

Review

# Children's Health in the Digital Age

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**Abstract:** Environmental studies, metabolic research, and state of the art neurobiology point towards the reduced amount of natural day and sunlight exposure of the developing child's organism as the consequence of increasingly long hours spent indoors online as the single unifying source of a whole set of health risks identified worldwide, as is made clear in this review of the current literature. Over exposure to digital environments, from abuse to addiction, now concerns even the youngest (ages 0 to 2), and triggers, as argued on the basis of clear examples herein, a chain of interdependent negative and potentially long-term metabolic changes. This leads to a deregulation of the serotonin and dopamine neurotransmitter pathways in the developing brain, currently associated with online activity abuse and/or internet addiction, and akin to that found in severe substance abuse syndromes. A general functional working model is proposed under the light of evidence brought to the forefront in this review.

**Keywords:** digital environments; over exposure; children; vitamin D; melatonin; myopia; sleep loss; depression; obesity internet addiction; serotonin; dopamine; oxidative stress

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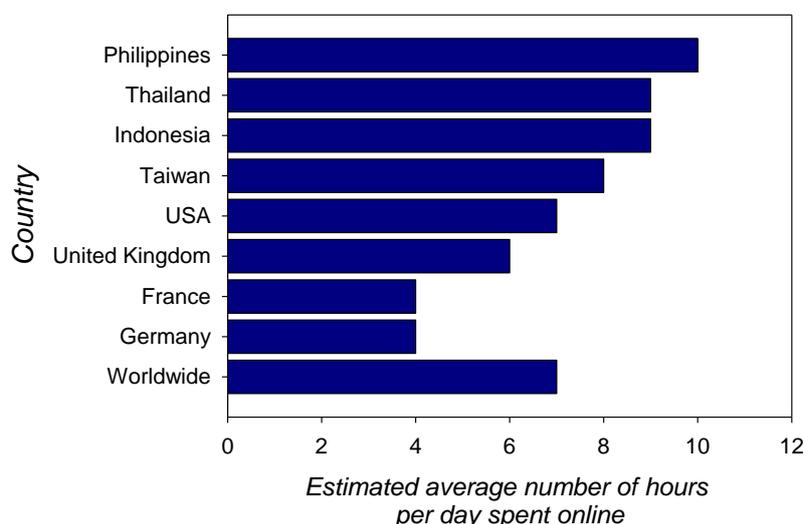
## Introduction

With rapidly spreading digitalization worldwide, more and more people and, in particular, increasingly younger children spend an increasing number of hours per day online reading on the screens of computers, tablets, and smart phones. This trend has been signaled to now include even the youngest from age 0 to 2 [1]. Results from recent studies suggest that this growing habit is likely to engender multiple health risks such as early myopia and blindness [2-10], obesity [11,12], sleep disorders, anxiety, and depression [13-18] leading to impaired performance at school and behavioral problems [19,20]. The potential impact of these health risks on our children's future lives and the well-being of future societies as a whole could be dramatic, and public awareness of this problem needs to be fostered in communities as well as on a worldwide scale. This review of environmental studies, metabolic research, and state of the art research in neurobiology points towards the reduced amount of natural day and sunlight exposure of the developing child's organism as a consequence of increasingly long hours spent indoors online as the single unifying source, or common denominator, of all the health risks already statistically identified in the literature. The cumulated lack of exposure to natural daylight environments during childhood and adolescence triggers a chain of interdependent negative and potentially long-term effects on the regulation of a child's physiology. This includes the deregulation of brain mechanisms ensuring far vision, or long-distance visual capacity, vitamin D levels, and neural circuitry, in particular the serotonin and dopamine transmitter pathways, in the still developing brain. Already identified risks of massive digitalization to the health of children and adolescents are identified in the first part of this paper. Complex causal links between different metabolic factors involved in a complex cause-effects chain from digital environment to brain and behavior are then brought to the forefront. The analysis leads to the conclusion that the health of future generations may be severely compromised if nothing is done to raise public awareness about the necessity for regulatory measures at all levels prompting children

to change and self-monitor their interactions with digital environments wherever possible to minimize risks already identified likely to already have taken their toll.

### 1. The health risks of children's over exposure to digital environments

In the middle age access to written sources like scrolls or bound manuscripts was the privilege of clerics and aristocracy. Books were written and copied by hand then, essentially by monks in monasteries, until Gutenberg revolutionized printing and made books available to all. People worldwide started reading and, over the centuries, shortsightedness caused by reading for long hours under poor light became more and more frequent [21]. Then, people learnt that it was important to read under good lighting conditions and to take breaks. Now, there is a new boost in myopia worldwide as a consequence of digital technology. Computers, the internet, smart phones, tablets and e-books have re-shaped our reading and learning habits entirely, and since 2014 there are officially more mobile devices than people in the world [22]. We can access hundreds of resources on almost any subject with just a click of a button and by using search engines, which is much more practical and efficient. Technology has also changed the way we use libraries. Instead of going outdoors to make our way to the library and search the shelves, we reserve the book we want online before fetching it at the library. While this saves us a lot of time, it has also conditioned us, and our children, into spending many more hours indoors reading small text on smaller and smaller screens online. Schools and universities around the world now offer tuition online, and for many pupils and students using a book, pen, and paper has become a thing of the past. Tablets that hold the contents of hundreds of books, video classes, online learning, online homework sessions and online exams enable students to stay connected with their schools 24 hours a day. According to data from the Global Web Index Survey, published online in 2019 [23], the average time spent by individuals between 16 and 64 years of age may be estimated to seven hours per day worldwide (Figure 1). In the USA in 2017, this number was estimated to amount to two hours and twenty minutes per day for children between zero and two years of age [24], and to four hours and thirty minutes for kids between eight and twelve years of age [24,25].



