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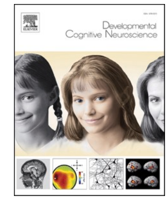

Neural activations to loss anticipation mediates the association between difficulties in emotion regulation and screen media activities among early adolescent youth: A moderating role for depression

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A R T I C L E I N F O

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A B S T R A C T

Background: Screen media activities (SMAs; e.g., watching videos, playing videogames) have become increasingly prevalent among youth as ways to alleviate or escape from negative emotional states. However, neural mechanisms underlying these processes in youth are incompletely understood.
Method: Seventy-nine youth aged 11–15 years completed a monetary incentive delay task during fMRI scanning. Neural correlates of reward/loss processing and their associations with SMAs were explored. Next, brain activations during reward/loss processing in regions implicated in the processing of emotions were examined as potential mediating factors between difficulties in emotion regulation (DER) and engagement in SMAs. Finally, a moderated mediation model tested the effects of depressive symptoms in such relationships.
Result: The emotional components associated with SMAs in reward/loss processing included activations in the left anterior insula (AI) and right dorsolateral prefrontal cortex (DLPFC) during anticipation of working to avoid losses. Activations in both the AI and DLPFC mediated the relationship between DER and SMAs. Moreover, depressive symptoms moderated the relationship between AI activation in response to loss anticipation and SMAs.
Conclusion: The current findings suggest that DER link to SMAs through loss-related brain activations implicated in the processing of emotions and motivational avoidance, particularly in youth with greater levels of depressive symptoms. The findings suggest the importance of enhancing emotion-regulation tendencies/abilities in youth and, in particular, their regulatory responses to negative emotional situations in order to guide moderate engagement in SMAs.

1. Introduction

Screen media activities (SMAs) are central to people's daily lives (Anderson and Subrahmanyam, 2017; Carter et al., 2016; Hutton et al., 2020). In particular, since the emergence of COVID-19 pandemic in early 2020, SMAs have taken increasingly prominent roles, with some people, including early adolescent youth, using SMAs to relieve anxiety and nervousness related to fear of infection and social isolation (Collaborators, 2021; Francisco et al., 2020; Stieger and Swami, 2021). Youth may be particularly susceptible to SMAs given their developing control systems and greater inclinations to embrace new technologies (Jeong et al., 2020). A recent survey by the China Internet Network Information Center (CNNIC) showed that more than 60% of Chinese adolescents frequently engaged in SMAs like playing videogames,

Abbreviations: SMAs, Screen Media Activities; DERS, Difficulties in Emotion Regulation Scale; AI, Anterior Insula; DLPFC, Dorsolateral Prefrontal Cortex; SDS, Self-Rating Depression Scale.

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watching short videos, engaging in online social activities and listening to music, and more than one-third of adolescents who used the internet have increased their online entertainment time to alleviate psychological concerns associated with the pandemic (CNNIC, 2021). Moderate engagement in SMAs could help adolescents reduce unpleasant feelings in real life by providing online social support and satisfying entertainment needs (Anderson and Subrahmanyam, 2017; Marciano et al., 2021). However, excessive SMAs may occupy a majority of leisure time and compromise cognitive development of adolescents and have been demonstrated to be closely related to present or future physical and mental health problems (Hutton et al., 2020; Nagata et al., 2022). Therefore, it is important to examine antecedents of SMAs in youths in order to provide specific guidance for future preventative and intervention initiatives that attempt to reduce the incidence of excessive SMAs.

1.1. Difficulties in emotional regulation and SMAs engagement

Adolescents often experience stress due to rapid physical, psychological, and interpersonal changes, which may lead to increased risk behaviors (Garakani et al., 2021; Li et al., 2021). Emotional regulation tendencies during this period are crucial for helping adolescents cope with stress and minimize risk behaviors (Beauchaine, 2015; Breaux et al., 2021). Better emotional regulation strategies have been linked to positive and healthy mental states in adolescents (Houck et al., 2016; Te Brinke et al., 2021). In contrast, adolescents with poor emotional regulation are more likely to adopt maladaptive coping strategies (such as avoidance and withdrawal), which could result in the development of various addictive behaviors (Hudak et al., 2022; Vintro-Alcaraz et al., 2022; von Deneen et al., 2022) and emotional disorders (Miklowitz et al., 2022; Price et al., 2022). Although SMAs do not involve substance intake, they may influence dopaminergic and other systems, and may help adolescents relieve stress and manage negative emotions in the short term (Dong et al., 2021; Laier and Brand, 2018). However, prolonged or excessive engagement in SMAs could be a maladaptive way to cope with emotional difficulties and stressful life events (Blasi et al., 2019; Brand et al., 2019; Zhang et al., 2020). Therefore, we hypothesized that difficulties in emotional regulation (DER) in early adolescent youth would positively predict their SMAs (Hypothesis 1).

1.2. The mediating roles of neural responses to reward/loss processing

In addition to the contribution of youth DER to the development of behavioral problems, various theories and empirical evidence highlight a role for neurodevelopment (Palmer et al., 2022; Vijayakumar et al., 2018). Reward/loss processing is considered a crucial indicator of adolescent neurodevelopment (Armbruster-Genc et al., 2022) and has been linked to adolescents' risk behaviors (Eckstrand et al., 2019; Ivanov et al., 2021). However, the relationship between SMAs, a potentially risky behavior in children and adolescents, and the neural mechanisms underlying reward/loss processing remains unclear. Given that the reward/loss stimuli may have either positive or negative emotional valences (Verdejo-Garcia et al., 2015), and reward/loss processing share overlapping neural mechanisms with emotional processing (Janak and Tye, 2015; Murray, 2007), we hypothesized that the neural activations during reward/loss processing would implicate brain areas related to emotional processing and be associated with SMAs.

Dysfunctions in emotional neurocircuitry (Elsayed et al., 2021; Gupta and Kujawa, 2022) may increase adolescent vulnerability to risk behaviors including SMAs (Brumback et al., 2016). Therefore, it is important to explore whether neural activations associated with emotion processing during reward/loss processing underlie the association between DER and SMAs. We hypothesized that neural responses during reward/loss processing, specifically neural activations implicated in emotional processing associated with SMAs, would serve as one potential linking mechanism explaining how DER would relate to more frequent engagement in SMAs in youth (Hypothesis 2).

1.3. A moderating role for depression

Excessive SMAs may be more likely to develop in people with depressed states (Kiraly et al., 2020), possibly as SMAs could potentially be used as a maladaptive coping way to relieve depressive symptoms or negative emotional stress (Wegmann and Brand, 2022). Studies have suggested that compared to adolescents with low levels of depressive symptoms, DER may be more likely to prevent adolescents with high levels of depressive symptoms from immediately disengaging from negative emotions in response to negative stimuli (Lazarov et al., 2018; Li et al., 2022). Difficulties disengaging could further increase adolescents' motivations to engage in SMAs (Kardefelt-Winther, 2014), and could also lead to higher risk for maladaptively using SMAs (Teng et al., 2021). In this case, high levels of depressive symptoms may strengthen the relationship between DER and SMAs among adolescents with high rather than low levels of depressive symptoms.

In addition, specific neural correlates of reward/loss processing have been linked to risk behaviors (e.g., substance intake) among individuals with high rather than low levels of depressive symptoms (Baskin-Sommers and Foti, 2015; Muench et al., 2018). This may occur as people with high levels of depressive symptoms may have impaired motivation and emotion systems involved in reward/loss processes, and thus may increase their motivation to consume substances to alleviate/avoid negative emotions (Koob and Dantzer, 2020; Sullivan, 2018). Similar to substance intake, engaging in SMAs may also help adolescents alleviate/avoid depressive symptoms and negative emotional stress (Kardefelt-Winther, 2014; Király et al., 2020). However, how precisely relationships between adolescents' reward/loss neural responsiveness and SMAs may be influenced by depressive symptoms remains incompletely understood. Thus, the present study explored whether there were moderating effects of depressive symptoms on the relationship between reward/loss neural responsiveness and SMAs.

1.4. The present study

Despite studies that have examined direct associations between DER and SMAs, the underlying mechanisms for the associations remain unclear (Blasi et al., 2019; Brand et al., 2019; Zhang et al., 2020). To fill this gap, the present study aimed to explore in early adolescents (a) neural activations associated with positive/negative events in relation to SMAs, (b) whether these neural activations could serve as linking mechanisms to explain how DER related to SMAs, and (c) whether depressive symptoms influenced associations among DER, neural activations associated with positive/negative events, and SMAs.

The monetary incentive delay (MID) task is a widely used experimental paradigm that can measure neural activations in response to positive events (rewards) or negative events (losses) among youth (Ivanov et al., 2021; Willinger et al., 2021). Thus, the MID task was used in this study to explore neural activations of reward/loss processing associated with SMAs. Specifically, SMAs-related neural activations in brain regions implicated in both reward/loss processing and emotional regulation, such as the dorsal striatum (DS), ventral striatum (VS), insula, and dorsolateral prefrontal cortex (DLPFC) were extracted (Chaarani et al., 2021; Goncalves et al., 2021; Yee et al., 2021).

2. Methods and materials

2.1. Participants

Data of the present study derived from a longitudinal study on child brain development and mental health. A total of 112 adolescents (45 females) between 10.92 and 15 years old (*M*age = 13.07 ± 0.73 years) were recruited through posted advertisements. Exclusion criteria included any neurological, psychiatric or psychotic disorders, which were confirmed by participants' parents. All participants and their parents provided written informed assent/consent prior to enrollment.

Of these participants, 18 were excluded due to the absence of imaging data, 13 were excluded due to the absence of SMAs information, and 2 were excluded due to head movement > 0.2 mm or 0.2°. Finally, seventy-nine youth (31 females; Range $_{age}$ = 10.92–15 years, M_{age} = 13.11 ± 0.76 years) were included in subsequent analyses.

