

HUMAN NEUROIMAGING STUDY



Brains online: structural and functional correlates of habitual Internet use

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ABSTRACT

In the past decades, the Internet has become one of the most important tools to gather information and communicate with other people. Excessive use is a growing concern of health practitioners. Based on the assumption that excessive Internet use bears resemblance with addictive behaviour, we hypothesized alterations of the fronto-striatal network in frequent users. On magnetic resonance imaging scans of 62 healthy male adults, we computed voxel-based morphometry to identify grey matter (GM) correlates of excessive Internet use, assessed by means of the Internet Addiction Test (IAT) and functional connectivity analysis and amplitude of low-frequency fluctuation (ALFF) measures on resting state data to explore the functional networks associated with structural alterations. We found a significant negative association between the IAT score and right frontal pole GM volume (P < 0.001, family wise error corrected). Functional connectivity of right frontal pole to left ventral striatum was positively associated with higher IAT scores. Furthermore, the IAT score was positively correlated to ALFF in bilateral ventral striatum. The alterations in the fronto-striatal circuitry associated with growing IAT scores could reflect a reduction of top-down modulation of prefrontal areas, in particular, the ability to maintain long-term goals in face of distraction. The higher activation of ventral striatum at rest may indicate a constant activation in the context of a diminished prefrontal control. The results demonstrate that excessive Internet use may be driven by neuronal circuits relevant for addictive behaviour.

Keywords Behavioural addiction, frontal pole, grey matter, Internet addiction, ventral striatum, voxel-based morphometry.

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INTRODUCTION

In the past decades, the Internet has become one of the most important tools to gather information and communicate with other people. Among adolescents and young adults, Internet use is nearly ubiquitous. Excessive use and loss of control over its use is a growing concern and has been shown to have adverse consequences. Anecdotal media reports as well as scientific studies suggest a link between Internet overuse and mental health problems. including depression and problematic alcohol consumption (Young & Rogers 1998; Babor & Higgins-Biddle 2001; Ko et al. 2008, 2012). In its extreme, the phenomenon has been termed 'Internet addiction disorder' or 'problematic Internet use'. Ivan Goldberg coined the term 'Internet addiction disorder' as a satiric joke in 1995.

First, empirical research applied the criteria for pathological gambling as defined by DSM-IV to diagnose Internet addiction as a compulsive disorder (Young 1998b). The debate whether excessive Internet use should be included in diagnostic manuals is still ongoing (Block, 2008). It is obvious that the distinction between characteristics of addiction and dimensions of new lifestyles based on technological progress is problematic and far from unambiguous (Bergmark, Bergmark & Findahl 2011). The question is whether people who neglect the rest of their lives to spend every waking moment at the monitor are addicted to the technology or to the behaviour that this technology enables. The things that people are addicted to on the Net could be the same things people get hooked on without Internet, namely, video gaming, pornography and shopping, e.g. Holden (2001). Apart from these activities,

people may become addicted to information *per se*. Interestingly, it has been shown that the habit of seeking information is not restricted to humans, but can also be observed in monkeys (Bromberg-Martin & Hikosaka 2009).

At present, it is increasingly argued that many behaviours are apt to produce short-term reward and provoke continued behaviour as well as diminished control (Holden 2001; Grant et al. 2010). It has been proposed that dopamine neurons take part in learning and sustaining many of these reward-dependent behaviours that we acquire. Habits have been proposed to 'hijack' the brain circuits that evolved to reward survival-enhancing behaviour. Typically, habitual and addictive behaviour has been associated with fronto-striatal circuits, including prefrontal brain regions that exert top-down control over the ventral striatum that is involved in reward-processing (Ashby, Turner & Horvitz 2010). Neuroscientific literature has demonstrated that many regular activities can alter brain structure, e.g. learning to become a taxi driver (Woollett & Maguire 2011), playing an instrument professionally (Gaser & Schlaug 2003) and learning to juggle (Draganski et al. 2004). Based on these observations, we predicted structural changes in the fronto-striatal network of participants showing tendencies for dependency such as tolerance, withdrawal, preoccupation, craving and impaired control of Internet usage and continued use despite clear evidence of adverse consequences.

