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#### A Developmental Science Perspective on Investing in Adolescence

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#### Preface:

This review summarizes the case for investing in adolescence as a period of rapid growth, learning, adaptation, and formational neurobiological development. Adolescence is a dynamic maturational period when young lives can pivot rapidly—in negative and positive directions. Scientific progress in understanding adolescent development provides actionable insights into windows of opportunity where policies can have a positive impact on developmental trajectories of health, education, social, and economic success. Given current global changes and challenges affecting youth, there is a compelling need to leverage these advances in developmental science to inform strategic investments in adolescent health.

#### Introduction:

It is well-recognized that the first few years of life represent a sensitive period for growth, early learning and brain maturation <sup>1</sup>. Accordingly, this scientific understanding of the formational effects of early experience has had significant impact on global policies and practices <sup>2,3</sup>. Recent scientific advances are now contributing to the growing recognition that adolescence is a second period of rapid growth and foundational learning associated with a distinct neuro-maturational changes<sup>4,5</sup>. There is great potential for leveraging these advances to inform strategies for investing resources during this pivotal time in the life course<sup>6,7</sup>.

Notably, the global stakes for choosing to invest in adolescence are increasing. Global demographics reveal a disproportionate surge in the number of adolescents in the world, including an unprecedented expansion of youth in low income regions. More than a billion adolescents are now coming of age amidst an accelerating array of social changes and global challenges. The revolutionary changes in information technology that are sweeping across the globe are having their greatest impact on adolescents. They are often the early adopters of new technology in ways that can amplify vulnerabilities (e.g., exploitation, radicalization) as well as opportunities (education, social connection, innovation, learning). These accelerating technological and social changes magnify the importance of understanding how (and when) to intervene to prevent harmful effects and to promote health.

In this review, we present a developmental science perspective on adolescence as a distinct maturational period that begins with the onset of puberty. Developmental science is the study of the patterns and processes of biological, cognitive, and behavioral changes that occur as an organism grows and matures. Here, we summarize our current understanding of developmental processes that occur during and subsequent to puberty. We describe some of the distinctive aspects of learning in adolescence that are thought to support acquisition of the culturally embodied knowledge, skills, and self-regulatory capacities needed to become independent and to integrate into adult society. We explore how a nuanced understanding of the distinctive features of this developmental period may inform intervention and policy, especially the developmental changes in learning and exploration that are amplified during adolescence. We specifically highlight the role that pubertal hormones may play in enhancing the motivational salience of status, prestige, and sex as important drivers of social learning and identity developmental science to inform intervention and policy—particularly in light of current global challenges.

#### **Puberty Begins a Distinct Developmental Period**

Adolescence encompasses the myriad developmental changes and foundational learning experiences that occur in the transition from childhood to the attainment of adulthood. This transition begins with onset of puberty—a biological process that drives sexual maturation, typically starting by age 10 in girls and by age 12 in boys (see Figure 1). Puberty begins with changes in the brain, which initiate a cascade of transformational changes in the body that include: rapid acceleration in physical growth (pubertal growth spurt), metabolic changes, changes in sleep and circadian regulation, and sexual maturation (i.e., sex-specific changes in facial structure, voice, muscle and fat distribution, body hair distributions, changes in skin and glandular secretions, breast, genital, adrenal and gonadal development)<sup>8</sup>. Hormones released from the gonads and adrenals, in turn, impact the brain, altering cognitive, emotional, and motivational processes that is sexually differentiated, testosterone and estrogens can be found in the brain and blood of both males and females with variable, and sometimes overlapping concentrations).

Developmental changes during adolescence also include structural and functional changes in the brain particularly neural systems involved in cognitive, emotional, social, and motivational processes <sup>4,9,10</sup>. These neural changes are associated with behavioral changes such as increases in sensation-seeking and a re-orientation of attention and motivation (toward peers, social evaluation, status and prestige, and sexual and romantic interests)<sup>11,12</sup>. Adolescent development also involves profound changes in social contexts, social roles, and social responsibilities<sup>13</sup>. Importantly, there are complex *interactions* between and among these levels of change. Indeed, learning and brain development are inextricably intertwined throughout this period as learning affects brain development, and maturational changes in the brain in turn affect learning and motivation.