The study protocol was approved by the Institutional Review Board of the State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University. Imaging data collection was performed using a 64-channel head and neck coil on a Siemens Prisma 3 T MRI scanner.

2.2. Screen media activities

SMAs were assessed using the adapted self-reported Screen Time Survey from the Adolescent Brain Cognitive Development (ABCD) Study (Nagata et al., 2021; Paulus et al., 2019). The survey inquired about SMAs during a typical weekday and a weekend day, respectively, not including time spent on school-related work. Two original items were removed because they involve the content of restricted movies and games, which is not eligible with current Chinese policies. The final SMAs assessment included six different activities: Watching television (TV) shows or movies, watching videos (e.g., Tiktok), playing video games, texting, video chatting (e.g., Wechat, QQ), and visiting social networking (e.g., microblog). A sample item was "On a typical weekday/weekend day, how many hours do you watch TV shows or movies." Items were rated on a 7-point scale (none, < 30 min, 30 min, 1 h, 2 h, 3 h, and > 4 h). A total score was calculated based on the formula: (the sum of six SMAs on weekdays × 5) + (the sum of six SMA modes on weekend days × 2). Cronbach' α in this study was 0.833.

2.3. DER and depressive symptoms

DER was assessed using the 36-item Difficulties in Emotion Regulation Scale (11 reverse scoring items; e.g., "I am clear about my feelings"), which includes nonacceptance of emotional responses (Nonacceptance, 6 items; e.g., "When I'm upset, I become angry with myself for feeling that way."), difficulties engaging in goal-directed behaviors (Goals, 5 items; e.g., "When I'm upset, I have difficulty getting work done."), impulse-control difficulties (Impulse, 6 items; e.g., "I experience my emotions as overwhelming and out of control."), lack of emotional awareness (Awareness, 6 items; e.g., "I pay attention to how I am feeling." (reverse scored), limited access to emotion-regulation strategies (Strategies; 8 items, e.g., "When I'm upset, I believe that I will remain that way for a long time."), and lack of emotional clarity (Clarity, 5 items; e.g., "I am clear about my feeling." (reverse scored) (Gratz and Roemer, 2004). Items were rated on a 5-point Likert scale (1 = *almost never* to 5 = *almost always*). Higher scores reflect more emotional regulation difficulties. Cronbach' α of the whole scale was 0.922.

Depressive symptoms were measured using the 20-item Self-Rating Depression Scale (SDS) (Zung, 1967). The SDS assesses subjective feelings of depressive symptoms (e.g., "I feel down-hearted and blue.") during the prior week. Items were rated using a 4-point Likert-like scale (from 1 = *none or a little of the time* to 4 = *most or all of the time*), with higher scores indicating more depressive symptoms. The SDS has been found to be a reliable and valid assessment tool in prior studies with Chinese adolescents (Lu et al., 2022). Cronbach's αwas 0.795.

2.4. Reward/loss processing

A modified version of the MID task from the ABCD Study was used to measure brain activations during anticipation and receipt of reward, loss, and no reward/loss (Casey et al., 2018). In the MID task, the cue picture was presented first for 2000 ms, indicating the valence (win/-lose/no incentive) and the stake amount (CNY 0/1/25). After the cue presentation, the screen presented a fixation "+ " (1500–4000 ms) as the jittered anticipatory delay. Then, when a black figure (i.e., the response target) consistent with the previous cue appeared, participants were required to press a button as quickly as they could in order to obtain a reward or avoid a loss. The presentation time of the response target was regulated by an adaptive algorithm to maintain a success rate of 60%. The result of a given trial (i.e., win CNY 1/25, not win CNY 1/25, lose CNY 1/25, not lose CNY 1/25, neither win nor lose + CNY 0/−0) was presented on the screen after the response was completed, regardless of whether the participant pressed the button or not. The process of a trial is illustrated in Fig. 1.

Before conducting the task, participants were instructed to complete a practice task in order to obtain their initial reaction time (RT). During the formal task, participants were required to complete a total of two runs, each containing 50 trials and lasting for approximately 10.6 min. In the present experiment, we focused on the following contrasts: (a) anticipation of reward (+ CNY 1/25) vs no incentive (± CNY 0), (b) anticipation of loss (- CNY1/25) vs. no incentive (± CNY 0), (c) receipt of reward (+ CNY 1/25) vs. no reward (+ CNY0), and (d) receipt of loss (- CNY 1/25) vs. avoidance of loss (- CNY 0).

After fMRI scanning, participants were asked to complete a MID post-imaging questionnaire. This questionnaire asked participants to rate how they felt when viewing different cues (including how excited/nervous they felt when they saw the following situations (win 1/25, loss 1/25) and how hard they tried in the following situations (win 1/25) during MID task performance to assess feelings and motivations regarding the values of wins and losses. Monetary rewards earned during task performance were provided to participants.

2.5. Data acquisition and preprocessing

Imaging data were acquired using a 3 T Siemens Prisma MRI scanner with a 64-channel head coil, at the State Key Laboratory of Cognitive Neuroscience and Learning of Bejing Normal University. Functional data during the MID task were acquired using T1 * -weighted echo-planar imaging sequence with multi-band acceleration factor of 6 and parallel imaging factor (iPAT) of 10, TR = 800 ms, TE = 30 ms, flip angle = 52 degrees, field of view (FOV) = 216 × 216 mm, in plane resolution of 2 × 2 mm 30 degrees of the anterior commissure-posterior commissure line to reduce the frontal signal dropout, slice thickness of 2.4 mm, 60 slices. For each functional run, 400 scans were acquired.

Gradient echo field maps were acquired for each participant, with the following imaging parameters: TR = 600 ms, TE 1 = 4.92 ms, TE 2 = 7.38 ms, flip angle = 60 degrees, FOV = 212 × 212 mm, in plane resolution of 2 × 2 mm, 60 slices with slice thickness of 2.4 mm. In addition, for each participant, high-resolution T1 weighted structural images were acquired using a magnetization prepared rapid gradient echo (MPRAGE) pulse sequence, 176 slices, TR = 2500 ms, TE = 2.45 ms, flip angle = 8 degrees, FOV = 256 × 256 mm, resolution = 1 × 1 × 1 mm.

Results included in this manuscript come from preprocessing performed using *fMRIPrep* 20.2.0 ((Esteban et al., 2019); RRID: SCR_016216), which is based on *Nipype* 1.5.1 ((Gorgolewski et al., 2011); RRID:SCR_002502). Details regarding functional and anatomical data preprocessing are shown in Supplementary methods. Participants with a mean head movement > 2 mm or 2° were removed.

2.6. First-level analyses

After preprocessing, data were analyzed with Statistical Parametric Mapping (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). We examined event-related blood oxygen level-dependent signals in a model with regressors of interest: anticipation ("small/large reward," "small/large loss," and "no reward/loss") and feedback ("small/large reward," "no small/large reward," "small/large loss," and "no small/large loss"). For each participant, we estimated a general

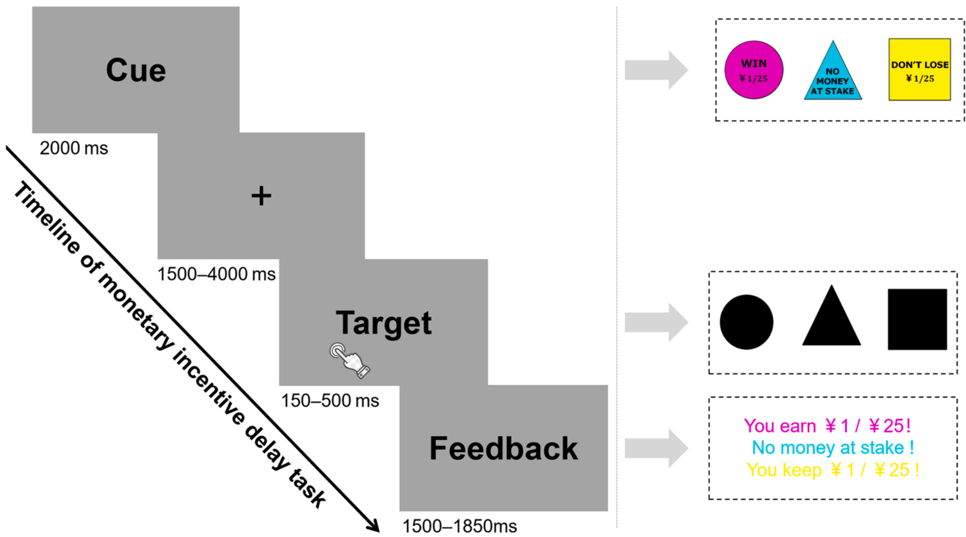

Fig. 1. The timeline of one trial in the monetary incentive delay (MID) task. In the MID task, the cue picture was first presented for 2000 ms, indicating the valence (win/lose/no incentive) and the stake amount (CNY 0/1/25). After the cue presentation, the screen presented a fixation "+ " (1500–4000 ms) as the jittered anticipatory delay. Then, when a black figure (i.e., the response target) consistent with the previous cue appeared, participants were instructed to press a button as quickly as they could in order to try to obtain a reward or avoid a loss.

linear model (GLM) with the onsets of "anticipation" and "feedback" for each trial convolved with a canonical hemodynamic response function entered as regressors in the model (Friston et al., 1995). Realignment parameters in all 6 dimensions were also entered in the model as nuisance covariates, and a high-pass filter with a cut-off of 128 s was applied to improve the signal-to-noise ratio.

