ORIGINAL ARTICLE

Systematic Review of the Utility of Functional MRI to Investigate Internet Addiction Disorder: Recent Updates on Resting State and Task-Based fMRI

Hamed Sharifat¹, Aida Abdul Rashid^{2, 3}, Subapriya Suppiah^{1, 2}

1 Centre for Diagnostic Nuclear Imaging, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

2 Department of Imaging, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

['] 3 Department of Diagnostic Imaging, Hospital Serdang, Jalan Puchong, 43000 Kajang, Selangor, Malaysia

ABSTRACT

Introduction: Internet addiction disorder (IAD) particularly the internet gaming disorder (IGD) is recognized as a type of addiction similar to substance abuse. This addiction carries similar social impact as the latter, as it can cause serious impairment of interpersonal relationship, and even deterioration of academic or occupational performances. Functional magnetic resonance imaging (fMRI) is able to act as a non-invasive objective biomarker to detect functional neuronal connectivity in areas of the brain affected by IAD by utilizing blood oxygenation level dependent (BOLD) imaging. **Methods:** A systematic review was conducted from original articles published from January 2014 to January 2017 that had the keywords "internet addiction" and fMRI. **Results:** Initial data collection had 170 articles, however after applying the inclusion and exclusion criteria, there were 34 articles in the final analysis (17 resting-state fMRI studies). The striatal nucleus and dopaminergic system demonstrated impaired functioning in subjects with IAD. **Conclusion:** Task-based and resting-state fMRI are able to detect areas of the brain that are activated in subjects with internet addiction, similar to those observed in subjects with substance abuse and other addictions. This review also introduces a newly arising subtype which is smartphone addiction disorder.

Keywords: Seed-based, Task-based, fMRI, Independent component analysis, Functional connectivity

Corresponding Author:

Dr. Subapriya Suppiah Tel: +60192051260 Fax: +60389472775 *Email: subapriya@upm.edu.my*

INTRODUCTION

Internet addiction disorder (IAD) particularly the internet gaming disorder (IGD) is recognized as a type of addiction similar to substance abuse.(1) This addiction carries similar social impact as the latter, as it can cause serious impairment of interpersonal relationship, and even deterioration of academic or occupational performances. As a matter of fact IAD consists of a spectrum of addiction disorders which includes IGD, cybersex and social networking. (2) Social networking using smartphones in particular, has risen as an insidious cause of psychosocial problems among adolescents and young adults especially due to the recognition of a sub-entity known as Problematic mobile phone use (PMPU). (3) Consequently, psychosocial studies as well as imaging studies have been carried out to subjectively assess these disorders.

Internet Gaming Disorder

Internet Gaming Disorder has been listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a non-substance abuse type of addiction disorder.(1) It is stated that certain individuals are likely to develop pathological behavior related Internet Gaming Disorder that may lead to stress and impairment of daily living.(4) This addiction is based on the concept of a craving; that involves a reward system which allows the addicted subjects to escape from real-life problems and act as a coping mechanism for them. (4) Development of tolerance has also been implicated in the diagnosis of IGD as it is a chronic and progressive condition. Increasing the time of being online and downloading faster softwares are some of the objective measurements involved in diagnosing IGD. (4) Most practitioners agree that it is a heterogeneous entity and they acknowledge that what unites many types of addictions is their similarities rather than their dissimilarities. (5)

Smartphone Addiction Disorder

Smartphone Addiction Disorder is fast gaining recognition as a distinct entity which is under the spectrum of IAD. The constant availability, portability and ease of selection of mobile applications to suit the users' requirements are implicated in causing this addiction.(6) Facebook and Instagram addictions thus have become more rampant as these mobile phone applications allow for instant messaging and being constantly online to update status or respond to tags. There are Smartphone Addiction Scale questionnaires (SAS)(7), (8) that have been developed to aid in detecting this condition.

Functional magnetic resonance imaging (fMRI)

There are various imaging modalities that are able to evaluate the brain functionally, namely diffusion tensor imaging that analyses tractography, positron emission tomography computed tomography (PET/CT) and functional magnetic resonance imaging (fMRI). PET/CT has a wide role in functionally imaging mainly for oncology imaging(9),(10),(11) and in infection and inflammation disorder;(12) but it is also able to give functional neurological information regarding activation of brain areas based on detection of cerebral glucose metabolism.

Nevertheless, its disadvantage is that it involves exposure to ionizing radiation and it is not able to demonstrate interactions among different areas of the brain as opposed to fMRI. Thus, fMRI has emerged as the imaging modality of choice to investigate IAD as it is able to allude to the complex neuronal interactions that occur in the addicted brain. There are two main methods of fMRI which include resting state fMRI (rsfMRI) and task-based fMRI.

Resting state fMRI (rs-fMRI)

Resting state fMRI data acquisition involves performing blood oxygen level dependent (BOLD) imaging in subjects when they are at rest in the fMRI scanner. The subjects are usually asked to fixate their vision upon a dot on the fMRI screen. Even when not performing an explicit task, there are low frequency brain activity fluctuations that are consistent and occur within the range of 0.01 – 0.08 Hz that occur in the brain at resting state.(13) Overall spontaneous fluctuations are taken into account and give an improved signal to noise ratio (SNR).

