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Effects of digital games training on hormonal responses and brain plasticity

Efeitos do treinamento com jogos digitais nas respostas hormonais e na plasticidade cerebral

Efectos del entrenamiento con juegos digitales sobre las respuestas hormonales y la plasticidad cerebral

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Abstract
Digital games are a ubiquitous part of almost all children's and adolescents' lives. At the same time gaming industry is ready to unlock new levels of growth in the coming years (Granik et al., 2014). A growing number of studies have already focused on the beneficial effects of digital games on various aspects of cognition and health. However, less emphasis has been given to the physiological biomarkers that operate in the background and cause various modifications in players' mental and emotional states as well as their ability to be aware and take control over their decisions and actions. Hormones and neurotransmitters regulate homeostasis and determine to a significant extent humans' health, state of mind, and self-awareness abilities. Neuroplasticity is now recognized as a crucial factor in acquiring new skills and abilities. The present study aims to investigate the impact of digital game-playing on hormone responses and neuroplasticity phenomena. To this objective, we conducted a literature review presenting the most representative experimental studies. The results showed that digital games have significant effects on hormone responses and neuroplasticity phenomena. Finally, we discuss the factors that may contribute to alterations in digital game players' homeostasis. The findings of this review aim to contribute to the discussion regarding the design of targeted, novel game-based intervention tools that have the potential to improve homeostasis, drive positive neuroplasticity, accelerate metacognitive learning, and thereby promote mental and emotional well-being for both typical populations, but most importantly, for people with learning disabilities, mental and other disorders.
Keywords: Digital games; Hormones; Neurotransmitters; Neuroplasticity; Mental and emotional health; Learning; Metacognition.

Resumo
Os jogos digitais são uma parte onipresente da vida de quase todas as crianças e adolescentes. Ao mesmo tempo, a indústria de jogos está pronta para alcançar novos níveis de crescimento nos próximos anos. Um número crescente de estudos já enfocou os efeitos benéficos dos jogos digitais em vários aspectos da cognição e da saúde. No entanto, menos ênfase tem sido dada aos biomarcadores fisiológicos que operam em segundo plano e causam várias modificações no estado mental e emocional dos jogadores, bem como em sua capacidade de estar ciente e assumir o controle de suas decisões e ações. Hormônios e neurotransmissores regulam a homeostase e determinam de forma significativa a saúde, o estado de espírito e as habilidades de autoconsciência dos seres humanos. A neuroplasticidade é agora reconhecida como um fator crucial na aquisição de novas competências e habilidades. O presente estudo tem como objetivo investigar o impacto do jogo digital nas respostas hormonais e nos fenômenos de neuroplasticidade. Para tanto, realizamos uma revisão da literatura apresentando os estudos experimentais mais representativos. Os resultados mostraram que os jogos digitais têm efeitos significativos nas respostas hormonais e nos fenômenos de neuroplasticidade. No entanto, fazemos uma ampla discussão sobre os fatores que podem contribuir para alterações na homeostase dos jogadores de jogos digitais. Os resultados desta revisão visam contribuir para a discussão sobre o design de novas ferramentas de intervenção baseadas em jogos que tenham o potencial de melhorar a homeostase, impulsionar a neuroplasticidade positiva, acelerar a aprendizagem metacognitiva e, assim, promover o bem-estar

mental e emocional para ambos. populações típicas, mas mais importante para pessoas com dificuldades de aprendizagem, transtornos mentais e outros.
Palavras-chave: Jogos digitais; Hormonas; Neurotransmissores; Neuroplasticidade; Saúde mental e emocional; Aprendizagem; Metacognição.

Resumen
Los juegos digitales son una parte omnipresente de la vida de casi todos los niños y adolescentes. Al mismo tiempo, la industria del juego está lista para desbloquear nuevos niveles de crecimiento en los próximos años. Un número creciente de estudios ya se ha centrado en los efectos beneficiosos de los juegos digitales en varios aspectos de la cognición y la salud. Sin embargo, se ha dado menos énfasis a los biomarcadores fisiológicos que operan en segundo plano y provocan diversas modificaciones en el estado mental y emocional de los jugadores, así como en su capacidad para tomar conciencia y tomar control sobre sus decisiones y acciones. Las hormonas y los neurotransmisores regulan la homeostasis y determinan en gran medida la salud, el estado mental y la capacidad de autoconciencia de los humanos. La neuroplasticidad ahora se reconoce como un factor crucial en la adquisición de nuevas habilidades y destrezas. El presente estudio tiene como objetivo investigar el impacto de los juegos digitales en las respuestas hormonales y los fenómenos de neuroplasticidad. Con este objetivo, realizamos una revisión de la literatura presentando los estudios experimentales más representativos. Los resultados mostraron que los juegos digitales tienen efectos significativos sobre las respuestas hormonales y los fenómenos de neuroplasticidad. Sin embargo, hacemos una extensa discusión sobre los factores que pueden contribuir a las alteraciones en la homeostasis de los jugadores de juegos digitales. Los hallazgos de esta revisión tienen como objetivo contribuir a la discusión sobre el diseño de herramientas de intervención novedosas y específicas basadas en juegos que tienen el potencial de mejorar la homeostasis, impulsar la neuroplasticidad positiva, acelerar el aprendizaje metacognitivo y, por lo tanto, promover el bienestar mental y emocional para ambos. poblaciones típicas, pero lo más importante para las personas con discapacidades de aprendizaje, trastornos mentales y de otro tipo.
Palabras clave: Juegos digitales; Hormonas; Neurotransmisores; Neuroplasticidad; Salud mental y emocional; Aprendizaje; Metacognición.

1. Introduction

Digital games are a ubiquitous part of almost all children’s and adolescents’ lives. At the same time gaming industry is ready to unlock new levels of growth in the coming years. A wide range of terms and definitions concerning digital games are proposed, mainly due to the existence of multiple digital media designed for gaming. As a result, the term "digital games" has become equivalent to a variety of terms, including computer games, digital games, electronic games, and video games. Digital games share some common features such as the gaming environment, the strong participation of the gamer, the element of interactivity, and the increased use of multimedia (Manesis, 2020).

Digital games’ classifications present various categories according to their objectives and characteristics. For instance, digital games can be divided into two general categories, namely commercial and serious games, depending on their objective (Choi et al., 2020). Serious games aim to use new gaming technologies for educational or training purposes (Papanastasiou et al., 2017). Unlike serious games, commercial video games are designed for the entertainment of players. However, a growing number of studies reveal that commercial tools may also be used not only for entertainment but also as brain training tools (Choi et al., 2020).

Common types of games are traditional games (i.e Tetris), action games, simulation games, and strategy games (Choi et al., 2020). Except for the type of game, several influence factors differentiate digital games’ outcomes. Users’ factors include players’ experience, playing style, motivation, age, gender, emotional status, and intended relaxation. System factors involve game genre, game structure, game mechanics and rules, technical system setup, and design characteristics. A crucial role also plays the context factors, interaction quality, and aesthetic aspects (Möller et al., 2013).

Studies have already shown that playing digital games can boost cognitive abilities as well as various aspects of human intelligence (Pappas et al., 2017; Kokkinakis et al., 2017). Expert video game players often outperform non-players on measures of attention, memory, speed, and executive control. Experts are more able to track objects moving at greater speeds, better detect changes to objects stored in visual short-term memory, switch more quickly from one task to another, and mentally rotate objects more efficiently (Boot et al., 2008). In addition, digital games are recognized as tools for gradual and profound skills training and development with a high potential to support expertise in different fields of human life (Stafford, 2022)

A growing number of studies indicate that digital games and especially serious games constitute effective strategies for training, and intervention for people with learning difficulties, special needs, and other disabilities (Papanastasiou et al., 2017). Gaming is now established as an alternative solution to traditional mental health treatment methods. Even commercial digital games provide evidence of their psychotherapeutic benefits in reducing symptoms of depression and anxiety (Kowal et al., 2021). In addition, they are now examined as a complementary intervention for various psychiatric or long-term degenerative disorders (Zayeni et al., 2020; Alves et al., 2018). Studies have also revealed that digital game playing is associated with analgesic effects and pain relief (Puig et al., 2020)

Playing digital games is also associated with positive feelings and well-being. Playing video games, appropriately designed, can boost cognitive health, emotional balance, and socialization (Barr et al., 2022; Pallavicini et al., 2018). Gaming is also associated with states of mind that are closely associated with peak performance and superior learning outcomes (Chen et al, 2020). Games have already been recognized as valuable educational tools with a significant potential to be applied in educational settings to support cognitive, motivational, affective, and social processes that underlie learning (Mayer, 2019). Most importantly, digital games have significant potential in learning procedures because they influence motivation and metacognition (Mayer, 2019). Digital games raise players' self-awareness because of cultivating players' sense of agency, while training players in applying self-regulation strategies (Hacker, 2017).