2.7. Second-level analyses

In group-level or random-effects analyses, we performed one-sample *t* tests of the whole brain on each of the four contrasts (i.e., anticipation of reward vs. no incentive, anticipation of loss vs. no incentive, receipt of reward vs. no reward, and receipt of loss vs. avoidance of loss). In addition, to investigate relationships between reward/loss processing and SMAs, we conducted whole-brain linear regressions with SMAs scores as the regressor. We performed whole-brain linear regression analyses on each of the 4 contrasts against SMAs with age, gender, monetary awards, and the post-questionnaire of the MID scores as covariates and reported the findings at voxel $p < 0.001$ uncorrected and cluster-level $p < 0.05$ FWE-corrected. The cluster thresholds varied across the task contrasts (contrast of anticipation of reward vs. no incentive: 79; contrast of anticipation of loss vs. no incentive: 138). In addition, the brain regions associated with SMAs in a given contrast (e.g., anticipation of loss vs. no incentive) were used as regions of interest (ROIs). Then the contrast β values of these ROIs were extracted to perform the mediation and moderated mediation analyses.

2.8. Statistical analyses

Mediating and moderating analyses were conducted using Mplus 8.3. First, the mediating model examined the mediating role of brain activations during MID task performance through which DER relate to SMAs. The indirect effect was considered significant if its 95% bootstrapped confidence interval from 5000 bootstrap samples did not include zero (Muthén and Asparouhov, 2015). Second, the moderated mediation model was conducted to examine the potential moderating role of depression. The significant moderating effect of depression would be illustrated by examining the conditional effects of targeted associations (e.g., DER → SMAs) at one standard deviation (*SD*) above and below the mean of the SDS. The MID post-imaging questionnaire scores and monetary rewards were considered to be particularly relevant to neural activations during the MID task. However, comparisons with and without MID post-imaging questionnaire scores and monetary rewards as covariates did not detect significant changes in the main results of the mediation and moderated mediation models (see Supplementary Materials). Given the potentially limited power of models, the post-imaging questionnaire scores and monetary rewards were not included in the subsequent mediation and moderated mediation models, and only age and gender were included as covariates.

3. Results

3.1. Behavioral results

The mean accuracy rate for the MID task was 57.9%. One-way ANOVAs were conducted on participates' reaction times (RTs) and accuracy rates under different MID cues (i.e., Win, Loss, and Neutral). The accuracy rates differed significantly across the three conditions ($F_{(2,\ 78)} = 39.060$, $p_{bonf} < 0.001$, $\eta^2 = 0.334$). Post-hoc analyses showed that the accuracy rate in the win condition was significantly higher than those in the loss ($t_{78} = 2.998$, $p_{bonf} = 0.011$, d = 0.337) and neutral conditions ($t_{78} = 7.531$, $p_{bonf} < 0.001$, d = 0.847). The accuracy rate in the loss condition was also significantly higher than that in the neutral condition ($t_{78} = 5.805$, $p_{bonf} < 0.001$, d = 0.653) (Fig. 2). There were no significant differences in the RTs across the three conditions ($F_{(2,78)} = 2.459$, $p_{bonf} = 0.108$, $\eta^2 = 0.031$), and we have provided additional comparison results for RTs relating to wins and losses in the supplementary material.

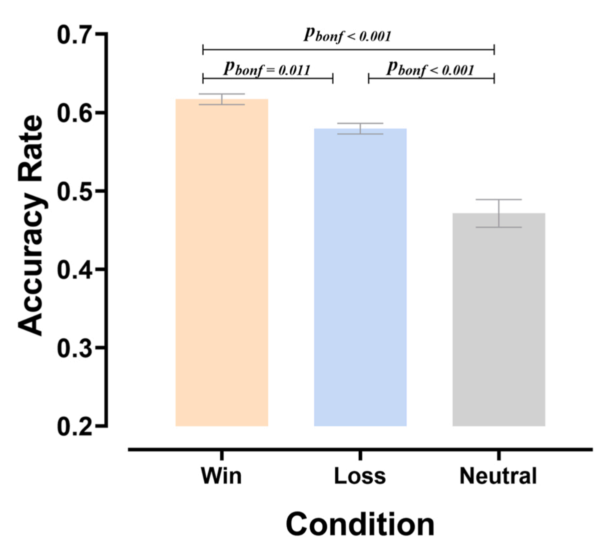

Fig. 2. The accuracy rates under different conditions.

3.2. Regional activations during the MID task in relation to SMAs

The brain activations of anticipation of reward vs. no incentive, anticipation of loss vs. no incentive, receipt of reward vs. no reward, and receipt of loss vs. avoidance of loss are presented in the Supplementary materials. For the contrast anticipation of win > no incentive, the activations in the left calcarine cortex and right lingual gyrus correlated positively with SMAs (Fig. 3A and Table 1). For the contrast anticipation of loss > no incentive, the activations in the left anterior insula (AI), left calcarine cortex, right DLPFC, and right lingual gyrus correlated positively with SMAs (Fig. 3B and Table1). No significant correlations emerged between activations in brain regions and SMAs for other contrasts.

3.3. The mediating model

First, there was a significant positive correlation between DER and SMAs in adolescents ($r = 0.292, p = 0.009$). We proceeded to examining potential mediating roles of emotional components (including the AI and DLPFC, which are considered important nodes in an emotion neurocircuit; Kebets et al., 2021), which were associated with SMAs in reward/loss processing (Fig. 4). The model fit the data well: $\chi^2(2) = 0.182, p = 0.928$, CFI = 1.000, RMSEA = 0.000, 90% CI, [0.000, 0.091], SRMR = 0.011. Bootstrapping results supported the proposed mediating effects: DER → AI/DLPFC → SMAs ($b_{AI} = 0.087$, $\beta_{AI} = 0.115$, 95% CI = [0.018, 0.218]; $b_{DLPFC} = 0.048$, $\beta_{DLPFC} = 0.063$, 95% CI = [0.007, 0.131]). The direct effect and indirect effects are presented in Table 2.

Since the data were cross-sectional, we also calculated possible alternate mediating pathways (neural activation to reward/loss → DER → SMAs), but no mediating effect was found. These results are presented in the Supplementary Material.

3.4. The moderated mediation model

Further, we explored the moderating effects of depressive symptoms in the identified associations. The moderated mediation model fit the data well: $\chi^2(1) = 0.011, p = 0.917$, CFI = 1.000, RMSEA = 0.000, 90% CI, [0.000–0.113], SRMR = 0.003. In the full model, the moderating effect of SDS was not significant in both the DER → SMAs and the neural activations → SMAs pathways, but SDS did demonstrate a trend level of a moderating effect in the relationship between AI activation and SMAs ($b = 0.343$, $\beta = 0.256$, $p = 0.076$) (Fig. 5A). The follow-up exploratory analyses indicated that depressive symptoms amplified the positive association between activation in the AI under loss anticipation and SMAs (Fig. 5B). Specifically, the AI activation significantly predicted the SMAs among adolescents with high levels of depressive symptoms (+1 *SD*, $b = 0.072$, $\beta = 0.558$, $p = 0.009$), but not among those with low levels of depressive symtoms (−1 *SD*, $b = 0.018$, $\beta = 0.139$, $p = 0.369$).

Given the small sample size in the moderated mediation model in the present study, we further removed the non-significant paths involving SDS in the model and ran the test again. The moderating effects of SDS in the relationship between AI and SMAs were significant ($b = 0.308$, $\beta = 0.230$, $p = 0.015$; see Supplementary Material). Moreover, the pattern of results remained the same when including the post-questionnaire MID scores and monetary awards in mediation and moderated mediation analyses (see Supplementary Material).

4. Discussion

The present study contributes to the literature on youth SMAs by identifying potential neural mechanisms underlying associations between DER and SMAs. Specifically, the neural activations in emotion-processing-related brain regions (i.e., AI and DLPFC) associated with SMAs served as linking mechanisms underlying the association between DER to SMAs in youth. Moreover, this study further identified the amplifying effect of youth depressive symptoms in such associations, providing insights for developing future targeted prevention and intervention efforts that aim to reduce the incidence of youth excessive engagement in SMAs.

4.1. Brain activations of reward/loss processing associated with SMAs

We found that the activations associated with SMAs were present in the anticipation phase. The anticipation of future positive or negative outcomes may arouse various emotional and motivational states prior to action (Robinson et al., 2014) and consequently may influence subsequent behaviors. Thus, neural activations during the anticipation phase associated with SMAs may reflect emotional and motivational states influencing engagement in SMAs.

First, the present study found that SMAs was associated positively with activation in the left calcarine cortex and right lingual gyrus during reward or loss anticipation. This finding was consistent with findings from prior studies suggesting that children and adolescents with problematic use of the internet and emotional problems may have abnormalities in these brain regions (Chen et al., 2021; Lorenz et al., 2013; Wang et al., 2019; Wilcox and Adinoff, 2016). Both the calcarine cortex and the lingual gyrus belong to the visual attention network (Gebodh and Kelly, 2017), which is implicated in attention and processing visual stimuli (Eggebrecht et al., 2017; Goodale and Milner, 1992). Thus, the findings speculatively suggest that youth with greater engagement in SMAs may be more sensitive to visual stimuli.

