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Influences of excessive smartphone use on subjective symptoms, mood, and autonomic nervous reactivity

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ABSTRACT

Influences of excessive smartphone use on subjective symptoms, anxiety, mood, autonomic nervous reactivity and salivary cortisol was assessed, by examining differences in these parameters including autonomic and endocrine system responses to a psychological stressor (Mental arithmetic), between excessive and non-excessive smartphone users, and between long time use period and short time use period in each user group, in 28 female college students (18 to 23 years old). Subjective symptoms assessed by Cornell medical index (CMI), and anxiety assessed by state-trait anxiety inventory (STAI), were significantly higher in excessive users, and physical symptoms in CMI and trait anxiety in STAI reduced significantly after 2 weeks of short time use period in excessive users. Repeated measures ANOVA revealed decreased autonomic nervous reactivity to mental arithmetic assessed by heart rate variability in excessive users, but not in non-excessive users, and improved reactivity after 2 weeks of short time use period in excessive users.

Keywords: smartphone use; Cornell medical index; state-trait anxiety inventory; mental arithmetic; heart rate variability

1. INTRODUCTION

Number of smartphone users are markedly increasing in these days and various health problems related with smartphone use are becoming a major issue. Munezawa and coworkers (2011) reported the association between sleep disturbance and mobile phone use after light out. Boumosleh and Jaalouk (2017) reported decreased sleep quality and sleeping hours due to smartphone use. Dewi and coworkers (2018) pointed out significant positive correlation between smartphone use at night, and sleep disturbance and depressive symptoms, in adolescents. Dharmadhikari et al. (2019) reported significant association of smartphone addiction with poorer sleep quality and higher perceived stress in medical students. Inoue et al. (2019) suggested increased breakfast skipping behavior and physical complaint in frequent smartphone users. Emotional exhaustion was also reported to be associated with smartphone addiction (Brubaker & Beverly, 2020). Zou et al. (2019) found significant association between smartphone addiction and hypertension, and suggested that smartphone addiction may be a new risk factor for high blood pressure in adolescents. Park et al. (2019) suggested disruptions of the autonomic nervous system using heart rate variability method in internet gaming disorder. Thus, excessive or night time smartphone use could possibly cause various physical and mental health problems. However, most of literatures dealing with smartphone related health problems were cross-sectional studies. Then, the possibility that the health problems may be attributable not to smartphone use time itself but to personality trait to use smartphone for a long time, is not completely excluded. Longitudinal study or survey to elucidate whether these health problems improve or not by reducing smartphone use time for a certain period, was not enough and had better be conducted more.

Nose et al. (2017) elucidated that evening smartphone use may alter sleep-wake cycle, and consequently diminish cardiac autonomic nervous activity after awakening, by the method of heart rate variability (HRV) analysis. Internet addiction or excessive online gaming is described to cause higher sympathetic activity and lower parasympathetic activity associated with autonomic dysregulation (Chang et al., 2015; Lin et al., 2014). Therefore, excessive smartphone use may have some influence on autonomic nervous system, as well as physical and mental subjective symptoms.

Cornell Medical Index is a self-administered health questionnaire created by Brodman et al. in 1949 that collects a large body of significant medical and psychiatric data without the physician's participation. State-Trait Anxiety Inventory (STAI) is a self-administered measure of trait and state anxiety (Spielberger et al., 1970). Profile of mood states (POMS) is designed to measure a person's affective states, with scores of six subscales, and is thought to be a useful tool for estimating moods repeatedly and has been a popular research tool among psychologists

(Yokoyama & Araki, 1994). A visual analogue scale (VAS) is also an effective tool to assess subjective momentary feeling, which varies continuously and cannot easily be directly measured (McCormack et al., 1988; Gould et al., 2001; Wewers & Lowe, 1990).

Numerous studies have indicated that a spectral analysis of heart rate variability (HRV) is a powerful tool for evaluating autonomic nervous functions non-invasively (Akselrod et al., 1985; Berger et al., 1989; Langewitz et al., 1991; Montano et al., 1994; Pagani et al., 1986; 1991; Pomeranz et al., 1985). Blood pressure is also considered to be related with autonomic nervous function or mental state (Conway et al., 1983; Steptoe & Sawada, 1989). Salivary cortisol measurement is a useful tool to evaluate hypothalamus– pituitary– adrenal axis (HPA axis) activity noninvasively (Giles et al., 2014; Qi et al., 2016).

Then, we studied influences of excessive smartphone use on mood and autonomic nervous system in female college students using POMS and VAS for mood estimation; HRV, systolic and diastolic blood pressure (BP) for an evaluation of autonomic nervous system; and salivary cortisol for an estimation of HPA axis status. Kim et al. (2021) tried to identify video game addiction using HRV Parameters and mentioned that the accuracy of the parameters was not enough. Numerous studies have demonstrated that autonomic nervous function is modulated by various factors such as a physical stimulus (Sun et al., 1993; Yamamoto et al., 1991) and a mental load (Langewitz et al., 1991; Pagani et al., 1991). More investigation using HRV parameters including the time course or reactivity of the parameters to some kind of stimulus in excessive smartphone users, may be necessary to elucidate the influence of the excessive use on autonomic nervous system. Therefore, applying 15 minutes of mental arithmetic as a psychological stimulus, we analyzed reactivity of autonomic, endocrine and mood to the stimulus, along with basal states in excessive smartphone users (long time users) and non-excessive smartphone users (short time users). First, parameters taken during usual (familiar) smartphone use condition in both groups were compared and analyzed. Next, these parameters were compared with those taken after 2 weeks of unusual (unfamiliar) smartphone use condition in each group to know the parameters change dependent on the smartphone use time.