Although there is extensive research regarding the impact of digital games on various aspects of human life (health, well-being, cognition, learning), less emphasis has been given to the physiological parameters that operate in the background and unconsciously contribute to various positive or negative outcomes. In addition, there is a growing interest regarding the impact of gaming on neuroplasticity phenomena.

The objective of the current review is to examine the impact of digital gaming on hormonal responses and neuroplasticity phenomena. Specifically, we aim to investigate whether and how digital games alter hormones that are closely related to anxiety, depression, aggression, or motivated learning, positivity, and effective self-regulation. In the second part of this study, we examine whether digital games playing influence neuroplasticity and neurogenesis phenomena. Through this study, we also expect to identify possible factors (i.e game genre, game’s content) that may contribute to diverse physiological responses. With this study, we expect to put more emphasis on the role of games on human homeostasis and shed more light on the physiological variables that induce specific cognitive and emotional states and incite players to specific behaviors.

2. Methodology

The objective of this narrative review was to present an overview of the available and most representative evidence on how digital game playing is associated with players’ hormone responses and neuroplasticity phenomena. The methodology was based on the guide lines of narrative reviews (Pare et al., 2015). The literature search was conducted in two scientific, online databases (Scholar Google and PubMed). To be included in this review, studies had to examine the effects of digital games (i.e. video games, computer games, virtual reality games) on hormones/neurotransmitters and other biomarkers which are responsible for neurogenesis and neuroplasticity phenomena. In our search, there were no restrictions regarding the age of the participants, or gender. Although we tried to give priority to the most recent research, in several cases we also included older ones. We focused on surveys written after 2010, however older surveys were also included when they met the survey requirements. Priority also was given to experimental studies and randomized controlled trials. For this study, we excluded non-digital games, and other physiological parameters (i.e heart rate, blood glucose, and blood pressure). After the full-text screening, the 30 remaining studies were included in the final analysis.

3. Results and Discussion

3.1 Digital Games on Brain Chemistry

Neurons in the human brain communicate with each other by releasing chemical messengers called neurotransmitters. Neurotransmitters are chemical signals released from presynaptic nerve terminals into the synaptic cleft. The subsequent binding of neurotransmitters to specific receptors on postsynaptic neurons briefly changes the electrical properties of the target cells. Hormones secreted by the endocrine system typically influence target cells far removed from the hormone-secreting cell. This “action at a distance” is achieved by the release of hormones into the bloodstream.

Neurotransmitters include acetylcholine, glutamate, and γ-aminobutyric acid (GABA). A significant role also plays the catecholamines like norepinephrine (noradrenaline), epinephrine (adrenaline), dopamine, and serotonin. Neuropeptides include oxytocin. Hormones and neurotransmitters play a significant role in the proper functioning of cognitive and emotional functions and have a major impact on human behavior (Kovacs, 2004; Drigas and Mitsea, 2021). According to Drigas and Mitsea (2021), hormones and neurotransmitters affect brain areas and physiological procedures that are associated with metacognitive abilities, which enable humans to be aware of and take control over cognition (Drigas and Mitsea, 2020-2022).

Dopamine: the ‘reward’ neurotransmitter

Dopamine is the neurotransmitter that is responsible for the feeling of pleasure and excitement. Dopamine is closely related to motivation and reward learning. However, dysregulation of dopamine levels may contribute to addictive behaviors (Dayan, 2002; Drigas and Mitsea, 2021). Koepp et al. (1998) used 11C-labeled raclopride and positron emission tomography scans to investigate whether endogenous dopamine is produced in the human striatum during a goal-directed motor task in a video game. For a monetary incentive, eight male volunteers played a computer game in which they learned to navigate a tank. It was found that raclopride binding to dopamine receptors in the striatum was decreased substantially during the video game compared to the baseline rates, consistent with higher dopamine production and binding to its receptors. Thus, video games can cause the production of dopamine in the brain's reward pathways, resulting in a sense of euphoria.

Testosterone: The tenacity hormone

Oxford et al. (2010) assessed the impact of playing violent games on testosterone levels. The participants were 14 three-member teams of undergraduate men (n=42), with a mean age of 19 years (S.D.=.97). Men who contributed the most to their teams' between-group victory showed testosterone increases immediately after the competition. The testosterone response during the between-group competition also suggests that violent multiplayer video games may be appealing to young men because they simulate male–male coalitional competition.

Cortisol: the stress hormone

Cortisol regulates various fundamental physiological functions and significantly influences cognitive abilities like memory. However, abnormal elevation of cortisol levels is associated with cognitive impairments, chronic disorders such as anxiety and depression, and neurodegeneration phenomena (Drigas and Mitsea, 2021).

Aliyari et al. (2018) investigated the impact of different types of video games on the stress hormone cortisol. A sample of 80 players, aged 18 to 30 years played a runner game, an exciting game, a fear game, and a puzzle game. Before and after the intervention, the saliva samples of the participants were collected to measure their levels of cortisol. The results showed that the puzzle game, which trains attention and concentration, reduced cortisol levels, while the runner, excitement, and fear games increased cortisol. The authors concluded that the digital game genre has a different impact on autonomous nervous systems and, as a result on stress hormones release.

Aliyari et al. (2020) investigated the effects of violent and football video games on cognitive functions, cortisol levels, and brain waves. A total of 64 participants competed in a single-elimination tournament. Saliva samples of all players were measured before and after the games for the evaluation of cortisol levels. The results showed that both games reduced cortisol levels.

Aliyari et al. (2015) evaluated the effects of the game Fifa 2015 on cognition and hormonal levels. Thirty-two subjects aged 20 years on average participated in playing the computer game. The impact of playing computer games on the cortisol concentration of saliva before and after the game showed that the amount of saliva plasma after playing the game dropped significantly. It was also revealed that sustained attention also increased after the game.

Hébert et al. (2005) investigated the effects of music on hormone levels in video game playing. Two groups of participants (one playing with techno music, the other one playing in silence) played a video game for ten minutes and gave four saliva samples for analysis of cortisol levels at regular intervals. The findings showed that the built-in sound environment of video games, here pop/techno music, increased cortisol levels.

Gentile et al. (2017) investigated the impact of violent content in video games on cortisol. One hundred and thirty-six children participated in the current study with an average age of 8 to 12 years old. Results showed that the violent video game increased cortisol more than the equally exciting non-violent game. The violent game also increased the accessibility of aggressive thoughts. The cortisol findings indicated that playing a violent video game may activate the sympathetic nervous system and elicit a fight-or-flight type response in children.

Epinephrine: the “excitement” neurotransmitter

Epinephrine mediates short-term responses to stressors by initiating behavioral and physiological changes that help a person cope with the stressful stimulus. Epinephrine interacts via various projections to the prefrontal cortex, midbrain, and locus coeruleus, areas that influence higher mental abilities (Drigas and Mitsea, 2021).

Phan-Hug et al. conducted a pilot study to evaluate the impact of videogame playing on various metabolic indicators including the hormone epinephrine. Twelve children were subjected to two distinct tests at a few weeks' intervals: (i) a 60-min video gaming session followed by a 60-min rest period and (ii) a 60-min reading session followed by a 60-min rest period. The results showed an increase in heart rate ($p = 0.05$) as well as a norepinephrine increase ($p = 0.03$) during the video gaming session when compared to the reading session. This pilot study also suggested that video game playing could induce a state of excitation sufficient to activate the sympathetic system.

Serotonin: the ‘balance’ hormone

Serotonin stands for mental balance and regulates mood and emotion. It improves self-confidence and self-satisfaction. Several cognitive domains appear to be sensitive to changes in serotonin such as memory, attentional functions notably focused and sustained attention, and cognitive flexibility (Schmitt et al., 2006; Drigas and Mitsea, 2021).

