is made possible by increases in the efficiency of reflective reprocessing of information via neural circuits that coordinate hierarchically arranged regions of the PFC (Bunge & Zelazo 2006). Increases in the efficiency of reflection are manifested behaviorally as children notice challenges (detect conflict), pause, consider their options, put things into context before responding, and monitor their ongoing efforts. Having paused, children are then in a position to exercise their EF skills (i.e., cognitive flexibility, working memory, and inhibitory control), often using self-directed speech as they do so. Indeed, the goal-directed control of attention is typically verbally mediated and involves the formulation and maintenance in working memory of explicit rules (e.g., Gooch et al. 2016). More complex rule representations allow for more flexibility and control in a wider range of situations than previously possible (Woolgar et al. 2015). The coordination of hierarchically arranged regions of the PFC into an activated network permits increases in the hierarchical complexity of rules that can be formulated and maintained in working memory (Zelazo et al. 2003). When children respond to situations reactively, without much reflection upon what they are doing, they are more likely to show classic EF failures (e.g., assuming that they know what to do; treating a new situation as if it were an old, familiar one).

The IR model describes both the cognitive and the neural processes associated with reflection and how these lead to specific EF skills and to consciously controlled behavior (see **Figure 2**). At the neural level, reflection involves the reprocessing of neural patterns via thalamocortical circuits involving the PFC and other cortical and subcortical regions. At the neurocognitive level, reflection involves the active, elaborative reprocessing of information. Information is processed and then reprocessed (reflected upon) as additional information is integrated into a richer, more detailed

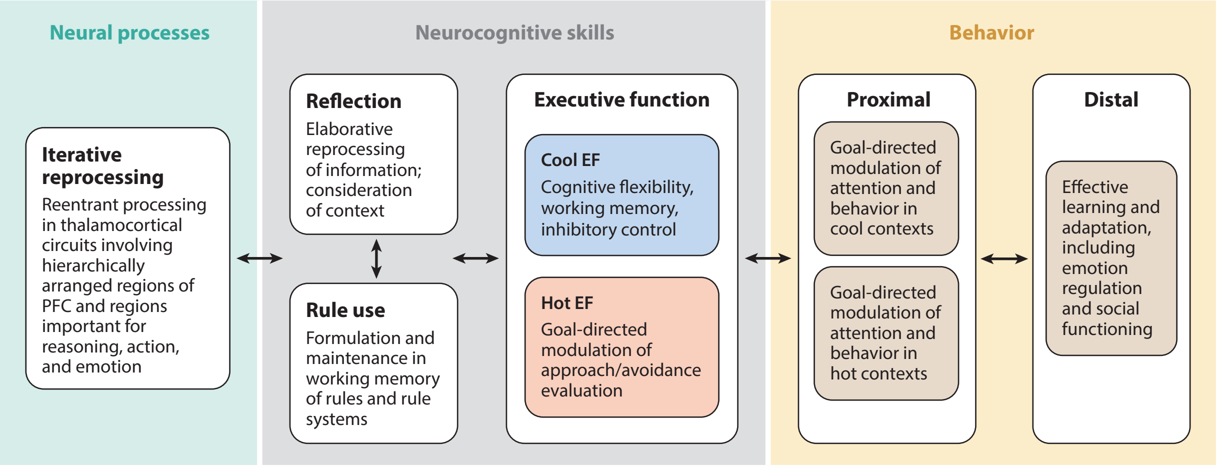

Figure 2

Outline of key processes in the iterative reprocessing model of EF skills (Cunningham & Zelazo 2007). Abbreviations: EF, executive function; PFC, prefrontal cortex. Figure adapted with permission from Zelazo (2015).

construal (i.e., interpretation). This kind of reprocessing depends on EF skills (e.g., sustaining focus on the object of reflection) and also enables their strategic use. At the behavioral level, cool and hot EF together allow for intentional learning and effective social functioning. It is well established, for example, that children's cool and hot EF skills predict their theory of mind, a key aspect of social cognition, concurrently and longitudinally (e.g., Carlson et al. 2004, Frye et al. 1995).

