Addictive Behaviors 105 (2020) 106334

Contents lists available at ScienceDirect

Addictive Behaviors

journal homepage: www.elsevier.com/locate/addictbeh

Structural and functional correlates of smartphone addiction

Juliane Horvath[a], Christina Mundinger[a], Mike M. Schmitgen[a], Nadine D. Wolf[a], Fabio Sambataro[b], Dusan Hirjak[c], Katharina M. Kubera[a], Julian Koenig[d,e], Robert Christian Wolf[a,*]

[a] Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Germany
[b] Department of Neurosciences, Padua Neuroscience Center, University of Padova, Padua, Italy
[c] Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
[d] University Hospital of Child and Adolescent Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
[e] Section for Experimental Child and Adolescent Psychiatry, Clinic for Child and Adolescent Psychiatry, Centre for Psychosocial Medicine, University Hospital Heidelberg, Heidelberg, Germany

HIGHLIGHTS

- We investigate brain function and structure in persons with "smartphone addiction" (SPA).
- Persons with SPA showed lower gray matter volume in insula and temporal cortex.
- Persons with SPA showed reduced resting-state activity of the anterior cingulate cortex.
- Anterior cingulate cortex volume and activity was associated with SPA-severity.
- The data suggest aberrant neural integrity of the salience network.

ARTICLE INFO

Keywords:
Smartphone
Addiction
Gray matter volume
Brain activity
Voxel-based morphometry
Resting-state fMRI

ABSTRACT

Popularity and availability of smartphones have dramatically increased in the past years. This trend is accompanied by increased concerns regarding potentially adverse effects of excessive smartphone use, particularly with respect to physical and mental health. Recently, the term "smartphone addiction" (SPA) has been introduced to describe smartphone-related addictive behavior and associated physical and psychosocial impairment. Here, we used structural and functional magnetic resonance imaging (MRI) at 3 T to investigate gray matter volume (GMV) and intrinsic neural activity in individuals with SPA (n = 22) compared to a control group (n = 26). SPA was assessed using the Smartphone Addiction Inventory (SPAI), GMV was investigated by means of voxel-based morphometry, and intrinsic neural activity was measured by the amplitude of low frequency fluctuations (ALFF). Compared to controls, individuals with SPA showed lower GMV in left anterior insula, inferior temporal and parahippocampal cortex ($p < 0.001$, uncorrected for height, followed by correction for spatial extent). Lower intrinsic activity in SPA was found in the right anterior cingulate cortex (ACC). A significant negative association was found between SPAI and both ACC volume and activity. In addition, a significant negative association between SPAI scores and left orbitofrontal GMV was found. This study provides first evidence for distinct structural and functional correlates of behavioral addiction in individuals meeting psychometric criteria for SPA. Given their widespread use and increasing popularity, the present study questions the harmlessness of smartphones, at least in individuals that may be at increased risk for developing smartphone-related addictive behaviors.

1. Introduction

Parallels between excessive smartphone use and behavioral addiction have been increasingly emphasized by recent research (Kwon, Lee et al., 2013; Lin et al., 2016). Accompanying such observations, the term "smartphone addiction" (SPA) has been introduced to describe excessive and psychosocially dysfunctional smartphone use that closely resembles addictive behavior (Kwon, Lee et al., 2013). Based on

* Corresponding author at: Center for Psychosocial Medicine, Department of General Psychiatry, Heidelberg University, Voßstraße 4, 69115 Heidelberg, Germany.
E-mail address: christian.wolf@med.uni-heidelberg.de (R. Christian Wolf).

https://doi.org/10.1016/j.addbeh.2020.106334
Received 23 November 2019; Received in revised form 29 January 2020; Accepted 31 January 2020
Available online 01 February 2020
0306-4603/ © 2020 Elsevier Ltd. All rights reserved.

research criteria of Internet Gaming Disorder (IGD), as included in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), several specific psychometric instruments for SPA have been developed (Kwon, Kim, Cho, & Yang, 2013; Kwon, Lee et al., 2013; Lin et al., 2014). Using such instruments, the prevalence of SPA has previously been estimated with 12–28%, particularly in students (Haug et al., 2015; Lin, Pan, Lin, & Chen, 2017; Lopez-Fernandez, 2017).

Following the inclusion of IGD in DSM-5 appendix, a growing body of neuroimaging research provided evidence for distinct loci of neural dysfunction associated with this condition (Weinstein, 2017; Yao et al., 2017). Similarities to other substance-related and behavioral addictions have been highlighted, especially regarding abnormal neural integrity of lateral prefrontal, orbitofrontal, cingulate and parietal areas and insula (Kuss, Pontes, & Griffiths, 2018). Unlike IGD, SPA is not considered or suggested as distinct category in any of the current diagnostic classification systems. Accordingly, there have been few neuroimaging studies in individuals with SPA, with very few recent exceptions (Chen, Liang, Mai, Zhong, & Qu, 2016; Chun et al., 2017; Hu, Long, Lyu, Zhou, & Chen, 2017; Lee, Namkoong, Lee, Lee, & Jung, 2019).

The term “smartphone addiction” and the differentiation of IGD and SPA have been criticized in the scientific literature. On the one hand due to arguments such as the lack of severe negative consequences compared to other forms of addiction (Panova & Carbonell, 2018), on the other hand because of the smartphone being merely the medium of accessing the Internet and especially social media/messenger applications, entailing overlaps between for example IGD, “smartphone addiction”, “WhatsApp use disorder” and “Facebook use disorder” (Leung et al., 2020; Montag, Wegmann, Sariyska, Demetrovics, & Brand, 2019; Sha, Sariyska, Riedl, Lachmann, & Montag, 2019). Alternative terms such as “problematic smartphone use” and concepts have been proposed (Montag et al., 2019; Panova & Carbonell, 2018). Montag et al. (2019), for example, suggested a concept of Internet use disorder, differentiating ways the Internet is assessed, comparing a mobile and non-mobile branch. A particularly appealing example for a model integrating e.g. individual characteristics, coping styles, affective and cognitive responses leading to and maintaining Internet use disorders is the I-PACE model, as suggested by Brand and colleagues (Brand, Young, Laier, Wölfling, & Potenza, 2016). This model has been revised and extended to Internet use disorder as well as other addictive behaviors, given the conceptual overlap between entities (Brand et al., 2019). Meshi et al. proposed a model for the underlying motivation and relevant neural systems in social media use regardless of the way social media are assessed (Meshi, Tamir, & Heekeren, 2015).