In addition, SMAs were associated positively with activations in the

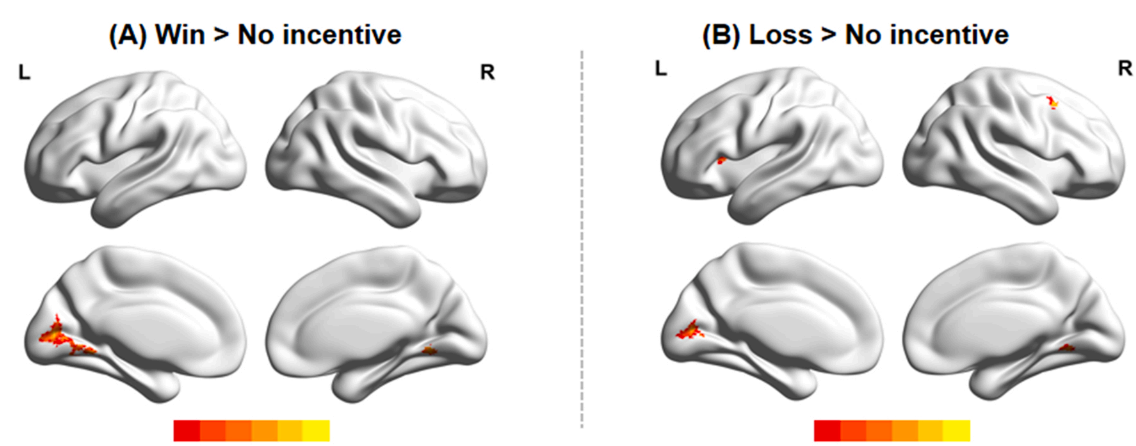

Fig. 3. Brain activations during reward/loss processing associated with SMAs. (A) Regional activations associated with SMAs during reward anticipation. (B) Regional activations associated with SMAs during loss anticipation.

Table 1
Brain activations associated with SMAs in different contrasts.

	Regions	BA[a]	x, y, z[b]			Max *t*	Number of voxels	Hemisphere[c]
Anticipation of win > no incentive								
Positive	Calcarine cortex	18	-13,	-79,	10	5.28	568	L
	Lingual Gyrus	18, 19	16,	-59,	-5	4.63	138	R
Negative	*NA*	–	–	–	–	–	–	–
Anticipation of loss > no incentive								
Positive	Dorsolateral Prefrontal Cortex	8	44,	12,	50	5.15	78	R
	Anterior Insula	13	-33,	18,	4	4.78	109	L
	Lingual Gyrus	18, 19	12,	-53,	-7	4.63	73	R
	Calcarine cortex	18	-13,	-79,	10	4.99	259	L
Negative	*NA*	–	–	–	–	–	–	–

Note. [a] Brodmann's area. [b] Peak Montreal Neurological Institute (MNI) coordinates. [c] The activation area was on the right side (R) or the left side (L)

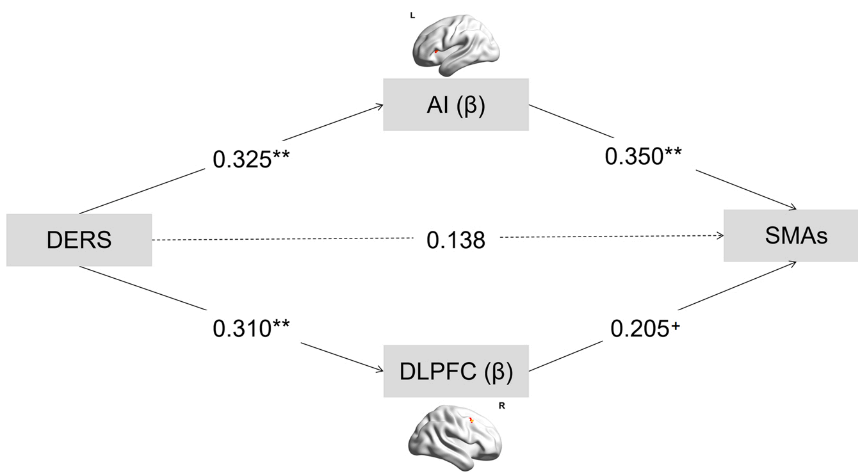

Fig. 4. The mediation model.

Table 2
Bootstrap testing of multiple mediation models for the AI and DLPFC.

Path	Unstandardized b	95% CI		Standardized β
	(SE)	Low	High	(SE)
Direct effect				
DER → SMAs	0.105 (0.080)	-0.043	0.272	0.139 (0.101)
Indirect effect				
DER → AI → SMAs	0.087(0.048)	0.018	0.218	0.115 (0.054)
DER → DLPFC → SMAs	0.048 (0.029)	0.007	0.131	0.063 (0.038)

Note. AI: Anterior Insula; DLPFC: Dorsolateral Prefrontal Cortex; DER: Difficulty in Emotion Regulation.

left AI and right DLPFC during loss anticipation. The DLPFC and AI have been considered as important nodes in emotion processing and emotional regulation circuits (Lai, 2021; Santos et al., 2019; Zhang et al., 2020). In particular, the DLPFC has been suggested as a central hub for facilitating connectivity of structures involved in processing and regulating affective states (Wu et al., 2019). Treatment protocols using the DLPFC as a neural target in interventions that aim to reduce depressive symptoms as well as addictive behaviors have been investigated and supported (Li et al., 2020; Neacsiu et al., 2021; Santos et al., 2019). The sustained recruitment of the DLPFC during emotional regulation may reflect continued attention to and autoregulation of negative stimuli (Shackman et al., 2009; Zhao et al., 2021). The AI is located deep in the anterior region of the lateral fissure of the brain and is associated with multiple psychological functions including interoception, emotion, motivation, and cognition (Quarmley et al., 2019; Reisch et al., 2020). In emotional networks, there is often a strong response to aversive stimuli (Fazeli and Buchel, 2018; Liljeholm and O'Doherty, 2014). A previous study suggested that changes in insular-mediated anticipation and prediction of future events may lead to heighten negative emotion, which may trigger avoidance behaviors (Gogolla, 2017). Furthermore, both DLPFC and AI activation were associated with anticipated aversive responses (Nitschke et al., 2006) and increased negative emotional avoidance motivation (Aupperle et al., 2015). Thus, albeit speculatively, motivations to avoid negative emotions may increase the use of compensatory SMAs (Ahmed et al., 2022). Therefore, the present study suggests that the greater AI and DLPFC activations during loss anticipation may be important neural foundations for increased SMAs in adolescents, possibly reflecting complex and relevant cognitive responses to negative stimuli. This may suggest that SMAs should be used moderately and not as a main avoidance coping strategy for managing negative emotions. It is notable that these results showed lateralization. However, given that the present study was exploratory, the lateralization results require further investigation and validation.

Previous studies have suggested that reward and loss constitute independent components (Fonagy and Luyten, 2018). Consistent with prior research, the present study found that longer response times and poorer accuracy to loss rather than reward stimuli were observed, suggesting that loss processing may have more complex cognitive components (Sozinov et al., 2020). Meanwhile, similar to another study (Goncalves et al., 2021), the present study observed that emotional responses under loss rather than reward anticipation appeared to be associated with SMAs in adolescents. Speculatively, this may reflect imbalanced development of reward/loss sensitivity in early adolescents (Feldmann et al., 2021), such that the loss anticipation modulates broader insula connections than the reward anticipation and thus is more closely associated with future motivated behaviors (Cho et al., 2013; Leong et al., 2021). However, the present study was unable to make effective inferences about this. Further longitudinal follow-up studies are warranted to explore and examine why emotional

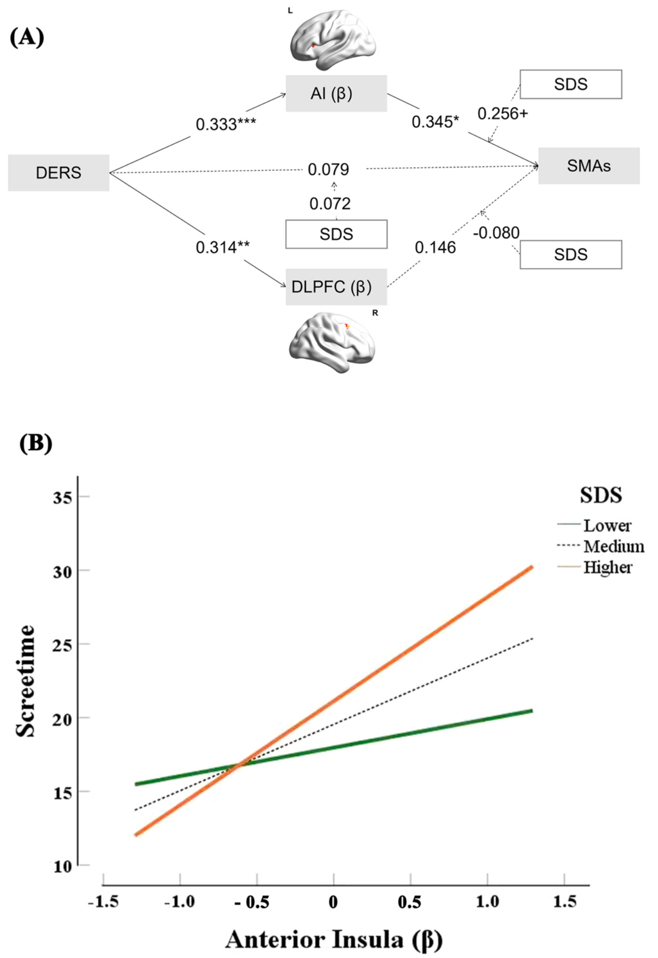

Fig. 5. Depressive symptoms moderated the associations among DER, AI activity during loss anticipation, and SMAs. (A) The path diagram of the moderated mediation model. (B) The simple slopes for the moderating effect of depression in the relationship between AI activity and SMAs. *Note.* Parameter estimates were standardized coefficients. For simplicity of presentation, control variables (age and gender) are not shown. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

responses in loss anticipation rather than reward anticipation may be a salient neural feature predicting SMAs during early adolescence.