Podrigalo et al. (2020) examined the metabolic and endocrine changes of forty-five schoolboys engaged in computer gaming. The participants were divided into two groups: the active players' group (n=26) and the control group which consisted of 19 schoolboys who did not play computer games at all. The results showed differences in homeostatic indicators between children belonging to the group of active players in comparison with those who do not have contact with computer games. The experimental group of active players showed increased levels of serotonin.

GABA: The relaxation hormone

Prena et al. (2020) measured the inhibitory neurotransmitter γ-aminobutyric acid before and after 30 minutes of a goal-directed spatial decision-making video game play. Thirty-seven participants aged 18 to 26 years old, were recruited. The sample consisted of the non-gamers group who played video games for under one hour a week and the gamers group who played at least five hours per week. While there were no significant variations in hippocampus GABA concentrations before and after gaming for both gamers and non-gamers, there was a significant quadratic relationship between spatial working memory task performance and post-gaming hippocampal GABA concentrations.

Oxytocin: the 'socialization' hormone

Oxytocin is a neuropeptide with a neurobehavioral role since it regulates a wide range of positive social behaviors. Oxytocin not only reduces amygdala reactivity but also increases the amygdala's connectivity with areas responsible for emotional regulation and social cognition. (Drigas and Mitsea, 2021; Yoon et al., 2020)

Aliyari et al. (2022) evaluated the electrophysiological and biochemical indicators of stress after playing a scary video game. Thirty volunteers were divided into two groups control and experimental. The saliva and blood samples were collected before and after the intervention to measure cortisol and salivary alpha-amylase levels, oxytocin, and brain-derived neurotrophic factor (BDNF). It was found that cortisol and alpha-amylase levels were significantly higher after the gameplay ($P<0.001$ for both). Oxytocin and BDNF plasma levels decreased after playing the scary game ($P<0.05$ for both). The authors concluded that perceived stress significantly elevates among players of scary video games, which adversely affects the emotional and cognitive capabilities, possibly via the strength of synaptic connections, and dendritic thorn construction of the brain neurons among players.

Grizzard (2013) examined the effect of cooperative play on the generosity and associated cooperative gameplay with increased production of oxytocin, a neuromodulating hormone related to bonding, trust, and social interaction. A random assignment (solo versus cooperative play) experiment with an offset control condition was conducted using a guitar-music video game as stimuli. Before and after gameplay, oxytocin was measured using salivary samples. However, the examination of this hypothesis was prevented by sudden and unexpected problems associated with analyzing oxytocin from salivary samples.

3.2 Digital Games on Neuroplasticity

Neuroplasticity can be defined as the brain's ability to change, remodel and reorganize for purpose of better ability to adapt to new situations (Demarine et al., 2014). The term plasticity refers to the changes in neural organization which may account for various forms of behavioral modifiability, either short-lasting or enduring, including maturation, adaptation to a mutable environment, specific and unspecific kinds of learning, and compensatory adjustments in response to functional losses from aging or brain damage (Berlucchi et al., 2009). Neural networks are not fixed but occur and disappear dynamically throughout our whole life, depending on experiences. When we regularly practice a single action, such as a sequence of motions or a mathematical problem, neural circuits emerge, resulting in a greater capacity to complete the trained task with less energy loss. Neuroplasticity may occur either at a structural or a functional level (Demarin et al., 2014). The technological revolution provides new game-based tools that may drive positive neuroplasticity, accelerate learning, and strengthen cognitive function, thereby promoting mental well-being in both healthy and impaired brains (Mishra et al., 2016). Recent studies support the idea that computerized training, including video games, can boost neuroplasticity phenomena and learning (Pappas and Drigas, 2019).

Kühn et al. (2014) investigated the structural neural changes resulting from a video game training intervention. It was hypothesized that a video game with a prominent navigation component, that is, the necessity to orient in a three-dimensional environment, and with orientation and strategic demands would have measurable neuroplasticity effects. A training group that consisted of 23 participants was instructed to play the video game Super Mario 64 on a portable Nintendo Dual Screen XXL console for at least 30 min per day over 2 months. A passive control group (n=25) had no task but underwent the same testing procedure as the training group 2 months apart. It was found a significant gray matter increase in the right hippocampal formation, right dorsolateral prefrontal cortex, and bilateral cerebellum in the training group. These brain areas play a crucial role in memory, intelligence, and metacognition. The researchers concluded that video game training could be used for people with smaller hippocampus and prefrontal cortex volume, for example in post-traumatic stress disorder, schizophrenia, and neurodegenerative disease.

West et al. (2018) investigated the impact of action video games on brain plasticity. In two studies, participants received 90 hours of training on either an action video game, a 3D-platform game (such as Super Mario 64), or an action role-playing game. All participants underwent magnetic resonance imaging (MRI) brain scans and their brain tissue density was measured. A randomized longitudinal training experiment demonstrated that first-person shooting games reduced grey matter within the hippocampus in participants using non-spatial memory strategies, while players who used hippocampus-dependent spatial strategies showed increased grey matter in the hippocampus after training. It was concluded that video games can be beneficial or detrimental to the hippocampal system depending on the navigation strategy that a player employs and the genre of the game.

Kühn et al. (2014) examined the magnetic resonance imaging scans of 152 14-year-old adolescents, to estimate the cortical thickness. Their examination revealed a robust positive association between cortical thickness and video gaming duration in the left dorsolateral prefrontal cortex and left frontal eye fields. These areas are responsible for executive control and strategic planning which in turn are essential cognitive domains for successful video gaming. Left frontal eye fields are a key region involved in visuomotor integration important for the programming and execution of eye movements and allocation of visuospatial attention.

Schaeffer et al. (2022) assessed the effects of exergaming on hippocampal volume and brain-derived neurotrophic factor levels in Parkinson's disease. Seventeen patients and eighteen healthy controls participated in a 6-week exergaming training program, combining visually stimulating computer games with physical exercise. Volumetric segmentation of hippocampal subfields on T1- and T2-weighted magnetic resonance imaging, as well as serum levels of brain-derived neurotrophic factor (BDNF), were studied before and after the training program. The results showed that physical exercise combined with computer games increases the brain-derived neurotrophic factor serum levels, as well as the volume of the hippocampus not only in healthy adults but also in patients with Parkinson's disease.

Similar studies outline the beneficial effects of video gaming combined with various types of exercises on brain plasticity. For instance, Cui et al. (2020) concluded that hippocampal neurogenesis induced by aerobic exercise is more likely to survive when simultaneously accompanied by cognitive stimulations, particularly when the cognitive goals are challenging.

West et al. (2017) assessed the effects of 3D-platform video game training (i.e., Super Mario 64) on grey matter in the hippocampus, cerebellum, and prefrontal cortex of older adults. Older adults aged 55 to 75 years old were randomized into three groups. The experimental group (n = 8) participated in a 3D-platform video game training over 6 months. An active control group took a series of self-directed, computerized music (piano) lessons (n = 12), while a no-contact control group did not engage in any intervention (n = 13). After training, the grey matter within the hippocampus, as well as the cerebellum, significantly increased in the video games training group.

Butler et al. (2020) investigated whether video gaming play could increase hippocampal volume in male patients with combat-related posttraumatic stress disorder (PTSD). Patients with combat-related PTSD were randomly assigned to either an experimental Tetris group (n = 20) or a control group (n = 20). Following therapy, hippocampal volume increased in the Tetris group, but not in the control group.

Momi et al. (2019) quantified the immediate and long-lasting cognitive and morphometric impact of a systematic gaming experience on a first-person shooter game. Thirty-five healthy participants were assigned to a video gaming and a control group and underwent a cognitive assessment and structural magnetic resonance imaging at baseline, immediately post-gaming, and after 3 months. Morphometric analysis revealed immediate structural changes involving bilateral medial and posterior thalamic nuclei, as well as bilateral superior temporal gyrus, right precentral gyrus, and left middle occipital gyrus. The involvement of posterior thalamic structures highlights a potential link between video games and thalamocortical networks related to attention mechanisms and multisensory integration processing.

Momi et al. (2021) used functional magnetic resonance imaging (fMRI) to quantify acute and long-lasting connectivity changes following a sustained gaming experience on a first-person shooter game. Thirty-five healthy participants were assigned to either gaming or a control group. The analysis of data revealed significantly greater connectivity between the left thalamus and left parahippocampal gyrus in the gamer group, both post-gaming and at a 3-month follow-up. The increased functional connectivity induced by action video games is associated with better spatial orientation, visual discrimination, and motor learning.