Despite the controversy on the term “smartphone addiction”, as described above, it is still the prevailing term in the extant literature. Additionally, the psychometric instruments used in this study explicitly refer to the concept of “smartphone addiction”. In this regard, we aimed at achieving at least a certain level of terminological congruency and used the term “smartphone addiction” to describe excessive smartphone use with a negative impact on daily functioning. In the upcoming years, a shift away from the term “smartphone addiction” towards more appropriate terms, as discussed above, might be observed, once consensus on these taxonomical issues is reached.

Here, we employed magnetic resonance imaging (MRI) to investigate brain structure and function in individuals with SPA. Gray matter volume (GMV) was investigated by means of voxel-based morphometry (VBM), and neural activity at rest (i.e. “intrinsic” neural activity) was studied using resting-state functional MRI (rs-fMRI). We focused on the amplitude of low frequency fluctuations (ALFF), which captures the relative magnitude of blood oxygen level dependent (BOLD) signal changes of intrinsic neural activity in distinct brain regions. This approach has been shown to be suitable to identify brain regions/networks with aberrant local functioning in patients with substance-use disorders and IGD (Liu et al., 2018; Meda et al., 2015; Turner et al., 2013; Yuan et al., 2013; Zhang et al., 2016b). We expected that individuals with SPA would exhibit neural changes in regions that have previously been robustly associated with addictive behavior and social media, i.e. prefrontal cortices, the anterior cingulate cortex (ACC), the striatum and the insula (Galandra, Basso, Cappa, & Canessa, 2018; Jin et al., 2016; Luijten et al., 2014; Meshi et al., 2015; Suckling & Nestor, 2017; Volkow, Koob, & McLellan, 2016; Volkow, Wang, Fowler, & Tomasi, 2012).

2. Materials and methods

2.1. Participants

A total of n = 48 smartphone users participated in the study (details illustrating the recruitment, exclusion and inclusion process are provided as Supplementary material). We included right-handed smartphone-owners within the age range of 18–30 years. Exclusion criteria were self-reported neurological diseases, severe medical conditions and a history of current or lifetime mental disorders (substance-use disorders, psychotic and affective disorders, gambling or excessive computer gaming, and neurodevelopmental disorders). Individuals scoring > 5 on the short-form Internet Gaming Disorder Scale (IGDS-sf, Pontes, Macur, & Griffiths, 2016) were also excluded from participation. General contraindications for MRI were ruled out.

We defined two user groups based on the short version of the Smartphone Addiction Scale (SAS-SV, Haug et al., 2015), where cut-off values of > 31 for males and > 33 for females were used to define a SPA-group (n = 22), as suggested previously (Kwon, Lee et al., 2013). Participants below the aforementioned cut-offs were assigned to a control group (n = 26). Due to rigorous data quality control (see also Supplementary material), data from another three participants had to be excluded, leading to a total of n = 21 participants in the SPA group and n = 23 individuals in the control group. Demographic and psychometric data are provided in Table 1. Prior to MRI, the Smartphone Addiction Inventory (SPAI, Lin et al., 2014) was administered to all participants. The SPAI is a 26-item questionnaire, assessing symptoms such as compulsive use, tolerance and withdrawal, health management or problems in interpersonal functioning. All participants completed the Beck Depression Inventory (BDI-II) and the Barratt Impulsiveness Scale (BIS-11) (Patton, Stanford, & Barratt, 1995; Wang & Gorenstein, 2013).

The study was approved by the Ethics Committee of the Medical Faculty at Heidelberg University and carried out in compliance with the Declaration of Helsinki. All participants provided written informed consent prior to inclusion in the study. All participants received monetary compensation (EUR 30) for their participation in this study.

Table 1
Demographics and clinical scores for individuals with smartphone addiction (SPA) and controls.

	SPA (n = 22)		Controls (n = 26)		*p* value
	Mean	SD	Mean	SD	
Age (years)	22.5	3.0	23.0	3.2	0.55
Education (years)	15.7	3.3	15.5	2.5	0.84
Gender (m/f)	7/15		8/18		0.94^{+}
Duration of smartphone use (h)					
working days	3.6	1.2	2.1	1.2	< 0.001*
weekend	4.4	2.0	2.2	1.3	< 0.001*
SPAI total score	57.2	10.0	35.7	6.0	< 0.001*
IGDS total score	0.6	1.1	0.4	0.7	0.42
BDI	9.5	6.9	4.4	4.2	0.003*
BIS total score	64.3	8.9	56.5	6.1	0.001*

Data are given as means and standard deviation (SD). SPAI: Smartphone Addiction Inventory; IGDS: Internet gaming Disorders Scale; BDI: Beck Depression Inventory; BIS: Barratt Impulsiveness Scale, vers. 11; $^{+}$ indicates $\chi 2$ test; *indicates significant findings (t-tests) at $p < 0.05$.

2.2. Neuroimaging data acquisition

A 3T Magnetom TIM Trio MR Scanner (Siemens, Erlangen) equipped with a 32-channel head coil was used to collect whole-brain structural and functional scans in a darkened room. The scanner protocol included four measurements including (in this particular order) a resting-state scan, three experimental paradigms, and a structural scan. Results from the experimental paradigms will be reported elsewhere.

For acquisition of structural data, 192T1-weighted images were acquired with an MP-RAGE pulse sequence in an axial orientation with the following parameters: repetition time = 1900 ms, echo time = 2.52 ms, field of view = 350 × 263 × 350 mm, flip angle = 9°, voxel size = 1 × 1 × 1 mm, 192 slices, slice thickness = 1 mm.

For rs-fMRI, participants were instructed to keep their eyes closed, not to fall asleep, and to not think about anything in particular. During rs-fMRI, 200 whole brain echo planar imaging (EPI) volumes were recorded in a transverse (axial) orientation with the following imaging parameters: repetition time = 2000 ms, echo time = 30 ms, field of view = 192 mm, flip angle = 90°, voxel size = 3 × 3 × 3 mm, 33 slices, distance factor between slices = 1 mm.

2.3. Data analysis

2.3.1. Data preprocessing

VBM of T1-weighted structural MRI (sMRI) images was calculated using the Computational Anatomy Toolbox, CAT12 (http://dbm.neuro.uni-jena.de/cat/) together with SPM12 (http://www.fil.ion.ucl.ac.uk/spm/). VBM included segmentation of images into gray matter, white matter, and cerebrospinal fluid, normalization using DARTEL, and smoothing of GMV segments using an 8-mm full-width half-maximum (FWHM) isotropic Gaussian kernel.