Task-based fMRI (tb-fMRI)

Task-based fMRI involves similar imaging techniques using echo planar imaging (EPI), albeit performed to elicit activation areas in the cerebral cortex based on a task performed by the subjects while in the fMRI scanner. Task-based fMRI fluctuations have more noise, thus reduced SNR, due to confusion and uncertainty that often occur when performing a given task. Furthermore, the increased neuronal metabolism that occurs during a task-based event is less than 5% of the total brain energy and focuses on only a small fraction of the brain's overall activity.

Currently, there is a need to understand the complexities involved in designing the study, recruiting the subjects and interpretation of fMRI scans for the objective assessment of IAD. Hence, we conducted a systematic review of all published original articles in SCOPUS database that investigated the pattern of functional connectivity on fMRI seen in subjects having Internet Addiction Disorder focusing on Internet Gaming Disorder.

MATERIALS AND METHODS

The most recent search for this review was performed on the 1st of September 2017. We searched the electronic database of SCOPUS; using the keywords or search terms "internet addiction" and "functional MRI", as well as "Internet Gaming Disorder" and "functional MRI". We filtered the search to include all full text journal articles in the English language published between the periods of January 2014 to August 2017.

Selection criteria

We selected studies that had defined cohorts with any accepted definition of "Internet Addiction Disorder" and utilized functional MRI to further investigate the disorder. We selected articles that conducted investigations using either resting state fMRI as well as task-based fMRI.

Next, we excluded articles that were from case reports and proceedings; articles that were predominantly based on other imaging modalities, as well as articles that only had the abstract in English but the full article was in a foreign language. We also excluded articles that predominantly analysed structural parameters or utilized other diagnostics tests such as electroencephalography as their main method of investigation.

Data collection and analysis

We screened all titles generated by the electronic database search engines. Two authors (HS and SS) independently assessed the abstracts of all potentially relevant studies. The identified full papers were assessed for eligibility and data were extracted to create tables that gave information on positive and negative correlations for functional connectivity of different regions of the brain. One independent assessor (AAR) performed a quality assessment using the QUADAS 2 tool. We grouped together studies that shared similar methodologies e.g. the use of resting state or task-based fMRI methods. We extracted data regarding study design, patient selection, whether healthy controls were included or not; as well as verification bias.

RESULTS

Main results

Our initial search recovered 170 articles. After applying the exclusion criteria, we had 35 articles for the final analysis; whereby 18 articles were from resting state fMRI (rs-fMRI) studies and 17 articles were from taskbased fMRI studies (Figure 1).

Resting state fMRI (rs-fMRI)

A total of 17 fMRI studies which aimed to identify functional connectivity in brain regions were reviewed [Table 1]. The majority of the studies used seed-based analysis.(14), (15), (16), (17), (15), (18), (19), (20), (21), (22), (23), (24), (25). The essence of seed-based analysis proposes to find the linear correlation of all the voxels in the brain with a pre-defined region of interest (ROI) which is termed the seed. Thus, based on this model, a seed-based functional connectivity map is formed.(13) The largest study that utilized this method of analysis was Chen et al., 2016 who recruited 115 number of subjects. (21) They detected increased functional connectivity of the posterior insula with the somatosensory and sensorimotor cortices in IGD subjects.

There were four studies (26),(27),(28),(29) that used the graph theoretical study analysis method [Table 1]. It applies a model to connect various regions and sub-regions of the brain that constitute a larger single network. It deals with the study of nodes and edges in the brain.

Lastly, one study utilized independent component analysis (ICA) method.(30) This involves employing mathematical algorithms to extract distinct resting state fMRI networks. The signals are decomposed to temporally and spatially independent components.

Overall, the rs-fMRI studies noted that there was impaired functional connectivity between areas of the insula and amygdala with the dorso lateral prefrontal cortex (DLPFC) and orbital frontal lobe which were related to impulsivity.

Task-based fMRI

A total of 18 fMRI studies which studied the brain activation seen in task-based fMRI [Table 2]. The commonly used task is the popular Go/NoGo task that tests for attention and concentration.(31), (32) ,(33), (34), (35) Whereas, some other studies utilized the Stroop task method. (36), (37),(38), (24) Other task-based paradigms included cue-reactivity methods that assessed their response and risk taking behaviours. (39), (40),(41), (42), (42), (43), (40), (44), (45) There are several ways to conduct task-based fMRI which include block-based paradigms and event-based paradigms. Ko et al (2014) detected positive correlation with impulsivity in subjects



Fig. 1 Evidence synthesis of articles related to fMRI and Internet Addiction Disorder.