MATERIAL AND METHODS

Participants

Sixty-four healthy male participants (mean = 28.9, SD = 6.62, range 21–45 years) were recruited by means of advertisements in newspapers and the Internet. We restricted our sample to males, since according to the present literature men are more prone to Internet addiction than women are (Tsitsika et al. 2008; Durkee et al. 2012). According to personal interviews (Mini-International Neuropsychiatric Interview; Sheehan, Lecrubier & Sheehan 1998), participants were free of psychiatric disorder. Other medical and neurological disorders relevant for the study as well as illegal and psychotropic drug use during the last year were excluded in a personal interview. In addition, exclusion criteria for all subjects were abnormalities in the magnetic resonance imaging (MRI) or any clinically relevant abnormalities. The study was approved by the local ethics committee of Charité University Clinic Berlin, Germany. After complete description of the study, the subjects informed written consent was obtained from all participants. The participants were right-handed as assessed by means of a handedness questionnaire (Oldfield, 1971).

Scanning procedure

Structural images were collected on a Siemens Tim Trio 3T scanner (Erlangen, Germany) and a standard 12-channel head coil was used. The structural images were obtained using a three-dimensional T1-weighted magnetization prepared gradient-echo sequence based on the ADNI protocol (http://www.adni-info.org; repetition time = 2500 ms; echo time = 4.77 ms; TI = 1100 ms, acquisition matrix = $256 \times 256 \times 176$ flip angle = 7° ; $1 \times 1 \times 1$ mm voxel size).

Questionnaire

We administered the Internet Addiction Test (Young 1998a) in its German version (Barke, Nyenhuis & Kröner-Herwig 2012) consisting of 20 items as a measure Internet usage. The questions were answered on a 6-point rating scale (0 = 'does not apply' to 5 = 'always'). The criteria for addiction are met with 80-100 points indicating that Internet usage is causing significant problems. The retest reliability of IAT in its German version is 0.83 and a significant correlation with time spent on the Internet in a typical week was demonstrated (Barke et al. 2012). In addition to this questionnaire, we administered a questionnaire to assess hours of Internet usage asking: 'How many hours on average do you spend using the Internet during a week day?', 'How many hours on average do you spend using the Internet during a day of the weekend?', 'For how long have you been using the Internet with this frequency?'. Based on the answers, we computed hours spend using the Internet during the week on average. Furthermore, the participants were asked 'How much of this time do you spend on the Internet for job related reasons (in percent)?', 'How much of this time do you spend on the Internet for private reasons (in percent)?' and 'How much of this time do you spend on the Internet for sexual reasons (in percent)?'. Additionally, we asked the participants 'Would you describe yourself as addicted to the Internet?'.

To assess sexually motivated Internet behaviour in more detail, we used the Internet Sex Screening Test (ISST), which has a Cronbach's alpha of 0.51–0.86 for its separate subscales (ISST, Delmonico & Miller 2003). To measure computer gaming, we used a scale for the assessment of pathological computer gaming, which has a Cronbach's alpha of 0.69 and construct validity has been

demonstrated by means of a confirmatory factor analysis [Computerspielverhalten Fragebogen (CSV-S), Wölfling, Müller & Beutel 2011]. To explore the associations between Internet use and markers of dependency and psychiatric disease, we administered the following questionnaires: Alcohol Use Disorder Identification Test (AUDIT, Babor & Higgins-Biddle 2001), Fagerström Test for Nicotine Dependence (Frecker & Fagerström 1991) and the Beck Depression Inventory (BDI, Beck *et al.* 1996).

