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Review Article

Neuroimaging findings in adolescent gaming disorder: a systematic review

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Abstract

Objectives: Gaming disorder is a growing concern affecting adolescents, exacerbated by the impact of recent COVID-19 restrictions. The World Health Organization has recently included gaming disorder in the 11th International Classification of Diseases (ICD-11). However, there is still an ongoing debate about the validity and reliability of the proposed clinical criteria, despite growing neurobiological evidence in this cohort. Systematic reviews in this area have focused mainly on adults or mixed adult/adolescent populations. Therefore, this systematic review explored the neuroimaging literature in adolescents (under 18 years old) with gaming disorder.

Methods: Using PRISMA 2020 guidelines, 3288 primary studies were identified from PubMed, CINAHL Plus, PsycINFO and Web of Science. After applying inclusion and exclusion criteria (appropriate title, abstract, comparison group used within study, English-language, neuroimaging and mean age under 18), 24 studies were included in this review.

Results: Functional and structural brain alterations in adolescent gaming disorder were noted across several imaging modalities, including electroencephalogram (EEG), functional magnetic resonance imaging (fMRI) and structural magnetic resonance imaging (MRI). Compared with healthy controls, adolescents with gaming disorder demonstrated neurological changes comparable to substance addiction, namely impairments in emotional regulation, reward-seeking, inhibition and increased risky decision-making. Positive brain adaptations in the areas of visuospatial processing and memory were observed.

Conclusions: A number of key brain regions are affected in adolescent gaming disorder. These findings can help clinicians understand adolescent presentations with gaming disorder from a neurobiological perspective. Future studies should focus on forming a robust neurobiological and clinical framework for adolescent gaming disorder.

Keywords: Adolescents; Gaming disorder; Internet gaming disorder; Neuroimaging; Systematic review

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Introduction

Gaming has become increasingly popular across the world during the COVID-19 pandemic (King et al., 2020), especially among adolescents (Donati et al., 2021). Governments and public health authorities, in an effort to curb the spread of COVID-19, utilised various measures to increase social distancing such as the cancellation of most social activities available to adolescents (Ko and Yen 2020). Gaming emerged as an acceptable activity during the pandemic for adolescents and was promoted by the World Health Organization (WHO) in their '#PlayApartTogether' campaign to encourage social distancing among young people (Donati et al., 2021). While the gaming industry is now reporting a decline in engagement in online gaming services as people return to more real-world pursuits (Gross 2022), overall levels of gaming are significantly higher than pre-pandemic levels (Howley 2022).

Gaming can be a positive activity to help adolescents cope with the stressors of social distancing restrictions, such as social isolation (Jones et al., 2014).. Gaming can have benefits as a coping strategy in times of heightened psychological stress (Russoniello et al., 2009), and casual levels of gameplay have been shown to reduce symptoms of anxiety, depression, stress and low mood over a 1-month period (Fish et al., 2014). Despite gaming's multiple benefits, increased frequency and duration of gaming can increase the risk of developing gaming disorder for a minority of individuals (Mihara and Higuchi 2017). An increase in gaming disorder rates among adolescents were observed in many studies over the course of the COVID-19 pandemic, with psychological distress and social isolation due to the pandemic cited as driving factors (Han et al., 2022). Worldwide, there is an estimated 3.05% prevalence rate of gaming disorder within the adolescent population, with significantly higher prevalence in the male population with a ratio of 2.5:1 (Stevens et al., 2021).

It is important to delineate the differences between non-problematic gaming and gaming disorder or an addiction to gaming. Gaming exists on a spectrum from non-problematic occasional gaming, through to problematic gaming and gaming

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disorder for a minority of individuals (Griffiths et al., 2017). Problematic gaming is an example of disordered gaming where there are significant disruptions to psychosocial functioning due to gaming (Griffiths et al., 2017). The International Classification of Diseases 11th Revision (ICD-11) have described gaming disorder as a 'pattern of persistent or recurrent gaming behaviour ('digital gaming' or 'video gaming'), which may be online (i.e. over the internet) or offline' with the following characteristics demonstrated over a 12-month period:

- 'Impaired control over gaming (e.g. onset, frequency, intensity, duration, termination, context)
- Increasing priority given to gaming to the extent that gaming takes precedence over other life interests and daily activities
- Continuation or escalation of gaming despite the occurrence of negative consequences' (World Health Organization 2018).

There was significant debate amongst scholars about the inclusion of gaming disorder in the ICD-11 (Griffiths et al., 2017), as well as critique of the terminology used in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) for Internet Gaming Disorder as an emerging disorder (Kuss et al., 2017), where the terms internet addiction, gaming addiction and gaming disorder are used interchangeably (American Psychiatric Association, 2013). For clarity, this review will use the term 'gaming disorder" to also describe gaming addiction and problematic gaming. Since the introduction of gaming disorder in the ICD-11, there still remains some ongoing debate amongst researchers as to the validity and reliability of the proposed clinical criteria for gaming disorder (Brand et al., 2020). In support of the validity of gaming disorder, there are a growing number of neuroimaging studies supporting gaming disorder as a distinct entity from a neurobiological perspective (Kuss et al., 2018, Vaccaro and Potenza 2019).

There have been a number of systematic reviews exploring the neurobiological findings associated with gaming disorder in adults. Magnetic resonance imaging (MRI) studies have shown impaired cognitive control and a deficiency in ventral striatal reward systems (Kuss et al., 2018). Alterations in the striatum, amygdala and orbitofrontal cortex have been associated with higher levels of video game craving in gaming-disordered adults (Choi et al., 2021). Electroencephalogram (EEG) findings in adult gaming disorder are similar to cocaine and alcohol addiction, with increased P300 latency and decreased P300 amplitudes suggesting poor attention capacity and allocation of attention (Kuss et al., 2018). While some systematic reviews have focused on younger age groups (Sugaya et al., 2019), these reviews mixed adult and adolescent samples in their findings. To our knowledge, there are no systematic reviews focused purely on the neurobiological findings of gaming disorder in an adolescent (under 18 years old) age group. This cohort are especially vulnerable given the developing nature of the adolescent brain and increasing rates of gaming. In addition, increased knowledge in this area would be of importance to child and adolescent mental health professionals treating under-18-year-old patients attending their services, especially given the recent inclusion of gaming disorder in ICD-11 and the potential for referrals of this nature to child and adolescent services. Therefore, this systematic review explored the neuroimaging literature in adolescents (under 18 years old) with gaming disorder.