Evidence for the important role of reflection in EF skills comes from experimental interventions. For example, Espinet et al. (2013) examined the effect of reflection training on DCCS performance (see the sidebar titled The Dimensional Change Card Sort: A Measure of Executive Function Skills). Children who failed this task were given a different version of it and taught to pause before responding, reflect on the nature of the task, and formulate higher-order rules for responding flexibly. Compared with children who received this different version but received only minimal yes/no feedback (without practice in reflection) and children who received no feedback at all (without practice in reflection), children who received ~20 min of reflection training showed significant improvements in performance on a subsequent administration of the task (with different stimuli). Improvements were also seen on other tasks, including a measure of far transfer, a false belief task that measures flexible perspective taking. These behavioral changes were accompanied by predictable changes in children's frontocentral neural activity; there was a decrease in the amplitude of the N2 component of the event-related potential, an anterior cingulate cortex (ACC)-mediated index of conflict detection, so that it resembled that of children with better EF skills. Trained children who reflected on the task and engaged their EF skills resolved the conflict inherent in the task, resulting in reduced N2 amplitude.

The IR model recognizes that top-down regulation is not a unitary phenomenon. First, it underscores the interdependence between EF and metacognition (e.g., Lyons & Zelazo 2011, Roebers 2017) and points to the fundamental role of reflection, which starts with conflict detection, occasions the recruitment of EF skills, and then allows for monitoring and attentional, cognitive, and behavioral flexibility. The efficiency of metacognitive reflection, corresponding to degrees of iterative reprocessing of information, is a fundamental dimension along which development occurs, and failures of reflection can help explain dissociations between knowing (on some level) and doing (e.g., Zelazo et al. 1996) as well as the pervasive lack of insight associated with

PFC damage and a range of clinical conditions (e.g., Ciurli et al. 2010). Reflection allows for more aspects of a situation to be noticed and integrated into a construal (or interpretation), yielding a richer, more nuanced evaluation of the situation and an appreciation of the options at one's disposal (cf. Trope & Liberman 2010). Cognitive behavioral therapy with children and adolescents is often focused on scaffolding and supporting reflection and emotion regulation in the context of stress (e.g., anxiety, overly negative appraisals regarding a setback, exposure to threat-relevant stimuli in a client with OCD).

Second, the IR model captures the continuum between hot and cool EF as well as the dynamic interaction between more bottom-up (e.g., limbic) and more top-down (cortical) influences on information processing and goal-directed behavior. Limbic regions interact reciprocally with cortical areas of the brain, including the orbitofrontal cortex (OFC), the ACC, and hierarchically arranged regions of the lateral PFC (ventrolateral PFC, dorsolateral PFC, and rostrolateral PFC). Information may be processed with relatively little reflection (i.e., few iterations of reprocessing), as when a simple evaluation may be sufficient for the current situation. However, detection of uncertainty can trigger reflection, in which case previously processed information from the limbic regions can be reprocessed by cortical regions including the PFC, resulting in a new evaluation. The IR model suggests ways to minimize more reactive responses and improve hot EF skills, including through supporting and scaffolding reflection and the use of rules. Hot EF processes can attenuate emotional reactivity, and these processes can themselves be controlled by cooler EF processes, including through self-directed speech.

In particular, there is a close correspondence between the development of the lateral PFC and increases in rule use: understanding, formulating, and following rules to regulate behavior (Bunge & Zelazo 2006, Crone & Steinbeis 2017). On the DCCS and other measures of rule use, performance improves markedly in the preschool period. With age and experience, children show increases in the complexity of the rules that they can formulate and use. Relatively simple rules (e.g., stimulus–response associations and their reversal) appear relatively early in development and are associated more with OFC. Over the course of the preschool years, children are able to use increasingly complex rules that depend on more complex neural networks integrating first the ventrolateral, then the dorsolateral, and finally the rostrolateral PFC in a dynamic way. For example, research has found that even 2.5-year-olds successfully use a single arbitrary rule to sort pictures, 3-year-olds can use a pair of rules (e.g., shape rules in the DCCS), and 5-year-olds can use a hierarchical set of rules, including a higher-order rule for switching between rule pairs (e.g., Zelazo et al. 2003).

Figure 3 highlights key interactions between more effortful, reflective processes and more automatic, bottom-up processes, whether those be mediated primarily by the striatum (habits, stimulus–response associations) or by the amygdala, among other regions (e.g., insula). Within each of the structures pictured in this simplified model, there are corresponding kinds of organization. For example, the dorsal ACC connects more strongly with the anterior and lateral regions of the PFC such as the dorsolateral PFC, whereas more ventral parts of the ACC connect more strongly with orbitofrontal and ventromedial regions (e.g., Bush et al. 2000).

