International Journal of Psychophysiology 158 (2020) 411–418

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Using novel mobile sensors to assess stress and smoking lapse

Motohiro Nakajima [a], Andrine M. Lemieux [a], Mark Fiecas [b], Soujanya Chatterjee [c], Hillol Sarker [d], Nazir Saleheen [c], Emre Ertin [e], Santosh Kumar [c], Mustafa al'Absi [a,*]

[a] Department of Family Medicine & Biobehavioral Health, University of Minnesota Medical School, Duluth, United States of America
[b] Division of Biostatistics, School of Public Health, University of Minnesota, United States of America
[c] Department of Computer Science, University of Memphis, United States of America
[d] IBM TJ Watson Research Center, United States of America
[e] Department of Electrical and Computer Engineering, The Ohio State University, United States of America

ARTICLE INFO

Keywords:
mHealth
Smoking
Abstinence
Lapse

ABSTRACT

Mobile sensors can now provide unobtrusive measurement of both stress and cigarette smoking behavior. We describe, here, the first field tests of two such methods, *cStress* and *puffMarker,* that were used to examine relationships between stress and smoking behavior and lapse from a sample of 76 smokers motivated to quit smoking. Participants wore a mobile sensors suite, called *AutoSense,* which collected continuous physiological data for 4 days (24-hours pre-quit and 72-hours post-quit) in the field. Algorithms were applied to the physiological data to create indices of stress (*cStress*) and first lapse smoking episodes (*puffMarker*). We used mixed effects interrupted autoregressive time series models to assess changes in heart rate (HR), *cStress*, and nicotine craving across the 4-day period. Self-report assessments using ecological momentary assessment (EMA) of mood, withdrawal symptoms, and smoking behavior were also used. Results indicated that HR and *cStress*, respectively, predicted smoking lapse. These results suggest that measures of traditional psychophysiology, such as HR, are not redundant with *cStress*; both provide important information. Results are consistent with existing literature and provide clear support for *cStress* and *puffMarker* in ambulatory clinical research. This research lays groundwork for sensor-based markers in developing and delivering sensor-triggered, just-in-time interventions that are sensitive to stress-related lapser risk factors.

1. Introduction

Despite the successes of anti-smoking public health campaigns (Shmulewitz et al., 2016), close to one in six American adults were regular smokers in 2014 (CDC, 2016). Advances in computing, smart phone technologies, and mHealth applications (apps) specific for health behaviors, such as smoking, have exploded in popularity over the past decade. Clinical trials of mHealth tools for smoking cessation have demonstrated the efficacy of these tools (Whittaker et al., 2009; Whittaker et al., 2012; Whittaker et al., 2016). While popular with both users and researchers, one weakness of mHealth smoking cessation tools is the over-reliance on self-reports for recording the precise timing of smoking via ecological momentary assessment (EMA) prompts. This burdens participants and does not eliminate the need for retrospective recording of lapses across the day. This, in turn, weakens the value of field assessment for smoking lapse. Objectively detecting smoking lapses using unobtrusive sensors has the potential to provide precise timing of smoking lapses as well as to reduce the burden on participants to remember to report the lapses.

In addition to unobtrusive recording of smoking behaviors, a true understanding of the factors that lead to smoking lapse will require mHealth systems that can not only record smoking behavior and EMA responding but that can also examine potential mediating or moderating factors that predict lapse or relapse (Whittaker et al., 2016). Stress is a known risk factor of smoking initiation (Holliday and Gould, 2016; Huizink et al., 2009), smoking maintenance (Shaw and al'Absi, 2010), and relapse (al'Absi, 2006; al'Absi et al., 2015; Childs and de Wit, 2010; Dupont et al., 2012; Lemieux and al'Absi, 2016; McKee et al., 2015). Negative affect reliably, but weakly, also leads to decreased smoking latency and increased number of puffs during ad libitum smoking sessions (Heckman et al., 2013; McKee et al., 2015), which relate to increased cravings for tobacco (Heckman et al., 2013), increased distress, increased withdrawal symptoms, and decreased positive affect (al'Absi et al., 2003). Early work with electronic diaries confirmed that

* Corresponding author at: University of Minnesota Medical School, 1035 University Drive, Duluth, MN 55812, United States of America.
E-mail address: malabsi@umn.edu (M. al'Absi).

https://doi.org/10.1016/j.ijpsycho.2020.11.005
Received 15 April 2019; Received in revised form 2 November 2020; Accepted 10 November 2020
Available online 13 November 2020

field-detected increases in negative affect precede smoking lapses (Minami et al., 2011; Shiffman and Waters, 2004). Stress queries using EMAs predicted smoking within 4 h of a lapse, particularly in combination with other risk factors (Businelle et al., 2016b), and stress-related EMAs can be used to trigger tailored interventions (Businelle et al., 2016a).

Creating a system to index stress that does not rely solely on self-report requires access to psychophysiological signals. Cardiovascular indices of stress are well characterized (al'Absi et al., 1997; Hellhammer et al., 2009). Cardiovascular responses to stress differ between chronic smokers and nonsmokers (al'Absi et al., 2013; al'Absi et al., 2003; Childs and de Wit, 2009; Girdler et al., 1997; Roy et al., 1994; Tsuda et al., 1996). For example, chronic smokers show blunted cardiovascular stress responses relative to nonsmokers (Wiggert et al., 2016), though in moderate to heavy smokers at rest, HR is higher than nonsmokers (Cagirci et al., 2009; Yuksel et al., 2016). Following cessation, resting HR decreases for successful abstainers (Harte and Meston, 2014; Stein et al., 1996; Yotsukura et al., 1998). In a study using ambulatory monitoring devices in the natural environment, HR was associated with cocaine use (Kennedy et al., 2015). This has not been directly tested with tobacco use.

In this study, we used *AutoSense*, a wearable system that collects multiple measures, including electrocardiography, respiration, galvanic skin conductance, skin and ambient temperatures, and 3-axis accelerometer motion sensing ((Ertin et al., 2011). When combined with a smartphone hosting accompanying software (called *mCerebrum*; see https://mhealth.md2k.org/), the sensors in *AutoSense* allow for two-way communication between the wearer and the system for EMA delivery and recording. Further, the computing power of the smartphone and proprietary software allows recording and processing of the incoming data. *AutoSense* has been used in over 25 published analyses of mobile sensor data, including smoking (Ali et al., 2012; Saleheen et al., 2015) and physiological activity related to stress (Hovsepian et al., 2015; Plarre et al., 2011; Sarker et al., 2016). *cStress* is a computational stress model that is calculated based on physiological and subjective data collected by *AutoSense*. *cStress* has been field-tested in three studies that show very promising initial results. In a recent validation trial of *cStress,* recall was 89%, false positives were 5%, and the accuracy was 72% when compared with self-reports (Hovsepian et al., 2015). *PuffMarker* is a computational model to detect cigarette smoking behavior from *AutoSense* and wrist sensors that are used to track arm movements. Using only respiration patterns and arm movements from 6-axis inertial sensors to distinguish smoking from walking or eating, *puffMarker* demonstrates 96.9% accuracy and 1.1% false positives (Saleheen et al., 2015). These works establish feasibility and reliability of obtaining the markers of stress and smoking from wearable sensors.