Rs-fMRI images were processed using the Data Processing Assistant for rs-fMRI (DPARSF) (Chao-Gan, 2014; Chao-Gan & Yu-Feng, 2010). ALFF calculation included (1) slice timing, (2) head motion correction, (3) spatial normalization, (4) smoothing with a 4-mm FWHM isotropic Gaussian kernel, (5) regressing out nuisance covariates including mean signals from white matter and cerebrospinal fluid as well as the Friston 24-parameter model (Friston, Williams, Howard, Frackowiak, & Turner, 1996).

2.3.2. Group inference

For GMV analyses, differences between the groups were calculated using an ANCOVA model adjusted for age, gender and total intracranial volume (TIV). An absolute threshold of 0.15 was used to prevent effects occurring at tissue border regions. For ALFF analyses, an ANCOVA model adjusted for age and gender was used. Head movement parameters, expressed in terms of mean framewise displacement (FD) were included as further nuisance variable. Derivatives of the six rigid-body realignment parameters estimated during standard volume realignment were used for FD calculation (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012).

To test for associations between SPAI scores and brain structure and function, two separate regression models across all subjects were implemented in SPM12. The models included individual GMV segments and ALFF maps, respectively, covaried for age, gender and TIV (for GMV) or FD (for ALFF). Since BDI scores significantly differed between individuals with SPA and controls, we repeated all GMV and ALFF analyses using BDI scores as an additional nuisance variable.

For the aforementioned analyses, inference of meaningful local group differences was based on a significance threshold of $p < 0.001$, uncorrected for height. In addition, using Gaussian random field theory, an empirically determined cluster extent threshold k was defined based on SPM resolution element ("resel") estimates within specific contrasts. Stereotaxic coordinates of significant between-group differences are reported as peak maxima within a cluster according to the MNI template. Anatomical denominations were derived from the Neuromorphometrics atlas (http://www.neuromorphometrics.com/), as implemented in SPM12.

For completeness, we explored functional connectivity (FC) differences in individuals with SPA vs. controls using a seed-based data analysis approach (Biswal, Yetkin, Haughton, & Hyde, 1995; Buckner, Krienen, & Yeo, 2013). We used the FC algorithms, as implemented in DPARSF (please see Supplementary data for methodological details), to investigate FC between-group differences in networks connected to the right ACC and left anterior insula, respectively. In brief, right ACC and left anterior insula masks, as defined by the Neuromorphometrics atlas, were employed to compute the correlation coefficient between the average time course of the data within each mask and the time courses of each voxel across the whole-brain. Resulting individual FC maps were z-transformed and considered for further analyses. Two one-sample t-tests (adjusted for age, gender and FD) were used to calculate individual right ACC and left anterior insula FC maps. Two ANCOVA models adjusted for age, gender and FD were computed to assess between-group differences. Since we considered this type of analysis as data-driven and exploratory, we chose a more liberal significance threshold of $p < 0.005$, uncorrected for height, followed by an extent threshold of *k* voxels (see previous paragraph).

3. Results

3.1. Demographics and psychometric assessment

Individuals with SPA and controls did not significantly differ with respect to age, gender, and education years. Unsurprisingly, individuals with SPA spent a significantly higher amount of time with their smartphone, and as expected, there was a significant between-group difference with respect to SPAI total score. BDI and BIS total scores were significantly different between the groups (see Table 1 for further details). Participants' specific smartphone using activities are provided in Table 2.

3.2. Gray matter volume

Compared to controls, individuals with SPA showed lower GMV in left anterior insula (x = 27, y = 17, z = −5, Z = 3.68, k = 326), left inferior temporal cortex (x = −27, y = −9, z = −48, Z = 3.99, k = 176 voxels) and left parahippocampal cortex (PHC, x = −14, y = −36, z = −3, Z = 3.90, k = 197); regions with increased GMV in SPA compared to controls were found in the left supramarginal gyrus (x = −44, y = −75, z = 9, Z = 3.91, k = 138); see Fig. 1.

Regression analyses revealed a negative association between SPAI scores and GMV in a cluster including the middle cingulate cortex and ACC (x = 12, y = 21, z = 29, Z = 3.91, k = 187); see also Fig. 2. Additional negative relationships between SPAI and GMV were detected in left posterior orbital gyrus (OFC, x = 33, y = 29, z = −11, Z = 3.99, k = 146) and right inferior occipital gyrus (x = 44, y = −75, z = 9, Z = 3.91, k = 138).

3.3. ALFF

Compared to controls, individuals with SPA showed lower ALFF in right ACC (x = 9, y = 27, z = 27, Z = 4.72, k = 14 voxels); see Fig. 1. Regions with increased ALFF in SPA compared to controls were not found.

Regression analyses revealed a negative correlation between SPAI scores and ALFF in right ACC (x = 9, y = 27, z = 27, Z = 3.88, k = 9) and bilateral precentral gyrus (left: x = −48, y = 6, z = 27, Z = 3.62, k = 6; right: x = 42, y = 0, z = 36, Z = 4.07, k = 5); see also Fig. 2. In addition, there was a positive association between SPAI scores and a cluster including the right fusiform gyrus, extending into the PHC (x = 33, y = −21, z = −30, Z = 4.33, k = 23).

Table 2
Specific smartphone using activities.

	> Once per day	Once per day	< Once per day	Never	Statistic
SPA					
Making phone calls	6/22	9/22	7/22	0/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Sending SMS/MMS	1/22	1/22	9/22	11/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Sending email	6/22	6/22	9/22	1/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Using social networks (e.g. Facebook, Twitter)	19/22	0/22	1/22	2/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Downloads (apps, profiles, ringtones)	1/22	1/22	18/22	2/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Taking pictures	8/22	7/22	7/22	0/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Using messengers (e.g. WhatsApp)	22/22	0/22	0/22	0/22	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Using Internet	19/20	1/20	0/20	0/20	$p > 0.05 \| p > 0.05 \| p > 0.05 \| p > 0.05$[a]
Controls	–	–	–	–	–
Making phone calls	2/26	14/26	10/26	0/26	–
Sending SMS/MMS	1/26	1/26	10/26	14/26	–
Sending email	4/26	5/26	15/26	2/26	–
Using social networks (e.g. Facebook, Twitter)	16/26	4/26	2/26	4/26	–
Downloads (apps, profiles, ringtones)	0/26	0/26	19/26	7/26	–
Taking pictures	9/26	7/26	10/26	0/26	–
Using messengers (e.g. WhatsApp)	26/26	0/26	0/26	0/26	–
Using Internet	18/26	6/26	2/26	0/26	–

SMS – Short Message Service, MMS – Multimedia Message Service, SD – standard deviation. Please note that different sample sizes in SPA are due to missing data. [a] χ^2-test between SPA and controls.

