Digital dementia in the internet generation: excessive screen time during brain development will increase the risk of Alzheimer’s disease and related dementias in adulthood

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Converging evidence from biopsychosocial research in humans and animals demonstrates that chronic sensory stimulation (via excessive screen exposure) affects brain development increasing the risk of cognitive, emotional, and behavioural disorders in adolescents and young adults. Emerging evidence suggests that some of these effects are similar to those seen in adults with symptoms of mild cognitive impairment (MCI) in the early stages of dementia, including impaired concentration, orientation, acquisition of recent memories, and social functioning, and self-care. Excessive screen time is known to alter gray matter and white volumes in the brain, increase the risk of mental disorders, and impair acquisition of memories and learning which are known risk factors for dementia. Chronic sensory overstimulation (i.e., excessive screen time) during brain development increases the risk of accelerated neurodegeneration in adulthood (i.e., amnesia, early onset dementia). This relationship is affected by several mediating/moderating factors (e.g., IQ decline, learning impairments and mental illness). We hypothesize that excessive screen exposure during critical periods of development in Generation Z will lead to mild cognitive impairments in early to middle adulthood resulting in substantially increased rates of early onset dementia in later adulthood. We predict that from 2060 to 2100, the rates of Alzheimer’s disease and related dementias (ADRD) will increase significantly, far above theCentres for Disease Control (CDC) projected estimates of a two-fold increase, to upwards of a four-to-six-fold increase. The CDC estimates are based entirely on factors related to the risk of Alzheimer’s disease and related dementias (ADRD); Mild cognitive impairment (MCI); Internet generation (iGen) or Generation Z; Anterograde amnesia.

1. Introduction

Researchers at the Centers for Disease Control and Prevention (CDC) project that the rate of Alzheimer’s disease and related dementias (ADRD) in the United States will increase 2-fold, from 1.6% to 3.3%, by 2060 [1]. These estimates are based on data for the ADRD burden of disease in 2014 for adults aged ≥65 years according to age, sex, race, and ethnicity factors which primarily represents individuals born between 1925–1945 (Silent Generation) and 1946–1964 (Baby Boomers) [1]. These factors do not account for significant and relevant differences between individuals born before 1965 and those born after 1980 (Millennials) and 1995 (Generation Z). The CDC estimates are based upon factors currently known about the Silent Generation and Baby Boomers who are aged ≥65 years today, whereas most of the population aged ≥65 years older in 2060 will be Millennials and Generation Z. There are at least two known critical factors that differ significantly between those born before 1965 and those born after 1980 which are related to the risk of neurodegenerative disorders such as ADRD: these are overall intelligence level (i.e., assessed by IQ testing) and excessive screen time (i.e., time spent on electronic media).

Growing evidence documents a negative (or reverse) Flynn Effect, which is a progressive decline in population intelligence (i.e., intelligence quotient or IQ test scores), on a global scale starting around 1975 and projected to continue into 2050 [2]. The projected global decline in intelligence of approximately 1.28 I.Q. points for 2000–2050 is thought to be related to environmental rather than genetic causes and to have started with Millennials and will include Generation Z [3]. Converging evidence shows that excessive screen time (i.e., more than 2–3 h/day exposure to electronic media including television, computers, and mobile devices such as

Keywords

Excessive screen time; Brain development; Alzheimer’s disease and related dementias (ADRD); Mild cognitive impairment (MCI); Internet generation (iGen) or Generation Z; Anterograde amnesia
Excessive Screen Time (2–3 h/day exposure to electronic media including television, computers, laptops, smartphones, tablets, and laptops), particularly during brain development, is related to increased risk of learning and memory impairments, attentional and emotional disorders, substance abuse, and changes in cortical gray and white matter volumes [4]. These observations are consistent with the cognitive-behavioral-brain reserve (CBBR) hypothesis of dementia, which suggests that more complex patterns of neural and mental activity in early, middle, and later life stages are associated with decreased risk of dementia, whereas less complex patterns are associated with an increased risk of dementia [5]. We propose that these two factors, declining intelligence and excessive screen time, which came to prominence for Millennials and Generation Z, will compound over time reducing the overall cognitive-behavioral-brain reserve of these individuals significantly increasing their risk of ADRD. We predict that from 2060 to 2100, the rates of ADRD will rise far above the CDC projected estimates up to a four- to six-fold increase. The CDC estimates are based entirely upon factors related to the age, sex, race and ethnicity of individuals born before 1950 who did not have access to mobile digital technology during critical periods of brain development. Our estimates include the documented effects of global declines in intelligence levels and excessive screen time for individuals born after 1980, Millennials and Generation Z, who will comprise most individuals ≥65 years old in 2060.

2. Theory

Converging evidence from biopsychosocial research in humans and in animal models demonstrates that chronic sensory stimulation via excessive screen time (i.e., defined as more than 2–3 h/day exposure to electronic media including television, computers, and mobile electronic devices) affects brain development, increasing the risk of cognitive, emotional, and behavioral disorders in adolescents and young adults by negatively impacting attention and concentration, learning and memory, emotional regulation and social functioning, physical health, and development of mental disorders and substance use. These effects are similar to the symptoms of mild cognitive impairment (MCI) seen in older adults that increase the risk of Alzheimer’s disease and Related Dementias (ADRDs). The current decline in global IQ, estimated to have started post-1975 and projected to continue into 2050, parallels significant population level increases in screen time and could also increase the risk of MCI and ADRD. Solid lines represent empirically-supported connections between factors and dotted lines represent theoretically-supported connections.