Data analysis

Voxel-based morphometry (VBM)

Structural data was processed by means of the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) and the SPM8 software package (http://www.fil.ion.ucl.ac .uk/spm) with default parameters. The VBM8 toolbox involves bias correction, tissue classification and affine registration. The affine registered grev matter (GM) and white matter (WM) segmentations were used to build a customized DARTEL (diffeomorphic anatomical registration through exponentiated lie algebra; Ashburner 2007) template. Then, warped GM and WM segments were created. Modulation was applied in order to preserve the volume of a particular tissue within a voxel by multiplying voxel values in the segmented images by the Jacobian determinants derived from the spatial normalization step. In effect, the analysis of modulated data tests for regional differences in the absolute amount (volume) of GM. Finally, images were smoothed with a full width at half maximum (FWHM) kernel of 8 mm. Statistical analysis was carried out by computing correlations of the Internet addiction sum sore and GM/WM volume for each voxel in the whole brain. Age and whole-brain volume were entered as covariates of no interest. The resulting maps were thresholded with P < 0.001 and the family wise error (FWE) method was used to correct for multiple comparisons combined with a non-stationary smoothness correction (Hayasaka & Nichols 2004).

Functional connectivity resting state analysis

The first five volumes were discarded to allow the magnetization to approach a dynamic equilibrium. Part of the data pre-processing, including slice timing, head motion correction (a least squares approach and a six-parameter spatial transformation) and spatial normalization to the Montreal Neurological Institute (MNI) template (resampling voxel size of $3 \times 3 \times 3$ mm³) were conducted using the SPM8 and Data Processing Assistant for Resting-State fMRI (DPARSF; Chao-Gan & Yu-Feng 2010). A spatial filter of 4 mm FWHM was used. Participants showing head motion above 3 mm of maximal translation (in any direction of x, y or z) and 1.0° of

maximal rotation throughout the course of scanning would have been excluded. After pre-processing, linear trends were removed. Then, the fMRI data were temporally band-pass filtered (0.01-0.08 Hz) to reduce lowfrequency drift and high-frequency respiratory and cardiac noise (Biswal et al. 1995). To reduce the effect of physiological artifacts, we removed effects of the following nuisance covariates: global mean signal, the six motion parameters, signal from cerebrospinal fluid and WM (Fox 2005; Kelly et al. 2008). We conducted an exploratory analysis by means of DPARSF computing functional connectivity maps with a seed region consisting of the cluster of GM volume reduction in right frontal pole that was found to be negatively correlated with the IAT score, identifying brain regions that were functionally connected.

The resulting whole-brain functional connectivity maps were correlated with the IAT score to identify brain regions that were jointly activated with right frontal pole weighed according to extensive Internet involvement.

Additionally, ALFF maps were created using DPARSF (Yang et al. 2007; Zang et al. 2007). The time series for each voxel was transformed to the frequency domain using fast Fourier transform (FFT) and the power spectrum was obtained. Since the power of a given frequency is proportional to the square of the amplitude of this frequency component in the original time series in time domain, the power spectrum obtained by FFT was square rooted and then averaged across 0.01-0.08 Hz at each voxel. This averaged square root constitutes what has been called the ALFF. The ALFF of each voxel was divided by the individual global mean of ALFF within a brain mask, which was obtained by removing the tissues outside the brain using software MRIcro (http://www .psychology.nottingham.ac.uk/staff/cr1/mricro.html) within DPARSF. The resulting whole-brain ALFF maps were correlated with the individuals' IAT score.

A height threshold of P < 0.001 was used and a cluster size correction by means of Monte Carlo simulation. Significant effects were reported when the volume of the cluster was greater than the Monte Carlo simulation determined minimum cluster size on the whole-brain volume (> 20 voxels), above which the probability of type I error was below 0.05 (AlphaSim, Ward 2000). Coordinates are reported in MNI space.

The correlations reported are based on Pearson correlation coefficients. For the variables used, we verified the fulfilment of the assumption of normality by means of Kolmogorov–Smirnov tests.

