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Internet addiction and functional brain networks: task-related fMRI study

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A common brain-related feature of addictions is the altered function of higher-order brain networks. Growing evidence suggests that Internet-related addictions are also associated with breakdown of functional brain networks. Taking into consideration the limited number of studies used in previous studies in Internet addiction (IA), our aim was to investigate the functional correlates of IA in the default mode network (DMN) and in the inhibitory control network (ICN). To observe these relationships, task-related fMRI responses to verbal Stroop and non-verbal Stroop-like tasks were measured in 60 healthy university students. The Problematic Internet Use Questionnaire (PIUQ) was used to assess IA. We found significant deactivations in areas related to the DMN (precuneus, posterior cingulate gyrus) and these areas were negatively correlated with PIUQ during incongruent stimuli. In Stroop task the incongruent_minus_congruent contrast showed positive correlation with PIUQ in areas related to the ICN (left inferior frontal gyrus, left frontal pole, left central opercular, left frontal opercular, left frontal orbital and left insular cortex). Altered DMN might explain some comorbid symptoms and might predict treatment outcomes, while altered ICN may be the reason for having difficulties in stopping and controlling overuse.

Internet – along with new technologies – has improved many aspects of our lives and it is now essential part of the everyday routine, including professional and social functioning. The benefits that Internet brought into our life are multiple, however, excessive use can contribute to various psychological and medical problems, such as depression¹, anxiety², body image disturbance³, sleeplessness⁴, and poor dietary behavior³. Problematic Internet use is considered as a relatively new, fast growing behavioral addiction⁵ that has a potential threat to public health⁶.

Though Internet addiction (IA) is not considered as a distinct mental disorder a more specific form, problematic video gaming, operationalized as ‘Internet gaming disorder’ (IGD), was included in Section 3 (‘Emerging Measures and Models’) of DSM-5, as a condition warranting further study⁷. It is important to note that the 11th revision of the International Classification of Diseases (ICD-11) also includes gaming disorder in section “Disorders Due to Substance Use or Addictive Behaviours”⁸. Several authors claim that it is important to distinguish between IA and IGD. E.g. Montag and colleagues investigated general Internet addiction and specific forms of Internet addiction (incl. video gaming, shopping, social network and pornography) in three European and one Asian country. They found that only online social network showed constant correlation patterns with generalized IA, other specific forms must be distinguished from IA during scientific investigations⁹. Over the last few years, researchers have increased efforts to investigate brain-related alterations to understand the phenomena deeper. These neuroimaging studies – utilizing mainly structural and functional magnetic resonance imaging (MRI) – identified abnormalities in frontal brain regions (orbitofrontal and prefrontal cortex) and the brain’s reward system (putamen, nucleus accumbens) that play crucial role in associative learning¹⁰ and cognitive control^{11,12}. Moreover, IA shares several aspects of substance addiction, such as obsessive thinking about the

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substance/Internet (daydreaming, rumination, and fantasizing), neglecting everyday activities, social life and essential needs and difficulties in controlling the use^{5,13}.

Another common brain-related feature of substance and behavioral addictions is the altered function of higher-order brain networks. Growing evidence suggests that addictions are not only associated with structural and functional breakdown of isolated regions but rather with system-level alterations between brain regions¹⁴. Functional brain imaging data have revealed that the human brain is topologically organized into a set of coherent spatio-temporal networks, such as default-mode network (DMN)¹⁵. The DMN was first mentioned by Shulman in 1997¹⁶ who noted several brain areas in the cerebral cortex that constantly decreased their activity while performing highly demanding tasks. It can be divided into two main subdivisions: the medial prefrontal cortex, and the posterior cingulate cortex with the nearby precuneus and lateral parietal cortex¹⁷. The DMN-related functional MRI (fMRI) studies can be divided into two types of design. In the resting-state experiments, the subjects lie passively (with closed eyes or with eyes focusing on a fixation cross) without any tasks during scanning. In task-related experiments, fMRI data are acquired during a certain cognitive task and researchers usually focus on deactivations in the brain¹⁸. However, there are some studies that revealed task-induced activations in the DMN, e.g. when internally directed/self-related cognition is required¹⁹.

Several studies revealed altered DMN in addictions. These researches focused primarily on gambling disorder²⁰ and Internet gaming disorder^{15,20} or substance addictions, such as heroin²¹, alcohol²², nicotine²³, and cannabis²⁴. It was also demonstrated that functional connectivity within DMN may predict successful quitting²⁵, the intensity of withdrawal-induced craving²⁶ and the degree of cognitive decline²⁷ in addictions. These observations suggest that dysfunctions in the DMN play important role in the pathogenesis and persistence of addictive disorders. To our knowledge the only study focusing on DMN in adult Internet addicts was conducted by Li and colleagues²⁸. They assessed grey matter volumetry and functional connectivity to investigate brain alterations in healthy young adults with an IA tendency. They found altered relationship between the dorsolateral prefrontal cortex (as key node of the cognitive control network) and the anterior cingulate/prefrontal cortices (as key nodes of the DMN).

Impaired inhibitory control is another important feature of addictions (including IA)^{29,30}. Pre-existing inhibitory control problems may increase vulnerability to develop addictive disorders, and may serve as a risk factor for their maintenance³¹. Dong *et al.* tried to identify neural correlates of response inhibition in IA. They used Stroop-related fMRI³⁰ and event-related brain potential²⁹ techniques and showed that cingulate and medial frontal cortices are impaired in IA. There are some practical and theoretical differences in our study, compared with that one conducted by Dong and colleagues. Firstly, they investigated only males with relatively low sample size (24 participants in total). Secondly, we claim, that in the lack of well-established diagnostic criteria and clear cutoff points, continuous measure of IA is recommended. Thirdly, since Stroop task is considered as a highly demanding task, in our study we focused on DMN activation as well (using different contrast in the higher level analysis). Congdon *et al.*³² suggested that brain areas related to response inhibition ability should be considered as elements of the “inhibitory control network” (ICN). According to their study, the inferior frontal and medial frontal gyri, the opercular, insular, orbital posterior cingulate and posterior parietal cortices are involved in the ICN.