Fig. 1. Schematic model of the effects of excessive screen time on various factors that contribute to the development of mild cognitive impairment and dementia. Excessive screen time (i.e., >2–3 h/day exposure to electronic media including television, computers, and mobile electronic devices) has been shown to affect brain development (i.e., structure and function) and increase the risk of cognitive, emotional, and behavioral disorders in adolescents and young adults by negatively impacting attention and concentration, learning and memory, emotional regulation and social functioning, physical health, and development of mental disorders and substance use. These effects are similar to the symptoms of mild cognitive impairment (MCI) seen in older adults that increase the risk of Alzheimer’s disease and Related Dementias (ADRDs). The current decline in global IQ, estimated to have started post-1975 and projected to continue into 2050, parallels significant population level increases in screen time and could also increase the risk of MCI and ADRD. Solid lines represent empirically-supported connections between factors and dotted lines represent theoretically-supported connections.
Fig. 2. Schematic model of the effects of excessive screen time on cognitive-behavioural brain reserve and implications for early onset of mild cognitive impairment and dementia. The cognitive-behavioural-brain reserve (CBBR) hypothesis of dementia postulates that more complex patterns of neural and mental activity in early, middle, and later life stages are associated with decreased risk of dementia as opposed to less complex patterns which are associated with increased risks. Brain development occurs in stages marked by periods of massive neuroplasticity (i.e., significant changes in gray and white matter) that correspond to cognitive-behavioural maturation. Neuroimaging studies of connectivity in the brain suggest several dynamic brain networks governing executive functions, intelligence, and social-emotional behaviour emerge early in brain development, increase their functional interactions during adolescence, and variations in patterns of connectivity can predict healthy and pathological trajectories of development into adulthood. Studies show that these cortical networks can be influenced by early environmental experiences including excessive screen time. If the neural circuits underlying these cognitive-behavioural abilities essential for general intelligence and lifetime adaptability are under- or abnormally-developed before adulthood, then it is likely that these changes will persist into early and middle adulthood and be more vulnerable to accelerated neurodegeneration in late adulthood therefore increasing the risk of early onset MCI and ADRDs.

estimated to have started post-1975 and projected to continue into 2050, could contribute to an overall cognitive decline in the world’s population increasing the risk of ADRD in individuals ≥65 years old in 2060 and beyond. It is estimated that these two factors, increasing rates of excessive screen time and declining IQ levels, will compound over time to reduce the overall cognitive-behavioural-brain reserve capacity for individuals born after 1975 and increase their rates of ADRD compared to those born before 1950 (refer to Figs. 1,2 and Table 1, Ref. [3, 4, 7–14, 16–21, 23, 25, 29–44]). Specifically, we predict that Millennials and Generation Z will have a 4- to 6-fold increase in ADRD in 2060 compared to recent estimates of ADRD in 2014 for the Silent Generation and Baby Boomers.

3. Hypothesis

We hypothesize that for individuals born after 1975, the effects of excessive screen exposure during critical periods of brain development and the global decline in IQ levels will compound over time leading to lower overall cognitive-behavioural-brain reserve. This will translate into a higher prevalence of MCI in early to middle adulthood resulting in substantially increased rates of ADRD in late adulthood. We predict that the rates of ADRD will rise far above the projected estimates from the CDC of a 2-fold increase from 2014 levels [1] up to a 4- to 6-fold increase in 2060 and beyond.

4. Evaluation of hypothesis

4.1 Critique of CDC estimates

Using data from the Centers for Medicare and Medicaid Services (CMS) and the United States (US) Census Bureau, Matthews and colleagues [1] estimated a 178% increase from 2014 to 2060 for the number of Americans projected to have ADRD. This reflects a growth in both aging and minority populations and assumes trends in 2014 will remain constant [1]. Matthews and colleagues [1] suggest that since their estimates are based solely upon unchangeable risk factors for ADRD, other modifiable factors such as educational attainment which tend to have protective effects against dementia may result in an overestimate for future decades. We will argue that not only is the Matthews and colleagues [1] projection not an overestimate, but it is a significant underestimate based upon additional data showing several critical differences between populations aged ≥65 in 2014 compared...
**Table 1. Effects of excessive screen time on cognitive-behavioural brain reserve early in life and implications for risk of MCI and ADRD.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Effects on Brain, Behaviour &amp; Cognition (CBBR)</th>
<th>Implications for risk of MCI &amp; ADRD</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain structure and function</td>
<td>Screen time associated with changes in occipital cortex (reduced volume, thinning, sulcal depth), prefrontal cortex (smaller orbitofrontal volume, thinning), temporal cortex (thinning), insula (reduced volume), limbic structures (smaller hippocampus, amygdala, ventral striatum), reduced functional connectivity in cortico-subcortical circuits, and microstructure abnormalities in gray and white matter</td>
<td>Early volume losses in areas governing sensorimotor functioning, executive functioning, and reward-learning areas could reduce overall CBBR and increase risk of cognitive-behavioural disorders including substance use disorders and thus increase risk of MCI and ADRD later in life</td>
<td>He et al. [29] (2017); Hong et al. [30, 31] (2013); Lee et al. [32] (2018); Paulus et al. [33] (2019); Weng et al. [34] (2013); Yuan et al. [35, 36] (2011, 2013)</td>
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<tr>
<td>Attention and concentration</td>
<td>Screen time associated with impairments in attention during development, cognitive capacity (working memory and functional fluid intelligence), vulnerability to distractions, poorer inhibition, reduced executive control (focused and sustained attention), shallow information processing, and poorer academic progress</td>
<td>Impairments in attention, concentration, and cognitive capacity similar to symptoms of MCI; if occurring early in life, these could reduce overall CBBR, adult IQ, and lifetime educational attainment which are known risk factors for MCI and ADRD</td>
<td>Carrier et al. [14] (2009); Christakis et al. [12] (2004); Christakis et al. [13] (2018); Loh &amp; Kanai [37] (2016); Ward et al. [16] (2017)</td>
</tr>
<tr>
<td>Learning and memory</td>
<td>Screen time associated with impaired development of sensorimotor skills, spatio-temporal abilities, problem solving and language acquisition, lower crystallized and fluid intelligence, poorer vocabulary and reading comprehension, reduced metacognitive and self-regulation skills, and superficial effort and retention of information, poorer long-term memory, cognitive development (analytical thinking), and academic performance</td>
<td>Impairments in learning and memory early in life could reduce overall CBBR, adult IQ and lifetime educational attainment which are known risk factors for MCI and ADRD; impairments in episodic and semantic memory in young adults likely to persist into middle and late adulthood increasing risk of early onset of MCI and ADRD symptoms</td>
<td>Glass &amp; Kang [9] (2018); Madigan et al. [7] (2019); Mangen et al. [8] (2013); Paulus et al. [33] (2019); Sparrow et al. [10] (2011); Tamir et al. [11] (2018)</td>
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<tr>
<td>Emotional regulation and social functioning</td>
<td>Screen time associated with poorer emotional regulation, inability to stay calm, reinforcing cognitive-emotional spirals, lower self-esteem, increased anxiety and depressed moods, lower productivity and curiosity, fewer social interactions, lower sociability, up- wards social comparison, uncooperative attitudes and behaviour, sexual activity</td>
<td>Symptoms of poor emotional regulation, self-care, and social functioning are characteristic of MCI which is a known risk factor for ADRD</td>
<td>Boers et al. [17] (2019); Hunt et al. [38] (2018); McNeil &amp; Thorsteinsson [23] (2017); Neophytou et al. [4] (2019); Twenge &amp; Campbell [20] (2018) Twenge et al. [21] (2019)</td>
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<tr>
<td>Mental disorders and substance use</td>
<td>Screen time associated with poorer mental health, overall risk of psychiatric conditions including externalizing psychopathology (e.g., attentional problems, hyperactivity, rule breaking and aggressive behaviour) and internalizing psychopathology (e.g., social anxiety, depression) and excess behaviour related to reward-learning disruptions (e.g., impulse control and addictive behaviours related to the internet and substances)</td>
<td>Psychiatric conditions are known risk factors for MCI and ADRD; chronic exposure to excessive audiovisual stimulation may affect the neuroimmunoendocrine system increasing allostatic load and risk of mental disease</td>
<td>Maras et al. [19] (2015); Neophytou et al. [4] (2019); Yen et al. [39] (2009); He et al. [29] (2017); Gommans et al. [25] (2015); Twenge &amp; Campbell [20] (2018)</td>
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<tr>
<td>Physical health</td>
<td>Screen time associated with poorer sleep, more sedentary lifestyle, reduced physical activity, lower cardiovascular fitness, increased incidence of being overweight or obese; may directly and indirectly affect the neuroimmunoendocrine system increasing allostatic load and increase risk of physical disease</td>
<td>Poor physical health is a known risk factor for MCI and ADRD</td>
<td>Martin [40] (2011); Twenge et al. [41] (2017); Wethington et al. [42] (2013)</td>
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<td>Global intelligence</td>
<td>Significant population level increases in screen time align with significant population level declines in intelligence despite population level increases in educational attainment (i.e., Reverse Flynn Effect)</td>
<td>Lower IQ and educational attainment tend to be risk factors for MCI and ADRD</td>
<td>Bratsberg &amp; Rogeber [3] (2018); Twenge et al. [43, 44] (2019)</td>
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*ADRD: Alzheimer’s disease-related dementia, MCI: Mild cognitive impairment.*
4.2 Neurological and cognitive-behavioural markers of MCI and ADRD