Methods

Using PRISMA 2020 guidelines, a systematic review on studies investigating neuroimaging findings in gaming disorder in an adolescent (under 18 years old) population. The methods for this review were adapted from similar systematic reviews conducted in gaming disorder (Kuss and Griffiths 2012, Yao et al., 2017, Kuss et al., 2018, Sugaya et al., 2019, Burleigh et al., 2020). All included studies met the following criteria: 1) adolescents with a sample mean age of under 18 years old, 2) studies focused on gaming disorder, 3) neuroimaging techniques used within the study, 4) primary studies (cross-sectional and cohort studies) and 5) papers in the English language. Exclusion criteria were 1) type of study (case reports, case series), 2) studies with a sample mean age of over 18 years old, 3) studies that mislabelled generalised internet addiction as gaming disorder, 4) inadequate or absent comparison groups and 5) non-English-language studies. Electronic databases used to search for primary studies were PubMed, PsycINFO, Web of Science and CINAHL Plus. Comprehensive search terms focused on population and intervention were entered into an advanced search engine including ('Addiction' OR 'Pathology' OR 'Disorder' OR 'Compulsive' OR 'Problem') AND ('Gaming' OR 'Internet') AND ('imaging' OR 'neurobiological' OR 'neuroscience' OR neuropsychological'). Search filters were applied to include child, adolescent and English-based papers while excluding literature reviews, systematic reviews and meta-analyses.

A total of 3288 papers were identified on initial searches. After removing duplicates (692 papers), application of exclusion criteria and screening of papers based on title, abstract, keywords and publication type, 24 studies were included for analysis in this review (see Table 1). A PRISMA flow diagram (see Fig. 1) is included as per the PRISMA 2020 statement guidelines (Page et al., 2021). Studies were assessed for their risk of bias with JBI's Critical Appraisal Tools (Ma et al., 2020). This systematic review was registered with PROSPERO and the ID number is CRD42021264905. To avoid confusion, the term gaming disorder will be used interchangeably with gaming addiction and problematic gaming.

Results

Electroencephalography (EEG)

Two studies conducted using task-based interventions and resting-state EEG compared gaming-disordered samples and the non-disordered adolescent controls. EEG can be used to detect event-related potentials (ERP), small voltages generated by the brain in response to different sensory, motor, or cognitive actions made by participants (Sur and Sinha 2009). During task-based interventions, adolescents with gaming disorder demonstrated less positive P3 amplitudes compared to controls in response inhibition tasks (Li et al., 2020). Less positive P3 amplitudes have been linked with increased task difficulty. Given that P3 amplitudes become less positive with increased difficulty within the task, adolescents with gaming disorder may have more difficulty inhibiting their responses compared with controls (Li et al., 2020). This finding, along with higher scores demonstrated on impulsivity scales, suggest that gaming disordered adolescents demonstrate abnormalities in inhibitory control systems (Li et al., 2020). Adolescents with gaming disorder in reward tasks showed a less positive feedback-related negativity (FRN) amplitude compared with controls after receiving a gain on a gambling task (Li et al., 2020). A blunted FRN response can be an indicator of reduced reward sensitivity (Li et al., 2020). There was no difference between FRN responses on the gambling task after a loss, indicating while gaming-disordered adolescents may share similar loss avoidance, they may have increased reward-seeking behaviours (Li et al., 2020).

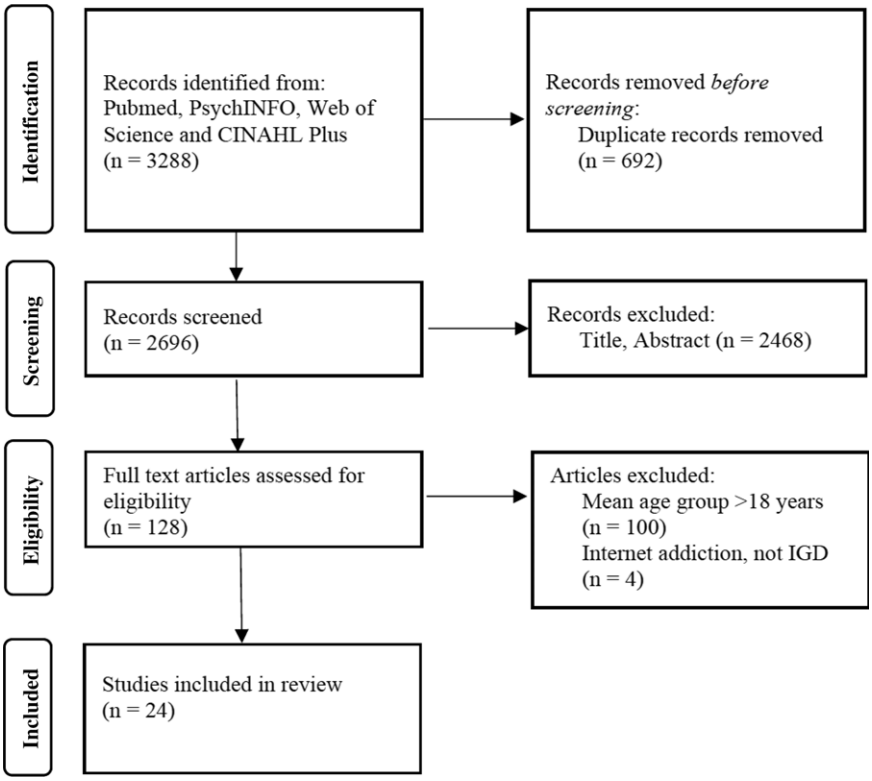

Figure 1. Prisma flow diagram of study selection.

