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## The roles of physical activity, exercise, and fitness in promoting resilience during adolescence: effects on mental well-being and brain development

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### Abstract

Adolescence is a critical yet vulnerable period for developing behaviors important for mental well-being. The existing literature suggests that physical activity (PA), exercise, and aerobic fitness promote well-being and reduce risk of mental health problems. In this review, we focus on PA, exercise, and fitness as modifiable resilience factors that may help to promote self-regulation via strengthening of top-down control of bottom up processes in the brain; thereby acting as a buffer against mental health problems during this period of vulnerability. First, we briefly review the link between PA, exercise, and aerobic fitness with mental well-being and reduced mental health problems in adolescence. Then, we present how impairments in self-regulation, which involves top-down control to modulate bottom-up processes, are common across a wide range of mental health disorders. Finally, we utilize the extant neuroimaging literature to highlight how neural systems underlying top-down control continue to develop across adolescence, and propose that PA, exercise, and aerobic fitness may facilitate resilience through strengthening both individual brain regions as well as large-scale neural circuits to improve emotional and behavioral regulation. Future neuroimaging studies assessing the effects of PA/exercise and aerobic fitness at various developmental stages in each sex and those that consider the characteristics (e.g. frequency, intensity, type) and social context of PA/exercise are vital to better understand both macro and micro-scale mechanisms by which these behaviors and attributes may facilitate mental health resilience during adolescent development.

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## Keywords

self-regulation; prefrontal cortex; internalizing symptoms; externalizing symptoms; emotion; neurodevelopment

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## INTRODUCTION

Adolescence is the transition between childhood and adulthood, encompassing biological growth, social role transitions, and hormonal changes (1). It is also a period of enhanced brain plasticity and cognitive flexibility designed to promote learning in order to respond and adapt to new roles, environments, and encounters (2–4). As such, adolescence is often defined as both a period of opportunity and vulnerability (3). The developing adolescent brain can adapt and learn to establish behaviors important for mental well-being. However, the malleability of the adolescent brain may also render it vulnerable to maladaptive responses to mental stress. One in five adolescents experience mental health problems (5), with half of all lifetime diagnoses occurring by age fourteen (6). Mental health problems can generally be divided into externalizing disorders, including conduct and oppositional disorders and attention deficit-hyperactivity disorder (ADHD), and internalizing symptoms, including anxiety and depression (7). The prevalence of externalizing symptoms among adolescents is about 19% while internalizing symptoms affects between 14–32% of U.S. adolescents, with both symptoms displaying largely similar developmental trajectories across adolescence (8). Due to the negative health consequences of these mental health problems, understanding how the symptoms develop, their subsequent prevention, and alleviation are major public health targets.

In this narrative review, we focus on physical activity (PA), exercise, and fitness as modifiable brain resilience factors that promote neural processes of self-regulation, thereby acting as a buffer against mental health problems during this period of vulnerability (9–11). PA is defined as any bodily movement that increases energy expenditure above resting, and encompasses occupational, sports, conditioning, and other activities (12). Exercise, a subset of PA, is defined as planned, structured, repetitive, and purposive PA to improve or maintain physical fitness (12) – a set of physiologic attributes (e.g., body composition, muscle strength, balance, cardiorespiratory effects) related to the ability to perform PA and exercise that have a relationship with good health (13, 14). *Aerobic* fitness refers to maximal oxygen consumption ( $VO_2\text{max}$ ) (15), or the ability of circulatory and respiratory systems to deliver oxygen during activity, and is commonly interchanged with the term *cardiorespiratory* fitness (13).

PA, exercise, and aerobic fitness during adolescence are thought to confer resilience – defined here as ‘the ability to withstand, recover, or grow, in the face of stressors and changing demands’ (16). Importantly, this broader definition of resilience not only includes recovery, but also the ability of resistance towards disease onset. Specifically, this broader term is used here as PA, exercise, and aerobic fitness may each contribute to resilience in terms of both recovery and resistance against mental health issues. We use a cognitive-affective neuroscience framework and build upon the extant PA/exercise/fitness

neuroimaging literature in youth to propose that PA, exercise, and aerobic fitness promote resilience by strengthening self-regulation through top-down control of bottom-up processing. Thus, this focused narrative review integrates concepts across the fields of behavioral research and exercise physiology, mental health, and cognitive developmental neuroimaging to provide a mechanistic framework that expands our understanding of how PA, exercise, and fitness promote mental health resilience across adolescence using Magnetic Resonance Imaging (MRI) neuroimaging (for detailed reviews of each of these literatures, see (17–19)). Specifically, in this review we: (1) briefly review the link between PA/exercise/aerobic fitness and mental health in adolescence; (2) present that impairments in self-regulation via top-down control are common across many mental health disorders; and (3) utilize the extant neuroimaging literature to highlight how neural systems of top-down control continue to mature during adolescence and that PA/exercise and fitness may strengthen these neural systems to reduce vulnerability to mental health problems. Overall, we discuss how during adolescence the parallel increase in mental health problems alongside decreased PA/exercise and fitness may play an important role in affecting optimal development of these neural systems.