2. METHODS

2.1 Participants

The study was approved by The Ethics Committee of our university beforehand and was performed according to the Declaration of Helsinki. At first, a flyer to ask

smartphone use time and contact address, was delivered to almost every student in the same course. Next, criteria for long time smartphone users and that for short time smartphone users were determined as, longer than 5 and half hours per day and less than 3 and half hours per day, respectively, based on the collected data from the flyers and reports about smartphone use time in college and university students (Inashima & Horio, 2019; Uemura & Uemura, 2015). Potential participants were recruited among students in the same course. After all, 28 female college students (14 for long time users and the other 14 for short time users) agreed and participated in this study after providing written informed consents. Smartphone use time was confirmed by smartphone application (screen time) and/or self-report during the previous week of the experiment, and 1 long time user and 2 short time users were excluded from the analysis since they did not meet the criteria. The age of long time smartphone users ranged from 18 to 23 years old ($M \pm SD = 20.15 \pm 1.63$ y.o.), and that of short time smartphone users ranged from 18 to 23 years old ($M \pm SD = 20.75 \pm 1.48$ y.o.). Their height and weight were 159.62 ± 6.37 cm ($M \pm SD$) and 53.36 ± 9.22 kg ($M \pm SD$) for long users, and 158.25 ± 5.40 cm and 49.08 ± 4.06 kg for short users, which were not significantly different. They asked to abstain from eating, drinking and smoking for at least three hours before experiments, and to sleep for 6 hours or more on the previous day. Strenuous exercise and heavy drink on the previous day were also prohibited.

2.2 Procedure

The experimental procedure is mostly the same as that of our previous experiment (Sakuragi, 2019). Each subject underwent one or two experiments, an experiment under their usual smartphone use condition and that under their unusual smartphone use condition of two weeks, each planned on 4 weeks apart days to reduce any influences of menstrual cycle. The procedure was the same except for average smartphone use time for two weeks just before the experiment. An experiment under the usual smartphone use condition was carried out first, and that under unusual one was carried out next (4 weeks after the first experiment). That is, a long time user underwent the experiment under their usual smartphone use condition (long time use) first, and underwent the experiment under their unusual smartphone use condition (short time use) next, and a short time user underwent the experiment under their usual smartphone use condition (short time use) first and underwent the experiment under their unusual smartphone use condition (long time use) next. A comparison between data from long time users and data from short time users was made first to know differences between the two groups. Then, a comparison between data from familiar (usual) smartphone use condition and data from unfamiliar (unusual) smartphone use condition was made to know whether any changes between the two conditions occur in each group. 12 out of 13 long time users

achieved shorter time use for 2 weeks, and 5 out of 12 short time users achieved longer time use for 2 weeks. The day and time of the two experiments was equally planned since mood and autonomic nervous activity could change depending on the day of the week and the time zone (Malliani et al., 1991). The experiments were planned on the third day to ninth day of their menses (follicular phase), to minimize the influences of a menstrual cycle which could affect mood and autonomic nervous activity.

The experimental room and the around was kept quiet and the room temperature was kept at 22 ± 2 degree Celsius. The subjects entered the room and were asked to fill out CMI and STAI questionnaires. They were also asked to fill out POMS questionnaires and to write down VAS for an evaluation of their basal mood state. Each subject sat upright on a chair, while disc electrodes were attached for chest electrocardiograms (ECG) with CM5 leads, and a thermistor for detecting respiration was also attached just under one nostril. Blood pressure (BP) and heart rate (HR) were also measured every 5 minutes throughout the experiments with a sphygmomanometer (BP-203X, Colin Japan). Mental arithmetic was addition or subtraction of 2 two-digit integers from 10 to 99, such as: $87 + 24$, $28 - 59$, which were generated by random variable (RANDBETWEEN (10, 99)). The mental arithmetic problems printed on sheets of A4 paper, were continuously provided for 15 minutes, and the subjects were instructed to calculate as fast and accurate as possible, and to mark the point they just finished at 5 minutes and 10 minutes after the start of mental arithmetic period for later analysis. ECG and respiration curves were recorded throughout the experiment. Data were stored on a personal computer equipped with a 12-bit analog-digital converter (ADTM-98, Canopus, Kobe, Japan) for subsequent offline analysis.