EEG can be used to compare spontaneous electrical activity of the brains during task-related events (Light et al., 2010). One study examined qualitative EEG (QEEG) in adolescents with gaming disorder and comorbid ADHD, compared to adolescents with ADHD, and adolescent healthy controls (Park et al., 2017b). Adolescents with comorbid ADHD and gaming disorder showed increased theta coherence in the electrodes in the temporal region, suggesting an increased stimulation of the working memory circuit in gaming disorder. Increased intra-hemispheric coherence was noted in the right parieto-occipital region in the gaming disorder group compared to controls, implying a consistent gaming stimulus activates visuospatial working memory circuits (Park et al., 2017b). Increased beta cortical activity observed in this study has been compared to similar increases in beta cortical activity arising from methylphenidate usage in ADHD, implying that gaming may result in increased attentional capacity and a subconscious means of enhancing attention (Park et al., 2017b)

Functional Magnetic Resonance Imaging (fMRI)

Eighteen functional MRI (fMRI) studies compared resting-state brain activity between gaming-disordered samples and the non-disordered adolescent controls. fMRI uses changes in blood oxygen levels in the brain to map different brain regions, traditionally when performing a specific task such as tapping your finger (Lv et al., 2018). Resting-state fMRI, which is fMRI conducted without the subject performing a task, uses spontaneous changes in blood oxygen levels to map the intrinsic brain activity (Lv et al., 2018).. Taken together, adolescents with gaming disorder demonstrate brain changes comparable with substance addiction, differences in functional connectivity, emotional regulation, inhibition and self-identity compared to controls. Compared with healthy controls, one study demonstrated increased cerebral blood flow in the left inferior temporal lobe, left parahippocampal gyrus, amygdala, right medial frontal lobe/anterior cingulate cortex, bilateral insula, right-middle temporal gyrus, right precentral gyrus, left supplementary motor area, left cingulate gyrus and right inferior parietal lobe of adolescents with gaming disorder (Feng et al., 2013). These areas correlate with traditional substance addiction pathways, such as the involvement of the insula in urges to use substances, prefrontal cortex involvement in drug seeking behaviour and craving, anterior cingulate cortex activation in video game craving, and parietal cortex activity as an underlying cause of inhibition failure (Feng et al., 2013).

At rest, three studies demonstrated increased functional connectivity in the left superior frontal cortex, left middle frontal cortex and right inferior temporal cortex (Du et al., 2017b), including the left frontal eye field to the dorsal anterior cingulate and right interior insula in adolescents with gaming disorder (Han et al., 2015). This increased functional connectivity within the dorsolateral prefrontal cortex (DLPFC), temporal lobe and left temporoparietal junction (TPJ) (Han et al., 2015) may correlate with improved performance in visuospatial and visual attention processing (Du et al., 2017b). These findings may represent the risk of over-connectivity in response to increased amounts of game play and may impact executive control networks, in turn impacting mental health (Han et al., 2015). This can be observed when measuring the connection efficiency between the dorsal striatum and left DLPFC between regular gamers and adolescents with gaming disorder (Chen et al., 2021). In adolescents with gaming disorder, increased dorsal striatum activity suppressed the left DLPFC, as opposed to the activity of the dorsal striatum stimulating the left DLPFC (Chen et al., 2021).

Compared with controls, two studies demonstrated that adolescents with gaming disorder were characterised by reduced functional connectivity between different brain regions and the

Table 1. Studies included in systematic review of adolescent gaming disorder (GD)

Author	Sample	Mean age + SD	GD assessment measures used	Sample Characteristics	Aims	Findings
Bae et al., 2016	ADHD + GD, $N = 28$ ADHD, $N = 27$ Controls, $N = 42$	ADHD + GD (15.7 years, SD = 1.7 years) ADHD (15.3 years, SD = 1.4 years) Controls (16.4 years, SD = 2.0 years)	Greater than >30 hours per week gaming, Young Internet Addiction Scale (YIAS) score >50, clinical symptoms of GD	All males recruited from hospital in South Korea	To examine metabolic differences in ADHD patients with GD, using proton MRS. The study hypothesised that N-acetyl-cysteine (NAA) levels would be reduced in all ADHD adolescents, along with reduced levels of glutamate (Glu) and glutamine (Gln) in ADHD + GD adolescents, compared to ADHD -only adolescents.	Levels of N-acetyl-aspartate (NAA) in both ADHD groups were lower compared to controls, with levels of glutamate and glutamine higher in the ADHD-only group compared to other two groups in the study. Decreased levels of NAA in both ADHD groups may suggest a common pathway of hypoactivity in the frontal lobe, with decreased levels of glutamate and glutamine in the gaming disorder and comorbid ADHD group (compared to ADHD-only group) possibly mediated by increased dopamine levels from increased levels of video gaming
Chen et al., 2021	GD, $N = 22$ Regular game users matched controls, $N = 26$	GD, (14.1 years, SD = 1.8 years) Controls (13.9 years, SD = 1.5 years)	Internet Addiction Test (IAT) >50, main use of internet for gaming, online gaming time 4–6+ hours per day for more than 2 years, meets DSM-5 criteria for GD	17 males & 5 females. All recruited from middle school in China	To explore the prefrontal-striatal circuits and resting-state functional connectivity as measures of impulsiveness and response inhibition in GD adolescents	GD group demonstrated higher impulsivity and impaired inhibition. Increased dorsal striatum activity suppressed the left dorsolateral prefrontal cortex (DLPFC) increasing inhibition, as opposed to the activity of the dorsal striatum stimulating the left DLPFC in healthy controls
Choi et al., 2018	GD, $N = 17$ Controls, $N = 17$	GD (13.38 years, SD = 2.69 years) Controls (15.33 years, SD = 0.98 years)	Young Internet Addiction Scale (YIAS) >50, abnormal use of online gaming based on DSM-5 criteria for IGD	Only males, GD recruited via hospital and controls via middle and high school, all in South Korea	To investigate whether adolescent boys make mental state inferences for their online game characters and whether adolescents who were diagnosed with GD perceived their personal game character to be similar to themselves	Adolescents with gaming disorder utilised the medial prefrontal cortex (MPC) and anterior cingulate cortex (ACC) when thinking about their game avatar, with even stronger activation of these regions compared to self-thoughts. These brain regions are linked with thoughts about the self and activated in healthy controls when thinking about aspects of their self, demonstrating that adolescents with gaming disorder identify more with their gaming avatar than their own self
Chun et al., 2015	GD, $N = 16$ Controls, $N = 19$	GD (13.63 years, SD = 1.03 years) Controls (13.37 years, SD = 1.03 years)	Korean Internet Addiction Proneness Scale (K-scale), significantly higher gaming use compared to controls	All males recruited form middle schools in South Korea	To investigate neural responses to swear words and cognitive control in adolescents with GD compared to controls. Frontolimbic regions (dACC, orbitofrontal cortex (OFC) and amygdala) were examined given their roles in monitoring, compulsive repetitive behaviour and affective response, respectively .	Stronger activation demonstrated in the right superior temporal gyrus in GD compared to controls when using negative words. Less activation in the left inferior frontal gyrus and caudate nucleus in GD compared to controls. Control subjects elicited higher activation of the dACC and right orbitofrontal cortex (rOFC), suggesting that gaming-disordered adolescents have less emotional sensitivity and less cognitive control in response to swear words