## RELATIONSHIPS AMONG PA, EXERCISE, AND FITNESS WITH MENTAL HEALTH IN ADOLESCENTS

The U.S. Physical Activity Guidelines recommend that youth ages 6–17 years accumulate at least 60 minutes of moderate-to-vigorous intensity PA per day for physical and mental health benefits (20). Recent systematic reviews and meta-analyses of study samples ranging from 20 to over 35,000 participants highlight the potential for PA to reduce and prevent symptoms associated with depression and anxiety, as well as ADHD and substance use disorders among youth (11, 18, 21, 22). Due to its wide-ranging benefits, exercise has also been proposed as a non-pharmacological treatment to alleviate depression (sub-clinical or clinical), anxiety, and externalizing disorders such as ADHD. Several recent reviews and meta-analyses of study samples ranging from 10 to 779 participants concluded that PA and exercise can improve internalizing and externalizing symptoms in youth (23–26), with depression and anxiety the two most-studied outcomes (27). However, relatively less is known about the role of fitness components and mental health in youth (28). One hypothesis is that higher levels of fitness components lead to greater mental well-being in youth (29, 30). Specifically, improvements in *aerobic* fitness are associated with better mental well-being (e.g., less depression; improved school and social functioning) in children and adolescents (30–34). Altogether these findings indicate that higher fitness levels, and low (40–54% of maximal heart rate (MHR) on VO<sub>2</sub>max test) and moderate (55–69% of MHR) intensity exercise buffer against internalizing and externalizing symptoms, particularly depression and ADHD. Recently, in an effort to increase the methodological quality of randomized control trials (RCTs) in this area, findings from a pilot study in 9–12 year-old children (N=27) suggested that the low-to-moderate intensity exercise intervention significantly reduced depressive and trait anxiety symptoms, whereas the high intensity intervention did not have any significant effects (35). However, limitations of prior studies include: a lack of experimental design with rigorous controls, a wide variety of exercise durations, intensities, and frequencies, little attention to the role of puberty or effects in

children under 16 years, and often no information provided on pre-trial PA or fitness levels – all of which may influence results.

Despite compelling evidence that PA/exercise and fitness are beneficial to mental health and may help to promote resilience in youth affected by mental health problems, the question remains as to *how* resilience is conferred. The potential mechanism(s) of these effects are likely multifaceted, and include stress-buffering effects, optimizing neuroendocrine and physiological responsiveness, reducing inflammation, and enhancing neuroplasticity (36, 37). In terms of the latter, below we discuss how PA/exercise may increase fitness components to confer resilience via ultimately promoting better self-regulation through structural and functional changes in how the brain may process and regulate information.

## SELF-REGULATION THROUGH TOP-DOWN PROCESSING AND MENTAL HEALTH

Self-regulation, broadly defined as the ability to “monitor and modulate cognition, emotion, and behavior” (38), occurs through the operation of two simultaneous ways in which we process information, known as top-down and bottom-up processes (Figure 1A). Bottom-up processes are more automatic and are derived from the sensory information provided by cues and stimuli in our environment, whereas top-down processes are more conscious and cognitively driven. This self-regulation framework involving two simultaneous information-processing systems has been useful for contemporary theories of emotional regulation (i.e. the ability to increase or decrease the intensity of an emotion in response to a given situation) and behavioral regulation (i.e. modulating behavior such as implementing executive function and/or self-control) (39). Considerable overlap exists in the neural circuitry that underlies such self-regulation capabilities, and dysregulation of information processing, including both emotional and behavioral regulation, has been identified as a potential risk phenotype of mental health disorders (40). Externalizing disorders are commonly conceptualized as dysfunction of top-down behavioral self-regulation, such as inattention, impulsivity, and hyperactivity, whereas other externalizing and internalizing disorders, such as conduct disorder, bipolar, anxiety, and depression, may reflect dysfunction of top-down emotional self-regulation (41). Although these disorders have traditionally been studied separately, impairment in self-regulation resulting in poor control of bottom up processes is thought to be a common transdiagnostic mechanism in individuals affected by mental illness (41, 42).

Depending on the type of cognitive information (e.g. emotion, memory, attention), a number of brain regions are involved in self-regulation at the neural level, including the prefrontal cortex (PFC), superior parietal lobe, and cerebellum (43, 44). In terms of top-down modulation of emotions, the orbitofrontal (OFC), ventral medial PFC (mPFC), and anterior cingulate cortex (ACC) are involved in a larger corticolimbic network, which helps to regulate bottom-up processing of emotional stimuli via the amygdala, ventral striatum, and hippocampus (45–47) (Figure 1B). The integration of top-down control over bottom-up emotional processes allows for better emotional control since the meaning assigned to emotional stimuli are not automatic, but rather are dependent on an individual’s experiences,

personality, and goals (48), thus allowing for adaptive strategies such as expressive suppression and cognitive appraisal (49). The PFC plays a significant and unique role during top down processing as it exerts both ‘modulatory’ and ‘directional’ influences over other brain regions involved in this intrinsic circuit. Top-down behavioral regulation also involves the dorsal lateral PFC (LPFC) and its interactions with brain regions involved in the larger frontoparietal network (FPN), including portions of the superior parietal lobe known as the intraparietal sulci (IPS) (50). The FPN supports key high-level cognitive tasks vital for self-regulation, including goal-directed attention and working memory, in order to flexibly interact with other cognitive and motor systems necessary for successful adaption of behavior depending on a current goal (51). Lastly, dorsal portions of the mPFC also interacts with the posterior cingulate (PCC) and the temporal parietal junction (TPJ) as part of the default mode network (DMN), which is most active at rest (i.e. absence of top-down and bottom-up processing and/or goal directed tasks), with primary functions including mentalizing, perspective-taking, and self-representation (52, 53). Unsurprisingly, poor PFC structural connectivity and dysfunction of these intrinsic large-scale networks (corticolimbic, FPN, DMN) involved in top-down control are common features seen in those affected by mental health problems and are thought to be a transdiagnostic risk factor (51, 54–56).