Kral et al. (2018) examined the effectiveness of an empathy training video game on empathic accuracy and related brain activation in 74 adolescents aged between 11 to 14 years. Participants completed a resting state functional MRI scan and an emotional accuracy task during an fMRI scan before and after 2 weeks of daily gameplay with either the empathy training game (n= 34) or a commercial video game (n = 40), as an active control condition. Engagement with the empathy training video game was associated with a higher increase in the right temporoparietal junction. Connectivity in empathy-related brain circuits (posterior cingulate–medial prefrontal cortex) was stronger after the gameplay. The more individuals engaged with the video game, the stronger the connectivity in brain circuits relevant to emotion regulation was. The researchers concluded that a video game designed to increase empathic accuracy produces functional neural changes in fewer than 6 hours of gameplay in adolescents.

Benady-Chorney et al. (2020) assessed the differences in resting state functional connectivity between action video game players compared to non-video game players on the hippocampus, the caudate nucleus, and the nucleus accumbens. Seventeen and sixteen non-action video game players were scanned using fMRI. Results showed that action video game players had increased resting state functional connectivity between the nucleus accumbens and the subgenual anterior cingulate cortex and between the caudate nucleus and the precentral gyrus. Action video game players also displayed decreased connectivity between the hippocampus and the superior temporal gyrus and between the nucleus accumbens and the ventral tegmental area. These results indicate that frequent action video game playing is associated with higher functional resting state functional connectivity activity in the reward circuit and lower functional activity within the hippocampus.

He et al. (2021) examined the structural brain differences associated with extensive massively-multiplayer video gaming. The results of this study showed that extensive massively-multiplayer video gamers (those who play about 3 h/day) are morphologically different from non-gamers in that they have reduced volumes, thinner cortices, and sometimes shallower sulci in regions that govern self-control (prefrontal areas). They also have a thinner superior parietal lobule sulcus, presumably reflecting increased concentration and visuomotor abilities.

Lee et al. (2012) examined changes in brain function during a complex visuomotor task following training using the Space Fortress video game. Participants underwent functional magnetic resonance imaging (fMRI) before and after 30 hours of training with one of two training regimens: Hybrid Variable-Priority Training, which focused on improving specific skills and managing task priority, or Full Emphasis Training, which simply practiced the game to obtain the highest overall score. Hybrid Variable-Priority Training learners reached higher performance on the game and showed less brain activation in areas (right dorsolateral prefrontal cortex) related to visuospatial attention and goal-directed movement after training. These findings indicated that brain areas involved in complex visuomotor processing decrease in activity as a result of training.

Gong et al. (2015) investigated the relationship between action video games and the plasticity of insular subregions and the functional networks, which are responsible for attentional and sensorimotor functions. Two groups of subjects were tested: the experts' group and the amateurs' group. It was revealed that action video gaming experts had enhanced functional connectivity and grey matter volume in insular subregions. In a later study, Gong et al. (2016) found that expert players in action video games exhibit better integration between Salience Network and Central Executive Network, which are responsible for attention and working memory.

Martinez et al. (2013) used a test-retest methodology to examine changes in resting-state functional connectivity following videogame training. The experimental group (n=10) was trained during a maximum of 16 h (2 h by session, two sessions by week) on a pack of reasoning puzzles (Professor Layton and The Pandora's Box, by Nintendo) under strict supervision in the laboratory. fMRI techniques revealed increased connectivity of the thalamus, hippocampus and prefrontal areas which are involved in various meta-cognitive processes.

Sadeghi et al. (2022) conducted a randomized controlled trial to compare physical training with virtual reality cognitive games on cognition, and serum-derived blood markers in individuals with multiple sclerosis. Forty-eight subjects were randomized to three groups: 18 received physical rehabilitation, 20 received VR-based cognitive rehabilitation, and 10 received no intervention. The VR cognitive rehabilitation program consisted of three games targeting sensorimotor integration, memory-based navigation, and visual search. Each intervention lasted 8 weeks for three 1-hour sessions per week. Results showed that virtual reality cognitive games increased neurotrophic factors, which are responsible for neurogenesis and improved memory and cognition.

4. Final Considerations

The first question of our research concerned the effect of digital games on hormones that are primarily responsible for the regulation of cognition, emotion, and behavior. The results of this review provided evidence regarding the impact of digital game-playing on hormones such as dopamine, cortisol, serotonin, oxytocin, and adrenaline. It was obvious that digital game playing alters hormones' responses. However, the ways this happens vary. In the case of cortisol, the core hormone of anxiety, it was found that games with violent content or games that stimulate feelings of high excitement or fear tend to increase cortisol levels. However, games that require attention and concentration tend to reduce cortisol levels. Interestingly, it was found that even the music used as a soundtrack can influence users' hormones. In addition, it was found that games, especially action games, induce a state of excitement and euphoria elevating hormones such as dopamine and adrenaline. The same tendency was observed with other hormones. For example, oxytocin, the hormone of socialization, appeared to decrease in scary games, but there were indications that in games that promote generosity, the results may be quite different.

The second research question concerned the impact of digital games training on neuroplasticity phenomena. The results revealed that digital games training is associated with neurogenesis and neuroplasticity phenomena. Specifically, studies revealed that game-playing is associated with structural neural changes. Experimental studies confirm volume increases in brain areas responsible for metacognition, executive control, self-awareness, and spatial working memory. Specifically, increases were observed in the hippocampus, prefrontal, and cerebellum. Interestingly, it was revealed that the player's experience as well as the type of strategy used play a significant role in neurogenesis phenomena. For instance, the users who use spatial strategies have more chances to increase the volume and connectivity of brain areas that govern higher mental abilities. These results are of great importance for both healthy populations and people with mental and emotional disorders. Healthy people can improve their skills and intelligence. People with reduced volume in crucial brain areas or with weak interconnectivity usually face various disorders (i.e depression) (Kuhn et al., 2014). Digital games have the potential to fire neurogenesis processes minimizing disabilities.

Except for volume increases, the finding revealed increased long-lasting connectivity between brain networks and areas which are responsible for attention, multisensory integration processing, and emotional regulation. For instance, enhanced connectivity was observed between the thalamus, hippocampus, and prefrontal (Martinez et al., 2013; Momi et al., 2019; 2021; Kral et al., 2018; Benady-Chorney et al., 2020).

In addition, studies revealed the elevation of the factors that contribute to neurogenesis and neuroplasticity phenomena. Playing digital games, especially when combined with physical exercise (exergames), accelerate the release of neurotrophic factors (Schaeffer et al., 2022; Sadeghiet et al., 2022).

This research had some limitations. Most limitations concerned the relationship between digital games and hormonal responses. We initially found that there was not enough research focusing on games' impact on hormone and neurotransmitter levels, while most research investigated hormone responses after playing violent games. For instance, while the relationship between digital games and motivation, reward system, addiction, and pleasure is well-known, only one research was found related to the effect of games on dopamine levels.

Now there is a multitude of digital games that are effectively used as tools to train new skills, improve mental abilities, and improve several dysfunctional health conditions in various psychiatric and neurodevelopmental disorders. Already, a growing number of studies have shown the beneficial effects of reducing stress, and depression and improving learning difficulties. However, there isn't an overwhelming amount of research explaining how these games have a beneficial effect on a physiological level. Thus, future research should further investigate the impact of digital game playing on various biomarkers, with a special focus on serious games, brain training and mental health digital games.

In addition, future experimental research should examine the factors (game content, music, characters, gender) influencing the effect of games on hormones and neurotransmitters. Such investigations could help to better understand the physiological processes involved in game playing. Systematic research should be done to determine those characteristics both in terms of content and in terms of the use of interfaces that can bring beneficial results.

In addition, future research should emphasize the beneficial role of digital games both on adults and young people's brains. Especially for young people and adolescents, because their brain is under constant growth. Such studies would provide new data for the design and construction of new digital games appropriate for assessment, training, and intervention for learning and various health conditions. This would be of great importance when applied to healthy populations to improve mental functions that maximize performance, but especially in more vulnerable populations such as people with learning disabilities and mental disorders.