Author (Year)	Sample Size IAD/ HC	Type of Analysis	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding /Additional Information
Bi <i>et al</i> (2015)	42 (21/21)	Seed-based analysis	IAD had ↓ VMHC of DLPFC and ↓ fractional anisotropy (FA) values in the genu of corpus callosum	VMHC of DLPFC was negatively correlated with the duration of IAD	functional-structural coupling disruption in IAD is likely due to ↓ reduced constraints that white matter connectivity pose on the brain function
Hong <i>et al</i> (2015)	22 (12/11)	Seed-based analysis	↑ FC between the DP and bilateral S1 cortices in IGD	↓ FC between DP with the posterior insula-parietal operculum.	↓ FC between the DP and bilateral S1 cortices in healthy controls.
Ko <i>et al</i> (2015)	60 (30/30)	Seed-based analysis	↑ Impulsivity and a greater severity of IGD. ↑ FC between bilateral amygdala over the contralateral insula.	Left amygdala and DLPFC FC was negatively correlated with impulsivity. Right amygdala FC to the left DLPFC and orbital frontal lobe was negatively correlated with impulsivity	Altered GMD over the amygdala might represent vulnerability to IGD, such as impulsivity.
Kim <i>et al</i> (2015)	31 (16/15)	Seed-based analysis	↑ ReHo in PCC of the IGD and AUD. Positive correlation of ReHo in the MFC, precuneus /PCC, and left ITC among those with IGD	↓ ReHo in right STG in IGD. ↓ ReHo in the anterior cingulate cortex of AUD.	↓ ReHo in the STG may be a candidate neurobiological marker for IGD.
Lin <i>et al</i> (2015)	29 (14/15)	Seed-based analysis	↑ FC between the left DP and bilateral caudal cingulate motor area.	The negative association between SCARED scores and FC strengths arise from dysfunction of corticostriatal circuits which are involved in affection regulation.	IAD is associated with alterations of corticostriatal functional circuits involved in the affective and motivation processing and cognitive control.
Park <i>et al</i> (2017)	39 (19/20)	Graph theoretical analysis	IGA induced brain functional networks, impulsivity à topological alterations frontolimbic FC.	IGA impulsivity à ↑global efficiency and↓local efficiency relative to the controls.	IAD brain could be in the state similar to pathological states in terms of topological characteristics of brain functional networks.
Wang <i>et al</i> (2015)	41 (17/24)	-Voxel mirrored homotopic connectivity (VMHC) -Seed-based analysis	IGD participants showed higher SFG activation after continuous wins than healthy controls.	Negative correlation was observed between VMHC in superior frontal gyrus (orbital part) and CIAS, in IAD	OFC plays an important role in the neuropathological mechanism of IGD.

Author (Year)	Sample Size IAD/ HC	Type of Analysis	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding /Additional Information
Wee <i>et al</i> (2014)	33 (17/16)	Graph theoretical analysis	Disruption in the FC between regions located in the frontal, occipital and parietal lobes; positively correlated with impulsiveness and the severity of emotion and prosocial behaviour problems with the functionally affected regions.	No significant correlation between regional network measures and other behavioural measures.	Correlation analysis demonstrates that the observed regional abnormalities are correlated with the IAD severity and behavioural clinical assessments.
Wang <i>et al</i> (2017)	69 (26/43)	Group independent component analysis (ICA)	IA group members showed Increased intra-hemispheric functional connectivity of the left FPN	IAD had ↓ inter- hemispheric FC of the right FPN, and dorsal medial PFC	IAD a/w imbalanced interactions among the DMN, and left and right fronto- parietal network, system-level neural underpinnings of addiction.
Wang <i>et al</i> (2016)	72 (37/35)	Graph theoretical analysis	IAD had ↑ FC SMC	IGD had ↓ regional centralities in the prefrontal cortex, left posterior cingulate cortex, right amygdala and bilateral lingual gyrus.	IGD: Impaired executive control & emotional management, but enhanced coordination among visual, sensorimotor, auditory & visuospatial systems.
Wen <i>et al</i> (2016)	47 (?/?)	Graph theoretical analysis	Majority of nodes that link the two (CIAS-R positive and CIAS-R negative) networks are located within the frontal lobe	Network that comprised of functional connections that were negatively related to CIAS- R scores.	IAD showed higher fronto-striatal and fronto- parietal activation during the Go/Nogo task.
Zhang <i>et al</i> (2016)	38 (19/19)	Seed-based analysis	They observed increased functional connectivity between frontal eye field and anterior insula	↓ FC with left posterior insula in bilateral SMA and middle cingulate cortex.	IGD is a/w altered insula-based network, that is, IGD, as one kind of internet addiction, is similar to substance addiction such as smoking, showing altered insula-based network.

Author (Year)	Sample Size IAD/ HC	Type of Analysis	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding /Additional Information
Chen <i>et al</i> (2016)	115 (74/41)	Seed-based analysis	IGD had ↑ FC between the anterior insula and a network of regions including anterior cingulate cortex (ACC), putamen, angular gyrus and precuneus.	IGD had ↓ FC in executive control network (ECN).	Posterior insula had ↑ FC with somatosensory and sensorimotor cortices in IGD subjects.
Chen <i>et al</i> (2014)	81 (29+22/ 30)	-Temporal correlation method -Seed-based analysis	Compared with the non-smokers with IGA, the smokers with IGA had ↑ FC of left middle frontal gyrus.	Smokers with IGA had ↓ FC with PCC in the right rectus gyrus.	Smokers with IGA had functional changes in brain areas related to motivation and executive function compared with the non-smokers with IGA.
Chen <i>et al</i> (2016)	60 (30/30)	Seed-based analysis	IGD had ↑ FC with contralateral insula than healthy controls.	IGD had ↓ FC with the left insula over the left dorsolateral prefrontal cortex (DLPFC) and orbital frontal lobe.	The elevated inter- hemispheric insula FC is found to be associated with impulsivity in IGD.
Han <i>et al</i> (2015)	31 (15 IGD/ 16AD)	Seed based analysis	IAD subjects have positive functional connectivity between the DLPFC, temporal lobe and striatal areas.	Both AD and IGD subjects have positive functional connectivity between the dorsolateral prefrontal cortex (DLPFC), cingulate and cerebellum.	Negative FC between the DLPFC and the striatal areas in IGD subjects, compared to AD, may be due to the earlier prevalence age, different comorbid diseases as well as visual & auditory stimulation.
Dong <i>et al</i> (2015)	71 (35/36)	Seed-based analysis	IGD had ↑ FC in the reward network when comparing with the healthy controls.	IGD subjects show decreased FC in the executive control network.	The inverse proportion between control network and reward network in IGD suggests that impairments in executive control lead to inefficient inhibition of enhanced cravings to excessive online game playing.