#### [Insert Figure #1: Puberty initiates a period of rapid growth and multi-level dynamic change]

The endpoint of adolescence is considerably more difficult to define scientifically. Becoming an adult cannot simply be equated with a measure of physical maturation such as attaining final adult height or reproductive maturity. There have been some recent attempts to define the end of adolescence in terms of cognitive and affective processes<sup>14</sup>. However, 'adulthood' is inherently intertwined with taking on certain social roles—and importantly, having the knowledge, skills, and social competence to succeed in these roles. It also involves societal recognition that the individual has the rights (and responsibilities) to exercise these roles. As a pragmatic matter, modern societies typically confer adult rights and responsibilities based on age. However, this is at best an approximate way to estimate maturation especially during adolescence when punctuated growth processes can result in dramatically different maturational development between individuals of the same age. Moreover, laws can vary widely (within and across countries) regarding which age is used to designate specific adult rights, roles, or responsibilities (e.g., the legal age for driving a car, voting in an election, marriage, serving in the armed forces, being sanctioned as an adult for committing crimes, using alcohol, cigarettes or other drugs, making personal decisions about health, owning a gun)<sup>15</sup>. Typically, these legal frameworks are primarily informed by cultural (and sometimes religious) values, rather than evidence about the developmental effects of exposure to particular learning experiences and independent decision making at different stages of development<sup>16</sup>.

#### Learning, Development, and Maturation in Adolescence

Adolescent development builds on considerable childhood learning, and allows us to acquire a new level of knowledge, skills, and cultural competence to successfully transition to an independent adult role. In adolescence, we gain cognitive, affective, and self-regulatory abilities that allow us to adaptively pursue new goals and priorities that can be increasingly abstract and extend far into the future <sup>4,17</sup>. We gain more nuanced understanding of the workings of adult society, which involves learning to reason about abstract concepts, future consequences, and a more mature understanding of self, others, and the complexities of adult social relationships <sup>17-21</sup>. We also acquire skills to navigate a growing range of novel, uncertain, and emotionally charged social situations (including a new level of cognitive, social, emotional and self-regulatory capacities <sup>22</sup>) and to apply these skills to an increasingly complex set of social relationships with peers, adults, and societal institutions.

In addition, in adolescence we also must adapt to fundamentally new aspects of our own emerging identity<sup>23</sup>, which includes learning how to relate to the world, and ourselves, as a suddenly and (often) mystifyingly sexual being<sup>24</sup>. We must discover in a new way—through an elaborate series of trials and errors, successes and failures, and with growing independence—who we are. That is, we must develop (within a family, cultural, and social context) an adult identity, with our own heartfelt goals, values, and priorities.

As supported by a large body of evidence, this developmental traverse from being a child to becoming an adult is fraught with a multitude of risks and vulnerabilities. These contribute to an enormous amount of death and disability through adolescent accidents, suicide, violence, depression, alcohol and substance use, sexually transmitted diseases, unwanted pregnancies, as well as the establishment of a wide range of health-related behavioral risk factors (such as smoking, drinking, substance use, unhealthy eating, and sedentary behavior) that will contribute to later lifetime health consequences <sup>25</sup>. Pivotal changes in educational trajectories during adolescence have increasingly important lifetime consequences, with educational attainment impacting career options and economic success<sup>15</sup>.

#### The Rapidly Changing World of Adolescence

We currently are witnessing dramatic and historically unprecedented changes in the demography and lifestyle of adolescents<sup>15</sup>. In 2015, the estimated global population of adolescents aged 10–19 years was 1.2 billion, which is approximately 16% of the world's population<sup>26</sup>. The vast majority of the world's adolescents—approximately 90%—live in lower- and middle-income countries (LMICs) where the barriers to achieving positive health and well-being are often the most complex and challenging. As such, nations that are already finding meeting the educational and health needs of adolescents challenging are likely to need increased resources to address these issues in the near future.

Technological innovations, especially in mobile computing (e.g., smartphones) and online social networks, are transforming the daily lives of adolescents <sup>27-29</sup>. Today's adolescents in middle and highincome countries are "digital natives"—individuals who have never experienced the world before the internet. The social capabilities of internet enabled devices tap into core adolescent motivations in powerful ways. Adolescents are particularly motivated to explore peer relationships, and social media provide almost ubiquitous access to these interactions<sup>29</sup>. Moreover, it provides these opportunities in ways that are particularly appealing to adolescents—relatively free of the reach of parental monitoring<sup>30</sup>. This creates unprecedented opportunities for positive social connection and support (e.g., the isolated teen who finds a community of like-minded individuals online), but it also intensifies adolescents' exposure to negative social encounters (e.g., ostracism, bullying, sexual exploitation, and violent radicalization). Adolescents' emerging interests in sex and sexuality are now met with an almost unlimited supply of free streaming highly explicit pornography. Importantly, these technologies can also add to the "digital divide", whereby social inequalities between those in well-sourced contexts (where parents, teachers, and social influences help to scaffold adolescents' learning and use of technology) and those growing up in impoverished contexts (who may be more vulnerable to the negative effects) are exacerbated <sup>31</sup>.

Other factors are also rapidly altering the lives of adolescents. Today, adolescents enter into puberty earlier, and take on independent adult roles (e.g., finishing formal education and entering the workforce, living apart from their family of origin, becoming fully financially independent) later than they did in past centuries, making adolescence a longer period of life than it was previously<sup>32</sup>.

