



Effects of smartphone restriction on cue-related neural activity

Mike M. Schmitgen^{a,b,1}, Gudrun M. Henemann^{a,b,1}, Julian Koenig^c, Marie-Luise Otte^{a,b}, Jakob P. Rosero^a, Patrick Bach^{b,d}, Sophie H. Haage^a, Nadine D. Wolf^{a,b}, Robert C. Wolf^{a,b,*}

^a Department of General Psychiatry, Center for Psychosocial Medicine, Heidelberg University, Germany

^b DZPG (German Center for Mental Health), partner site Mannheim/Heidelberg/Ulm (ZIHUB), Germany

^c Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany

^d Department of Addictive Behavior and Addiction Medicine, Central Institute of Mental Health, Mannheim, Germany

ARTICLE INFO

Handling editor: Andrew Lepp

Keywords:

Functional magnetic resonance imaging

Receptor systems

Smartphone

Addiction

Cue-reactivity

Multimodal data analysis

ABSTRACT

With the increasing popularity of smartphones in the past decades, physical, social, and psychological consequences of excessive smartphone use (ESU) have been increasingly debated. Cue-reactivity (CR) has been discussed as a core mechanism driving this behavior, and previous studies have highlighted distinct neural mechanisms underlying CR in individuals with ESU. Here, we used a functional MRI (fMRI) CR-paradigm to investigate the effects of smartphone restriction over 72 h in 25 young adult smartphone users. The CR-task used contrasts of images showing smartphones vs. neutral stimuli and active vs. inactive smartphones. Region-of-interest based correlations with psychometric scores were performed, and activity changes after 72 h were investigated on a neurochemical level using neurotransmitter probability maps. CR-related brain activity changes over time were most prominent in the nucleus accumbens and anterior cingulate cortex ($p < 0.001$). Such changes were significantly associated with dopamine- and serotonin-receptor probabilities ($p_{FDR} < 0.05$). Significant associations between parietal cortex activity and craving were detected ($p < 0.05$). This study provides evidence for CR-related modulation of neural activity in key regions of salience, motor-inhibition, and reward processing after 72 h smartphone restriction. The identified neural mechanisms may substantially promote addictive behavior in people at risk for ESU.

1. Introduction

Smartphones are ubiquitous in everyday life and integral components of the daily routines of many individuals. Excessive smartphone use (ESU) may show behavioral similarities to addictive disorders (Lin, Chiang et al. 2016). While several validated psychometric instruments include the term “smartphone addiction” (Kwon, Kim et al. 2013a,b; Kwon, Lee et al. 2013a,b; Lin, Chang et al. 2014) (SPA), this term has been frequently criticized for its inaccurate description of a complex with multiple cognitive, affective and behavioral facets. In addition, it is an ongoing debate whether SPA could be regarded as a distinct clinical entity or as a variant of technology-related addictive behaviors, or none of the above (Montag, Wegmann et al. 2019). Yet, regardless of such eminent taxonomic or nosological questions, mounting evidence clearly suggests that ESU may lead to a plethora of adverse somatic and psychosocial effects (Demirci, & AkgönülAkpınar, 2015; Sohn et al., 2019).

Adapting a dimensional perspective that renounces a categorical distinction between SPA and non-SPA, ESU could be located on a continuum of smartphone-use behavior, where intensity and frequency of smartphone-use and related detrimental physical or psychosocial effects may fulfill ICD-11 criteria for gaming disorder (Darvesh et al., 2020) at the extreme end.

In the past years, ESU has increasingly attracted neuroscientific interest, which is not surprising given the interpersonal and societal impact imposed by the rapidly growing number of smartphone users worldwide and given the inclusion of Internet Gaming Disorder (IGD) in DSM-5 appendix and, more recently, the inclusion of gaming disorder in ICD-11. Interventions and neural mechanisms in IGD have already been investigated for about a decade (Sharma & Weinstein, 2024). In contrast to IGD (Zheng et al., 2019), ESU/SPA has been less studied using systems neuroscience methods, such as multimodal imaging. Since ESU, like IGD, can be considered a technology-related behavioral addiction or

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

¹ These authors contributed equally to this publication.

potentially a variant of IGD, the investigation of smartphone restriction could provide valuable insights. Specifically, it may help understanding how the restriction effects e.g. the cue reactivity (CR)-related neural activation and whether these effects could shed further light on craving processes. This, in turn, could serve as a foundation for investigating neuromechanistic parallels to IGD and other technology-related addictive behaviors. Furthermore, several studies have shown that individuals with ESU exhibit distinct structural and functional differences compared with subjects without ESU, and that the spatial distribution of these differences shows a close correspondence with other addictive disorders, such as IGD or substance-use disorders (Lin, Chang et al. 2022). In a previous cross-sectional study, we have shown neural activity differences related to CR processing in individuals with ESU vs. non-ESU, particularly in regions of salience and reward processing (Schmitgen, Horvath et al., 2020). In this previous study, we introduced a CR-experiment including two types of cues – smartphones in non-operating and operating states, related to different psychological states: increased attention towards smartphones per se in ESU for cues irrespective of being turned on or off on the one hand, and increased urge to interact with smartphones in ESU for cues presenting operating smartphones on the other hand (Schmitgen, Horvath et al., 2020). Incorporation of a task capable of differentiating between these processes bears potential to provide deeper insight on the unconscious processes of “wanting” and “liking” in addictive disorders (Anselme & Robinson, 2016). On a neurochemical level, previous studies showed associations between dopamine and opioid receptor distributions and addictive disorders and craving (Volkow, Wang et al. 2011; Itzhak-Israeli et al., 2024). In this line, we have also shown that the found patterns of CR-related activity are tightly connected with opioidergic transmission, further strengthening the notion that the development of ESU (as much as other addictive disorders) is tightly linked to reward processing (Henemann, Schmitgen et al., 2023a,b).

So far it is unclear whether functional changes in individuals with ESU are stable over time or whether brain activity is modulated in specific contexts of smartphone use. Although a former study found increased craving already after 24 h of smartphone restriction, it could not find differences in mood and anxiety (Wilcockson, & OsborneEllis, 2019). Another study reported an increase in withdrawal symptoms and fear of missing out, but no influence on positive and negative affect after 72 h of smartphone restriction (Eide et al., 2018). The neural mechanisms underlying such effects are unclear, yet they could be driven by CR-related mechanisms (Dieterich and Endrass 2022). To fill this gap of knowledge, we build on our previous cross-sectional findings on CR-related neural processing in ESU (Schmitgen, Horvath et al., 2020; Henemann, Schmitgen et al., 2023a,b). Here, we considered an independent sample of smartphone users recruited as part of an ongoing longitudinal study using multimodal neuroimaging and digital ambulatory assessments. Using functional MRI (fMRI), we investigated CR-related neural changes after 72 h smartphone restriction. Given our previous cross-sectional data, suggesting CR-related activity increases in key regions of the salience network, such as the anterior cingulate cortex (ACC) (Schmitgen, Horvath et al., 2020), we predicted that neural activity in these regions would increase further after 72 h withdrawal. In addition, we aimed to relate such changes to neurochemical processes derived from cross-modal correlations with a set of previously reported specific PET/SPECT receptor probability maps (Dukart, Jech et al. 2020; Dukart, Holiga et al. 2021). Finally, we explored associations between CR-related neural markers and distinct psychometric scores indicating the magnitude of smartphone use, craving and affective symptoms. Previous studies on CR in addictive disorders (McClernon et al., 2009; Lou et al., 2012; Huang et al., 2018; Allenby et al., 2020; Zhang, Hu et al. 2020) reported associations between brain activity changes, CR and craving. Therefore, we expected to find individual craving scores to be related to activity changes, especially in ACC and craving-associated brain regions.

2. Materials and methods

2.1. Participants

In this study, we included 25 young adult smartphone users (inclusion criterion age between 18 and 30 years; 13 female) of an ongoing longitudinal project on ESU. Participants were recruited using flyers and posters distributed at Heidelberg University campus, city center, and via ads on social media platforms. Inclusion criteria were as described in Horvath et al., 2020: sufficient German language skills, right-handedness, age 18–30 years, no general contraindications for MRI or self-reported neurological or mental illness, no IGD, as indicated by cut-off scores of <6 on the short form of Internet Gaming Disorder Scale (IGDS-sf) (Lemmens, & ValkenburgGentile, 2015).

For sample size determination, G*Power (<https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower>; last visited October 11, 2024) was used, based on effect sizes derived from our previous study (Schmitgen, Horvath et al., 2020) that was conducted in an entirely independent sample. The suggested sample sizes were at least 12 participants per group to achieve a power of at least 0.95 at an α error probability of 0.05.

Written informed consent was given by all participants prior to inclusion in our study. The Ethics Committee of the Medical Faculty at Heidelberg University approved our study, which was carried out in compliance with the Declaration of Helsinki. All participants received monetary compensation for their participation in our study, a fixed amount (50 €) for participation in two MRIs and a variable amount based on the number of completed EMA questionnaires and results of another experimental paradigm.