## **PA/EXERCISE AND FITNESS FACILITATE RESILIENCE BY STRENGTHENING BRAIN SELF-REGULATION MECHANISMS DURING ADOLESCENCE**

PA and exercise may act as resilience factors by exerting neuroplastic effects via promoting structure and function of neural circuits involved in self-regulation that are continuing to develop during adolescence. The key brain regions involved in emotional and behavioral self-regulation are not fully developed at birth, and continue to develop across childhood and adolescence (2, 4). Cortical regions that process sensorimotor information as well as the subcortical limbic structures (i.e. amygdala, hippocampus, and striatum) (57) involved in bottom-up emotional processing mature prior to the protracted development of the PFC which is uniquely involved in top-down control processing (2, 4). Therefore, there is a tentative bias towards bottom-up processing as the relatively immature PFC is building and refining its role in supporting top-down control capabilities to regulate emotions and behavior (2). Beyond structural changes to the PFC, structures involved in the large-scale corticolimbic, FPN, and DMN brain networks (58), and white matter pathways sub-serving these networks (59), continue to mature across childhood and adolescence (60). That is, there is increased coordination of higher order cognitive processes in adolescents (61, 62) and age-related differences are seen in functional connections between the PFC and amygdala within the corticolimbic network (63). Structural and functional developmental changes in the PFC and integration with the structures of these related intrinsic large-scale networks ultimately lead to progressive improvements in key components of cognitive control, including working memory and attention to relevant, but inhibition of irrelevant, stimuli in adolescents (64, 65). Furthermore, the development of these top-down processes allows for the ability to control bottom-up reactions to external cues that foster essential mental strategies for adaptive cognitive and emotional functioning (57, 66–68). Importantly,

this early maturation of bottom-up brain regions (i.e. sensorimotor, limbic) relative to the protracted top-down brain areas (i.e. PFC, superior parietal lobe, etc.) overlap with the developmental timing in which mental health problems begin to emerge during the adolescent years (Figure 2A/B). Coincidentally, an age-related decline in PA and exercise occur during this same transition from childhood to adolescence (69–71) (Figure 2C). Building upon the extant cross-sectional and RCT PA, exercise, and fitness studies using MRI (Table 1), we hypothesize that PA, exercise, and fitness may positively affect PFC brain structure and function, along with intrinsic large-scale networks (corticolimbic, FPN, DMN), to allow for better top-down control as a potential neural mechanism of resilience against mental health problems during adolescence (Figure 3).

Cross-sectional studies have linked aerobic fitness with cortical gray matter morphometry in the PFC, as well as motor, parietal, superior temporal and occipital regions (72–76) and greater white matter volume in inferior fronto-opercular, inferior temporal, cingulate, and middle occipital and fusiform gyri in youth; although findings have been mixed (77, 78). Aerobic fitness has also been linked to larger subcortical volumes, including the hippocampus (73, 78, 79) and basal ganglia (73, 76, 80), as well as improvements in hippocampal-dependent processes, such as memory encoding (81) and working memory (82, 83). These regions and white matter connections uniquely contribute to various aspects of self-regulation including: goal-oriented behavior and thought (e.g. inferior fronto-opercular) (84–89), voluntary motor control and inhibition (e.g. basal ganglia) (90), emotion and behavior regulation (e.g. cingulate) (91) as well as valence of visual stimuli (e.g. inferior temporal) including faces via the fusiform (92). Hippocampal volumes have also been found to mediate the association between PA (e.g., sports participation) and depression symptoms among male children (93). In addition to brain structure, the structural connectivity between brain regions, as measured by diffusion weighted MRI (DWI), is an important component to the aforementioned larger scale networks that are involved in emotional and behavioral self-regulation. Cross-sectional studies suggest PA is related to overall greater fractional anisotropy (FA) (94, 95) across the entire brain. Moreover, aerobic fitness as well as RCT studies have linked exercise to differences in FA within specific white matter tracts, including: the superior corona radiata (SCR) and superior longitudinal fasciculus (SLF) that are long range tracts connecting the PFC to other brain regions such as the superior parietal lobe; the corpus callosum (CC) (96–99) that integrates motor, sensory, and cognitive processes between the two hemispheres (100); the uncinate fasciculus (UF) (101) that connects the PFC to corticolimbic regions, such as the hippocampus and amygdala (102); and in the motor (corticospinal) tract (103). Thus, as the identified white matter structural pathways linked to PA and exercise innervate the PFC and sub-serve cognitive functioning (e.g. CC, SLF, SCR) (88, 104, 105) and emotional systems (e.g. UF) (106), these findings may suggest that regular exercise may exert widespread effects on PFC white matter connectivity to strengthen top-down control systems that are involved in behavioral regulation. Notably, these exercise-related differences in PFC structure, connectivity with other self-regulatory brain regions, and hippocampal volumes and associated behaviors overlap with brain regions and cognitive functions involved in the larger-scale functional networks such as the DMN and FPN.