Ding et al., 2014	GD, $N = 17$ Controls, $N = 17$	GD (16.41 years, SD = 3.20 years) Controls (16.29 years, SD = 2.95 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, clinical interview, subgroup addicted to violent games (or similar) recruited	Both GD and control groups contained 14 males & 3 females. GD recruited from the psychiatry department in China	To investigate differences in response inhibition between GD and controls, and to explore facets of trait impulsivity that may be linked with abnormal brain activation in GD	No differences in behavioural performance between groups. GD adolescents demonstrated hyperactivity during inhibition tasks in left superior medial frontal gyrus, right ACC, right superior/middle frontal gyrus, left inferior parietal lobule, left precentral gyrus and left precuneus and cuneus compared to controls. GD adolescents significantly hypoactive during inhibition tasks in bilateral middle temporal gyrus, bilateral inferior temporal gyrus and right superior parietal lobule compared to controls
Du et al., 2017a	GD, $N = 33$ Controls, $N = 32$	GD (16.82 years, SD = 3.46 years) Controls (17.28 years, SD = 3.01 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, online gaming >4 hours per day, Young Internet Addiction Test (YIAT) >50	All males recruited in China	To evaluate the relationship between impulsivity and white matter integrity using diffusion tensor imaging (DTI) in adolescent GD	Higher correlations between non-planning impulsiveness (NI) score and fractional anisotropy values of right corticospinal tract and right occipital white matter region observed in GD compared to controls. Other forms of impulsivity (attentional impulsiveness, motor impulsiveness) did not show correlation between groups
Du et al., 2016	GD, $N = 25$ Controls, $N = 27$	GD (17.28 years, SD = 3.42 years) Controls (17.48 years, SD = 2.87 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, online gaming >4 hours per day, Young Internet Addiction Test (YIAT) >50	All males recruited form China	To identify altered structural correlates of impulsivity using voxel-based morphology (VBM) in GD adolescents	Correlations between higher impulsivity scores and decreased grey matter volume of the right dorsomedial prefrontal cortex (dmPFC), bilateral insula, OFC, right amygdala and left fusiform gyrus in GD compared to controls
Du et al., 2017b	GD, $N = 27$ Controls, $N = 35$	GD (17.07 years, SD = 3.55 years) Controls (16.8 years, SD = 2.34 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, online gaming >4 hours per day, Young Internet Addiction Test (YIAT) >50	All male subjects recruited from a general hospital in China	To investigate the abnormal spontaneous brain activity with resting-state functional connectivity disturbance (rsFCD) and to detect the relationship between altered rsFCD and visual-related behavioural performance (visual attention and visual spatial working memory)	No significant intergroup differences in behavioural performance. GD adolescents showed increased rsFCD in brain regions involved in working memory, spatial orientation and attention processing. Increased functional connectivity demonstrated in the left superior frontal cortex, left middle frontal cortex and right inferior temporal cortex may correlate with improved performance in visuospatial and visual attention processing in GD

(*Continued*)

Table 1. (*Continued*)

Author	Sample	Mean age + SD	GD assessment measures used	Sample Characteristics	Aims	Findings
Feng et al., 2013	GD, $N = 15$ Controls, $N = 18$	GD (16.93 years, SD = 2.34 years) Controls (16.33 years, SD = 2.61 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, psychiatrist interview	GD subjects consisting of 13 males, 2 females. Controls, 14 male, 4 female. All recruited from a mental health centre, China	To investigate the effects of GD on resting cerebral activation patterns in adolescent brains. To examine any similarities seen in subjects with drug addiction. To determine relationships between altered cerebral blood flow (CBF) and behavioural and personality measures in subjects with GD	GD adolescents with demonstrated increased cerebral blood flow in the left inferior temporal lobe, left parahippocampal gyrus, amygdala, right medial frontal lobe/anterior cingulate cortex, bilateral insula, right-middle temporal gyrus, right precentral gyrus, left supplementary motor area, left cingulate gyrus and right inferior parietal lobe. These areas correlate with addiction pathways seen in substance addiction, such as the involvement of the insula, prefrontal cortex, ACC and parietal cortex
Han et al., 2015	GD, $N = 24$ GD + Major Depressive Disorder (MDD), $N = 40$ GD + ADHD, $N = 14$ Controls, $N = 73$	GD (15.2 years, SD = 1.9 years) GD + MDD (13.9 years, SD = 1.6 years) GD + ADHD (14.6 years, SD = 2.0 years) Controls - No disorder (14.8 years, SD = 1.9 years) Controls - MDD (14.2 years, SD = 2.0 years) Controls - ADHD (14.6 years, SD = 1.5 years)	Young Internet Addiction Scale (YIAS) >50, online game play >4 hours per day, clinical symptoms of GD, psychiatrist interview	All males recruited from a mental health unit, South Korea	To assess whether internet video gameplay would increase brain connectivity within brain attentional networks in subjects with GD and in subjects with GD and comorbid ADHD/MDD	Increased right sided connections between the right DLPFC to right TPJ, right auditory cortex to right motor cortex, right auditory cortex to SMA and right auditory cortex to dorsal anterior cingulate are associated with increased gameplay in adolescent gaming disorder. These findings may represent the risk of over-connectivity in response to increased game play and may impact executive control networks, in turn impacting mental health
Han et al., 2021	GD, $N = 20$ ADHD, $N = 26$ ADHD + GD, $N = 29$ Controls, $N = 38$	GD (14.6 years, SD = 1.2 years) ADHD (14.2 years, SD = 1.9 years) ADHD + GD (14.6 years, SD = 1.2 years) Controls (14.8 years, SD = 2.0 years)	Young Internet Addiction Scale (YIAS) >50, online game play >2 hours per day	All males recruited in South Korea	To compare brain changes within the attentional network, frontal cortices and subcortices in GD compared to ADHD, ADHD + GD and controls	Adolescents with GD demonstrated decreased functional connectivity between the right-middle frontal gyrus and the left cingulate gyrus, to the caudate. One year of treatment for ADHD & GD symptoms increased the functional connectivity between cortex and subcortex in all ADHD and GD participants with good prognoses
Han et al., 2018	GD, $N = 26$ Controls, $N = 30$	GD (16.81 years, SD = 0.75 years) Controls (17.0 years, SD = 0.89 years)	Young's Diagnostic Questionnaire (YDQ), psychiatrist interview	Only males. GD recruited via hospital and controls via general public, all in China	To investigate the therapeutic mechanisms of CBT in GD subjects, including the regulation of abnormal prefrontal-striatal regions	Pre-treatment adolescent GD showed increased amplitude of low-frequency (ALFF) values in the bilateral putamen, right medial OFC, bilateral supplementary motor area (SMA), left postcentral gyrus and left ACC. Post-treatment with CBT, the ALFF values in the treatment group significantly decreased in the left superior OFC and the left putamen, and functional connectivity between these brain regions increased post-CBT