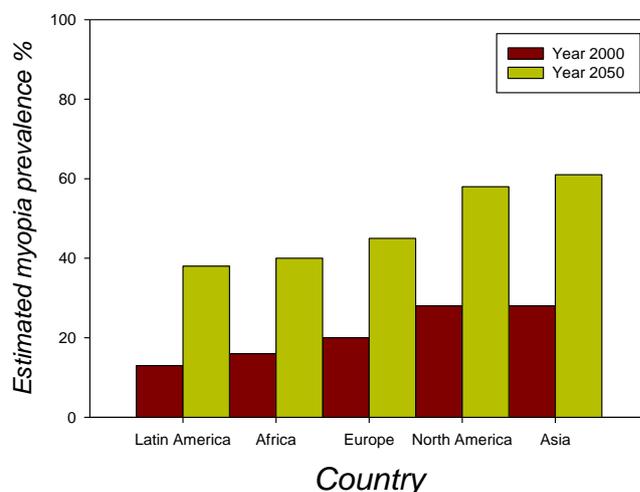
**Figure 1.** Estimated average time (number of hours per day) spent online by individuals between 16 and 64 years of age. Times vary, as shown here, between countries. The average time spent online is currently estimated to seven hours per day worldwide, and expected to increase further. In the USA in 2017, this number was estimated to amount to two hours and twenty minutes per day for children between zero and two years of age, and to four hours and thirty minutes for kids between eight and twelve years of age [ref web].

A pilot study was conducted in the framework of the EU project ECIT (Empowering Citizens' rights in Emerging Information Technology). ECIT was aimed at identifying new threats to children by

digital technologies beyond social networks to develop recommendations, and to empower children's rights by preventing and mitigating risk issues through education, school/community co-vigilance, and a reorientation of digital and personal interactions through raised awareness and parental guidance. Research has mainly targeted 9-16 years old, but some have shown that children are going online at an increasingly younger age [1]. Very young children cannot be made aware of the risks they incur when gaming online, and despite the substantial increase in online activity in very young children, research is lagging behind. This is alarming and points toward an urgent need for more research fast, as this growing habit promotes the early onset and speedy progress of axial myopia, which ultimately leads to blindness if it is not treated as early as possible, as demonstrated by recent studies on the dramatic increase in early myopia and blindness due to an excessive exposure to digital screens in younger and younger children worldwide.

### 1. 1. Myopia and early blindness

Recent evidence for a dramatic rise of myopia and early blindness in children as a consequence of excessive exposure to computer and smart phone screens [2-9] sends out a severe warning signal to governments, parents, and clinicians worldwide. Especially in East and Southeast Asia childhood myopia has risen dramatically during the last 60 years [4-10], as extensively documented in reports on studies which comprehensively describe and analyze the history, epidemiology, and the presumed causes of the worldwide "myopia boom" [3]. This trend is unequivocally linked to the general society trend where adults spend a large part of their time online, and where children start out way too early in life looking at the screens of computers, tablets and smart phones for hours every day. The specific form of early myopia this habit engenders is due to an excessive growth of the eye in the longitudinal direction [2] and referred to as axial myopia. If left untreated, the disease progresses relentlessly and leads to severely impaired vision and, ultimately, blindness. In East and Southeast Asia, about 95% of the population needs glasses or contact lenses to restore functional clear vision beyond an arm's length. This statistic [2] exceeds by far the estimates from an earlier report, published four years ago [3], of expected increase in myopia prevalence in different countries of the world including Asia between the years 2000 and 2050 (Figure 2). It can be expected that current statistics from other countries are also likely to already exceed the predictions made for 2050 in this earlier report. The most likely explanation for this worrisome trend towards rapidly increasing myopia worldwide is that kids now become myopic early in childhood because their eyes grow too fast as a result of excessive time spent reading close-up on increasingly smaller screens of digital devices (computers, tablets, smart phones).



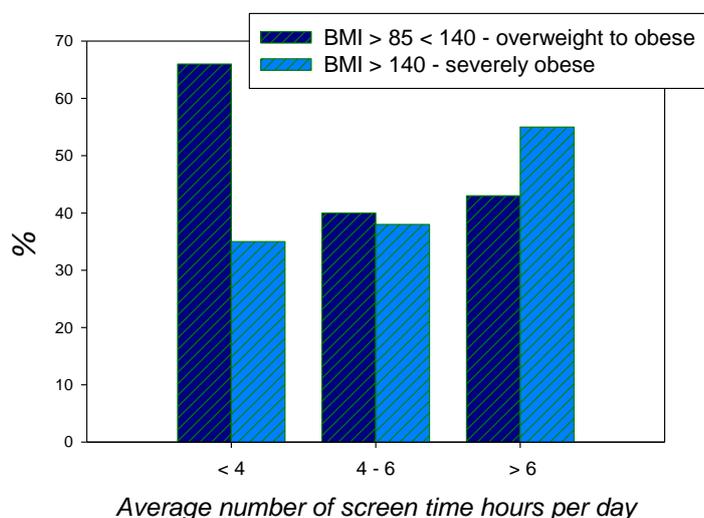
**Figure 2.** Estimated increase in myopia prevalence in populations from different countries of the world including Asia between the years 2000 and 2050 [3]. The percentages shown here are based on

data from an earlier report published five years ago. Current statistics from a more recent review [2] reveal that in 2019 only 5% of the total populations of East and Southeast Asia still had normal (uncorrected) vision. This leads to suggest that higher percentages than shown here above are to be anticipated for the year 2050 if nothing gets done to stop the worldwide trend of myopia in children.

This entails that kids do not get enough outdoor activity and suffer a cumulated lack in exposure to sufficient amounts of daylight. Myopia is estimated to currently affect 108 million people worldwide and identified as the second most common cause of global blindness [21]. The worldwide economic burden of uncorrected distance vision impairment, of which myopia is the main cause, is currently estimated to 202 billion Dollars per annum. With the rising prevalence of myopia in young children, this economic burden will also rise. In addition, myopia is associated with other complications such as myopic macular degeneration, retinal detachment, cataract, and glaucoma. Once myopia has set in, treatment must be initiated as early as possible to stop the progression towards total blindness.