EXECUTIVE FUNCTION DIFFICULTIES AS A TRANSDIAGNOSTIC INDICATOR: DIMENSIONAL CHARACTERIZATIONS OF PSYCHOPATHOLOGY AND THE ROLE OF ATYPICAL EXECUTIVE FUNCTION ACROSS CONDITIONS

Difficulties with EF have been documented in a wide range of conditions with childhood or youth onset, including learning difficulties and learning disorders (e.g., Toll et al. 2011), externalizing disorders or disruptive behavior problems such as ADHD (e.g., Petrovic & Castellanos 2016) and

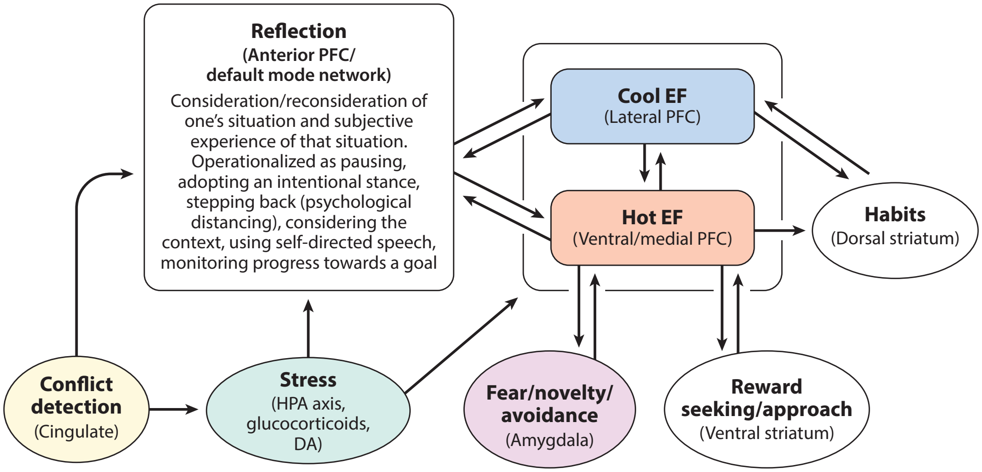

Figure 3

Neurocognitive processes (and structures) involved in fluid reasoning, intentional action, emotion regulation, and social function. Abbreviations: DA, dopamine; EF, executive function; HPA, hypothalamic pituitary axis; PFC, prefrontal cortex.

CD/oppositional defiant disorder (ODD) (e.g., Rubia 2011), internalizing disorders such as anxiety and depression (e.g., Nelson et al. 2018, Shi et al. 2019) and OCD (e.g., Pietrefesa & Evans 2007), and thought disorders such as ASD (e.g., O'Hearn et al. 2008) and schizophrenia (e.g., Bansal et al. 2019). Building on research in developmental psychopathology that recognized a broad distinction between internalizing and externalizing problems (Achenbach et al. 1987), dimensional approaches to the structure of psychopathology have now found considerable support for the hierarchical, bifactor model in which the general p factor reflects impairments common to all categories as well as the severity of distress (e.g., Caspi et al. 2014, Castellanos-Ryan et al. 2016, Lahey et al. 2017).

Neuroimaging and behavioral research with adult patients provides support for the hierarchical structure of psychopathology. For example, meta-analyses (e.g., McTeague et al. 2017) indicate a transdiagnostic pattern of atypical brain activation in regions corresponding to the multiple demand network (left lateral PFC, right insula, right intraparietal sulcus, and anterior midcingulate/presupplementary motor cortex) (Duncan 2013), which is activated across different EF tasks and likely reflects relatively general processes (e.g., reflection, task analysis and decomposition, sequencing, monitoring) common to all EF skills. A meta-analysis of 16,000 individuals with diverse conditions found transdiagnostic gray matter volume reduction in dorsal anterior cingulate and bilateral anterior insula (McTeague et al. 2017). In healthy controls, lower gray matter volume in these regions was associated with worse EF. Across disorders, there was hypoactivation in the right anterior insula/ventrolateral PFC. Network analysis of symptoms in a sample of 849 adolescents (13–20 years) found that when a measure of IQ, interpreted as an index of cool EF, was added to the symptom network, it showed the largest number of connections to other nodes (symptoms), making it the most central node to its network (Madole et al. 2019). In contrast, self-reported emotional control was the 11th most central node. For internalizing and aggression symptoms, the average between-cluster edge weight, an index of comorbidity among clusters of symptoms, was lower for teens at both the lower and higher extremes of emotional control.