2.2. Procedure (see Fig. 1 for a flowchart of the study procedure)

2.2.1. Screening

During recruitment, participants performed the short version of the Smartphone Addiction Scale (SAS-SV) (Haug et al., 2015) and the short form of the Internet Gaming Disorder Scale (IGDS-sf) (Wartberg, et al., 2017).

The SAS-SV is an instrument that captures the magnitude of physical, psychological, and social problems caused by smartphone use. It comprises 10 items with a maximum score of 60.

The IGDS-sf comprises 9 items and it captures psychological and social problems caused by computer gaming in a binary manner (yes/no questions) within the last year.

Participants below and above the threshold for ESU according to SAS-SV (>31 for males and >33 for females) and IGDS-sf scores <6 entered the study.

2.2.2. Baseline psychometric assessment (T0)

Upon inclusion in the study, all participants completed a second smartphone-related scale, i.e. Smartphone Addiction Inventory (SPAI) (Lin, Chang et al. 2014) to capture the overall magnitude of smartphone use and the magnitude of distinct smartphone-use dimensions at a first of three on-site appointments (T0). It comprises 26 items with a maximum score of 104 distributed over four factors. In this regard, a confirmatory factor analysis of the SPAI suggested a five-factor model (SPAI-I), which better fits a European population than the original SPAI (Lin, Chang et al. 2014; Pavia et al., 2016). In this study, the original four SPAI factors and the five SPAI-I factors were calculated and used in data analysis (see Table 1 for demographic and psychometric data).

Further psychometric scores that were obtained at T0 (baseline) comprised the Beck Depression Inventory (BDI-II) (Beck et al., 1961) and the Mannheim Craving Scale (MaCS) (Nakovics et al., 2009).

The BDI-II is a questionnaire designed to measure depressive symptoms over the last two weeks. It comprises 21 items and has a maximum score of 63.

The MaCS is an instrument that captures the magnitude of craving

Table 1

Demographics and psychometric scores by group and differences between groups.

	Full sample n = 25 (mean)	SD	Min- Max	Non-ESU n = 13 (mean)	SD	Min- Max	ESU n = 12 (mean)	SD	Min- Max	Statistic (df)	<i>p</i> _{ESU vs non- ESU}	Effect size
Age	23.04	1.70	20–26	23.62	1.09	22–25	22.42	4.27	20–26	1.81 (15.99) ^a	0.09	0.74 ^b
Sex (m/f)	12/13	–	–	5/8	–	–	7/5	–	–	0.99 (1) ^c	0.32	0.20 ^d
<i>T0 (72 h before restriction)</i>												
BDI total	4.36	5.02	0–16	3.54	4.54	0–12	5.25	5.55	0–16	67 ^e	0.56	–0.12 ^f
SPAI total	48.28	13.93	28–76	39.00	8.85	28–55	58.33	11.22	37–76	14 ^e	< 0.001	–0.69 ^f
SPAI withdrawal	13.48	4.27	6–21	10.38	2.87	6–15	16.83	2.69	12–21	–5.78 (23) ^a	< 0.001	–2.31 ^b
SPAI compulsive behavior	15.52	4.73	9–26	12.92	3.71	9–20	18.33	4.14	11–26	–3.45 (23) ^a	0.002	–1.38 ^b
SPAI tolerance	6.00	2.29	3–10	4.62	1.80	3–9	7.50	1.78	5–10	18.5 ^e	0.001	–0.65 ^f
SPAI functional impairment	13.28	4.47	8–24	11.08	2.69	8–17	15.67	4.87	9–24	–2.95 (23) ^a	0.007	–1.18 ^b
SPAI-I total	43.88	12.57	26–69	35.54	8.14	26–50	52.92	10.05	34–69	–4.77 (23) ^a	< 0.001	–1.91 ^b
SPAI-I time spent	8.56	2.72	5–14	6.46	1.71	5–10	10.83	1.47	9–14	5 ^e	< 0.001	–0.80 ^f
SPAI-I compulsivity	5.68	1.80	4–10	4.85	1.57	4–9	6.58	1.62	4–10	29.5 ^e	0.007	–0.54 ^f
SPAI-I daily life interference	12.72	3.91	8–23	10.46	2.18	8–15	15.17	3.95	10–23	19.5 ^e	0.001	–0.64 ^f
SPAI-I craving	11.20	3.86	6–19	8.92	2.60	6–13	13.67	3.52	6–19	–3.85 (23) ^a	< 0.001	–1.54 ^b
SPAI-I sleep interference	5.72	2.46	3–11	4.85	1.91	3–9	6.67	2.71	3–11	–1.96 (23) ^a	0.06	–0.78 ^b
MaCS total	22.64	7.01	12–40	18.85	5.98	12–34	26.75	5.71	17–40	–3.37 (23) ^a	0.002	–1.35 ^b
<i>T2 (after 72 h restriction)</i>												
BDI total	3.32	4.98	0–21	2.15	3.02	0–9	4.58	6.39	0–21	60 ^e	0.32	–0.20 ^f
MaCS total	22.08	7.62	13–40	17.38	4.07	13–26	27.17	7.36	17–40	–4.16 (23) ^a	< 0.001	–1.66 ^b

Abbreviations: SD - standard deviation, Min - minimum value, Max - maximum value; m - male, f - female; BDI - Beck-Depression-Inventory, SPAI - Smartphone Addiction Inventory, SPAI-I - SPAI five-factor model, MaCS - Mannheimer Craving Scale.

^a t-value.

^b Cohen's d.

^c χ^2 .

^d ϕ .

^e Wilcoxon W.

^f r. Significant results in bold font.

across a variety of substance-use disorders. It comprises 12 items with a maximum score of 60, three visual analogue scales, and one question on the last usage in days.

Also, at the end of T0, participants received a device for collecting Ecological Momentary Assessment (EMA) data on craving and other variables such as well-being, daily activities, and smartphone use. All participants completed two MRI-sessions, which were 72 h apart, one directly before the restriction of smartphone-use (T1) and one directly before the end of the 72 h restriction period (T2). The first of two MRI-sessions (second on-site appointment) was performed 72 h after T0. At the end of T1, a smartphone restriction phase for 72 h started. Apart from EMA, no interventions or procedures were applied during the 72 h between T0 and T1.

2.2.2.1. MRI data acquisition. Whole-brain MRI-images were acquired using a 3 T SIEMENS MAGNETOM Prisma Fit MRI-scanner (SIEMENS, Erlangen) equipped with a 32-channel head coil in a darkened room. The head of the participants was fixated using foam cushions to minimize head motion. The scanner protocol was comprised of five functional measurements including (in this order) a resting state scan, the cue-reactivity experiment based on Schmitgen et al., 2020 (Schmitgen, Horvath et al., 2020), three further experimental paradigms, and a structural scan.

Parameters of the sequence used during the CR experiment were as follows: 293 whole brain echo planar imaging (EPI) volumes were recorded in transversal orientation, repetition time = 2.22 s, echo time = 29 ms, field of view = 192 mm, flip angle = 85°, voxel size = 3 × 3 × 3 mm, 33 slices, distance factor between slices = 33 %.

Parameters of the structural T1 MPRAGE sequence were: 192 slices recorded in sagittal orientation, repetition time = 1.90 s, echo time = 2.52 ms, field of view = 256 mm, flip angle = 9°, voxel size = 1 × 1 × 1 mm, distance factor between slices = 50 %.

2.2.2.2. CR-task. We applied the modified block-design CR-task as described in Schmitgen et al., 2020 (Schmitgen, Horvath et al., 2020), which is based on the CR-task by Beck et al., 2012. In brief, during the task, blocks of five pictures were presented for 20 s (i.e. 4 s per picture) and a fixation cross (ITI; 25 blocks, one before the start of the experiment and 24 between blocks of pictures) was presented for 4.8 s between the blocks of pictures. The blocks of pictures either contained neutral images (NEU; 12 blocks), inactive smartphones (OFF; six blocks), or smartphones in use (ON; six blocks; see Fig. 2). Block order and pictures within blocks were pseudorandomized between participants and between MRI-sessions.

