Towards detecting cocaine use using smartwatches in the NIDA clinical trials network: Design, rationale, and methodology

August F. Holtyn[a,*], Eugene Bosworth[a], Lisa A. Marsch[b], Bethany McLeman[b], Andrea Meier[b], Elizabeth C. Saunders[b], Emre Ertin[c], Md Azim Ullah[d,e], Shahin Alan Samiei[d], Monowar Hossain[d], Santosh Kumar[d,e], Kenzie L. Preston[f], Massoud Vahabzadeh[f], Dikla Shmueli-Blumberg[g], Julia Collins[g], Jennifer McCormack[g], Udi E. Ghitza[h]

[a] Johns Hopkins University School of Medicine, 5200 Eastern Ave, Baltimore, MD, 21224, USA
[b] Geisel School of Medicine at Dartmouth, 46 Centerra Parkway, Suite 315, Lebanon, NH, 03766, USA
[c] Ohio State University, 512 Dreese Lab, 2015 Neil Avenue, Columbus, OH, 43210, USA
[d] Center of Excellence for Mobile Sensor Data-to-Knowledge (MD2K), The University of Memphis FedEx Institute of Technology, Suite 335, Memphis, TN, 38152, USA
[e] The University of Memphis, Department of Computer Science, 375 Dunn Hall, Memphis, TN, 38152, USA
[f] National Institute on Drug Abuse Intramural Research Program, 251 Bayview Blvd, Baltimore, MD, 21224, USA
[g] Emmes Corporation, 401 N Washington, Suite 700, Rockville, MD, 20850, USA
[h] National Institute on Drug Abuse, 6001 Executive Boulevard, Rm 3105, MSC 9557, Bethesda, MD, 20892, USA

ARTICLE INFO

ABSTRACT

Cocaine use in clinical trials is often measured via self-report, which can be inaccurate, or urine drug screens, which can be intrusive and burdensome. Devices that can automatically detect cocaine use and can be worn conveniently in daily life may provide several benefits. AutoSense is a wearable, physiological-monitoring suite that can detect cocaine use, but it may be limited as a method for monitoring cocaine use because it requires wearing a chestband with electrodes. This paper describes the design, rationale, and methodology of a project that seeks to build upon and extend previous work in the development of methods to detect cocaine use via wearable, unobtrusive mobile sensor technologies. To this end, a wrist-worn sensor suite (i.e., MotionSense HRV) will be developed and evaluated. Participants who use cocaine (N = 25) will be asked to wear MotionSense HRV and AutoSense for two weeks during waking hours. Drug use will be assessed via thrice-weekly urine drug screens and self-reports, and will be used to isolate periods of cocaine use that will be differentiated from other drug use. The present study will provide information on the feasibility and acceptability of using a wrist-worn device to detect cocaine use.

1. Introduction

Cocaine use disorder is a significant public health concern that has serious negative health and social consequences for both the individual user and society. In 2017, 2.2 million persons aged 12 or older in the United States were current (past-month) users of cocaine [1]. The National Survey on Drug Use and Health (NSDUH) estimated that 1.0 million Americans aged 12 and over used cocaine for the first time in 2017; approximately 2700 initiates per day [1]. Efforts aimed at developing effective treatments for cocaine addiction depend critically on the ability to accurately detect cocaine use. Participant self-reports have been used to measure cocaine use, but self-reports of drug use may be of questionable validity, as they can suffer from recall or social desirability biases. Detection of drug (cocaine) metabolites in urine provides a more objective measure but requires frequent in-person visits and can be intrusive. Both of these approaches lack the temporal precision needed to identify antecedents and precipitants of cocaine use [2].