Hong et al., 2015	GD, $N = 12$ Controls, $N = 11$	GD (13.41 years, SD = 2.31 years) Controls (14.81 years, SD = 0.87 years)	Young Internet Addiction Test (YIAT), self-reported online gaming as primary disorder	All males from South Korea	To analyse resting-state brain activity in GD, focusing on the relationship between putamen functional connectivity and proxy measures of video game exposure	Decreased functional connectivity was observed between the dorsal putamen and left insula-operculum in GD. Time spent gaming online was found to positively predict increased functional connectivity between the putamen and bilateral postcentral cortices, with control subjects showing significantly lower connectivity in the same brain regions. Higher addiction scores correlated with greater functional connectivity between the dorsal putamen and left parahippocampal cortex in GD
Hwang et al., 2020	GD, $N = 42$ Controls, $N = 41$	GD (14.6 years, SD = 1.1 years) Controls (14.8 years, SD = 2.0 years)	Psychiatrist interview, DSM-5 criteria for GD	Only males recruited via online clinic (GD) or OPD (Controls), through a hospital in South Korea	To investigate whether the GD adolescents show disrupted family relationships and explore the association between family relationships and brain activity within the reward circuit.	Adolescent GD demonstrated decreased brain connectivity from the cingulate to the striatum. Positive correlations between functional connectivity values and Family Environmental Scale-R scores were identified between the left cingulate and the left and right lentiform nucleus, while functional connectivity values from the left cingulate to the left & right lentiform nucleus were negatively correlated with YIAS scores, a measure of internet addiction
Kwak et al., 2020	GD, $N = 14$ Pro-gamer controls, $N = 12$	GD (16.5 years, SD = 1.2 years) Pro-gamers (17.1 years, SD = 0.3 years)	Currently diagnosed with GD attending the clinical service, Young Internet Addiction Scale (YIAS) >50	All males recruited in a hospital in South Korea	To assess effects of long-term game play on brain activity within attentional system between GD and pro-gamers.	Pro-gamers improved problem behaviours compared to GD group. Both groups showed increased brain activity in parietal lobe. GD group showed higher brain activity within left OFC, in addition to increased activity in the left subcallosal gyrus, left orbital and left inferior frontal gyrus, compared to pro-gamers
Lee et al., 2020	GD, $N = 17$ Controls, $N = 18$	GD (13.7 years, SD = 0.9 years) Controls (13.4 years, SD = 1.0 years)	Korean Internet Addiction Proneness Scale (K-scale), main online purpose was playing 'League of Legends'	All males recruited from the local community playing the multiplayer online game 'League of Legend' in South Korea	To identify alterations in functional connectivity related to decision-making in adolescents with GD, in particular the default mode network, salience network and executive central network.	Increased functional connectivity in GD was observed between the posterior superior temporal sulcus (pSTS) and the posterior cingulate cortex (PCC) and anterior insular cortex (AIC) compared to controls, proxy measures for the social brain network and social processing respectively, implying that gaming disorder may inhibit social brain functioning in adolescents
Lee et al., 2015	GD, $N = 18$ Controls, $N = 18$	GD (13.6 years, SD = 0.9 years) Controls (13.4 years, SD = 0.9 years)	Korean Internet Addiction Proneness Scale (K-scale), gaming main purpose for internet use, psychologist interview with DSM-5 criteria for GD	All males recruited from local community in South Korea	To assess emotional regulation in adolescent GD, using activity of the dorsal ACC as a measure of cognitive control. To examine functional connectivity during emotional processing in adolescent GD	GD adolescents showed weaker dACC activation and stronger insular activations compared to controls. Weaker dACC involvement in the dorsal attention network and stronger activation of the right insula could imply that GD adolescents were more distracted by emotional interference.

(*Continued*)

Table 1. (*Continued*)

Author	Sample	Mean age + SD	GD assessment measures used	Sample Characteristics	Aims	Findings
Li et al., 2020	GD, $N = 31$ Controls, $N = 32$	GD (15.81 years, SD = 1.68 years) Controls (15.91 years, SD = 1.73 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, psychiatrist interview	Recruited from a mental health centre in China. M:F ratio 28:3. Subjects all from China	To examine inhibitory control and reward-seeking behaviours in GD using EEG markers on inhibition and gambling tasks	GD adolescents demonstrated less positive P3 amplitudes in response inhibition tasks. Less positive P3 amplitudes have been linked with increased task difficulty, suggesting GD adolescents may have more difficulty inhibiting their responses. GD adolescents in reward tasks showed a less positive feedback-related negativity (FRN) amplitudes after receiving a gain on a gambling task, indicating reduced reward sensitivity. No difference between FRN responses on the gambling task after a loss, indicating while gaming-disordered adolescents may share similar loss avoidance, they may have increased reward-seeking behaviours
Park et al., 2017a	GD, $N = 19$ Controls, $N = 20$	GD (13.61 years, SD = 0.98 years) Controls (13.35 years, SD = 0.88 years)	Korean Internet Addiction Proneness Scale (K-scale), game time >10 hours per week or half of total time spent online	All males recruited from middle school in South Korea	To assess GD adolescent impulsiveness and whether topological alterations of the brain are related to degree of impulsivity	GD adolescents demonstrated higher regional global efficiency in the fronto-sensorimotor, frontal-temporal, frontal-limbic and temporal region, correlated with increased impulsivity.
Park et al., 2017b	GD + ADHD, $N = 16$ ADHD only, $N = 15$ Controls, $N = 14$	GD + ADHD (14.6 years, SD = 1.9 years) ADHD only (13.7 years, SD = 0.8 years) Controls (14.4 years, SD = 1.7 years)	Young Internet Addiction Scale (YIAS) >50, psychiatrist interview using DSM-5 criteria for GD	All males recruited from a mental health centre in Korea	To investigate whether ADHD comorbid with GD or without comorbidity demonstrated any neurophysiological differences in QEEG testing	Adolescents with comorbid ADHD and gaming disorder showed increased theta coherence in the electrodes in the temporal region, suggesting increased stimulation of the working memory circuit in gaming disorder. Increased intra-hemispheric coherence was noted in the right parieto-occipital region in the gaming disorder group, implying a consistent gaming stimulus activates visuospatial working memory circuits
Qi et al., 2015	GD, $N = 23$ Controls, $N = 24$	GD (17.26 years, SD = 3.56 years) Controls (17.42 years, SD = 3.05 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, Internet Addiction Test (IAT) >50, game play >4 hours per day	All males recruited in China	To investigate whether changes in risk level during decision-making are altered in adolescents with GD compared to controls	Lower activation of other frontal structures, such as the right DLPFC, demonstrated negative correlation with impulsivity scores during risky decision making in adolescent gaming disorder. This decreased activation of the right DLPFC has been observed in other substance misuse disorders and may reflect impaired executive control, leading to increased inhibition