The technological revolution provides new opportunities for neuroscientists to design targeted, novel game-based tools that drive positive neuroplasticity, accelerate learning, and strengthen cognitive function, thereby promoting mental well-being in both healthy and impaired brains (Mishra et al., 2016). Digital games in the education domain as well as in all aspects of everyday life are very productive and successful, facilitate and improve assessment, intervention, decision making, educational procedures, and all the scientific and productive procedures via Mobiles games (Stathopoulou et al., 2018, 2020, 2022, Kokkalia et al. 2016, Drigas & Pappanastasiou, 2014), various ICTs applications (Drigas et. al, 2004, 2005, 2015, 2016, Drigas & Kokkalia, 2017, Pappas et al., 2018, 2019, Drigas & Leliopoulos 2013, Papanastasiou et al., 2018, 2020, Alexopoulou et al., 2019, Kontostavlou & Drigas 2019) AI & STEM games (Vrettaros et al., 2009, Anastasopoulou et al., 2020, Lytra & Drigas, 2021), and educational robotics games (Drigas & Mitsea, 2021-2022, Kokkalia et al., 2017,).

The New Technologies (NT) and more specifically Digital Technologies provide the tools for access, analysis and transfer of information and its management and utilization of new knowledge. Information and Communication Technologies (ICT), the unprecedented technological capabilities of man, have a catalytic effect, create a new social reality and shape the Information Society (Pappas et Drigas, 2015, 2016, Drigas & Koukiannakis, 2004, 2006, 2009, Drigas & Kontopoulou, 2016, Theodorou & Digas, 2017, Drigas & Kostas, 2014, Bakola et al., 2019, 2022, Drigas & Politi-Georgousi, 2019, Karyotaki et al., 2022).

Concluding, it's necessary to refer that the combination of digital games with theories and models of metacognition, mindfulness, meditation, and emotional intelligence cultivation accelerates and improves more over the educational, productive, and decision-making practices and results (Drigas & Mitsea, 2020, 2021, 2022; Mitsea et al., 2019, 2020, 2021, 2022; Drigas & Papoutsi, 2020, Kokkaliaet al., 2019, Pappas & Drigas, 2019, Pappoutsi & Drigas, 2016, Karyotaki & Drigas, 2015, 2016, Papoutsi et al., 2019, 2021, Chaidi & Drigas 2022, Drigas & Karyotaki 2019, Mitsea et al., 2020, 2021, Angelopoulou & Drigas, 2021; Tairimpampa et al., 2018, Kapsi et al., 2020, Drigas et al., 2021, 2022, Galitskaya & Drigas, 2021).

References

Anagnostopoulou, P., Alexandropoulou, V., Lorentzou, G., Lykothanasi, A., Ntaountaki, P., & Drigas, A. (2020). Artificial intelligence in autism assessment. *International Journal of Emerging Technologies in Learning*, 15(6), 95-107. https://doi.org/10.3991/ijet.v15i06.11231

Aliyari, H., Sahraei, H., Erfani, M., Mohammadi, M., Kazemi, M., Daliri, M. R., ... & Farajdokht, F. (2020). Changes in cognitive functions following violent and football video games in young male volunteers by studying brain waves. *Basic and clinical neuroscience*, 11(3), 279.

Aliyari, H., Sahraei, H., Daliri, M. R., Minaei-Bidgoli, B., Kazemi, M., Agaei, H., ... & Dehghanimohammadabadi, Z. (2018). The beneficial or harmful effects of computer game stress on cognitive functions of players. *Basic and clinical neuroscience*, 9(3), 177.

Aliyari, H., Golabi, S., Sahraei, H., Sahraei, M., Minaei-Bidgoli, B., & Daliri, M.R., et al (2022). Perceived Stress and Cognition Function Quantification in a Scary Video Game: An Electroencephalogram Features and Biochemical Measures. *Basic and Clinical Neuroscience*. doi: http://dx.doi.org/10.32598/bcn.2022.3811.1

Aliyari, H., Kazemi, M., Tekieh, E., Salehi, M., Sahraei, H., Daliri, M. R., ... & Aghdam, A. R. (2015). The effects of fifa 2015 computer games on changes in cognitive, Hormonal and brain waves functions of young men volunteers. *Basic and clinical neuroscience*, 6(3), 193.

Alves, M. L., Mesquita, B. S., Morais, W. S., Leal, J. C., Satler, C. E., & dos Santos Mendes, F. A. (2018). Nintendo Wii™ versus Xbox Kinect™ for assisting people with Parkinson's disease. *Perceptual and motor skills*, 125(3), 546-565.

Bakola, L. N., & Drigas, A. (2020). Technological Development Process of Emotional Intelligence as a Therapeutic Recovery Implement in Children with ADHD and ASD Comorbidity. *International Journal of Online and Biomedical Engineering (IJOE*), 16(03), 75. https://doi.org/10.3991/ijoe.v16i03.12877

Bakola, L., Chaidi, I., Drigas, A., Skianis, C., & Karagiannidis, C. (2022). Women with Special Educational Needs. Policies & ICT for Integration & Equality. *Technium Social Sciences Journal*, 28, 67–75. https://doi.org/10.47577/tssj.v28i1.5708

Bakola, L., N., Rizos, N., D., Drigas, A. S., 2019, "ICTs for Emotional and Social Skills Development for Children with ADHD and ASD Co-existence"*International Journal of Emerging Technologies in Learning* (iJET), https://doi.org/10.3991/ijet.v14i05.9430

Barr, M., & Copeland-Stewart, A. (2022). Playing video games during the COVID-19 pandemic and effects on players' well-being. *Games and Culture*, 17(1), 122-139.

Benady-Chorney, J., Aumont, É., Yau, Y., Zeighami, Y., Bohbot, V. D., & West, G. L. (2020). Action video game experience is associated with increased resting state functional connectivity in the caudate nucleus and decreased functional connectivity in the hippocampus. *Computers in Human Behavior*, 106, 106200.

Berlucchi, G., & Buchtel, H. A. (2009). Neuronal plasticity: historical roots and evolution of meaning. *Experimental brain research*, 192(3), 307-319.

Boot, W. R., Kramer, A. F., Simons, D. J., Fabiani, M., & Gratton, G. (2008). The effects of video game playing on attention, memory, and executive control. *Acta psychologica*, 129(3), 387-398.

Butler, O., Herr, K., Willmund, G., Gallinat, J., Kühn, S., & Zimmermann, P. (2020). Trauma, treatment and Tetris: video gaming increases hippocampal volume in male patients with combat-related posttraumatic stress disorder. *Journal of Psychiatry and Neuroscience*, 45(4), 279-287.

Chaidi I. and Drigas, A. S., "Autism, Expression, and Understanding of Emotions: Literature Review," *Int. J. Online Biomed*. Eng., vol. 16, no. 02, pp. 94–111, 2020. https://doi.org/ 10.3991/ijoe.v16i02.11991

Chaidi, I., & Drigas, A. (2022, August 8). Digital games & special education. *Technium Social Sciences Journal*, 34, 214–236. https://doi.org/10.47577/tssj.v34i1.7054

Chen, Y. L., & Hsu, C. C. (2020). Self-regulated mobile game-based English learning in a virtual reality environment. *Computers & Education*, 154, 103910.

Choi, E., Shin, S. H., Ryu, J. K., Jung, K. I., Kim, S. Y., & Park, M. H. (2020). Commercial video games and cognitive functions: video game genres and modulating factors of cognitive enhancement. *Behavioral and Brain Functions*, 16(1), 1-14.

Cui, X., Gui, W., & Li, J. (2020). Combined training of aerobic exercise and 3D video game to improve hippocampal and memory functions in older adults: An RCT trial: Update on pharmacologic and nonpharmacologic interventions. *Alzheimer's & Dementia*, 16, e039795.

Dayan, P., & Balleine, B. W. (2002). Reward, motivation, and reinforcement learning. *Neuron*, 36(2), 285-298.

Demarin, V., & Morović, S. (2014). Neuroplasticity. *Periodicum biologorum*, 116(2), 209-211.

Drigas, A., & Mitsea, E. (2020). The 8 pillars of metacognition. *International Journal of Emerging Technologies in Learning* (iJET), 15(21), 162-178.

Drigas, A., & Mitsea, E. (2021). Metacognition, Stress-Relaxation Balance & Related Hormones. *Int. J. Recent Contributions Eng. Sci. IT*, 9(1), 4-16.