A few initial cross-sectional and RCT studies of brain function and blood flow also support the notion that exercise may influence neural resources required for top-down control (107–111) and learning (112) among youth. Lower-fit children demonstrate different patterns of activation in somatosensory, insula, ACC, parietal, and the middle PFC during tasks of sustained attention and inhibition (108, 110), and two RCTs found exercise resulted in differences in PFC activity during the anti-saccade task (109, 113). Another cross-sectional study found that lower-fit adolescent males had lower activity in PFC regions, as well as impaired decoupling of the hippocampus to the DMN when encoding new memories compared to their higher-fit peers (112). Beyond task activation, two additional studies provide initial evidence that aerobic fitness may influence intrinsic functional organization of large-scale networks, including resting-state brain activity patterns in the DMN, cognitive control (i.e. notably similar to the FPN described here), and motor networks (107), as well as increased cerebral blood flow to the hippocampus (114). Thus, exercise-related differences are found in the DMN at rest and in various FPN regions during goal-directed top-down cognitive tasks, like paying attention, inhibiting a motor response, or learning new memories.

Taken together, structural and functional MRI findings suggest that PA and exercise may confer resilience at the neural level through structure and function of the PFC, as well as potential integration and refinement of the PFC with other brain regions involved in large-scale networks, such as the FPN, DMN, and corticolimbic systems. In turn, strengthening these systems to improve top-down control of bottom-up processes may ultimately lead to enhanced modulation of behavioral self-regulation such as attention or impulse control, as well as emotional self-regulation of positive and negative emotionality and/or emotion-expressive behavior. Specifically, exercise-related improvements in FPN activation and DMN deactivation may enhance attention, inhibition, and working memory capacities, ultimately increasing the capacity to change one's attention, suppress negative affect, and/or implement cognitive reappraisal strategies to modify duration and/or intensity of undesirable or aversive feelings. Improved cognitive control may also promote a healthier self-concept, higher self-esteem, and/or advanced coping and problem-solving skills which could also be protective (115, 116). Thus, PA and exercise may refine these key neural systems, offering reductions in internalizing and externalizing symptoms via increased cognitive control, ultimately decreasing risk for mental health problems during the vulnerable adolescent developmental period.

## **FUTURE STUDIES TO INVESTIGATE THE LINK BETWEEN PA/EXERCISE, SELF-REGULATION VIA TOP-DOWN CONTROL, AND MENTAL HEALTH RESILIENCE**

Using the extant PA/exercise/fitness and MRI literature as well as a cognitive-affective neuroscience framework, we propose increased PA/exercise and improved fitness may facilitate self-regulation via improved top-down control over more prominent de facto bottom-up processes during adolescence as a potential resilience mechanism to promote well-being and mitigate risk for mental health problems. Additional multi-disciplinary studies are necessary to directly assess this plausible neural mechanism. As such, we

highlight key considerations for future studies that are needed to address the remaining fundamental questions (Supplement Box 1) as to how PA/exercise and fitness impact brain development to better identify the neural mechanism(s) that promote resilience during adolescence.

### **1. Possible developmental and sex-specific effects:**

The studies to date have included mostly children and/or pre-adolescents (see age details in Table 1). Given that the brain is malleable with dynamic patterns of brain maturation across childhood and adolescence (4, 59, 117), it is likely that PA and exercise may modify brain structure and function of particular neural circuitries based on the age and/or developmental stage and the sex of the individual. Since the PFC and self-regulation are still undergoing dynamic growth as individuals' transition from childhood to adulthood, PA and exercise may have larger effects on these systems in adolescence as compared to other periods of the lifespan. In addition, sex differences in mental health problems emerge during the transition from childhood to adolescence, with increased internalizing problems in females and increased externalizing problems in males (118, 119). Interestingly, some evidence suggests that the age-related PA decline during the transition from childhood to adolescence (69–71) are steeper and begin earlier in females as compared to males (120, 121). This is important because sex differences in PA and exercise levels may also contribute to sex differences seen in mental health prevalence rates (9–11). Compounding the challenge of understanding developmental and sex effects of PA/exercise and risk for mental health problems during adolescence, are the physical and hormonal changes that occur with puberty. The timing of pubertal maturation (e.g., maturing earlier vs. same time/later to peers) has been theorized to contribute to the development of internalizing symptoms in females (122–124), and sex differences in brain maturation (125–128) have been linked to pubertal maturation (126, 129). Differences in rising levels of sex steroids in males and females (e.g. testosterone, estradiol) may also contribute to sex differences in brain development that may lead to the prevalent imbalance of internalizing versus externalizing symptoms that are seen between females and males. Yet few of the PA and exercise neuroimaging studies have reported on the pubertal development of their samples (see Supplemental Material). Studies are needed to help disentangle how sex differences in PA/exercise, patterns of brain maturation, and pubertal processes may uniquely combine to contribute to risk versus resilience of mental health problems in males and females during adolescence.

### **2. Multi-modal MRI to assess changes in large-scale networks and self-regulation with PA and exercise:**

The aforementioned MRI studies suggest PA/exercise and aerobic fitness are associated with key structural and functional changes in brain regions, such as the PFC and hippocampus, in children and adolescents. Future MRI studies are needed to more fully characterize how PA and exercise affect large-scale networks, including those that involve PFC-related circuitry to implement top-down control. In addition, despite the compelling literature on PA, exercise, and emotional well-being, it surprisingly remains unknown if PA and exercise impact brain structure and function of the corticolimbic system and brain activity patterns of emotional regulation across adolescence. Future studies are needed beyond examining a specific brain region and/or behavioral construct to more fully examine how PA and exercise