Qi et al., 2016	GD, $N = 24$ Controls, $N = 24$	GD (17.17 years, SD = 3.51 years) Controls (17.42 years, SD = 3.05 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, Internet Addiction Test (IAT) >50, game play >4 hours per day, psychiatrist interview	All males recruited in China	To investigate the manner in which different outcomes affected the covariance between risk level and brain activation during decision-making processes in adolescents with GD	After a risky decision-making task, adolescents with GD showed an increased activation of prefrontal cortex structures (left inferior frontal cortex, bilateral ventromedial PFC) when experiencing negative feedback, suggesting increased resources were needed to evaluate risk values post-receiving negative feedback on a risky decision
Wang et al., 2015	GD, $N = 17$ Controls, $N = 24$	GD (16.94 years, SD = 2.73) Controls (15.87 years, SD = 2.69)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, psychiatrist interview	GD group – 13 males, 4 females. Control group – 18 males, 6 females. All recruited via hospital in China	To examine the interhemispheric synchronous changes of the brain using voxel-mirrored homotopic connectivity (VMHC) in participants with GD	Interhemispheric connections between the right and left prefrontal lobes and orbitofrontal cortex (superior frontal gyrus, inferior frontal gyrus, superior frontal gyrus and middle frontal gyrus) were reduced compared to controls in adolescent GD
Weng et al., 2013	GD, $N = 17$ Controls, $N = 17$	GD (16.25 years, SD = 3.02 years) Controls (15.54 years, SD = 3.19 years)	Young's Diagnostic Questionnaire (YDQ) – 5 of 8 criteria, online gaming reported as primary activity	GD group – 13 females, 4 males. Control group – 15 females, 2 males. All recruited via hospital in China	To investigate morphological brain differences between GD and controls using voxel-based morphometry (VBM) and tract-based spatial statistics (TBSS)	GD adolescents showed significant grey matter atrophy in the right OFC, bilateral insula and right supplementary motor area. Grey matter volumes of the right OFC, bilateral insula and fractional anisotropy (FA) values of the right external capsule were positively correlated with increased GD scores

dorsal striatum. Adolescents with gaming disorder demonstrated decreased functional connectivity between the right-middle frontal gyrus and the left cingulate gyrus, to the caudate (Han et al., 2021), and decreased functional connectivity between the dorsal putamen and left insula-operculum (Hong et al., 2015). Time spent gaming online was found to positively predict increased functional connectivity between the putamen and bilateral postcentral cortices, with control subjects showing significantly lower connectivity in the same brain regions (Hong et al., 2015). Higher scores on the Young Internet Addiction Test (YIAT), used as a measure of gaming disorder in this study, correlated with greater functional connectivity between the dorsal putamen and left parahippocampal cortex in gaming-disordered adolescents (Hong et al., 2015). Increased functional connectivity in gaming-disordered adolescents was observed between the posterior superior temporal sulcus (pSTS) and the posterior cingulate cortex (PCC) and anterior insular cortex (AIC) compared to controls (Lee et al., 2020). These brain regions were used as proxy measures for the social brain network and social processing respectively, implying that gaming disorder may inhibit social brain functioning in adolescents (Lee et al., 2020). Dysfunction in the social brain network, such as deficits in social cognition and mentalisation, is related to executive dysfunction and cognitive problems in adolescents (Lee et al., 2020).

Changes in amplitude of low-frequency fluctuations (ALFF), a parameter that reflects the power of regional spontaneous neuronal activity (Zang et al., 2007), were measured alongside functional connectivity in gaming disorder in adolescents pre- and post-receiving cognitive behavioural therapy (CBT) (Han et al., 2018). The pre-treatment adolescent group showed significantly increased ALFF values in the bilateral putamen, right medial orbitofrontal cortex (OFC), bilateral supplementary motor area (SMA), left postcentral gyrus and left anterior cingulate (ACC) compared to healthy controls (Han et al., 2018). Post-treatment with CBT, the ALFF values in the treatment group significantly decreased in the left superior OFC and the left putamen, and functional connectivity between these brain regions significantly increased post-CBT (Han et al., 2018). Increased OFC activity is mirrored in another study examining functional ALFF between gaming-disordered adolescents and student pro-gamers, in addition to increased activity in the left subcallosal gyrus, left orbital and left inferior frontal gyrus. Both pro-gamers and gaming-disordered adolescents demonstrated increased parietal lobe activity and increased activity within the attention network of the brain, however pro-gamers improved from a behavioural and emotional perspective during the study, whereas the gaming-disordered adolescents showed no improvement (Kwak et al., 2020).