The purpose of this study was to examine the relationship between stress and smoking lapse in the field environment at the actual, precise time of lapse. Whether stress, as indexed by *cStress,* is associated with smoking lapse as indexed by *puffMarker,* has not been directly tested in the field. Based on the relevant literature, we hypothesized that greater levels of stress would lead to a lapse. We also anticipated that an increase in cardiovascular activity (i.e., heart rate) would signal an impending smoking lapse. Another purpose was to replicate the feasibility of *puffMarker* with additional sample to the previous report (Saleheen et al., 2015). We expected that those who were classified as lapsers would have greater levels of tobacco exposure (as assessed by carbon monoxide; CO) than those who were classified as abstainers. In addition, in light of the literature showing associations between stress, craving, and relapse (al'Absi et al., 2005; Morrell et al., 2008), we explored the relationship between *cStress* and self-reported craving.

2. Methods

2.1. Overview of the study design

This study included multiple laboratory visits. They were: 1) on-site medical screening; 2) pre-quit field session (wearing *AutoSense* for 24 h while particpants smoked on their own pace); 3) quit field session (wearing *AutoSense* during the first 72 h of smoking cessation); 4) post-cessation visit.

2.2. Participants

Participants initiated contact with study staff as instructed by recruitment flyers placed around the University of Minnesota on the Duluth and Minneapolis campuses and by postings on social media or online classifieds (Craigslist). A preliminary phone screening was followed by an on-site medical screening to assess eligibility. Recruited smokers were accepted if they had a strong desire to quit ($\geq$ 4 on a 5 point scale), smoked a minimum of 5 or more cigarettes per day, reported no current nor prior history of significant medical or psychiatric care, drank <2 alcoholic beverages per day, and had normal sleep patterns (no shift work, bed between 9:00 PM and 12:00 AM and awake between 6:00 AM and 8:00 AM). Pregnant women and those with current medical or psychiatric care were excluded. The Institutional Review Board of the University of Minnesota approved of, and provided oversight for, the consent forms signed by all participants. Although 76 chronic smokers completed data collection, *puffMarker* lapse was not available for 10 participants due to lapses that occurred after the final *AutoSense* wear period but before the final lab visit. Given this, data are presented for the 66 participants with both *puffMarker* lapse and EMA recordings from the *AutoSense* system. The average age of this sample was 37.6 years (SD = 12.2). They had a BMI of 29.6 (SD = 8.9) and completed 13.5 years of education (SD = 1.9). Approximately half (n = 32; 49%) of the sample was women. They smoked an average of 15.3 cigarettes per day at baseline (SD = 7.2). The mean score on the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991) was 4.0 (SD = 2.2), suggesting that these smokers were moderately dependent on nicotine.

2.3. Measures

2.3.1. Self-report and physiological measures in the field using AutoSense

All participants were carefully instructed on the wear and use of *AutoSense*. The system includes a chest band, fit with a strain gauge, for measurement of respiration, a two-lead electrocardiogram (ECG), and a 3-axis accelerometer. Two inertial sensors, in the form of wrist-bands, with 3-axis accelerometer and 3-axis gyroscope were also worn on each wrist. Signals from the 3-accelerometer placed on the chest were used to screen high physical activity. That is, if the majority of ten-second window inside the minute was classified as moderate-to-high activity, that entire minute was labeled as physical activity and removed from the analysis (Hovsepian et al., 2015). We adapted methods that focused on threshold-based approach to detect physical movement (Rahman et al., 2014). As a result, we limited the application of *cStress* to data with no or low physical activity intervals. ECG was sampled at 128 HZ and Respiration was sampled at 21.3 HZ (Hovsepian et al., 2015). R-R intervals (interbeat interval) were extracted from ECG and respiration cycles were extracted from respiration measurements. These were then used to compute 51 features from 1 min worth of measurements. Features computed from ECG signals included: mean R-R interval, 80th percentile of R-R intervals, variance of R-R intervals, quartile deviation, low frequency power (LF: 0.1–0.2 Hz), medium frequency power (MF: 0.2–0.3 Hz), high frequency power (HF: 0.3–0.4 Hz), and HF:LF ratio. Respiration-related features included: breath rate; mean inspiration: expiration (IE) ratio; median IE ratio; median stretch; and inspiration minute volume (Hovsepian et al., 2015). We used three steps to retain valid signals (e.g., each minute of data was examined for ECG data that retained standard characteristic morphologies, automated detection of R peaks of the QRS complex, and normalization of the R-R intervals to remove any components due to subject or session (Hovsepian et al., 2015). We conducted a laboratory study administering validated stress tasks to collect data on the 'ground-truth' of stress response (Hovsepian et al., 2015). Participants wore Autosense device for continuous measurement of physiological and subjective measures throughout the study. A standardized lab stress protocol with clear onset of stressors enabled to create a fine-tuned model of physiological stress response (Hovsepian et al., 2015). Selected discriminative features were then used to train a machine learning model to produce stress likelihood in each minute of data. These features were used to develop the *cStress* algorithm that was used to compute *cStress* scores for each participant.

Each participant was given a smart phone that continuously received and recorded sensor data from *AutoSense*. It was also used for prompting self-report assessments using EMAs (see below). Technical details of the system, algorithm development, and validation for *cStress* and *puffMarker* can be found elsewhere (Ertin et al., 2011; Hovsepian et al., 2015; Saleheen et al., 2015). Briefly, raw data were streamed from the *AutoSense* sensors to the smartphone and stored for later uploading. The data were then culled for missing or incomplete signal epochs and the *cStress* and *puffMarker* algorithms were applied to produce minute-to-minute output values. *cStress* uses ECG and respiration measurements, described above, when not confounded by significant physical activity (detected by accelerometers in *AutoSense* chest band). Data classified as physical activity were removed in light of previous studies reporting potential confounding effects of physical activity on the link between cardiovascular measures and stress (Kamarck et al. 2012). *puffMarker* uses respiration features (described above) collected from the *AutoSense* chest band and hand-to-mouth movements captured via 6-axis inertial sensors (3-axis accelerometers and 3-axis gyroscopes) worn on wrists (Saleheen et al., 2015). Outputs included a binomial variable for *puffMarker* (smoking detected yes/no; Saleheen et al., 2015) and the probability (p) that the minute represents a stressed response for *cStress;* probability range of 0–100. The *puffMarker* classifier of individual puffs on lab data has been shown to have excellent cross-validation with 96.9% accuracy in the recall rate and a false positive rate of 1.1% (Saleheen et al., 2015). From the output of this puff detection model, a smoking lapse event was identified if four or more puffs are detected in close proximity.