CR-experiments are commonly used to study behavioral and substance addictions and are known to elicit cravings in heavy consumers (Dieterich and Endrass 2022) and smartphone restriction leads to withdrawal symptoms, including craving in heavy smartphone users (Eide et al., 2018). In this context, we combined restriction and a CR-experiment to examine the association between craving and CR on a behavioral and neuronal level. We chose a restriction period of 72 h to ensure capturing effects on craving and withdrawal symptoms and at the same time to prevent discouraging potential participants from entering the study. During this 72 h period of smartphone restriction, participants were asked to renounce to use their smartphone, substitute devices, and software as much as possible, e.g. for activities entirely unrelated to

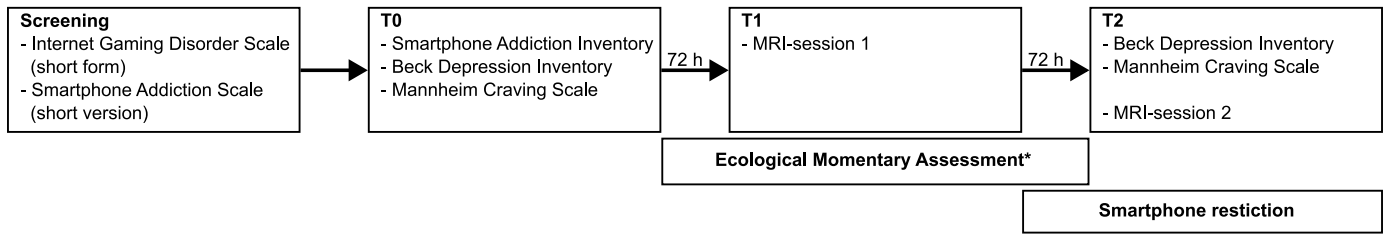


Fig. 1. Flowchart of study-procedure.

First, a screening of potential participants comprising the short version of the Internet Gaming Disorder Scale and the short version of the Smartphone Addiction Scale was performed. If eligible, participants were invited to the first on-site meeting for collecting baseline psychometric data and handing out a device for Ecological Momentary Assessment (T0). Seventy-two hours after T0, the first MRI session was performed (T1). After the MRI-session the smartphone restriction phase started. Seventy-two hours after T1, the third on-site meeting took place, comprising psychometry and the second MRI-session (T2). Ecological Momentary Assessment stopped at the beginning and smartphone restriction stopped at the end of T2. *Findings on Ecological Momentary Assessment will be reported elsewhere. This figure was created using Inkscape (<https://inkscape.org/>; last visited August 11, 2024).

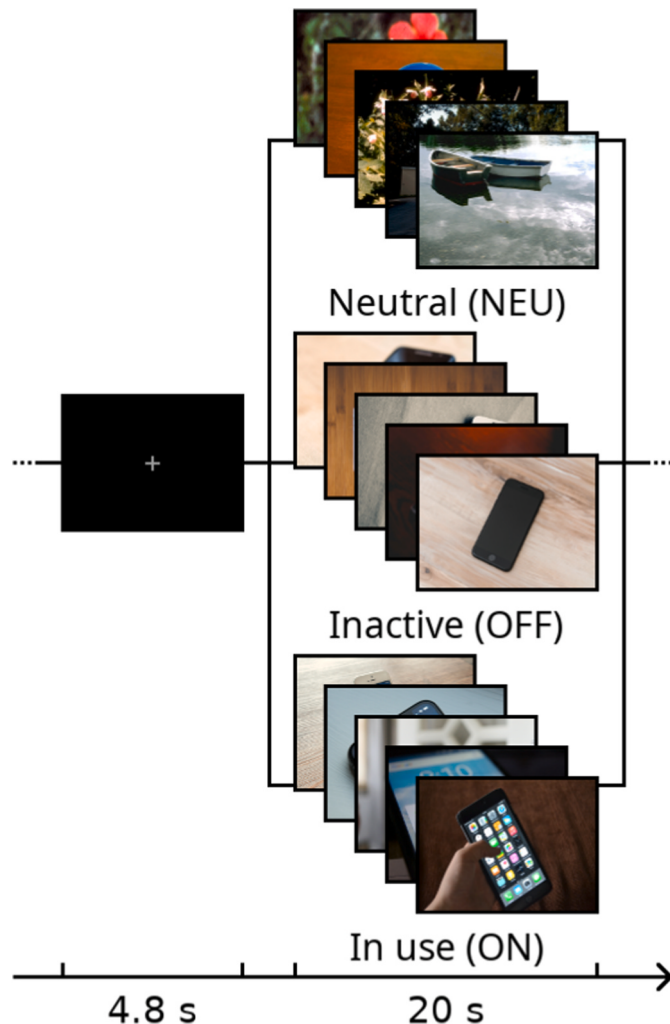


Fig. 2. Schematic overview of the CR-task.

This figure was created using GIMP (<https://www.gimp.org/>; last visited 01/21/2024).

work or activities related to daily living and communication with significant others. Smartphone restriction was not monitored via examination of screen time on private phones, however, further information on craving and other variables such as well-being, daily activities, and smartphone use were collected using EMA starting at the end of T0 and ending at the beginning of T2. The EMA-based data have not yet been analyzed and will be reported elsewhere after completion and detailed

evaluation.

2.2.3. MRI-session 2 (T2)

On the third on-site appointment, directly before the end of the 72 h restriction period, psychometry in terms of BDI (with instructions adapted for the study-specific repeated assessments) and MaCS was acquired again and the second MRI-session (identical order of measurements acquired as during T1) was performed (T2; see Table 1 for demographic and psychometric data).

2.3. Data analysis

2.3.1. Psychometric data

BDI and MaCS were tested for changes over time via paired t-tests or robust methods via bootstrap and M-estimator, if differences were not normally distributed [R function *bootdpci* from the WRS package]). Seven participants (three ESU and four non-ESU) showed missing values in psychometric data (SPAI, BDI or MaCS). In most cases (two ESU and three non-ESU), only singular items of one of the questionnaires were omitted. We consider two major reasons that account for this data loss, i. e. participant's time constraints or inattentiveness. Missing values were handled as follows: Given the categorical analyses that considered group as a factor (see Table 1 for demographics and psychometric scores), median scores of missing items were calculated per group, and respective missing values were replaced by the medians, a standard imputation method for missed items (<https://tahera-firdose.medium.com/filling-missing-values-with-mean-and-median-76635d55c1bc>; last visited December 11, 2024).

2.3.2. Functional MRI

2.3.2.1. Functional MRI data preprocessing. FMRI images were pre-processed using the Data Processing Assistant for rs-fMRI (DPABI/DPARSF) (Yan et al., 2016). In accordance with our previous study (Schmitgen, Horvath et al., 2020), preprocessing included slice timing, realignment, reorientation of functional and structural data, automated mask-creation, brain extraction, coregistration of the T1 image to functional images, SPM new segment and DARTEL using affine regularization for European participants, normalization by DARTEL to a voxel-size of $3 \times 3 \times 3$ mm, and smoothing using a FWHM of $9 \times 9 \times 9$ mm. Head movement >3 mm or 3° was defined as an exclusion criterion.

2.3.2.2. Functional MRI data statistical analysis, individual data. Statistical fMRI data analysis was conducted using SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/>; last visited September 01, 2024). As in our previous study (Schmitgen, Horvath et al., 2020), 1st level models (block design) were set up using the following regressors:

PHONE vs. NEU model: ITI, blocks of pictures showing ON or OFF (PHONE), blocks of pictures showing NEU, and six movement

parameters.

ON vs. OFF model: ITI, blocks of pictures showing NEU, blocks of pictures showing OFF, blocks of pictures showing ON, and six movement parameters.

2.3.2.3. Functional MRI data statistical analysis, group data. On 2nd level, SPM one sample t-tests for contrasts of PHONE vs. NEU and ON vs. OFF at the first MRI session were set up to visualize T1 activation patterns (see [Supplementary Fig. 1](#) and [Supplementary Table S1](#)).

We followed a dimensional and a subsequent categorical approach. The primary analysis considered ESU as a cognitive-behavioral continuum, so that no clear-cut distinction was made whether participants fulfilled psychometric cut-offs for “SPA” or not, as determined by the SAS-SV. We considered this approach as important given that excessive smartphone use is a dimensional phenomenon and that clear-cut categories, such as “smartphone addiction” still await more precise definitions, beyond what has been so far suggested by psychometric research. The secondary analysis, i.e. the categorical approach, was conducted to allow comparisons with previous research in ESU/SPA ([Abdul Rashid et al., 2021](#); [Montag & Becker, 2023](#), [León Méndez, Padrón et al., 2024](#)), including our own previous studies ([Horvath, Mundinger et al., 2020](#), [Schmitgen, Horvath et al., 2020](#), [Hirjak et al., 2022](#), [Schmitgen, Wolf et al., 2022](#), [Henemann, Schmitgen et al., 2023a, b](#)). For this purpose, we determined participant subgroups of ESU and non-ESU as determined by SAS-SV cutoffs ([Kwon, Kim et al. 2013a,b](#), [Horvath, Mundinger et al., 2020](#), [Schmitgen, Horvath et al., 2020](#), [Hirjak et al., 2022](#), [Schmitgen, Wolf et al., 2022](#), [Henemann, Schmitgen et al., 2023a,b](#)) and focused on group-by-time interactions in the model referred below.

To test for changes of neural activations over time (T2 vs. T1), SPM flexible factorial models (factors: group [ESU, non-ESU], time) were set up for contrasts of PHONE vs. NEU and ON vs. OFF. All SPM models used age and sex as covariates of no interest, and a significance threshold of $p < 0.001$ (uncorrected for multiple comparisons) was chosen on voxel-level, followed by cluster-extent correction using Gaussian random field theory (i.e. an empirically determined extent threshold of k based on SPM resolution elements). Unless reported otherwise, all fMRI data analyses are based on whole-brain data, including the above-mentioned cluster-extent correction.