3.4. Covariation for BDI

Detailed results are presented as Supplementary data. In brief, lower anterior insula and left inferior temporal cortex GMV differences in individuals with SPA were confirmed, but not in PHC and supramarginal cortex. In GMV regression analyses, additional negative associations were found in right posterior OFC, medial segment of the right superior frontal gyrus, and right supplementary motor area. The right inferior occipital gyrus results did not reach statistical significance. For ALFF analyses, between-group differences in right ACC were confirmed. Also, a significant relationship between SPAI total scores, right ACC and left precentral gyrus activity was confirmed.

3.5. Functional connectivity analyses

In one-sample t-tests positive FC of the right ACC was significant in cortical midline regions including posterior cingulate cortex and precuneus, as well as in bilateral thalamus, striatum, insula, lateral prefrontal, orbitofrontal and temporoparietal regions. A similar pattern was found for FC of the left anterior insula. In both networks, lower FC was found in regions of the inferior parietal lobule (IPL) in participants with SPA compared to controls. In particular, for right ACC FC, lower connectivity was found in left supramarginal and angular gyrus, as well as in right angular gyrus. For right anterior insula FC, lower FC was found in right supramarginal gyrus (see also Supplementary data for stereotaxic coordinates, Z-scores and figures).

4. Discussion

In this multimodal MRI study, we investigated brain volume and intrinsic neural activity in individuals with SPA. Three main findings emerged: First, individuals with SPA showed significantly lower GMV in the insula and in regions of the temporal cortex compared to controls. Second, ACC activity was significantly lower in individuals with SPA compared to controls. Third, associations between SPAI scores and GMV and ALFF, respectively, converged on the ACC.

The insula has been robustly associated with addictive behavior (e.g. Suckling & Nestor, 2017; Zhang et al., 2016a), with accumulating evidence supporting differential contributions of anterior vs. posterior regions. Specifically, the anterior insula has been associated with stimulus-related salience processing and craving, whereas the posterior insula has been attributed to interoception (Zhang et al., 2016a). It is noteworthy that previous studies in individuals with IGD have also shown decreased GMV in left insula together with increased intrinsic FC between anterior insula and ACC and other brain regions associated with craving, salience, self-monitoring and attention (Wang et al., 2015; Zhang et al., 2016a). Decreased GMV of the insula has also been reported in substance-related addiction (Suckling & Nestor, 2017).

The second important finding of the present study is the lower activity of ACC in individuals with SPA compared to controls.

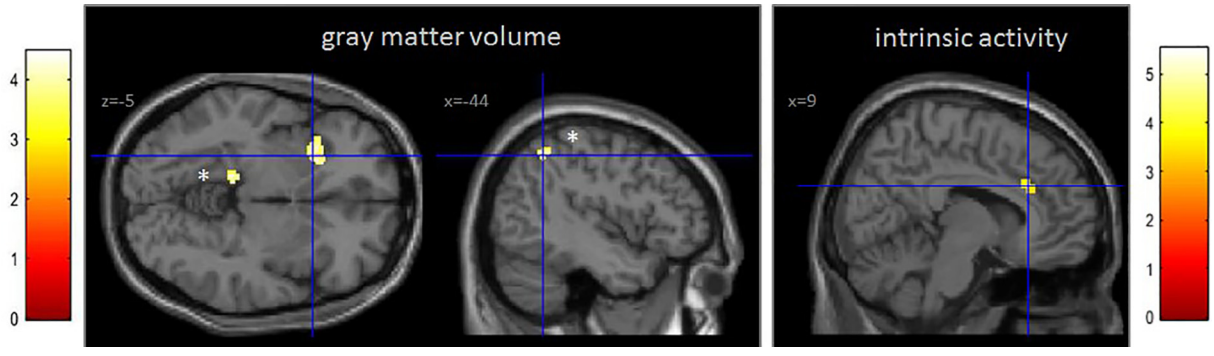


Fig. 1. Left: GMV differences in individuals with SPA compared to controls. Lower GMV is shown for the left anterior insula and left PHC. Increased GMV in SPA individuals was found in left supramarginal gyrus. * indicates that these regions did not survive covariation for BDI scores. Shown are results of 2nd level ANCOVA, $p < 0.001$ uncorrected for height, $k > 80$ voxels. Right: Intrinsic activity differences in individuals with SPA compared to controls. Lower activity in SPA individuals was found in right ACC. Shown are results of 2nd level ANCOVA, $p < 0.001$ uncorrected for height, $k > 5$ voxels. The color bars represent T-values.