Economically, adolescents increasingly take on the role of active consumers, with their own disposable cash and credit accounts making them independently responsible for purchasing decisions <sup>33</sup>. As a result, adolescents are now the direct target of marketing efforts (including marketing of financial products) that no longer need to be filtered through parental control. Although many of these secular changes are particularly pronounced for adolescents living in high income countries, the environment in LMICs is rapidly changing to reproduce these phenomena, often in contexts where there is less education and regulation to buffer their potentially deleterious effects (e.g., the rapid changes in point of sale advertising for alcohol, tobacco, and unhealthy snack foods in LMICs <sup>34</sup>).

Given the importance of successful adolescent development for adult attainment of social, educational, and financial success, achieving these goals will require policy initiatives and investments aimed at adolescents. A recent study found evidence for high returns from such investments<sup>7</sup>. However, there is significant variation between countries, with returns expected to be greatest in low-income countries. A range of interventions, including those targeting physical, mental, and sexual health, road traffic injuries, child marriage, and increasing the extent and quality of secondary schooling, are all predicted to be associated with especially high benefit to cost ratios<sup>7</sup>. Accordingly, there have been many calls for comprehensive and increasing investments in adolescent health and wellbeing in both national and international policy<sup>15,35,36</sup>.

We support these proposals to invest in the lives of adolescents, and moreover assert that in order to have the most positive impact, such investments must be guided by science. To ensure they are not too diffuse they should also be carefully targeted to epochs in which they might have the greatest impact.

#### Informing strategic investment in adolescence

Maturational periods of rapid growth and change can create opportunities for pivotal influences on developmental trajectories. This principle can be illustrated by rates in physical growth (see Box 1). For example, it is easy to intuit the likely impact of experiencing a severe famine during a period of accelerated growth. Given the extra nutritional and metabolic demands of rapid growth it makes sense that being an infant *or* being in the midst of a pubertal growth spurt, during a period of malnutrition, could have particularly deleterious long-term effects. Indeed, analyses of data from the famine during the Nigerian Civil war <sup>37</sup> and from the famine in Cambodia 1975-1979 <sup>38</sup> show that experiencing famine as an adolescent resulted in more significant stunting of adult height than does exposure to famine during other life stages. Another study has shown that being in early adolescence during historical periods of adverse experiences such as war or famine is particularly associated with a shortened life

#### expectancy <sup>39</sup>.

However, periods of rapid growth and maturational change can also create opportunities. For example, establishing healthy bone density during the adolescent growth spurt (by getting enough calcium, vitamin D, and exercise) can be protective against developing osteoporosis in later life<sup>40</sup>. Similarly, adolescence creates an opportunity to normalize the risk trajectory of developing polycystic ovarian syndrome during adulthood amongst females with very low birthweight, through insulin sensitization (via metformin treatment) when administered during pubertal maturation<sup>41</sup>.

These examples highlight a general principle about *modifiable* inflection points in developmental trajectories. We believe there are parallels in adolescent development in cognitive, affective, social, and motivational domains, which could provide modifiable inflection points for developmental trajectories in behavioral, educational and mental health outcomes. Peri-pubertal changes in learning and motivation and in the neural systems underpinning these changes, may provide these inflection points.

#### Brain development and changes in learning

Both human and animal models have provided evidence for distinctive neurodevelopmental changes during adolescence. Most famously, the grey matter in higher order brain regions becomes thinner and prunes synapses during adolescence <sup>42-44</sup>. However, some specific brain connections are formed primarily in early to mid-adolescence, which may potentiate new forms of motivation and and/or new learning. For example, dopaminergic <sup>45</sup> and amygdala neurons <sup>46,47</sup>increasingly innervate the frontal cortices, and the frontal cortex shows striking changes in top down innervation of the amygdala<sup>48</sup>. There is strengthening of functional connectivity between cortical regions implicated in cognitive control and the basal ganglia (relative to more affective regions), altering the ratio of cognitive versus affective inputs in a region that serves as an arbiter of value based decision-making<sup>49</sup>. Gains in special inhibitory synapses may open bursts of neuroplasticity <sup>10,50,51</sup>, potentially to transiently enhance learning from experience in a sensitive period (Box 2).

Mid to late adolescence is also a period of more global refinement and stabilization for the brain. The grey matter regions implicated in higher cognition now slow their rate of thinning<sup>52</sup>, the outgrowth of new cortical synapses declines<sup>47,53</sup>, and the total density of synapses on pyramidal neurons decreases<sup>43,44</sup>, . Myelination increases <sup>54,55</sup> and perineuronal nets form in the extracellular space around some neurons<sup>50,56</sup>. Together, these processes are thought to bring greater stabilization and efficiency which may enhance function but could potentially limit further change<sup>50,56,57</sup>.