ADRDs are progressive brain disorders characterized by gradual and increasing impairments in attention, concentration, and orientation, short-term and long-term memory, activities of daily living, and reasoning and decision making abilities [22, 46]. At the end stages of ADRD, individuals are usually non-verbal, non-ambulatory and unresponsive to their surroundings [46]. The progression from early to end stages of ADRD also include profound changes in personality, mood and social interactions, including anterograde amnesia (i.e., inability to acquire new memories), retrograde amnesia (i.e., trouble recalling past memories), and even psychiatric symptoms such as delusions and hallucinations [46, 47]. Those with ADRD also show poorer social functioning and self-care routines, score higher on tests of anxiety, and have greater sleep disturbances [48, 49].

Studies show that regional and global cerebral atrophy rates are well correlated with progressive cognitive-behavioural declines characteristic of Alzheimer’s disease (AD) [50–55]. Progressive cerebral atrophy is associated with the stages of AD [52, 54]. Pre-symptomatic and mildly affected individuals show significant volume loss in the hippocampus and posterior cingulate and neocortical temporoparietal cortices; in contrast, moderately and severely symptomatic individuals show more widespread cerebral atrophy, particularly in the inferolateral areas and frontal lobes with some sparing of the primary motor and sensory areas and cerebellum [52, 54]. Volumetric changes in the hippocampus, entorhinal cortex, whole brain, and ventricles predicted conversions from preclinical (i.e., no symptoms) to clinical stages of MCI or AD and from MCI to AD and were more reliable predictors than standard psychometric measures [53]. For individuals over age 60, gray matter volume decreases of approximately 2% per year are seen in patients with AD compared to controls [50] and significant losses in white matter essential for communication between brain regions [30, 34, 35, 51, 56]. Reduced cortical thickness in the posterior cingulate gyrus is characteristic of AD in both typical and atypical clinical presentations [57]. These findings demonstrate that cerebral volume is a robust indicator of MCI and ADRD in middle to late adulthood. Factors that may increase cerebral volume loss in early adulthood, or even prevent cerebral volume growth in childhood and adolescence, may greatly accelerate the cognitive-behavioural signs of neurodegeneration in middle adulthood and significantly increase the rates of MCI and ADRD. We will argue that excessive screen time in childhood, adolescence, and early adulthood impairs brain development leading to reduced overall CBBR before middle adulthood increasing the risk of neurodegeneration potentially 10 to 20 years earlier than expected.

4.3 Global declines in intelligence may increase risk of MCI and dementia in 2060

The Flynn effect refers to the increasing performance over time on intelligence tests across the population throughout the 20th century [3, 58–61]. Studies show increases of approximately 2.50 to 3.00 IQ points per decade with proposed explanations focusing on biological factors (e.g., nutrition, pathogen stress, fertility) and environmental factors (e.g., education, family size, technology, test-taking behaviour) and the interactions between them, referred to as ‘social multipliers’ (i.e., any environmental factor that confers an advantage improving test performance) [62]. Analyses show substantial gains in fluid IQ (i.e., reasoning-based performance) that are greater than gains for crystallized IQ (i.e., knowledge-based performance), greater gains for adults than children, and positive correlations with economic gains (i.e., GDP growth) [62]. Results also show a deceleration or reversal of gains in recent decades [62].