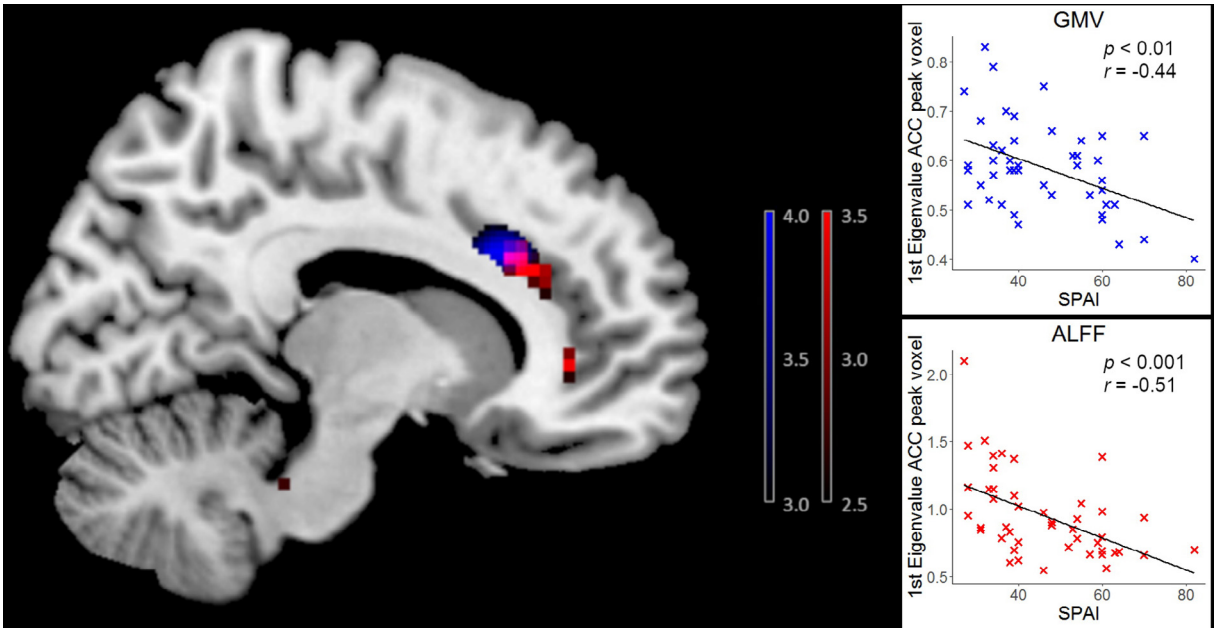


Fig. 2. Across all participants, the cingulate cortex showed a negative relationship between SPAI and GMV (blue) and ALFF (red), respectively. Shown are results of whole-brain regression analyses covaried for age, gender, TIV (VBM) or FD (ALFF), $p < 0.001$ uncorrected for height, $k > 80$ (VBM) and $k > 5$ voxels (ALFF). The color bars represent T-values (please note a different scaling, chosen for illustrative purposes). Plots illustrate relationships between SPAI total score and GMV or ALFF parameter estimates, respectively (1st ACC peak voxel eigenvariate). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Furthermore, the associations between SPAI scores and GMV and ALFF, respectively, converged on the ACC. The ACC has been identified as part of the reward system and relevant for craving and inhibitory control, showing lower activity in individuals with substance use disorders without exposure to drug stimuli, whereas activation was identified as a correlate of cue-elicited craving (Volkow et al., 2012). It is noteworthy that in studies on IGD, a reduction of GMV of ACC has also been described, with the effect being negatively correlated with cognitive control performance and impulsivity of the affected individuals (Jin et al., 2016; Lee, Namkoong, Lee, & Jung, 2018; Lee, Park, Namkoong, Kim, & Jung, 2018; Wang et al., 2015). A systematic review and meta-analysis by Yao and colleagues highlighted both structural and functional alterations of ACC in IGD (Yao et al., 2017). Moreover, a recent study investigating addictive WeChat use provided further evidence for reduced ACC volume (Montag et al., 2018). In the present multimodal study, we observed both structural and functional contributions of ACC to SPA. In accordance with other researchers (Yao et al., 2017), the findings of this study clearly show that ACC alterations are not specific to SPA (or any other behavioral addictions). Rather, given the relevance of the ACC for a plurality of dimensions and psychological processes in human behavior, altered neural integrity of this brain area rather reflects a transnosologic neural signature across several mental disorders (McTeague et al., 2017).

On a neural systems level, insula and ACC have been described as key regions of the "salience network" which mediates the interplay between executive systems and of the so-called "default mode network" (DMN) (Volkow et al., 2012). The DMN is more active during rest, e.g. with a possible role in mind-wandering and thinking about oneself, others and the personal future (Volkow et al., 2012; Zhang & Volkow, 2019). Neural changes in key nodes of the DMN, including insula and ACC, have been observed in substance-related disorders as well as behavioral addictions, possibly as a neural correlate of functions as self-awareness and emotional regulation impaired in addicted individuals (Volkow et al., 2012; Zhang & Volkow, 2019). ACC and anterior insula have been frequently referred to in the context of aberrant salience processing in addiction (Menon, 2015; Zilverstand, Huang, Alia-Klein, & Goldstein, 2018), a notion that is well-supported by findings of the present study. It is noteworthy that in exploratory FC analyses, lower functional coupling between both right ACC and left anterior insula networks converged on the IPL, which has been consistently identified as a DMN key regions. The IPL is a region involved in various processes as reflexive processes, social cognition and memory (Igelström & Graziano, 2017), yet in the context of addictive behavior, the IPL has been consistently implied in salience processing, particularly in those processes requiring directed attentional control (Zilverstand et al., 2018). This said, it is not surprising that in substance use disorders, activation in this network has been associated with craving and drug-seeking behavior (Kühn & Gallinat, 2011; Zilverstand et al., 2018). Eventually, the structural and functional changes in IPL have also been described in the context of salience processing and cue reactivity in individuals with IGD (Lee, Namkoong et al., 2018; Zhang et al., 2016c), once again emphasizing the relevance of this region for addictive behavior.

In addition to ACC and insula, several other brain regions were identified to show significant differences in individuals with SPA compared to controls, i.e. left inferior temporal cortex, left PHC, left supramarginal gyrus, left posterior OFC and right inferior occipital gyrus in terms of GMV. Regression analysis revealed associations between SPAI scores and intrinsic neural activity of bilateral precentral gyrus and a cluster including right fusiform gyrus extending into the PHC. The pattern of neural change, as observed in this study, shows a close spatial correspondence with neuroimaging data in IGD (e.g. Sun et al., 2014). For instance, alterations of volume or activity of parahippocampal and temporal gyri have been described in individuals with IGD, linked to alterations of visual and auditory processing, social cognition and memory (Aminoff, Kveraga, & Bar, 2013; Kuss et al., 2018; Squire, Stark, & Clark, 2004; Sun et al., 2014). Also, activity of left precentral gyrus has been previously associated with impaired response inhibition in individuals with IGD (Kuss et al., 2018). Alterations in OFC involved in decision making, inhibitory and behavioral control have also been found in individuals with IGD, such as reduced GMV of OFC (Lee, Park et al., 2018; Zhou et al., 2019). In line with recent findings by Zhou et al., we found the severity of the behavior to be negatively associated with OFC GMV. Based on longitudinal data, Zhou

et al. suggest that increasing engagement with the medium (here online gaming activity) leads to increased addiction symptoms and decreased OFC structural integrity. In the absence of longitudinal data, we can only speculate on similar mechanisms in SPA, implicating a loss of OFC structural integrity in a loss of regulatory control, leading to excessive use and addictive behavior. Complementing these studies, recent work by Lee and coworkers provided evidence for orbitofrontal GMV reductions in individuals with problematic smartphone use. Moreover, and in good agreement with our findings, right OFC GMV was also negatively associated with smartphone use behavior, as assessed by the Smartphone Addiction Proneness Scale (Lee et al., 2019). It is possible that the pattern of structural variation in OFC and ACC, as detected in persons with in IGD as well as in individuals with SPA, could be reflective of a neural signature that is common to several technology-related addictive behaviors (Baggio et al., 2018). Yet, neuroimaging studies directly comparing e.g. individuals with IGD and SPA are needed to derive robust conclusions.