Hierarchical, dimensional approaches to the structure of psychopathology converge well with the Research Domain Criteria (RDoC) initiative (e.g., Insel et al. 2010). RDoC identifies behavioral functions with clear relations to neural systems that are likely to be dysfunctional in psychopathology. RDoC provides a way to map processes across multiple levels of analysis (from symptomatology to neurocognitive function to genes), and in particular, it captures several functions that collectively make up reflection and EF skills: attention, working memory, language, and cognitive (effortful) control.

Building on the current RDoC formulation, the IR model adds a characterization of cognitive control that captures additional variation along two partially orthogonal continua: levels of conscious reflection, with corresponding levels of EF (attentional control); and the hot–cool dimension. Reflection has been closely linked to EF skills both in developmental (e.g., Lyons & Zelazo 2011, Roebers 2017) and in neuropsychological research (e.g., Ciurli et al. 2010). Evidence indicates that metacognitive reflection can be scaffolded and supported using autonomy-supportive techniques that encourage openness, exploration, curiosity, and agency (Marulis et al. 2020, Zelazo 2015), and studies also have shown that reflection facilitates cognitive flexibility and the far transfer of trained skills (e.g., Espinet et al. 2013, Hadley et al. 2020, Pozuelos et al. 2019). The IR model, which allows for degrees of reflection and captures dynamic transactions between automatic and reflective processes over time, contrasts with more static dual process models that draw a sharper distinction between implicit and explicit processes (e.g., Greenwald & Banaji 1995). Teachman et al. (2019) considered the implications of the IR model for a variety of conditions (anxiety, posttraumatic stress disorder, major depressive disorder, OCD, and alcohol use disorder) and noted that whereas evidence indicates that disorder-specific implicit beliefs are associated with symptomatology, implicit processes can still be influenced by strategic control through reflective reprocessing (e.g., Cunningham et al. 2008).

The hot–cool EF dimension has proven useful in addressing both comorbidity across diagnostic categories and heterogeneity within them. Consideration of hot and cool EF has helped characterize a wide range of conditions, including ADHD (e.g., Geurts et al. 2006, Petrovic & Castellanos 2016), ASD (e.g., Zimmerman et al. 2016), antisocial personality disorder (e.g., De Brito et al. 2013), CD (e.g., Rubia 2011), developmental coordination disorder (e.g., Rahimi-Golkhandan et al. 2016), fetal alcohol syndrome disorders (e.g., Kully-Martens et al. 2013), OCD (e.g., Güngör et al. 2018), sequelae of prematurity (e.g., Hodel et al. 2016), psychotic symptoms in at-risk youth (e.g., MacKenzie et al. 2017), and the consequences of traumatic brain injury (e.g., Fonseca et al. 2012). The literature also includes failures to find differences between hot and cool EF across clinical conditions or across subtypes within a condition (e.g., Hybel et al. 2017).

The hot–cool distinction has sharpened our understanding of ADHD, including differentiating it from highly comorbid disruptive behavior disorders, such as ODD and CD (e.g., Rubia 2011). Whereas the most common and consistent correlates of ADHD are measures of cool EF, there is growing appreciation of the role of hot EF difficulties such as high delay aversion, high temporal discounting, and emotion dysregulation (Petrovic & Castellanos 2016). These findings support the idea that there are two neurodevelopmental pathways leading to ADHD, one involving difficulties in cool EF and one involving difficulties in hot EF and motivation (e.g., Sonuga-Barke 2003).

ADVERSE CHILDHOOD EXPERIENCES, STRESS, AND EXECUTIVE FUNCTION DEVELOPMENT

Within particular samples, EF skills show considerable heritability, and twin studies indicate that genetic influences on a general EF factor are correlated with genetic influences on a general psychopathology factor (Paige Harden et al. 2019). However, the development of EF skills depends crucially on experience, and there is growing evidence that EF skills can be improved by practice and influenced by a wide range of circumstances and experiences, such as SES, stress, and the quality of early childhood care (e.g., Masten et al. 2012, Zelazo et al. 2018). Children growing up in poverty typically perform worse on EF than their more affluent peers (Noble et al. 2015). Lower EF is also associated with higher levels of stress in childhood, likely because stress impairs EF, and impaired EF in turn leads to more stress (e.g., Blair & Raver 2016).