Each experiment consisted of six parts: a pre POMS and VAS period of about 5 minutes (basal) followed by basal saliva sampling; basal recording of 10 minutes; mental arithmetic (MA) period of 15 minutes; 1st post POMS and VAS period of 5 minutes (after MA) for an evaluation of whatever mood states were induced by the MA; post-MA rest period of 30 minutes which were interrupted by post MA saliva sampling 10 minutes after MA, and 2nd post POMS and VAS period of 5 minutes (after Rest) for an evaluation of current mood states.

Subjects were asked to keep their eyes open and to keep quiet, and not to fall asleep, avoiding any disruptive movements of their heads or hands throughout the experiments.

2.3 Measures

Cornell Medical Index (CMI). — Subjective symptoms were assessed by the CMI which consists of 18 sections and 195 items. The A–L sections (144 items) represent physical state and the M–R sections (51 items) represent

mental state. Participants answered “yes” or “no” to indicate the presence or the absence of a symptom or a disorder. If the answer was “yes,” it indicated that the patient had symptoms and received a score of 2. On the other hand, a “no” answer indicated that the patient had no symptoms and was scored at one point (Costa & McCrae, 1977). This study used the Japanese version of the CMI, which was created by Kanehisa and colleagues (2001). CMI data were manually scored and summed for physical, mental and C.I.J. symptoms. C (cardiovascular system), I (fatigability), and J (frequency of illness) scores have been found effective to assess neurotic tendencies along with mental symptom scores.

State-Trait Anxiety Inventory (STAI) — The STAI is a commonly used measure of trait and state anxiety, and has 20 items for assessing trait anxiety and 20 for state anxiety (Spielberger et al., 1970). It is often used in psychological research as an indicator of anxiety. This study used the Japanese version of the STAI, which was created by (Mizuguchi et al., 1970).

Profile of mood states (POMS). Comprehensive mood was assessed by the POMS which was designed to measure a person’s mood states, and includes six subscales: Tension-anxiety; T-A, Depression-dejection; D, Anger-hostility; A-H, Vigor; V, Fatigue; F, and Confusion; C. Subjects are given a score for each trait according to their responses to certain statements which include key words such as unhappy, tense, careless, and cheerful. For each statement, subjects state how they feel at that moment, or how they felt over the previous day, few days, or week, by choosing one of the following responses: not at all; a little; moderately; quite a lot; extremely. Internal consistency for the Profile of Mood States was reported at 0.74, 0.81, 0.85, 0.89, 0.90, 0.73 Cronbach alpha rating for T-A, D, A-H, V, F, C, respectively (Kitaoka-Higashiguchi et al, 2005). Score for each scale was converted into T-score for parametric statistical analysis (Yokoyama & Araki, 1994).

Visual analogue scale (VAS). — Subjective momentary feelings about fatigue and irritation were evaluated by the VAS which was a horizontal line, 100 mm in length, anchored by word descriptions at each end, and a participant marks on the line the point that they feel represents their current feeling state (Gould et al., 2001; McCormack et al., 1988; Wewers & Lowe, 1990). Each score was determined by measuring the distance from the left end to the point they marked. The VAS was used for the assessment of fatigue and irritation. Higher ratings on each scale indicated more fatigued and more irritated.

Heart rate variability (HRV). — Heart rate varies according to respiration and blood pressure variation, and the extent of variation of heart rate is usually dependent on the autonomic nervous activity. HRV can be divided into two main components by spectral analysis, i.e., a high-frequency component (HF)

which corresponds to respiratory sinus arrhythmia and reflects parasympathetic nerve activity, and a low-frequency component (LF) which corresponds to Mayer wave related sinus arrhythmia and relates to both sympathetic and parasympathetic nerve activities (Akselrod et al., 1985; Berger et al., 1989; Montano et al., 1994; Pagani et al., 1986; Pomeranz et al., 1985). Therefore, we can know the level of autonomic nervous activity to a certain extent by the spectral analysis of HRV.

Blood pressure (BP). — Blood pressure is determined by cardiac output $\times$ total peripheral resistance, which are mainly regulated by endocrine system and autonomic nervous system. Short-term control of BP is mainly achieved by sympathetic and parasympathetic activity which will affect diameters of veins and arteries, heart rate and force of cardiac contraction, to adjust blood supply and its distribution in the body. Then, systolic and diastolic BP may be influenced by local circulation change, possibly made by vasoconstriction or vasodilatation, along with the change of autonomic nervous activity.

Salivary cortisol (Cortisol). — Salivary cortisol is known to increase after a stressful event and frequently used to evaluate the stress level (Giles et al., 2014; Qi et al., 2016). Salivary samples were collected by each subject through a cotton swab (Salivettes®: Sarstedt, Germany) keeping under her tongue for 2 minutes, thereafter, centrifuged at 1500g for 2 minutes and frozen at -20 degree Celsius until later analysis. Free cortisol levels were assayed in duplicate, employing Salimetrics® Cortisol Enzyme Immunoassay Kit (Salimetrics, Germany), and determined by a 4 parametric logistic regression analysis according to the manual provided by the Salimetrics®. Those samples whose intra-assay coefficient were over 20% (possibly caused by technical difficulties), were excluded from the analysis.