Eventually, it is worth noting that, although study participants did not present with clinically relevant depression, BDI score nonetheless had a significant effect on the results of the analysis. This finding is in line with previous research suggesting increased subthreshold depression levels in smartphone users, particularly in those with lower educational achievement and higher SPA scores (Alhassan et al., 2018). Here, after controlling for BDI scores as a potential nuisance variable, findings regarding structural and functional changes in ACC, insula, OFC, left precentral gyrus, left inferior temporal cortex and right middle cingulate cortex remained stable. Differences in PHC, supramarginal cortex and right fusiform gyrus were not confirmed in this study when controlling for BDI scores, which might be explained by the fact that these regions are associated with neural changes in depression rather than in addictive behavior - especially regarding the PHC, that is considered relevant for memory and visual processes (Aminoff et al., 2013; Kaiser et al., 2016; Yu et al., 2018), but also right fusiform gyrus relevant for visual processes (Arnone et al., 2016; Demenescu et al., 2011; Weiner & Zilles, 2016). Thus, future neuroimaging research in individuals with SPA (as much as in other behavioral addictions, such as IGD) may want to rule out potential effects of subclinical depression.

We acknowledge potential shortcomings of this study, such as the modest sample size and the lack of a formal clinical evaluation of potentially confounding comorbid mental disorders. Though mental disorders were not reported by participants prior to study inclusion, due to the lack of structured interviews we cannot fully rule out the possibility of other mental health conditions that may have an impact on GMV or ALFF. Also, the cross-sectional design doesn't allow inference on temporal development and stability of these findings, as much as the correlations do not imply causality. It is also important to note that we investigated neural activity within an experimentally poorly controlled environment, i.e. during resting-state conditions. Neural activity patterns during active task conditions could substantially differ from resting-state brain activity patterns in individuals with SPA. Thus, future research will need to additionally consider specific activation paradigms in this population, in analogy to task-designs employed in addiction research. Eventually, the lack of whole-brain voxel-wise correction for multiple comparisons is another limitation that needs to be considered. A conservative correction (e.g. using family-wise error [FWE] correction) for multiple comparisons would have rendered all whole-brain based findings non-significant, at the same time highly increasing the probability of false negative findings. We fully acknowledge the difficulties of this trade-off. Yet, we also believe that the neurobiological plausibility our findings and the regional overlap between our study and a plethora of previous neuroimaging studies and meta-analyses in addiction research further indicate the significance of our results (e.g. McTeague et al., 2017; Wang et al., 2015; Yao et al., 2017; Zilverstand et al., 2018). This said, the findings of this study warrant replication and extension by future research.

Keeping the presented limitations in mind, the present study provides first evidence for common neural underpinning mechanisms of behavioral addiction in individuals with SPA. This study clearly needs replication as much as extension in larger cohorts, including longitudinal assessments, ecological momentary assessment and task-based functional MRI. Yet, at the same time, this study provides important data and preliminary evidence, suggesting addiction-related differences in neural processes in the context of smartphone use, particularly with respect to the salience network. Given the widespread use and increasing popularity of smartphones, the present study challenges assumptions towards the harmlessness of smartphones, at least in individuals that may be at increased risk for developing addictive behaviors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

6. Contributors

RCW, JH, CM, MMS were responsible for the study concept and design. JH, CM and MMS contributed to the acquisition of human data. CM, MMS and RCW performed the data analysis. JH and FS assisted with data analysis and interpretation of findings. JH, CM, MMS and RCW drafted the manuscript. NDW, FS, DH, KMK, and JK provided critical revision of the manuscript for important intellectual content. All authors critically reviewed content and approved the final version of the manuscript for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We thank our study participants for their time and interest in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2020.106334.

References

Alhassan, A. A., Alqadhib, E. M., Taha, N. W., Alahmari, R. A., Salam, M., & Almutairi, A. F. (2018). The relationship between addiction to smartphone usage and depression among adults: A cross sectional study. *BMC Psychiatry, 18*(1), 148.

Aminoff, E. M., Kveraga, K., & Bar, M. (2013). The role of the parahippocampal cortex in cognition. *Trends in Cognitive Sciences, 17*(8), 379–390.

Arnone, D., Job, D., Selvaraj, S., Abe, O., Amico, F., Cheng, Y., & McIntosh, A. M. (2016). Computational meta-analysis of statistical parametric maps in major depression. *Human Brain Mapping, 37*(4), 1393–1404.

Baggio, S., Starcevic, V., Studer, J., Simon, O., Gainsbury, S. M., Gmel, G., & Billieux, J. (2018). Technology-mediated addictive behaviors constitute a spectrum of related yet distinct conditions: A network perspective. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors, 32*(5), 564–572.

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic Resonance in Medicine, 34*(4), 537–541.

Brand, M., Wegmann, E., Stark, R., Müller, A., Wölfling, K., Robbins, T. W., & Potenza, M. N. (2019). The Interaction of Person-Affect-Cognition-Execution (I-PACE) model for addictive behaviors: Update, generalization to addictive behaviors beyond internet-use disorders, and specification of the process character of addictive behaviors. *Neuroscience and Biobehavioral Reviews, 104*, 1–10.