Taking into consideration the limited number of studies and methods used in previous functional studies in IA, our aim was to investigate the functional correlates of IA in the DMN and in the ICN. To observe these relationships, task-related fMRI responses to verbal Stroop and non-verbal Stroop-like tasks were investigated. We hypothesized that blood-oxygen-level dependent (BOLD) signal changes in the regions of the DMN and ICN are correlated with IA scores. In the lack of well-established diagnostic criteria, we decided to use a multidimensional continuous measure of IA.

Materials and Methods

Participants. Our study was conducted through online recruiting. A total of 602 adults participated in the online survey on problematic internet use. According to gender, age and MRI safety parameters sixty healthy Caucasian university students (30 males) aged between 18 and 30 (mean \pm SD: 22.0 \pm 2.08 years) were included. All participants underwent a brief interview by a clinical psychologist and neurological expert to screen out participants with a current psychiatric and neurologic diagnosis. Subjects with chronic illnesses, neurological or psychiatric disorders were not included (for more details about the selection procedure, see the Fig. 1). All subjects had right-hand dominance according to the Edinburgh Handedness Inventory (Oldfield, 1971). Participants spend on average 2.75 (SD = 2.74) hours online per day and consider themselves 45.27% (SD = 29.05) addicted to the Internet. They were either paid or received course credits for their participation and were naive with regard to the purpose of the experiment.

The study was approved by the Regional Research Ethics Committee of the Clinical Center, University of Pécs.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

Assessment. Without clear diagnostic criteria, it is highly recommended to measure excessive Internet use with a continuous questionnaire without using unclear cut-off scores¹¹. Therefore, we used the Problematic Internet Use Questionnaire (PIUQ), a validated self-report scale with good reliability and validity characteristics^{13,33}. The questionnaire contains 18 items, each scored on a 5-point Likert-type scale ranging from 1 (never) to 5 (always). A confirmatory factor analysis verified the three factor model of questionnaire, each subscale contains six items. Obsession subscale refers to obsessive thinking about the Internet (daydreaming, rumination and fantasizing) and withdrawal symptoms caused by the lack of Internet use (anxiety, depression). (“How often do you feel tense, irritated, or stressed if you cannot use the Internet for as long as you want to?”). Neglect subscale

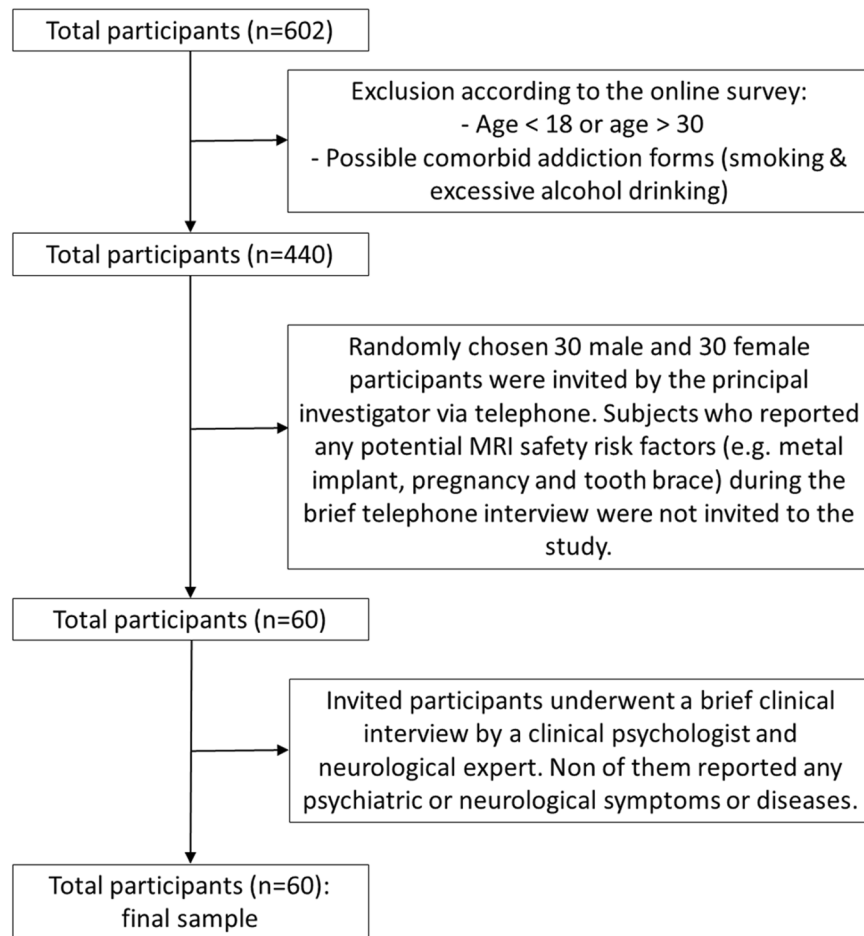


Figure 1. The selection of the final sample. 602 subjects completed the online survey. 139 of them reported smoking habits or excessive alcohol drinking and 28 individuals did not fall within the expected age range (18–30). Since there was overlap between the groups (5 subjects), totally 162 subjects were excluded at this stage of the process. Finally, 30 male and 30 female participants with no neurological and psychiatric symptoms and no risk factors related to MRI measurements were chosen randomly from the remaining 440 subjects.

contains items about neglecting everyday activities, social life and essential needs (“How often do you spend time online when you’d rather sleep?”). Control disorder subscale reflects difficulties in controlling time spent on the Internet (“How often do you realize saying when you are online, ‘just a couple of more minutes and I will stop?’”). Since in this study we focused on global psychological consequences of Internet addiction, we used PIUQ total score in statistical analyses, that was computed by summing the scores on all the items of the scale.