Two studies explored gaming disorder from an emotional regulation perspective. In a fMRI study examining swear word processing in adolescent gaming-disordered subjects, stronger activation was demonstrated in the right superior temporal gyrus compared to controls when using negative words (Chun et al., 2015). There was less activation in the left inferior frontal gyrus and caudate nucleus compared to controls - areas related to language, emotional processing and automatic processing of swear words (Chun et al., 2015). Control subjects elicited higher activation of the dorsal anterior cingulate gyrus (dACC) and right orbitofrontal cortex (rOFC) in response to swear words (Chun et al., 2015). During a Stroop task, gaming-disordered adolescents showed weaker dACC activation and stronger insular activations compared to controls (Lee et al., 2015). Combined with the

weaker dACC involvement in the dorsal attention network, stronger activation of the right insula could imply that gaming-disordered adolescents were more distracted by the emotional interference of angry faces during the Stroop task (Lee et al., 2015).

Compared to the weakened involvement and activation of the dACC in emotional regulation studies, the right ACC was found to be hyperactive in studies investigating impulse inhibition in adolescent gaming disorder (Ding et al., 2014). Activation of right sided brain structures, such as the right ACC, is consistent with other studies related to gaming disorder. However, predominately left sided structures (left superior medial frontal gyrus, left inferior parietal lobe, left precentral gyrus, left precuneus, left cuneus) were found to be significantly hyperactive in impulse inhibition tasks in adolescent gaming disorder (Ding et al., 2014). Interhemispheric connections between the right and left prefrontal lobes and orbitofrontal cortex (superior frontal gyrus, inferior frontal gyrus, superior frontal gyrus and middle frontal gyrus) were reduced compared to controls in adolescent gaming disorder (Wang et al., 2015). These findings suggest that the right hemisphere may be fully engaged, requiring the left hemisphere to play a role in response inhibition (Ding et al., 2014). In addition, higher regional global efficiency in the fronto-sensorimotor, frontal-temporal, frontal-limbic and temporal region correlated with increased impulsivity in gaming disorder (Park et al., 2017a).

Lower activation of other frontal structures, such as the right DLPFC, demonstrated negative correlation with impulsivity scores during risky decision-making in adolescent gaming disorder (Qi et al., 2015). After a risky decision-making task, adolescents with gaming disorder showed an increased activation of prefrontal cortex structures (left inferior frontal cortex, bilateral ventromedial PFC) when experiencing negative feedback, suggesting increased resources were needed to evaluate risk values post-receiving negative feedback on a risky decision (Qi et al., 2016). This decreased activation of the right DLPFC has been observed in other substance misuse disorders and may reflect impaired executive control, leading to increased inhibition (Qi et al., 2015). While lower activation may be observed in the right DLPFC in risky decision-making, increased right sided connections between the right DLPFC to right TPJ, right auditory cortex to right motor cortex, right auditory cortex to SMA and right auditory cortex to dorsal anterior cingulate are associated with increased gameplay in adolescent gaming disorder (Han et al., 2015).

The effects of relationships and identity in adolescent gaming disorder were the focus of two fMRI studies. While examining the interaction between family relationships and functional connectivity, adolescents with gaming disorder demonstrated decreased brain connectivity from the cingulate to the striatum (Hwang et al., 2020). Positive correlations between functional connectivity values and Family Environmental Scale-R scores were identified between the left cingulate and the left and right lentiform nucleus, while functional connectivity values from the left cingulate to the left & right lentiform nucleus were negatively correlated with YIAS scores, a measure of internet addiction (Hwang et al., 2020). In terms of self-identity, significant differences in brain region activation have been seen between healthy controls and adolescent gaming disorder when comparing thoughts about themselves versus thoughts about their game avatar (Choi et al., 2018). Adolescents with gaming disorder utilised the medial prefrontal cortex (MPC) and ACC when thinking about their game avatar, with even stronger activation of these regions compared to self-thoughts (Choi et al., 2018). These brain regions are linked with thoughts about the self and activated in healthy controls when thinking about aspects of their self, demonstrating that adolescents with gaming disorder identify more with their gaming avatar than their own self (Choi et al., 2018).

Structural Magnetic Resonance Imaging (MRI)

Three structural MRI studies were included in this review. Structural MRI measures differences in grey and white matter structures to provide information on microstructural changes in adolescents with gaming disorder. Using voxel-based morphometry (VBM) and tract-based spatial statistics (TBSS) to investigate microstructural changes, adolescent subjects showed significant grey matter atrophy in the right orbitofrontal cortex, bilateral insula and right SMA (Weng et al., 2013). Grey matter volumes of the right orbitofrontal cortex, bilateral insula and fractional anisotropy (FA) values of the right external capsule were positively correlated with increased YIAT scores (Weng et al., 2013).

Higher impulsivity scores were correlated with decreased grey matter volumes in similar brain regions (bilateral insula, orbitofrontal cortex), as well as the right dorsomedial prefrontal cortex (dmPFC), right amygdala and left fusiform gyrus (Du et al., 2016). In relation to white matter changes and impulsivity, gaming-disordered adolescents showed higher correlations between non-planning impulsiveness (NI) score and FA values of right corticospinal tract and right occipital white matter region (Du et al., 2017a). Other forms of impulsivity (attentional impulsiveness, motor impulsiveness) did not show any correlation between groups (Du et al., 2017a). These findings demonstrated dysfunction of these brain areas involved in behaviour inhibition, attention and emotion regulation might contribute to impulse control problems in gaming-disordered adolescents.

Proton Magnetic Resonance Spectroscopy (MRS)

Proton MRS is an imaging technique used to assess regional brain chemistry (Novotny et al., 1998) and has been utilised in one study in adolescent gaming disorder. Adolescents with gaming disorder and attention-deficit hyperactivity disorder (ADHD) were examined using proton MRS and measured against both healthy controls and adolescents with ADHD (Bae et al., 2016). Levels of N-acetyl-aspartate (NAA) in both ADHD groups were lower compared to controls, with levels of glutamate and glutamine higher in the ADHD-only group compared to other two groups in the study (Bae et al., 2016). Decreased levels of NAA in both ADHD groups may suggest a common pathway of hypoactivity in the frontal lobe, with decreased levels of glutamate and glutamine in the gaming disorder and comorbid ADHD group (compared to ADHD-only group) possibly mediated by increased dopamine levels from engagement in video gaming (Bae et al., 2016).