Author	Sample Size	Type of	Positive correlates	Negative correlates	Finding /Additional
(Year)	IAD/ HC	Analysis	(brain areas)	(brain areas)	Information
Jin <i>et al</i> (2016)	46 (25/21)	Seed-based analysis and VBM	IGD had ↓ grey matter volume in PFC regions including the bilateral DLPFC, OFC, ACC and the right SMA.	IGD had ↓ FC between several cortical regions and our seeds, including the insula, and temporal and occipital cortices.	IGD may share similar neural mechanisms with substance dependence at the PFC-striatal circuit level.

AUD: Alcohol use disorder; BOLD imaging : Blood oxygenation level dependent imaging; CIAS-R: Chen internet addiction scale-revised; DLPFC: Dorsolateral prefrontal cortex; DMN: Default mode network; DP: Dorsal putamen; ECN: Executive control network; EPI: Echo planar imaging; FC: Functional connectivity; GMD: Gray matter density; IAD: Internet addiction disorder; IGD: Internet gaming disorder; ITC: Inferior temporal cortex; MFC: Medial frontal cortex; PCC: Posterior cingulate cortex; PFC: Prefrontal cortex; Re-Ho: Regional homogeneity; S1: Primary somato sensory cortex; SCARED: Screen for child anxiety related emotional disorders; SMA: Supplementary motor area; STG: Superior temporal gyrus; VMHC: Voxel-mirrored homotopic connectivity; VBM: Voxel based morphometrics

Author (Year)	Sample Size IA/HC	Type of Task	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding/Additional Information
Ko <i>et al</i> (2014)	49 (26/23)	Event-based using Go/NoGo task/ paradigm	IGD had higher score for impulsivity than control group. The DLPFC had ↑ activation; positively correlated with impulsivity in subjects with borderline personality disorder.	Contrast values of the bilateral caudate nucleus and left orbital frontal lobe were significantly correlated with the score of lack of self- control among all IGD groups.	The fronto-striatal network involved in response inhibition and the salience network, anchored by the anterior cingulate and insula contributes to error processing
Li <i>et al</i> (2014)	41 (18/23)	Event-based using Go/NoGo task/ paradigm	Core brain regions in the response inhibition network including the corpus striatum exhibited stronger activation	IAD revealed \downarrow GMD, \downarrow orbitofrontal cortical thickness, abnormal white matter fractional anisotropy (FA), impaired brain activity and \downarrow FC	IAD is a behavioural disorder and has aberrant connectivity in the response inhibition network.
Lee <i>et al</i> (2016)	48 (24/24)	Event-based (Risky decision making task)	IGD showed ↓ front insular activations in response to high-risk uncertain conditions. Control group showed stronger activation within the dorsal attention network, which implies stronger top- down goal-directed attention during the decision-making task.	IGD had ↓ activations in the inferior frontal gyrus, anterior insular cortex, precentral gyrus, inferior temporal gyrus and superior parietal lobe	Young adults with IGD showed impaired anterior insular activation during risky decision making, which might make them vulnerable when they need to adapt to new situations and environments.