Self-report assessments using EMAs, installed on the smart phone first asked whether participants were available for responding to questions or whether they preferred a delay (e.g., due to driving). Twelve random prompts were sent daily to record recent smoking with the question "How many cigarettes have you had since the last prompt?". A zero response was classified as no smoking and responses with one or higher were classified as smoking. These prompts also included mood items related to positive affect and distress (items were adapted from Lundberg and Frankenhaeuser, 1980) as well as withdrawal symptoms and craving (Minnesota Withdrawal Scale (MNWS); Hughes and Hatsukami, 1986). Other questions asked contextual information and current behavior (not reported here). The phone also logged user response patterns, such as the number of EMAs that were completed but delayed and the amount of time required to complete an EMA.

2.3.2. Self-report measures collected in the laboratory (baseline measures)

Questionnaires regarding demographics (sex, age, and education), history of smoking, drug and alcohol use, and caffeine consumption were collected at a pre-cessation on-site medical screening session. Smoking history included age at smoking onset, average cigarettes per day, and years smoking at the current rate. Severity of smoking dependency was assessed using the FTND (Heatherton et al., 1991). Expired carbon monoxide (CO) was measured using Bedfont Micro+ monitors (coVita, Haddonfield, NJ). A questionnaire to assess each user's personal experience with the *AutoSense* device was also administered. This form included statements about participants' experience during data collection (e.g.,"It was easy to enter my response today"), phone usage (e.g., "The phone interfered with my social interactions"), and chest band usage (e.g., "The chest band caused physical discomfort today."). Participants responded with one of four options: Strongly agree, Agree, Disagree, and Strongly Disagree.

2.4. Procedures

The pre-quit and quit lab visits began between noon and 1:00 PM to control for diurnal variability. The first day of pre- and quit labs consisted of reviews of smoking history, study procedures, and training for use of *AutoSense*. Participants left that afternoon with instructions on using the system, including EMA prompt responses, and they were required to wear the *AutoSense* system until bedtime, when *AutoSense* was removed and recharged overnight. The next morning, the system was put on immediately upon waking and worn until they returned to the lab later that day. During the pre-quit field session, participants were able to smoke at their own pace. After the pre-quit session, participants set a quit day and agreed that the start of their 72-h abstinence was to begin when they came to their lab visit on their quit date. There were approximately two weeks between the pre-quit and the second (post-quit) sessions; and participants were allowed to smoke ad libitum during this interim period. For the next 72 h following that second visit, the participants were encouraged to remain abstinent and they returned to the laboratory each day for psychosocial support and to assess potential problems with the use of *AutoSense*. Smoking lapse was reviewed at each visit and lapsers were encouraged to re-start their abstinence. Self-reported measures and CO samples collected in post-quit visits were used to determine smoking abstinence. On the final day of the 72-h period, *AutoSense* was returned to the laboratory, participants were debriefed, and they were compensated for their time and effort.

2.5. Data reduction and analysis

2.5.1. Signal processing & algorithm calculation

The first smoking episode (lapse) was unobtrusively identified using the *puffMarker* algorithm. Given that the *puffMarker* designation used here was restricted to the first lapse, we avoid the term "relapse" due to its very specific clinical definitions and meaning (Hughes et al., 2003) that are not captured in this analysis of the first lapse. Consistent with our previous procedures (Hovsepian et al., 2015), we retained for analysis only those minutes throughout recording that had no missing nor distorted signals and no evidence of high physical activity (e.g. exercise), as measured by the magnitude of accelerometers in *AutoSense* worn around the chest. From the total time of acceptable recordings, the raw probability that each a minute represented a stress state (range 0–100) was computed for each participant. In addition, *AutoSense* recorded HR per minute over the entire recording period using raw ECG waveforms.

2.5.2. Assessing baseline smoking measures as a function of lapse classification by puffMarker

For descriptive purposes, the *puffMarker* assigned lapse groups were compared using *t*-test on smoking variables (FTND, cigarettes per day, CO) to characterize these smokers. In all cases, omnibus tests of significance were set at $p < .05$.

2.5.3. Assessing changes in subjective mood and withdrawal symptoms (EMA) as a function of lapse classification by puffMarker

All continuous variables were assessed for normality and log-transformed as needed prior to analysis. We used MANOVA models to assess positive affect, distress, withdrawal symptoms, and craving from the EMAs across time. Grouping variables included assessment of *puffMarker* lapse status (abstain/lapse) and sex (male/female).

2.5.4. Assessing the relationship between the onset of the first lapse and HR and cStress using mixed effects autoregressive interrupted time series models

Restricted to the participants who lapsed, we used interrupted time series models to analyze the temporal characteristics of HR and *cStress* before and after the first lapse. For each participant who lapsed, we temporarily registered their HR and *cStress* data to the time that they lapsed so that these temporal profiles are comparable across participants. We used mixed effects autoregressive interrupted time series models of the form

$$y_{it} = \phi y_{i,t-1} + b_{0i} + (\beta_0 + (\beta_1 + b_{1i})t + \beta_2 craving_i(t))\mathbf{1}(pre - lapsed_i(t)) + (\gamma_0 + (\gamma_1 + c_{1i})t + \gamma_2 craving_i(t))\mathbf{1}(post - lapsed_i(t)) + \varepsilon_{it}$$

where y_{it} denotes either HR or *cStress* for participant i at time t, ϕ captures the temporal dependence in HR or *cStress* measurements, β_0 and γ_0 are fixed effects that capture the population-level average, b_{0i} is a random intercept that accounts for the heterogeneity in each participant's baseline HR or *cStress*, β_1 and γ_1 are fixed effects that capture population-level temporal trends, with b_{1i} and c_{1i} as random effects to capture participant-specific deviations, β_2 and γ_2 are fixed effects that capture the effect of craving, $\mathbf{1}(pre - lapsed_i(t))$ and $\mathbf{1}(post - lapsed_i(t))$ are indicator functions, where the former is equal to 1 at all time points prior to participant i's first lapse and 0 afterwards, and the latter is equal to 0 at all time points prior to participant i's first lapse and 1 afterwards, respectively. To place the EMA reports on the same time scale as the *cStress* and HR data, we assumed that the craving as reported from the EMA is constant between two random prompts. In other words, we assumed that their craving at one random prompt remained the same unless this changes as determined by the next random prompt. Given the time stamps of the random prompts, we could then temporally register each participant's craving with the *cStress* and HR data. We also considered two variants of this model, the first where we do not account for craving, and the second where we do not account for the lapse. The latter model is the simplest time series model we considered, and we henceforth refer to this as the null model. Furthermore, in order for the models to be temporally localized around the moment of the first lapse, we restricted the time indices *t* to be within a certain range from the time of the first lapse, where the range was picked by maximizing a leave-one out mean-square prediction error criteria, yielding a window of 93 and 83 min pre- and post-lapse for HR and *cStress*, respectively. Finally, we estimate all parameters in each model using restricted maximum likelihood (REML).