The reversal of this trend in IQ gains, referred to as the negative Flynn effect, has been documented in several countries in post-1975 birth cohorts [2, 3, 58, 62]. The main contributors to the Flynn effect are thought to be environmental and generate within-family variation based upon exposure differences (e.g., age at exposure, exposure duration), although the specific mechanisms underlying these environmental effects are unclear [3]. The negative Flynn effect may reflect a ceiling effect for environmental advantages (e.g., saturation or diminishing returns) or increases in social multipliers detrimental to IQ (e.g., dysgenic fertility, immigration, declining educational standards) [3, 62]. Although exposure to technology is postulated to positively affect IQ by providing greater visual stimulation, evidence does not support a link between increased fluid IQ and frequency of visual media exposure [62]. In fact, evidence is emerging that excessive screen time may be a significant negative social multiplier contributing to the deceleration and decline of population IQ. The negative Flynn effect starting post-1975 is paralleled by a decline in vocabulary, documented from 1974 to 2016 for American adults; this is despite an increase in educational attainment (e.g., 11.83 to 13.68 years of school completed), which is generally correlated with verbal intel-
ligence [43]. During this same time period, there has been a significant decrease in reading print (e.g., books, magazines, newspapers) and a critical increase in digital screen exposure (e.g., television, computers, tablets, smartphones) [44]. In a study examining reading comprehension, it was found that students who read from print scored significantly higher on reading comprehension tests than those who read the text digitally [8]. Several explanations were proposed: (i) navigation via scrolling on screens is known to negatively interfere with mental representations of text, (ii) multitasking on a computer (e.g., switching screens to read or answer questions) has hidden cognitive processing and memory costs (e.g., increasing challenges of dividing attentional resources), and (iii) metacognitive and self-regulation skills (i.e., ability to monitor and adapt one’s cognitive performance to a task) may have been engaged more with print media, traditionally used for effortful learning, compared to digital media, often used for quick and superficial information gathering [8]. Evidence suggests there are detrimental consequences of excessive screen time for attention, learning, memory, and language development [4]. Research shows that screen time is increasingly replacing time spent on academics for adolescent and young adult students [43, 44, 62] and constant use of digital devices is associated with worse reading comprehension, word reading and vocabulary [8], which may impact overall IQ levels.

4.4 Significant differences in screen time exposure for individuals born before and after 1975

The amount of screen time exposure during critical periods of brain development differs significantly for the Silent Generation (born 1925 to 1945), Baby Boomers (born 1946 to 1964), and Generation X (born 1965 to 1979) compared to Millennials (born 1980 to 1995) and Generation Z (born 1996 to 2012). Compared to previous generations, the average 17–19-year-old spends approximately 6 hours a day on mobile digital devices (MDD) (e.g., smartphones, tablets, and laptop computers) [44] whereas individuals born before 1965, the Silent Generation and Baby Boomers, at the same age spent zero hours on MDD. Generation Z is the first in history to never know a world without the Internet; Generation Z surpasses passes Millennials on social media use by almost 3 hours each day [64].

Adolescent screen time use has changed dramatically from 2.5 hours a day of TV viewing in 1970 to almost 8 hours a day of TV viewing, internet use, texting, and social media use in 2016 [44]. This represents at least a 3-fold increase in screen use for adolescents as these numbers were reported for leisure time and do not include screen use at work, school or studying [44]. Even the time spent viewing television may be fundamentally different across cohorts as Generation Z increasingly engages in multiscreen use [65–68] which is known to have negative effects on cognitive processing including attention, memory, learning, and comprehension [69–73]. Overall, Generation Z spends more time online and texting and less time with more traditional media such as magazines, books, and television than previous generations [44].

4.5 The effects of screen time on brain development and implications for cognitive-behavioural-brain reserve in adulthood

Excessive screen time affects brain structure and function, particularly during development, which greatly impacts attentional and inhibitory control, focused concentration, learning, memory, reasoning, and creativity [10, 74–76]. These basic capacities are essential for executive control in goal-directed and decision-making behaviours which underlie human intelligence and the essential “ability to adapt to uncertain, changing, and open-ended environments” [63, p.1]. If the neural circuits underlying these cognitive-behavioural abilities essential for general intelligence and lifetime adaptability are under- or abnormally-developed before adulthood, then it is likely that these changes will persist into early and middle adulthood and be more vulnerable to accelerated neurodegeneration in late adulthood. Brain development occurs in stages and is marked by periods of massive plasticity (i.e., major neuronal and synaptic rearrangement), particularly the perinatal and periaadolescent transitions, the latter of which is characterized by significant gray matter reductions and white matter increases that correspond to cognitive-behavioural maturation [77–79]. Neuroimaging studies of connectivity in the brain suggest several dynamic brain networks governing executive functions, intelligence, and social-emotional behaviour emerge early in brain development, increase their functional interactions during adolescence, and variations in patterns of connectivity can predict healthy and pathological trajectories of development into adulthood [22, 80–82]. Changes in these cortical networks are thought to be influenced by early environmental experiences, including childhood abuse [83], urban upbringing [84], and screen time [33], and may have serious lifetime impacts on general cognitive ability, social-emotional behaviour, psychopathology, and substance use and abuse. Studies show that abnormal patterns of regional connectivity, specifically in frontal and parietal lobe connections, are also found in neurodegenerative conditions including ADRDs, particularly frontotemporal dementia and AD [22].

Preliminary data from The Adolescent Brain and Cognitive Development (ABCD) Study, a multi-site longitudinal neuroimaging study, shows the significant impact that screen time has on the relationship between cognitive-behavioural maturational markers and normal patterns of brain development in children and adolescents [33, 85]. The study identified several associations between screen time, brain structure (e.g., cortical thickness, gray matter volume, and sulcal depth), and cognition (e.g., fluid and crystallized intelligence) and mental health (e.g., internalizing and externalizing psychopathologies) [33]. First, results showed a robust association between screen time and changes in visual system structural patterns (i.e., reduced volume, thinner cortex, variations in sulcal depth), which may negatively affect the functioning of other cortical networks, such as cognitive...
control regions, that interact with sensorimotor areas [33]. Second, results showed a strong association between screen time, externalizing (but not internalizing) psychopathology, and changes in cortical and limbic structures (e.g., smaller orbitofrontal volume, thinner occipital and temporal cortices, thinner hippocampi) [33], which may help explain the comitant rise in screen time and disorders of attention and hyperactivity (reviewed in [4]). Third, results showed a more complex pattern of association between screen time, particularly type (e.g., gaming versus social media), and brain structure changes and measures of fluid and crystallized intelligence. For fluid intelligence, gaming activity showed positive associations with prefrontal cortex thinning, whereas social media activity showed negative associations with hippocampal thickness and temporal lobe volume [33]. In contrast, for crystallized intelligence, screen time in general and social media activity showed strong negative associations with occipital and orbitofrontal volume [33]. In a study of young adults, it was demonstrated that excessive social media use is associated with gray matter volume reduction in the bilateral amygdala and right ventral striatum but not the prefrontal cortex [29], suggesting that excess behaviour arises from a developmental disruption of reward-learning [29].