Table 2. Data collection of task-based fMRI studies

Author (Year)	Sample Size IA/HC	Type of Task	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding/Additional Information
Dieter <i>et al</i> (2017)	95 (51/44)	Event-based (Anxious words- based Affective Go/NoGo task together with Stroop task)	Specific internet addiction showed ↑ impulsivity, social anxiety and ↓ emotional competence.	↓ left MTG activation during interference of socially anxious words in internet gaming and relative to social network addicts.	A sub-sample of healthy controls (n=23) and specific internet addicts (n=25) underwent fMRI while completing an Emotional Stroop Task (EST) with socially anxious, positive, negative and neutral words.
J. Liu <i>et al</i> (2016)	38 (19/19)	Event-based (Internet video game stimuli)	IGD had ↑ activation in the right side involving superior parietal lobe, insular lobe, precuneus, cingulated gyrus, STG, and left brainstem. IGD subjects showed laterality activation of the right cerebral hemisphere.	No activation of the striatum was observed for IGD member.	Number of activated voxels between the two groups differed: an average of 1078 voxels activated in the IGD group compared with only 232 in the control group.
Wang <i>et al</i> (2016)	40 (19/21)	Event-based (Probability discounting task - Decision making)	IGD showed ↑ task- related activity in DMN The ECN correlate positively with probability discounting rates.	The IGD indicated less engagement in the ECN than HC when making the risky decisions. The activities of DMN correlate negatively with the reaction time.	IGD subjects prefer the risky decision- making to the fixed options and showed ↓ reaction time compared to HC. IGD showed altered modulation in DMN and deficit in ECN, causing IGD subjects to continue to play online games.
Wang <i>et al</i> (2017)	39 18/21	Event-based (delay discounting task)	IGD had ↑ higher delay discounting rates than HC. The delay discounting rates were positively correlated with the modulation of the two networks and the reaction time.	IGD have ↑ sensitivity to reward and decreased ability to control their impulsivity effectively, which leads to myopic decision making.	↑ delay discounting rates indicated that the people with IGD put more emphasis on instantaneous rewards and give up the choices in a long run.
Xing <i>et al</i> (2014)	34 (17/17)	Event-based (colour-word Stroop task)	The impaired cognitive control in IGD was validated by more errors during the incongruent condition in color- word Stroop task.	The fractional anisotropy values of the right salience network tract were negatively correlated with the errors during the incongruent condition in IGD adolescents.	The structural connectivity was not correlated with functional connectivity in neither IGD adolescents nor healthy controls.

Author (Year)	Sample Size IA/HC	Type of Task	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding/Additional Information
Ding <i>et al</i> (2014)	34 (17/17)	Event-based using Go/NoGo task/ paradigm	IGA group was significantly hyperactive during No-Go trials in the left superior medial frontal gyrus, right anterior cingulate cortex, right superior/ middle frontal gyrus, left inferior parietal lobule, left precentral gyrus, left precuneus and cuneus. Activation of the left superior MFG positively associated with CIAS-R	IA subjects showed decreased regional homogeneity (ReHo) in the temporal, occipital, and parietal brain regions.	prefrontal cortex may be involved in the circuit modulating impulsivity, while its impaired function may relate to high impulsivity in adolescents with IGA.
J. Zhang <i>et al</i> (2016)	59 (40/19)	Event-based (cue-reactivity task)	IGD subjects showed stronger activation in multiple brain areas, including the dorsal striatum, brainstem, substantia nigra and anterior cingulate cortex.	IGD subjects indicated ↓ activation in the posterior insula. IGD had ↓ insular FC with the lingual gyrus and precuneus after receiving CBI.	Craving behavioural intervention (CBI) is effective in ↓ craving and severity in IGD, and it may exert its effects by altering insula activation and its FC with regions involved in visual processing and attention bias.
K. Yuan <i>et al</i> (2017)	87 (43/44)	Event-based (Stroop task)	Nucleus accumbens (NAc) volumes were positively correlated with internet addiction test scores in IGD. The caudate volume and DLPFC-caudate RSFC was correlated with the impaired cognitive control.	The cognitive control deficits in IGD were correlated with the reduced frontostrital RSFC strength.	neuropsychological changes are associated with IGD, and IGD should be considered a psychological illness.
Y. Zhang <i>et al</i> (2016)	40 (19/21)	Event-based (Stroop task)	Compared with HC group, IGD subjects showed ↑ activations when facing Internet gaming- related stimuli in regions including the inferior parietal lobule, the middle occipital gyrus and the dorsolateral prefrontal cortex.	fMRI signals in the left and right postcentral gyrus and left temporal gyrus were significantly decreased for IGD subjects compared with HC group.	IGD subjects show impairment in both visual and cognitive control ability while dealing with gaming- related words.

Author (Year)	Sample Size IA/HC	Type of Task	Positive correlates (brain areas)	Negative correlates (brain areas)	Finding/Additional Information
G. Dong <i>et al</i> (2015)	71 (35/36)	Event-based (Stroop task)	IGD subjects, FC measures in ECNs were positively correlated with brain activations in executive-control regions across groups. Positive trends were found between FC in ECNs and brain activations in Stroop task in IGD	FC measures in ECNs were negatively correlated with Stroop effect. Negative trends were found between Stroop effect and FC in ECNs in IGD and HC groups separately.	Higher FC in ECNs may underlie better executive control and may provide resilience with respect to IGD whereas, ↓ FC in ECNs may represent an important feature in understanding and treating IGD.
C. Chen <i>et al</i> (2015)	30 (15/15)	Event-based Go/Nogo task	The control group exhibited activation of the right supplement motor area (SMA), dorsolateral prefrontal cortex, and caudate for response inhibition.	The IGD group had a higher impulsivity and lower activity of the right SMA/pre- SMA in comparison to the control group.	dysfunctional activation of the SMA for response inhibition is one of the candidate mechanisms of IGD.
L. Liu <i>et al</i> (2017)	62 (39/23)	Event-based Cue-reactivity task	IGD participants exhibited ↑ cue- induced activations within both the ventral and DS when compared with HCs. Positive associations were found between activations within the right putamen, pallidum and left caudate and duration of IGD.	Within the IGD group, activity within the left ventral striatum (VS) was correlated negatively with cue-induced craving. Cue-induced activity within the left putamen was negatively associated with right VS volumes among IGD participants.	transition from ventral to dorsal striatal processing may occur among individuals with IGD, a condition without the impact of substance intake.
G. Dong et al (2016)	36 (20/16)	Event-based Risk-taking and risky decision- making	HC versus IGD subjects showed ↑ activation in the left IFG and STG. The IFG may signal subjective risk and contribute to the formation	IGD subjects selected more risk- disadvantageous trials and demonstrated less activation of the anterior cingulate, posterior cingulate and middle temporal gyrus. During risky decision-making and as compared to HCs, IGD subjects showed ↓ response times and ↓ activations of the IFG and STG.	IGD subjects show impaired executive control in selecting risk- disadvantageous choices, and they make risky decisions more hastily and with less recruitment of regions implicated in impulse control.