These changes across diverse brain systems in adolescence not only shape behavior, but also learning in ways that could have lifelong impact. Across development, our capacity for learning does not just gradually (and monolithically) increase, but rather learning and motivation change in non-linear ways, and can show qualitative and well as quantitative shifts. If we focus on highly specific forms of learning using carefully designed tasks, we can observe that some forms of learning are 'better' (meaning more accurate or more efficient) in adolescents<sup>58-61</sup>, while other forms are 'better' in adults, and others in children<sup>62-64</sup>. Overall, what seems to be happening are developmental shifts in how the brain attends to, integrates, and retains information<sup>6,65</sup>. The dependence of brain changes on age alone versus pubertal development is debated, although evidence that pubertal processes play a critical role is increasing<sup>66-69</sup>. There is considerable complexity in this field of study, but in a nutshell, during early- to mid-adolescence there appears to be distinctive enhancements in: 1) exploration<sup>62</sup>, sensation seeking, and sensitivity to novelty<sup>59,69-71</sup>, 2) learning from situations when information needs to be integrated in time from multiple experiences with imperfect (probabilistic) feedback<sup>58,60,71</sup> (a process that may be especially important for acquiring social, emotional, and cultural competence, which cannot be easily mastered by memorizing rules or simply reasoning one's way through complex rapidly changing social situations), 3) learning from negative feedback or about negative associations<sup>60,71</sup>, and 4) learning from peer social information (both positive and negative)<sup>4,72</sup>.

In particular, processing of social information and feedback may undergo distinctive developmental changes in adolescence. Influential reviews have described adolescence as a period of "social reorientation" <sup>4,9,12,73</sup>, which includes increases in sensitivity to social evaluation and the importance of social status and popularity<sup>18</sup>. The adolescent social reorientation is thought to be associated with changes in neural systems involved in the development of social cognition <sup>74</sup>—especially *affective* responses to social acceptance and social rejection<sup>75,76</sup> and neural changes that are thought to enhance the motivational salience of engaging with peers<sup>77</sup>, which may motivate behavior and serve to enhance learning. (While acknowledging this increasing salience of peer relationships, the quality of family relationships continues to be a significant influence on adolescent development and health, and provides a compelling example of bidirectional influences between social and biological development.) (See Box 1).

#### [Insert Box 1: The Role of Parenting in Social Learning and Brain Development During Adolescence]

#### Animal models and sensitive periods for learning

It may be informative to consider the social learning that occurs during adolescence as the product of a potential "sensitive period." Over time, evolutionary influences have shaped each species' development in order to regulate the timing of different forms of learning. Sensitive periods for learning are timed when important information is available and most useful to the adaptive development of the organism <sup>78-80</sup>. Humans and laboratory research animals have been found to share similar early sensitive periods in sensory regions, for example in binocular visual regions where there is a critical balance in the input from two eyes<sup>50</sup>. Humans also have multiple early sensitive periods in the acquisition of language<sup>78,81</sup>. It is tantalizing to consider the range of sensitive periods for human cognitive, affective, and, importantly, social development that are not yet fully understood or discovered, which could be leveraged to enhance the impact of interventions. We can look to sensitive periods for learning and social behavior in other species for clues. Here we focus on sensitive period biology that may have ties to puberty onset.

Human social learning during adolescence may share some parallels with sensitive periods for the acquisition of song learning in song birds. The timing of song learning in songbirds differs by species and involves imprinting on a song model (a "tutor") through social interaction<sup>78</sup>. Some birds learn their song from their father and go through puberty in the first 90 days of life<sup>78</sup>. Others time their learning (and gonadal hormone/ receptor fluctuations) to allow song plasticity during different periods<sup>78,82,83</sup>, for example when they arrive in a new territory and should imitate the songs of their new neighbors<sup>78,84</sup>. Gonadal hormones are thought to regulate the neurobiology of song learning by altering both motor flexibility and the salience of social cues. Changes in salience are thought to ensure appropriate selection of the song to be copied (i.e., the correct species, time, and context)<sup>85-88</sup> and selection of an appropriate mate<sup>85-90</sup>.

In mammals, frontal neocortical areas, which play a critical role in higher cognition, self-regulation, and social behaviors, develop late—from the time of pubertal milestones and into early adulthood<sup>10,45-47,67</sup>. In laboratory mice, the onset of puberty has been found to rapidly alter frontal cortex neurobiology, changing inhibitory neurotransmission mechanisms previously identified as key regulators of sensitive periods in the neocortex (see Box 2)<sup>10,51</sup>. Changes in frontal cortex inhibitory neurotransmission can also be connected to changes in learning<sup>10,91</sup>, suggesting a causal link between puberty and adolescent shifts in learning.