4.2. The mediating effects of SMAs-related activations in the AI and DLPFC during loss anticipation in the relationship between DER and SMAs

In addition to replicating the positive relationship between DER and SMAs (Ji et al., 2021; Marchica et al., 2020), the present study further identified neural activations during loss anticipation as an underlying neural mechanism that accounted for the association between DER and SMAs. Specifically, activations in the AI and DLPFC during loss anticipation served as linking mechanisms in the associations between DER and SMAs. The loss cues signified possible negative outcomes, which may have inadvertently increased participants' psychological stress and emotional responses during the anticipation phase (Kermer et al., 2016; Weidacker et al., 2021). The activation in the AI was associated with greater negative anticipation, suggesting greater aversion to loss (Rothenberg et al., 2019; Sheppes and Gross, 2015). Therefore, adolescents with DER may have shown greater activation of the AI during loss anticipation due to their increased sensitivity to aversive stimuli, which may have promoted their avoidance motivation (Gogolla, 2017) and facilitated avoidance behaviors, including possible engagement in SMAs. Moreover, the DLPFC is involved in emotion processing (Kohn et al., 2014), and has been implicated in approach/avoidance behaviors (Aupperle et al., 2015; Rolle et al., 2022). Studies have demonstrated the DLPFC hyperactivity in individuals with DER, which might be involved in attentional regulation of emotional information (Rive et al., 2015; Robinson et al., 2008). In the present study, adolescents with DER had increased recruitment of the DLPFC during loss anticipation, suggesting possible increased attention to negative stimuli (Barnhofer et al., 2021). Furthermore, activation in the right DLPFC has been associated with increased motivation for avoidance behavior (Gueguen et al., 2021; Xia et al., 2021). Therefore, increased activation in the DLPFC during loss anticipation in adolescents with DER may speculatively promote avoidance behaviors. SMAs may represent common negative-emotion avoidance behaviors among adolescents, which may help them escape from negative states, seek online support, and meet social needs (Marino et al., 2020). However, SMAs may also be maladaptive as they may be reinforced and develop into addictions, which in turn may compromise individuals' cognitive and neural development (Brand et al., 2019, 2016). While these possibilities are currently speculative and warrant further direct examination, they are in line with prior data and theoretical models.

As multimodal integration sites, the AI and DLPFC have been associated with other subcortical emotion-related brain regions such as the amygdala, striatum, and thalamus, which have also been implicated in various advanced cognitive functions (Fang et al., 2020; Royer et al., 2020). The extensive connections of the AI or DLPFC with subcortical brain regions have been implicated in excessive SMAs, including gaming and internet addictions (Dong et al., 2019; Zeng et al., 2021). These cortical-subcortical associations should also be examined in future studies.

The present results did not support alternate pathways for the relationships among DER, brain activations and SMAs. However, considering that the present data were cross-sectional, it is important to explore other possibilities (e.g., brain activations → DER → SMAs) in future longitudinal studies.

4.3. The moderating effect of SDS

In the present study, a moderating effect of depressive symptoms in the association between DER and SMAs was not found. However, the present study provided some evidence for the moderating effect of depressive symptoms in the relationship between the AI activation during loss anticipation and SMAs. Further exploration revealed that the AI activation during loss anticipation significantly and positively predicted SMAs among adolescents with higher levels of depressive symptoms, while such an association was not found among those with lower levels of depressive symptoms. These findings are in line with the proposition of a negative reinforcement theory such that depressive/negative states may strengthen the relationship between internal disrupted emotion/neurocircuitry regulation and external risk behaviors (e.g., substance-seeking) to alleviate/avoid negative emotions and maintain a emotional homeostatic (Koob and Dantzer, 2020), although additional research is needed to investigate this possibility. Individuals with high levels of depressive symptoms have demonstrated impaired cognitive functioning (e.g., emotion dysregulation) (Grahek et al., 2019) and disrupted emotional neurocircuitry (Andreescu et al., 2019; Workman and Raab-Graham, 2017). Therefore, they may be more vulnerable to abnormal activation in the AI in response to negative stimuli (Zhang et al., 2022), and could be more likely to do something to manage negative emotions aroused by AI activation (Fauth-Bühler et al., 2014). Considering that SMAs may be one common, easily available compensatory way to disengage individuals from negative emotions (Kardefelt-Winther, 2014), it is not surprising that the AI activation during loss anticipation leads to increased SMAs for those adolescents with high levels of depressive symptoms.

In sum, the present study suggests that effects of AI activation during processing of negative stimuli on SMAs in adolescents varied across different levels of depression. However, molecular mechanisms of possible AI-related homeostatic influences were not studied here and require further examination in future studies. Meanwhile, considering the potential risks, excessive SMAs among adolescents, especially those with high levels of depressive symptoms, need to be identified and targeted in interventions. Strengthening adolescents' acquisition of effective emotion-regulation skills may constitute a promising way to address daily negative emotions and reduce the incidence of excessive SMAs.

4.4. Limitations

Some limitations should be noted. First, the cross-sectional design limited the exploration of potentially causal relationships among DER, neural activations during reward/loss processing, and SMAs. Given the potentially complex natures of emotion processing and youth engagement in SMAs, future studies are warranted to examine the unfolding processes of these dynamic relationships. Second, engagement in SMAs was based primarily on youth self-report. Adolescents and their significant others (e.g., parents) may have disparate perceptions of media use, either in forms or magnitude. Future studies may want to employ multi-informant reporting (e.g., from both parents and adolescents) in assessing SMA and more objective measures of engagement in SMAs. Third, the present study focused on the relationship between escaping from negative mental states and SMAs, but did not consider possible roles of other motivations. Future studies should consider potential influences of other relevant motivations such as seeking online support and social affiliation with respect to SMAs in adolescents. Fourth, while age was included in models, different pubertal stages may associate differentially with age across subjects. Future studies should also assess and consider pubertal stage. Fifth, some additional variables, such as parental restrictions on SMAs, may be important and warrant consideration in future studies. Sixth, limited information on screen media use were collected, and future studies could consider additional measures of problematic use of SMAs in youth (e.g., the Bergen Social Media Addiction Scale (Andreassen et al., 2012)). Finally, this study emphasized the independent roles of the AI and DLPFC activations under loss anticipation. As important hub nodes, it remains worthwhile to explore how their activations at a network level may influence relationships between DER and SMAs.

5. Conclusion

In conclusion, the present study demonstrated that the activations in the AI and DLPFC during loss anticipation may be a biological basis for linking the relationship between DER and SMAs. Greater DER in youth contributed to more frequent engagement in SMAs through brain activations possibly linked to higher emotional reactions (AI activation) and greater cognitive attention and regulation to negative events (DLPFC activation). In particular, for adolescents with high rather than low depressive symptoms, DER were associated more strongly with SMAs through specific neural correlates implicated in emotional responses to negative events. Therefore, this study suggests the importance of considering youth emotional problems with respect to engagement in SMAs. Further, it seems important to help youth in a timely manner to appropriately cope with negative emotions and enhance their emotional-regulation capabilities.

CRediT authorship contribution statement

Jia-Lin Zhang: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Nan Zhou:** Methodology, Writing – review & editing. **Kun-Ru Song:** Data curation, Formal analysis, Investigation. **Bo-Wen Zou:** Data curation, Investigation. **Lin-Xuan Xu:** Investigation. **Yu Fu:** Investigation. **Xiao-Min Geng:** Investigation. **Zi-Liang Wang:** Investigation. **Xin Li:** Investigation. **Marc N. Potenza:** Writing – review & editing. **Yun Nan:** Resources, Project administration. **Jin-Tao Zhang:** Conceptualization, Supervision, Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declared that there were no competing interests exist. Marc N. Potenza has consulted for and advised Opiant Pharmaceuticals, Idorsia Pharmaceuticals, Baria-Tek, AXA, Game Day Data and the Addiction Policy Forum; has been involved in a patent application with Yale University and Novartis; has received research support from the Mohegan Sun Casino and Connecticut Council on Problem Gambling; has participated in surveys, mailings or telephone consultations related to drug addiction, impulse control disorders or other health topics; and has consulted for law offices and gambling entities on issues related to impulse control or addictive disorders. The other authors report no disclosures.

Data availability

Data will be made available on request.

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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.

Data statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2022.101186.

References

Ahmed, Abdalla, Mohamed, Mohamed, Shamaa, 2022. Relation between internet gaming addiction and comorbid psychiatric disorders and emotion avoidance among adolescents: A cross-sectional study. Psychiatry Res 312, 114584. https://doi.org/10.1016/j.psychres.2022.114584.

Anderson, Subrahmanyam, 2017. Digital screen media and cognitive development. Pediatrics 140 (Suppl 2), S57–S61. https://doi.org/10.1542/peds.2016–1758 C.

Andreassen, Torsheim, Brunborg, Pallesen, 2012. Development of a facebook addiction scale. Psychol. Rep. 110 (2), 501–517. https://doi.org/10.2466/02.09.18.Pr0.110.2.501-517.

Andreescu, Ajilore, Aizenstein, Albert, Butters, Landman, Taylor, 2019. Disruption of neural homeostasis as a model of relapse and recurrence in late-life depression. Am. J. Geriatr. Psychiatry 27 (12), 1316–1330. https://doi.org/10.1016/j.jagp.2019.07.016.

Armbruster-Genc, Valton, Neil, Vuong, Freeman, Packer, McCrory, 2022. Altered reward and effort processing in children with maltreatment experience: A potential indicator of mental health vulnerability. Neuropsychopharmacology 47 (5), 1063–1070. https://doi.org/10.1038/s41386-022-01284-7.

Aupperle, Melrose, Francisco, Paulus, Stein, 2015. Neural substrates of approach-avoidance conflict decision-making. Hum. Brain Mapp. 36 (2), 449–462. https://doi.org/10.1002/hbm.22639.