Author	Sample Size	Type of Task	Positive correlates	Negative correlates	Finding/Additional
(Year)	IA/HC		(brain areas)	(brain areas)	Information
J. Kim <i>et al</i> (2014)	30 (15/15)	Event-based	Activation in the reward- related subcortical system, self-related brain region, and other brain areas for the contrasts, but these brain areas showed almost no activation in IAD. IAD showed significant activation in the DLPFC	The neural response showed negative correlation between the level of activation in the left STG and the duration of Internet game use per day in IAD.	IAD showed reduced levels of self-related brain activation and ↓ reward sensitivity irrespective of the type of reward and feedback.

AUD: Alcohol use disorder; BOLD imaging: Blood oxygenation level dependent imaging; CIAS-R: Chen internet addiction scalerevised; DLPFC: Dorsolateral prefrontal cortex; DMN: Default mode network; DP: Dorsal putamen; ECN: Executive control network; EPI: Echo planar imaging; FC: Functional connectivity; GMD: Gray matter density; IAD: Internet addiction disorder; IGD: Internet gaming disorder; ITC: Inferior temporal cortex; MFC: Medial frontal cortex; PCC: Posterior cingulate cortex; PFC: Prefrontal cortex; Re-Ho: Regional homogeneity; S1: Primary somato sensory cortex; SCARED: Screen for child anxiety related emotional disorders; SMA: Supplementary motor area; STG: Superior temporal gyrus; VMHC: Voxel-mirrored homotopic connectivity; VBM: Voxel based morphometrics

with borderline personality disorder and IGD.(31) These experiments detected that subjects with IGD were more sensitivity to reward and had increased impulsivity and a tendency to choose immediate rewards.

DISCUSSION

Resting state fMRI studies were able to identify reduced functional connectivity between bilateral amygdala and the contralateral insula as well as increased functional connectivity between the dorsolateral prefrontal cortex and temporal lobes with the insula and striatal areas. These findings were all attributed to the changes that pointed to increased impulsivity among subjects with IAD. (29)

In the task-based fMRI studies, there was evidence that subjects with IAD had shorter response time compared with healthy controls. This implied that subjects with IAD might not think things through thoroughly and make hasty judgements i.e. increased impulsivity, and exhibit risky-decision making habits. (39) Furthermore, individuals having IAD also impaired response inhibition as evidenced by aberrant connectivity in the response inhibition network.(32) This disrupted functional connectivity raises the alarm that these individuals are at risk as they are vulnerable to exploitation when exposed to a new environment.

It is recommended that in future fMRI study designs be formulated to objectively assess other spectrums of IAD particularly social networking involving smartphone addiction to demonstrate whether similar neuronal changes occur that are compatible with changes previously recorded in IAD.

CONCLUSION

Functional MRI, involving both resting state and taskbased fMRIs, have provided a visual and statistical evaluation of neuronal connectivity in the brain in subjects with Internet Addiction Disorder. It has shown significant evidence of impulsivity in subjects with IAD with a certain level of improved visuospatial connectivity. The implications of these findings have the potential for objective assessment and detection of IAD as well as a tool for monitoring response to cognitive behavior therapy as a means to treat this condition.

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REFERENCES

1. American Psychiatric Association [APA], American Psychiatric Association. Diagnostic and statistical manual of mental disorders [Internet]. 5th ed. Arlington, VA: American Psychiatric Association; 2013. Available from: http://psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596