Stimuli. Using Presentation software (Neurobehavioral Systems, Inc., Berkeley, CA, USA), the visual stimuli were presented via MRI-compatible goggles (VisualSystem, NordicNeuroLab AS, Bergen, Norway) and subjects’ responses were collected via MRI-compatible response buttons (ResponseGrip, NordicNeuroLab AS, Bergen, Norway).

Since indirect behavioral evidences suggest that language network and verbal processes might be impaired in IA³⁴, we decided to use two different tasks in this study for controlling this possible interfering effect: verbal Stroop task and non-verbal Stroop-like task.

Verbal stroop task. A series of colored words were displayed against a black background. Half of the words were written in the same ink color as the meaning of the word (congruent stimuli, e.g., the word “green” displayed in green color), while the other half were written in colors other than the word’s meaning (incongruent stimuli, e.g., the word “green” displayed in blue color). Four colored words (blue, green, red, and yellow) and their corresponding colors were used. Subjects had to choose the ink color (and neglect the meaning) of the words by using the four response buttons (left thumb = red; left index = blue; right thumb = green; right index = yellow). Colored circle thumbnails were presented on the bottom of screen to aid the subjects in which button to use for different colors (Fig. 1).

Non-verbal stroop-like task. A series of white arrows pointing either left or right was displayed against a black background either on the left or right side of a centered fixation cross. Half of the stimuli were pointing in the same direction as their position on the screen (congruent stimuli, e.g., a leftward pointing arrow on the

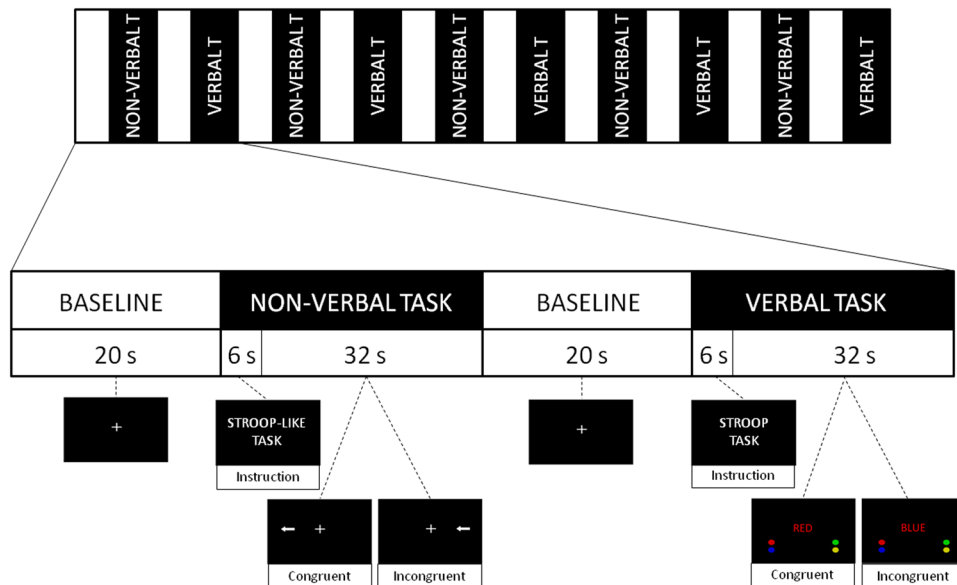


Figure 2. Verbal Stroop and Non-verbal Stroop-like task: design and stimuli examples. The experiment started with a baseline session. It was followed by task sessions that were presented successively. Subjects had to choose the direction of the arrows (Stroop-like task) or ink color of the words (Stroop task).

left side of the fixation cross), while the other half were pointing in an opposite direction as their position on the screen (incongruent stimuli, e.g., leftward pointing arrow on the right side of the fixation cross). Subjects had to choose the direction (and neglect the position) of the arrows by pressing one of the two buttons with their left or right index fingers.

Experimental design. Stimulus presentations were analogous in both tasks. Stimuli were presented for 1200 ms each, with an interstimulus duration of 800 ms. Sixteen stimuli were presented in each session (32 s), with 8 congruent and 8 incongruent stimuli, presented pseudo randomly. Half of the stimuli required left-handed, while the other half required right-handed responses within each session.

The experiment started with a 20 s baseline session with a fixation cross in the center of the screen. The baseline section was followed by the first nonverbal Stroop-like task session that started with a 6 s instruction period followed by the congruent and incongruent stimuli. Then, a 20 s baseline session with fixation cross was conducted following by the verbal Stroop task (again, starting with 6 s instruction period). The verbal Stroop and non-verbal Stroop-like task sessions were presented successively, always interleaved with 20 s baseline. The whole experiment consisted of 5–5 repetitions with 10 baseline sessions, resulting in a total measurement time of 580 s (Fig. 2). Reaction times (RTs) and error rates (ERs) were recorded for each condition (verbal_congruent, verbal_incongruent, non-verbal_congruent, non-verbal_incongruent).