To conduct statistical inference about the model parameters, we used the non-smoking data from each participant's pre-quit days to create a pseudo-data set from which we repeated our analyses in order to create a null distribution for the model parameters. Our algorithm was as follows. First, for each participant, we randomly selected one of their pre-quit sessions. Second, because the participants had not yet lapsed during a pre-quit session, we randomly selected a time point within the pre-quit session to declare as their pseudo-lapse time. We thus created a pseudo-data set using the timestamp of the pseudo-lapse time and the EMA, HR, and *cStress* data recorded and temporally registered during the pre-quit session. Third, we fit the above models on the pseudo-data set to obtain estimates of the model parameters. Fourth, we repeated each of the above steps 10,000 times to obtain a null distribution for each model parameter. Finally, we compared our estimates of the model parameters from the lapse sessions to their respective null distributions to obtain *p*-values. The random construction of the pseudo-lapse time ensured that any relations between the pseudo-lapse time with their HR and *cStress* were purely coincidental, yielding a valid null distribution for each model parameter. Furthermore, by using data from each participant's own pre-quit sessions, our null distributions better reflected the variability that arises from within and between participants.

3. Results

3.1. Lapse description

puffMarker classified 38 individuals as lapsed and 28 as abstinent and the post-quit interview revealed that 42 people claimed to have lapsed and 24 were abstinent. Only two smokers who were identified as a lapser by *puffMarker* did not disclose via self-report that they had returned to smoking. In contrast, 6 cases (9%: 6/66) who self-reported a smoking lapse were classified as non-lapsers by *puffMarker*. Three of these cases were mis-classified due to significant sensor data loss, 2 cases were mis-classified due to smoking while not wearing the device, and 1 case was due to missing relapse information in the laboratory visit and therefore demonstrating that these were not a false negative. As a result, the sensitivity of *puffMarker* in lapse episode was 85% (36/42). CO levels taken on the last day of the 72-hour session were higher among those who were classified as lapsers by *puffMarker* (mean = 8.8 ppm; SEM = 1.2) than among those who were classified as abstainers (mean = 5.0 ppm; SEM = 0.9), $p = .02$. Lapsers identified by interviews (mean = 9.4 ppm; SEM = 1.1) had higher CO levels than abstainers (mean = 3.4 ppm; SEM = 0.5), $p < .001$. These results support the validity of lapse/abstinent classification. There was no significant difference between abstainers and lapsers (defined by *puffMarker*) on any of the demographic variables except years of education (see Table 1). There were also no lapse group differences in baseline FTND, average cigarettes per day, nor MNWS in a baseline session (medical screening).

In total, participants initiated 3838 self-report assessment of EMAs during the 72-hour post-quit study period. Of those, the delay option was used in 197 (5.1%) recordings and 138 (3.6%) of the total EMAs were incomplete, indicating very high compliance with EMA prompts. On average, it took 2.0 min (SD = 0.8) to complete one EMA. A significant smoking status by sex interaction was found in the total number of EMAs completed ($p = .02$). A greater number of EMAs were completed by male lapsers (mean = 53.3; SEM = 2.1) than male abstainers (mean = 45.6; SEM = 2.7), $p = .03$, with no differences between female lapsers (mean = 49.7; SEM = 1.8) and abstainers (mean = 52.6; SEM = 2.2), $p = .31$. Analysis of the device experience questionnaire found that lapsers were more likely than abstainers to endorse that the phone interfered with their daily activities during the study period (51% vs. 19%, $p = .008$).

3.2. Self-reported mood (EMA) and withdrawal change from pre-quit to 72-h abstinence

As expected, mood and withdrawal symptoms collected via EMA shifted over the three days of abstinence. Positive affect declined slightly

Table 1
Baseline sample characteristics for *puffMarker* defined lapse.

		Lapse status from *puffMarker*				
		Abstained		Lapsed		
		Count		Count		p-Value
Race[a]	White/Caucasian	20		24		0.48
	Non-Caucasian	7		12		
Sex	female	14		18		0.83
	male	14		20		
		Mean	SEM	Mean	SEM	
Age of participant		37.4	2.3	37.7	1.9	0.93
Years of education		14.1	0.4	13.0	0.3	0.01
Body mass index		29.4	1.4	29.8	1.7	0.90
Caffeine consumption (cups)		1.4	0.4	1.9	0.6	0.50
Age of smoking onset		16.0	1.2	14.9	0.6	0.39
Cigarettes per day		14.9	1.3	15.6	1.3	0.73
Duration at this level		14.8	2.6	13.1	1.8	0.59
FTND		3.7	0.4	4.3	0.4	0.28

Note. All continuous tests utilized t-test.

across the sessions ($p = .06$). Distress ($p = .02$) and withdrawal symptoms ($p < .001$) increased from baseline to the first day of abstinence (ps < 0.04; see Fig. 1). Craving remained stable during the first two days of abstinence then declined significantly ($p = .03$) from the second to the final day ($p = .02$). There were no *puffMarker* lapse category main effect, sex main effect, or interaction between *puffMarker* and time in positive affect, distress, withdrawal symptoms, and craving.

3.3. HR & *cStress* prediction of first lapse

We illustrate the temporal trends in HR and *cStress* in Fig. 2a and present the data in Table 2. For HR, we see an increase in heart rate leading up to the onset of the first lapse, and then a slower increasing temporal trend in HR after the first lapse. On the other hand, *cStress* increases prior to the first lapse, and then decreases after the first lapse. We model and test for these temporal trends using the interrupted time series models.

Results from the interrupted time series models are shown in Table 2. The null model only has an autoregressive term and the intercepts is also presented in Table 2. Model 1 has only the temporal trend pre/post-lapse, and Model 2 has both the temporal trend and is adjusted for craving pre/post-lapse. From Table 2, we see that the HR increases prior to the first lapse time ($p < .05$), with no evidence of a temporal trend after the first lapse. Without accounting for craving, there is also evidence of increasing *cStress* values up to the lapse time ($p < .05$); however, temporal changes in *cStress* before and after the lapse may be explained by its negative association with the craving scores both before and after the lapse. We computed the AIC for each model for each of the HR and *cStress* data, from which we can use to compare fit. For HR, the AIC values were 20,870.21, 20,798.39, and 20,798.03 for the null model and Models 1 and 2, respectively. This suggests that accounting for the temporal trend and the onset of the first lapse improves model fit; and accounting for craving yielded a slightly better fit to the HR data. Statistically, the Null vs. Model 1 was significant ($p < .001$) and Model 1 vs. Model 2 was not significant ($p = .11$), confirming that the improvement in model fit after accounting for the time effect. Accounting for craving led to a better fit (lower AIC), but the improvement was not statistically significant.