Brand, M., Young, K. S., Laier, C., Wölfling, K., & Potenza, M. N. (2016). Integrating psychological and neurobiological considerations regarding the development and maintenance of specific Internet-use disorders: An Interaction of Person-Affect-Cognition-Execution (I-PACE) model. *Neuroscience and Biobehavioral Reviews, 71*,

252–266.
Buckner, R. L., Krienen, F. M., & Yeo, B. T. T. (2013). Opportunities and limitations of intrinsic functional connectivity MRI. *Nature Neuroscience, 16*, 832–837.
Chao-Gan, Y. (2014). DPARSF. Retrieved from http://rfmri.org/DPARSF.
Chao-Gan, Y., & Yu-Feng, Z. (2010). DPARSF: A MATLAB toolbox for "pipeline" data analysis of resting-state fMRI. *Frontiers in Systems Neuroscience, 4*, 13.
Chen, J., Liang, Y., Mai, C., Zhong, X., & Qu, C. (2016). General deficit in inhibitory control of excessive smartphone users: Evidence from an event-related potential study. *Frontiers in Psychology, 7*, 511.
Chun, J.-W., Choi, J., Kim, J.-Y., Cho, H., Ahn, K.-J., Nam, J.-H., & Kim, D.-J. (2017). Altered brain activity and the effect of personality traits in excessive smartphone use during facial emotion processing. *Scientific Reports, 7*(1), 12156.
Demenescu, L. R., Renken, R., Kortekaas, R., van Tol, M.-J., Marsman, J. B. C., van Buchem, M. A., & Aleman, A. (2011). Neural correlates of perception of emotional facial expressions in out-patients with mild-to-moderate depression and anxiety. A multicenter fMRI study. *Psychological Medicine, 41*(11), 2253–2264.
Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S., & Turner, R. (1996). Movement-related effects in fMRI time-series. *Magnetic Resonance in Medicine, 35*(3), 346–355.
Galandra, C., Basso, G., Cappa, S., & Canessa, N. (2018). The alcoholic brain: Neural bases of impaired reward-based decision-making in alcohol use disorders. *Neurological Sciences, 39*(3), 423–435.
Haug, S., Castro, R. P., Kwon, M., Filler, A., Kowatsch, T., & Schaub, M. P. (2015). Smartphone use and smartphone addiction among young people in Switzerland. *Journal of Behavioral Addictions, 4*(4), 299–307.
Hu, Y., Long, X., Lyu, H., Zhou, Y., & Chen, J. (2017). Alterations in white matter integrity in young adults with smartphone dependence. *Frontiers in Human Neuroscience, 11*, 532.
Igelström, K. M., & Graziano, M. S. A. (2017). The inferior parietal lobule and temporoparietal junction: A network perspective. *Neuropsychologia, 105*, 70–83.
Jin, C., Zhang, T., Cai, C., Bi, Y., Li, Y., Yu, D., & Yuan, K. (2016). Abnormal prefrontal cortex resting state functional connectivity and severity of internet gaming disorder. *Brain Imaging and Behavior, 10*(3), 719–729.
Kaiser, R. H., Whitfield-Gabrieli, S., Dillon, D. G., Goer, F., Beltzer, M., Minkel, J., & Pizzagalli, D. A. (2016). Dynamic resting-state functional connectivity in major depression. *Neuropsychopharmacology, 41*(7), 1822–1830.
Kühn, S., & Gallinat, J. (2011). Common biology of craving across legal and illegal drugs – A quantitative meta-analysis of cue-reactivity brain response. *The European Journal of Neuroscience, 33*(7), 1318–1326.
Kuss, D. J., Pontes, H. M., & Griffiths, M. D. (2018). Neurobiological correlates in internet gaming disorder: A systematic literature review. *Frontiers in Psychiatry, 9*, 166.
Kwon, M., Kim, D.-J., Cho, H., & Yang, S. (2013). The smartphone addiction scale: Development and validation of a short version for adolescents. *PloS One, 8*(12), e83558.
Kwon, M., Lee, J.-Y., Won, W.-Y., Park, J.-W., Min, J.-A., Hahn, C., & Kim, D.-J. (2013). Development and validation of a smartphone addiction scale (SAS). *PloS One, 8*(2), e56936.
Lee, D., Namkoong, K., Lee, J., & Jung, Y.-C. (2018). Abnormal gray matter volume and impulsivity in young adults with Internet gaming disorder. *Addiction Biology, 23*(5), 1160–1167.
Lee, D., Namkoong, K., Lee, J., Lee, B. O., & Jung, Y.-C. (2019). Lateral orbitofrontal gray matter abnormalities in subjects with problematic smartphone use. *Journal of Behavioral Addictions, 8*(3), 404–411.
Lee, D., Park, J., Namkoong, K., Kim, I. Y., & Jung, Y.-C. (2018). Gray matter differences in the anterior cingulate and orbitofrontal cortex of young adults with Internet gaming disorder: Surface-based morphometry. *Journal of Behavioral Addictions, 7*(1), 21–30.
Leung, H., Pakpour, A. H., Strong, C., Lin, Y.-C., Tsai, M.-C., Griffiths, M. D., & Chen, I.-H. (2020). Measurement invariance across young adults from Hong Kong and Taiwan among three internet-related addiction scales: Bergen Social Media Addiction Scale (BSMAS), Smartphone Application-Based Addiction Scale (SABAS), and Internet Gaming Disorder Scale-Short Form (IGDS-SF9) (Study Part A). *Addictive Behaviors, 101*, 105969.
Lin, Y.-H., Chang, L.-R., Lee, Y.-H., Tseng, H.-W., Kuo, T. B. J., & Chen, S.-H. (2014). Development and validation of the Smartphone Addiction Inventory (SPAI). *PloS One, 9*(6), e98312.
Lin, Y.-H., Chiang, C.-L., Lin, P.-H., Chang, L.-R., Ko, C.-H., Lee, Y.-H., & Lin, S.-H. (2016). Proposed diagnostic criteria for smartphone addiction. *PloS One, 11*(11), e0163010.
Lin, Y.-H., Pan, Y.-C., Lin, S.-H., & Chen, S.-H. (2017). Development of short-form and screening cutoff point of the Smartphone Addiction Inventory (SPAI-SF). *International Journal of Methods in Psychiatric Research, 26*(2).
Liu, R., Liu, B.-X., Ma, M., Kong, D., Li, G., Yang, J., & Dong, Y. (2018). Aberrant prefrontal-parietal-cerebellar circuits in alcohol dependence. *Neuropsychiatric Disease and Treatment, 14*, 3143–3150.
Lopez-Fernandez, O. (2017). Short version of the Smartphone Addiction Scale adapted to Spanish and French: Towards a cross-cultural research in problematic mobile phone use. *Addictive Behaviors, 64*, 275–280.
Luijten, M., Machielsen, M. W. J., Veltman, D. J., Hester, R., de Haan, L., & Franken, I. H. A. (2014). Systematic review of ERP and fMRI studies investigating inhibitory control and error processing in people with substance dependence and behavioural addictions. *Journal of Psychiatry & Neuroscience : JPN, 39*(3), 149–169.