Imaging data acquisition and visual analysis. All measurements were performed on a 3 T Magnetom TIM Trio human whole-body MRI scanner (Siemens AG, Erlangen, Germany) with a 12-channel head coil. Functional images were acquired using a 2D single-shot echo-planar imaging (EPI) sequence (TR/TE = 2000/30 ms; Flip angle = 76°; 36 axial slices with a thickness of 3 mm; FOV = 192 × 192 mm²; matrix size = 64 × 64; receiver bandwidth = 2170 Hz/pixel; no gap; interleaved slice order to avoid crosstalk between contiguous slices). For distortion correction purposes, field mapping sequence (TR/TE1/TE2 = 400/4.92/7.38 ms; Flip angle = 60°; 36 axial slices; FOV = 228 × 228 mm²; matrix size = 76 × 76; receiver bandwidth = 259 Hz/pixel) with the same voxel size, orientation and adjustment parameters as the fMRI scan was acquired right after the fMRI measurement. Anatomical images were obtained using an isotropic T1-weighted 3D-MPRAGE sequence (TR/TI/TE: 2530/1100/3.37 ms; Flip angle = 7°; 176 sagittal slices with a thickness of 1 mm; FOV = 256 × 256 mm²; matrix size = 256 × 256; receiver bandwidth = 200 Hz/pixel). The MPRAGE anatomical images were visually checked by MRI experts. There were no brain abnormalities according to the visual analysis of the MR images.

Functional MRI data processing and analysis. Pre-processing and statistical analyses were performed using FEAT (fMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, <http://www.fmrib.ox.ac.uk/fsl>). Pre-processing included MCFLIRT motion correction, slice timing correction, brain extraction, spatial smoothing with 5 mm full width at half maximum, and a high-pass temporal filter of 104 s (estimated using FSL's cutoffcalc tool). The temporal filtering applied to the data was used for the model as well. Whole brain general linear model (GLM) time-series statistical analyses of individual data sets were carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction.

Task	Condition	Mean (SD) or Median (min-max)	t/Z	rho
Correlation with PIUQ				
Verbal Stroop RT ^a	Cong.	0.87 (0.09)	4.96***	0.077
	Incong.	0.96 (0.17)		0.077
Verbal Stroop ER ^b	Cong.	1 (0–18)	5.80***	–0.01
	Incong.	5 (0–18)		–0.02
Non-verbal Stroop RT ^a	Cong.	0.65 (0.10)	8.43***	–0.11
	Incong.	0.68 (0.10)		–0.12
Non-verbal Stroop ER ^b	Cong.	0 (0–4)	4.16***	0.15
	Incong.	1 (0–5)		0.04

Table 1. Differences in task performances between conditions and correlations with PIUQ. ^aPaired samples t-test, mean (SD) and t values are presented; ^bWilcoxon signed-rank test, median (min-max) and Z scores are presented; ***p < 0.001, RT – reaction time, ER – error rate, PIUQ – Problematic Internet Use Questionnaire, rho – Spearman’s correlation coefficient.

First level analysis included five regressors: verbal (Stroop task) congruent, verbal incongruent, non-verbal (Stroop-like) congruent and non-verbal incongruent conditions, and an additional regressor to model BOLD changes induced by the task instructions.

The single-session data sets were registered into the MNI152 standard space using a two-step process. First, functional (EPI) image of each subject was registered to that subject’s T1 structural scan using BBR (6 degrees-of-freedom) incorporating simultaneous B0 field unwarping (i.e. distortion correction) with a combination of FUGUE and BBR tools^{35,36}. Then, each subject’s T1 image was registered to the 2 mm MNI152 standard space T1 image using a 12 degrees-of-freedom linear fit followed by nonlinear registration (FNIRT, warp resolution = 8 mm). Next, for each subject, these two registrations were combined and applied to the first-level statistical maps to take them into standard space.

Second-level mixed-effects analyses were carried out using FLAME (FMRIB’s Local Analysis of Mixed Effects, stage 1 and 2) with outlier de-weighting to investigate the following questions:

- Deactivation pattern during high-demand incongruent condition (verbal and non-verbal separately).
- Correlation between PIUQ and BOLD signal change during high-demand incongruent condition (verbal and non-verbal tasks separately).
- Activation pattern during the incongruent condition (verbal and non-verbal separately).
- Correlation of PIUQ with BOLD signal change between incongruent and congruent conditions (incongruent_minus_congruent; verbal and non-verbal separately).

Statistical maps were considered to be significant at $Z > 2.3$ and a family-wise error corrected cluster significance threshold of $p = 0.05$.

Brain areas were considered to be part of the DMN if the following assumptions were satisfied for the local maximas (LMs): a) deactivation measured during incongruent condition and b) according to the Harvard-Oxford Cortical Structural Atlas (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases>) the LMs are in the areas related to the DMN (incl. medial prefrontal, posterior cingulate cortex, precuneus or lateral parietal cortex)¹⁷.

Brain areas were considered to be part of the ICN if the following assumptions were satisfied for the LMs: a) activation measured during incongruent_minus_congruent contrast indicating congruency effect or interference effect; b) according to the Harvard-Oxford Cortical Structural Atlas the LMs are in the areas related to the ICN (incl. inferior frontal and medial frontal gyri, the opercular, insular, orbitofrontal, posterior cingulate and posterior parietal cortices)³².

Statistical analyses for behavioral data. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp. Released 2013. Armonk, NY, USA). Mean reaction time (RT) and error rate (ER) differences between congruent and incongruent stimuli were assessed by paired samples t-test or Wilcoxon signed-rank test depending on the distribution of the data. Since PIUQ scores did not show normal distribution, Spearman’s rank correlation was used to study the associations between RTs/ERs and PIUQ.

Results

Behavioral results. The mean of the total score on the PIUQ for our sample is 32.85 (SD = 12.4, 95% CI: [29.62–36.08]).