RESULTS

Participants had an average sum score of 22.2 points (SD = 13.6, range 0–62) on the IAT. None of the

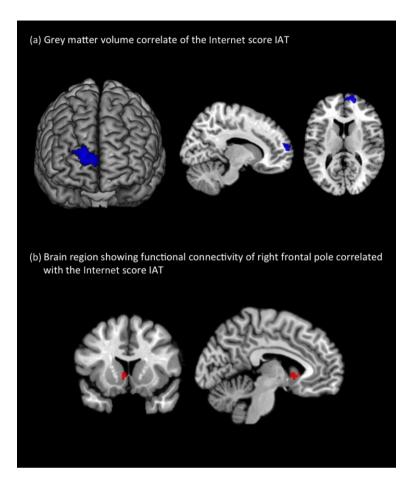


Figure I (a) Brain region showing a significant negative correlation between Internet score (IAT) and grey matter volume in right frontal pole (MNI: 14, 64, 14, BA 10; P < 0.001, FWE corrected). (b) Positive correlation between Internet score (IAT) and functional connectivity map of the right frontal pole in left ventral striatum (MNI: –3, 11, –3; P < 0.001, Monte Carlo cluster corrected)

participants was classified as having an Internet addiction based on the IAT score. However, when being asked explicitly, 15 participants indicated that they are 'addicted' to the Internet. On average, participants reported 41.6 hours of Internet use per week (SD = 45.7) of which 34% were ascribed to job-related, 61.6% to private and 9.7% to sexually related Internet usage on average (cave: percentages do not add up to 100%; participants did indicate the three percentages independently of one another). 20.6% of the participants held a university degree, 15.9% held polytechnic degree, 28.6% were skilled workers and 34.9% did not complete vocational training.

The IAT score was positively associated with the depression score [BDI: r(64) = .372, P < 0.01], the Internet sex questionnaire [ISST: r(64) = .508, P < 0.001] and the pathological computer gaming score [CSV-S: r(64) = .640, P < 0.001], but only marginally positively associated with alcohol use [AUDIT: r(64) = .244, P = 0.052] and not associated with the Fagerström score of nicotine dependence [r(64) = .026, P = 0.841]. Interestingly, the IAT score was not significantly associated with the reported Internet hours per week [r(64) = .135, P = 0.286], showing that the variance captured by the IAT goes beyond the time devoted to Internet usage.

When correlating the IAT score with GM segmentations, we found a significant negative association in the right frontal pole when controlling for age and wholebrain volume (MNI coordinate: 14, 64, 14, BA 10; P < 0.001, FWE corrected; Fig. 1). No region showed a significant positive correlation between GM volume and IAT score and no significant correlations were found in WM segmentations. In order to control for the possible confounding factor of Internet sex addiction, we computed the correlation between IAT score and GM in frontal pole while controlling for the ISST score. We still found the negative association between IAT score and frontal pole GM volume [r(61) = -.310, P < 0.05]. Controlling for depressivity in a similar partial correlation did also not affect the negative association between IAT score and frontal pole GM volume [r(61) = -.342, P < 0.01], the same holds true when controlling for the computer gaming score [r(61) = -.252, P < 0.05].

We used the subscales of the IAT proposed in a previously published factor analysis to predict GM volume in frontal pole by means of a multiple regression analysis. The subscales suggested were called salience, excessive use, neglect of work, anticipation, lack of control and neglect of social life (Widyanto & McMurran 2004). GM volume in frontal pole was significantly predicted from

the factor salience ($\beta = -.24$, P < 0.05), the other IAT factors did not contribute significantly to the prediction (total model: $R^2 = 0.23$, P < 0.05).