- 2. Lopez-Fernandez O. How Has Internet Addiction Research Evolved Since the Advent of Internet Gaming Disorder? An Overview of Cyberaddictions from a Psychological Perspective. Curr Addict Reports. 2015;2(3):263–71.
- 3. Billieux J, Maurage P, Lopez-Fernandez O, Kuss DJ, Griffiths MD. Can Disordered Mobile Phone Use Be Considered a Behavioral Addiction? An Update on Current Evidence and a Comprehensive Model for Future Research. Curr Addict Reports. 2015;2(2):156–62.
- 4. Kuss DJ, Griffiths MD, Pontes HM. DSM-5 diagnosis of Internet Gaming Disorder: Some ways forward in overcoming issues and concerns in the gaming studies field. J Behav Addict. 2017;6(2):133–41.
- 5. Griffiths MD. Behavioural addiction and substance addiction should be defined by their similarities not their dissimilarities. Addiction. 2017;112(10):1718–20.
- 6. Gökçearslan Ş, Mumcu FK, Haşlaman T, Çevik YD. Modelling smartphone addiction: The role of smartphone usage, self-regulation, general selfefficacy and cyberloafing in university students. Comput Human Behav. 2016;63:639–49.
- Kwon M, Lee JY, Won WY, Park JW, Min JA, Hahn C, et al. Development and Validation of a Smartphone Addiction Scale (SAS). PLoS One. 2013;8(2).
- 8. Ching SM, Yee A, Ramachandran V, Lim SMS, Sulaiman WAW, Foo YL, et al. Validation of a Malay version of the smartphone addiction scale among medical students in Malaysia. PLoS One. 2015;10(10):1–11.
- 9. Suppiah S, Chang WL, Hassan HA, Kaewput C. Systematic Review on the Accuracy of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography/Magnetic Resonance Imaging in the Management of Ovarian Cancer: Is Functional Information Really Needed? World J Nucl Med . 2017; 16 (3):176-185.
- Suppiah S, Andi Anggeriana Andi Asri, Fathinul Fikri Ahmad Saad, Hasyma Abu Hassan, Norhafizah Mohtarrudin CWL, Mahmud R, Nordin AJ. Contrast-Enhanced 18F-FDG PET/ CT in Preoperative Assessment of Suspicious Adnexal Masses and Proposed Diagnostic Imaging Algorithm: A single centre experience in Malaysia. Malaysian J Med Heal Sci. 2017;13(1):1–8.
- 11. Suppiah S, Fathinul Fikri AS, Mohad Azmi NH, Nordin AJ. Mapping 18F-Fluorodeoxyglucose metabolism using PET/CT for the assessment of treatment response in Non-Small Cell Lung Cancer patients undergoing Epidermal Growth Factor Receptor inhibitor treatment: A singlecentre experience. Malaysian J Med Heal Sci. 2017;13(1):23–30.

- 12. Suppiah S, Zakaria MH, Khalid B, Saini SM, Othman N. Diagnostic Dilemma of Reactive Arthritis Aided by Multimodality Imaging using MRI, CECT and 18F-FDG PET/CT Scans. Malaysian J Med Heal Sci. 2017;13(1):73–7.
- 13. Smitha K, Akhil Raja K, Arun K, Rajesh P, Thomas B, Kapilamoorthy T, et al. Resting state fMRI: A review on methods in resting state connectivity analysis and resting state networks. The Neuroradiology Journal. 2017;30(4): 305-317.
- 14. Bi Y, Yuan K, Feng D, Xing L, Li Y, Wang H, et al. Disrupted inter-hemispheric functional and structural coupling in Internet addiction adolescents. Psychiatry Res - Neuroimaging. 2015;234(2):157–63.
- 15. Kim H, Kim YK, Gwak AR, Lim JA, Lee JY, Jung HY, et al. Resting-state regional homogeneity as a biological marker for patients with Internet gaming disorder: A comparison with patients with alcohol use disorder and healthy controls. Prog Neuro-Psychopharmacology Biol Psychiatry. 2015;60:104–11.
- 16. Hong SB, Harrison BJ, Dandash O, Choi EJ, Kim SC, Kim HH, et al. A selective involvement of putamen functional connectivity in youth with internet gaming disorder. Brain Res. 2015;1602(C):85–95.
- 17. Ko CH, Hsieh TJ, Wang PW, Lin WC, Yen CF, Chen CS, et al. Altered gray matter density and disrupted functional connectivity of the amygdala in adults with Internet gaming disorder. Prog Neuro-Psychopharmacology Biol Psychiatry. 2015;57:185–92.
- 18. Lin F, Zhou Y, Du Y, Zhao Z, Qin L, Xu J, et al. Aberrant corticostriatal functional circuits in adolescents with Internet addiction disorder. Front Hum Neurosci. 2015;9(6):356.
- 19. Wang Y, Yin Y, Sun YW, Zhou Y, Chen X, Ding WN, et al. Decreased prefrontal lobe interhemispheric functional connectivity in adolescents with internet gaming disorder: A primary study using restingstate fMRI. PLoS One. 2015;10(3):1–11.
- 20. Zhang JT, Yao YW, Li CSR, Zang YF, Shen ZJ, Liu L, et al. Altered resting-state functional connectivity of the insula in young adults with Internet gaming disorder. Addict Biol. 2016;21(3):743–51.
- 21. Chen CY, Yen JY, Wang PW, Liu GC, Yen CF, Ko CH. Altered functional connectivity of the insula and nucleus accumbens in internet gaming disorder: A resting state fMRI study. Eur Addict Res. 2016;22(4):192–200.
- 22. Chen X, Wang Y, Zhou Y, Sun Y, Ding W, Zhuang Z, et al. Different resting-state functional connectivity alterations in smokers and nonsmokers with internet gaming addiction. Biomed Res Int.;2014,Article ID 825787:9 http:// dx.doi.org/10.1155/2014/825787
- 23. Han JW, Han DH, Bolo N, Kim BA, Kim BN, Renshaw PF. Differences in functional connectivity between alcohol dependence and

internet gaming disorder. Addict Behav. 2015; 41:12-9. doi: 10.1016/j.addbeh.2014.09.006.