For *cStress*, the AIC values were − 3872.745, −3890.85, and − 3894.10 for the null model and Models 1 and 2, respectively. This suggests that accounting for both the onset of the first lapse and for craving improves model fit relative to the null model that only accounts for temporal autocorrelation and Model 1 that accounts for the onset of the first lapse and temporal trends, but not craving. Statistically, there were significant differences between Null vs. Model 1 ($p < .001$) and Model 1 vs. Model 2 ($p = .03$), indicating the improvement in model fit after accounting for both the time effect and craving. Model 2 demonstrates that with craving accounted for, the increase in HR pre-lapse is significant for both Models 1 and 2 ($p < .01$, see Table 2 and Fig. 2), but *cStress* does not show pre- and post-lapse temporal trends.

4. Discussion

We provide novel findings in this study of two new mHealth tools designed to identify unobtrusively physiological stress states (*cStress*) and lapse (*puffMarker*) during a clinical study of smoking cessation. First, we note that controlling false positives when detecting rare events, such as smoking lapse using sensors that collect and analyze data continuously is challenging. This is because in 12 h of sensor wearing per day, there are over 15,000 respiration cycles, each of which can contain a smoking puff. A model with as low as 1% false positive rate will produce 150 false positives per day. In contrast, the first lapse detection from *puffMarker* did not produce a false positive first lapse detection for 22 (out of 24) abstinent participants. Collectively, participants wore sensors for 66 person days, resulting in a very low false positive rate. Second, HR and *cStress* showed somewhat different patterns of changes related to a first smoking lapse episode. Both HR and *cStress* showed an increase prior to a lapse episode. However, while HR increased post-lapse, *cStress* decreased after a lapse episode. Third, EMA distress and withdrawal symptoms changed from pre-quit to abstinence (Hughes and Hatsukami, 1986; Morrell et al., 2008; Shiffman and Paty, 2006), although there were no differences between abstainers and lapsers.

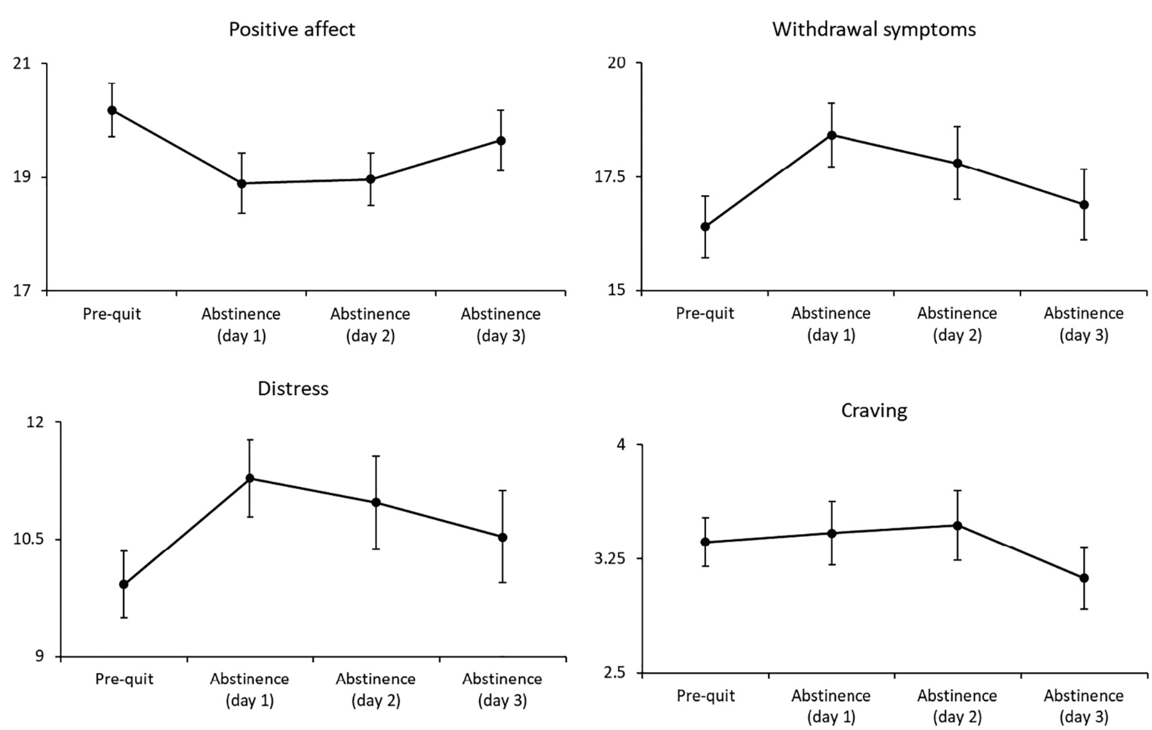

Fig. 1. Withdrawal symptoms across the 72-hour abstinence ($n = 66$). Note. All noted effects represent a main effect of time. There were no main effects of sex nor *puffMarker* and there were no *puffMarker* interactions.