influence large-scale networks of cognitive control and emotional processing, with a focus on targeting already identified transdiagnostic functional and structural phenotypes (130). PA and exercise intervention studies should consider using both resting-state protocols as well as fMRI tasks that directly assess changes to self-regulatory systems that contribute to emotional self-regulation and bias, such as emotional Stroop or emotional reappraisal tasks (131–133). Given that internetwork communication continues to integrate with age across development (60, 117), PA and exercise may promote PFC integration into the corticolimbic and FPN networks to facilitate self-regulation via strengthening top-down control abilities. For example, acute exercise in both young and old adults show that just 30 minutes of moderate intensity exercise results in synchrony among brain regions involved in the corticolimbic, FPN, and DMN (134). It is likely that this pattern may also hold true for adolescents; yet the consequences of continual PA and exercise may be more long-lasting in that the adolescent brain is continuing to mature and largely remains under construction. Strengthening such top-down systems during development could ultimately lead to improvements in impulse control, inhibition of thoughts and actions, and modulation of intense emotions – all of which are important to self-regulation and may ultimately help mitigate risk for emotional health problems during this critical period of maturation.

### **3. Understanding how PA/exercise and fitness characteristics optimize mental health benefits:**

The type (i.e. aerobic, strength), frequency, and intensity of PA/exercise that may be optimal for promoting resilience during adolescence remains unknown. In addition, in order to better address potential confounders, future studies need to provide more details on baseline participant characteristics beyond those related to mental health, such as general PA, sports participation, and fitness levels. Although beyond the scope of this review, there are also multiple behavioral and neurocognitive mechanisms that link aerobic fitness and mental health in youth (e.g., higher fitness leads to greater participation in social activities that help develop relationships; higher self-efficacy and esteem for activity behaviors; and greater social and problem-solving skills) that may promote resilience. In addition, the question remains of how the prosocial context of PA/exercise and fitness level may reduce mental health symptoms in both sexes -- albeit through potentially different psychosocial avenues. For example, team sports may provide benefits beyond individualized sports through positive social interactions with peers that provide social support and increase self-esteem (135–137). Both cross-sectional (138) and longitudinal (139) studies indicate that adolescents who participate in team sports report greater mental/emotional well-being (135, 140), compared to those who participate in individual sports. A recent meta-analysis highlighted domain-specific (e.g., PA for transportation vs. PA in physical education class) benefits of PA which are likely due to the interplay of multiple psychosocial and biological mechanisms (141). Additionally, sex differences may exist in how the prosocial environment of PA and exercise may uniquely promote well-being and mental health. Organized sports emphasizing competition may provide emotional benefits for males (142, 143), while physical education classes emphasizing self-efficacy and mastery may be more beneficial for females (142). The emotional benefits of PA and exercise may also be maximized when the behavior is intrinsically motivated (e.g., engaging in PA/exercise for inherent feelings of pleasure and accomplishment) (144–146). In the context of PA, young males may be more

intrinsically-motivated to be active and therefore derive more pleasure from activity compared to young females, who may be more extrinsically-motivated (viewing PA as a means to an end goal, i.e. weight maintenance) (147, 148). A greater understanding of the relative contribution of each of the different mechanisms at hand will maximize the benefit of PA/exercise and provide more evidence that PA and exercise can act as resilience factors against mental health symptoms.