Significant differences were found between congruent and incongruent stimuli in RTs and ERs regarding both the verbal Stroop and the non-verbal Stroop-like task (Table 1). No significant correlations were found between task performance scores (incl. reaction times – RT, error rates – ER and congruency effect [incongruent_minus_congruent for RTs and ERs) and PIUQ total.

fMRI results. The correlations between PIUQ and BOLD fMRI results for incongruent and incongruent_minus_congruent contrasts are presented in Table 2 (see also Fig. 3). During the incongruent stimuli in the verbal Stroop task, significant negative correlations were found in the bilateral posterior cingulate gyri and bilateral

Cluster	Area	#voxels	Max. Z-score	MNI coordinates		
				x	y	z
PIUQ INCONGRUENT						
	<i>Verbal Stroop task</i>					
1.	Left posterior cingulate gyrus ^a	506	4.09	0	-42	34
	Right precuneus ^a			14	-50	46
	Right posterior cingulate gyrus ^a	434	3.78	8	-40	30
2.	Left precuneus ^a			-4	-58	10
	<i>Non-verbal Stroop-like task</i>					
1.	Left precuneus ^a	386	3.95	-2	-60	52
	Right precuneus ^a			8	-68	50
2.	Right middle frontal gyrus ^a	378	4	40	8	38
	Right precentral gyrus ^a			42	2	42
PIUQ INCONGRUENT_MINUS_CONGRUENT						
	<i>Verbal Stroop task</i>					
1.	Left inferior frontal gyrus pars opercularis ^b	275	3.45	-50	16	0
	Left frontal pole ^b			-36	40	8
	Left central opercular cortex ^b			-38	8	10
	Left frontal opercular cortex ^b			-42	24	2
	Left frontal orbital cortex ^b			-44	20	-6
	Left insular cortex ^b			-42	10	-2
	<i>Non-verbal Stroop-like task</i>	n.s.				

Table 2. Correlations between PIUQ and fMRI BOLD signal changes. ^aNegative correlation ^bpositive correlation; n.s. not significant; MNI coordinates are listed for the local maximas.

precuneus. During the incongruent stimuli in non-verbal Stroop-like task, significant negative correlations were detected in the bilateral precuneus, the right middle frontal gyrus and right precentral gyrus. BOLD signal was decreased with the severity of Internet addiction in both tasks.

Incongruent_minus_congruent contrast for Stroop task positively correlated with PIUQ in several left sided cortical areas including the inferior frontal gyrus (pars opercularis), frontal pole, central and frontal opercular cortex, frontal orbital cortex and insular cortex. The same contrast for non-verbal Stroop-like task showed no significant relationship with PIUQ.

Compared to the baseline, significant deactivations were found in the areas related to the DMN during incongruent stimuli in Stroop and Stroop-like tasks (see Fig. S1). Areas related to the ICN showed significant activation during incongruent stimuli in Stroop task (Fig. S2).

Discussion

In this study, functional correlates of Internet addiction were demonstrated during verbal Stroop and non-verbal Stroop-like task in young adult Internet users. Since the different task-related fMRI contrasts represent different psychological and neural domains they will be discussed separately.

Incongruent stimuli induced BOLD signal changes were found to be negatively correlated with PIUQ in bilateral precuneus and posterior cingulate gyri (PCG) during Stroop task and bilateral precuneus, during Stroop-like task. Moreover, we found significant deactivations in these areas during incongruent stimuli for both verbal Stroop and non-verbal Stroop-like tasks. Brain areas in the cerebral cortex with constantly decreasing activity during demanding tasks are considered being part of the DMN¹⁶. Previous studies investigating Internet addiction and Internet gaming disorder (IGD) also found alterations in the DMN. However, these studies revealed the involvement of the anterior part of the network and used merely resting-state fMRI. Li *et al.*²⁸ demonstrated decreased anticorrelation between the right dorsolateral prefrontal cortex and the anterior part of the DMN (medial prefrontal cortex and anterior cingulate gyrus) that might lead to dysfunctions of the cognitive control network and DMN, including diminished cognitive efficiency. Wang *et al.* also revealed reduced functional connectivity in the anterior part of the DMN, as well as decreased interactions between the salient network and DMN in adolescents³⁷. Authors claim that this may serve as neural background of the uncontrolled Internet use and they also suggest that IA may share similar neurobiological abnormalities than other addictions. Similar impaired connectivity patterns were found in IGD¹⁵. In addition, functional connectivity among DMN regions were in negative correlation with anger and depression³⁸, as well as with executive control dysfunction³⁹. The results of our study have significant contribution to advance our knowledge on the field. We are the first to show that task-related changes in activation of DMN-related structures are also significantly related to IA. The highlighted areas (precuneus and PCG) are parts of the posterior part of the DMN and previous studies revealed that the middle frontal gyrus observed in the current study is also strongly related to the DMN⁴⁰.

Impaired DMN may explain some comorbid symptoms that often occur in IA, thereby it may have important clinical implications. Firstly, many evidences indicate that DMN plays an important role in cognition, particularly in attention and memory processes. Wide range of studies showed that vigilance⁴¹, semantic processing⁴²,