# [Insert Box 2 Puberty Affects Brain Development, Learning and Plasticity -- Insights From Animal Studies]

In rats, the adolescent period is characterized by social learning such as rough and tumble play and learning about sexual encounters. Interestingly, male rats need exposure to testosterone during adolescence in order to display rapid learning from sexual experience, and do not recover this learning if testosterone is replaced in adulthood<sup>5,92</sup>. Thus, in rodents, as in birdsong, we can see a repeated pattern, whereby developmental signals (specifically, the pubertal rise in gonadal hormones) may prime the brain's ability to learn during an adolescent sensitive period when 1) the information is available in the environment and 2) developmentally appropriate. When the temporal intersection of these processes is prevented, as when a developing adolescent is deprived of critical learning opportunities, the trajectory towards developing the capacities required to take up independent adult roles can be derailed or disrupted<sup>5,78,92</sup>.

#### Developmental timing, investments, and interventions

If comparable sensitive period processes occur in association with pubertal maturation in humans, this could inform developmental timing and targets for interventions. For example, if pubertal hormones underpin distinct changes in social learning, leveraging these insights by designing interventions that target this window of opportunity could have large positive effects on developmental trajectories.

The sharp rise in testosterone at the onset of puberty in both boys and girls is associated with shifts in social and affective information processing<sup>70,93-95</sup> and increased prioritization of social status feedback<sup>93</sup>. A recent review of decades of research into the behavioral effects of testosterone in animals and humans concluded that testosterone increases 'motivation to gain social status'<sup>96</sup>. Consistent with that conclusion, testosterone administration can increase status-enhancing behaviors in both prosocial and antisocial ways <sup>97</sup>. In humans, the process of earning prestige may sculpt behavior in a manner that is separate from gaining status through aggressive dominance<sup>98</sup> The specific types of learning—and criteria for earning prestige—relevant to social success are highly variable. Importantly, these are not only, or even primarily, determined by our biology.

A unique feature of our species, and potentially a distinct leverage point for intervention, is the role of human culture in shaping social learning relevant to prestige and admiration. Cultural values for prestige vary widely. For example, a Tibetan Buddhist community that confers the highest prestige on kindness and compassion will create different social learning opportunities for admiration-seeking youth than a warrior society, or a highly materialistic culture. Developmental science cannot yet fully explicate how and when these values are learned and maintained at the neural level. Yet, there appears to be promising evidence supporting these as potential leverage points for positive change in adolescence.

In designing interventions, it is important to note that adolescents are not simply passive learners

conforming to adult values. Complaints about youth's rebellious contempt toward adult authority go back to the time of Socrates. While adolescents are strongly influenced by family and cultural values, they also are naturally seeking greater autonomy and independence. Dutifully acquiring knowledge and skills from accomplished adults represents one path for gaining status and prestige. An alternative pathway is to discover novel approaches or simply an innovative twist or refinement that leads to success. These tendencies are evident today as adolescents worldwide are the early adopters of expertise with new technology (as well as frequent contributions to the leading edge of the latest trends in music, fashion, and innovative use of language).

From this perspective, adolescence can be conceived of as an inflection point for pivotal change in human development in a very broad sense. Adolescent risk taking, together with status seeking, both often maligned, may actually have contributed to unique group level capacities to exploit and preserve serendipitous innovations throughout human history. An extended (adolescent) developmental period of exploratory social learning—when an individual is also highly sensitive to social evaluation and the motivational salience of earned prestige through valued contribution—could have played a critical role in humans' remarkable capacity for rapid expansion, adoption and refinement of innovation through human culture. We speculate that interventions that support and provide social scaffolding for healthy pro-social versions of innovation and success during this sensitive window of social learning and adolescent identity develop, could potentially have large positive impacts on health and education.

#### **Policy and intervention**

The developmental science of adolescence is advancing rapidly, and we have only reviewed a small proportion of the field. We have selected work that exemplifies the growing understanding of adolescence as a period of critical investment opportunity because of the specific types of learning that are potentiated during this period of development. In addition to scientific advances in understanding the enormous potential for growth and positive development, we also have focused on areas of scientific progress that are providing insights into leverage points for specific policies and interventions.. The emerging evidence points towards investments that place a strong emphasis on creating mastery learning experiences that maximize social learning and enhance status and autonomy at a key time in an individual's development of social identity and competence.

Translating our understanding of developmental processes to target specific outcomes will, of course, require careful attention to contextual norms around sex, gender, and culture. As an exemplar, let us further explore how an enhanced understanding of adolescent sensitivity to social evaluation and the motivational salience of earning prestige might create a window of opportunity for positive social learning experience to address gender inequalities. Consider, for example, the harmful social learning experiences for girls coming into adolescence in a social context that admires bold courageous behavior in boys but disapproves of these qualities in girls. In contrast, girls who attend schools or clubs where prestige and admiration signals are comparable across genders, could have very different social learning experiences<sup>99</sup>. Given that puberty in girls typically starts between the ages of 10 - 12 years old, this may be a particularly important time to promote gender equality by providing opportunities for girls to discover, through experiential learning, that they can excel and gain admiration and prestige for their bold successes (at an age when they also are typically bigger, stronger, and more socially competent than same age boys). A formative learning experience during this key developmental window is likely to also positively influence the well-established gender differences in rates of mental disorders, which typically emerge during adolescence, which also are likely to be related to differences in the social experiences of girls and boys during these formative periods in early adolescence<sup>100,101</sup>.