### 1. 2. Obesity

Excessive online activity has recently been associated with a significantly higher Body Mass Index (BMI) in pre-adolescent children [11,12], pointing towards a link between digitalization and childhood obesity. Current statistics on childhood obesity collected by the World Health Organization Commission on ending childhood obesity [26] reveal that the number of overweight or obese infants aged 0 to 5 years has increased from 32 million in 1990 to 41 million in 2016. This number is currently projected by the WHO to reach 60 million worldwide by 2035, and ensuring that our kids follow the right diet will not be enough to prevent this from happening. Obesity is deemed one of the most challenging public health problems faced by developed and developing countries worldwide. Screen media exposure is deemed a well documented cause of obesity in children and obesity a well documented consequence of screen media exposure [27-31]. Exposure to 'screen media' in this context refers to exposure to content on any screen including that of tablets, computers, smart phones or TV sets. The most recent evidence for a direct link between the severity of childhood obesity and the number of screen time hours comes from a cross-sectional survey study within the Childhood Obesity Multi Program Analysis and Study System (COMPASS) on consecutive patients seeking treatment at five tertiary care weight management programs located within geographically diverse children's hospitals of the United States [29]. Results from this survey indicate that the severity of a child's obesity increases with the number of hours of daily screen time (Figure 3).



**Figure 3.** Results of a recent survey from the USA revealing the link between the severity of obesity and the number of screen time hours per day in children treated for obesity in different hospitals across the country [29].

To explain the link between screen time and obesity in children, previous theories used the assumption that excessive screen time reduces time spent being physically active and, as a consequence, the child will gain weight. However, recent epidemiologic studies on the one hand point towards much more complex causal links [32,33], and experimental studies on the effects of reduced screen time have on measurable increases in physical activity did not yield conclusive results [29,31]. This suggests that the lack of physical activity is not a self-sufficient direct link between long screen times and obesity. There is stronger evidence for increased energy intake as a prominent causal link between screen times and childhood obesity. Epidemiologic studies have shown that children who spent more screen time statistically consume fewer fruits and vegetables and more energy snacks, soft drinks, or fast food, and receive a higher percentage of their energy from fats and a higher total energy intake [30]. Eating while viewing increases children's daily energy intake [28], as demonstrated by studies where children were reported to consume a large proportion of their daily calories and meals during screen time while watching. However, the reasons for this change in the eating habits of kids exposed to longer screen times are only beginning to be unraveled. They relate to complex metabolic changes involving a variety of factors that will be made clear later herein.

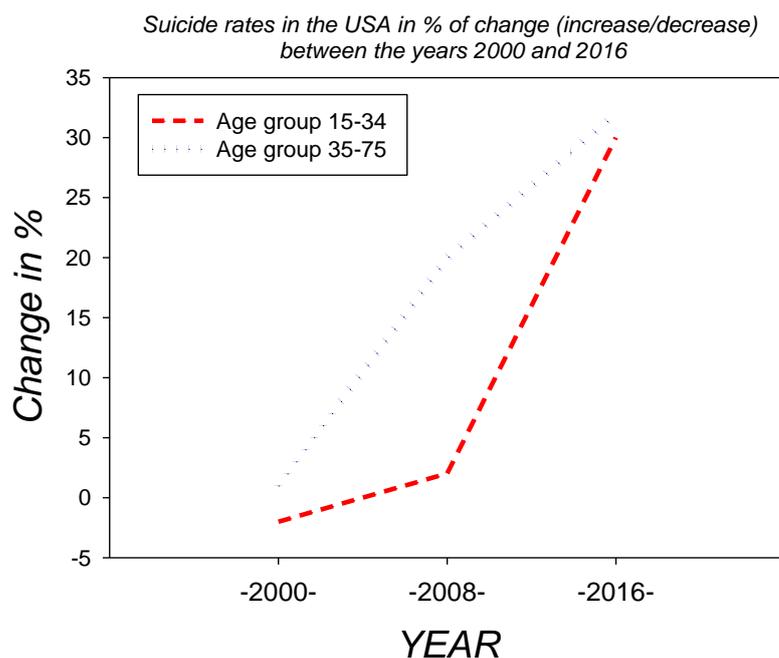
### 1. 3. *Sleep disorders, anxiety, depression*

Long hours of exposure to digital technology or online activity have been associated with loss of sleep and/or symptoms of depression in young students [13]. When children or students have to get up early for school or college, delayed bedtimes due to online reading until late can take a serious toll. Several studies have linked delayed bedtimes to poor performance in school, impaired learning, and psychological problems [18-20]. Electronic media, especially when used before bedtime, have a negative impact on the sleep of children and adolescents [34-48], and while shorter total sleep times have been consistently related to media use, coherent brain-behavior models of the underlying mechanisms are still lacking. However, it has become quite clear now that over exposure to digital environments, and the metabolic changes it produces in children, has a measurably negative impact on their cognitive development [49]. Significant relationships between digital device exposure and sleep variables tested in different studies include shorter times spent in bed and shorter total sleep times [36,37,39], delayed bedtimes or longer sleep onset latency, more frequent night waking, delayed wake-up times [38, 41-46], daytime sleepiness or tiredness, bed time resistance, sleep anxiety [13-20], sleep-disordered breathing pathologies and sleep-wake transition disorders [19, 20] and excessive daytime somnolence [36-46]. Populations tested range from children of age 5 to adolescents of age 19. Virtually no data are available on the effects of the duration of exposure to digital environments, which have been estimated to 2.5 hours per day on average for the youngest aged between 0 and 2 years of age in the USA recently [24,51]. Recent evidence for negative physiological and psychological effects of excessive exposure to digital environments in kids younger than 5 years of age is available [50-51], but more research is urgently needed here. Most importantly, maladapted and excessive use of the internet results in a new syndrome now officially referred to as Internet Addiction (IA) or Internet Addiction Disorder (IAD). This syndrome [52] most widely, and severely, affects young people, and is associated with various other negative consequences on health and behaviour including sleep disorders, depression, and cognitive dysfunction beyond, as we will see in the next sub-chapter. Large survey studies, behavioural experiments, and molecular and/or functional imaging approaches have been employed over recent years to extend the analysis of the neurobiological changes as a consequence of excessive online activities, and to pin down the major neurochemical correlates of internet addiction.