Also, for completeness, SPM two sample t-tests were set up to examine differences between ESU and non-ESU at T1 and T2 (see [Supplementary Table S1](#)).

2.3.2.4. Correlations between region of interest fMRI activation and psychometric scores. Further, raw activation within brain regions detected in the longitudinal contrasts (PHONE > NEU T1 vs. T2 and ON > OFF T1 vs. T2; left and right hemisphere separately for close to midline structures) was extracted using MarsBaR (version 0.45 ([Brett et al., 2002](#)), differences between T1 and T2 were calculated according to the direction of the respective effects, and used for Spearman correlations with psychometric scores in R (version 4.3.1; <https://www.r-project.org/>; last visited 01/21/2024). Anatomical masks were created using the Neuromorphometrics atlas implemented in SPM12. Here, due to the explorative nature of this analysis, a nominal significance level of $p < 0.05$ was chosen and no correction for multiple comparisons was applied.

2.3.2.5. Cross-modal correlations between fMRI activation patterns and PET/SPECT-derived receptor maps. Finally, cross-modal Spearman correlations of activation patterns of PHONE > NEU at T2 – T1 and ON > OFF at T1 – T2 with neurotransmitter/receptor maps (all 30 neurotransmitter maps available and implemented in JuSpace at the time of data analysis) were calculated via JuSpace toolbox (version 1.5; <https://github.com/juryxy/JuSpace>; last visited 01/27/2025) ([Dukart, Holiga et al. 2021](#)). The JuSpace toolbox allows for cross-modal correlations between imaging data and PET/SPECT-derived receptor maps

implemented in the toolbox. In JuSpace, pair-wise option was chosen to calculate differences between T1 and T2 contrast images of each subject and Spearman correlations with PET/SPECT-based neurotransmitter/receptor maps were calculated. Data were adjusted for spatial autocorrelation and 10000 permutations were used during computation of exact p -values. For these analyses a nominal significance level of $p < 0.05$ was chosen and FDR-correction was applied.

3. Results

3.1. Demographics and psychometric scores

Considering the dimensional analysis, neither BDI nor MaCS showed significant changes between T0 and T2. The categorical analysis approach (ESU vs. non-ESU) revealed significantly higher MaCS-scores in ESU at baseline and at follow-up, yet significant time-dependent effects were not detected. BDI scores did not significantly differ between the groups, neither at baseline, nor at follow-up (see [Table 1](#) for further details).

3.2. Changes of brain activation over time

Following the dimensional approach, i.e. treating all participants as whole group with different levels of potentially excessive smartphone use, SPM flexible factorial model of the contrast PHONE > NEU at T2 > T1 showed increased activation in left anterior cingulate gyrus and left caudate, reaching into left nucleus accumbens (NAcc) area (verified via small volume correction using an anatomical mask from the Neuromorphometrics atlas implemented in SPM12) after 72 h of smartphone restriction (see [Fig. 3](#) and [Table 2](#); PHONE > NEU at T1 > T2 did not show any significant clusters). The contrast ON > OFF at T1 > T2 revealed greater activation in left middle frontal gyrus, left superior parietal lobule, and left inferior occipital gyrus at T1, which is equivalent to decreased activation at T2, i.e. after 72 h of smartphone restriction (see [Fig. 3](#) and [Table 2](#); ON > OFF at T2 > T1 did not show any significant clusters).

Following the categorical approach, Time-by-group interaction contrasts using group as factor showed an interaction effect in bilateral superior parietal lobule in the ON > OFF contrast (see [Fig. 3](#) and [Table 2](#); no other contrast showed a significant effect). Post-hoc tests indicate that this effect was driven by activation in these regions in non-ESU at T2 (SPM One-sample t-tests of each group separately at T1 and T2 separately).

For completeness, see [Supplemental Table S1](#) for T1-effects and brain activation differences between groups at T1 and T2.

3.3. Associations between psychometric scores and changes of brain activation

In the contrast of PHONE > NEU at T2 – T1 left NAcc area showed significant positive correlation with BDI at T0 ($\rho = 0.59$, $p = 0.002$), right NAcc area showed significant positive correlation with BDI at T0 ($\rho = 0.59$, $p = 0.002$) and BDI at T2 ($\rho = 0.44$, $p = 0.026$), and right caudate showed significant correlation with BDI at T0 ($\rho = 0.45$, $p = 0.025$).

In the contrast of ON > OFF at T1 – T2 left middle frontal gyrus showed significant negative correlation with SPAI-I sleep interference ($\rho = -0.45$, $p = 0.023$) and left superior parietal lobule showed positive correlation with MaCS total score at T2 ($\rho = 0.41$, $p = 0.043$).

None of the changes in brain activation were significantly correlated with changes in psychometric scores.

3.4. Changes of cross-modal correlations over time

For the contrast PHONE > NEU 5HT1b, D1, MU, NMDA, and mGluR5 transmitter systems showed changes in cross-modal correlations

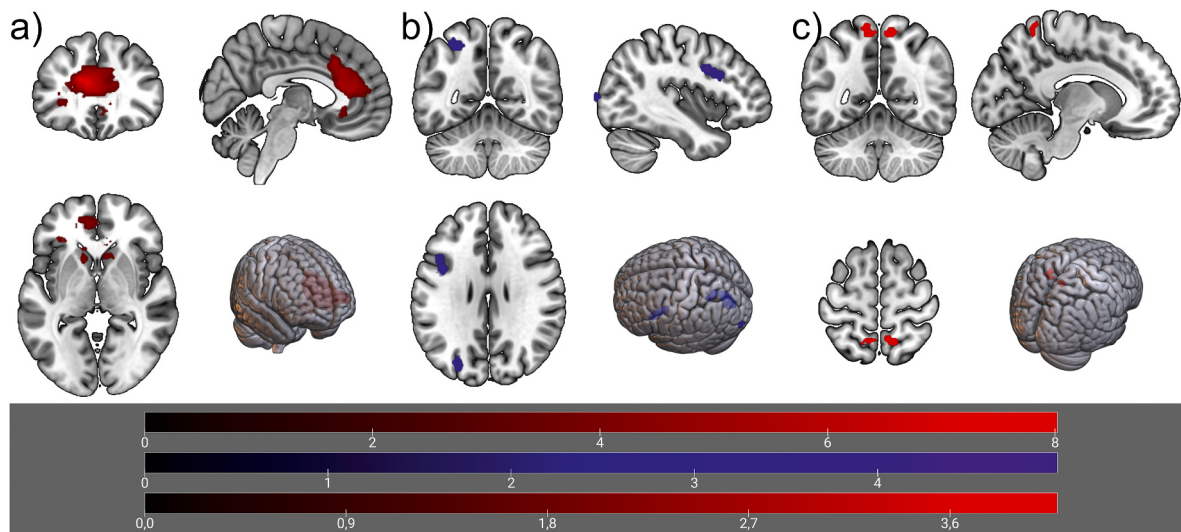


Fig. 3. CR-related brain activity over time. a) PHONE > NEU T2 – T1 (red) at $p < 0.001$, $k = 7$. b) ON > OFF T1 – T2 (blue) at $p < 0.001$, $k = 9$. c) Time-group interaction T2 > T1 and ESU > non-ESU of ON > OFF (red) at $p < 0.001$, $k = 9$. Color bars depict T-values of the respective contrasts, top: a), middle: b), bottom c). This figure was created using GIMP and MRICroGL (<https://www.nitrc.org/projects/mricrogl>; last visited 01/21/2024).

Table 2
Changes of brain activation over time.

Brain area	Cluster size k (voxel)	T value (peak voxel)	Peak voxel coordinates (MNI)		
			x	y	z
<i>PHONE > NEU T2-T1; $k = 7$</i>					
L anterior cingulate gyrus	1302	8.20	−9	30	18
L caudate	21	4.86	−12	21	−6
<i>PHONE > NEU T1-T2; $k = 7$</i>					
−	−	−	−	−	−
<i>ON > OFF T2-T1; $k = 9$</i>					
−	−	−	−	−	−
<i>ON > OFF T1-T2; $k = 9$</i>					
L middle frontal gyrus	65	5.05	−39	6	30
L superior parietal lobule	170	5.00	−24	−75	42
L inferior occipital gyrus	10	3.86	−36	−93	6
<i>Time-group interaction T2 > T1 & ESU > non-ESU of PHONE > NEU; $k = 7$</i>					
−	−	−	−	−	−
<i>Time-group interaction T1 > T2 & non-ESU > ESU of PHONE > NEU; $k = 7$</i>					
−	−	−	−	−	−
<i>Time-group interaction T2 > T1 & ESU > non-ESU of ON > OFF; $k = 9$</i>					
L superior parietal lobule	22	4.16	−12	−51	72
R superior parietal lobule	17	4.11	9	−54	63
<i>Time-group interaction T1 > T2 & non-ESU > ESU of ON > OFF; $k = 9$</i>					
−	−	−	−	−	−

between T1 and T2, whereas 5HT1b and D1 survived FDR-correction (see Fig. 4). For the contrast ON > OFF D1, GABAA, SERT, and VACHT systems showed changes in cross-modal correlations between T1 and T2, none of these results survived FDR-correction (see Fig. 4).