## CONCLUSION

PA/exercise and fitness during adolescence are linked to brain structure and function implicated in cognitive and emotional systems associated with mental health. With many unanswered questions concerning these behaviors, attributes, and resilience during this sensitive period of adolescent development, future research is necessary to determine if neuroplastic effects of PA/exercise may lead to resilience of mental health problems via integration of the PFC and related circuitry into large-scaled cognitive and emotional systems, including top-down control of bottom-up processes. Initial neuroimaging studies suggest PA/exercise and fitness may be vital to both healthy brain development as well as mental health among adolescents worldwide. Across borders and cultures, PA/exercise and fitness likely play a crucial role in helping the adolescent brain flourish.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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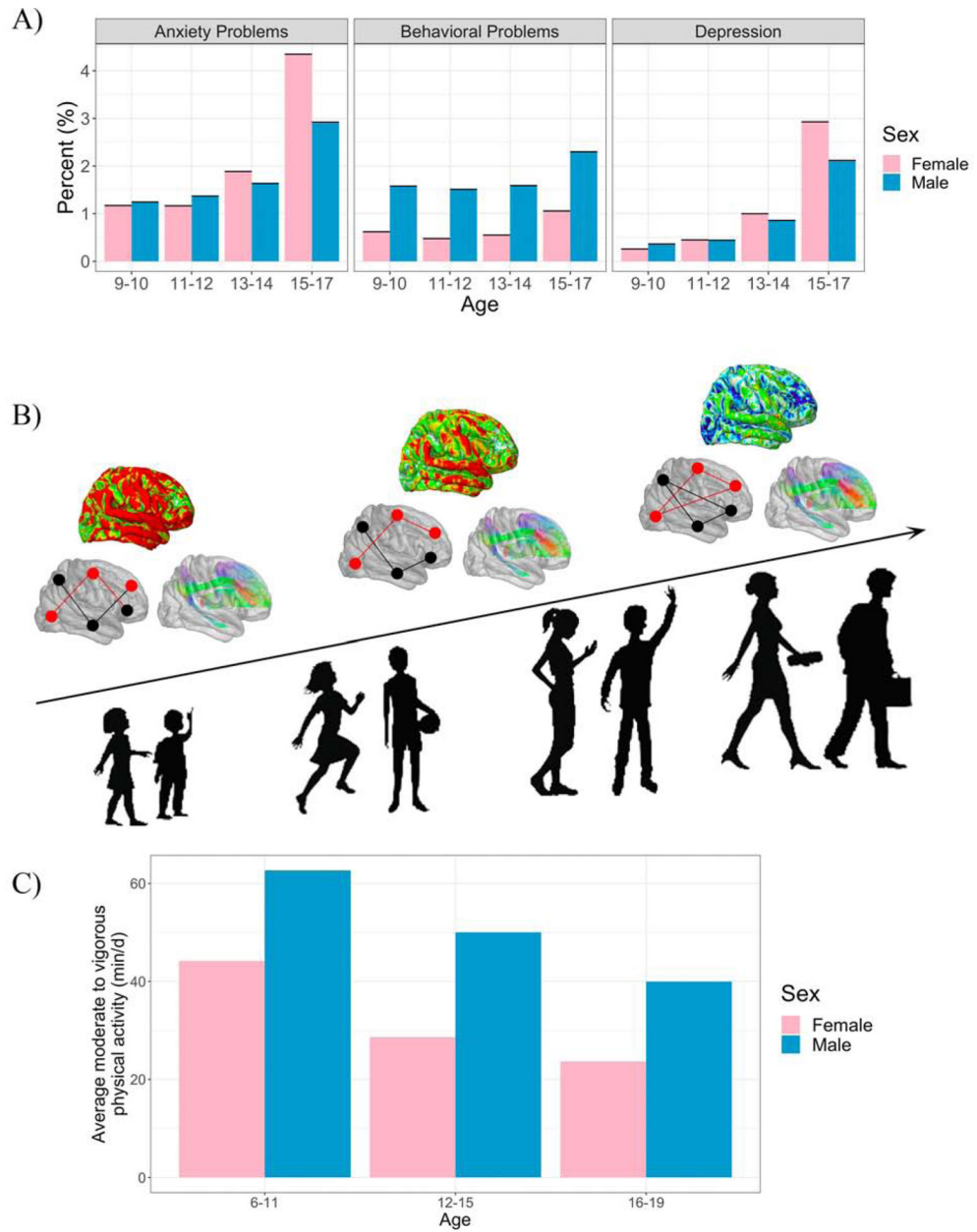
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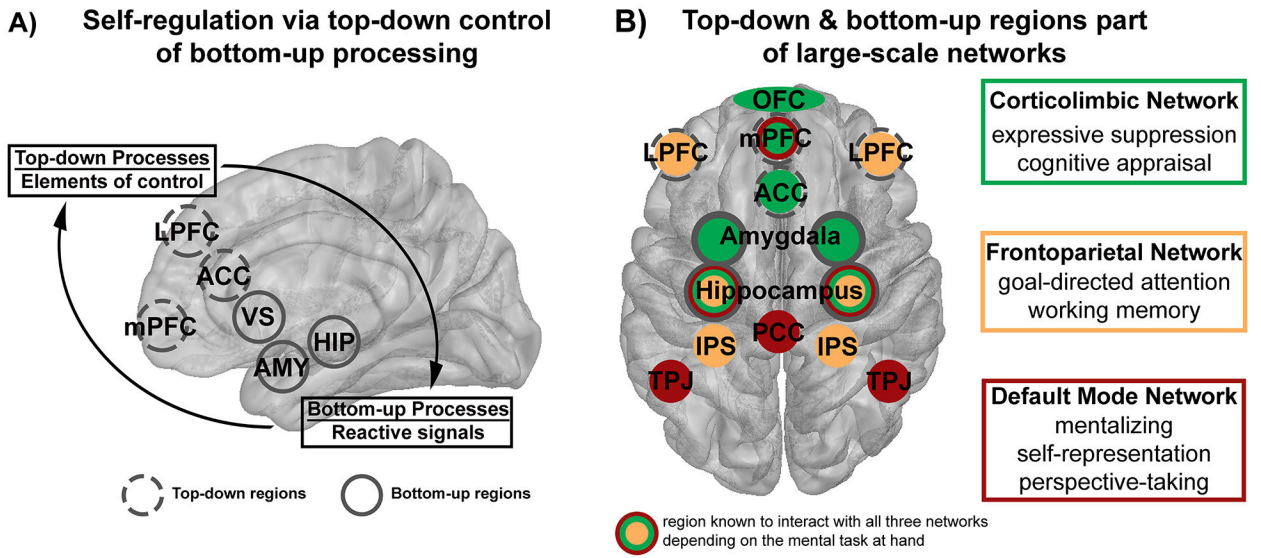
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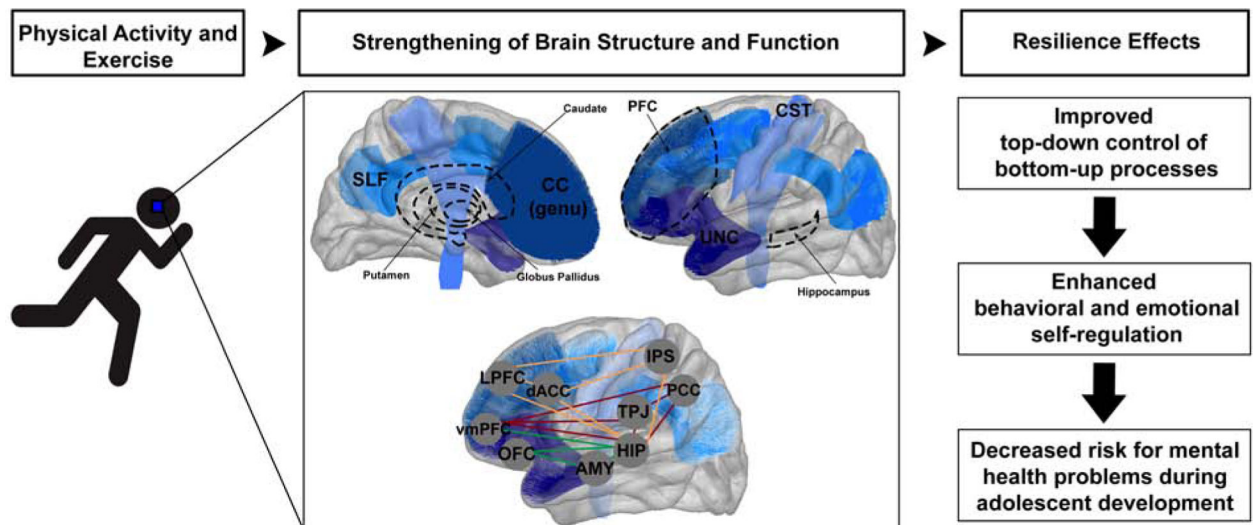
**Figure 1.**