Taken together, these results contribute to evidence from brain imaging and behaviour studies that support the dual system theory of excess problematic behavior [86] which proposes that the development of these abnormal behaviors arises from imbalances between the reward system (mesolimbic dopamine amygdala-striatal) which becomes hyperactive and the inhibition system (prefrontal regions) which becomes hypo-active [29]. Such imbalances have important implications for focusing attention, learning, memory, intelligence, social-emotional regulation, and behavioural addictions. Based on models of drug, alcohol, and gambling addictions, characteristic traits of internet addiction include fixation with playing online games, repeated failed attempts at cessation, increased negative affect, neglecting significant relationships or activities, and the development of tolerance and withdrawal symptoms [30, 35, 36]. Studies show internet addiction is associated with important changes in both gray and white matter in the developing brain, including volumetric loss and functional impairments related to behavioural abnormalities (e.g., impaired cognitive ability and control) [30, 34–36, 87]. For example, individuals with internet addiction showed abnormalities in cortical thickness in several areas involved in cognitive control including the frontal lobe, left lateral orbitofrontal cortex, insula cortex, lingual gyrus, right postcentral gyrus, entorhinal cortex, and inferior parietal cortex [35]. The frontal lobe performs executive functions, such as planning and organizing, and undergoes massive changes from puberty until mid-twenties [74]. The frontal lobe along with volume loss in the striatum, which includes the reward pathway and suppression of impulses, is seen to be affected by gray matter atrophy and white matter volumes; those with gaming addiction showed significant gray matter atrophy in the right orbitofrontal cortex, bilateral insula, and right supplementary motor area [34]. A functional magnetic resonance imaging study found that there is less efficient information processing and a reduced impulse inhibition in those with an internet addiction disorder, along with an increased sensitivity to rewards and an insensitivity to loss was exhibited [88, 89]. It was identified that those with an internet addiction disorder had abnormal spontaneous brain activity that correlated with poor task performance [35].

Thus, these studies suggest that early reductions in brain volume and functional capacity during brain development may increase the risk of MCI and ADRD which are characterized by significant white and gray matter loss and a deterioration in instrumental activities of daily living. This is consistent with the cognitive-behavioural-brain reserve (CBBR) hypothesis of dementia. Studies show that brain reserve is positively correlated with IQ, educational attainment, and engagement in cognitively stimulating occupational and leisurely activities, and negatively correlated with the transition from MCI to dementia [5, 90].

### 4.6 Main developmental effects of screen time on learning and memory

The term digital dementia was first coined by the neuroscientist Manfred Spitzer to refer to the literal ‘mind-deteriorating’ effects of digital technology; specifically, that excessive use of digital devices is associated with cognitive impairments characteristic of dementia, such as decreased attention and impaired memory, and these effects are being seen increasingly in younger adults not expected to be experiencing neurodegeneration characteristic of old age [91–93]. For example, Generation Z children began regularly watching television by 3 months of age [94] compared to 4 years of age for Generation X children [95]. Previous research indicates that earlier and longer exposures to screen time are associated with increased risk of psychiatric conditions (i.e., attentional problems and hyperactivity, anxiety, and depression) [19, 39], further suggesting that Generation Z children would be more likely to exhibit learning and memory impairments when compared to Generation X children.

Excessive screen time was found to be associated with problems in meeting developmental milestones for motor skills, spatio-temporal abilities, problem solving and language acquisition [7]. Content, pace, and degree of exposure were associated with dysfunction in attention, learning, and memory for both infants and children [6, 13]. For example, observational experiments in humans and animals determined that excessive sensory stimulation and exposure to fast-paced television during infancy and childhood resulted in cognitive and behavioural deficits [13]. Similarly, television programs which encourage active participation facilitated greater vocabulary acquisition when compared to passive programming [6]. A decline in performance of cognitive tasks was also observed in children who had over two hours of screen time per day and children exposed to seven
or more hours of screen time per day revealed significantly reduced orbitofrontal thickness [32], a fundamental structure in the reward circuit pathway responsible for decision-making and addiction disorders in adolescence and adulthood [25, 31, 96].

The consequences of digital technology are associated with prolonged effects in adulthood. For example, post-secondary students scored significantly higher on midterms and exams in classrooms that prohibited the use of electronic devices in comparison to classrooms that did not prohibit the use of electronic devices [9]. In the general population, long-term effects of excessive screen time were associated with reductions in long-term memory and cognitive development [9]. In addition, many adults rely on technology and smartphones as opposed to cultivating self-imposed analytical thinking [76]. For instance, three studies examining smartphone use and cognition determined that individuals who thought more intuitively were more likely to rely on their smartphones for information when compared to individuals who thought more analytically [76]. Since search engines allow easy access of information, users are more prone to remember where to locate a fact instead of remembering the fact itself [10]. This can be seen when dealing with difficult questions: users tend to think more about searching for solutions online as they have a decreased recollection of the information and an enhanced recollection for where to access it [10].

Excessive screen time involving task switching between multiple screens also has harmful effects on memory, especially explicit memory which consists of episodic and semantic memory [97]. Episodic memory involves the recollection of autobiographical events from the past occurring in specific spatial and temporal contexts [98]. However, an overuse of digital recording of events (e.g., digital pictures, videos, etc.) may result in a loss of episodic memories as one begins to rely on external storage for memory rather than encoding it in the brain [97]. In a study evaluating the effects of using social media to record or share one’s experiences, it was found that participants who did not use social media consistently remembered their experiences more accurately than those who used social media [11]. These results suggest that using digital media may prevent people from remembering the very events they are attempting to preserve [11]. Semantic memory is described as the general knowledge and recall of factual information [98]. Information on the internet is often presented in hypertexts permitting users to scan information superficially which can lead to poor memory recollection [37]. Digital media adapts at a rapid pace, producing fundamental changes in written word or text (e.g., internet shorthand such as acronyms, keyboard symbols and abbreviations) [99]. Constant literary changes impede one’s ability to internalize the categorical rules of language like verb conjugation, spelling, and punctuation. Today, penmanship is dramatically diminished, which may drastically impact future generations more significantly because it serves as a tool for learning and consolidating memories [99].

In a study that evaluated the concept of digital dementia, the starting age and amount of mobile device use were potential factors leading to cognitive decline in males and females either under 20 years old or over 21 [75]. Excessive screen time is also associated with decreased attention and memory ability, alongside a greater amount of stress endured [75]. Generation Z may be a high-risk population for ADRD due to their heavy reliance on technology during critical periods of brain development and maturation. Many symptoms of excessive screen time parallel early cognitive decline as language and memory are severely impaired.