4. Discussion

We used a longitudinal approach to investigate effects of smartphone restriction in smartphone users, considering ESU as a dimensional continuum of smartphone use intensity and frequency. Three main findings emerged in this study: 1. No significant increase of craving-related behavior was observed after 72 h of restriction, 2. After 72 h of

restriction, CR-related brain activity changes were observed in craving-related regions, 3. Associations between changes of brain activation over time and addiction-related neurotransmitter systems were found.

For psychometry, neither BDI nor MaCS showed significant changes after 72 h of smartphone restriction, suggesting that participants neither experienced significant changes in mood nor in craving. Unaffected mood is consistent with a previous study (Wilcockson, Osborne and Ellis 2019). On the other hand, as a subjective impression, several participants reported improved mood and quality of life after 72 h of smartphone restriction. Therefore, future longitudinal studies on ESU should consider including qualitative interviews on mood, quality of life, compliance, and coping strategies during and/or after the restriction phase. Regarding unaffected craving, MaCS-differences might be higher for participants with ESU as for those without, thus in our dimensional approach effects for ESU are less visible. In fact, numerically our data shows different progression between ESU and non-ESU over time (see Table 1). Moreover, the employed MaCS, being a Craving Scale developed for substance use disorders, might not gather craving related to smartphone restriction ideally. Another possible explanation for the data not confirming our hypothesis is that the 72-h restriction period may have been too short to evoke a significant effect and/or sampling-rate of the MaCS was chosen too coarse.

To examine neurobiological correlates of craving, imaging studies comprising relatively short-time abstinence or restriction are helpful. For substance disorders, short-time smoking abstinence for 24 h in smokers revealed increased activity in the ACC and participants with higher ACC-activity after abstinence were more likely to relapse (Allenby et al., 2020). In line with these findings, we show increased activation of a sub-region of the ACC, the left anterior cingulate gyrus, after smartphone restriction. After a 12-h smoking abstinence, Allenby et al. showed increased activity in parietal, occipital, and central cortical regions as well as in the dorsal striatum and in thalamic areas in response to smoking cues. While we found increased activation in the left caudate in addition to changes in the left anterior cingulate gyrus, areas affected by smartphone and smoking abstinence (Allenby et al., 2020) seem to differ, as our results also highlight regions with reduced activity. Moreover, previous work found evidence for a positive correlation between pre-intervention craving intensity and activation in the dorsomedial prefrontal cortex (dmPFC) including superior frontal gyrus, ACC, and supplementary motor area, in a CR-task after 24-h of smoking abstinence (McClernon, Kozink et al. 2009). Our results did not fully

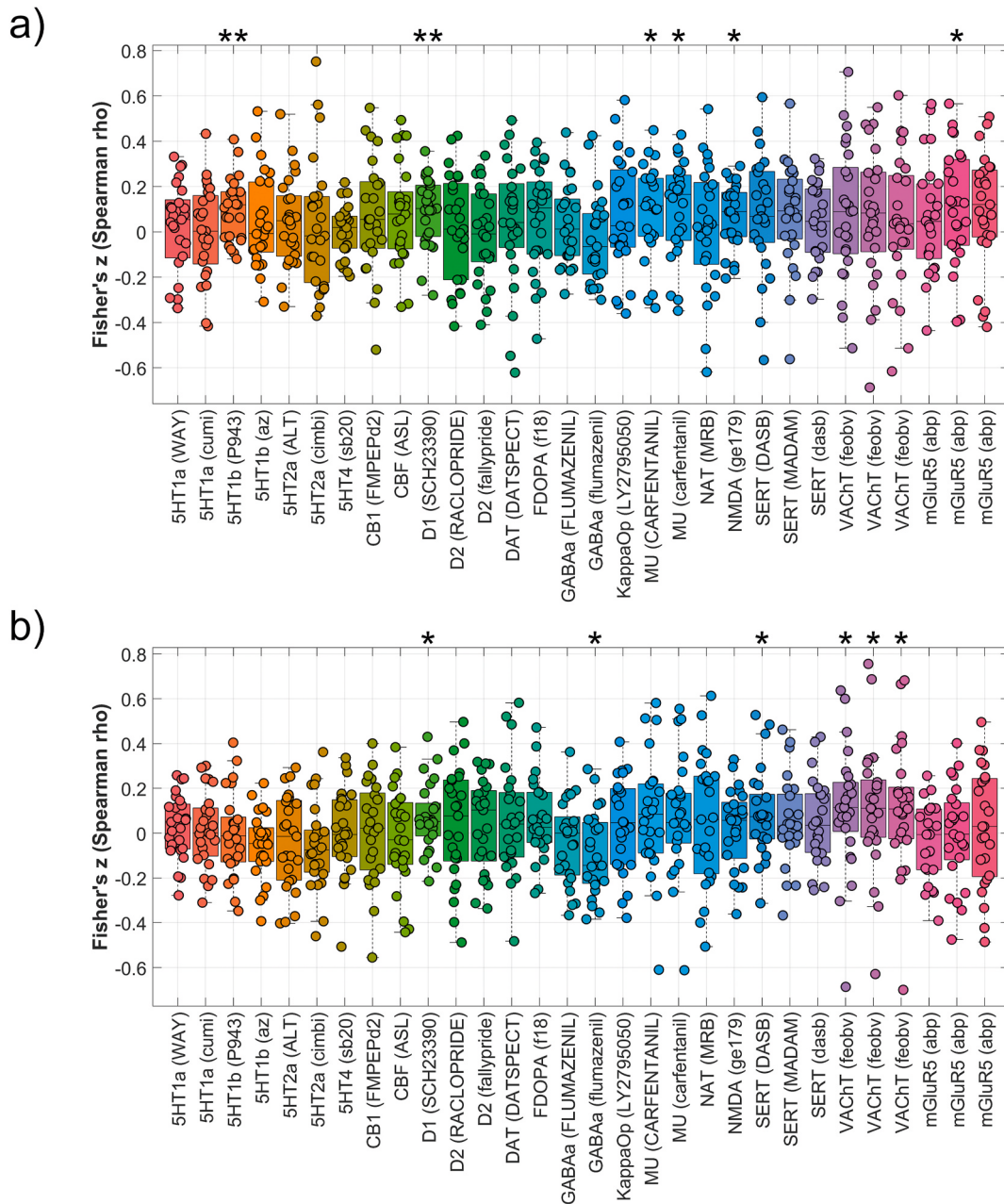


Fig. 4. Cross-modal Spearman correlations between changes of brain activation and receptor probability maps.

a) PHONE > NEU at T2 - T1, * exact $p < 0.05$, ** survives FDR correction. b) ON > OFF at T2 - T1, * exact $p < 0.05$. This figure was created using GIMP and JuSpace.

replicate these findings, since we only found associations of activation differences between T1 and T2 with depression severity, quality of sleep, and craving at T0 or T2, but not with changes between T0 and T2. It was also postulated that increased activation in visuospatial and reward circuitries underly abstinence-induced craving in smokers (Wang et al., 2007). In heroin addiction, after a short-term abstinence, increased activation was found in bilateral temporal, occipital, posterior cingulate cortex (PCC), ACC, thalamus, cerebellum, and left hippocampus during a CR-task (Lou, Wang et al. 2012). In patients with alcohol addiction, increased activation was measured in bilateral PCC, right angular gyrus, left pregenual ACC, right dorsal ACC, dmPFC, left orbitofrontal cortex, right occipitotemporal gyrus, left angular gyrus, right hippocampus, left parahippocampal gyrus, left amygdala, left NAcc, right ventral striatum, left thalamus, and bilateral cerebellum in a CR task in response to alcoholic cues after a 24 h-abstinence, whereas left anterior insula showed decreased activation (Huang et al., 2018). Thus, while increased

activation of the ACC, or respective sub-regions, seems to generalize across different addiction modalities, it is suggested that differences between behavioral and substance addiction are reflected in neuroimaging post restriction. Interestingly, in patients with IGD, a study examined effects on brain activity after a forced gaming break, reporting decreased (not increased) activation in ACC, parahippocampal gyrus, and in dorsolateral prefrontal cortex in a CR-task (Zhang, Hu et al. 2020). However, unlike the present study, the study did not include repeated fMRI before and after gaming restriction and addressed only cross-sectional differences compared to healthy controls. Thus, the finding of increased activation in ACC is consistent with previous studies examining abstinence in addictive disorders and is considered a correlate of craving and impulsive behavior (McClernon et al., 2009; Lou et al., 2012; Allenby et al., 2020; Zhao, Sallie et al. 2021).