McTeague, L. M., Huemer, J., Carreon, D. M., Jiang, Y., Eickhoff, S. B., & Etkin, A. (2017). Identification of common neural circuit disruptions in cognitive control across psychiatric disorders. *The American Journal of Psychiatry, 174*(7), 676–685.
Meda, S. A., Wang, Z., Ivleva, E. I., Poudyal, G., Keshavan, M. S., Tamminga, C. A., & Pearlson, G. D. (2015). Frequency-specific neural signatures of spontaneous low-frequency resting state fluctuations in psychosis: Evidence From Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) Consortium. *Schizophrenia Bulletin, 41*(6), 1336–1348.
Menon, V. (2015). Salience network. In A. W. Toga (Ed.). *Brain mapping. An encyclopedic reference* (pp. 597–611). London, UK: Academic Press.
Meshi, D., Tamir, D. I., & Heekeren, H. R. (2015). The emerging neuroscience of social media. *Trends in Cognitive Sciences, 19*(12), 771–782.
Montag, C., Wegmann, E., Sariyska, R., Demetrovics, Z., & Brand, M. (2019). How to overcome taxonomical problems in the study of Internet use disorders and what to do with "smartphone addiction"? *Journal of Behavioral Addictions,* 1–7.
Montag, C., Zhao, Z., Sindermann, C., Xu, L., Fu, M., Li, J., & Becker, B. (2018). Internet communication disorder and the structure of the human brain: Initial insights on WeChat addiction. *Scientific Reports, 8*(1), 2155.
Panova, T., & Carbonell, X. (2018). Is smartphone addiction really an addiction? *Journal of Behavioral Addictions, 7*(2), 252–259.
Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology, 51*(6), 768–774.
Pontes, H. M., Macur, M., & Griffiths, M. D. (2016). Internet gaming disorder among Slovenian primary schoolchildren: findings from a nationally representative sample of adolescents. *Journal of Behavioral Addictions, 5*(2), 304–310.
Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage, 59*(3), 2142–2154.
Sha, P., Sariyska, R., Riedl, R., Lachmann, B., & Montag, C. (2019). Linking internet communication and smartphone use disorder by taking a closer look at the Facebook and WhatsApp applications. *Addictive Behaviors Reports, 9*, 100148.
Squire, L. R., Stark, C. E. L., & Clark, R. E. (2004). The medial temporal lobe. *Annual Review of Neuroscience, 27*, 279–306.
Suckling, J., & Nestor, L. J. (2017). The neurobiology of addiction: The perspective from magnetic resonance imaging present and future. *Addiction (Abingdon, England), 112*(2), 360–369.
Sun, Y., Sun, J., Zhou, Y., Ding, W., Chen, X., Zhuang, Z., & Du, Y. (2014). Assessment of in vivo microstructure alterations in gray matter using DKI in Internet gaming addiction. *Behavioral and Brain Functions: BBF, 10*, 37.
Turner, J. A., Damaraju, E., van Erp, T. G. M., Mathalon, D. H., Ford, J. M., Voyvodic, J., & Calhoun, V. D. (2013). A multi-site resting state fMRI study on the amplitude of low frequency fluctuations in schizophrenia. *Frontiers in Neuroscience, 7*, 137.
Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *The New England Journal of Medicine, 374*(4), 363–371.
Volkow, N. D., Wang, G.-J., Fowler, J. S., & Tomasi, D. (2012). Addiction circuitry in the human brain. *Annual Review of Pharmacology and Toxicology, 52*(1), 321–336.
Wang, H., Jin, C., Yuan, K., Shakir, T. M., Mao, C., Niu, X., & Zhang, M. (2015). The alteration of gray matter volume and cognitive control in adolescents with internet gaming disorder. *Frontiers in Behavioral Neuroscience, 9*, 64.
Wang, Y.-P., & Gorenstein, C. (2013). Psychometric properties of the Beck Depression Inventory-II: A comprehensive review. *Revista brasileira de psiquiatria (Sao Paulo, Brazil : 1999), 35*(4), 416–431.
Weiner, K. S., & Zilles, K. (2016). The anatomical and functional specialization of the fusiform gyrus. *Neuropsychologia, 83*, 48–62.
Weinstein, A. M. (2017). An update overview on brain imaging studies of internet gaming disorder. *Frontiers in Psychiatry, 8*, 185.
Yao, Y.-W., Liu, L., Ma, S.-S., Shi, X.-H., Zhou, N., Zhang, J.-T., & Potenza, M. N. (2017). Functional and structural neural alterations in internet gaming disorder: a systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews, 83*, 313–324.
Yu, S., Shen, Z., Lai, R., Feng, F., Guo, B., Wang, Z., & Gong, L. (2018). The orbitofrontal cortex gray matter is associated with the interaction between insomnia and depression. *Frontiers in Psychiatry, 9*, 651.
Yuan, K., Jin, C., Cheng, P., Yang, X., Dong, T., Bi, Y., & Tian, J. (2013). Amplitude of low frequency fluctuation abnormalities in adolescents with online gaming addiction. *PloS One, 8*(11), e78708.
Zhang, J.-T., Yao, Y.-W., Li, C.-S. R., Zang, Y.-F., Shen, Z.-J., Liu, L., & Fang, X.-Y. (2016a). Altered resting-state functional connectivity of the insula in young adults with Internet gaming disorder. *Addiction Biology, 21*(3), 743–751.
Zhang, S., Li, X., Lv, J., Jiang, X., Guo, L., & Liu, T. (2016b). Characterizing and differentiating task-based and resting state fMRI signals via two-stage sparse representations. *Brain Imaging and Behavior, 10*(1), 21–32.
Zhang, Y., Lin, X., Zhou, H., Xu, J., Du, X., & Dong, G. (2016c). Brain activity toward gaming-related cues in internet gaming disorder during an addiction stroop task. *Frontiers in Psychology, 7*, 714.
Zhang, R., & Volkow, N. D. (2019). Brain default-mode network dysfunction in addiction. *NeuroImage, 200*, 313–331.
Zhou, F., Montag, C., Sariyska, R., Lachmann, B., Reuter, M., Weber, B., & Becker, B. (2019). Orbitofrontal gray matter deficits as marker of Internet gaming disorder: Converging evidence from a cross-sectional and prospective longitudinal design. *Addiction Biology, 24*(1), 100–109.
Zilverstand, A., Huang, A. S., Alia-Klein, N., & Goldstein, R. Z. (2018). Neuroimaging impaired response inhibition and salience attribution in human drug addiction: A systematic review. *Neuron, 98*(5), 886–903.