Barnhofer, Reess, Fissler, Winnebeck, Grimm, G.ärtner, Hölzel, 2021. Effects of mindfulness training on emotion regulation in patients with depression: Reduced dorsolateral prefrontal cortex activation indexes early beneficial changes. Psychosom. Med. 83 (6), 579–591. https://doi.org/10.1097/psy.0000000000000955.

Baskin-Sommers, Foti, 2015. Abnormal reward functioning across substance use disorders and major depressive disorder: Considering reward as a transdiagnostic mechanism. Int. J. Psychophysiol. 98 (2), 227–239. https://doi.org/10.1016/j.ijpsycho.2015.01.011.

Beauchaine, 2015. Future directions in emotion dysregulation and youth psychopathology. J. Clin. Child Adolesc. Psychol. 44 (5), 875–896. https://doi.org/10.1080/15374416.2015.1038827.

Blasi, Giardina, Giordano, Coco, Tosto, Billieux, Schimmenti, 2019. Problematic video game use as an emotional coping strategy: Evidence from a sample of mmorpg gamers. J. Behav. Addict. 8 (1), 25–34. https://doi.org/10.1556/2006.8.2019.02.

Brand, Wegmann, Stark, Muller, Wolfling, Robbins, Potenza, 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. Neurosci. Biobehav. Rev. 104, 1–10. https://doi.org/10.1016/j.neubiorev.2019.06.032.

Brand, Young, Laier, Wolfling, Potenza, 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. Neurosci. Biobehav. Rev. 71, 252–266. https://doi.org/10.1016/j.neubiorev.2016.08.033.

Breaux, Dvorsky, Marsh, Green, Cash, Shroff, Becker, 2021. Prospective impact of covid-19 on mental health functioning in adolescents with and without adhd: Protective role of emotion regulation abilities. J. Child Psychol. Psychiatry, Allied Discip. 62 (9), 1132–1139. https://doi.org/10.1111/jcpp.13382.

Brumback, Worley, Nguyen-Louie, Squeglia, Jacobus, Tapert, 2016. Neural predictors of alcohol use and psychopathology symptoms in adolescents. Dev. Psychopathol. 28 (4pt1), 1209–1216. https://doi.org/10.1017/s0954579416000766.

Carter, Rees, Hale, Bhattacharjee, Paradkar, 2016. Association between portable screen-based media device access or use and sleep outcomes: A systematic review and meta-analysis. JAMA Pediatr. 170 (12), 1202–1208. https://doi.org/10.1001/jamapediatrics.2016.2341.

Casey, Cannonier, Conley, Cohen, Barch, Heitzeg, Workgroup, 2018. The adolescent brain cognitive development (abcd) study: Imaging acquisition across 21 sites. Dev. Cogn. Neurosci. 32, 43–54. https://doi.org/10.1016/j.dcn.2018.03.001.

Chaarani, Hahn, Allgaier, Adise, Owens, Juliano, Consortium, 2021. Baseline brain function in the preadolescents of the abcd study. Nat. Neurosci. 24 (8), 1176–1186. https://doi.org/10.1038/s41593-021-00867-9.

Chen, Xia, Zhao, Kuang, Jia, Gong, 2021. Characteristics of intrinsic brain functional connectivity alterations in major depressive disorder patients with suicide behavior. J. Magn. Reson. Imaging 54 (6), 1867–1875. https://doi.org/10.1002/jmri.27784.

Cho, Fromm, Guyer, Detloff, Pine, Fudge, Ernst, 2013. Nucleus accumbens, thalamus and insula connectivity during incentive anticipation in typical adults and adolescents. Neuroimage 66, 508–521. https://doi.org/10.1016/j.neuroimage.2012.10.013.

Collaborators, 2021. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the covid-19 pandemic. Lancet 398 (10312), 1700–1712. https://doi.org/10.1016/S0140-6736(21)02143-7.

Dong, Wang, Zhang, Du, Potenza, 2019. Functional neural changes and altered cortical–subcortical connectivity associated with recovery from internet gaming disorder. J. Behav. Addict. 8 (4), 692–702. https://doi.org/10.1556/2006.8.2019.75.

Dong, Zhang, Zhornitsky, Le, Wang, Li, Zhang, 2021. Depression mediates the relationship between childhood trauma and internet addiction in female but not male chinese adolescents and young adults. J. Clin. Med. 10 (21) https://doi.org/10.3390/jcm10215015.

Eckstrand, Hanford, Bertocci, Chase, Greenberg, Lockovich, Phillips, 2019. Trauma-associated anterior cingulate connectivity during reward learning predicts affective and anxiety states in young adults. Psychol. Med. 49 (11), 1831–1840. https://doi.org/10.1017/S0033291718002520.

Eggebrecht, Elison, Feczko, Todorov, Wolff, Kandala, Pruett, 2017. Joint attention and brain functional connectivity in infants and toddlers. Cereb. Cortex 27 (3), 1709–1720. https://doi.org/10.1093/cercor/bhw403.

Elsayed, Vogel, Luby, Barch, 2021. Labeling emotional stimuli in early childhood predicts neural and behavioral indicators of emotion regulation in late adolescence. Biol. Psychiatry.: Cogn. Neurosci. Neuroimaging 6 (1), 89–98. https://doi.org/10.1016/j.bpsc.2020.08.018.

Esteban, Markiewicz, Blair, Moodie, Isik, Erramuzpe, Gorgolewski, 2019. Fmriprep: A robust preprocessing pipeline for functional mri. Nat. Methods 16 (1), 111–116. https://doi.org/10.1038/s41592-018-0235-4.

Fang, Potter, Nguyen, Zhang, 2020. Dynamic reorganization of the cortical functional brain network in affective processing and cognitive reappraisal. Int. J. Neural Syst. 30 (10) https://doi.org/10.1142/s0129065720500513.

Fauth-Bühler, Zois, Vollstädt-Klein, Lemenager, Beutel, Mann, 2014. Insula and striatum activity in effort-related monetary reward processing in gambling disorder: The role of depressive symptomatology. NeuroImage: Clin. 6, 243–251. https://doi.org/10.1016/j.nicl.2014.09.008.

Fazeli, Buchel, 2018. Pain-related expectation and prediction error signals in the anterior insula are not related to aversiveness. J. Neurosci. 38 (29), 6461–6474. https://doi.org/10.1523/JNEUROSCI.0671-18.2018.

Feldmann, Landes, Kohls, Bakos, Bartling, Schulte-K.örne, Greimel, 2021. Neural processes of reward and punishment processing in childhood and adolescence: An event-related potential study on age differences. Dev. Cogn. Neurosci. *47*. https://doi.org/10.1016/j.dcn.2020.100896.

Fonagy, Luyten, 2018. Conduct problems in youth and the rdoc approach: A developmental, evolutionary-based view. Clin. Psychol. Rev. 64, 57–76. https://doi.org/10.1016/j.cpr.2017.08.010.

Francisco, Pedro, Delvecchio, Espada, Morales, Mazzeschi, Orgiles, 2020. Psychological symptoms and behavioral changes in children and adolescents during the early phase of covid-19 quarantine in three european countries. Front. Psychiatry 11, 570164. https://doi.org/10.3389/fpsyt.2020.570164.

Friston, Holmes, Poline, Grasby, Williams, Frackowiak, Turner, 1995. Analysis of fmri time-series revisited. Neuroimage 2 (1), 45–53. https://doi.org/10.1006/nimg.1995.1007.

Garakani, Zhai, Hoff, Krishnan-Sarin, Potenza, 2021. Gaming to relieve tension or anxiety and associations with health functioning, substance use and physical violence in high school students. J. Psychiatr. Res. 140, 461–467. https://doi.org/10.1016/j.jpsychires.2021.05.055.

Gebodh, Vanegas, Kelly, 2017. Effects of stimulus size and contrast on the initial primary vsual cortical response in humans. Brain Topogr. 30 (4), 450–460. https://doi.org/10.1007/s10548-016-0530-2.

Gogolla, 2017. The insular cortex. Curr. Biol. 27 (12), R580–R586. https://doi.org/10.1016/j.cub.2017.05.010.

Goncalves, Turpyn, Niehaus, Mauro, Hinagpis, Thompson, Chaplin, 2021. Neural activation to loss and reward among alcohol naive adolescents who later initiate alcohol use. Dev. Cogn. Neurosci. 50, 100978 https://doi.org/10.1016/j.dcn.2021.100978.

Goodale, Milner, 1992. Separate visual pathways for perception and action. Trends Neurosci. 15 (1), 20–25. https://doi.org/10.1016/0166-2236(92)90344-8.

Gorgolewski, Burns, Madison, Clark, Halchenko, Waskom, Ghosh, 2011. Nipype: A flexible, lightweight and extensible neuroimaging data processing framework in python. Front. Neuroinform. 5, 13. https://doi.org/10.3389/fninf.2011.00013.

Grahek, Shenhav, Musslick, Krebs, Koster, 2019. Motivation and cognitive control in depression. Neurosci. Biobehav. Rev. 102, 371–381. https://doi.org/10.1016/j.neubiorev.2019.04.011.

Gratz, Roemer, 2004. Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. J. Psychopathol. Behav. Assess. 26 (1), 41–54. https://doi.org/10.1023/B:JOBA.0000007455.08539.94.

Gueguen, Lopez-Persem, Billeke, Lachaux, Rheims, Kahane, Bastin, 2021. Anatomical dissociation of intracerebral signals for reward and punishment prediction errors in humans. Nat. Commun. 12 (1) https://doi.org/10.1038/s41467-021-23704-w.

Gupta, Dickey, Kujawa, 2022. Neural markers of emotion regulation difficulties moderate effects of covid-19 stressors on adolescent depression. Depress Anxiety 39 (6), 515–523. https://doi.org/10.1002/da.23268.