2.4 Data analysis

POMS data were summed to generate six sub-scales: T-A, D, A-H, V, F and C. These summed raw scores were converted into T-scores for parametric statistical analysis according to the POMS manual (Yokoyama & Araki, 1994). Combined score named total mood disturbance (TMD) was also calculated and analyzed (Kitaoka-Higashiguchi et al., 2005).

ECG data were digitized at a sampling frequency of 1 kHz on a personal computer. After detecting every R-wave peak, consecutive R-R intervals on the ECG were calculated, excluding ectopic beats and abrupt discharges in R-R intervals. Spectral analysis was applied to the time series data of R-R intervals for each 5 min block, using the maximum-entropy method (MemCalc Version 2.5, Suwa Trust) (Ohtomo et al., 1994). After calculating the power-spectral density, the magnitude of the power for HRV was obtained by measuring areas

under the spectral density curves. The values were divided into two major bands, a low-frequency component (LF; 0.04-0.15 Hz) and a high-frequency component (HF; 0.15-0.5 Hz). Thereafter, the amplitude of each frequency band was calculated as twice the power magnitude and the square root thereof. We considered HF amplitude (HF) as an index of parasympathetic nervous function and LF/HF amplitude (LF/HF) as a marker of relative sympathetic activity (Malliani et al., 1991; Pagani et al., 1986). Systolic BP and diastolic BP were measured for every 5 min.

Ten-minute data just prior to the MA period were used to establish pre-MA basal activity (basal 1 and basal 2). Fifteen-minute data for the MA period were divided into 3 five-minute blocks, and represented as MA 1, 2, 3. Thirty-minute data for the post-MA period were also divided into 6 five-minute blocks, and represented as post 1, 2, 3, 4, 5 and 6.

2.5 Statistical analysis

Student's *t*-test was carried out first, to clarify the differences of subjective symptoms and anxiety between long time smartphone users and short time smartphone users. Next, to examine whether the subjective symptoms and anxiety during usual smartphone use period would change to those during unusual period dependent on the smartphone use time, paired *t*-test was applied to the data from each group. Pearson's correlation coefficient was also calculated to know whether there was a linear correlation between smartphone use time and subjective symptoms or anxiety.

A repeated measures ANOVA is referred to as a within-subjects ANOVA and is suitable to investigate changes in values over time from the same participants, and can examine the difference of trend of values taken under different conditions. Therefore, to clarify the influences of long time smartphone use on mood, interactions between users (long user and short user: between subjects variable) and time course (basal, before MA and after Rest: within-subjects variable), interactions between period (long period and short period: within-subjects variable) and time course (basal, before MA and after Rest: within-subjects variable) in either users were examined by repeated measures analysis of variance (repeated measures ANOVA). Similarly, to elucidate the influence of excessive smartphone usage on autonomic nervous system, repeated measures ANOVA were performed at 2 steps as follows: 1step; group (long users and short users: between-subjects variable) $\times$ time course of the parameters (basal 1, basal 2 through MA 1, 2, 3 to post 1 to post 6: within-subjects variable) interaction were analyzed. 2nd step; main effect of trend (time course of the parameters) was examined to be significant in each group, to know the reactivity to the stimulus. Similarly, period (long period and short

period: within-subjects variable) $\times$ time course (basal 1, basal 2 through MA 1, 2, 3 to post 1 to post 6) interaction were analyzed at first. Main effect of trend (time course) was examined to be significant in each period at second, to know the reactivity to the stimulus. Since HF amplitudes in short time users seemed higher than those in long time users at all time-points, and HF amplitudes during short use period seemed higher than those during long use period at almost all time-points, Student's *t*-test and paired *t*-test was applied to know whether the values were significantly different between both users, and between both periods at each time point. Effect size (Cohen's *d* for student's *t*-test and paired *t*-test, *r* for Pearson's correlation coefficient and partial η^2 for repeated measures ANOVA) was also calculated to help readers better understand the importance of the findings in this study (Cohen, 1988; Faul et al., 2007; Mizumoto & Takeuchi, 2008). Statistical analysis was performed on a personal computer using Statview Ver. 5.0 (HULINKS), and differences with a probability value of less than 0.05, and correlation coefficient with a probability value of less than 0.01 were considered significant.

3. RESULTS

3.1 Influences on subjective symptoms and anxiety

Figure 1 shows CMI-scores obtained from long users and those obtained from short users. *T*-test revealed significantly higher physical score ($p = .0100$, $d = 1.172$), mental score ($p = .0227$, $d = 1.027$), and C.I.J. score ($p = .0084$, $d = 1.233$) in long users. Paired *t*-test revealed significantly lower physical score ($p = .0197$, $d = 0.301$) for short use period compared to that for long use period, in long users. Mental score and C.I.J. score did not decrease to significant level after short time use period of two weeks in long users. Three CMI scores did not significantly change after long time use period of two weeks in short users.