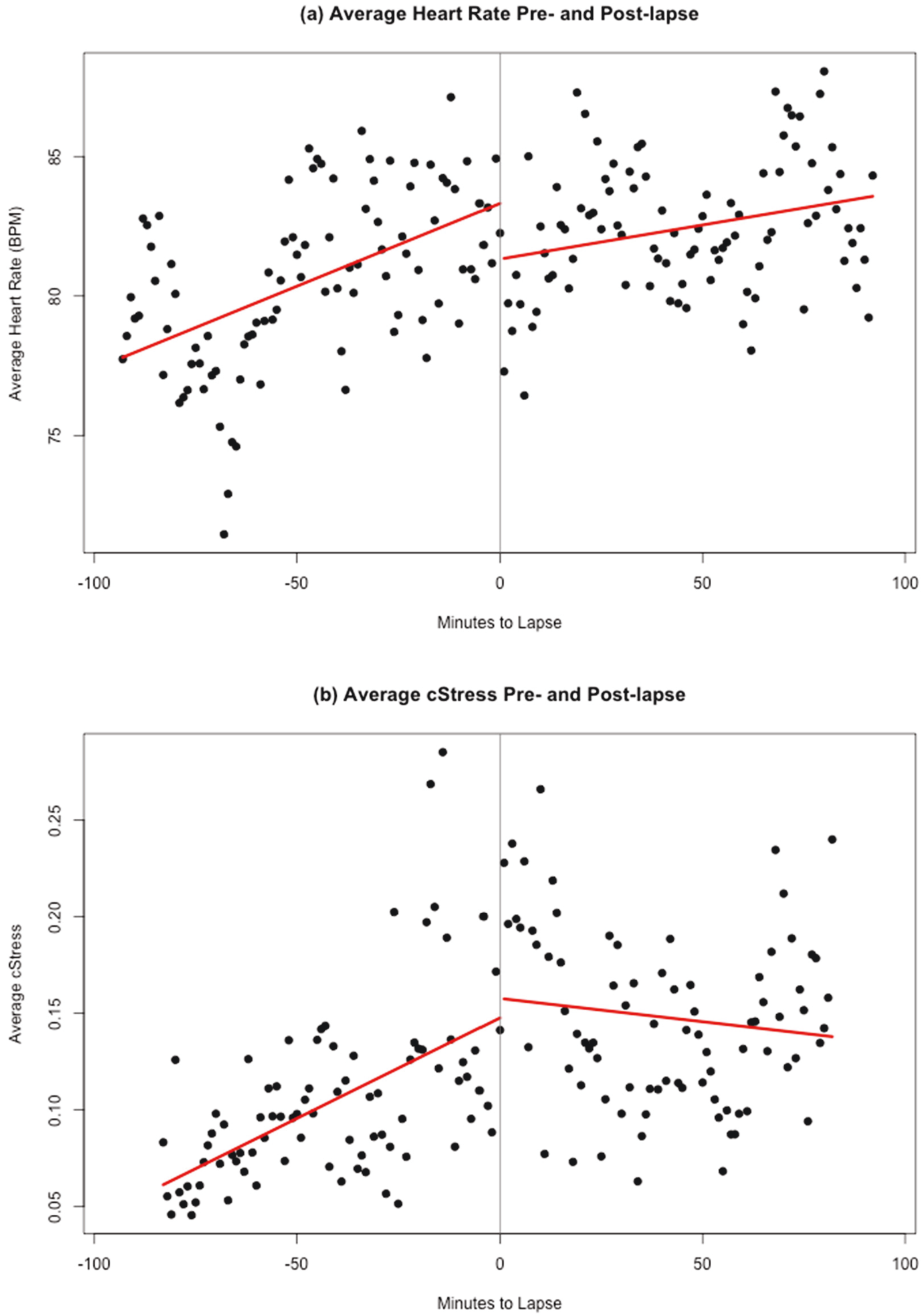

Fig. 2. (a) Average heart rate pre-/post-lapse. (b) Average *cStress* pre-/post-lapse. In each figure, the red lines correspond to the temporal trends in either the average heart rate or average *cStress*, pre- and post-lapse. The vertical gray lines correspond to the onset of the first lapse. The analysis included 22 individuals who had HR and cStress data and also lapsed. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fourth, adding craving to the time series model did not improve the HR model, but it did reveal a significant negative association with *cStress*. Temporal changes were not significant pre- nor post-lapse for *cStress* when craving was considered.

Time series analysis of *cStress* at the time of lapse suggests that *cStress* was associated with lapse when taking into account craving. While underlying mechanisms are not clear at this time, this likely reflects the complex, multifactorial nature of *cStress*. *cStress* was developed based upon multiple indices calculated from ECG and respiration signals. Which aspects of this algorithm are sensitive to self-reported craving and to smoking relapse needs to be determined in future work. In addition, future research should examine psychophysiological changes during withdrawal phase of quitting and their relationships to lapse in the natural environment.

Table 2
Model parameter estimates (se) for each interrupted time series model. The entries for time and craving effects for *cStress* are $\times 10^3$. Resampling-based p-values: * $p < .05$, ** $p < .01$, *** $p < .001$. The analysis included 22 individuals who had HR and *cStress* data and also lapsed.

	Null Model		Model 1: Time		Model 2: Time + Craving	
	Heart rate	*cStress*	Heart rate	*cStress*	Heart rate	*cStress*
Autocorrelation parameter (ϕ)	0.543 (0.015)***	0.651 (0.015)***	0.473 (0.016)***	0.618 (0.015)***	0.471 (0.016)***	0.617 (0.015)***
Time effect, pre-lapse (β_1)			0.032 (0.011)**	0.444 (0.161)	0.034 (0.010)*	0.478 (0.158)
Time effect, post-lapse (γ_1)			0.018 (0.011)	−0.169 (0.164)	0.018 (0.012)	−0.214 (0.157)
Craving effect, pre-lapse (β_2)					−0.036 (0.286)	−6.757 (3.467)*
Craving effect, post-lapse (γ_2)					−0.507 (0.296)	−8.025 (2.526)*

The current study provides unique findings and demonstrates the feasibility and utility of mobile sensors and these two mHealth tools, but it is not without limitations. Limitations in this study are related primarily to issues of EMA timing and data acquisition. Data loss due to signal loss is a critical weakness of the existing *AutoSense* system that warrants further work. While we used multiple steps to retain valid signals (see Methods section), the exact amount of data that was lost due to loss in the ECG/respiration signal is unknown. Although these initial results are promising, increased data retention for processing will be important in future studies, particularly within prospective smoking cessation studies which are time-consuming and expensive. Better data retention would also facilitate further analysis of sex differences, which was limited in this study due to sample size. Issues related to missing sensor signals and data loss during processing are not unusual in sensor-based studies, such as EEG, EMG, and EKG (Venkatachalam et al., 2011), but could be improved to minimize subject loss. Methodologically, reliance on baseline self-report measures and on low-density of EMAs across waking hours are also limitations. Future analyses will benefit from EMA-based assessment of affect, craving, and withdrawal immediately preceding smoking and lapse behaviors. Inclusion of these measures in algorithms may improve computational models to predict smoking behavior and relapse. Improvement in data collection timing and sequencing (e.g., triggered by passive sensing of stress) in future studies will set the stage for using this technology to cue delivery of interventions. Finally, due to technical challenges in preprocessing, we examined temporal trends for HR and *cStress* surrounding the first lapse using separate models. Future research should examine HR and *cStress* in one model.

These results have important implications for future development and refinement of sensor-enabled, just-in-time interventions. For example, associations between *cStress* and smoking behaviors may differ between individuals; and that difference may be important in predicting lapse. In future studies, smokers who show a negative association between *cStress* and cigarettes smoked per day immediately preceding a planned quit date (suggesting a strong association between stress relief and smoking) may have greater sensitivity to the stress of withdrawal and may be at higher risk of lapsing. Finally, further work to clarify the sources of proposed differences in rate of response between HR and *cStress* would be helpful. The current data suggest that HR and *cStress* are not redundant, both are important sources of information for predicting a lapse.

In conclusion, the mobile sensor *AutoSense* shows excellent promise for use in clinical studies of smoking and other addictions, particularly field studies of natural smoking behavior. The current study of these mHealth tools supports the use of *cStress* and *puffMarker* as unobtrusive markers of lapse and relapse and the physiological disturbance associated with stress. Utilizing *puffMarker* in future studies of smoking cessation will allow for more precise analysis of lapse behaviors and will facilitate development of phone-based, just-in-time mHealth interventions (Nahum-Shani et al., 2018; Rabbi et al., 2017). It will also allow for correlation with not only physiological signals via *cStress,* but also with other markers of the hypothalamic-pituitary-adrenal axis and autonomic activity. Despite the limitations of the current study, this analysis supports the appropriateness of taking the next step in refinement of the system and *cStress*. Such just-in-time mHealth interventions are likely to have important application to not only studies of stress and addiction but also studies of stress and other health behaviors or chronic medical conditions.