AutoSense was a wearable, physiological-monitoring suite that was developed to detect cocaine use [3,4]. AutoSense included a flexible band worn around the chest that measured breathing via respiratory inductive plethysmography, heart rate via a two-lead electrocardiograph (ECG), and physical activity via a three-axis accelerometer. The measurements collected by these wearable sensors were transmitted using wireless radio to a smartphone in real-time [3,5]. The AutoSense suite has been worn by over 200 participants for over 20,000 h as part of various field studies [4,6]. From these field studies, computational models using the data from AutoSense were developed to detect cocaine use [3,4] as well as other health states, such as physiological stress and smoking [7,8]. The detection of cocaine use was accomplished through the development of a computational model that used measures of heart rate (i.e., interbeat intervals) and physical activity collected by the sensors in the AutoSense suite. Specifically, a dynamical systems model was developed that estimated the effect of recovery by the parasympathetic nervous system on heart rate after physical activity, the dampening of heart rate recovery due to excitation of the sympathetic nervous system by cocaine, and the weakening of this dampening effect due to metabolism of cocaine. The model obtained 100% recall on 58 days (554 h) of data collected in the laboratory setting for a false positive rate of 0.87/day. When tested on 922 days (10,449 h) of field data, the model maintained a false positive rate of 1.1/day [3]. All of the participant-reported cocaine use events in the field setting were detected by this computational model for which high-quality sensor data were obtained. However, the model depended on high-quality sensor data being collected during periods of cocaine use; about 80% of the 142 participant-reported cocaine use events were missed due to: a) participants not having worn the sensors (e.g., after removing the AutoSense suite at the end of the day; 50 use events), b) sensor malfunction (6 use events), c) missing data (6 use events), or d) poor data quality (53 use events) [3].

To improve wearability and sensor data yield, the present study seeks to develop methods to detect cocaine use via wearable, unobtrusive mobile sensor technologies that will not require wearing ECG electrodes. To this end, a wrist-worn sensor suite (i.e., a smartwatch) will be developed and evaluated. After initial smartwatch development, a field test will be conducted to: a) characterize the feasibility of using the smartwatch to collect high-quality physiological data that are necessary to detect cocaine use, and b) evaluate whether a modified computational model, developed for use with the sensor data collected via the smartwatch, can detect cocaine use. This paper describes the design, rationale, and methodology behind the smartwatch development process and the field test to evaluate the novel smartwatch device.

2. Material and methods

2.1. The novel smartwatch: MotionSense HRV

To create a less obtrusive physiological-monitoring system, the present study will develop a wrist-worn sensor suite (i.e., MotionSense HRV). Development of a new wrist-worn device – as opposed to using an existing smartwatch – is necessary for several reasons. Many of the existing (and commercial) smartwatches do not provide heart rate measures, such as interbeat intervals, with the level of precision

required to detect cocaine use. Heart rate detection from smartwatches is typically accomplished using photoplethysmography (PPG) sensors that contain light-emitting diodes (LEDs) and photodetectors. Light reflectance from the LEDs (typically green- or infrared-LEDs) and photodetectors are used to detect pulse waveform characteristics from the radial artery. However, the detection of heart rate from PPG sensors on a wrist-worn device is a challenging task because the physiological signals can be contaminated by large motion artifacts caused by a user's movement. These motion artifacts create noisy data, which can infer false or mis-detected beats. Therefore, many existing smartwatches target the average heart rate measure in identifying periodic components in short-term (~1 min) recordings; they only provide sporadic interbeat interval data not suitable for the application of advanced computational models. The main cause of the aforementioned motion artifacts is the movement of the sensor (LEDs and photodetectors) and skin as the sensor comes in and out of contact with the body. In general, it is not viable to distinguish LED-photodetector pairs that are in good contact in real time while the user is in motion. One strategy to address this problem is to continuously sample all of the sensor pairs; however, this leads to high power consumption and short battery life. Commercially-available smartwatches have limited battery life with continuous sensor sampling, which is required for accurate interbeat interval monitoring.

To overcome the limitations of currently available PPG-based smartwatches, this project will develop MotionSense HRV. MotionSense HRV will include a 3-axis accelerometer and 3-axis gyroscope for measuring physical activity and motion, a multispectral (red-, green-, infrared-LEDs) PPG sensor, and a microcontroller that will perform interchip communication and wireless communication to the smartphone. The novel PPG sensor array will consist of multiple LEDs and photodetectors laid out on an interlaced grid on flexible substrate so that at least a subset of LED-photodetector pairs has good skin contact at any time. Because power consumption and battery life are dominated by active time of the LEDs, MotionSense HRV will randomly sample a subset of LED-photodetector pairs. The proportion of sensor pairs sampled will be adjusted based on the accelerometer readings. As the wearer transitions from a stationary to moving state, the sensor will increase the number of sensor pairs it scans. The brightness of the LEDs will be adjusted to improve signal-to-noise ratio while aiming to maintain a sufficient battery life.