To date, only very few studies investigated neural cue-reactivity in ESU. Our group could show altered cue-reactivity in ESU in the medial

prefrontal cortex, the ACC and parts of the occipital and temporal gyri with lower activation being correlated to higher compulsivity scores on the Smartphone Addiction Inventory (Oweda, Schmitgen et al., 2024; Schmitgen, Horvath et al., 2020). Further studies substantiated structural alterations and functional alterations in ESU and smartphone addiction in reward processing circuits, involving the ACC, caudate, insula and amygdala, as well as executive control networks, including the dorsolateral prefrontal cortex, which were associated with altered reward sensitivity (for reviews see (Montag & Becker, 2023, Leon Mendez, Padron et al. 2024)). Regarding the role of the caudate and NAcc in ESU, prior work reported lower functional connectivity between the NAcc and orbitofrontal cortex (OFC), as well as between the middle cingulate cortex and OFC in adolescents who used their smartphones excessively, which might implicate disrupted reward processing (Chun et al., 2018). Considering data on the role of the caudate and NAcc in addiction and cue-reactivity in general, these brain regions seem to play a key role in excessive drug using behavior and habit formation (Zhou et al., 2019) and might also apply for excessive non-substance related behavior.

The contrast ON > OFF at T1 – T2 showed decreased activation in left middle frontal gyrus, left superior parietal lobule and angular gyrus, and left inferior occipital gyrus after smartphone restriction. The results demonstrate a decreased activation in areas related to visual processing, language, and memory processing as well as motor functions and inhibitory processes (Heitzeg et al., 2014). This reduction was observed when participants were presented with cues of active smartphones, compared to smartphones that were not in use after restriction. Interestingly, other studies of abstinence found increased activation in some of the beforementioned areas: Increased activation of occipital regions was reported for abstinence in heroin addiction (Lou et al., 2012) and higher activation of the left angular gyrus was also shown after abstinence in alcohol addiction (Huang et al., 2018). The angular gyrus is considered a part of the Default Mode Network (DMN) which is assumed to act as a “cross-modal hub”, directing attention to important information, among other functions (Seghier, 2013). Given the hypo-activation in left angular gyrus as well as in areas of visual processing, it can be speculated that the cues of activated smartphones compared to turned-off versions seem to be less stimulating after smartphone restriction. Taken together with our findings in PHONE > NEU T2 – T1 and our behavioral findings, this could indicate two competing processes: Images of smartphones per se evoking neural craving processes while smartphones in use seem less stimulating. This in turn could explain why no change of craving was observed on the behavioral level. Also, the observed increase of activation of ACC in PHONE > NEU T2 – T1 might indicate that participants learned to better recruit neuronal resources for controlling impulsive/reactive responses (Brand, Young et al. 2016; Brand, Wegmann et al. 2019) after 72 h of smartphone restriction. This seems to be particularly true for operating smartphones, as we observed decreased activation of occipital regions in ON > OFF after 72 h of smartphone restriction, reflecting a decrease of salience of operating smartphones after restriction. In terms of the distinction between “wanting” and “liking” this might indicate a decrease of the “wanting” component after restriction, especially regarding operating smartphones, while the “liking” component may remain unaffected after 72 h of smartphone restriction. Moreover, taken together and especially regarding our finding in NAcc and our findings associated with reward, inhibitory control, salience, executive function, and memory, our findings are in accordance with the I-PACE model (Brand, Young et al. 2016; Brand, Wegmann et al. 2019). The I-PACE model illustrates the associations between CR, craving and reduced inhibitory control which lead to habituation and thus play a central part in development and perpetuation of addictive disorders (Brand, Young et al. 2016; Brand, Wegmann et al. 2019). Underlying brain circuits involve fronto-striatal areas, dorsolateral prefrontal areas, and the dorsal striatum (Brand, Wegmann et al. 2019), including functional networks predominantly processing reward, habit, salience, executive, memory, and self-directed networks

(Zilverstand et al., 2018). Several studies suggested that changes in brain activation in ESU seem to involve several brain networks such as reward, affective, and cognitive processes and might show similarities to other addictive behaviors (Montag & Becker, 2023). Clearly, further studies, specifically tailored to these aspects, are needed to test these assumptions.

Time-by-group interactions showed increased activation in superior parietal lobule, which is associated with sensorimotor processing, an indispensability for the skillful use of tools (Yalachkov & Naumer, 2011). The post-hoc effect found in superior parietal lobule in non-ESU at T2 might indicate stronger suppressive processes in motor preparation in non-ESU. Conversely, these findings point towards neural craving signaling, which is more present in participants more prone to excessively using their smartphone after 72 h of restriction.

When examining the relationships between brain activity changes and behavior in PHONE > NEU T2 – T1, bilateral NAcc showed significant positive correlations with BDI at baseline and right NAcc also with BDI at T2. Additionally, the right caudate showed positive correlation with BDI at baseline. Both regions are known to play a significant role in reward processing and major depressive disorder (Pizzagalli et al., 2009). This might indicate that changes of reward processing during smartphone restriction happen and support improved mood but depend on severity of depressiveness before smartphone restriction. Also, the weaker correlation observed between the activation of these regions and BDI-scores at T2 in combination with the lower BDI-scores at T2 suggests that the improvement in mood following smartphone use restriction may be modulated by these regions. In ON > OFF T1 – T2, decrease of left middle frontal gyrus and left superior parietal lobule activation after 72 h of restriction showed negative correlation with SPAI-I sleep interference and positive correlation with MaCS total score at T2, respectively. The negative correlation between middle frontal gyrus and SPAI-I sleep interference might reflect that the ability to suppress the urge to use the smartphone (mediated by frontal motor-inhibitory processes), e. g. during bedtime, improves quality of sleep. The positive correlation between superior parietal lobule and MaCS at T2 indicates a neural craving signal after 72 h of smartphone restriction.

Cross-modal correlations showed significant changes for PHONE > NEU at T2 – T1 for receptor probability maps of D1 and 5HT1b-Systems. This finding suggests that neural changes in smartphone restriction might be mediated through the respective neurotransmitter systems, which are already known to be relevant in the process of addiction (Volkow, Fowler et al. 2009; Kirby et al., 2011; Müller & Homberg, 2015, Volkow, Michaelides and Baler 2019; Alonso, O'Connor et al. 2022). Changes in DA transmission were described to be associated with craving in an animal model (Alonso, O'Connor et al. 2022). However, the role of DA dysfunctions in behavioral addictions i.e. in gambling disorder remains ambiguous (Potenza, 2018). Additionally, MU, NMDA, and mGluR5 receptor maps showed associations with changes of brain activation but did not survive correction for multiple comparisons. All these neurotransmitter systems have been reported to be associated to addiction, with the MU-opioid receptor system, in particular, potentially being linked to our findings in the NAcc (Gomez-Andres, Cunillera et al. 2022). Considering our cross-modal findings for ON > OFF at T1 – T2, D1, GABAA, SERT, and VACHT showed associations, but did not survive FDR-correction. As discussed before, the serotonin and dopamine transmitter systems are involved in addiction-specific processes. Also, GABA and Acetylcholine are known to play a major role in alcohol- and nicotine addiction, respectively (Tomkins & Sellers, 2001).

While our study has several strengths and novel aspects, such as being the first to investigate cue reactivity in ESU in a longitudinal setting, accounting for the effects of a phase of smartphone restriction and analyzing correlations with psychometric scores and receptor probability maps, potential shortcomings of our study must be acknowledged as well: First, although the participants were instructed to completely abstain from smartphone use, no control mechanisms were implemented to verify whether participants used their smartphones

occasionally. Moreover, our data does not disentangle craving for smartphone use and craving for social interaction, nowadays two tightly intertwined processes. Although our data shows relatively robust findings without unraveling these processes, future studies should clearly aim to address this aspect. Second, although participants negated any psychiatric comorbidities, we did not perform detailed interviews of such, hence we cannot fully eliminate the possibility of potentially confounding mental diseases. Third, the study's sample size is relatively modest and in our correlation analyses, we partially report findings uncorrected for multiple comparisons. Implications drawn from our results therefore should be treated with scientifically adequate caution. Fourth, a third group without smartphone restriction could have been added as another control group. We decided otherwise, since we strongly suspected this would have exceeded the limits of feasibility and interpretability of our study. For further validation of our findings, future research should use larger, more diverse samples and consider implementing a third participant group without smartphone restriction as control.

In conclusion, our study presents novel evidence considering the underlying neural mechanisms of smartphone restriction in a longitudinal setting. Although no increased behavioral correlate of craving in terms of scores of the MaCS was found, our data suggest that craving-related neural processes in terms of brain-activation changes over time, ROI-based brain-behavior correlations, and correlations to addiction-associated neurotransmitter-systems are evoked by 72 h of smartphone restriction. Especially ACC, regions involved in reward processing, such as NAcc, and regions linked to processes of motor-behavior and -inhibition, as well as multisensory integration seem to play a key role in restriction of smartphone usage. Smartphone restriction seems to show parallels to abstinence of respective drugs in other addictions or even craving food (Pelchat, Johnson et al. 2004) in some aspects, and remarkably so in our continuous study collective, involving self-reported ESU and non-ESU participants. Further research is clearly necessary to examine the effects of smartphone restriction in more detail, especially regarding other task-related activity.