The important influence of experience on EF development is seen not only at the level of behavior but also at the level of the brain. Research on the effects of practice shows how practice-induced changes in brain function (i.e., how one uses one's brain) produce relatively persistent changes in brain structure (e.g., Zatorre et al. 2013). These changes include experience-related decreases and increases in gray matter as well as increases (and possibly decreases) in white matter (for review, see, e.g., Kaller et al. 2017). Whereas decreases in gray matter mostly reflect synaptic pruning, increases in gray matter can reflect axon sprouting, dendritic branching and synaptogenesis, neurogenesis, changes in glial cells, and the development of new blood vessels (angiogenesis). Increases in white matter reflect mainly myelination but also axon branching, packing density, axon diameter, fiber crossing, changes in astrocytes, and angiogenesis. Experience also changes other aspects of brain structure, including the density of receptors for particular neurotransmitters, such as dopamine (DA) (e.g., McNab et al. 2009). Collectively, this research shows that the activation of specific neural pathways, repeated over time, changes those pathways, rendering them more efficient.

Adversities associated with poverty include inconsistent caregiving, neglect or maltreatment, malnutrition, and exposure to loud noise, all of which can lead to high levels of sustained and uncontrollable stress (e.g., Blair & Raver 2016). Children from low-SES families are also exposed to more chaos (e.g., Matheny et al. 1995) and less environmental support for language acquisition [e.g., fewer words (Schmitt et al. 2011)] and for EF skills [e.g., fewer opportunities to play games that require attention regulation (Korucu et al. 2019)]. For example, inconsistent schedules and the lack of family routines make it difficult for children to predict and anticipate sequences of events (essential for goal-directed behavior such as planning and delay of gratification), and these lifestyle factors often disrupt sleep (e.g., Koopman-Verhoeff et al. 2019) and elicit high levels of chronic and recurring stress (e.g., Lupien et al. 2009)—effects that are likely to impair PFC and EF development (e.g., Kolb et al. 2017, Shonkoff et al. 2012). Lower SES has been found to be related to higher hair cortisol in children and youth (Vliegenthart et al. 2016). Correlations have been reported between hair cortisol and hippocampal and ACC volume, and these relations were found to be mediated by SES (parent education), such that lower SES was positively related to higher levels of cortisol, which in turn were related to smaller regional brain volumes (Merz et al. 2020). In a cross-sectional study of 1,099 typically developing individuals (3–20 years), cortical surface area partially mediated the relation between SES and cool EF skills but not the relations between SES and vocabulary or reading (Noble et al. 2015). Electrophysiological evidence has shown atypical prefrontal function in low-SES infants as young as 6 months (Tomalski et al. 2013).

Exposure to ACEs (e.g., Felitti et al. 1998), including abuse and household dysfunction, follows a gradient of poverty. A study found that 44% of homeless parents reported 4 or more (of 10) ACEs compared with 12% in national (CDC) data, and there was a link from parents' ACE exposure to children's ACE exposure and to child problems (Narayan et al. 2017). More generally, the relation between trauma exposure and adverse outcomes is well established, and growing evidence also suggests that negative effects on neurocognitive and social development are mediated at least in part by the toxic effects of stress on the development of the PFC (e.g., Hanson et al. 2010) and on EF skills and school performance (e.g., Shonkoff et al. 2012). SES is negatively related to EF skills in childhood, and EF skills partially account for the relation between SES and school success (better than IQ or language) (e.g., Nesbitt et al. 2013). SES has also been found to interact with parental history of ADHD to determine ADHD prevalence (Rowland et al. 2018), and it has been proposed that EF might mediate the relation between stress and externalizing problems (Johnson 2015). There is also evidence that good EF skills can serve as a protective factor against academic risks associated with poverty. Children who are (or have been) homeless and highly mobile are more likely than other children to perform poorly in school, but having good EF skills increases their odds of success in school despite being homeless (Masten et al. 2012).

Physiological responses to stress, including hypothalamic–pituitary–adrenal (HPA) axis activity, result in the release of glucocorticoids (cortisol) as well as catecholamines such as DA and norepinephrine (NE) that play a central role in PFC function (Butts et al. 2011). Cortisol, DA, and NE facilitate neural activity in the PFC in an inverted U-shaped fashion, and high levels overwhelm PFC function, resulting in more reactive and unregulated responses (e.g., Robbins & Arnsten 2009). Serotonin (5-HT) appears to play a more important role in hot EF (e.g., Roberts 2011). Disruption of HPA axis function by exposure to high levels of uncontrollable stress undermines EF skills both in the moment, because it hijacks one's attention (e.g., Liston et al. 2009), and over time because of the toxic effects on neural structures important for EF (PFC and hippocampus; see Kolb et al. 2017). Research with children indicates that exposure to chronic stress is correlated over time with initially elevated stress hormone levels and subsequent blunted levels (and other disrupted stress physiology) along with diminished EF skills (e.g., Hostinar et al. 2014). A recent longitudinal study of 815 high-risk mother–offspring pairs found predictive relations between early family stress (0–5 years) and both internalizing ($b = 0.30$) and externalizing ($b = 0.29$) problems at age 20 years but no evidence of disorder-specific effects (Conway et al. 2018). Other research has suggested that the strongest correlations with stress are with the general p factor (e.g., Shanmugan et al. 2016).