Acknowledgement

The authors wish to acknowledge their support by the National Science Foundation under award numbers IIS-1231754, ACI-1640813 and IIS-1722646, National Institute of Health grants R01DA016351 and R01DA027232 under the trans-NIH OppNet initiative R01DA035502 (by NIDA), National Institutes of Health grant R01DA016351, National Institutes of Health and National Institute on Drug Abuse grant R01DA027232, and funds provided by the trans-NIH Big Data-to-Knowledge (BD2K) initiative U54EB020404 (by NIBIB). We thank Shahin Alan Samiei for his help with data management (University of Memphis) and the study coordinators at Universities of Minnesota and Memphis. The authors declare no conflict of interest in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2020.11.005.

References

al'Absi, M., 2006. Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. Int. J. Psychophysiol. 59, 218–227.
al'Absi, M., Bongard, S., Buchanan, T., Pincomb, G.A., Licinio, J., Lovallo, W.R., 1997. Cardiovascular and neuroendocrine adjustment to public speaking and mental arithmetic stressors. Psychophysiology 34, 266–275.
al'Absi, M., Wittmers, L.E., Erickson, J., Hatsukami, D., Crouse, B., 2003. Attenuated adrenocortical and blood pressure responses to psychological stress in ad libitum and abstinent smokers. Pharmacol. Biochem. Behav. 74, 401–410.
al'Absi, M., Hatsukami, D., Davis, G.L., 2005. Attenuated adrenocorticotropic responses to psychological stress are associated with early smoking relapse. Psychopharmacology 181, 107–117.
al'Absi, M., Nakajima, M., Grabowski, J., 2013. Stress response dysregulation and stress-induced analgesia in nicotine dependent men and women. Biol. Psychol. 93, 1–8.
al'Absi, M., Nakajima, M., Allen, S., Lemieux, A., Hatsukami, D., 2015. Sex differences in hormonal responses to stress and smoking relapse: a prospective examination. Nicotine Tob. Res. 17, 382–389.
Ali, A., Hossain, S., Hovsepian, K., Rahman, M., Plarre, K., Kumar, S., 2012. mPuff: Automated detection of cigarette smoking puffs from respiration measurements. Proc. ACM IPSN.
Businelle, M.S., Ma, P., Kendzor, D.E., Frank, S.G., Vidrine, D.J., Wetter, D.W., 2016a. An ecological momentary intervention for smoking cessation: evaluation of feasibility and effectiveness. J. Med. Internet Res. 18, e321.
Businelle, M.S., Ma, P., Kendzor, D.E., Frank, S.G., Wetter, D.W., Vidrine, D.J., 2016b. Using intensive longitudinal data collected via mobile phone to detect imminent lapse in smokers undergoing a scheduled quit attempt. J. Med. Internet Res. 18, e275.
Cagirci, G., Cay, S., Karakurt, O., Eryasar, N., Kaya, V., Canga, A., Yesilay, A.B., Kilic, H., Topaloglu, S., Aras, D., Demir, A.D., Akdemir, R., 2009. Influence of heavy cigarette smoking on heart rate variability and heart rate turbulence parameters. Ann. Noninvasive Electrocardiol. 14, 327–332.
CDC, 2016. Current Cigarette Smoking Among Adults in the United States, vol. 2016.

Childs, E., de Wit, H., 2009. Hormonal, cardiovascular, and subjective responses to acute stress in smokers. Psychopharmacology 203, 1–12.

Childs, E., de Wit, H., 2010. Effects of acute psychosocial stress on cigarette craving and smoking. Nicotine Tob. Res. 12, 449–453.

Dupont, P., Reynaud, M., Aubin, H.J., 2012. Stress and smoking in treament-seeking smokers. Rev. Med. Liege 67, 195–201.

Ertin, E., Stohs, N., Kumar, S., Raij, A., Al'Absi, M., Shah, S., Mitra, S., Kwon, T., Jeong, J. W., 2011. AutoSense: Unobtrusively wearable sensor suite for inferring the onset, causality, and consequences of stress in the field. In: SenSys 2011 - Proceedings of the 9th ACM Conference on Embedded Networked Sensor Systems, pp. 274–287.

Girdler, S.S., Jamner, L.D., Jarvik, M., Soles, J.R., Shapiro, D., 1997. Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. Psychosom. Med. 59, 294–306.

Harte, C.B., Meston, C.M., 2014. Effects of smoking cessation on heart rate variability among long-term male smokers. Int J Behav Med 21, 302–309.

Heatherton, T.F., Kozlowski, L.T., Frecker, R.C., Fagerstrom, K.O., 1991. The Fagerstrom test for nicotine dependence: a revision of the Fagerstrom tolerance questionnaire. Br. J. Addict. 86, 1119–1127.

Heckman, B.W., Kovacs, M.A., Marquinez, N.S., Meltzer, L.R., Tsambarlis, M.E., Drobes, D.J., Brandon, T.H., 2013. Influence of affective manipulations on cigarette craving: a meta-analysis. Addiction 108, 2068–2078.

Hellhammer, D.H., Wust, S., Kudielka, B.M., 2009. Salivary cortisol as a biomarker in stress research. Psychoneuroendocrinology 34, 163–171.

Holliday, E., Gould, T.J., 2016. Nicotine, adolescence, and stress: a review of how stress can modulate the negative consequences of adolescent nicotine abuse. Neurosci. Biobehav. Rev. 65, 173–184.

Hovsepian, K., al'Absi, M., Ertin, E., Kamarck, T., Nakajima, M., Kumar, S., 2015. cStress: towards a gold standard for continuous stress assessment in the mobile environment. Proc ACM Int Conf Ubiquitous Comput 2015, 493–504.

Hughes, J.R., Hatsukami, D., 1986. Signs and symptoms of tobacco withdrawal. Arch. Gen. Psychiatry 43, 289–294.

Hughes, J.R., Keely, J.P., Niaura, R.S., Ossip-Klein, D.J., Richmond, R.L., Swan, G.E., 2003. Measures of abstinence in clinical trials: issues and recommendations. Nicotine Tob. Res. 5, 13–25.

Huizink, A.C., Greaves-Lord, K., Oldehinkel, A.J., Ormel, J., Verhulst, F.C., 2009. Hypothalamic-pituitary-adrenal axis and smoking and drinking onset among adolescents: the longitudinal cohort tracking adolescents' individual lives survey (TRAILS). Addiction 104, 1927–1936.