4.7 Effects of excessive screen time on attentional disorders

The rise of infant television viewing started in the late 1990s and has only become progressively more common [100]. The United States has seen a 10-fold rise in the incidence of attention-deficit disorder diagnoses in the past 20 years [100]. Television exposure early on is associated with attentional problems; in one study, 10% of children aged 1 to 3 developed attentional problems as early as the age of 7 [12]. Children viewed an average of 2.2 hours of television per day at age 1 and 3.6 hours per day at age 3. A one point standard deviation increase in the number of hours of television watched at age 1 is linked with a 28% rise in the likelihood of having attentional problems at age 7 [12].

Furthermore, increased multitasking on digital devices, particularly during study time, increases the risk of poor academic progress for adolescents and young adults [9, 14]. Interestingly, another study proposing a brain drain hypothesis for the effects of digital technology on cognition demonstrated that even when people are successful at maintaining sustained attention and avoid checking their phones, the mere presence of these devices still reduces available cognitive capacity [16]. The presence of a smartphone can adversely affect two measures of cognitive capacity, working memory capacity and functional fluid intelligence; both were negatively affected in those who had the highest rates of smartphone dependence [16].

Lastly, “digital natives”, such as Generation Z, are generations that grow up with internet technologies and drift towards a shallow information processing behavior distinguished by rapid attention shifting [37]. They also display higher incidence of internet-related addictive behaviors that reflect changed reward-processing and self-control mechanisms. Neuroimaging investigations have indicated associations between these internet-related cognitive effects and fundamental alterations in the brain [37]. A study that analyzed multitasking between different generations found that Millennials and Generation Z reported more multitasking than Generation X, who reported more multitasking than the Baby Boomers [14]. Generation Z differs significantly than Baby Boomers as they engage in heightened multitasking activities which are related to increased distractibility and poor executive control abilities [14]. Attention is necessary for all cognitive activities, and impairments in attention in adoles-
cience and early adulthood that persist into middle and late adulthood may greatly reduce overall brain reserve leading to greater risk and early signs of MCI and ADRD [101, 102].

4.8 Effects of excessive screen time on social emotional functioning and self-care

Generation Z individuals see their friends in person an hour less a day than Millennials did at similar ages [41]. On average, Generation Z adolescents in Grade 12 spend approximately 2 hours a day texting, 2 hours a day on the internet (including gaming) and 2 hours a day on social media for a total of 6 hours a day of screen time [44]. When the smartphones became more available around 2010, fewer adolescents reported that they were happy [20]. Adolescents who scored high on-screen use were significantly more likely to display poor emotion regulation, an inability to stay calm, irritability, uncooperative attitudes, lower productivity and curiosity, and damaged sociability [20]. Poor mental health is correlated with excessive screen time (any more than 2 hours per day), less sleep, or decreased in-person interactions [44]. Excessive screen use contributes to a sedentary lifestyle which is associated with reduced physical activity, lower vascular fitness, and an increased incidence of being overweight or obese [40]. In a 2007 survey it was found that 20.8% of 6 to 11-year olds and 26.1% of 12 to 17-year olds engaged in excessive screen time. Having a TV in their bedroom, for both groups, was strongly associated with excessive screen time. For the older age group, it was also strongly associated with obesity [42]. Excessive screen time on social media has negative impacts on sleep duration and/or sleep quality [41]. Adolescents in 2015 were 16–17% more likely to report sleeping less than 7 hours a night compared to those in 2009 [41]. Screen time, such as electronic device use, social media, and reading news online, rose during this time period [41]. This was linked with heightened odds of short sleep duration, with a clear exposure-response relationship for electronic devices after 2 or more hours of use per day [41]. Experimental studies show that limiting social media use to less than 30 minutes per day may lead to significant improvements in well-being (e.g., significant reduction in loneliness and depression) [38]. Symptoms of impaired self-care, emotional regulation, and social functioning are characteristic of MCI and ADRD [48]. Impairments in instrumental activities of daily living in adolescence and early adulthood that persist or worsen in middle adulthood could lead to diminished brain and cognitive-behavioural reserves increasing the risk of early onset dementia.

4.9 Effects of excessive screen time on the development of psychiatric disorders

Studies show that early sociobiological embedding of stressors tends to have enduring lifetime effects rather than transient ones and increases the risk of lifetime physical and mental illness and social problems [103]. Brain structure and function, which is the most malleable during development, is continually remodeled by environmental factors and is particularly sensitive to acute and chronic stressors which exert their effects through the neuro-immuno-endocrine system [103]. Although neuroplastic changes in response to stressors may confer adaptive advantages in the short-term (allostasis), the persistence of changes that are abnormal and irreversible can be maladaptive later in life under accumulating pressures of the biopsychosocial environment (allostatic load and overload) [103]. Excessive screen time can act as both a non-normative stimulus, exerting its effects at a sub-stress threshold level, and as an acute and chronic stressor, increasing the risk of psychiatric problems during development and later in life [4]. Evidence is emerging that excessive social media use is a significant psychosocial stressor contributing to mental health problems in adolescents and young adults, for example, by lowering global self-esteem and heightening the risk of internet addiction, and increasing the prevalence of psychopathology including attentional, hyperactivity, anxiety, and depressive disorders [4]. Unlike offline face-to-face social connection, online virtual social interaction is associated with greater incidence of internalizing problems such as social anxiety and depression [4, 20]. Specifically, the association between screen time and depression was proposed and tested with three explanatory hypotheses: displacement, upward social comparison, and reinforcing spirals [17]. Upward social comparison suggests that the impact of screen time on mental health depends on the kind of content being viewed; for example, when individuals compare themselves with others who they consider are in more favorable positions (e.g., those with perfect bodies and lives) [17]. Reinforcing spirals also posit that screen time effects are mediated through content; however, reinforcing spirals add that individuals try to obtain and choose information consistent with their thoughts which may then become increasingly negative in nature [17]. The displacement hypothesis suggests that all screen time adversely affects mental health because it displaces time one could be engaging in physical exercise and other healthy behaviours [17]. It was found that the upward social comparison and reinforcing spirals hypotheses explained associations between social media, television, and depression more than the displacement hypothesis [17]. Since those on social media platforms share the most idealized versions of themselves, it becomes commonplace for individuals to compare their real-life experiences with those of others who highlight positive moments, causing deleterious effects on self-esteem and life satisfaction [17]. Of the four types of screen use assessed (i.e., social media, TV viewing, video gaming, and computer use), only greater levels of social media and computer use were associated with depression, but not TV viewing or video gaming [17]. However, in a study on the relationship between screen time and psychological distress, internet addiction was associated with greater online video gaming and sexual activity, higher anxiety levels, and low email use [23]. Individuals with internet addiction also had increased avoidance coping mechanisms and higher rumination whilst having worsened self-care behaviors, such as seeking social support and getting adequate sleep [23]. Screen
time potentially worsens— or in some cases creates— mental health problems which some speculate may lead to premature neurodegeneration and increased risk of premature cognitive decline in later adulthood [4].