#### 1. 4. Digital addiction

IAD is a disabling condition that calls for full consideration as it has a severe impact on young people's brain functioning. Internet addiction disorder (IAD), sometimes also called pathologic/problematic internet use (PIU), is widely defined in terms of an impulse control disorder characterized by uncontrolled Internet use [52-68]. The disorder is associated with significant functional impairment and/or clinically measurable distress, anxiety, depression and other psychopathological symptoms [59-63]. IAD is not (yet) classified as a mental disorder in the Diagnostic and Statistical Manual of Mental Disorders - Fifth edition (DSM-5), but a subtype of IAD, the internet gaming disorder (IGD), which specifically refers to videogame addiction, has been included in Section 3 of the DSM 5 [62]. It is currently envisaged to include IAD and IGD also into the International Classification of Diseases for mortality and morbidity statistics ICD-11 [63]. A meta-analysis on IAD performed six years ago [56] and involving more than 89000 participants from 31 nations reported a global prevalence estimate for IAD of 6% worldwide. The highest estimates for IAD prevalence were scored for the Middle East in terms of about 12% of the reference population, the lowest for Northern and Western Europe, with about 2.5% of the reference population. These estimates were made six years ago. A study conducted on Indian college students [57] identified male gender, continuous online availability, predominant use of the internet for new friendships/relationships as major risk factors. Higher computer skills and easy Internet access in teenagers and young adults represent an augmented risk for IAD [56,57,58]. Internet addiction (IA) has emerged as a universal issue, but its international estimates vary considerably. Two factors have been considered to explain cross-national variations [53-58]. One is internet accessibility, which varies between continents and nations and predicts that IA prevalence should be positively related to the internet penetration rate per capita. The other factor, referred to as real life quality, predicts that IA prevalence should be inversely related to the global national index of life satisfaction and/or other specific national indices of environmental and lifestyle quality. Personal technology usage (PTU) has hit young people in the USA, with 92% internet penetration, currently the highest worldwide, "fast and hard", as pointed out in a recent article on the effects of PTU on children and youth [68]. This recent online article published by the US Naval Institute Proceedings describes the internet in terms of a virtual hypodermic mechanism that delivers a digital drug content in a highly effective manner, particularly via the smartphone. This drug seems to hamper children's ability to manage and balance time, energy, attention, and thereby leads to lifestyle changes and behavioral deficits. The mediating effects of insomnia and associations between problematic Internet use including Internet Addiction (IA), Online Social Networking Addiction (OSNA) and depression among adolescents [51-61] have been highlighted in a population of more than thousand secondary school students from Guangzhou in China [61], which has about 70% internet penetration, i.e. about 30% less than the USA or Europe. Levels of depression, insomnia, IA, and OSNA were assessed using the Center for Epidemiological Studies Depression Scale (CESDS) [69], the Pittsburgh Sleep Quality Index (PQI) [70], Young's Diagnostic Questionnaire for Internet Addiction (YDQIA) [71], and the Online Social Networking Addiction Scale (OSNAS) [72]. The results from this cross-sectional study reveal that a high prevalence of IA and OSNA is associated with increased risk of developing depression among adolescents, both directly and/or as a consequence of insomnia associated with the addictive behaviour [60,61]. Insomnia therefore is a factor that may be a trigger and/or a chronically developing consequence of IA and OSNA. Likely depression predicts IA and OSNA, and vice versa, among those subjects who were free from either problem at baseline [61]. Conclusions from this study suggest that it may be effective to consider problematic Internet use, insomnia, and depression jointly as all three seem to be clearly interdependent in the light of these and other findings [58-61]. The high incidence of depression and increasing suicide rates in teenagers has become a worldwide concern that calls for an urgent scrutiny. Depressed individuals might go into online social networking as a secure and non-threatening means of communication with the outside world and as a means for alleviating anxiety related to personal problems. Thus, excessive internet use appears to be a maladapted coping strategy [68] that accelerates the development of digital addiction on the one hand, and augments the withdrawal from interpersonal

offline activities that could lead to effective coping with real world problems. As a consequence the young person, instead of coping or learning to cope with problems through real-world interaction with others, spirals further and further down the slippery slope of depression, insomnia and, ultimately, loneliness. A study published in 2017 the *American Journal of Epidemiology* [73] has shown that teenagers are particularly vulnerable in this respect and that the trend towards online technology-induced teenage depression and associated symptoms may well reach epidemic proportions if nothing gets done to stop it. Recent national statistics made available in a US Naval Institute Publication [68] show estimates for suicide rates in individuals for two age ranges across the years 2000-2019 in terms of % of change per annum. The curves reveal an alarming trend towards increase, which has been particularly steep for ages 15-34 between years 2008 and 2016 (Figure 4). The narrative of the publication links this trend to digital addiction.



**Figure 4.** Estimates for suicide rates in the USA, which has an internet penetration index of 92% of the global population, between the years 2000 and 2016. Estimates are expressed here in % of change (increase/decrease) per annum showing an alarmingly steep increase for the age group of 15 to 34 year old individuals. The data shown here have been replotted on the basis of a report published by the US Naval Institute in 2018 [68] which points towards a link between the increase shown here and digital addiction, especially in younger individuals. The hypothesis is consistent with data from scientific studies, summarized here above, showing a tight connection between internet addiction, insomnia, and depression in young males and females.