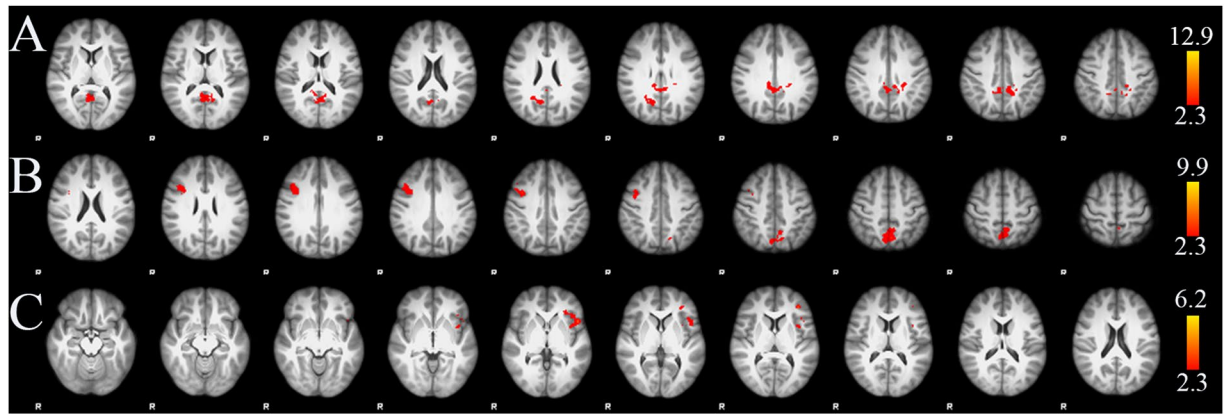


Figure 3. Group level negative associations between PIUQ and BOLD signal changes during incongruent condition in verbal Stroop task (A) and non-verbal Stroop-like task (B). Group level positive associations between PIUQ and BOLD signal changes during incongruent_minus_congruent contrast in Stroop task (C). Images were thresholded using clusters determined by $Z > 2.3$ and a corrected cluster significance threshold of $p = 0.05$. Axial slices are shown in radiological convention for MNI slice coordinates from $Z = 8$ to 48 mm in (A), $Z = 22$ to 62 mm in (B) and $Z = -16$ to 24 mm in (C).

episodic, autobiographical memory⁴³ and creative problem solving⁴⁴ are strongly associated with DMN activation, moreover, diminished vascular functionality for the DMN in mid-life may serve as a preclinical marker for brain dysfunction in later life⁴⁵. These observations may implicate long term negative effect of IA on cognition - similarly to those presented in nicotine addiction²⁷, and suggest that DMN alterations serve as the common neuro-functional background behind IA and attention-related deficits⁴⁶. Although, it must be noted that IA is still a relatively young phenomenon and more evidences are needed to prove this assumption. Secondly, according to previous studies connectivity within DMN can be changed with pharmacotherapies via bottom-up and with cognitive behavioral therapy (CBT) via top-down mechanisms in some psychiatric disorders (for review see⁴⁷), however, the exact mechanisms are unclear. Furthermore, individual variations in pre-treatment functional connectivity may be a reliable predictor of treatment efficacy in schizophrenia⁴⁸, major depression⁴⁹ and smoking²⁷. It is important to note that these studies did not investigate the DMN as a holistic functional brain system, they focused rather on its connection with other networks (executive control network)²⁷, on a highlighted component of the DMN (dorsolateral prefrontal cortex)⁴⁸ and subnetworks of the DMN (anterior and posterior subnetworks; abnormal functional connectivity within the posterior part was normalized after antidepressant treatment, while anterior subnetwork remained persistent against treatment)⁴⁹. Since CBT seems to be successful methods for improving IA status⁵⁰, individual differences in DMN might also predict treatment outcome and be reliable and objective tool for assessing therapeutic efficacy. Further studies are needed to explore this.

In Stroop task the incongruent minus congruent contrast showed significant positive correlation with PIUQ in the left inferior frontal gyrus, left frontal pole, left central opercular, left frontal opercular, left frontal orbital and left insular cortex. Activation in these areas were reported to be correlated with individual differences in task performances requiring good inhibition ability^{32,51}. Congdon *et al.* used Stop-signal task-related probabilistic ICA (independent component analysis) and referred two components that included similar regions found in our study³². They demonstrated that engagement of networks that include these regions is positively related to response inhibition that is the ability to suppress a habitual response or routine behavior, including motor actions and higher-order responses (thoughts, emotions etc.). Therefore, these networks are essential to stop problematic behaviors - such as excessive Internet use. Ergo, it is not surprising that Internet addiction was found to be associated with impaired inhibition in previous studies^{30,52}. Here we suggest that a special “inhibitory control network (ICN)” that was found by Congdon and colleagues³² should be considered as a possible pathogenic factor in the development of IA. However, significant correlations were only found during the Stroop task as an important unexpected result. The most plausible explanation is that the Stroop-like non-verbal task was not sensitive enough to detect individual differences due to the relatively simple nature of the task even in incongruent condition. Despite there were significant differences between incongruent and congruent conditions in RT and ER, incongruency effect did not occur in an expected way. Another possible explanation might be that the verbal domain is altered in IA. This is supported by the presence of left hemisphere specialization in our study that is known to be typical for language processing⁵³. At this stage of knowledge, this explanation seems highly speculative, and further studies are needed.

Some limitations must be considered. First, the cross-sectional nature of the study limits our ability to discriminate between cause and effect. Does excessive Internet use lead to brain-related changes or vice versa? Secondly, IA is known to have various comorbid symptoms such as depression, attention deficit hyperactivity disorder, anxiety disorders etc. Although, we excluded patients with diagnosed comorbid diseases, subjects with subclinical symptoms may have influenced our results. Another limitation is related to recruitment through online platforms. The major problems with this method are that the representativeness of the sample cannot be fully determined and problematic Internet users could be overrepresented in the sample.

Taken together, our results suggest that problematic Internet use in healthy young adults has functional brain correlates in regions that are related to the DMN. Since similar associations were found in IGD⁵⁴, smoking¹⁸ and other substance related addictions²¹ our results suggest long-term negative effects of IA on brain functions. As described before, DMN is strongly related to human cognitive performance and some features of the DMN were able to predict therapy outcomes in psychiatric disorders. Therefore, we suggest, that altered DMN might explain some comorbid symptoms (including attention deficit) and might predict treatment outcomes (for further information about Internet-related changes in human cognition see the review article of Loh & Kanai⁵⁵). Although we must highlight, that in the lack of well-designed, reliable researches, these assumptions are speculative at the moment. Activation in the ICN was also found to be correlated with problematic Internet use suggesting that difficulties in stopping and controlling overuse are not results of “weak character of the person” but the impaired brain mechanisms responsible for behavioral inhibition. However, it must be highlighted that, since we investigated only healthy young people, our conclusions should be applied only to this group. Longitudinal studies and studies with other age groups (e.g. adolescents) are highly needed to test if these findings can be generalized to other groups and whether these functional correlates are the result of overall additive tendencies or specific to maladaptive Internet use. It would be also important to know that controlled Internet use or complete abstinence could reduce these brain-related changes.