4.10 Limitations of the hypothesis and counterarguments on the evidence

Given the significant increases in average daily use of digital technology, we are concerned about the possibility of a rising trend in ADRD attributed to excessive screen time. To date, few studies have assessed the relationship between excessive screen time during development and ADRD, which is concerning because the ADRD burden is expected to at least double by 2060 [1]. The estimates provided in Matthews and colleagues (2019) [1] were from a nationally representative sample, ADRD was physician-diagnosed in a clinical setting, and sociodemographic characteristics (i.e., age, race, sex, and ethnicity) were included. We considered the same estimates as outlined in Matthews and colleagues [1] and also considered the effects of screen time and type, by age, and developmental stage. Statistical analyses by sex, race, or ethnicity were omitted because the data is not available or is not significant for these factors. Matthews and colleagues [1] also note that estimates did not include socioeconomic factors, such as education, which is a known risk factor in ADRD research [104]. To address this, our proposed hypothesis considered education attainment and IQ. Our report is the first to propose and explore the relationship between ADRD and screen time during development. Future research should consider additional factors, for example the serious short- and long-term implications of excessive screen time for the development of youth and young adult CBRR. These should include the short term implications of overall increased screen time from greater digital technology use both at home and at school (e.g., increased anxiety, depression, substance abuse, suicidal ideation and attempts etc.) and their long term consequences (e.g., permanent effects on brain development that will affect learning, memory and intelligence level, poorer school performance, greater risk of internalizing and externalizing psychological disorders, poorer overall health and economic outcomes, etc.). Future research should examine the lifelong implications of excessive screen time because it represents a significant proportion of daily activity during development, equal or greater than time spent on traditional educational activities (i.e., face-to-face instructional learning, reading from print, learning to hand write words and numbers). Additionally, physical activity should be included as a covariate because research shows that a reduction in physical activity is associated with increased screen time [105] and risk of developing ADRD [106–108].

While research on ADRD and screen time during development is limited, the current literature indicates that cognitive activity and physical activity are the two major modifiable risk factors for ADRD [106] and both cognitive and physical activity have also shown associations with screen time [109]. However, counterarguments on the evidence are mixed and inconclusive as to whether brain structure and physiology are associated with cognitive activity [106]. For example, cognitive activities may cross domains (i.e., completing a puzzle with a friend is both a cognitive activity and a social activity) and no such methods exist to classify the rate of cognitive activities (i.e., high cognitive activity versus a low cognitive activity), introducing noise into the variable [106]. Prospective research should continue to monitor the long-term effects of excessive screen time, including the ABCD study [33] that records the amount of screen use, amongst other factors, and the incidence of dementia in a large population in 2060. Preliminary results, for example in 2020 and 2040, could help inform future health policy decisions and potential preventative actions. Ideally research should focus on a number of factors including the influence of duration and type of media in order to inform appropriate guidelines and recommendations. A predicted effective approach would be to focus on informing the public on the dangers of excessive screen time use.

5. Consequences of the hypothesis and discussion

The projected estimates of those with ADRD, as reported in Matthews and colleagues (2019) [1], will double from 1.6% to 3.3%, meaning 13.9 million Americans are predicted to have ADRD in 2060. We, however, predict that from in 2060 to 2100, the rates of ADRD will rise far above the CDC’s projected estimates of a 2-fold increase to up to a four- to six-fold increase. With our prediction this would mean that up to 26.7 to 48.0 million Americans aged ≥65 years could potentially show signs of ADRD between 2060 and 2100 as Millennials and Generation Z become the majority of the elderly population. In minority populations, the disproportionate prevalence of ADRD could amplify current socio-economic disparities leading to worse health outcomes for those with ADRD and their subsequent caregivers [1]. If our proposed hypothesis is correct, then there are substantial consequences to excessive screen time for Millennials and Generation Z, and future generations to follow, which include their children and grandchildren. There are three main courses of action available to address the implications of our hypothesis: treatment, mitigation, and prevention. Perhaps the easiest, but most costly, will be treatment, whereas the least costly but most difficult will be prevention. As such, mitigation may be the most pragmatic and effective overall.

First and foremost, for the majority of Millennials and Generation Z, the negative effects of excessive screen time on development and cognitive-behavioural-brain reserve have already occurred. Thus, any negative effects can only be treated in late adulthood or potentially mitigated before then. It is possible for the youngest Generation Z individuals that these effects could potentially be reversed with targeted intervention. If nothing is done to address the concerns raised here over the next 40 years, then treatment of MCI and ADRD will be the main course of action. The health care system is
not prepared to handle the future social and economic burden of an ADRD patient population estimated to more than double or triple in size by 2060. For example, the ratio of potential caregivers to patients is currently 7-to-1 for adults in the high-risk age group, but this support is anticipated to decrease to 4-to-1 by 2030 [110]. If our projected estimates are correct it will be far lower by 2060. Furthermore, caregivers often report experiencing work disruption, decreased income and personal savings, poorer physical health increased rates of psychological distress and depression, and have increased mortality risks [111–113]. The full and future socioeconomic costs to society of ADRD are challenging to gauge, specifically in light of new and converging data suggesting that factors unique to youth and young adults today, such as declining global IQ and rapidly increasing rates of screen time, may increase their risk of accelerated neurodegeneration in early and middle adulthood and rates of ADRD in late adulthood. Recent estimates of the worldwide costs of ADRD in 2015 were equivalent to 1.1% of the global gross domestic product (GDP) and more than 85% of these costs occur in high-income countries such as the US and Canada [114]. Global economic costs of ADRD are projected to double from $1 trillion to $2 trillion (USD) in the next decade alone (e.g., from 2018 to 2030) [114, 115]. If our predictions are correct, and the prevalence of ADRD will increase by more than double the current projected rates estimated by Matthews and colleagues [1], this could cripple or even collapse the healthcare systems in North America.