Figure 2 shows STAI-scores obtained from long users and those obtained from short users. *T*-test revealed significantly higher state anxiety score ($p = .0400$, $d = 0.909$), and trait anxiety score ($p = .0072$, $d = 1.231$) in long users. Paired *t*-test revealed significantly lower trait anxiety score ($p = .0351$, $d = 0.257$) for short use period compared to that for long use period, in long users. State anxiety score did not significantly change after short time use period of two weeks in long users. Both anxiety scores did not significantly change after long time use period of two weeks in short users, however, state anxiety score seems somewhat higher after long time use period ($p = .0752$).

Significant correlations between smartphone use time and physical ($r =$

.636, $p < 0.01$), mental ($r = .561$, $p < 0.01$), and C.I.J. score ($r = 0.714$, $p < 0.01$) in CMI, and trait anxiety ($r = .515$, $p < 0.01$) in STAI, were showed by Pearson's correlation coefficient applied to 1st experiment data set (taken during familiar condition), but not when applied to 2nd experiment data set (taken during unfamiliar condition).

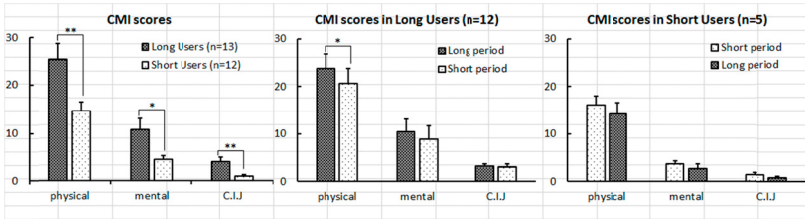


Figure 1. CMI-scores during usual period in long, and short users, during usual (long period) and unusual period (short period) in long users, and during usual (short period) and unusual period (long period) in short users. Asterisks (*) denote significant differences revealed by *t*-test or paired *t*-test

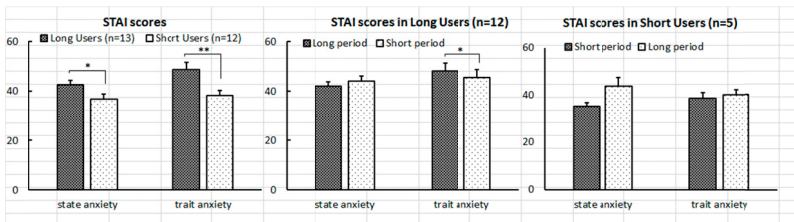


Figure 2. STAI-scores during usual period in long, and short users, during usual (long period) and unusual period (short period) in long users, and during usual (short period) and unusual period (long period) in short users. Asterisks (*) denote significant differences revealed by *t*-test or paired *t*-test

3.2 Influences on mood

Repeated measures ANOVA revealed no significant interaction of users (long user and short user) $\times$ time course (basal, before MA and after Rest) in each subscale of POMS. In long time users, repeated measures ANOVA revealed significant interaction of period (long period or short use period) $\times$ time course (basal, before MA and after Rest) in C subscale ($F(2,22) = 7.13, p = .00341$, partial $\eta^2 = 0.393$), and in TMD ($F(2,22) = 4.46, p = .0236$, partial $\eta^2 = 0.289$), that is, time courses of C score and TMD score were bidirectional in long use period and unidirectional in short use period. In short time users, repeated measures ANOVA revealed significant interaction of period (long period or short period) $\times$ time course (basal, before MA and after Rest) in A-H subscale ($F(2,8) = 5.03, p = .00385$, partial $\eta^2 = 0.557$), that is, A-H score change was less in long use period compared to that in short use period (Figure 3).

3.3 Autonomic nervous response

Autonomic nervous activity was assessed by HF amplitude and LF/HF amplitude of HRV, and its reactivity was evaluated applying 15 minutes of mental arithmetic to the subjects. Respiratory sinus arrhythmia (corresponds to HF: 0.15 to 0.5Hz) was separated from low frequency band (0.04 to 0.15Hz), since respiratory frequency from every subject was higher than 9/min (corresponds to 0.15 Hz).

Figure 4 shows trends of HF amplitudes in both users, both periods in each users throughout the experiments. There was no significant interaction of group (long users and short users) $\times$ time course (basal 1, basal 2 through MA 1, 2, 3 to post 1 to post 6) in HF amplitude, while significant main effect of trend was observed in short users ($F(10,110) = 3.69, p = .0003$, partial $\eta^2 = 0.251$), but not in long users. HF amplitudes in short time users seemed higher than those in long time users at all time-points, however, no significant difference was found by *t*-test. That is, parasympathetic activity (indicated by HF amplitude) was not necessarily higher in short users, but clearly reduced and recovered in response to MA stimulus in short users, but not in long users. In long time users, repeated measures ANOVA revealed significant interaction of period (long period or short period) $\times$ time course (basal 1, basal 2 through MA 1, 2, 3 to post 1 to post 6) in HF amplitude ($F(10,110) = 1.97, p = .0435$, partial $\eta^2 = 0.152$). That is, HF amplitudes in long time users exhibited no significant main effect of trend during long period, while exhibited significant main effect of trend after two weeks of short use period ($F(10,110) = 3.80, p = .0002$, partial $\eta^2 = 0.257$). In short time users, repeated measures ANOVA revealed no significant interaction of period $\times$ time course in HF amplitude,