## 2. The early deregulation of neurotransmitter pathways in the child's developing brain: towards a unifying model account

What science needs most now is a working model that provides a unifying account of brain-behaviour function underlying the health issues identified here, as they are quite clearly intertwined as multiple cause of one and the same environmental fact, which is excessive exposure to electronic device technology. Molecular and functional imaging findings on neurobiological mechanisms of internet addiction, focusing on magnetic resonance imaging (MRI) and nuclear imaging modalities including positron emission tomography and single photon emission computed tomography have become available [64-66]. MRI studies reveal structural changes in the frontal cortex associated with functional abnormalities in Internet addicted subjects [66]. Nuclear imaging findings indicate that IA is associated with dysfunction of the brain dopaminergic systems [64,65],

indicating that de-regulation of the prefrontal cortex may underlie reward specific uncontrolled behavior in internet overuse in addicted subjects. Results from a set of independent studies [74-78], mostly conducted in East Asia on young male subjects with internet gaming disorder, were recently analyzed in a comprehensive metareview [79]. This analysis led to conclude on functional alterations, similar to those observed in substance abuse, in brain regions involved in cognitive control functions [74-76], and reward/punishment sensitivity balance [76]. These findings connect with other functional evidence from neurobiology, as will become clear herein further below. The narrative will highlight the complex cause-effect chain that links increased exposure to digital environments to decreased exposure to healthy natural daylight and increased exposure to artificial light sources at the wrong time of day, deficient vitamin D and melatonin levels in the body, perturbed circadian rhythms as a consequence and, ultimately, the progressive deregulation of the serotonin transmitter pathways in the human brain. This generates a newly emerging syndrome of cognitive and emotional dysfunctioning akin to that found in severe substance abusers. It will be highlighted how these deregulatory mechanisms are triggered, and progressively develop into a syndrome, in children now including even the youngest aged 0 to 2 [51], as a consequence of over exposure to digital environments.

## 2. 1. *Exposure to the wrong kind of light at the wrong time*

Myopia is estimated to globally affect 108 million people worldwide and is identified as the second most common cause of global blindness, and the worldwide economic burden of uncorrected distance vision impairment, of which myopia is the main cause, is currently estimated to 202 billion Dollars per annum [80-82]. With the rising prevalence of myopia in children, this economic burden will also rise [80-83]. In addition, myopia is associated with other complications such as myopic macular degeneration, retinal detachment, cataract, and glaucoma. Once myopia has set in, prismatic or bifocal lenses, and specially designed multifocal soft contact lenses, and outdoors eye exercises have shown positive results in slowing myopia progression [84-88], which ultimately leads to blindness. Lifestyles which place emphasis on sports and outdoor living and where kids grow up accordingly, as in countries like Canada, Australia, or New Zealand, may explain why these countries have the lowest occurrence of myopia in the world. When kids are spending time outdoors, they are actively using and training their long distance vision by focusing on objects further away in the visual field. This is even more critically important in very young children (age zero to two) with still developing visual systems and brains. The development of visual capacity in very young kids takes place over many months [89]. Although current research into the brain development that may limit visual function at an early age suggests a relatively mature neural organization in human infants, despite such anatomical maturity, there is a high degree of visual plasticity with critical sensitive periods [90] of visual functional maturation, highlighted by a differential time-course for the development of form and motion sensitive visual capabilities in normally developing children [91]. It has been suggested that during a critical period, kids are particularly vulnerable to any abnormal visual experience [89]. The growing trend in very young kids to spend their time indoors with their eyes glued to the screen of a smart phone or a computer may, indeed, qualify as an 'abnormal visual experience' and prevent them from exercising their far vision capacities under well-balanced natural viewing conditions, as those from times before the digital age. Like our muscles, our brain and visual capacities tend to weaken when we do not use them properly, especially during functional development in childhood. Results from clinical studies examining the association between hours spent outdoors and prevalent myopia, incident myopia, and myopic progression [85-88] produced pooled odds ratios and 95% confidence intervals for each additional hour spent outdoors per week from a meta-analysis. The pooled ratios indicated odds of myopia reduced per 2% per additional hour of time spent outdoors per week [85,86]. Prospective cohort studies provided estimates of risk of incident myopia and myopic progression as a function of time spent outdoors indicating that increasing time spent outdoors significantly reduced both the risk of incident myopia and the speed of myopic progression. Whether daily exposure to very bright light per se might protect kids from developing near-sightedness is not known, and the mitigating

effects of time spent outdoors are probably mostly due to the fact that outdoor play allows practicing far vision [87,88]. What is known, however, is that a sufficient amount of exposure to daylight is critically important to preserving good health, and to mitigate risks of developing depression and other mood disorders [92]. The temporal organization of human physiology in terms of circadian rhythms [93-96] is critical to our health, and especially to that of our children. Since electric light was invented, however, pervasive exposure to artificial light sources at night has blurred the boundaries between day and night, making it more difficult for humans to synchronize all sorts of biological processes. Many physiological systems are under the control of circadian rhythms, which influence our sleep-wake behavior, hormone secretion, cellular functions and even gene expression. Circadian disruption by nighttime light perturbs all those processes, and is associated with an increase in the incidence of cancer, metabolic dysfunction, and mood disorders [93,94,96]. Electronic tablet computer screens and smartphone screens can emit more than 40 Lux, depending on the size of the screen. More and more children (and their parents) leave electronic devices such as computers switched on in their bedroom while sleeping [100]. As a consequence, the amount of artificial light exposure at night is, indeed, unprecedented in human history. Exposure to light at night perturbs the circadian system because light is the major entraining cue used by the body to discriminate day and night, and when exposure to light is not timed properly or becomes constant, biological and behavioral rhythms are desynchronized, which has severe consequences for a child's (and an adult's) health. Excessive daytime sleepiness as a result of a perturbed day-night rhythm has been, indeed, linked quantitatively to obesity, anxiety, and sleep disorders in young children [97-99]. With the widespread use of portable electronic devices and the normalization of screen media devices in the bedroom, insufficient sleep is now affecting 30% of toddlers, preschoolers, school-age children and the majority of adolescents [102]. In recent literature reviews of studies investigating the link between youth screen media use and sleep, 90% of included studies found an association between screen media use and delayed bedtime and/or decreased total sleep time [47,48]. Proposed mechanisms include displacement of time that would have been spent sleeping, psychological stimulation due to blue light source exposure in the evening or even at night, and increased physiological alertness [100]. This pervasive phenomenon of pediatric sleep loss has widespread implications due to the associations between insufficient sleep and increased risk of childhood obesity [97,98] disrupted psychological well-being [97-99] and impaired cognitive function [49,103]. There is a clear need for more research on the effects of screen media on sleep loss and health consequences in children and adolescents on the one hand, and a need for more general information to motivate society stakeholders to foster healthy online behavior to ensure healthy sleep habits. Indeed, as reviewed in the previous chapter here above, the habit of spending longer and longer hours reading online has recently been associated with childhood obesity, loss of sleep and/or symptoms of depression in increasingly younger individuals, and sleep disorders and insomnia in young individuals have both been linked to online addiction. Thus, a holistic analysis of the current evidence reviewed here points towards higher risks of early myopia, obesity, sleep disorder, depression, and online addiction in children who spend too much time online exposed to artificial light sources, often at the wrong time of day, as a consequence lack exposure to healthy outdoor light.