CRedit authorship contribution statement

Mike M. Schmitgen: Writing – original draft, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Gudrun M. Henemann:** Writing – original draft, Methodology, Investigation. **Julian Koenig:** Writing – review & editing. **Marie-Luise Otte:** Writing – original draft, Methodology, Investigation. **Jakob P. Rosero:** Investigation. **Patrick Bach:** Writing – review & editing. **Sophie H. Haage:** Investigation. **Nadine D. Wolf:** Writing – review & editing, Conceptualization. **Robert C. Wolf:** Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization.

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.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. We thank Gianmarco Brancato and Meliha Imamovic for support in recruiting participants and MRI acquisition, Sophia Niarchos and Laura Bakker for language editing, and our study participants for their time and interest in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chb.2025.108610>.

Data availability

Data will be made available on request.

References

- Abdul Rashid, A., Suppiah, S., Syed Nasser, N., Sharifat, H., Mohamad, M., Loh, J. L., Ibrahim, B., Ibrahim, N. S. N., Mohad Azmi, N. H., Abdul Rahim, E., Ahmad Apandi, L. M., Ab Hamid, S., Ngee Thai, Y., Ching, S. M., & Hoo, F. K. (2021). The neurobiology of smartphone addiction in emerging adults evaluated using brain morphometry and resting-state functional MRI. *Neuroscience Research Notes*, 4(4), 19–28.
- Allenby, C., Falcone, M., Wileyto, E. P., Cao, W., Bernardo, L., Ashare, R. L., Janes, A., Loughead, J., & Lerman, C. (2020). Neural cue reactivity during acute abstinence predicts short-term smoking relapse. *Addiction Biology*, 25(2), Article e12733.
- Alonso, I. P., O'Connor, B. M., Bryant, K. G., Mandalaywala, R. K., & España, R. A. (2022). Incubation of cocaine craving coincides with changes in dopamine terminal neurotransmission. *Addict Neurosci*, 3.
- Anselme, P., & Robinson, M. J. (2016). Wanting, "liking," and their relation to consciousness. *J Exp Psychol Anim Learn Cogn*, 42(2), 123–140.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, 4, 561–571.
- Beck, A., Wüstenberg, T., Genauck, A., Wrase, J., Schlagenhaut, F., Smolka, M. N., Mann, K., & Heinz, A. (2012). Effect of brain structure, brain function, and brain connectivity on relapse in alcohol-dependent patients. *Archives of General Psychiatry*, 69(8), 842–852.
- Brand, M., Wegmann, E., Stark, R., Müller, A., Wölfling, K., Robbins, T. W., & Potenza, M. N. (2019). The Interaction of Person-Affect-Cognition-Execution (I-PACE) model for addictive behaviors: Update, generalization to addictive behaviors beyond internet-use disorders, and specification of the process character of addictive behaviors. *Neuroscience & Biobehavioral Reviews*, 104, 1–10.
- Brand, M., Young, K. S., Laier, C., Wölfling, K., & Potenza, M. N. (2016). Integrating psychological and neurobiological considerations regarding the development and maintenance of specific Internet-use disorders: An Interaction of Person-Affect-Cognition-Execution (I-PACE) model. *Neuroscience & Biobehavioral Reviews*, 71, 252–266.
- Brett, M., Anton, J.-L., Valabregue, R., & Poline, J.-B. (2002). "Region of interest analysis using an SPM toolbox. *NeuroImage*, 16 [Abstract].
- Chun, J. W., Choi, J., Cho, H., Choi, M. R., Ahn, K. J., Choi, J. S., & Kim, D. J. (2018). Role of frontostriatal connectivity in adolescents with excessive smartphone use. *Front Psychiatry*, 9, 437.
- Darvesh, N., Radhakrishnan, A., Lachance, C. C., Nincic, V., Sharpe, J. P., Ghassemi, M., Strauss, S. E., & Tricco, A. C. (2020). Exploring the prevalence of gaming disorder and internet gaming disorder: A rapid scoping review. *Systematic Reviews*, 9(1), 68.
- Demirci, K., Akgönül, M., & Akpınar, A. (2015). Relationship of smartphone use severity with sleep quality, depression, and anxiety in university students. *J Behav Addict*, 4(2), 85–92.
- Dieterich, R., & Endrass, T. (2022). Neural correlates of cue reactivity and the regulation of craving in substance use disorders. *Zeitschrift für Klinische Psychologie und Psychotherapie*, 51(3–4), 263–270.
- Dukart, J., Holiga, S., Rullmann, M., Lanzenberger, R., Hawkins, P. C. T., Mehta, M. A., Hesse, S., Barthel, H., Sabri, O., Jech, R., & Eickhoff, S. B. (2021). JuSpace: A tool for spatial correlation analyses of magnetic resonance imaging data with nuclear imaging derived neurotransmitter maps. *Human Brain Mapping*, 42(3), 555–566.
- Dukart, J., Jech, R., Ruziska, F., Vyzamal, J., Rullmann, M., Hesse, S., Barthel, H., Sabri, O., & Eickhoff, S. (2020). JuSpace: A tool for spatial correlation analyses of functional and structural magnetic resonance imaging data with positron emission tomography derived receptor maps. *Biological Psychiatry*, 87(9), S190.
- Eide, T. A., Aarestad, S. H., Andreassen, C. S., Bilder, R. M., & Pallesen, S. (2018). Smartphone restriction and its effect on subjective withdrawal related scores. *Frontiers in Psychology*, 9, 1444.
- Gomez-Andres, A., Cunillera, T., Rico, I., Naval-Baudin, P., Camins, A., Fernandez-Coello, A., Gabarrós, A., & Rodriguez-Fornells, A. (2022). The role of the anterior insular cortex in self-monitoring: A novel study protocol with electrical stimulation mapping and functional magnetic resonance imaging. *Cortex*, 157, 231–244.
- Haug, S., Castro, R. P., Kwon, M., Filler, A., Kowatsch, T., & Schaub, M. P. (2015). Smartphone use and smartphone addiction among young people in Switzerland. *J Behav Addict*, 4(4), 299–307.
- Heitzeg, M. M., Nigg, J. T., Hardee, J. E., Soules, M., Steinberg, D., Zubieta, J. K., & Zucker, R. A. (2014). Left middle frontal gyrus response to inhibitory errors in children prospectively predicts early problem substance use. *Drug and Alcohol Dependence*, 141, 51–57.
- Henemann, G. M., Schmitgen, M. M., Wolf, N. D., Hirjak, D., Kubera, K. M., Sambataro, F., Bach, P., Koenig, J., & Wolf, R. C. (2023a). Cognitive domain-independent aberrant frontoparietal network strength in individuals with excessive smartphone use. *Psychiatry Research-Neuroimaging*, 329.
- Henemann, G. M., Schmitgen, M. M., Wolf, N. D., Hirjak, D., Kubera, K. M., Sambataro, F., Lemenager, T., Koenig, J., & Wolf, R. C. (2023b). Neurochemical