A) Schematic of the prefrontal cortex’s role involved in emotional and behavioral self-regulation through top-down (dashed circles) and bottom-up (solid circles) processes and B) Brain regions involved in top-down and bottom-up processing interact with other brain regions as part of large-scale networks, such as the cortic limbic (green), frontoparietal (yellow), and the default mode (red) networks to generate complex thoughts and behaviors. Abbreviations: LPFC: lateral prefrontal cortex; mPFC: medial prefrontal cortex; ACC: anterior cingulate cortex; AMY: amygdala; HIP: hippocampus; VS: ventral striatum; IPS: intraparietal sulcus; TPJ: temporoparietal junction; PCC: posterior cingulate cortex; OFC: orbitofrontal cortex



**Figure 2.** Schematic of emotional, neurodevelopment, and physical activity changes that occur simultaneously across adolescence. A) Prevalence of behavioral problems and internalizing disorders emerge with age across adolescence (based on data from the 2018 National Survey of Children’s Health (149)). B) Regional and network specific changes occur in structural and functional brain maturation, including decreases in cortical thickness (red to blue), increases in white matter development (bundle thickness), and refinement of functional brain networks (circles, lines). C) Meanwhile, moderate to vigorous physical activity levels significantly decline as children transition into adolescence (based on data from the 2003–2006 National Health and Nutrition Examination Survey (69)). Images were created using the QIT software package (150).





**Figure 3.**

Theoretical model as to how PA/exercise and fitness impacts brain structure and function to promote resilience against mental health problems during adolescence. MRI studies in children and adolescence have shown PA/exercise and fitness relate to white matter fiber tracts (blue) and morphometric and brain activity differences in specific brain regions (dashed lines). We hypothesize that these structural and functional differences occurring with PA and exercise (to enhance fitness) may contribute to resilience against mental health problems through facilitating the integration of top-down control of bottom-up processes within the large-scale corticolimbic (green), frontoparietal (yellow), and default mode (red) networks to enhance behavior and emotional self-regulation during adolescent development. Abbreviations: CC: corpus callosum; SLF: superior longitudinal fasciculus; CST: corticospinal tract; UNC: uncinate fasciculus; PFC: prefrontal cortex; LPFC: lateral prefrontal cortex; vmPFC: ventromedial prefrontal cortex; dACC: dorsal anterior cingulate cortex; AMY: amygdala; HIP: hippocampus; VS: ventral striatum; IPS: intraparietal sulcus; TPJ: temporoparietal junction; PCC: posterior cingulate cortex; OFC: orbitofrontal cortex

**Table 1.**

Cross-sectional and intervention studies of physical activity (PA), exercise (EX), or aerobic fitness (AF) and brain MRI in children and adolescents. Abbreviations: RCT: randomized control trial; sMRI: structural MRI; DWI: diffusion weighted imaging; fMRI: functional MRI; ASL: arterial spin labeling; TBSS: tract-based spatial statistics; ROI: region of interest