## 2. 2. *Resulting functional consequences of vitamin D and melatonin deficiency*

A critically important factor to good health quite clearly is the amount of daylight our children get while they develop, which in our current digital society is reduced to insufficient rates worldwide. These rates are likely to be even more insufficient as digitalisation progresses further. Exposure to healthy daylight is essential to the regulation of vitamin D and melatonin production in the human body [104-106], as both vitamin D and melatonin ensure important and closely related metabolic functions in the regulation of eating habits and sleep [107-115]. Vitamin D helps delay age-related changes in the human body including degenerative changes in the visual system [116]. Knowing that the outer retina has the highest metabolic demand in the body, retinal health is also dependent on sufficient levels of Vitamine D and melatonine in the body [116-119]. Exposure to as much daylight

as possible contributes to healthy vision, and may play a hitherto unsuspected role in the prevention of early vision loss in children exposed to digital environments by preventing the accelerated ageing of their retina [117,118]. Exposure to daylight increases levels of retinal dopamine in the visual system of myopic kids and slows down the progression of myopia [2]. The right amount of daylight, especially sunlight, helps produce adequate levels of vitamin D in the human body, and a well-regulated rhythm of daylight and nightlight exposure helps produce adequate levels of melatonin. Since both are functionally related, insufficiency in both engenders health risks [120-130] such as obesity [121], poor sleep [112,113,129], depression [120,122,126], and addictive behaviours [121,128] well beyond formerly identified physiological issues related to poor bone growth and muscle function [123-125]. There is now growing evidence that vitamin D ensures the healthy function of the neurotransmitter dopamine in the central nervous system [120-122] leading to new insights into the importance of vitamin D to the health of children beyond the mere recognition of its importance for calcium homeostasis and bone growth [124,125]. Vitamin D significantly impacts the immune systems in charge of preventing infections and regulating autoimmunity [130]. The neurohormonal effects of vitamin D and melatonin deficiency on brain development and behavior, linking to cognitive impairment and mental health disorders [120-122,126,128], highlight the interdependency between their metabolic regulation and the regulation of the dopamine neurotransmitter pathways in the brain [126,129,131,132,133-135]. The health consequences of vitamin D deficiency include the development of symptoms of dementia due to an increase in cerebral soluble and insoluble peptides, and a decrease of its anti-inflammatory/antioxidant properties in the brain [134]. The reduction of buffering of increased calcium in the brain also may cause hypoxic brain damage, and promote the development of depression, borderline schizophrenia and other mental illnesses [121,125]. The fact that obesity rates in children have risen dramatically worldwide in recent years may correlate with low levels of circulating vitamin D3 in their body, which significantly correlates with a high adiposity index [127]. The mechanism of exactly how vitamin D contributes to/interacts with melatonin production and healthy sleep are just beginning to be elucidated. It appears that it might have something to do with vitamin D regulation of tryptophan hydroxylase (TRPH) expression – the rate-limiting enzyme in serotonin and consequently melatonin production [136]. Vitamin D potentiates the expression of neuronal TRPH to stimulate the appropriate production of serotonin in the brain, and without sufficient serotonin production, melatonin levels will not rise appropriately to give the body the signal to go to sleep at night [136,137,138]. Vitamin D regulation in the body is closely linked to melatonin regulation, and both are critically influenced by the right amount of light a child is exposed to at the right time of day. Like vitamin D, melatonin is an antioxidant that scavenges free radicals in organism, and has anti-inflammatory [139], antitumor [140], and antiangiogenic effects [141]. Melatonin is a hormone mainly produced by the pineal gland when lights are out [129]. A subgroup of photosensitive retinal ganglion cells is responsible for mediating the light-dark cycles that regulate melatonin secretion in the body, and the melatonin release function obeys a circadian rhythm and correlates with sleep patterns [137,138]. Patients with circadian rhythm sleep disorders, including blind patients with no light-induced suppression of melatonin, benefit from melatonin treatment [142,143]. Melatonin is synthesized in the retina and other parts of the body. Recent studies have highlighted the antioxidative, antiapoptotic, and autophagic effects of melatonin on oxidative damage to retinal cells and photoreceptors [144]. Thus, like vitamin D, melatonin is important to the healthy development of a healthy retina and visual system. Melatonin has been found effective in the treatment of insomnia and depression [145,146]. The hormone is produced by the human body at night and, like vitamin D, it influences dopaminergic neurotransmitter release functions in the brain [122]. Significant effects of dopamine release under the influence of melatonin have been demonstrated in specific areas of the mammalian brain, and our further understanding of diurnal variation in dopamine is critical for understanding and treating the multitude of psychiatric disorders, including digital addiction, that originate from perturbations of the dopamine system. [147]. These elements all taken into consideration suggest that excessive indoor times spent online by children is likely to have a negative effect on a variety of dopamine-dependent behaviors. A pilot

study specifically explored the association between peripheral blood dopamine level and internet addiction disorder (IAD) in adolescents [148], knowing that chemical drug abuse cocaine and pathological gambling have neurobiological effects resulting in increased peripheral dopamine levels. The results of this study showed that peripheral blood dopamine levels in adolescents with internet addiction were twice as high compared with those of healthy controls [148]. This provides further evidence that dopamine pathway regulation is dysfunctional in digital addicts.