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References

- Kim, K. *et al.* Internet addiction in Korean adolescents and its relation to depression and suicidal ideation: A questionnaire survey. *International Journal of Nursing Studies* **43**, 185–192 (2006).
- Norkett, L. Quantitative research. *Nurs. Stand.* **27**, 59–59 (2013).
- Rodgers, R. F., Melioli, T., Laconi, S., Bui, E. & Chabrol, H. Internet Addiction Symptoms, Disordered Eating, and Body Image Avoidance. *Cyberpsychology, Behav. Soc. Netw.* **16**, 56–60 (2013).
- Cheung, L. M. & Wong, W. S. The effects of insomnia and internet addiction on depression in Hong Kong Chinese adolescents: An exploratory cross-sectional analysis. *J. Sleep Res.* **20**, 311–317 (2011).
- Young, K. S. Internet Addiction: The Emergence of a New Clinical Disorder. *CyberPsychology Behav.* **1**, 237–244 (1998).
- Mihajlov, M. & Vejmelka, L. Internet addiction: A review of the first twenty years. *Psychiatr. Danub.* **29**, 260–272 (2017).
- Király, O., Griffiths, M. D. & Demetrovics, Z. Internet Gaming Disorder and the DSM-5: Conceptualization, Debates, and Controversies. *Curr. Addict. Reports* **2**, 254–262 (2015).
- Reed, G. M. *et al.* Innovations and changes in the ICD-11 classification of mental, behavioural and neurodevelopmental disorders. *World Psychiatry* **18**, 3–19 (2019).
- Montag, C. *et al.* Is it meaningful to distinguish between generalized and specific Internet addiction? Evidence from a cross-cultural study from Germany, Sweden, Taiwan and China. *Asia-Pacific. Psychiatry* **7**, 20–26 (2015).
- Day, J. J., Roitman, M. F., Wightman, R. M. & Carelli, R. M. Associative learning mediates dynamic shifts in dopamine signaling in the nucleus accumbens. *Nat. Neurosci.* **10**, 1020–1028 (2007).
- Altbäcker, A. *et al.* Problematic internet use is associated with structural alterations in the brain reward system in females. *Brain Imaging Behav.* **10**, 953–959 (2016).
- Kühn, S. & Gallinat, J. Brains online: Structural and functional correlates of habitual Internet use. *Addict. Biol.* **20**, 415–422 (2015).
- Demetrovics, Z., Szeredi, B. & Rózsa, S. The three-factor model of Internet addiction: The development of the Problematic Internet Use Questionnaire. *Behav. Res. Methods* **40**, 563–574 (2008).
- Steele, V. R., Ding, X. & Ross, T. J. Addiction: Informing drug abuse interventions with brain networks. *Connectomics* 101–122, <https://doi.org/10.1016/b978-0-12-813838-0.00006-6> (2019).
- Zhang, J. T. *et al.* Altered coupling of default-mode, executive-control and salience networks in Internet gaming disorder. *Eur. Psychiatry* **45**, 114–120 (2017).
- Shulman, G. L. *et al.* Common Blood Flow Changes across Visual Tasks: II. Decreases in Cerebral Cortex. *J. Cogn. Neurosci.* **9**, 648–663 (1997).
- Raichle, M. E. The Brain's Default Mode Network. *Annu. Rev. Neurosci.* **38**, 433–447 (2015).
- Ding, X. & Lee, S.-W. Changes of Functional and Effective Connectivity in Smoking Replenishment on Deprived Heavy Smokers: A Resting-State fMRI Study. *PLoS One* **8**, e59331 (2013).
- Zhang, R. & Volkow, N. D. Brain default-mode network dysfunction in addiction. *Neuroimage* **200**, 313–331 (2019).
- Yuan, K. *et al.* Core brain networks interactions and cognitive control in internet gaming disorder individuals in late adolescence/early adulthood. *Brain Struct. Funct.* **221**, 1427–1442 (2016).
- Ma, N. *et al.* Abnormal brain default-mode network functional connectivity in drug addicts. *PLoS One* **6**, e16560 (2011).
- Arcurio, L. R., Finn, P. R. & James, T. W. Neural mechanisms of high-risk decisions-to-drink in alcohol-dependent women. *Addict. Biol.* **20**, 390–406 (2015).
- Lin, F., Wu, G., Zhu, L. & Lei, H. Altered brain functional networks in heavy smokers. *Addict. Biol.* **20**, 809–819 (2015).
- Wetherill, R. R. *et al.* Cannabis, cigarettes, and their co-occurring use: Disentangling differences in default mode network functional connectivity. *Drug Alcohol Depend.* **153**, 116–123 (2015).
- Weiland, B. J., Sabbineni, A., Calhoun, V. D., Welsh, R. C. & Hutchison, K. E. Reduced executive and default network functional connectivity in cigarette smokers. *Hum. Brain Mapp.* **36**, 872–882 (2015).
- Huang, W. *et al.* The development and expression of physical nicotine dependence corresponds to structural and functional alterations in the anterior cingulate-precuneus pathway. *Brain Behav.* **4**, 408–417 (2014).
- Cole, D. M. *et al.* Nicotine replacement in abstinent smokers improves cognitive withdrawal symptoms with modulation of resting brain network dynamics. *Neuroimage* **52**, 590–599 (2010).
- Li, W. *et al.* Brain structures and functional connectivity associated with individual differences in Internet tendency in healthy young adults. *Neuropsychologia* **70**, 134–144 (2015).
- Dong, G., Zhou, H. & Zhao, X. Male Internet addicts show impaired executive control ability: Evidence from a color-word Stroop task. *Neurosci. Lett.* **499**, 114–118 (2011).
- Dong, G., DeVito, E. E., Du, X. & Cui, Z. Impaired inhibitory control in ‘internet addiction disorder’: A functional magnetic resonance imaging study. *Psychiatry Res. Neuroimaging* **203**, 153–158 (2012).
- de Wit, H. Impulsivity as a determinant and consequence of drug use: a review of underlying processes. *Addict. Biol.* **14**, 22–31 (2009).
- Congdon, E. *et al.* Engagement of large-scale networks is related to individual differences in inhibitory control. *Neuroimage* **53**, 653–663 (2010).