A NEURODEVELOPMENTAL MODEL OF THE ROLE OF EXECUTIVE FUNCTION IN ATYPICAL DEVELOPMENT

Research on the development of EF skills helps explain why EF difficulties are such a pervasive feature in developmental psychopathology. First, EF skills provide a necessary foundation for deliberate learning and intentional action, which are crucial for flexible adaptation to changing circumstances and challenges. Indeed, EF skills are essential for the intelligent exercise of agency, which is perhaps the most higher-order, emergent, abstractly defined, and most cherished of human functions. Disruption of these skills therefore has widespread behavioral and developmental consequences (e.g., Moffitt et al. 2011), cutting across academic and social domains and across diagnostic categories.

Second, higher-order skills are especially vulnerable to disruption because of their position in a hierarchy; deficits in any one of the many subnetworks involved may lead to subsequent difficulties in controlling those networks. Neural development generally proceeds in a bottom-up fashion, with lower-order somatosensory and visual cortical networks developing first, followed by higher-order association networks such as those involving the PFC that integrate information from the lower-order areas (e.g., Gogtay et al. 2004). PFC areas grow on top of and around earlier-developing regions, allowing them to interact reciprocally with those lower-order areas, including orchestrating and modulating them in a top-down fashion but also being modified by them in a bottom-up way. As a result, the atypical development of lower-order networks and the functions they fulfill feeds forward over time and has the potential to disrupt the later-developing PFC networks supporting EF skills. For example, disruption of HPA axis function feeds forward to affect the PFC and hippocampus, among other regions.

Third, the window of opportunity for influencing EF skills is wide, for better and for worse. Although PFC function and EF skills emerge in infancy and allow even young children to behave

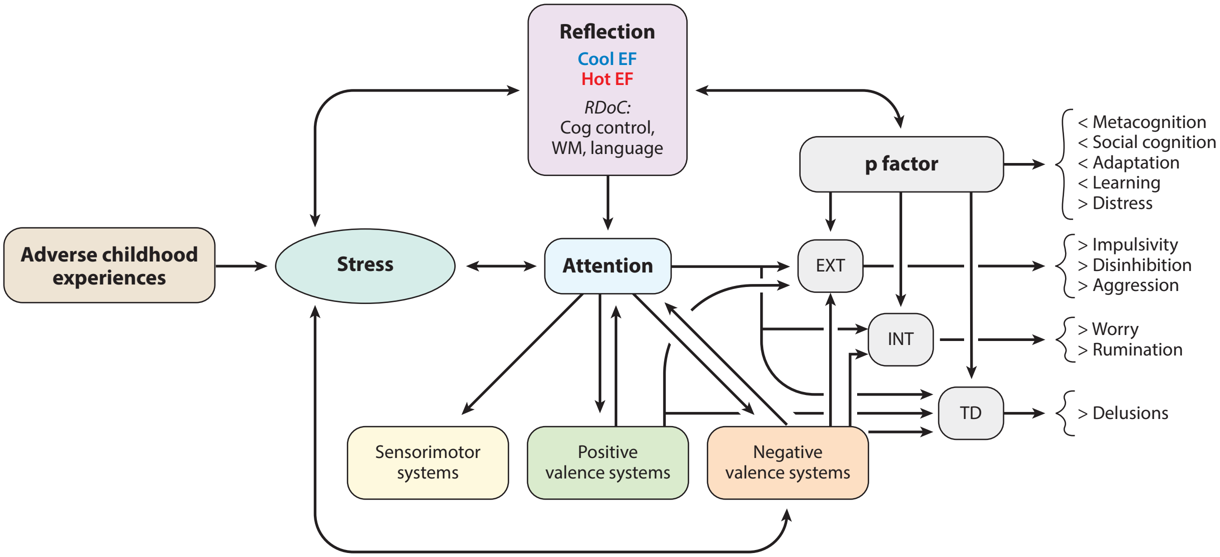

Figure 4

A simplified neurodevelopmental model of the etiology of general psychopathological risk. Abbreviations: Cog, cognitive; EF, executive function; EXT, externalizing; INT, internalizing; RDoC, Research Domain Criteria; TD, thought disorder; WM, working memory.