### 2. 3. *Early deregulation of neurotransmitter pathways in the developing brain*

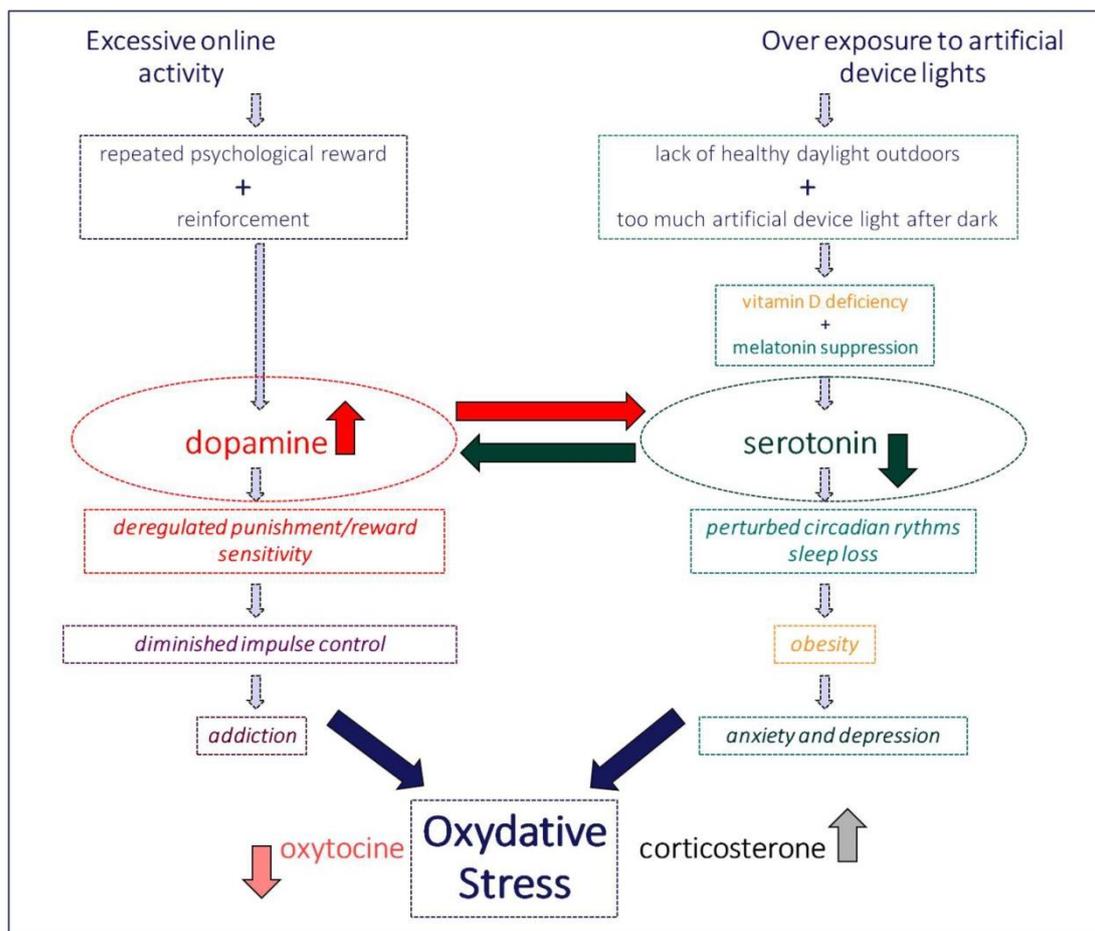
As discussed here above, exposure to daylight directly increases levels of retinal dopamine in the visual system of myopic kids and slows down the progression of myopia. Also, as the review here above has shown, sufficient amount of exposure to natural daylight “outdoors” regulates vitamin D levels, while both the right amount of daylight at the right time, and “lights out” at the right time (before going to bed) regulate melatonin levels, knowing that the latter is produced when lights are out, and the body stops producing it under daylight exposure. Sufficient levels of both vitamin D and melatonin are necessary for a healthy retina and visual cell function, healthy eating habits, and healthy sleep patterns, as also reviewed in detail here above. Both vitamin D and melatonin deficiency caused by excessive exposure to digital environments, especially during childhood, severely interfere with the healthy regulation of the neurotransmitter serotonin in the body [149, 150], while the reward circuitries involved in digital addiction change the regulation of the dopamine pathways in the brain [148]. This points towards a tightly interwoven cause-effect chain linking too much time spent on digital devices indoors on the one hand, and digital addiction on the other, to a general deregulation of neurotransmitters involved in the cognitive control of a child’s whole metabolism, from eating habits and sleep patterns to general intellectual capacity.

Serotonin is a neurotransmitter that contributes to the healthy regulation of a large number of physiological processes, and its production depends on healthy levels of both vitamin D and melatonin. Both melatonin and vitamin D synthesis are affected by light, and vitamin D is directly involved in melatonin secretion [150,151]. Serotonin is both an excitatory and an inhibitory neurotransmitter found in enteric neurons and in the brain [149-150]. Serotonin synthesis requires magnesium, zinc, and vitamin B6 and vitamin C as cofactors. In the pineal gland and the retina, the enzyme *N*-acetyltransferase converts serotonin to *N*-acetyl serotonin, which in turn is converted to melatonin and released into the bloodstream and cerebrospinal fluid by the enzyme 5-hydroxyindole-*O*-transferase, a process that requires the active form of vitamin B6 [149]. As a consequence, the serotonin neurotransmitter pathways ensure central brain control of the rhythm of sleep/wake periods and the immune response of the whole organism. This control breaks down in a so-called serotonin-and-melatonin- deficiency syndrome frequently diagnosed in elderly patients [152]. This syndrome may be seen as a correlate of premature ageing and, when present in the young, rings a serious alarm bell indicating that the mind-body system is under severe stress. Serotonin has an important role in decision making behaviour [153,154]. Serotonergic antidepressant, anxiolytic and antipsychotic drugs are extensively used in the treatment of neuropsychiatric disorders characterized by impaired decision making [153]. High serotonin levels are generally associated with improved reversal learning, improved attentional set shifting, decreased delay discounting, and increased response inhibition [154].