33. Koronczai, B. *et al.* Confirmation of the Three-Factor Model of Problematic Internet Use on Off-Line Adolescent and Adult Samples. *Cyberpsychology, Behav. Soc. Netw.* **14**, 657–664 (2011).
34. Nie, J., Zhang, W. & Liu, Y. Exploring depression, self-esteem and verbal fluency with different degrees of internet addiction among Chinese college students. *Compr. Psychiatry* **72**, 114–120 (2017).
35. Greve, D. N. & Fischl, B. Accurate and robust brain image alignment using boundary-based registration. *Neuroimage* **48**, 63–72 (2009).
36. Jenkinson, M., Bannister, P., Brady, M. & Smith, S. Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *Neuroimage* **17**, 825–841 (2002).
37. Wang, L. *et al.* Altered default mode, fronto-parietal and salience networks in adolescents with Internet addiction. *Addict. Behav.* **70**, 1–6 (2017).
38. Dong, G., Li, H., Wang, L. & Potenza, M. N. The correlation between mood states and functional connectivity within the default mode network can differentiate Internet gaming disorder from healthy controls. *Prog. Neuro-Psychopharmacology Biol. Psychiatry* **77**, 185–193 (2017).
39. Wang, L. *et al.* Dysfunctional default mode network and executive control network in people with Internet gaming disorder: Independent component analysis under a probability discounting task. *Eur. Psychiatry* **34**, 36–42 (2016).
40. Uddin, L. Q., Kelly, A. M., Biswal, B. B., Castellanos, F. X. & Milham, M. P. Functional connectivity of default mode network components: correlation, anticorrelation, and causality. *Hum. Brain Mapp.* **30**, 625–37 (2009).
41. Hinds, O. *et al.* Computing moment-to-moment BOLD activation for real-time neurofeedback. *Neuroimage* **54**, 361–368 (2011).
42. Binder, J. R. & Desai, R. H. The neurobiology of semantic memory. *Trends in Cognitive Sciences* **15**, 527–536 (2011).
43. Philippi, C. L., Tranel, D., Duff, M. & Rudrauf, D. Damage to the default mode network disrupts autobiographical memory retrieval. *Soc. Cogn. Affect. Neurosci.* **10**, 318–326 (2015).
44. Kühn, S. *et al.* The Importance of the Default Mode Network in Creativity-A Structural MRI Study. *J. Creat. Behav.* **48**, 152–163 (2014).
45. Haight, T. J. *et al.* Vascular risk factors, cerebrovascular reactivity, and the default-mode brain network. *Neuroimage* **115**, 7–16 (2015).
46. Yen, J.-Y., Ko, C.-H., Yen, C.-F., Wu, H.-Y. & Yang, M.-J. The Comorbid Psychiatric Symptoms of Internet Addiction: Attention Deficit and Hyperactivity Disorder (ADHD), Depression, Social Phobia, and Hostility. *J. Adolesc. Heal.* **41**, 93–98 (2007).
47. Weingarten, C. P. & Strauman, T. J. Neuroimaging for psychotherapy research: current trends. *Psychother. Res.* **25**, 185–213 (2015).
48. Kumari, V. *et al.* Dorsolateral Prefrontal Cortex Activity Predicts Responsiveness to Cognitive-Behavioral Therapy in Schizophrenia. *Biol. Psychiatry* **66**, 594–602 (2009).
49. Li, B. *et al.* A treatment-resistant default mode subnetwork in major depression. *Biol. Psychiatry* **74**, 48–54 (2013).
50. Winkler, A., Dörsing, B., Rief, W., Shen, Y. & Glombiewski, J. A. Treatment of internet addiction: A meta-analysis. *Clin. Psychol. Rev.* **33**, 317–329 (2013).
51. Goghari, V. M. & MacDonald, A. W. The neural basis of cognitive control: Response selection and inhibition. *Brain Cogn.* **71**, 72–83 (2009).
52. Dong, G., Lu, Q., Zhou, H. & Zhao, X. Impulse inhibition in people with Internet addiction disorder: Electrophysiological evidence from a Go/NoGo study. *Neurosci. Lett.* **485**, 138–142 (2010).
53. Vigneau, M. *et al.* Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *NeuroImage* **30**, 1414–1432 (2006).
54. Ding, W. N. *et al.* Altered Default Network Resting-State Functional Connectivity in Adolescents with Internet Gaming Addiction. *PLoS One* **8**, e59902 (2013).
55. Loh, K. K. & Kanai, R. How Has the Internet Reshaped Human Cognition? *Neuroscientist* **22**, 506–520 (2016).

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Author contributions

G.D. was responsible for writing the manuscript and supervising the whole process. G.P., A.N.Z., I.O. and G.O. were responsible for M.R.I. measurements and the statistical analysis. R.H., S.A.N., B.L. and D.T. were responsible for the manuscript review and critique. N.K., T.D., Z.D. and J.J. contributed equally to the conception, organization, and execution of the research project.

Competing interests

The authors declare no competing interests.

Additional information

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