in a goal-directed fashion (and hence to learn EF skills by using them), the development of EF skills and the neural networks upon which they depend extends into adulthood. PFC-dependent EF skills are among the last to mature in part because they require the prior development of more fundamental networks and skills. This protracted period during which both behavior and neural networks develop—that is, adapt to relevant environmental challenges—is indicative of extended relative malleability. A long window of plasticity is useful for the acquisition of EF skills because these skills depend importantly on environmental influences including social and cultural support (e.g., language, autonomy support, play). At the same time, however, the extended malleability of EF skills leaves them vulnerable for longer to disruption from a wide range of influences, such as poverty, abuse, chaos, and stress. **Figure 4** depicts a simplified model of the role of atypical development of EF skills, especially reflection and aspects of common EF, in producing general (p factor) features of psychopathology as well as risk for more specific features.

EXECUTIVE FUNCTION SKILLS AS A TARGET OF TRANSDIAGNOSTIC INTERVENTION

The importance of EF skills for flexible adaptation to changing circumstances, together with the protracted plasticity of these skills, makes them a promising target of transdiagnostic therapeutic intervention (e.g., Marchette & Weisz 2017). EF skills can now be reliably and validly measured in children as young as 18 months of age through the use of standardized direct behavioral assessments that can be administered repeatedly across a wide range of ability levels (Zelazo et al. 2016). Early detection of EF difficulties may allow for intervention during periods of relative plasticity in EF-related neural systems, including during the preschool years, the transition to adolescence, and late adolescence (e.g., Zelazo & Carlson 2012). Indeed, a growing body of research suggests that EF skills can be cultivated through scaffolded practice (Espinet et al. 2013) and autonomy-supportive caregiver–child interactions (Meuwissen & Carlson 2018). As with other neurocognitive skills, the repeated engagement and use of EF skills in problem solving at ever-increasing levels of challenge strengthen these skills and increase the efficiency of the corresponding neural circuitry. Evidence suggests that individual EF skills and sometimes fluid intelligence can be improved through training (e.g., Diamond & Lee 2011, Jaeggi et al. 2008, Mackey et al. 2011). Preschool and kindergarten curricula (e.g., Tools of the Mind) and modular programs designed to complement these curricula (e.g., PATHS) have been shown to lead to better EF skills and academic achievement (e.g., Riggs et al. 2006).

Although research to date has often failed to find evidence that trained EF skills generalize to different skills or contexts (far transfer) (e.g., Melby-Lervåg et al. 2016), most interventions have not been well designed to promote far transfer. Research on learning shows clearly that to promote the far transfer of any skill, it is important to train that skill in a wide range of contexts (e.g., Smith 1982). Newer evidence also indicates the importance not only of practicing EF skills in a variety of contexts but also of encouraging children to reflect upon them metacognitively so that they learn the purpose and utility of EF skills as well as how and when to apply those skills in new situations (Espinet et al. 2013, Hadley et al. 2020, Pozuelos et al. 2019). Interventions focusing on reflection, decentering, metacognition, and psychological distancing have also been found effective for individuals with various forms of psychopathology (e.g., Travers-Hill et al. 2017).

Scaffolded training at increasing levels of challenge together with a metacognitive component has the potential to buffer children against the disruptive effects of stress and might usefully address both cool and hot EF. One way to address hot EF is by practicing mindfulness, which is a particular way of paying attention—on purpose, in the present moment, and nonjudgmentally (Kabat-Zinn 1990). During mindfulness, an individual pays attention to a particular mental object (e.g., the experience of one's breathing), notices but does not dwell on distracting thoughts or feelings, and gently returns attention to the object of focus. The proximal goal of mindfulness meditation is therefore to train one's attention to be more reflective, focused, and deliberate. Additionally, the practice of paying attention to a specific mental object while ignoring distractors has the benefit of training people to recognize but not dwell on negative emotions—to be more nonjudgmental and accepting of themselves. Mindfulness practice has been shown to be beneficial in many domains, such as pain management, stress reduction, and the treatment of anxiety and depression (e.g., Dunning et al. 2019).