Drigas, A., & Mitsea, E. (2021). 8 Pillars X 8 Layers Model of Metacognition: Educational Strategies, Exercises &Trainings. *International Journal of Online & Biomedical Engineering*, 17(8).

Drigas A., and Koukianakis L. An open distance learning e-system to support SMEs e-enterprising. In proceeding of 5th WSEAS International conference on Artificial intelligence, knowledge engineering, data bases (AIKED 2006). Spain

Drigas A., Papoutsi C. (2020). The Need for Emotional Intelligence Training Education in Critical and Stressful Situations: The Case of COVID-19. *Int. J. Recent Contrib. Eng. Sci. IT* 8 (3), 20–35. 10.3991/ijes.v8i3.17235

Drigas A., Pappas M, and Lytras M., "Emerging technologies for ict based education for dyscalculia: Implications for computer engineering education," *International Journal of Engineering Education*, vol. 32, no. 4, pp. 1604–1610, 2016.

Drigas A.S., Kouremenos D (2005) An e-learning system for the deaf people. In: WSEAS transaction on advances in engineering education, vol 2, issue 1, pp 20–24

Drigas, A. & Kokkalia, G. 2017. ICTs and Special Education in Kindergarten. *International Journal of Emerging Technologies in Learning* 9 (4), 35–42.

Drigas, A. S. and Politi-Georgousi, S. (2019). Icts as a distinct detection approach for dyslexia screening: A contemporary view. *International Journal of Online and Biomedical Engineering (iJOE)*, 15(13):46–60.

Drigas, A. S., & Karyotaki, M. (2019). A Layered Model of Human Consciousness. *International Journal of Recent Contributions from Engineering*, Science & IT (iJES), 7(3), 41- 50. https://doi.org/10.3991/ijes.v7i3.11117

Drigas, A. S., and Vlachou J. A., "Information and communication technologies (ICTs) and autistic spectrum disorders (ASD)," *Int. J. Recent Contrib. Eng. Sci. IT (iJES)*, vol. 4, no. 1, p. 4, 2016. https://doi.org/10.3991/ijes.v4i1.5352

Drigas, A. S., J.Vrettaros, L.Stavrou, D.Kouremenos, E-learning Environment for Deaf people in the E-Commerce and New Technologies Sector, WSEAS *Transactions on Information Science and Applications*, Issue 5, Volume 1, November 2004.

Drigas, A. S., John Vrettaros, and Dimitris Kouremenos, 2005. "An e-learning management system for the deaf people," AIKED '05: Proceedings of the Fourth WSEAS International Conference on Artificial Intelligence, *Knowledge Engineering Data Bases*, article number 28.

Drigas, A. S., Karyotaki, M., & Skianis, C. (2018). An Integrated Approach to Neuro-development, Neuroplasticity and Cognitive Improvement. *International Journal of Recent Contributions from Engineering, Science & IT (iJES)*, 6(3), 4-18.

Drigas, A. S., Koukianakis, L, Papagerasimou, Y. (2006) "An elearning environment for nontraditional students with sight disabilities.", Frontiers in Education Conference, 36th Annual. *IEEE*, p. 23-27.

Drigas, A. S., Koukianakis, L,: Government online: An e-government platform to improve public administration operations and services delivery to the citizen. WSKS (1), volume 5736 de Lecture Notes in Computer Science, 523–532. *Springer*, 2009.

Drigas, A., Mitsea, E., Skianis, C., 2022, Clinical Hypnosis & VR, Subconscious Restructuring-Brain Rewiring & the Entanglement with the 8 Pillars of Metacognition X 8 Layers of Consciousness X 8 Intelligences. *International Journal of Online & Biomedical Engineering* 18 (1)

Drigas, A., & Bakola, L. N. (2021). The 8x8 Layer Model Consciousness-Intelligence-Knowledge Pyramid, and the Platonic Perspectives. *Int. J. Recent Contributions Eng. Sci. IT*, 9(2), 57-72.

Drigas, A., & Kontopoulou, M. T. L. (2016). ICTs based Physics Learning. *International Journal of Engineering Pedagogy (iJEP)*, 6(3), 53-59. https://doi.org/10.3991/ijep.v6i3. 5899

Drigas, A., & Kostas, I. (2014). On Line and other ICTs Applications for teaching math in Special Education. *International Journal of Recent Contributions from Engineering, Science & IT (iJES)*, 2(4), pp-46. http://dx.doi.org/10.3991/ijes.v2i4.4204

Drigas, A., & Mitsea, E. (2020). The Triangle of Spiritual Intelligence, Metacognition and Consciousness. *International Journal of Recent Contributions from Engineering, Science & IT (iJES)*, 8(1), 4-23. https://doi.org/10.3991/ijes.v8i1.12503

Drigas, A., & Mitsea, E. (2021). 8 Pillars X 8 Layers Model of Metacognition: Educational Strategies, Exercises &Trainings. *International Journal of Online & Biomedical Engineering*, 17(8). https://doi.org/10.3991/ijoe.v17i08.23563

Drigas, A., & Mitsea, E. (2021). Metacognition, stress-relaxation balance & related hormones. *International Journal of Recent Contributions from Engineering, Science & IT (iJES)*, 9(1), 4–16. https://doi.org/10.3991/ijes.v9i1.19623

Drigas, A., & Papanastasiou, G. (2014). Interactive White Boards in Preschool and Primary Education. *International Journal of Online and Biomedical Engineering (iJOE)*, 10(4), 46–51. https://doi.org/10.3991/ijoe.v10i4.3754

Drigas, A., & Papoutsi, C. (2019). Emotional Intelligence as an Important Asset for HR in Organizations: Leaders and Employees. *International Journal of Advanced Corporate Learning*, 12(1).

Drigas, A., & Dourou, A. (2013, July 25). A Review on ICTs, E-Learning and Artificial Intelligence for Dyslexicâ??s Assistance. International Journal of Emerging Technologies in Learning (IJET), 8(4), 63. https://doi.org/10.3991/ijet.v8i4.2980

Drigas, A., Kokkalia, G. & Lytras, M. D. (2015). Mobile and Multimedia Learning in Preschool Education. *J. Mobile Multimedia*, 11(1/2), 119–133.

Drigas, A., & Leliopoulos, P. (2013). Business to Consumer (B2C) E-Commerce Decade Evolution. *International Journal of Knowledge Society Research*, *4*(4), 1–10. https://doi.org/10.4018/ijksr.2013100101

Drigas, A., & Mitsea, E. (2020). A Metacognition Based 8 Pillars Mindfulness Model and Training Strategies. *International Journal of Recent Contributions From Engineering, Science & IT (IJES)*, 8(4), 4. https://doi.org/10.3991/ijes.v8i4.17419

Drigas, A., & Mitsea, E. (2021). Neuro-Linguistic Programming & VR via the 8 Pillars of Metacognition X 8 Layers of Consciousness X 8 Intelligences. *Technium Social Sciences Journal*, 26, 159–176. https://doi.org/10.47577/tssj.v26i1.5273

Drigas, A., Mitsea, E., & Skianis, C. (2021). The Role of Clinical Hypnosis & VR in Special Education. *International Journal of Recent Contributions From Engineering*, Science & IT (IJES), 9(4), 4–18. https://doi.org/10.3991/ijes.v9i4.26147

Drigas, A., & Mitsea, E. (2022). Breathing: a Powerfull Tool for Physical & Neuropsychological Regulation. The role of Mobile Apps. *Technium Social Sciences Journal*, *28*, 135–158. https://doi.org/10.47577/tssj.v28i1.5922

Drigas, A. S., Koukianakis, L. G., & Papagerasimou, Y. V. (2005). A system for e-inclusion for individuals with sight disabilities. *Wseas transactions on circuits and systems*, *4*(11), 1776-1780.

Doulou, A., & Drigas, A. (2022). Electronic, VR & Augmented Reality Games for Intervention in ADHD. *Technium Soc. Sci. J.*, *28*, 159.

Gentile, D. A., Bender, P. K., & Anderson, C. A. (2017). Violent video game effects on salivary cortisol, arousal, and aggressive thoughts in children. *Computers in Human Behavior*, 70, 39-43.