- correlates of cue reactivity in individuals with excessive smartphone use. *Eur Addict Res*, 29(1), 71–75.
- Hirjak, D., Henemann, G. M., Schmitgen, M. M., Götz, L., Wolf, N. D., Kubera, K. M., Sambataro, F., Leménager, T., Koenig, J., & Wolf, R. C. (2022). Cortical surface variation in individuals with excessive smartphone use. *Developmental Neurobiology*, 82(4), 277–287.
- Horvath, J., Mundinger, C., Schmitgen, M. M., Wolf, N. D., Sambataro, F., Hirjak, D., Kubera, K. M., Koenig, J., & Christian Wolf, R. (2020). Structural and functional correlates of smartphone addiction. *Addictive Behaviors*, 105, Article 106334.
- Huang, Y., Mohan, A., De Ridder, D., Sunaert, S., & Vanneste, S. (2018). The neural correlates of the unified percept of alcohol-related craving: A fMRI and EEG study. *Scientific Reports*, 8(1), 923.
- Itzhak-Israeli, P. S., Yael, H., Matsree, E., Pe'er-Nissan, H., Lancman, S. O., R. B., G. L., Motiei, M., Betzer, O., Gispán, I., Popovtzer, R., Anker, Y., Ma, F., & Y. G. (2024). A novel delta opioid receptor specific peptide reduces craving in an animal model of cocaine seeking. *Addiction Neuroscience*, 12, Article 100159.
- Kirby, L. G., Zeeb, F. D., & Winstanley, C. A. (2011). Contributions of serotonin in addiction vulnerability. *Neuropharmacology*, 61(3), 421–432.
- Kwon, M., Kim, D. J., Cho, H., & Yang, S. (2013a). The smartphone addiction scale: Development and validation of a short version for adolescents. *PLoS One*, 8(12), Article e83558.
- Kwon, M., Lee, J. Y., Won, W. Y., Park, J. W., Min, J. A., Hahn, C., Gu, X., Choi, J. H., & Kim, D. J. (2013b). Development and validation of a smartphone addiction scale (SAS). *PLoS One*, 8(2), Article e56936.
- Lemmens, J. S., Valkenburg, P. M., & Gentile, D. A. (2015). The internet gaming disorder scale. *Psychological Assessment*, 27(2), 567–582.
- Leon Mendez, M., Padron, I., Fumero, A., & Marrero, R. J. (2024). Effects of internet and smartphone addiction on cognitive control in adolescents and young adults: A systematic review of fMRI studies. *Neuroscience & Biobehavioral Reviews*, 159, Article 105572.
- Lin, H. M., Chang, Y. T., Chen, M. H., Liu, S. T., Chen, B. S., Li, L., Lee, C. Y., Sue, Y. R., Sung, T. M., Sun, C. K., & Yeh, P. Y. (2022). Structural and functional neural correlates in individuals with excessive smartphone use: A systematic review and meta-analysis. *Int J Environ Res Public Health*, 19(23).
- Lin, Y. H., Chang, L. R., Lee, Y. H., Tseng, H. W., Kuo, T. B., & Chen, S. H. (2014). Development and validation of the smartphone addiction inventory (SPAI). *PLoS One*, 9(6), Article e98312.
- Lin, Y. H., Chiang, C. L., Lin, P. H., Chang, L. R., Ko, C. H., Lee, Y. H., & Lin, S. H. (2016). Proposed diagnostic criteria for smartphone addiction. *PLoS One*, 11(11), Article e0163010.
- Lou, M., Wang, E., Shen, Y., & Wang, J. (2012). Cue-elicited craving in heroin addicts at different abstinence time: An fMRI pilot study. *Substance Use & Misuse*, 47(6), 631–639.
- McClernon, F. J., Kozink, R. V., Lutz, A. M., & Rose, J. E. (2009). 24-h smoking abstinence potentiates fMRI-BOLD activation to smoking cues in cerebral cortex and dorsal striatum. *Psychopharmacology (Berl)*, 204(1), 25–35.
- Montag, C., & Becker, B. (2023). Neuroimaging the effects of smartphone (over-)use on brain function and structure—a review on the current state of MRI-based findings and a roadmap for future research. *Psychoradiology*, 3, Article kkad001.
- Montag, C., Wegmann, E., Sariyska, R., Demetrovics, Z., & Brand, M. (2019). How to overcome taxonomical problems in the study of Internet use disorders and what to do with "smartphone addiction. *J Behav Addict*, 1–7.
- Müller, C. P., & Homberg, J. R. (2015). The role of serotonin in drug use and addiction. *Behavioural Brain Research*, 277, 146–192.
- Nakovics, H., Diehl, A., Geiselhart, H., & Mann, K. (2009). [Development and validation of an overall instrument to measure craving across multiple substances: The mannheimer craving scale (MaCS)]. *Psychiatrische Praxis*, 36(2), 72–78.
- Oweda, J., Schmitgen, M. M., Henemann, G. M., Gerdes, M., & Wolf, R. C. (2024). Machine learning based classification of excessive smartphone users via neuronal cue reactivity. *Psychiatry Research Neuroimaging*, Article 111903.
- Pavia, L., Cavani, P., Di Blasi, M., & Giordano, C. (2016). Smartphone Addiction Inventory (SPAI): Psychometric properties and confirmatory factor analysis. *Computers in Human Behavior*, 63, 170–178.
- Pelchat, M. L., Johnson, A., Chan, R., Valdez, J., & Ragland, J. D. (2004). Images of desire: Food-craving activation during fMRI. *NeuroImage*, 23(4), 1486–1493.
- Pizzagalli, D. A., Holmes, A. J., Dillon, D. G., Goetz, E. L., Birk, J. L., Bogdan, R., Dougherty, D. D., Iosifescu, D. V., Rauch, S. L., & Fava, M. (2009). Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. *Am J Psychiatry*, 166(6), 702–710.
- Potenza, M. N. (2018). Searching for replicable dopamine-related findings in gambling disorder. *Biological Psychiatry*, 83(12), 984–986.
- Schmitgen, M. M., Horvath, J., Mundinger, C., Wolf, N. D., Sambataro, F., Hirjak, D., Kubera, K. M., Koenig, J., & Wolf, R. C. (2020). Neural correlates of cue reactivity in individuals with smartphone addiction. *Addictive Behaviors*, 108, Article 106422.
- Schmitgen, M. M., Wolf, N. D., Sambataro, F., Hirjak, D., Kubera, K. M., Koenig, J., & Wolf, R. C. (2022). Aberrant intrinsic neural network strength in individuals with "smartphone addiction": An MRI data fusion study. *Brain and Behavior*, 12(9).
- Seghier, M. L. (2013). The angular gyrus: Multiple functions and multiple subdivisions. *The Neuroscientist*, 19(1), 43–61.
- Sharma, R., & Weinstein, A. M. (2024). Recent treatment and novel imaging studies evaluating treatment of internet gaming disorder: A narrative review. *Front Psychiatry*, 15, Article 1408560.
- Sohn, S., Rees, P., Wildridge, B., Kalk, N. J., & Carter, B. (2019). Prevalence of problematic smartphone usage and associated mental health outcomes amongst children and young people: A systematic review, meta-analysis and GRADE of the evidence. *BMC Psychiatry*, 19(1), 356.
- Tomkins, D. M., & Sellers, E. M. (2001). Addiction and the brain: The role of neurotransmitters in the cause and treatment of drug dependence. *Canadian Medical Association Journal*, 164(6), 817–821.
- Volkow, N. D., Fowler, J. S., Wang, G. J., Baler, R., & Telang, F. (2009). Imaging dopamine's role in drug abuse and addiction. *Neuropharmacology*, 56, 3–8.
- Volkow, N. D., Michaelides, M., & Baler, R. (2019). The neuroscience of drug reward and addiction. *Physiological Reviews*, 99(4), 2115–2140.
- Volkow, N. D., Wang, G. J., Fowler, J. S., Tomasi, D., & Telang, F. (2011). Addiction: Beyond dopamine reward circuitry. *Proc Natl Acad Sci U S A*, 108(37), 15037–15042.
- Wang, Z., Faith, M., Patterson, F., Tang, K., Kerrin, K., Wileyto, E. P., Detre, J. A., & Lerman, C. (2007). Neural substrates of abstinence-induced cigarette cravings in chronic smokers. *Journal of Neuroscience*, 27(51), 14035–14040.
- Wartberg, L., Kriston, L., & Thomasius, R. (2017). The prevalence and psychosocial correlates of internet gaming disorder. *Dtsch Arztebl Int*, 114(25), 419–424.
- Wilcockson, T. D. W., Osborne, A. M., & Ellis, D. A. (2019). Digital detox: The effect of smartphone abstinence on mood, anxiety, and craving. *Addictive Behaviors*, 99, Article 106013.
- Yalachkov, Y., & Naumer, M. J. (2011). Involvement of action-related brain regions in nicotine addiction. *Journal of Neurophysiology*, 106(1), 1–3.
- Yan, C. G., Wang, X. D., Zuo, X. N., & Zang, Y. F. (2016). Dpabi: Data processing & analysis for (Resting-State) brain imaging. *Neuroinformatics*, 14(3), 339–351.
- Zhang, J., Hu, Y., Li, H., Zheng, H., Xiang, M., Wang, Z., & Dong, G. (2020). Altered brain activities associated with cue reactivity during forced break in subjects with Internet gaming disorder. *Addictive Behaviors*, 102, Article 106203.
- Zhao, Y., Sallie, S. N., Cui, H., Zeng, N., Du, J., Yuan, T., Li, D., De Ridder, D., & Zhang, C. (2021). Anterior cingulate cortex in addiction: New insights for neuromodulation. *Neuromodulation: Technology at the Neural Interface*, 24(2), 187–196.
- Zheng, H., Hu, Y., Wang, Z., Wang, M., Du, X., & Dong, G. (2019). Meta-analyses of the functional neural alterations in subjects with Internet gaming disorder: Similarities and differences across different paradigms. *Progress In Neuro-Psychopharmacology & Biological Psychiatry*, 94, Article 109656.
- Zhou, X., Zimmermann, K., Xin, F., Zhao, W., Derckx, R. T., Sassmannshausen, A., Scheele, D., Hurlmann, R., Weber, B., Kendrick, K. M., & Becker, B. (2019). Cue reactivity in the ventral striatum characterizes heavy cannabis use, whereas reactivity in the dorsal striatum mediates dependent use. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 4(8), 751–762.
- Zilverstand, A., Huang, A. S., Alia-Klein, N., & Goldstein, R. Z. (2018). Neuroimaging impaired response inhibition and salience attribution in human drug addiction: A systematic review. *Neuron*, 98(5), 886–903.