Kennedy, A.P., Epstein, D.H., Jobes, M.L., Agage, D., Tyburski, M., Phillips, K.A., Ali, A. A., Bari, R., Hossain, S.M., Hovsepian, K., Rahman, M.M., Ertin, E., Kumar, S., Preston, K.L., 2015. Continuous in-the-field measurement of heart rate: correlates of drug use, craving, stress, and mood in polydrug users. Drug Alcohol Depend. 151, 159–166.

Lemieux, A., al'Absi, M., 2016. Stress psychobiology in the context of addiction medicine: from drugs of abuse to behavioral addictions. Prog. Brain Res. 223, 43–62.

Lundberg, U., Frankenhaeuser, M., 1980. Pituitary-adrenal and sympathetic-adrenal correlates of distress and effort. J. Psychosom. Res. 24, 125–130.

McKee, S.A., Potenza, M.N., Kober, H., Sofuoglu, M., Arnsten, A.F., Picciotto, M.R., Weinberger, A.H., Ashare, R., Sinha, R., 2015. A translational investigation targeting stress-reactivity and prefrontal cognitive control with guanfacine for smoking cessation. J. Psychopharmacol. 29, 300–311.

Minami, H., McCarthy, D.E., Jorenby, D.E., Baker, T.B., 2011. An ecological momentary assessment analysis of relations among coping, affect and smoking during a quit attempt. Addiction 106, 641–650.

Morrell, H.E., Cohen, L.M., al'Absi, M., 2008. Physiological and psychological symptoms and predictors in early nicotine withdrawal. Pharmacol. Biochem. Behav. 89, 272–278.

Nahum-Shani, I., Smith, S.N., Spring, B.J., Collins, L.M., Witkiewitz, K., Tewari, A., Murphy, S.A., 2018. Just-in-time adaptive interventions (JITAIs) in mobile health: key components and design principles for ongoing health behavior support. Ann. Behav. Med. 52, 446–462.

Plarre, K., Raij, A., Hossain, S., Ali, A., Nakajima, M., al'Absi, M., Ertin, E., Kamarck, T., Kumar, S., Scott, M., Siewiorek, D., Smailagic, A., Wittmers, L., 2011. Continuous inference of psychological stress from sensory measurements collected in the natural environment. ACM IPSN 97–108.

Rabbi, M., Philyaw-Kotov, M., Lee, J., Mansour, A., Dent, L., Wang, X., Cunningham, R., Bonar, E., Nahum-Shani, I., Klasnja, P., Walton, M., Murphy, S., 2017. SARA: a mobile app to engage users in health data collection. Proc ACM Int Conf Ubiquitous Comput 2017, 781–789.

Rahman, M.M., Bari, R., Ali, A.A., Sharmin, M., Raij, A., Ertin, E., Epstein, D., Preston, K., Kedia, S., Kennedy, A., Jobes, M., Al'Absi, M., Ward, K., Kumar, S., 2014. Are we there yet? Feasibility of continuous stress assessment via physiological sensors in field. ACM BCB 2014.

Roy, M.P., Steptoe, A., Kirschbaum, C., 1994. Association between smoking status and cardiovascular and cortisol stress responsivity in healthy young men. Int J Behav Med 1, 264–283.

Saleheen, N., Ali, A.A., Hossain, S.M., Sarker, H., Chatterjee, S., Marlin, B., Ertin, E., al'Absi, M., & Kumar, S. (2015). puffMarker: a multi-sensor approach for pinpointing the timing of first lapse in smoking cessation. Proceedings of the 2015 ACM International Joint Conference on Pervasive and Ubiquitous Computing (pp. 999–1010). Osaka, Japan: ACM.

Sarker, H., Tyburski, M., Rahman, M.M., Hovsepian, K., Sharmin, M., Epstein, D.H., Preston, K.L., Furr-Holden, C.D., Milam, A., Nahum-Shani, I., al'Absi, M., & Kumar, S. (2016). Finding significant stress episodes in a discontinuous time series of rapidly varying mobile sensor data. Proc SIGCHI Conf Hum Factor Comput Syst, 2016, 4489–4501.

Shaw, D., al'Absi, M., 2010. Blunted opiate modulation of prolactin response in smoking men and women. Pharmacol. Biochem. Behav. 95, 1–5.

Shiffman, S., Waters, A.J., 2004. Negative affect and smoking lapses: a prospective analysis. J. Consult. Clin. Psychol. 72, 192–201.

Shiffman, S., Paty, J., 2006. Smoking patterns and dependence: contrasting chippers and heavy smokers. J. Abnorm. Psychol 115, 509–523.

Shmulewitz, D., Stohl, M., Keyes, K.M., Brown, Q., Saha, T.D., Hasin, D., 2016. Effects of state-level tobacco environment on cigarette smoking are stronger among those with individual-level risk factors. Nicotine Tob. Res. 18 (10), 2020–2030.

Stein, P.K., Rottman, J.N., Kleiger, R.E., 1996. Effect of 21 mg transdermal nicotine patches and smoking cessation on heart rate variability. Am. J. Cardiol. 77, 701–705.

Tsuda, A., Steptoe, A., West, R., Fieldman, G., Kirschbaum, C., 1996. Cigarette smoking and psychophysiological stress responsiveness: effects of recent smoking and temporary abstinence. Psychopharmacology 126, 226–233.

Venkatachalam, K.L., Herbrandson, J.E., Asirvatham, S.J., 2011. Signals and signal processing for the electrophysiologist: part I: electrogram acquisition. Circ. Arrhythm. Electrophysiol. 4, 965–973.

Whittaker, R., Borland, R., Bullen, C., Lin, R.B., McRobbie, H., Rodgers, A., 2009. Mobile phone-based interventions for smoking cessation. Cochrane Database Syst. Rev. 7 (4), Cd006611.

Whittaker, R., McRobbie, H., Bullen, C., Borland, R., Rodgers, A., Gu, Y., 2012. Mobile phone-based interventions for smoking cessation. Cochrane Database Syst. Rev. 11, Cd006611.

Whittaker, R., McRobbie, H., Bullen, C., Rodgers, A., Gu, Y., 2016. Mobile phone-based interventions for smoking cessation. Cochrane Database Syst. Rev. 4, Cd006611.

Wiggert, N., Wilhelm, F.H., Nakajima, M., al'Absi, M., 2016. Chronic smoking, trait anxiety, and the physiological response to stress. Subst. Use Misuse 51, 1619–1628.

Yotsukura, M., Koide, Y., Fujii, K., Tomono, Y., Katayama, A., Ando, H., Suzuki, J., Ishikawa, K., 1998. Heart rate variability during the first month of smoking cessation. Am. Heart J. 135, 1004–1009.

Yuksel, R., Yuksel, R.N., Sengezer, T., Dane, S., 2016. Autonomic cardiac activity in patients with smoking and alcohol addiction by heart rate variability analysis. Clin Invest Med 39, 27519.