In order to investigate brain regions functionally associated with the region of GM reduction in the right frontal pole, we computed the whole-brain functional connectivity between voxels within this cluster and the whole brain. The resulting connectivity maps were correlated with the IAT score to explore differences in frontal pole connectivity related to extensive Internet involvement. We found that a region within the left ventral striatum (MNI coordinate: -3, 11, -3) was positively associated with the Internet score (P < 0.001, Monte Carlo cluster corrected), implicating that subjects who were more attached to the Internet had a stronger connectivity between right frontal pole and left ventral striatum. When comparing the values within the observed connectivity cluster between participants that called themselves 'Internet addicted' and those who did not, we found significantly stronger connectivity between frontal pole and ventral striatum in the self-reported Internet addicted participants [t(62) = -4.47, P < 0.001].

In order to explore the functional connectivity result in more detail, we computed a whole-brain correlation between activity in ALFF and the IAT score. We found a positive association in bilateral ventral striatum (P < 0.001, Monte Carlo cluster corrected, -7~14~-9), indicating that higher Internet addiction scores were associated with higher activity of the ventral striatum during resting state. In addition, the ALFF measure within the activated region was negatively correlated with the GM volume in the frontal pole [r(62) = -.363, P < 0.01].

DISCUSSION

Within the scope of the present study, we investigated structural and functional neural correlates of subclinical Internet addiction. The Internet addiction scores were positively associated with self-reported scores of depression, Internet sex addiction and pathological computer gaming, which is in line with previous investigations of the comorbid psychopathology of high Internet use (Morrison & Gore 2010; Carli et al. 2012; Ko et al. 2012). In the seminal study on Internet addiction, the subjects classified as Internet dependent spent 38.5 hours/week on the Internet (Young 1996). This is in the range of the self-reported hours of 41.6 per week in the present study. However, applying the criteria of the IAT, none of the participants would be classified as having an Internet addiction. When being asked for a subjective self-rating, 15 participants indicated that they would consider themselves 'addicted' to the Internet. Since there is no agreement on the diagnosis of Internet addiction (Mitchell

2000; Holden 2001; Weinstein & Lejoyeux 2010), we decided to use the Internet addiction scale as a continuous measure of the addictive tendencies present in Internet use. Surprisingly, the IAT score was not correlated with self-reported Internet hours/week. This clearly indicates that the variance captured by the Internet addiction score goes beyond the time devoted to Internet usage and shows that dependency symptoms such as tolerance, withdrawal, preoccupation, craving and impaired control of Internet usage and continued use despite clear evidence of adverse consequences are not necessarily associated with the amount of hours spend on the Internet.

The present study has shown that the IAT score is associated negatively with GM volume in the right frontal pole. This relationship remains significant when controlling for correlated variables such as depressivity, Internet sex addiction or computer gaming. Importantly, this analysis shows that the association between the GM reduction in frontal pole is indeed specific for excessive Internet use and not because of the activities that people might get hooked on in the Net such as video gaming or pornography or potential precondition or consequences of Internet addiction such as depressive mood.

From the proposed subscales of the IAT, namely, salience, excessive use, neglect of work, anticipation, lack of control and neglect of social life (Widyanto & McMurran 2004), salience predicted the volumetric decrease in the frontal pole best. The salience factor captures the personal importance and preoccupation with the Internet, which seems to be the most important factor in the volumetric reduction.

It is difficult to relate the present structural finding to previous reports on the neural correlates of excessive Internet use because many of the previous studies do not specify whether people primarily play video games or watch pornography on the Internet. However, a study using cortical thickness as the dependent measure found reduced thickness in the right orbitofrontal cortex in male adolescents (Hong et al. 2013; Yuan et al. 2013) within the proximity of the volumetric reduction observed in the present study. A previous VBM study likewise found GM volume reductions in the frontal pole or at least adjacent to it, although the authors label the location as orbitofrontal cortex (Yuan et al. 2011). Concerning WM changes, another study on Internet addicted adolescent subjects has shown a reduction in fractional anisotropy in frontal WM adjacent to the frontal pole GM reduction we observed (Lin et al. 2012). Outside of the context of Internet addiction, the frontal pole has been associated with learning about which kinds of goalgeneration processes produce particular outcomes, hence improving future choices (Tsujimoto, Genovesio & Wise 2011). In functional imaging studies, it has been associated with so-called branching processes and multitasking. Its supposed role in this context is to allocate attention between two tasks that are ongoing so that long-term goals can be represented while another more immediate goal from another task can be followed (Koechlin *et al.* 1999; Koechlin & Hyafil 2007; Okuda *et al.* 2007). A volumetric reduction of this area might make it difficult to keep potential long-term goals such as not spending too much time on the Internet in mind and make it difficult to maintain in the face of the entertainment of the Net.

