including neurostimulation (transcranial magnetic stimulation, transcranial direct-current stimulation), cognitive remediation, and physical exercise.[18] With renewed interest in this area, and a growing recognition of cognition as a neurobiologically and clinically distinct feature of MDD, there is genuine potential for improving the treatment of cognitive impairment in depression in the future.

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Emotion and Cognitive Control: An Essential Partnership for Adaptive Behavior

Rachel E. Brough, MA; Alyssa J. Asmar, MA; and Kimberly S. Chiew, PhD

Cognitive control (sometimes referred to as executive function) is a set of cognitive processes that enable individuals to adaptively and flexibly guide their behavior across different situations to achieve desired goals. Cognitive control comprises several interrelated but partly distinct skills, including inhibition of prepotent responses, maintaining and updating content in working memory, and flexibly shifting mental sets.[1] Disruptions to cognitive control, as well as to emotional processes, are implicated in a wide range of psychiatric disorders, including schizophrenia, depression, bipolar disorder, anxiety disorders, obsessive-compulsive disorder (OCD), and substance use disorders. Importantly, while these disorders present with diverse symptomology, disruptions in both emotion and cognitive control appear to be transdiagnostic and have been argued for as core indicators of psychopathology.[2] Understanding emotion as a factor that can interact with cognitive control, both adaptively and maladaptively, might be important for advancing mechanistic accounts of psychopathology as well as identifying potential points for intervention and treatment.

A Bidirectional Relationship

Given robust evidence of altered cognitive control and emotion functioning in psychopathology, a key element to consider is the role of cognitive control in regulating emotion. "Emotion regulation" draws on cognitive control to alter emotional experience and behavior—for example, "looking for the silver lining," reframing a negative situation, or "keeping one's cool" and inhibiting an emotional response.[3] Cognitive control enables individuals to set adaptive emotional goals and flexibly select, implement, and adjust emotion-regulation strategies to pursue such goals across diverse contexts. In psychopathology, disruptions in cognitive control and emotional functioning may be intertwined, leading to emotion dysregulation. Poorer cognitive control might be associated with a reduced ability to inhibit unwanted thoughts and update the contents of working memory, as well as increasing rigidity in the selection and use of emotion-regulation strategies, leading to ineffective regulation and worse emotional outcomes. For example, if individuals have difficulty mobilizing cognitive control to inhibit maladaptive thought patterns or to flexibly replace them with more adaptive interpretations, they may be more prone to using maladaptive emotion-regulation strategies such as rumination. Such inflexibility is commonly seen in psychiatric conditions such as depression and OCD.[4]

In addition to a burgeoning literature examining the role of cognitive control in emotion regulation, extensive evidence indicates a bidirectional relationship between emotion and cognitive control. Cognitive control can be deployed to regulate emotion, but emotional states can also modulate cognitive control processes. Such emotional modulation of cognitive performance can lead to variable processing outcomes. For example, anticipation of reward pursuit has been linked with increased attentional focus, typically resulting in improved cognitive control performance across a variety of tasks.[5] In contrast, induction of positive mood without direct reward incentives has been associated with attentional broadening and improved performance on tasks requiring creativity and cognitive flexibility.[6] Importantly, such broadening also appears to come at the cost of increased distraction and ability to stay on task,[6] suggesting that different emotional states can promote distinct cognitive modes with unique advantages and drawbacks. Negative emotional states can also have variable consequences for cognitive control. For instance, sad mood inductions have led to enhanced attentional focus and improved cognitive control,[7] while the presentation of high-intensity negative images has been associated with poorer cognitive control, perhaps due to competition for cognitive resources.[8] Altogether, while reward-related positive emotions have generally benefited cognitive control to a greater extent than negative emotions, different emotional states can promote variable modes of attentional processing and cognitive control, the adaptiveness of which might depend on the situation and context.