2.2. Study design

This project will evaluate MotionSense HRV using a single-site, non-treatment, 16-day, observational field study with a target sample size of 25 participants. Eligible volunteers will be adults who use cocaine and are enrolled in a clinical trial (R01 DA037314; hereafter referred to as the *parent trial*) conducted at the study site, the Center for Learning and Health at Johns Hopkins University School of Medicine in Baltimore, MD. The patient population in the present study will be targeted because it is similar to the population used in the prior AutoSense cocaine field study [3,4]. After completing a baseline assessment, participants will be asked to wear two MotionSense HRV devices, one on each wrist, and the AutoSense chestband for 14 days during waking hours. Participants will be asked to wear two MotionSense HRV devices to maximize data capture from the devices and to account for within-subject differences in wrist anatomy and wearing style. Participants also will be asked to wear the AutoSense chestband so that direct comparisons can be made between MotionSense HRV and AutoSense. Participants will be asked to carry a study-provided smartphone during their study participation. The smartphone will have mCerebrum software installed (for a description of the mCerebrum software, see Ref. [9]) that will continuously collect data via wireless radio from MotionSense HRV and AutoSense. These data will be uploaded to Cerebral Cortex (cloud software hosted by MD2K Center of Excellence).

During the 14-day study period, participants will attend the study

site every weekday, during which study staff will perform checks to ensure that the study devices are working and being worn properly, address any issues related to wearing the devices, and provide participants with feedback regarding incentives earned for wearing the devices. After the first week, participants will be paid for their study participation to date. After the 14-day period, participants will complete a study debriefing meeting at which they will return the devices, complete a questionnaire of device usability and acceptability, and will be paid for their final week of study participation. Drug use will be assessed via thrice-weekly urine drug screens and participant self-reports. This study is approved by the Johns Hopkins Medicine Institutional Review Board, and all participants will provide written informed consent.

2.3. Study objectives

The two primary objectives of the field study will be to: 1) characterize the feasibility of using MotionSense HRV to collect reliable physiological measures (e.g., heart rate, physical activity) in the natural field setting, characterize the conditions under which high-quality data can be obtained from MotionSense HRV, identify common failure scenarios, and understand wearability and usage patterns. 2) Adapt the computational model for detecting cocaine use, so that it can be applied to the data obtained from MotionSense HRV.

2.4. Study site

The field test will be conducted at the Center for Learning and Health. This site was selected because it provides an ideal setting for recruitment and implementation of this study. Specifically, the study site offers access to participants who are already providing thrice-weekly urine samples for drug testing and self-reports of drug use; offers access to participants with relatively high rates of cocaine use, suggesting that the number of cocaine use events obtained at the study site will be comparable to the use events in the original AutoSense cocaine field study [3]; and is in close proximity to the NIDA Intramural Research Program where the original AutoSense cocaine field study was conducted and expertise on the use of AutoSense will be available.

2.5. Sample size justification

The goal is to recruit a sample of 25 participants, which will result in a total of 50 weeks of data collection. Based on rates of cocaine use in the parent clinical trial, it is anticipated that this sample size will allow for approximately 150 instances of cocaine use during those 50 weeks. This would result in about the same number of cocaine use events that were reported in prior AutoSense field study publications (n = 142 in Ref. [3]; n = 147 in Ref. [4]) and will allow for an estimate of the proportion of events detectable by our smartwatch-based algorithm. In particular, n = 150 will result in a 95% confidence interval of ± 8.0% around the true detection probability of our technique using the normal approximation to the binomial distribution.