however, HF amplitudes in short time users exhibited significant main effect of trend during short period ($F(10,40) = 2.21$, $p = .0451$, partial $\eta^2 = 0.347$), while exhibited no significant main effect of trend after two weeks of long use period. HF amplitudes during short use period seemed higher than those during long use period at almost all time-points, however, no significant difference was revealed by paired t -test, except for post 5 values in long time users ($p = .0479$, $d = 0.505$), and post 6 values in short time users ($p = .0286$, $d = 0.707$). There was no significant interaction of users (long user or short user) $\times$ trend nor main effects of user or trend in LF/HF amplitude. LF/HF amplitudes in long time users exhibited no significant main effect of trend during both periods. LF/HF amplitudes in short time users exhibited significant main effect of trend during short period ($F(10,40) = 2.91$, $p = .0079$, partial $\eta^2 = 0.421$), while exhibited no significant main effect of trend after two weeks of long use period (data not shown).

Figure 5 shows trends of systolic and diastolic blood pressure (BP) and heart rate (HR) throughout the experiments. Repeated measures ANOVA revealed no significant interaction of users (long time users or short time users) $\times$ time course (basal 1, basal 2 through MA 1, 2, 3 to post 1 to post 6), nor significant interaction of period (long period or short period) $\times$ time course in both users, in systolic BP (sBP), in diastolic BP (dBP), and in HR. Mean systolic and diastolic BPs, and HRs in long time users seemed higher than those in short time users at all time-points, despite main effects of users were not significant. Student's t -test showed significant differences at basal 1 ($p = .0049$, $d = 1.299$), basal 2 ($p = .0141$, $d = 1.140$), MA 1 ($p = .0138$, $d = 1.112$), and MA 2 ($p = .0348$, $d = 0.936$) in sBP, at basal 1 ($p = .0331$, $d = 0.946$), basal 2 ($p = .0045$, $d = 1.353$), and MA 1 ($p = .0106$, $d = 1.161$) in dBP, and at basal 2 ($p = .0376$, $d = 0.947$), MA 2 ($p = .0147$, $d = 1.101$), post 1 ($p = .0322$, $d = 0.978$), and post 3 ($p = .0425$, $d = 0.897$) in HR.

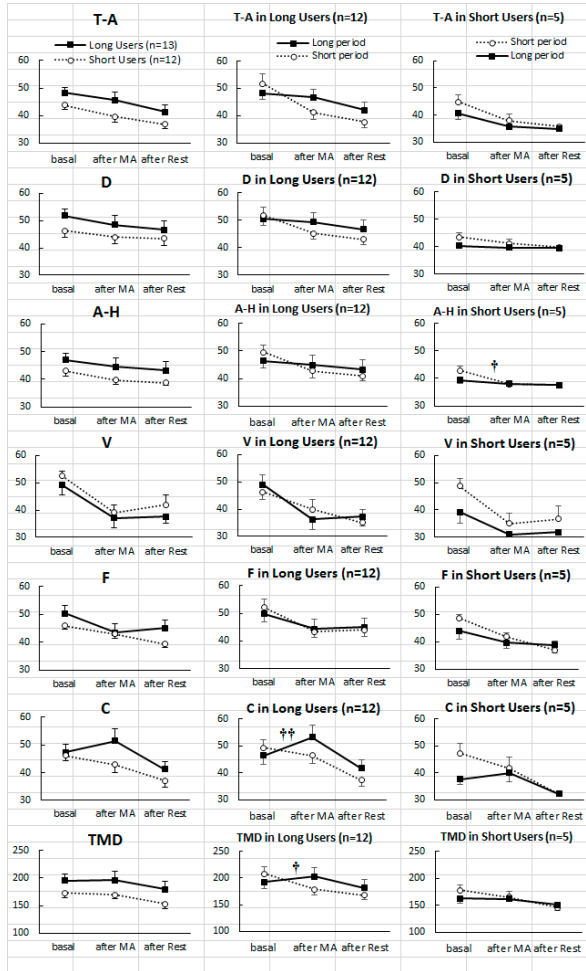


Figure 3. Changes in T-scores of A-H, C, TMD of POMS during usual period in long, and short users, during usual (long period) and unusual period (short period) in long users, and during usual (short period) and unusual period (long period) in short users. Closed square: scores during long use period (Long period), open circle: scores during short use period (Short period). All values are represented as $M \pm SE$. A dagger (†) and daggers (††) denote significant period $\times$ time course interaction revealed by repeated measures ANOVA, at level of $p < 0.05$ and $p < 0.01$, respectively