The neurotransmitter dopamine is produced in the *substantia nigra*, ventral tegmental area, and hypothalamus of the human brain. Dysfunction of the dopamine system has been related to a variety of nervous system diseases [155,156]. Dopamine levels in the brain and the periphery (blood) increase in response to any type of reward and to a number of functionally identified chemical substances and/or non-chemical drugs [155], which include sex, gambling and, most recently, the “digital drug” [149]. Dopamine transmitter pathway deregulation is a consequence of oxidative stress in the body [155]. Interactions between the serotonergic and dopaminergic transmitter pathway systems, both at the anatomical and the functional level, have been identified [156]. In

mammals, the central serotonergic system modulates the activity of dopaminergic neurons in the circuits connecting the *substantia nigra* to the *striatum* and the ventral tegmental area. Substances like reserpine and amphetamine induce symptoms that closely resemble those associated with depression and/or schizophrenia, and the pharmacological treatment of both directly targets the serotonergic and dopaminergic neurotransmitter systems [156]. Both dopamine and serotonin play an important role in drug and alcohol dependence by mediating the mechanism of dopamine reward and withdrawal symptoms. Patients with Internet Gaming Disorder (IGD) show a significant decrease in the level of availability of dopamine in the striatum and a reduced availability of serotonin [157]. This appears consistent with recent functional magnetic resonance imaging studies showing that IGD adolescents and adults have reduced gray matter volume in regions associated with attention motor coordination executive function, and lower white matter measures in brain regions that control for both serotonin and dopamine dependent decision-making, behavioral inhibition, and emotional regulation, leading to increased risk-taking and diminished impulse control ability common to all forms of addiction [158].

All these elements of evidence here above taken into account, it becomes clear that a unifying working model account of the whole set interdependent early childhood metabolic disorders and health problems that are the consequence of over exposure to digital environments may be proposed (Figure 5).



**Figure 5.** Excessive online activity and, ultimately, digital addiction inevitably go along with an over exposure to artificial device lights. Each of these two produces clearly identified changes in metabolic rates that negatively affect either the dopamine or the serotonin transmitter pathways in the child's still developing brain. Anticipated long-term consequence of such early brain deregulation are incommensurable. The working model shown above fully takes into account evidence from state-of-the-art research studies, reviewed in this paper.

### 3. Conclusions

This focused review of critical elements from the current literature shows quite unequivocally that the projection of increasingly excessive times spent online indoors [159] by increasingly younger children is likely to put their physical and psychological development and general health at risk, in the short and long term perspective. Early childhood myopia, disturbed circadian rhythms, sleep loss, depression and, ultimately, addiction and the deregulation of central control functions in the brain, initiated by lack of exposure to healthy outdoor light conditions, are the main risks identified here. Myopia is estimated to globally affect 108 million people worldwide and is identified as the second most common cause of global blindness. The worldwide economic burden of uncorrected distance vision impairment, of which myopia is the main cause, is currently estimated to 202 billion Dollars per annum. With the rising prevalence of myopia in children, this economic burden will also rise. In addition, myopia is associated with other complications such as myopic macular degeneration, retinal detachment, cataract, and glaucoma. School-based clinical trials have demonstrated that increasing the amount of time that children spend outdoors to a little more than two hours a day can significantly slow the onset of myopia. It may be necessary to implement mandatory outdoor programs in schools, and the regular monitoring of visual acuity of children from age two worldwide. Those children who have already become myopic should be referred for clinical treatment as soon as possible to slow down the progression of their myopia. The recent rise in depression or oxidative stress syndrome [160] in teenagers and even younger children is also alarming. As pointed out earlier here, scientific studies have linked depression in students to their online behavior. There may be other factors involved as well, however, a devoted public campaigning aimed at raising levels of awareness worldwide that too much screen time is not only good for the eyes, but also for the soul of children, teens, and adults, seems to be a good idea from many points of view. Statistics on childhood obesity collected by the World Health Organization lead to conclude that the number of overweight or obese infants aged 0 to 5 years has increased from 32 million in 1990 to 41 million in 2016. It is currently projected to reach 60 million worldwide by 2035, and ensuring that our kids follow the right diet may not be enough to prevent this from happening. While times spent online by our children are likely to increase further, scientific experts reckon that the currently recommended doses of food supplementation fall way short of what is needed to obtain the necessary levels for optimal health. A worldwide food supplementation program [161,162] seems urgently needed to prevent the progress of vitamin D and/or melatonin deficiency related health problems in kids (and also adults). Plant generative organs (e.g., flowers, fruits), and especially seeds, have been proposed as having the highest melatonin concentrations. While reinforcing a worldwide supplementation program could certainly have a dramatic impact on children's health worldwide, the first step to take is to raise public awareness of the tight link between time spent online indoors and a severely compromised long-term brain health of kids and teens. Diet control and food supplements can help here, but are clearly not the sole solution. The spreading disease of digital overexposure or abuse [163-165] worldwide is likely to have already taken a toll on even the youngest (toddlers between 0 and 2 years of age), not yet measurable in terms of short and long term consequences on their bodies and brains, but risks to have a dramatic negative impact, worldwide, soon. In short: we must get our kids off the digital hook - the time to act is now.

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