Houck, Barker, Hadley, Brown, Lansing, Almy, Hancock, 2016. The 1-year impact of an emotion regulation intervention on early adolescent health risk behaviors. Health Psychol. 35 (9), 1036–1045. https://doi.org/10.1037/hea0000360.

Hudak, Bernat, Fix, Prince, Froeliger, Garland, 2022. Neurophysiological deficits during reappraisal of negative emotional stimuli in opioid misuse. Biol. Psychiatry. https://doi.org/10.1016/j.biopsych.2022.01.019.

Hutton, Dudley, Horowitz-Kraus, De.Witt, Holland, 2020. Associations between screen-based media use and brain white matter integrity in preschool-aged children. JAMA Pediatr. 174 (1), e193869 https://doi.org/10.1001/jamapediatrics.2019.3869.

Ivanov, Parvaz, Velthorst, Shaik, Sandin, Gan, Consortium, 2021. Substance use initiation, particularly alcohol, in drug-naive adolescents: Possible predictors and consequences from a large cohort naturalistic study. J. Am. Acad. Child Adolesc. Psychiatry 60 (5), 623–636. https://doi.org/10.1016/j.jaac.2020.08.443.

Janak, Tye, 2015. From circuits to behaviour in the amygdala. Nature 517 (7534), 284–292. https://doi.org/10.1038/nature14188.

Jeong, Yim, Lee, Lee, Potenza, Jo, Kim, 2020. Low self-control and aggression exert serial mediation between inattention/hyperactivity problems and severity of internet gaming disorder features longitudinally among adolescents. J. Behav. Addict. 9 (2), 401–409. https://doi.org/10.1556/2006.2020.00039.

Ji, Yin, Zhang, Wong, 2021. Risk and protective factors of internet gaming disorder among chinese people: A meta-analysis. Aust. N. Z. J. Psychiatry 56 (4), 332–346. https://doi.org/10.1177/00048674211025703.

Kardefelt-Winther, 2014. A conceptual and methodological critique of internet addiction research: Towards a model of compensatory internet use. Comput. Hum. Behav. 31, 351–354. https://doi.org/10.1016/j.chb.2013.10.059.

Kebets, Favre, Houenou, Polosan, Perroud, Aubry, Piguet, 2021. Fronto-limbic neural variability as a transdiagnostic correlate of emotion dysregulation. *Transl. Psychiatry, 11*(1), 545. https://doi.org/10.1038/s41398-021-01666-3.

Kermer, Driver-Linn, Wilson, Gilbert, 2016. Loss aversion is an affective forecasting error. Psychol. Sci. 17 (8), 649–653. https://doi.org/10.1111/j.1467-9280.2006.01760.x.

Kiraly, Potenza, Stein, King, Hodgins, Saunders, Demetrovics, 2020. Preventing problematic internet use during the covid-19 pandemic: Consensus guidance. Compr. Psychiatry 100, 152180. https://doi.org/10.1016/j.comppsych.2020.152180.

Király, Potenza, Stein, King, Hodgins, Saunders, Demetrovics, 2020. Preventing problematic internet use during the covid-19 pandemic: Consensus guidance. Compr. Psychiatry *100*. https://doi.org/10.1016/j.comppsych.2020.152180.

Kohn, Eickhoff, Scheller, Laird, Fox, Habel, 2014. Neural network of cognitive emotion regulation — an ale meta-analysis and macm analysis. Neuroimage 87, 345–355. https://doi.org/10.1016/j.neuroimage.2013.11.001.

Koob, Dantzer, 2020. Drug addiction: Hyperkatifeia/negative reinforcement as a framework for medications development. Pharmacol. Rev. 73 (1), 163–201. https://doi.org/10.1124/pharmrev.120.000083.

Lai, 2021. Fronto-limbic neuroimaging biomarkers for diagnosis and prediction of treatment responses in major depressive disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 107, 110234. https://doi.org/10.1016/j.pnpbp.2020.110234.

Laier, Wegmann, Brand, 2018. Personality and cognition in gamers: Avoidance expectancies mediate the relationship between maladaptive personality traits and symptoms of internet-gaming disorder. Front. Psychiatry 9, 304. https://doi.org/10.3389/fpsyt.2018.00304.

Lazarov, Ben-Zion, Shamai, Pine, Bar-Haim, 2018. Free viewing of sad and happy faces in depression: A potential target for attention bias modification. J. Affect. Disord. 238, 94–100. https://doi.org/10.1016/j.jad.2018.05.047.

Leong, Ho, Colich, Sisk, Knutson, Gotlib, 2021. White-matter tract connecting anterior insula to nucleus accumbens predicts greater future motivation in adolescents. Dev. Cogn. Neurosci. *47*. https://doi.org/10.1016/j.dcn.2020.100881.

Li, Cai, Yang, Cui, Huang, Jing, Wang, 2022. A review of attentional bias modification trainings for depression. CNS Neurosci. Ther. https://doi.org/10.1111/cns.14022.

Li, Hartwell, Henderson, Badran, Brady, George, 2020. Two weeks of image-guided left dorsolateral prefrontal cortex repetitive transcranial magnetic stimulation improves smoking cessation: A double-blind, sham-controlled, randomized clinical trial. Brain Stimul. 13 (5), 1271–1279. https://doi.org/10.1016/j.brs.2020.06.007.

Li, Vanderloo, Keown-Stoneman, Cost, Charach, Maguire, Birken, 2021. Screen use and mental health symptoms in canadian children and youth during the covid-19 pandemic. JAMA Netw. Open 4 (12), e2140875. https://doi.org/10.1001/jamanetworkopen.2021.40875.

Liljeholm, Dunne, O'Doherty, 2014. Anterior insula activity reflects the effects of intentionality on the anticipation of aversive stimulation. J. Neurosci. 34 (34), 11339–11348. https://doi.org/10.1523/JNEUROSCI.1126-14.2014.

Lorenz, Kruger, Neumann, Schott, Kaufmann, Heinz, Wustenberg, 2013. Cue reactivity and its inhibition in pathological computer game players. Addict. Biol. 18 (1), 134–146. https://doi.org/10.1111/j.1369-1600.2012.00491.x.

Lu, Yu, Zhao, Guo, 2022. Mental health and related factors of adolescent students during coronavirus disease 2019 (covid-19) pandemic. Psychiatry Investig. 19 (1), 16–28. https://doi.org/10.30773/pi.2020.0416.

Marchica, Mills, Keough, Derevensky, 2020. Exploring differences among video gamers with and without depression: Contrasting emotion regulation and mindfulness. Cyber, Behav., Soc. Netw. 23 (2), 119–125. https://doi.org/10.1089/cyber.2019.0451.

Marciano, Ostroumova, Schulz, Camerini, 2021. Digital media use and adolescents' mental health during the covid-19 pandemic: A systematic review and meta-analysis. Front Public Health 9, 793868. https://doi.org/10.3389/fpubh.2021.793868.

Marino, Canale, Vieno, Caselli, Scacchi, Spada, 2020. Social anxiety and internet gaming disorder: The role of motives and metacognitions. J. Behav. Addict. 9 (3), 617–628. https://doi.org/10.1556/2006.2020.00044.

Miklowitz, Weintraub, Singh, Walshaw, Merranko, Birmaher, Schneck, 2022. Mood instability in youth at high risk for bipolar disorder. J. Am. Acad. Child Adolesc. Psychiatry. https://doi.org/10.1016/j.jaac.2022.03.009.

Muench, Schwandt, Jung, Cortes, Momenan, Lohoff, 2018. The major depressive disorder gwas-supported variant rs10514299 in tmem161b-mef2c predicts putamen activation during reward processing in alcohol dependence. Transl. Psychiatry 8 (1). https://doi.org/10.1038/s41398-018-0184-9.

Murray, 2007. The amygdala, reward and emotion. In: Trends Cognit. Sci., 11, pp. 489–497. https://doi.org/10.1016/j.tics.2007.08.013.

Muthén, Asparouhov, 2015. Causal effects in mediation modeling: An introduction with applications to latent variables. Struct. Equ. Model.: A Multidiscip. J. 22 (1), 12–23. https://doi.org/10.1080/10705511.2014.935843.

Nagata, Chu, Ganson, Murray, Iyer, Gabriel, Baker, 2022. Contemporary screen time modalities and disruptive behavior disorders in children: A prospective cohort study. J. Child Psychol. Psychiatry. https://doi.org/10.1111/jcpp.13673.

Nagata, Cortez, Cattle, Ganson, Iyer, Bibbins-Domingo, Baker, 2021. Screen time use among us adolescents during the covid-19 pandemic: Findings from the adolescent brain cognitive development (abcd) study. JAMA Pediatr. https://doi.org/10.1001/jamapediatrics.2021.4334.

Neacsiu, Beynel, Powers, Szabo, Appelbaum, Lisanby, LaBar, 2021. Enhancing cognitive restructuring with concurrent repetitive transcranial magnetic stimulation: A transdiagnostic randomized controlled trial. Psychother. Psychosom. 1–13. https://doi.org/10.1159/000518957.

Nitschke, Sarinopoulos, Mackiewicz, Schaefer, Davidson, 2006. Functional neuroanatomy of aversion and its anticipation. Neuroimage 29 (1), 106–116. https://doi.org/10.1016/j.neuroimage.2005.06.068.

Palmer, Pecheva, Iversen, Hagler, Sugrue, Nedelec, Dale, 2022. Microstructural development from 9 to 14 years: Evidence from the abcd study. Dev. Cogn. Neurosci. 53, 101044 https://doi.org/10.1016/j.dcn.2021.101044.