Mindfulness practice has also been found to improve EF skills (e.g., Schonert-Reichl et al. 2015) and may be particularly effective when combined with reflection training and EF skills training (Zelazo et al. 2018). From this perspective, mindfulness combines aspects of cognitive training (e.g., reflection and adaptive practice of attention regulation skills, such as sustaining attention for longer and longer) along with emotion regulation strategies (acceptance and reappraisal, psychological distancing) to deal with influences, such as anger and stress, that can hijack our EF skills and result in reactive behavior. The combination of paying attention in a goal-directed way while also contextualizing and consequently attenuating the impact of emotions and their consequences makes mindfulness well suited to address both top-down (reflective) and bottom-up (reactive) influences on behavior and has been shown to improve hot EF skills. For example, in one measure of emotion regulation (Buodo et al. 2002), participants are asked to categorize a tone as high versus low pitch while viewing stimuli that vary in their affective valence (positive, negative, or neutral). Emotional interference is measured as the increase in reaction time in the presence of negative versus neutral pictures. In a randomized controlled trial with adults, only participants who received 7 weeks of mindfulness practice (e.g., compared with an active control group receiving relaxation practice) showed a reduction in the emotional interference effect, which was accompanied by a corresponding reduction in the amplitude of participants' skin conductance responses to the affective pictures as well as a reduction in their ratings of the pictures' affective intensity (Ortner et al. 2007). Together, these findings suggest that mindfulness practice led to rapidly occurring and relatively automatic changes in the way the pictures were processed.

CONCLUSION

A simplified model of the emergence of psychopathology in childhood and adolescence leads from ACEs and other sources of toxic stress to the disruption of the development of neural systems supporting reflection and both hot and cool EF skills and then to an increased risk for general, transdiagnostic features of a wide range of clinical conditions. The role of EF difficulties in this developmental pathway can be understood as a consequence of (*a*) the fundamental role that EF skills play in learning and adaptation, (*b*) the hierarchical nature of both EF skills and the neural systems that support them, and (*c*) the relative plasticity of EF skills over an extended period of time. Research points to the promise of both hot and cool EF skills as a general target for therapeutic and preventive intervention. Indeed, a growing body of research suggests that EF skills can be cultivated through scaffolded training. It is proposed that intervention efficacy can be enhanced by mitigating disruptive bottom-up influences, such as stress, and that skills training that includes a reflective, metacognitive component can help promote the far transfer of trained skills. The need for preventive and therapeutic interventions supporting EF skills and brain health in children exposed to adversity is substantial.

SUMMARY POINTS

1. The IR model of EF skills and their development emphasizes the importance of metacognitive reflection and captures the continuum between hot and cool EF.
2. The structure of psychopathology symptoms can be modeled using a hierarchical, bifactor model consisting of a general factor (p) that accounts for transdiagnostic impairments, such as impairments in reflection and EF skills, and at least two lower-order factors, such as internalizing and externalizing.
3. Difficulties with both hot and cool EF skills are transdiagnostic indicators of atypical development: (<EF) → (>p).
4. Stress interferes with EF and its development: (>stress) → (<EF).
5. Early exposure to high levels of sustained and uncontrollable stress predicts transdiagnostic features of atypical development: (>stress) → (>p).
6. There is evidence that the link from high stress to high p is mediated by low EF: (>stress) → (<EF) → (>p).
7. EF skills mediate the relation between stress and general psychopathology features at least in part because of their fundamental importance for agency and intentional action, their hierarchical structure, and their protracted plasticity.
8. Evidence indicates that EF skills can be promoted, perhaps especially during periods of high relative plasticity (e.g., early childhood and the transition to adolescence). Interventions should address metacognitive reflection (noticing uncertainty, pausing, considering context, monitoring) to promote far transfer of trained EF skills, and they might be more effective if they target both cool and hot EF skills (e.g., by combining reflection training, EF skill training, and mindfulness).

FUTURE ISSUES

1. Additional longitudinal research with measures at multiple levels of analysis is needed to characterize the neurodevelopmental pathways from stress to EF skills to general features of psychopathology as well as to examine potential moderators of these pathways, such as SES, gender, and culture.
2. Research on the relations between psychopathology and personality has the potential to inform an extension of this model that captures individual differences within the typical range.
3. Large-scale randomized controlled trials with active control conditions are needed to establish the nature and efficacy of a unified protocol for promoting EF skills across childhood and adolescence. A unified protocol might include adjustments for age as well as options tailored to individuals with internalizing, externalizing, or thought disorder symptoms or some combination of these and/or other symptoms.
4. More research is needed on the relative plasticity of reflection and EF skills across age. Different types of intervention targeting different EF-related processes might be more or less effective during different developmental periods.

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RELATED RESOURCES

The website for the Harvard Center on the Developing Child (**https://developingchild.harvard.edu**) contains accessible information about stress and the development of EF skills.