Discussion

Examining the results from the four imaging modalities outlined, adolescents with gaming disorder demonstrate brain changes comparable with substance addiction, differences in emotional regulation, inhibition and self-identity, as well as some positive cognitive adaptations due to consistent gameplay. Adolescent gaming disorder demonstrated common findings in several brain regions associated with traditional substance addiction pathways. The insula, a brain region crucial in the conscious urge and the emotional connection towards substances in addiction (Naqvi and Bechara 2009), demonstrated reduced grey matter volume

(Weng et al., 2013) and was associated with increased internet addiction scores (Weng et al., 2013) and emotional sensitivity (Lee et al., 2015). Modifications in dorsal putamen connections have been hypothesised as a biological mechanism for moving from voluntary to habitual use in substance related disorders (Hong et al., 2015). Reduced reward sensitivity and increased reward-seeking behaviour are cornerstones of dopamine dysfunction in substance misuse (Volkow et al., 2010), with blunted FRN responses in task-based EEG studies demonstrating this finding in adolescent gaming disorder (Li et al., 2020). Given the increased dopamine from increased engagement in video gaming (Bae et al., 2016), the common biochemical pathways with ADHD-only adolescents demonstrated during this review (Bae et al., 2016) and ADHD being 2–3 times more likely than the general population to develop a substance misuse disorder (Schellekens et al., 2020), this provides further neurological similarity between substance misuse disorders and adolescent gaming disorder. Finally, effective treatments for substance misuse, such as CBT, was noted to improve connectivity in the orbitofrontal cortex in adolescent gaming disorder (Han et al., 2018). It is noteworthy that this is a region associated with compulsion and drive to take substances (Volkow and Fowler 2000).

Adolescence is a period where there is a greater vulnerability to disruption of normal emotional development and a predisposition to strong emotional states (Dahl 2004). Previous studies have shown that adolescents with gaming disorder can present with dysfunctional emotional regulation strategies (Yen et al., 2018). In this review, adolescents with gaming disorder demonstrated higher activations of the dACC and OFC, two areas that play roles in cognitive control and emotional regulation, respectively, suggesting that gaming-disordered adolescents have less emotional sensitivity, less cognitive control (Chun et al., 2015), and are more distracted by emotional interference compared to controls (Lee et al., 2015). These findings suggest that adolescents, given their heightened vulnerability, may be susceptible to the emotional regulation sequalae of gaming disorder.

Adolescents demonstrate higher levels of risk taking and poor impulse control compared to adults, largely due to the slower development of brain regions involved in inhibition, such as the prefrontal cortex and anterior cingulate cortex (Blakemore and Robbins 2012). Adolescents with gaming disorder demonstrated increased activity in these regions and other frontal brain regions, even compared to their non-addicted peers, when attempting inhibition tasks (Şalvarli and Griffiths 2022). This higher activation is suggested to represent a failure to recruit pathways that could be crucial for cognitive control and response inhibition (Park et al., 2017a), such as when evaluating risks after negative feedback (Qi et al., 2016). With higher effort being placed in inhibition tasks, other brain structures not normally involved in inhibition are recruited (Ding et al., 2014) and brain regions normally involved in inhibition can be suppressed (Chen et al., 2021).

Self-identity development is an important stage of adolescence (Beyers and Çok 2008) and previous studies have examined whether or not increased internet usage is due to increasing internet addiction or self-exploration of adolescent identity and understanding of themselves (Israelashvili et al., 2012). Similar exploration and testing of alterative ideas and beliefs can be seen in adolescent gaming disorder (Young 2009). The MPC and ACC are important for adolescent self-evaluation (Pfeifer and Berkman 2018) and these regions are active during gaming-disordered adolescent thoughts related to their gaming avatar, implying changes in self-identity (Choi et al., 2018). The family microsystem plays an important role in identity formation (Beyers and Çok 2008) with gaming-disordered adolescents showing disrupted family relationships, which was associated with the severity of the disorder and disconnectivity within the brain's reward circuit (Hwang et al., 2020). Alongside self-identity, adolescents with gaming disorder can demonstrate lower social competence (Torres-Rodríguez et al., 2018), with aberrations in social brain functioning demonstrated in this review (Lee et al., 2020).

Multiple studies demonstrated brain changes associated with positive adaptations to increased engagement in gaming. Increased functional connectivity in brain regions associated with visuospatial memory (Park et al., 2017b) and visuospatial attention processing (Du et al., 2017b) can have a positive effect on performance in gaming. Higher visuospatial processing has been demonstrated in studies recruiting naïve gamers to play shooter-type video games, with an associated improved accuracy of attention allocation (Granic et al., 2014). Increased connectivity between auditory circuits and brain regions (right DLPFC, right motor cortex, dorsal anterior cingulate) in adolescent gaming disorder demonstrate the adaptation of the salience network to process and integrate information more effectively from multiple senses during gameplay (Han et al., 2015). Regular gamers of shooter-type games are more efficient at allocating their attentional resources during a pattern recognition challenge, demonstrating their ability to filter out irrelevant information more effectively compared to controls (Granic et al., 2014).

There are several limitations noted within this systematic review. First, many of the studies included in this review have small sample size and were conducted in Asian populations, likely given an increased focus on possible problematic gaming in Asian populations. This limits the ability to generalise to a worldwide population. The intended age group to review were those aged under 18, however some studies despite a mean age under 18 may have had a standard deviation exceeding 18 years old. Hence a small number of subjects in the review may exceed the 18-year-old age range. Within the papers selected for this review, there were differing definitions of gaming disorder, with this term used interchangeably with internet addiction, excessive gaming, online gaming disorder and problematic gaming. This is a known issue within gaming disorder research (Griffiths 2018). In addition to differing definitions of gaming disorder, the majority of questionnaires used in this review measure internet addiction primarily and not specifically gaming disorder. These questionnaires were used alongside clinical evidence of gaming disorder to denote gaming disorder in these studies. Given the widespread nature of this method in these studies, this appears to be the accepted practice in researching gaming disorder in this population. Further research should focus on gaming-disorder specific questionnaires in order to decrease bias and confusion between what findings constitute internet addiction and/or gaming disorder. The studies included in the literature review are cross-sectional studies. Longitudinal studies would be required to establish causal relationships between altered brain structures and gaming disorder.

This review highlighted a number of key brain regions that can be affected in the adolescent brain due to gaming disorder. These findings can help clinicians understand adolescent presentations with gaming disorder and recognise important facets of clinical presentation from a neurobiological perspective. Referrals for gaming disorder treatment have been increasing internationally (King et al., 2022) so it is important clinicians have a greater understanding of gaming disorder as a whole. Future studies

should focus on forming a more robust neurobiological and clinical framework for adolescent gaming disorder.

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