The perspective we present on prestige learning also provides a novel approach to risk taking tendencies in adolescence—often considered the *sine qua non* of unhealthy adolescent behavioral tendencies. Research has shown that adolescents often find risk taking behaviors reinforcing, and moreover, that such behaviors can enhance their social reputation<sup>102,103</sup>. Indeed, courage is a quality that is admired almost uniformly across human cultural contexts, and showing courage in ways that are aligned to cultural values is a powerful route to earning prestige. As promoted through positive youth development frameworks, having pro-social opportunities to demonstrate courage—through sports, drama, civic engagement, or supporting social justice—are likely to have enhanced positive effects during this developmental period<sup>104</sup>. Such experiences may not only prevent anti-social and self-injurious paths, but also may promote healthy trajectories and identity development. Moreover, the proclivity to take risks—especially if it creates gains in status or prestige—now affects youth in new ways as adolescents can post videos of daring acts or innovative creation on online and get thousands of 'likes' from all over the world. Social media amplifies the social reinforcement associated with risk-taking behavior.

Moving to more traditional approaches to prevention and early intervention for health problems in adolescence, Yeager and colleagues<sup>105</sup> have focused on the relative failure of many traditional behavioral interventions during adolescence because well intentioned efforts to instruct adolescents to make positive changes to improve their health often indirectly (or directly) imply that adolescents require adult expertise and are unable to make the right choices on their own. Interventions that honor adolescents' sensitivity to status and respect appear to more effectively capture adolescent attention and motivation and result in improved behavioral outcomes<sup>105</sup>. These same developmental science insights have implications for education policy—especially middle school. The importance of student driven learning (autonomy), collaborative learning (social engagement in learning) and school and classroom climates that honor adolescent sensitivities to status, respect, and purpose, are likely to have powerful positive effects on learning—particularly in this formative period<sup>105</sup>.

#### Insert [Table 1] about here

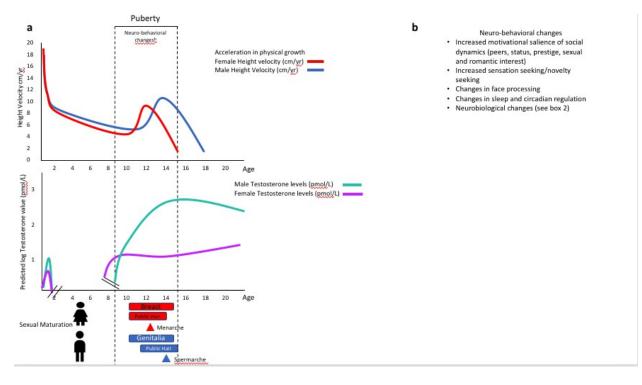
Applying a developmental science lens to strategic investment and intervention requires consideration of a number of principles. First developmental epidemiology<sup>106</sup> can provide information about which opportunities and/or problems arise during different life stages, and thus, can provide clues as to appropriate, developmentally informed prevention and intervention targets. Second, there should be an understanding of an underlying developmental process that results in greater sensitivity to interventions at this stage of life<sup>105,107</sup>. Finally, the process must be modifiable though educational, clinical, public health, policy, or other interventions and have protective effects. In this sense, the developmental perspective can contribute not only to precision medicine<sup>108</sup> and precision public health<sup>109</sup>, but also to precision public policy, by identifying ways to target investment and intervention for maximum benefit. Bearing in mind these three principles, Table 1 presents examples of developmental processes that putatively show sensitive periods during adolescence, along with examples of developmentally informed investment and intervention strategies. These are, however, simply exemplars of potential candidates. Other potential targets could include substance misuse, mental health, parenting, sexual and romantic relationships, nutrition, physical activity, and use of digital technologies, to name but a few.

As developmental science progresses to provide a more mechanistic understanding of developmental processes, it will lead to greater precision in understanding developmental risk factors and identifying the timing, mechanistic targets, and best contexts to improve adolescent trajectories. This program of research is challenging, as it requires the evaluation of the differential effects of similar learning interventions across multiple developmental phases. However, some promising examples of such studies

are emerging<sup>110,111</sup>. Ultimately the full integration of adolescent developmental science, intervention science, and public policy will require a comprehensive evidence base that thoroughly evaluates which kinds of interventions can be potentiated through optimal matching to specific developmental windows of opportunity.