Second, significant efforts could be made to mitigate the negative effects of screen time for Millenial and Generation Z adults with interventions targeted at reducing screen time, treating physical and mental health problems associated with screen time during early adulthood, and promoting factors known to increase cognitive-behavioural-brain reserve. Proper management of health, lifestyle, and wellness choices can reduce the risk of ADRD. A significant reduction in screen time will help mitigate the incidence of ADRD through preventing cognitive impairment. For example, correlational and experimental studies show that reducing screen time can improve concentration, learning, and memory [9, 12, 116], psychological well-being [117–119], reduce experiences of anxiousness and depressed moods [120], improve sleep [121] and overall mental health [63]. Studies in humans and animals models show that environmental enrichment can reduce or reverse some of the effects of deprivation, non-normative stimulation and even acute or chronic stress [122, 123] at the behavioural and neural levels [109, 124–126]. Evidence suggests that brain structure volume is influenced by environmental enrichment [106]. For instance, the London taxi driver study found that taxi drivers who drove passively (i.e., following fixed routes) had more prominent signs of hippocampal atrophy when compared to taxi drivers who drove actively (i.e., driving routes exclusively from memory) [127]. The latter raises the question as to whether students who passively take notes (i.e., on a laptop or tablet) may be more at risk for ADRD than students who take notes actively (i.e., longhand) [109], given that active participation increases cognitive-behavioural-brain reserve [106]. Additionally, increasing physical activity can prevent ADRD by improving cognitive reserve [106]. Physical activity, defined as 20 minutes of high-intensity training for 3 or more days per week or moderate-intensity training for 5 or more days per week, has been shown to decrease hippocampal, prefrontal and cingulate cortex atrophy [128, 129], all hallmarks of ADRD. By minimizing screen time, physical and mental health and environmental enrichment will improve, reducing the risk of ADRD. Correspondingly, improving physical and mental health and encouraging environmental enrichment can help to minimize screen time, and in turn lower the risk of ADRD. Thus, highlighting that the relationship between ADRD and screen time, physical and mental health, and cognitive reserve is bidirectional (i.e., improving one variable, directly affects another variable, and vice versa).

Last but not least, for future generations, it is still possible to completely avoid the detrimental effects of screen time and thus preventive measures should be the predominant focus. Excessive screen time is associated with negative physical, mental and social health effects as well as learning and behavioral disadvantages; as such potentially drastic measures should be implemented to decrease both the duration and consistency of screen use. For example, public and private investments (i.e., scholarships, awards, bursaries, and grants) could be used to encourage students from elementary through post-secondary school to replace digital learning with traditional learning. Students who can demonstrate more time engaging in non-digital enrichment activities when compared to digital enrichment activities can be eligible to apply for or receive monetary compensation. Data shows that institutional aid motivates students and encourages persistence towards program completion and graduation [130]. Additionally, education should be created to focus more on enriched environments promoting spatio-temporal learning and higher order analytic abilities, which both contribute to minimizing the risk of developing ADRD [7, 106]. Legislation can be implemented such that there are legal and economic costs (i.e., fines and incarceration) for individuals/companies who exploit the addictive nature of technology. Penalties should be of similar nature to how the US government prosecuted and convicted Big Tobacco companies for deceiving the public and racketeering [131]. Also, digital-free zones and mass public education campaigns can be implemented in public places such as schools, workplaces, places of worship, shopping malls, and restaurants with signs that promote physical activity and environmental enrichment, both proven to reduce the risk of ADRD [106]. In the short-term, the implementation of these measures will assist with reducing screen time, improve sleep and overall mental health, and have long-term implications for preventing ADRD.
6. Summary and conclusions

Estimates of the projected 2-to-4-fold increase in ADRDs for 2060 are based on age, sex, race, and ethnicity, and do not take into account significant and relevant differences in the populations used to make these predictions (i.e., Silent Generation and Baby Boomers) and the populations who will be represented in this growing burden of disease in 2060 (i.e., Millennials and Generation Z). We have identified two known critical factors that differ significantly between individuals born before 1965 and those born after 1980 which are related to the risk of MCI and ADRD: excessive screen time and intelligence. Excessive screen time has been empirically demonstrated to affect brain development and increase the risk of cognitive, emotional, and behavioural disorders in adolescents and young adults by negatively impacting attention and concentration, learning and memory, emotional regulation and social functioning, physical health, and development of mental disorders and substance use. These effects are similar to the symptoms of MCI seen in older adults that increase the risk of ADRDs. The current decline in global intelligence, estimated to have started post-1975 and projected to continue into 2050, parallels significant population level increases in screen time and could also increase the risk of MCI and ADRD. We have provided a detailed model of the effects of excessive screen time on CBBR expected to contribute to the increased risk of MCI and ADRD in Millennials and Generation Z in 2060 and beyond. The CBBR hypothesis of dementia postulates that more complex patterns of neural and mental activity in early, middle, and later life stages are associated with decreased risk of dementia as opposed to less complex patterns which are associated with increased risks. Studies show that these cortical networks and associated cognitive-behavioural abilities can be influenced by early environmental experiences including excessive screen time. If the neural circuits underlying these cognitive-behavioural abilities essential for general intelligence and lifetime adaptability are under- or abnormally-developed before adulthood, then it is likely that these changes will persist into early and middle adulthood and be more vulnerable to accelerated neurodegeneration in late adulthood therefore increasing the risk of early onset MCI and ADRDs. We present three main courses of action focused on treatment, mitigation, and prevention as measures to counteract the potential 4-to-6-fold increase in rates of ADRD post-2060 which could result in widespread societal and economic distress in an already overburdened healthcare system in North America.

Abbreviations

ABCD, Adolescent Brain and Cognitive Development; ADRD, Alzheimer’s disease and related dementias; CBBR, cognitive-behavioural brain reserve; CDC, Centres for Disease Control; GDP, gross domestic product; IQ, intelligence quotient; MCI, mild cognitive impairment; MDD, mobile digital devices.

Author contributions
LAM conceived and designed the study; LAM, MT, TMC, RE contributed to analyzing the data and writing the manuscript; LAM added graphics and edited the manuscript.

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