Gong, D., He, H., Liu, D., Ma, W., Dong, L., Luo, C., & Yao, D. (2015). Enhanced functional connectivity and increased gray matter volume of insula related to action video game playing. *Scientific reports*, 5(1), 1-7.

Gong, D., He, H., Ma, W., Liu, D., Huang, M., Dong, L., ... & Yao, D. (2016). Functional integration between salience and central executive networks: a role for action video game experience. *Neural plasticity*, 2016.

Granic, I., Lobel, A., & Engels, R. C. (2014). The benefits of playing video games. *American psychologist*, 69(1), 66.

Grizzard, M. N. (2013). *Cooperative video game play and generosity: Oxytocin production as a causal mechanism regarding prosocial behavior resulting from cooperative video game play*. Michigan State University.

Hacker, D. J. (2017). The role of metacognition in learning via serious games. In *Handbook of research on serious games for educational applications* (pp. 19-40). IGI Global..

He, Q., Turel, O., Wei, L., & Bechara, A. (2021). Structural brain differences associated with extensive massively-multiplayer video gaming. *Brain imaging and behav*ior, 15(1), 364-374.

Hébert, S., Béland, R., Dionne-Fournelle, O., Crête, M., & Lupien, S. J. (2005). Physiological stress response to video-game playing: the contribution of built-in music. *Life sciences*, 76(20), 2371-2380.

Kapsi, S., Katsantoni, S., Drigas, A., 2020, The Role of Sleep and Impact on Brain and Learning. *Int. J. Recent Contributions Eng. Sci. IT* 8 (3), 59-68

Karyotaki, M., & Drigas, A. (2016). Latest trends in problem solving assessment. *International Journal of Recent contributions from Engineering, Science & IT (iJES)*, *4*(2), 4-10.

Karyotaki, M., & Drigas, A. (2015). Online and other ICT Applications for Cognitive Training and Assessment. *International Journal of Online and Biomedical Engineering.* 11(2), 36-42.

Karyotaki, M., Bakola, L., Drigas, A., & Skianis, C. (2022). Women's Leadership via Digital Technology and Entrepreneurship in business and society. *Technium Soc. Sci. J.*, *28*, 246.

Kokkalia, G., Drigas, A. S., & Economou, A. (2016). Mobile learning for preschool education. *International Journal of Interactive Mobile Technologies*, *10*(4).

Kokkalia, G., Drigas, A. Economou, A., & Roussos, P. (2019). School readiness from kindergarten to primary school. *International Journal of Emerging Technologies in Learning*, 14(11), 4-18.

Kokkalia, G., Drigas, A., & Economou, A. (2016). The role of games in special preschool education. *International Journal of Emerging Technologies in Learning (iJET),* 11(12), 30-35.

Kokkalia, G., Drigas, A., Economou, A., Roussos, P., & Choli, S. (2017). The use of serious games in preschool education. *International Journal of Emerging Technologies in Learning*, 12(11), 15-27. https://doi.org/10.3991/ijet.v12i11.6991

Kontostavlou, E.Z., & Drigas, A.S. (2019). The Use of Information and Communications Technology (ICT) in Gifted Students. *International Journal of Recent Contributions from Engineering, Science and IT*, 7(2), 60-67. doi:10.3991/ijes.v7i2.10815

Koepp, M. J., Gunn, R. N., Lawrence, A. D., Cunningham, V. J., Dagher, A., Jones, T., & Grasby, P. M. (1998). Evidence for striatal dopamine release during a video game. *Nature*, 393(6682), 266-268.

Kokkinakis, A. V., Cowling, P. I., Drachen, A., & Wade, A. R. (2017). Exploring the relationship between video game expertise and fluid intelligence. *PloS one*, 12(11), e0186621.

Kovács, G. L. (2004). The endocrine brain: pathophysiological role of neuropeptide-neurotransmitter interactions. *EJIFCC*, 15(3), 107.

Kowal, M., Conroy, E., Ramsbottom, N., Smithies, T., Toth, A., & Campbell, M. (2021). Gaming your mental health: a narrative review on mitigating symptoms of depression and anxiety using commercial video games. *JMIR Serious Games*, 9(2), e26575.

Kral, T. R., Stodola, D. E., Birn, R. M., Mumford, J. A., Solis, E., Flook, L., ... & Davidson, R. J. (2018). Neural correlates of video game empathy training in adolescents: a randomized trial. *npj Science of Learning*, 3(1), 1-10.

Kühn, S., Gleich, T., Lorenz, R. C., Lindenberger, U., & Gallinat, J. (2014). Playing Super Mario induces structural brain plasticity: gray matter changes resulting from training with a commercial video game. *Molecular psychiatry*, 19(2), 265-271.

Kühn, S., Lorenz, R., Banaschewski, T., Barker, G. J., Büchel, C., Conrod, P. J., ... & IMAGEN Consortium. (2014). Positive association of video game playing with left frontal cortical thickness in adolescents. *PloS one*, 9(3), e91506.

Lee, H., Voss, M. W., Prakash, R. S., Boot, W. R., Vo, L. T., Basak, C., ... & Kramer, A. F. (2012). Videogame training strategy-induced change in brain function during a complex visuomotor task. *Behavioural Brain Research*, 232(2), 348-357.

Lytra, N., & Drigas, A. (2021). STEAM education-metacognition–Specific Learning Disabilities. *Scientific Electronic Archives*, *14*(10).

Martinez, K., Solana, A. B., Burgaleta, M., Hernández-Tamames, J. A., Álvarez-Linera, J., Román, F. J., & Colom, R. (2013). Changes in resting-state functionally connected parietofrontal networks after videogame practice. *Human Brain Mapping*, 34(12), 3143-3157.

Manesis, D. (2020). Digital Games in Primary Education. In (Ed.), Game Design and Intelligent Interaction. *IntechOpen*. https://doi.org/10.5772/intechopen.91134

Mayer, R. E. (2019). Computer games in education. *Annual review of psychology*, 70, 531-549.

Mishra, J., Anguera, J. A., & Gazzaley, A. (2016). Video games for neuro-cognitive optimization. *Neuron,* 90(2), 214-218.

Mitsea E., Drigas, A. S., Mantas , P., "Soft Skills & Metacognition as Inclusion Amplifiers in the 21st Century," *Int. J. Online Biomed. Eng. IJOE*, vol. 17, no. 04, Art. no. 04, Apr. 2021. https://doi.org/10.3991/ijoe.v17i04.20567

Mitsea, E., Lytra, N., Akrivopoulou, A., Drigas, A., 2020, Metacognition, Mindfulness and Robots for Autism Inclusion. *Int. J. Recent Contributions Eng. Sci. IT* 8 (2), 4-20

Mitsea, E., Drigas, A., & Skianis, C. (2022). ICTs and Speed Learning in Special Education: High-Consciousness Training Strategies for High-Capacity Learners through Metacognition Lens. *Technium Soc. Sci. J.*, *27*, 230.

Mitsea, E., Drigas, A., & Skianis, C. (2022). Metacognition in Autism Spectrum Disorder: Digital Technologies in Metacognitive Skills Training. *Technium Soc. Sci. J.*, *31*, 153.

Mitsea, E., Drigas, A., & Skianis, C. (2022). Mindfulness Strategies for Metacognitive Skills Training in Special Education: The Role of Virtual Reality. *Technium Soc. Sci. J.*, *35*, 232.

Mitsea, E., Drigas, A., & Skianis, C. (2022). Mindfulness for Anxiety Management and Happiness: The Role of VR, Metacognition, and Hormones. *Technium BioChemMed*, *3*(3), 37-52.

Mitsea, E., Drigas, A., & Skianis, C. (2022). Breathing, Attention & Consciousness in Sync: The role of Breathing Training, Metacognition & Virtual Reality. *Technium Soc. Sci. J.*, *29*, *79. hemMed*, 3(3), 37-52.

Mitsea, E., Drigas, A., & Skianis, C. (2022). Cutting-Edge Technologies in Breathwork for Learning Disabilities in Special Education. *Technium Soc. Sci. J.*, *34*, 136.

Mitsea, E., & Drigas, A. (2019). A Journey into the metacognitive learning strategies. *International Journal of Online & Biomedical Engineering*, 15(14).