Paulus, Squeglia, Bagot, Jacobus, Kuplicki, Breslin, Tapert, 2019. Screen media activity and brain structure in youth: Evidence for diverse structural correlation networks from the abcd study. Neuroimage 185, 140–153. https://doi.org/10.1016/j.neuroimage.2018.10.040.

Price, Scelsa, Zeman, Luebbe, 2022. Profiles of adolescents' sadness, anger, and worry regulation: Characterization and relations with psychopathology. Emotion. https://doi.org/10.1037/emo0001084.

Quarmley, Gur, Turetsky, Watters, Bilker, Elliott, Wolf, 2019. Reduced safety processing during aversive social conditioning in psychosis and clinical risk. *Neuropsychopharmacology, 44*(13), 2247-2253. https://doi.org/10.1038/s41386-019-0421-9.

Reisch, Wegrzyn, Woermann, Bien, Kissler, 2020. Negative content enhances stimulus-specific cerebral activity during free viewing of pictures, faces, and words. Hum. Brain Mapp. 41 (15), 4332–4354. https://doi.org/10.1002/hbm.25128.

Rive, Mocking, Koeter, van Wingen, de Wit, van den Heuvel, Schene, 2015. State-dependent differences in emotion regulation between unmedicated bipolar disorder and major depressive disorder. JAMA Psychiatry 72 (7). https://doi.org/10.1001/jamapsychiatry.2015.0161.

Robinson, Monkul, Tordesillas-Gutiérrez, Franklin, Bearden, Fox, Glahn, 2008. Fronto-limbic circuitry in euthymic bipolar disorder: Evidence for prefrontal hyperactivation. Psychiatry Res.: Neuroimaging 164 (2), 106–113. https://doi.org/10.1016/j.pscychresns.2007.12.004.

Robinson, Yager, Cogan, Saunders, 2014. On the motivational properties of reward cues: Individual differences. Neuropharmacology 76, 450–459. https://doi.org/10.1016/j.neuropharm.2013.05.040.

Rolle, Pedersen, Johnson, Amemori, Ironside, Graybiel, Etkin, 2022. The role of the dorsal–lateral prefrontal cortex in reward sensitivity during approach–avoidance conflict. Cereb. Cortex 32 (6), 1269–1285. https://doi.org/10.1093/cercor/bhab292.

Rothenberg, Di. Giunta, Lansford, Lunetti, Fiasconaro, Basili, Cirimele, 2019. Daily associations between emotions and aggressive and depressive symptoms in adolescence: The mediating and moderating role of emotion dysregulation. J. Youth Adolesc. 48 (11), 2207–2221. https://doi.org/10.1007/s10964-019-01071-6.

Royer, Paquola, Larivière, Vos de Wael, Tavakol, Lowe, Bernhardt, 2020. Myeloarchitecture gradients in the human insula: Histological underpinnings and association to intrinsic functional connectivity. Neuroimage *216*. https://doi.org/10.1016/j.neuroimage.2020.116859.

Santos, Carvalho, Van Ameringen, Nardi, Freire, 2019. Neuroimaging findings as predictors of treatment outcome of psychotherapy in anxiety disorders. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 91, 60–71. https://doi.org/10.1016/j.pnpbp.2018.04.001.

Shackman, Mc.Menamin, Maxwell, Greischar, Davidson, 2009. Right dorsolateral prefrontal cortical activity and behavioral inhibition. Psychol. Sci. 20 (12), 1500–1506. https://doi.org/10.1111/j.1467-9280.2009.02476.x.

Sheppes, Suri, Gross, 2015. Emotion regulation and psychopathology. Annu. Rev. Clin. Psychol. 11, 379–405. https://doi.org/10.1146/annurev-clinpsy-032814-112739.

Sozinov, Laukka, Lyashchenko, Siipo, Nopanen, Tuominen, Alexandrov, 2020. Greater learning transfer effect for avoidance of loss than for achievement of gain in finnish and russian schoolchildren. Heliyon 6 (6). https://doi.org/10.1016/j.heliyon.2020.e04158.

Stieger, Lewetz, Swami, 2021. Emotional well-being under conditions of lockdown: An experience sampling study in austria during the covid-19 pandemic. J. Happiness Stud. 1–18. https://doi.org/10.1007/s10902-020-00337-2.

Sullivan, 2018. Depression effects on long-term prescription opioid use, abuse, and addiction. Clin. J. Pain. 34 (9), 878–884. https://doi.org/10.1097/ajp.0000000000000603.

Te Brinke, Menting, Schuiringa, Dekovic, Weisz, de Castro, 2021. Emotion regulation training as a treatment element for externalizing problems in adolescence: A randomized controlled micro-trial. Behav. Res. Ther. 143, 103889 https://doi.org/10.1016/j.brat.2021.103889.

Teng, Pontes, Nie, Griffiths, Guo, 2021. Depression and anxiety symptoms associated with internet gaming disorder before and during the covid-19 pandemic: A longitudinal study. J. Behav. Addict. 10 (1), 169–180. https://doi.org/10.1556/2006.2021.00016.

Verdejo-Garcia, Verdejo-Roman, Rio-Valle, Lacomba, Lagos, Soriano-Mas, 2015. Dysfunctional involvement of emotion and reward brain regions on social decision making in excess weight adolescents. Hum. Brain Mapp. 36 (1), 226–237. https://doi.org/10.1002/hbm.22625.

Vijayakumar, Op. de Macks, Shirtcliff, Pfeifer, 2018. Puberty and the human brain: Insights into adolescent development. Neurosci. Biobehav. Rev. 92, 417–436. https://doi.org/10.1016/j.neubiorev.2018.06.004.

Vintro-Alcaraz, Munguia, Granero, Gaspar-Perez, Sole-Morata, Sanchez, Fernandez-Aranda, 2022. Emotion regulation as a transdiagnostic factor in eating disorders and gambling disorder: Treatment outcome implications. *J. Behav. Addict., 11*(1), 140-146. https://doi.org/10.1556/2006.2022.00004.

von Deneen, Hussain, Waheed, Xinwen, Yu, Yuan, 2022. Comparison of frontostriatal circuits in adolescent nicotine addiction and internet gaming disorder. J. Behav. Addict. 11 (1), 26–39. https://doi.org/10.1556/2006.2021.00086.

Wang, Qin, Li, Yao, Sun, Li, Luo, 2019. Abnormal functional connectivity in cognitive control network, default mode network, and visual attention network in internet addiction: A resting-state fmri study. Front. Neurol. 10, 1006. https://doi.org/10.3389/fneur.2019.01006.

Wegmann, Antons, Brand, 2022. The experience of gratification and compensation in addictive behaviors: How can these experiences be measured systematically within and across disorders due to addictive behaviors. Compr. Psychiatry *117*. https://doi.org/10.1016/j.comppsych.2022.152336.

Weidacker, Kim, Nord, Rua, Rodgers, Voon, 2021. Avoiding monetary loss: A human habenula functional mri ultra-high field study. Cortex 142, 62–73. https://doi.org/10.1016/j.cortex.2021.05.013.

Wilcox, Pommy, Adinoff, 2016. Neural circuitry of impaired emotion regulation in substance use disorders. Am. J. Psychiatry 173 (4), 344–361. https://doi.org/10.1176/appi.ajp.2015.15060710.

Willinger, Karipidis, Dimanova, Walitza, Brem, 2021. Neurodevelopment of the incentive network facilitates motivated behaviour from adolescence to adulthood. Neuroimage 237, 118186. https://doi.org/10.1016/j.neuroimage.2021.118186.

Workman, Niere, Raab-Graham, 2017. Engaging homeostatic plasticity to treat depression. Mol. Psychiatry 23 (1), 26–35. https://doi.org/10.1038/mp.2017.225.

Wu, Zheng, Zhan, Dong, Peng, Zhai, Wu, 2019. Covariation between spontaneous neural activity in the insula and affective temperaments is related to sleep disturbance in individuals with major depressive disorder. Psychol. Med. 51 (5), 731–740. https://doi.org/10.1017/s0033291719003647.

Xia, Li, Wang, Xia, Lin, Zhang, Zhang, 2021. Functional role of dorsolateral prefrontal cortex in the modulation of cognitive bias. *Psychophysiology, 58*(10). https://doi.org/10.1111/psyp.13894.

Yee, Crawford, Lamichhane, Braver, 2021. Dorsal anterior cingulate cortex encodes the integrated incentive motivational value of cognitive task performance. J. Neurosci. 41 (16), 3707–3720. https://doi.org/10.1523/JNEUROSCI.2550-20.2021.

Zeng, Wang, Zheng, Zhang, Dong, Potenza, Dong, 2021. Gender-related differences in frontal-parietal modular segregation and altered effective connectivity in internet gaming disorder. J. Behav. Addict. 10 (1), 123–134. https://doi.org/10.1556/2006.2021.00015.

Zhang, Dong, Zhao, Chen, Jiang, Du, Dong, 2020. Altered neural processing of negative stimuli in people with internet gaming disorder: Fmri evidence from the comparison with recreational game users. J. Affect. Disord. 264, 324–332. https://doi.org/10.1016/j.jad.2020.01.008.

Zhang, Huang, Li, Liu, Zhang, Li, Liu, 2022. Neural mechanisms underlying the processing of emotional stimuli in individuals with depression: An ale meta-analysis study. Psychiatry Res. *313*. https://doi.org/10.1016/j.psychres.2022.114598.

Zhao, Mo, Bi, He, Chen, Xu, Zhang, 2021. The vlpfc versus the dlpfc in downregulating docial pain using reappraisal and distraction strategies. J. Neurosci. 41 (6), 1331–1339. https://doi.org/10.1523/JNEUROSCI.1906-20.2020.

Zung, 1967. Factors influencing the self-rating depression scale. Arch. Gen. Psychiatry 16 (5), 543–547.