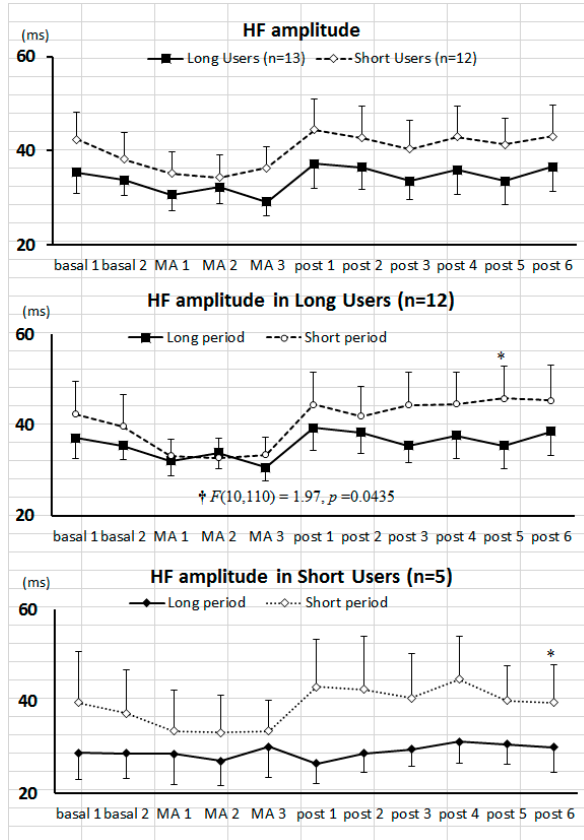


Figure 4. Time courses of HF amplitude during usual period in long, and short users, during usual (long period) and unusual period (short period) in long users, and during usual (short period) and unusual period (long period) in short users. Closed square: scores during long use period (Long period), open circle: scores during short use period (Short period). All values are represented as $M \pm SE$. A dagger (†) denotes significant ($p < 0.05$) period $\times$ time course interaction revealed by repeated measures ANOVA. An asterisk (*) denotes significant difference between both conditions revealed by paired t -test, at level of $p < 0.05$

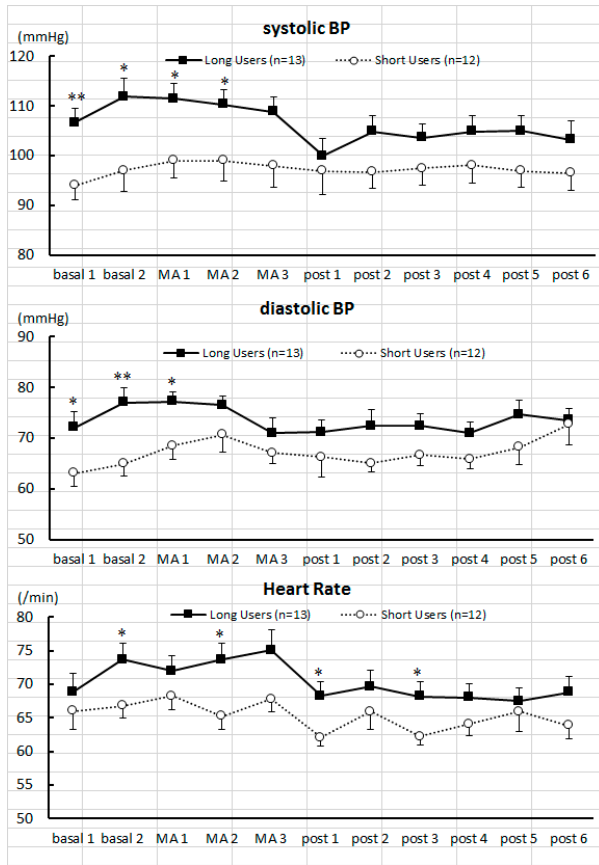


Figure 5. Time courses of systolic BP, diastolic BP and heart rate during usual period in long, and short users. Closed square: scores in long users, open circle: scores in short users. All values are represented as $M \pm SE$. An asterisk (*) and asterisks (**) denote significant differences between both users revealed by t-test, at level of $p < 0.05$ and $p < 0.01$, respectively

3.4 Hypothalamo-pituitary adrenal axis activity

Hypothalamo-pituitary adrenal axis activity was evaluated by salivary cortisol concentration. Samples whose intra-assay coefficient of variance more than 20 percent were excluded from the analysis to improve the reliability of the assay, and data from 11 long users and 11 short time users were used for between subjects analysis, and data from 8 long users and 4 short time users were used for within subjects analysis. Finally, overall intra-assay coefficient of variance was 6.07 percent. Repeated measures ANOVA revealed no significant interaction of users (long time users or short time users) $\times$ change (from basal to MA period), nor significant interaction of periods (long use period or short use period) $\times$ change (from basal to MA period) in both users (data not shown).