2.6. Study assessments

The study assessments are shown in Table 1. Some data will be gathered as part of the parent trial, while others will be collected solely for the purpose of this study. The baseline assessment captures participant demographic information (age, sex, race, ethnicity, weight, etc), recent and lifetime substance use, HIV status and testing, quality of life, current health status, and documentation of all concomitant, prescribed medications.

Drug use will be assessed by urine drug screens and participant self-reports. Results of thrice-weekly (Mondays, Wednesdays, and Fridays) urine drug screens will be abstracted from the parent trial. Participant self-reported drug use will be collected via a modified use-specific

Timeline Followback (US-TLFB) and ecological momentary assessment (EMA) throughout the study. The US-TLFB procedure will be administered every weekday throughout the 16-day study and will assess participant's self-reported use of substances since the previous US-TLFB assessment (or baseline) and the approximate time of day during which each substance was used. The US-TLFB will document use of any substance, including illicit (e.g., cocaine, heroin) and licit (e.g., cigarettes, caffeine, alcohol, prescription medications) drugs. As a part of the parent trial, participants will make real-time self-reports of their drug use on an electronic diary on a smartphone as part of an EMA. Participants will be prompted three times per day by the smartphone, at random times during their waking hours, to self-report on their drug use, and will be asked to initiate an entry on their smartphone whenever they use heroin, cocaine, or another stimulant. Data from these EMA procedures will be abstracted from the parent trial. The US-TLFB and the EMA procedures will document the dose, route, and time of substance use. Urine drug screens and participant self-reports of drug use will be used to isolate periods of cocaine use that will be differentiated from confounds such as other stimulant drug use (e.g., amphetamines).

2.7. Outcome measures

The outcome measures of this study will include: (1) physiological measures, including heart rate and heart rate variability (e.g., interbeat interval) from PPG sensors in MotionSense HRV and ECG sensors in AutoSense, and physical activity from accelerometers and gyroscopes. (2) Device wearability (e.g., acceptability and burden), measured via participant responses to the device usability and acceptability questionnaire. (3) Drug use measured via urine drug screens and participant-reported drug use from the US-TLFB and EMA. (4) Data yield from MotionSense HRV and AutoSense. (5) Algorithmic detection of cocaine use via computational models.

2.8. Statistical analyses

Descriptive statistics will be used to evaluate data yield and characterize common failure scenarios (e.g., poor sensor data quality, missing data due to poor sensor attachment, sensor malfunction, missing data due to device removal) of each sensor suite (i.e., AutoSense and MotionSense HRV). Average data yield as well as common failure scenarios of AutoSense and MotionSense HRV will be compared using independent samples t-tests. Descriptive statistics also will be used for the analyses of acceptability and usability via questionnaires.

Evaluation of the computational model for the algorithmic detection

Table 1
Schedule of study assessments.

	Baseline	Active Study	Debrief
Contact Information Form[a]	×		
Pregnancy[a]	×		
Adverse Events Reporting	×	×	×
Compliance Measures	×	×	×
Urine Drug Screen (UDS) [a]	×	×	×
Ambulatory Physiological Assessment using Mobile Sensors	×	×	
Ecological Momentary Assessment (EMA)[a]		×	
Eligibility Form	×		
PhenX Core Tier 1	×		
Concomitant Medications Form	×		
Photographs of Smartwatch Wrist Placement	×		
Timeline Followback (TLFB) [b]	×	×	×
Usability and Acceptability Questionnaire			×

[a] Collected as part of the parent clinical trial.
[b] Assessed every weekday during study period.

of cocaine use will be performed using precision and recall. To perform this evaluation, rates of true positive and false positive cocaine detection events will be compared. True positive events will be defined as events (out of all self-reported cocaine use events confirmed by urinalysis) where cocaine use was detected using the computational model during which data quality from the sensors is sufficient. False positive events will be defined as events where cocaine use was detected using the computational model during which data quality from the sensors is sufficient and when cocaine use is confirmed to have not taken place (from both urinalysis and self-report). Rates of true positive and false positive cocaine detection events from AutoSense and MotionSense HRV will be compared using independent samples t-tests.