However, cause and effect are not clear in cross-sectional studies. The observed volumetric differences in frontal pole could likewise be a precondition rather than a consequence of frequent Internet use and a tendency for dependence. Individuals with lower frontal pole volume might struggle more to stop surfing in the Net, which may lead to higher Internet addiction scores. Future studies should investigate the influence of excessive Internet use longitudinally over time to exclude the possibility that the reduction in frontal pole lead to higher Internet consumption.

The functional connectivity analysis with a seed in the frontal pole revealed that the left ventral striatum was positively associated with the Internet addiction score, indicating that subjects who were more attached to the Internet had a stronger connectivity between right frontal pole and left ventral striatum. The connectivity was stronger for participants that classified themselves as 'Internet addicted' than those who did not. It is clearly surprising that the connectivity of a brain region that is reduced in GM volume is increased with increasing Internet addiction scores.

Alterations in the fronto-striatal circuit and the dopaminergic system have previously been described in Internet addiction. A functional neuroimaging study suggested that Internet addicts have an enhanced reward sensitivity and decreased loss sensitivity (Dong, Huang & Du 2011). Contrary to our present finding, positron emission tomography studies have shown that the dopamine transporter expression level of the striatum was decreased (Hou et al. 2012) and the dopamine D2 receptors were reduced in Internet addicts (Kim et al. 2011). Albeit in the common cue reactivity paradigms with addiction-related cues participants with a dependence to alcohol, nicotine and cocaine consistently show an over-activation of the ventral striatum (Kühn & Gallinat 2011). A recent study comparing functional connectivity in resting state in patients with stimulant dependence and with obsessivecompulsive disorder found that both groups showed reduced connectivity in OFC regions. This reduced connectivity significantly correlated with increased compulsivity in both cases (Meunier et al. 2012).

Limitations

One potential drawback of the study is that we decided to limit our population to male subjects and that we focussed on excessive Internet use, not on Internet addiction. Strictly speaking, we can therefore only generalize the current findings to men and to excessive Internet use. Future studies should test whether similar brain regions are involved in women with excessive Internet use and whether the same brain regions are affected in Internet addiction.

Moreover, future studies may consider to use behavioural measures to assess Internet use instead of self-report instruments as administered in the present study since they may be subject to trivialization of the participants. Similarly, one may consider to measure depressivity based on the rating of a psychiatrist instead of self-reports.

Conclusions

To summarize, the present study demonstrated an association between IAT score and a GM reduction in right frontal pole. This structural reduction was accompanied by an enhanced resting state connectivity with the left ventral striatum. This finding is complemented by a positive association between IAT score and ALFF in bilateral ventral striatum. Taken together, the alterations in the fronto-striatal circuitry resemble changes reported in substance addiction. Seen in this light, the striatal overactivation may be a consequence of the reduced top-down control being exerted by the frontal pole.

However, the observed volumetric reduction in frontal pole and the over-activation of the ventral striatum during rest could likewise be a precondition rather than a consequence of frequent Internet consumption. Individuals with lower frontal pole volume might fall prey to the rewards of the Internet more easily and experience pleasure more strongly because of a lack of control, which may lead to higher IAT scores in turn. In order to clarify this, future studies should investigate the effects of excessive Internet use longitudinally.

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Disclosure

The authors have no conflict of interest to report.

Authors Contribution

SK and JG were responsible for study concept and design. SK performed the experiments, and SK and JG wrote the

article. All authors critically reviewed the content and approved the final version submitted for publication.

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