- 24. Dong G, Lin X, Hu Y, Xie C, Du X. Imbalanced functional link between executive control network and reward network explain the online-game seeking behaviors in Internet gaming disorder. Sci Rep. 2015;5:9197.
- 25. Jin C, Zhang T, Cai C, Bi Y, Li Y, Yu D, et al. Abnormal prefrontal cortex resting state functional connectivity and severity of internet gaming disorder. Brain Imaging Behav [Internet]. 2016;10(3):719–29.
- 26. Wen T, Hsieh S. Network-Based Analysis Reveals Functional Connectivity Related to Internet Addiction Tendency. Front Hum Neurosci. 2016;10:1–13.
- 27. Wee C-Y, Zhao Z, Yap P-T, Wu G, Shi F, Price T, et al. Disrupted brain functional network in internet addiction disorder: a resting-state functional magnetic resonance imaging study. PLoS One. 2014;9(9):e107306.
- 28. Wang L, Wu L, Lin X, Zhang Y, Zhou H, Du X, et al. Dysfunctional default mode network and executive control network in people with Internet gaming disorder: Independent component analysis under a probability discounting task. Eur Psychiatry. 2016;34:36–42.
- 29. Park CH, Chun JW, Cho H, Jung YC, Choi J, Kim DJ. Is the Internet gaming-addicted brain close to be in a pathological state? Addict Biol. 2017;22(1):196– 205.
- Wang Y, Wu L, Zhou H, Lin X, Zhang Y, Du X, et al. Impaired executive control and reward circuit in Internet gaming addicts under a delay discounting task: independent component analysis. Eur Arch Psychiatry Clin Neurosci. 2017;267(3):245–55.
- 31. Ko C-H, Hsieh T-J, Chen C-Y, Yen C-F, Chen C-S, Yen J-Y, et al. Altered brain activation during response inhibition and error processing in subjects with internet gaming disorder: A functional magnetic imaging study. Eur Arch Psychiatry Clin Neurosci. 2014; 264(8):661-72.
- 32. Li B, Friston KJ, Liu J, Liu Y, Zhang G, Cao F, et al. Impaired Frontal-Basal Ganglia Connectivity in Adolescents with Internet Addiction. Sci Rep. 2015;4(1):5027.
- 33. Dieter J, Hoffmann S, Mier D, Reinhard I, Beutel M, Vollstädt-Klein S, et al. The role of emotional inhibitory control in specific internet addiction an fMRI study. Behav Brain Res. 2017;324:1–14.
- 34. Ding W, Sun J, Sun Y-W, Chen X, Zhou Y, Zhuang Z, et al. Trait impulsivity and impaired prefrontal

impulse inhibition function in adolescents with internet gaming addiction revealed by a Go/No-Go fMRI study. Behav Brain Funct. 2014;10(1):20.

- 35. Chen CY, Huang MF, Yen JY, Chen CS, Liu GC, Yen CF, et al. Brain correlates of response inhibition in Internet gaming disorder. Psychiatry Clin Neurosci. 2015;69(4):201–9.
- 36. Xing L, Yuan K, Bi Y, Yin J, Cai C, Feng D, et al. Reduced fiber integrity and cognitive control in adolescents with internet gaming disorder. Brain Res. 2014;1586:109–17.
- 37. Yuan K, Yu D, Cai C, Feng D, Li Y, Bi Y, et al. Frontostriatal circuits, resting state functional connectivity and cognitive control in internet gaming disorder. Addict Biol. 2017;22(3):813–22.
- 38. Zhang Y, Lin X, Zhou H, Xu J, Du X, Dong G. Brain activity toward gaming-related cues in internet gaming disorder during an addiction Stroop task. Front Psychol. 2016;7(5):1–9.
- 39. Lee D, Lee J, Yoon KJ, Kee N, Jung Y-C. Impaired anterior insular activation during risky decision making in young adults with internet gaming disorder. NeuroReport Rapid Commun Neurosci Res. 2016;27(8):605–9.
- 40. Liu L, Yip SW, Zhang JT, Wang LJ, Shen ZJ, Liu B, et al. Activation of the ventral and dorsal striatum during cue reactivity in Internet gaming disorder. Addict Biol. 2017;22(3):791–801.
- 41. Liu J, Li W, Zhou S, Zhang L, Wang Z, Zhang Y, et al. Functional characteristics of the brain in college students with internet gaming disorder. Brain Imaging Behav. 2016;10(1):60–7.
- 42. Wang L, Shen H, Lei Y, Zeng L-L, Cao F, Su L, et al. Altered default mode, fronto-parietal and salience networks in adolescents with Internet addiction. Addict Behav. 2017;70:1–6.
- 43. Zhang JT, Yao YW, Potenza MN, Xia CC, Lan J, Liu L, et al. Effects of craving behavioral intervention on neural substrates of cue-induced craving in Internet gaming disorder. NeuroImage Clin. 2016;12:591–9.
- 44. Dong G, Potenza MN. Risk-taking and risky decision-making in Internet gaming disorder: Implications regarding online gaming in the setting of negative consequences. J Psychiatr Res. 2016;73:1–8.
- 45. Kim JE, Son JW, Choi WH, Kim YR, Oh JH, Lee S, et al. Neural responses to various rewards and feedback in the brains of adolescent Internet addicts detected by functional magnetic resonance imaging. Psychiatry Clin Neurosci. 2014;68(6):463–70.