However, whether emotional influences promote or impair cognitive control is not simply a function of positive vs negative valence. Instead, it is also important to consider the dimension of emotion *intensity*. In general, evidence suggests that too much or too little emotion, regardless of valence, might be less optimal for cognitive control than a moderate level of emotion (a Goldilocks effect). When emotional arousal is excessively high, whether positive or negative, cognitive control processing is typically impaired. This has been observed across a range of psychiatric disorders. For example, patients with bipolar disorder who are experiencing mania, a state of heightened positive emotion, have been found to display impaired cognitive control performance, including conflict processing, working memory, and goal management tasks.[9] Similarly, individuals with higher trait anxiety, who typically experience heightened negative emotion, have shown impairments in inhibitory control, task switching, and conflict resolution.[10]

On the opposite end of the emotional intensity spectrum, a relative lack of emotion, or apathy, may also be detrimental to cognitive control performance, particularly in the context of psychopathology. For example, in older adults with depression, increased apathy has been linked to worse performance on a battery of cognitive control tasks.[11] Interestingly, a recent study conducted by Westbrook et al demonstrated that individuals with depression exhibited lower levels of cognitive effort relative to those without depression, but these effort reductions were mitigated by a sad mood induction.[12] Given that cognitive effort is thought to be essential for successful cognitive control,[12] these results suggest that the induction of emotion, even if negative, can benefit cognitive control in individuals experiencing apathy. This may be particularly true if the emotional experience is validating and/or controllable, as might be the case for sad emotions induced through controllable means, such as music or films, in depression.[13] Thus, negative emotions may not always be detrimental to cognitive performance. When examining interactions between emotion and cognitive control, it is important to consider emotion goals—how individuals *want* to feel—as these goals may influence both how they choose to regulate their emotions as well as the potential impact of emotions on cognitive control outcomes.[14] Emotion goals might thus be a crucial element to the bidirectional relationship between emotion and cognitive control, with implications for daily functioning.

Neurotransmitter System Activity

Neurobiological evidence indicates that the complex and bidirectional relationships observed between emotion and cognitive control processes are supported by multiple interacting neurotransmitter systems. Decades of evidence implicate dopamine as integral to both cognitive control and reward processing.[15,16] More recently, dopamine neuromodulation has also been identified as a key mechanism by which emotion and motivation may influence cognitive control.[15] The effects of dopamine on cognitive control have been argued to follow a nonlinear, inverted-U pattern, whereby increased dopamine benefits cognitive control performance up to a point, beyond which further increases are associated with performance decrements.[17] This pattern is consistent with the Goldilocks effect discussed previously, whereby moderate levels of emotion may be associated with optimal cognitive control performance relative to very low or high levels of emotion. While the dopamine system has been most extensively studied in cognitive control research, other neurotransmitter systems have also been implicated in interactions between emotion and cognitive control. Serotonin and norepinephrine neurotransmitter systems have been implicated in threat responses and negative emotion[18,19]; as such, they may play a complementary role to the dopamine system, which has been largely associated with reward processing and positive emotions.[16]

In addition, similarly to the inverted-U account of dopamine, moderate levels of both serotonin and norepinephrine, relative to high or low levels, have been associated with better cognitive and emotional outcomes.[18,20] For instance, serotonin depletion is associated with increased threat sensitivity and difficulties with impulse control, while heightened serotonin levels are associated with exaggerated behavioral inhibition.[18] Both reductions and excesses in serotonin activity have been associated with elevated risk for psychopathology.[18] Meanwhile, moderate levels of norepinephrine may facilitate improved cognitive performance by enhancing the allocation of attention and cognitive resources toward highly salient and/or goal-relevant stimuli.[19] However, with excessive norepinephrine activity, arousal levels become overwhelming, performance begins to decline, and individuals shift from goal-directed to more habitual responding.[20] Disruptions in these and other neurotransmitter systems have been implicated across a range of psychiatric disorders. While attempts to alter neurotransmitter activity with medication (including monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, selective serotonin-norepinephrine reuptake inhibitors, and benzodiazepines, among others) have been largely successful in ameliorating symptoms for many patients, there is still much to learn about their functioning, as they work in complex and interactive manners to shape cognitive control and emotional experience.

TABLE. Key Points to Consider Regarding the Relationship Between Emotion and Cognitive Control

1. Emotional and cognitive control disturbances are transdiagnostic in psychopathology.
2. Disruptions in cognitive control can lead to emotion dysregulation, as the ability to regulate emotion is dependent on cognitive control abilities.
3. Emotional states, both negative and positive, can adaptively enhance cognitive control abilities.
4. The intensity of these emotional states can also impair cognitive control if they are too intense (as in mania) or not intense enough (as in apathy). Moderate levels of emotional intensity are typically optimal for cognitive control performance.
5. Imbalances in neurotransmitter system activity are often associated with disruptions in cognitive control and psychopathology. Too much or too little neurotransmitter activity can lead to dysfunction, while moderate levels of activity might be most adaptive.