#### Conclusion

The developmental science of adolescence is providing new insights into windows of opportunity where we can have especially strong positive impact on trajectories of health, education, social, and economic success across the lifespan. This emerging science points towards adolescence as a time of enhanced growth and a sensitive period for learning—one where adolescents' sensitivity to belonging, feeling valued and respected, and finding a way to make a valued contribution (i.e., to earn prestige and admiration), is also linked to adolescents' search for meaning and larger purpose. This social and affective learning can shape the development of 'heartfelt' goals and priorities such as those associated with experiences of inspiration, creativity, and innovation. Given current global changes, and the specific challenges affecting youth, there is a compelling need to understand the potential for strategic investments in adolescents to unleash this potential. From the global perspective, strategic investment of very limited resources, and the potential acceleration of economic inequalities and amplification of vulnerabilities and opportunities by the information technology revolution, makes the integration of insights from developmental science into public policy even more compelling. The stakes of investing in adolescents are rapidly increasing—especially if we are going to create sustainable growth, address climate change, and reduce social inequities—all matters critical to the achievement of the United Nations sustainable development goals. Strategic and developmentally informed investments in youth could contribute to a positive impact on the adolescent themselves, their future lives as leaders in adult society, and the next generation to whom they will be parents $^{7,15}$ .



#### Figure 1: Puberty initiates a period of rapid growth and multi-level dynamic change

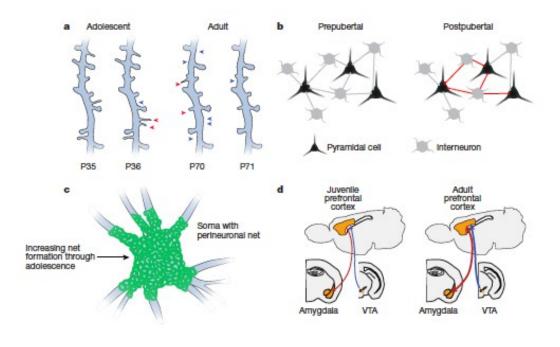
**Figure 1 caption:** As illustrated in the red and blue solid lines above (height velocity as a function of age in girls and boys) growth is very rapid in infancy and then slows during childhood. Growth rates accelerate at the onset of puberty and then decelerate in later stages of puberty. This dynamic pubertal "growth spurt" begins about 18 months earlier in girls than in boys—and is part of a large suite of physical manifestations of sexual maturation (which in girls includes breast and genital development, pubic and axillary hair and menarche, and in boys includes genital development, pubic, axillary and facial hair). Other physical changes include sexually dimorphic changes in facial architecture, changes in skin and sebaceous glands (e.g. acne and body odor) and deepening of the voice in boys.

Pubertal maturation also influences neuro-behavioral development, particularly social, emotional, and motivational processes such as the well-recognized increases in sensation-seeking, and a re-orientation of attention and motivational salience toward peers, social evaluation, status and prestige, and sexual and romantic interests." Pubertal maturation also influences (and is influenced by) the rapidly changing social contexts in which adolescent learning and development are occurring. Taken together these multi-level changes (and their bidirectional interactions) create a dynamic period of growth, development, learning and adaptation. Understanding these dynamic developmental processes can inform targets (and developmental timing) for early intervention, prevention, and policy.

Despite the strong cultural belief that the importance of parenting wanes compared to that of peers during adolescence, empirical research clearly demonstrates that parenting is a strong determinant of adolescent health and well-being during this period of life, often more so than peer processes <sup>112,113</sup>. Moreover, recent empirical research has suggested that parenting processes during adolescence provide a compelling example of bi-directional relationships between environmental learning/experiences and biological development, potentially setting up cascading effects of either vulnerability or resilience. For example, individual differences in adolescent brain development are associated with adolescents' behavior during parent-child interactions<sup>114</sup>, suggesting that neurobiology may influence interpersonal behavior in family contexts. However, early adolescent parent-child relationships also prospectively predict patterns of future adolescent brain development<sup>115</sup>, and brain function has been shown to serve a mediating link between family relationships and future psychopathology<sup>116</sup>. Finally, the quality of parent-child relationship during early adolescence has been shown to buffer some of the potentially deleterious effects of low socioeconomic status earlier in life on adolescent brain development<sup>117</sup>. Family processes during early adolescence are therefore potentially influenced by, and influence, both neurobiological development and functional outcomes. What is most important here, is the potential role of family relationships as modifiable aspects of developmental processes during a maturational window of dynamic change. Greater precision in understanding the specific maturational changes (such as pubertal maturational changes in social information processing, and motivational salience) could provide insights into developmental timing, targets, and processes that play a critical role in these mutually interacting developmental processes in ways that inform leverage points for adolescent focused public policy and clinical interventions. For example, although recent meta analytic reviews have supported the role parenting intervention in the prevention of anxiety and depression<sup>118</sup>, effect sizes are small, and few of these approaches have been informed by an explicitly developmental science perspective on the timing and targets of these interventions.