Möller, S., Schmidt, S., & Beyer, J. (2013, July). Gaming taxonomy: An overview of concepts and evaluation methods for computer gaming QoE. In *2013 Fifth International Workshop on Quality of Multimedia Experience (QoMEX)* (pp. 236-241). IEEE.

Momi, D., Smeralda, C. L., Di Lorenzo, G., Neri, F., Rossi, S., Rossi, A., & Santarnecchi, E. (2021). Long-lasting connectivity changes induced by intensive first-person shooter gaming. *Brain Imaging and Behavior*, 15(3), 1518-1532.

Momi, D., Smeralda, C., Sprugnoli, G., Neri, F., Rossi, S., Rossi, A., ... & Santarnecchi, E. (2019). Thalamic morphometric changes induced by first-person action videogame training. *European Journal of Neuroscience*, 49(9), 1180-1195.

Oxford, J., Ponzi, D., & Geary, D. C. (2010). Hormonal responses differ when playing violent video games against an ingroup and outgroup. *Evolution and Human Behavior*, 31(3), 201-209.

Pallavicini, F., Ferrari, A., & Mantovani, F. (2018). Video games for well-being: A systematic review on the application of computer games for cognitive and emotional training in the adult population. *Frontiers in psychology*, 9, 2127.

Papanastasiou, G., Drigas, A., Skianis, C., & Lytras, M. D. (2017). Serious games in K-12 education: Benefits and impacts on students with attention, memory and developmental disabilities. *Program*, *51*(4), 424-440.

Papanastasiou, G., Drigas, A., Skianis, C., and Lytras, M. (2020). Brain computer interface based applications for training and rehabilitation of students with neurodevelopmental disorders. A literature review. *Heliyon* 6:e04250. doi: 10.1016/j.heliyon.2020.e04250

Papoutsi, C. & Drigas, A. (2016). Games for Empathy for Social Impact. *International Journal of Engineering Pedagogy* 6(4), 36-40.

Papoutsi, C. and Drigas, A. (2017) Empathy and Mobile Applications. *International Journal of Interactive Mobile Technologies* 11. 57. https://doi.org/10.3991/ijim.v11i3.6385

Papoutsi, C., Drigas, A., & Skianis, C. (2021). Virtual and augmented reality for developing emotional intelligence skills. *Int. J. Recent Contrib. Eng. Sci. IT (IJES)*, *9*(3), 35-53.

Pappas, M. A., & Drigas, A. S. (2019). Computerized Training for Neuroplasticity and Cognitive Improvement. *Int. J. Eng. Pedagog*., 9(4), 50-62.

Pappas M, Drigas A, Papagerasimou Y, Dimitriou H, Katsanou N, Papakonstantinou S, et al. Female Entrepreneurship and Employability in the Digital Era: The Case of Greece. *Journal of Open Innovation: Technology, Market, and Complexity*. 2018; 4(2): 1.

Pappas M, Drigas A. Computerized Training for Neuroplasticity and Cognitive Improvement. International Journal of Engineering Pedagogy. 2019;.(4):50-62

Pappas Marios A, Demertzi, E., Papagerasimou, Y, Koukianakis, L., Voukelatos, N, Drigas, A. S., 2019. Cognitive Based E-Learning Design for Older Adults. *Social Sciences* 8, 1 (Jan. 2019), 6. https://doi.org/10.3390/socsci801000

Pappas, M. A., & Drigas, A. S. (2015). ICT Based Screening Tools and Etiology of Dyscalculia. *International Journal of Engineering Pedagogy*, 5(3)

Pappas, M., & Drigas, A. (2016). Incorporation of artificial intelligence tutoring techniques in mathematics. *International Journal of Engineering Pedagogy*, 6(4), 12–16. https://doi.org/10.3991/ijep.v6i4.6063

Pappas, M., Demertzi, E., Papagerasimou, Y., Koukianakis, L., Kouremenos, D., Loukidis, I. and Drigas, A. 2018. E-Learning for deaf adults from a user-centered perspective. *Education Sciences* 8(206): 3-15.

Pappas, M.A., & Drigas, A.S. (2015). ICT based screening tools and etiology of dyscalculia. *International Journal of Engineering Pedagogy*, 3, 61-66.

Paré, G., Trudel, M. C., Jaana, M., & Kitsiou, S. (2015). Synthesizing information systems knowledge: A typology of literature reviews. *Information & Management*, *52*(2), 183-199.

Stathopoulou A., Loukeris D., Karabatzaki Z., Politi E., Salapata Y., and Drigas, A. S., "Evaluation of Mobile Apps Effectiveness in Children with Autism Social Training via Digital Social Stories," *Int. J. Interact. Mob. Technol. (iJIM*); Vol 14, No 03, 2020

Phan-Hug, F., Thurneysen, E., Theintz, G., Ruffieux, C., & Grouzmann, E. (2011). Impact of videogame playing on glucose metabolism in children with type 1 diabetes. *Pediatric diabetes*, 12(8), 713-717.

Podrigalo, L. V., Iermakov, S. S., & Jagiello, W. (2020). Metabolic and Endocrine Changes Determined in Saliva of Adolescents Engaged in Computer Gaming. *BioMed Research International*, 2020.

Prena, K., Cheng, H., & Newman, S. D. (2020). Hippocampal neurotransmitter inhibition suppressed during gaming explained by skill rather than gamer status. *Frontiers in human neuroscience*, 14, 585764.

Puig, M. A., Alonso-Prieto, M., Miró, J., Torres-Luna, R., de Sabando, D. P. L., & Reinoso-Barbero, F. (2020). The association between pain relief using video games and an increase in vagal tone in children with cancer: analytic observational study with a quasi-experimental pre/posttest methodology. *Journal of Medical Internet Research*, 22(3), e16013.

Sadeghi, M., Kordi, M., Devos, H., & Khaligh-Razavi, S. M. (2022). VR-Cognitive Games are Complementary to Physical training for an Optimum Rehabilitation Strategy in Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation*, 103(12), e145.

Stafford, T., & Vaci, N. (2022). Maximizing the potential of digital games for understanding skill acquisition. Current Directions in Psychological Science, 31(1), 49-55.

Schaeffer, E., Roeben, B., Granert, O., Hanert, A., Liepelt-Scarfone, I., Leks, E., ... & Berg, D. (2022). Effects of exergaming on hippocampal volume and brain-derived neurotrophic factor levels in Parkinson’s disease. *European journal of neurology*, 29(2), 441-449.

Schmitt, J. A. J., Wingen, M., Ramaekers, J. G., Evers, E. A. T., & Riedel, W. J. (2006). Serotonin and human cognitive performance. Current pharmaceutical design, 12(20), 2473-2486.

Stathopoulou, A., Karabatzaki, Z., Kokkalia, G., Dimitriou, E., Loukeri, P.I., Economou, A., and Drigas, A. (2018). Mobile assessment procedures for mental health and literacy skills in education. *International Journal of Interactive Mobile Technologies* (iJIM), 12(3):21-37. https://doi.org/10.3991/ijim.v12i3.8038

Stathopoulou, A., Karabatzaki, Z., Tsiros, D., Katsantoni, S., & Drigas, A. (2019). Mobile Apps the Educational Solution for Autistic Students in Secondary Education. *International Journal of Interactive Mobile Technologies (iJIM)*, *13*(02), 89. https://doi.org/10.3991/ijim.v13i02.9896

Stathopoulou, et all Mobile assessment procedures for mental health and literacy skills in education. *International Journal of Interactive Mobile Technologies*, 12(3), 21-37, 2018,

West, G. L., Konishi, K., Diarra, M., Benady-Chorney, J., Drisdelle, B. L., Dahmani, L.,& Bohbot, V. D. (2018). Impact of video games on plasticity of the hippocampus. *Molecular psychiatry*, 23(7), 1566-1574.

West, G. L., Zendel, B. R., Konishi, K., Benady-Chorney, J., Bohbot, V. D., Peretz, I., & Belleville, S. (2017). Playing Super Mario 64 increases hippocampal grey matter in older adults. *PloS one,* 12(12), e0187779.

Yoon, S., & Kim, Y. K. (2020). The role of the oxytocin system in anxiety disorders. *Anxiety Disorders*, 103-120.

Zayeni, D., Raynaud, J. P., & Revet, A. (2020). Therapeutic and preventive use of video games in child and adolescent psychiatry: a systematic review. *Frontiers in psychiatry*, 11, 36.