AUTHOR	YEAR	STUDY DESIGN	SAMPLE SIZE	AGE	PA/ EX/ AF	MRI TYPE	BRAIN ANALYSIS	BRAIN OUTCOME
Chaddock (79)	2010	Cross-sectional	N=49, 59% Female	9–10 years	AF	sMRI	ROI: hippocampus, NAc	Volume
Chaddock (80)	2010	Cross-sectional	N=55, 55% Female	9–10 years	AF	sMRI	ROI: dorsal striatum (caudate nucleus and putamen), ventral striatum (NAc), and globus pallidus	Volume
Herting (78)	2012	Cross-sectional	N=34, 0% Female	15–18 years	AF	sMRI	ROI: hippocampus, total gray and white matter	Volume
Chaddock-Heyman (72)	2015	Cross-sectional	N=48, 54% Female	9–10 years	AF	sMRI	ROI: frontal (anterior, middle, superior), parietal (superior, inferior), temporal (superior, middle, inferior), and lateral occipital regions	Cortical thickness
Herting (75)	2016	Cross-sectional	N=34, 0% Female	15–18 years	AF	sMRI	Whole brain	Cortical thickness, surface area, volume
Esteban-Cornejo (73)	2017	Cross-sectional	N=101, 41% Female	8–11 years	AF	sMRI	Whole brain gray matter	Volume
Esteban-Cornejo (74)	2019	Cross-sectional	N=101, 41% Female	8–11 years	AF	sMRI	ROI: frontal (right premotor cortex, right supplementary motor cortex, and left IFG), temporal (left IFG, right parahippocampal gyrus, and right superior temporal gyrus), and occipital (right calcarine cortex) regions	Cortical thickness, surface area
Esteban-Cornejo (77)	2019	Cross-sectional; Two samples	1) N = 100, 40% Female	1) 8–11 years	AF	sMRI	Whole brain white matter	Volume
			2) N = 142, 55% Female	2) 7–9 years	AF	sMRI	Whole brain white matter	Volume
Gorham (93)	2019	Cross-sectional	N=4191, 48% Female	9–11 years	PA	sMRI	ROI: hippocampus	Volume
Ruotsalainen (76)	2019	Cross-sectional	N=60, 67% Female	12–16 years	PA; AF	sMRI	ROI: putamen, pallidum, caudate, NAc, thalamus, and hippocampus; paracentral lobule, postcentral gyrus, posterior cingulate cortex, precentral gyrus, superior frontal gyrus, lateral OFC, ACC (rostral anterior and caudal anterior division), MFG (rostral and caudal divisions), and medial OFC (medial OFC and frontal pole)	Volume
Chaddock-Heyman (96)	2014	Cross-sectional	N=24, 38% Female	9–10 years	AF	DWI	TBSS; Tractography ROIs: CC, corona radiata, SLF, posterior thalamic	White matter microstructure

AUTHOR	YEAR	STUDY DESIGN	SAMPLE SIZE	AGE	PA/ EX/ AF	MRI TYPE	BRAIN ANALYSIS	BRAIN OUTCOME
							radiation, and cerebral peduncle	
Herting (103)	2014	Cross-sectional	N=34, 0% Female	15–18 years	PA; AF	DWI	TBSS; Tractography ROIs: forceps major and minor, arcuate fasciculus, anterior thalamic radiation, corticospinal tract, inferior fronto- occipital fasciculus, ILF, UF	White matter microstructure
Krafft (98)	2014	RCT	N=18, 50% Female	8–11 years	EX	DWI	Tractography ROI: SLF	White matter microstructure
Schaeffer (101)	2014	RCT	N=18, % Female Not Reported	8–11 years	EX	DWI	Tractography ROI: UF	White matter microstructure
Chaddock-Heyman (97)	2018	RCT	N=143, 51% Female	7–9 years	EX	DWI	TBSS; Tractography ROIs: CC, corona radiata, SLF, posterior thalamic radiation, and UF	White matter microstructure
Rodriguez-Ayllon (95)	2019	Cross-sectional	N=103, 41% Female	8–11 years	PA	DWI	Tractography ROI: cingulum, corticospinal tract, forceps major and minor, ILF, SLF, UF	White matter microstructure
Rodriguez-Ayllon (94)	2020	Cross-sectional	N=2532, 50% Female	10 years	PA	DWI	Whole brain tractography	White matter microstructure
Ruotsalainen (99)	2020	Cross-sectional	N=59, 66% Female	12–16 years	PA; AF	DWI	TBSS ROI: body and genu of CC, the bilateral superior corona radiata, the bilateral SLF and the bilateral UF	White matter microstructure
Davis (109)	2011	RCT	N=20, 40% Female	7–11 years	EX	Task fMRI	ROI: frontal eye field, supplementary eye field, PFC, posterior parietal cortex	Anti-saccade
Voss (110)	2011	Cross-sectional	N=28, 53% Female	9–10 years	AF	Task fMRI	Whole brain; ROI: ACC, post-central gyrus, pre-central gyrus, left superior parietal lobule, SMA, precuneus, left central opercular cortex, left insular cortex, left temporal lobe, left putamen, left thalamus, left frontal pole, left MFG	Flanker
Chaddock (108)	2012	Cross-sectional	N=32, 50% Female	9–10 years	AF	Task fMRI	Whole brain; ROI: left MFG, right MFG, SMA, ACC, left and right superior parietal lobule	Flanker
Chaddock-Heyman (111)	2013	RCT	N=23, 57% Female	8–9 years	EX	Task fMRI	ROI: right anterior PFC, ACC	Modified Flanker with Nogo trials
Herting (112)	2013	Cross-sectional	N=34; 0% Female	15–18 years	AF	Task fMRI	ROI: hippocampus	Verbal Associative Learning
Krafft (113)	2014	RCT	N=43, 65% Female	8–11 years	EX	Task fMRI	Whole brain	Anti-saccade & Flanker
Krafft (107)	2014	RCT	N=22, 67% Female	8–11 years	EX	Resting state fMRI	ROI of 4 networks: default mode, salience, cognitive control, and motor	Cognitive, Default, & Motor Networks

AUTHOR	YEAR	STUDY DESIGN	SAMPLE SIZE	AGE	PA/EX/AF	MRI TYPE	BRAIN ANALYSIS	BRAIN OUTCOME
Chaddock-Heyman (114)	2016	Cross-sectional	N=73, 56% Female	7–9 years	AF	ASL	ROI: hippocampus, brainstem	Cerebral blood flow

NAc, nucleus accumbens; OFC, orbitofrontal cortex; CC, corpus callosum; MFG, middle frontal gyrus; ACC, anterior cingulate cortex; PFC, prefrontal cortex; SMA, supplementary motor area; SLF, superior longitudinal fasciculus; ILF, inferior longitudinal fasciculus; UF, uncinate fasciculus; IFG, inferior frontal gyrus;

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