#### Box 2: Puberty Affects Brain Development, Learning and Plasticity -- Insights From Animal Studies

The mammalian brain is remodelled during adolescence, particularly in associative cortical regions. Studies of human brains and animal models have shown that pruning of cortical synapses, as well as gaining of select new synapses in the neocortex, occurs during adolescence. These changes may reflect loss of juvenile forms of plasticity as well as potentially adolescent-specific sensitive periods. Whereas some of these changes have been shown to be puberty-dependent, others are thought to be pubertyindependent. Shifts in pubertal timing could potentially alter the sequence and/or phase overlap of different maturational events. In a, a schematic of a dendritic segment is shown at four time points, illustrating both the pruning and stabilization of spines (protrusions where synapses can form) that occur during adolescence. The first two time points are 24 h apart in early adolescence, whereas the second two are 24 h apart in early adulthood. When comparing adolescent time points to the adult time points, a decrease in spine density can be observed (lost spines are indicated by blue arrowheads). In addition, at the younger age, it has been shown that a greater fraction of the spines are lost or gained (red arrowheads) over 24 h, compared to the adult brain. These transient spines are thought to reflect the dendrite 'sampling' of the local space for potential new synaptic connections. As spine gains and losses become more infrequent, opportunities for rewiring and neuroplasticity are thought to lessen. Thus, during adolescence when dendritic spines become less dense and more stable, experience-dependent learning may be solidified, connectivity may become more efficient, and plasticity may become more limited. It remains debated whether spine changes are related to gonadal hormone effects at puberty<sup>42,116</sup>. In b, the schematic shows the increased inhibitory neurotransmission on to frontal cortical pyramidal neurons that occurs after puberty (indicated by red lines). This increase in a special form of neurotransmission has been shown to be organized by ovarian hormones at puberty in female mice<sup>51</sup>. The image in b is based on data from refs 10, 51. Changes in inhibition are thought to regulate the balance of excitation and inhibition and could initiate a transient sensitive period for plasticity<sup>50</sup>. A schematic of a perineuronal net surrounding the soma of a neuron is shown in c. Perineuronal nets increasingly form during adolescence in the neocortex<sup>58</sup> and amygdala<sup>56</sup>, particularly around inhibitory neurons. These changes may limit plasticity and potentially sensitive periods across the brain<sup>56,58</sup> and in multiple species<sup>57</sup>. The schematic in d shows cross-sections of the rodent brain that highlight new long-range connections, which continue to form during adolescence. This is notable, because pruning of connectivity generally predominates in this phase (as in a). The arrows indicate increasing innervation of the prefrontal cortex by amygdala inputs<sup>46,47</sup> (red) and dopaminergic inputs from the ventral tegmental area (VTA)<sup>45,69</sup> (blue) during the adolescent transition. The schematic also shows that top-down prefrontal cortex innervation of the amygdala (red) undergoes marked growth during adolescence<sup>48</sup>. Human imaging studies have shown that similar prefrontal-amygdala remodelling may be occurring in human brains<sup>117</sup>. It has been shown that the increase in dopaminergic innervation of the prefrontal cortex, does not show sex-specific changes at pubertal milestones<sup>118</sup> but the role of amygdala connectivity during puberty has not been tested, to our knowledge.



## Table 1 - Examples of matching intervention strategies to developmental changes during adolescence

Developmental Changes	Intervention Strategies
Period of rapid physical growth and increased metabolic demands	<ul> <li>Mitigate risk of famine and malnutrition<sup>38</sup></li> <li>Establish healthy bone 'bank' through optimal calcium, vitamin D , and exercise<sup>40</sup></li> </ul>
Increased tendency to explore, seek novelty & excitement	•Create opportunities for positive risk taking resulting in healthy, positive, productive, high arousal learning <sup>102,103</sup> •Provide context for self-directed, discovery/ exploratory learning
Pubertal changes in sleep and circadian regulation	•Couple later school start times with prevention and intervention efforts to improve and regularize sleep <sup>123</sup> •Provide sleep interventions to youth at increased risk for mental health problems <sup>124</sup>
Motivation for status, prestige, and respect	<ul> <li>Design health promotion and behavioral interventions in ways that honor adolescents' sensitivity to autonomy, respect and prestige<sup>105</sup></li> <li>Train adult teachers/facilitators to treat adolescents with respect and appropriately enhance autonomy<sup>125</sup></li> </ul>
Motivation for social learning	<ul> <li>Leverage social relationships to reinforce positive behavior<sup>93,97</sup></li> <li>Support adolescents in processing social information and understanding social experiences</li> <li>Structure learning experiences to include, rather than ignore, social context<sup>72,74</sup></li> <li>Enhance collaborative social learning in education settings<sup>19</sup></li> </ul>
Identity development and heartfelt goals	<ul> <li>Introduce positive role models and mentors who exemplify feeling-based values and inspired goals<sup>23</sup></li> <li>Create mastery curve learning opportunities that gradually become more challenging</li> </ul>

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