4. DISCUSSION

Significant correlations between smartphone use time, and CMI scores and trait anxiety in 1st experiment (familiar condition), disappeared at 2nd experiment (unfamiliar condition). Smartphone use time would possibly be a major cause for the subjective symptoms and anxiety. Unusual smartphone use may have required much effort, which would consequently confound the correlations at 2nd experiment. The fact that 1 out of 13 long time users could not achieve shorter time use, and 7 out of 12 short time users could not achieve longer time use, would also support the difficulty to complete unusual smartphone use for 2 weeks. Subjective symptoms assessed by CMI were more (worse) in long time users, and physical scores, but not mental scores in CMI, significantly improved (reduced) after two weeks of short use period. Mental symptoms would be influenced by various factors, and beneficial effect on mental symptoms of increased sleep time or improved physical condition induced by decreased smartphone use might be counteracted by dissatisfaction or frustration caused by unusual insufficient smartphone use. Two weeks may not be enough for improvement of mental symptoms, however, two weeks would be enough to improve physical symptoms. Anxiety assessed by STAI were higher in long time users than in short time users. Trait anxiety, but not state anxiety, significantly reduced after two weeks of short use period in long time users. Trait anxiety are considered not to vary easily and to remain fairly consistent during usual life, while state anxiety is considered to vary easily depending on the situation (Spielberger et al., 1970). Quinones and colleagues (2015) reported higher levels of trait anxiety in women with endometriosis who would have been persistently under high-stressed state, even though the levels

of state anxiety in women with endometriosis were not significantly different from those in healthy controls. We also reported higher trait anxiety in female college students during highly demanding and stressful period (Sakuragi, 2017). Then, I considered that trait anxiety is one of the most important parameters to detect persistent stress. Therefore, long time smartphone use may cause persistently stressed state which would be reflected in relatively high trait anxiety score during long use period. These facts would suggest adverse effects of long time smartphone use on mental health as well as physical health.

In long users, changes of C subscale and TMD in POMS under long use period were bidirectional, while those under shorter use period were unidirectional and somewhat higher basal scores decreased more and resulted in less scores after the rest of 30 minutes. The time courses of the other subscales were not significantly different. In not excessive users, changes of A-H subscale in POMS under short use period were unidirectional and decreased more than those under longer period. Basal mood was assessed immediately after entering the experimental room, then, the basal mood scores may represent tense or nervous mood state in the unfamiliar place (experimental room). Higher basal mood scores and steady reduction under short period may represent prompt response and adaptation of mood to the unfamiliar experimental situation. The reason why subjects during short use period do not react clearly to MA is unknown, however, 15 minutes mental arithmetic may not so stressful to the subjects during short use period.

High frequency component of HRV is usually called respiratory sinus arrhythmia, and its peak frequency would generally correspond respiratory frequency, and parasympathetic activity is generally evaluated by HF power or amplitude of HRV, as in the present study (Akselrod et al., 1985; Malliani et al., 1991). HF amplitudes in short users clearly responded to and recovered from MA as shown in Figure 4, but those in long users did not. Average HF amplitudes in short users seemed higher than those in long users at all time-points, though statistical significance was not observed. That is, parasympathetic activity assessed by HF amplitude in HRV would be higher and more responsive in short users. Reactivity of parasympathetic nervous system in long users improved after two weeks of short use period, while reactivity of HF amplitudes in short users worsened after two weeks of long use period. Reactivity of LF/HF amplitudes in short users worsened after two weeks of long use period. Mean systolic and diastolic BPs, and HRs in long time users seemed higher than those in short time users at all time-points, and were significantly higher at some time points, despite repeated measures ANOVA revealed no significant findings in systolic BP (sBP), in diastolic BP (dBP), and in HR. Taken together, longtime smartphone use would cause sympathetic predominant state which consequently result in decreased

autonomic reactivity, and may have negative effects on maintaining health. Furthermore, any significant differences could not be detected in basal values between two groups or between two conditions, however, significant differences could be found in the time course of HF amplitude values. Parameters of HRV would have fairly large individual differences, and tiny differences may be concealed in the individual differences. HRV reactivity in response to acute psychological stress is used to indicate self-regulation (Liu et al., 2020). Excessive smartphone use might contribute to diminished self-regulation which may partially relate to subjective symptoms and anxiety. Oh and coworkers (2020) tried to discriminate adjustment disorder from major depressive disorder by comparing autonomic reactivity to psychological stimuli, and indicated the importance of both basal activity and reactivity of HRV. Manser et al. (2021) proposed HRV reactivity as a biomarker for cognitive impairments, and suggested the possibility of the early detection of cognitive impairment. Taken together, reactivity of HRV parameters to some stimulus and their time course may be indicative of self-regulation and be more sensitive to detect tiny changes. It might be better to analyze not only basal HRV values but also HRV reactivity to a stimulus including response and recovery phases, to improve sensitivity of HRV parameters.

Salivary cortisol levels did not represent any significant influences. This may partially due to small sample size.

There are some limitations to consider in this study. Our sample size was small, and several salivary samples were not available due to large intra-assay coefficient of variance. Larger sample size with detailed analysis may have more consistent and clear results. We employed only female college students as subjects in this study. Then, there may be some differences by age or gender, and may not be generalized to persons in wide age range.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of our university held on 26th September, 2019. After receiving an explanation of the study, all participants gave written informed consent for participation before taking part in this study.

Consent for publication

Not applicable.

Availability of data and material

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

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Competing interests

The author declares that there is no competing interests regarding the publication of this paper.

Authors' contributions

SS designed the experiments, analyzed data and drafted the manuscript. The author read and approved the final approval.

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