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Concluding Thoughts

In conclusion, the relationship between emotion and cognitive control is complex and bidirectional: cognitive control is involved in the regulation of emotions, and emotions can influence cognitive control performance (see **Table**). Critically, a moderate level of emotional intensity may typically be most optimal for adaptive cognitive control outcomes, and patterns of neurotransmitter system activity may underlie this relationship. These complex interactions between emotion and cognitive control are important to consider in the characterization and treatment of psychiatric disorders.

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Are There Sex Differences in Cognition and Does It Matter?

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Sex differences in the brain, behavior, and cognition have been a topic of considerable interest in psychological and psychiatric research. Over the years, studies have sought to understand how biological and environmental factors shape cognitive abilities and brain functioning in males and females. Although many cognitive capabilities overlap between sexes, differences have been observed in various domains, such as spatial reasoning, verbal abilities, emotional processing, and memory. Differences between males and females are also reported in the prevalence and presentation of many neuropsychiatric conditions that are defined by their cognitive symptoms, including neurodevelopmental (eg, attention-deficit/hyperactivity disorder [ADHD]) and neurodegenerative (eg, Alzheimer disease) conditions. This article provides a synthesis of key findings on sex differences in cognition, exploring the possible causes and implications for clinical practice.

Terminology

The term *sex* refers to the biological attributes of sex chromosomes, gene expression, neuroanatomical features, and sex hormones that are used to categorize an individual as male (XY with testes), female (XX with ovaries), or intersex (reflecting variations across sex chromosomes, sex hormones, and neuroanatomical features). *Gender* refers to the psychosocial construct that encapsulates gender identity and expressions shaped by the environment, cultural and societal norms, roles, and behaviors. Both sex and gender exist on a spectrum and can influence cognition and the brain.[1,2]

Possible Biological Foundations of

Brain Structure, Connectivity, and Function: Research over many decades has unambiguously reported that total brain volume is larger in males than females. Some comprehensive reviews suggest that sex differences in brain volume (total brain volume and regional brain volumes) parallel sex differences in male and female body size.[3] In contrast, sophisticated analysis of the largest single-study neuroimaging data set (UK Biobank with > 40,000 participants) concluded that sex differences in height and weight did not account for sex differences in total brain volume and that once global brain size was taken into account, there remain numerous regional sex differences in both directions, albeit of small effect sizes.[4] However, sex differences in overall brain size or size of specific brain regions do not necessarily translate into differences in cognitive performance. Another key area often discussed in terms of sex differences in the brain is the efficiency of the communication (called connectivity) between brain hemispheres and brain regions. With the caveat of many mixed and inconclusive findings (often neglecting to account for differences in brain size), several studies suggest females have more efficient connectivity between brain hemispheres and locally between brain regions,[3] although literature remains mixed and a recent analysis of the large UK Biobank found males to have higher efficiency in connections between brain regions.[5]

Hormonal Influences: Sex hormones such as estrogen, progesterone, and testosterone influence the brain, behavior, and cognition throughout the lifespan. Males and females synthesize sex hormones in different quantities, with differential secretion of these hormones during the prenatal and pubertal periods, which are life phases thought to be particularly important for shaping sex differences in the organization of the brain.[6] For females, sex hormone levels continue to fluctuate across the lifespan—during the menstrual cycle, pregnancy, and through the menopause transition, with additional influences on hormone levels associated with the use of exogenous hormones (contraceptive pill or hormone therapy use during menopause). Testosterone, predominantly higher in males, has been associated with improved spatial skills, whereas estrogen, more abundant in females, is thought to enhance verbal abilities and memory performance.[7] These hormonal differences may help explain why, on average, males outperform females on visual-spatial tasks, whereas females tend to have superior performances on fine motor tasks, verbal fluency, and verbal memory.[8]

Cognitive Domain Differences

Sex differences in cognition have been observed across various cognitive domains, including spatial abilities, language, memory, and emotional process-