3. Discussion

This project seeks to build upon, and extend, methods to detect cocaine use from wearable sensors [3,5]. A wrist-worn device will be developed and a field test conducted to determine the feasibility and acceptability of using a wrist-worn device to detect cocaine use. Detection of cocaine use via wearable sensors worn on the wrist could become a novel and convenient technology to aid in clinical trials examining cocaine use.

The development of methods to detect health-related events, such as cocaine use, from wearable sensors involves several challenges that we plan to address in the proposed project [3]. First, wearable sensors that can be used conveniently in daily life, provide reliable data collection in the natural field setting, and last for a long enough duration to capture the health events of interest are needed. In this project, we will develop a wrist-worn device that can reliably detect interbeat intervals and can last the entire day on a single charge of battery with continuous sensor data collection. Second, a rigorous study needs to be conducted to collect data from the sensors – with appropriate labeling of the times when the health event of interest occurred – to train the computational model to detect the health event. This project will use Timeline Followback, ecological momentary assessment, and urine drug screens to rigorously identify instances of cocaine use. This project also will collect data on potentially important covariates (e.g., participant demographics, concomitant substance use) that can be used to facilitate accurate detection of cocaine use. Third, a robust computational model needs to be developed that is able to detect the health event of interest from streaming sensor data in the natural environment. This project seeks to adapt an existing computational model for detecting cocaine use, so it can be applied to the interbeat interval and physical activity data obtained from wrist-worn sensors.

The results of this study may have implications for future research of this type. Detection of cocaine use from devices that can be worn conveniently in daily life can provide several benefits. First, this approach could be used to pinpoint the precise timing of cocaine use, which in turn could be used to develop a cocaine user's risk profile to identify predictors of cocaine use, which could in turn trigger the delivery of interventions. Second, this method could be used to initiate self-report to collect contextual information that could point to the potential triggers or circumstances surrounding each use event. Finally, this approach may nicely complement self-report methods that can suffer from temporal inaccuracy. It could also reduce costs and improve convenience of measurement by reducing the frequency of urine specimen collection. In sum, the investigation of sensor suites that can be worn unobtrusively on the wrist may prove to be a convenient method

to collect continuous, high-quality physiological data that are necessary in the inference of health states such as cocaine use.

Conflict of interest

No authors have any conflicts of interest to declare related to this study or this publication.

Role of funding source

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2019.100392.

References

[1] Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indications in the United States: Results from the 2017 National Survey on Drug Use and Health. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Rockville, MD.

[2] D.M. Donovan, G.E. Bigelow, G.S. Brigham, et al., Primary outcome indices in illicit drug dependence treatment research: systematic approach to selection and measurement of drug use end-points in clinical trials, Addiction 107 (4) (2013) 694–708.

[3] S.M. Hossain, A.A. Ali, M.M. Rahman, et al., Identifying drug (cocaine) intake events from acute physiological response in the presence of free-living physical activity, Proceedings of the 13th IEEE/ACM International Symposium on Information Processing in Sensor Networks (IPSN), 2014, pp. 71–82.

[4] A.P. Kennedy, D.H. Epstein, M.L. Jobes, et al., Continuous in-the-field measurement of heart rate: correlates of drug use, craving, stress, and mood in polydrug users, Drug Alcohol Depend. 151 (2015) 159–166.

[5] E. Ertin, N. Stohs, S. Kumar, et al., AutoSense: unobtrusively wearable sensor suite for inferring the onset, causality, and consequences of stress in the field, Proceedings of the 9th ACM Conference on Embedded Networked Sensor Systems (SenSys), 2011, pp. 274–287.

[6] M.M. Rahman, R. Bari, A.A. Ali, et al., Are we there yet?: feasibility of continuous stress assessment via wireless physiological sensors, Proceedings of the 5th ACM Conference on Bioinformatics, Computational Biology, and Health Informatics (BCB), 2014, pp. 479–488.

[7] K. Hovsepian, M. al'Absi, E. Ertin, et al., cStress: towards a gold standard for continuous stress assessment in the mobile environment, Proceedings of the 2015 ACM International Joint Conference on Pervasive and Ubiquitous Computing, (UbiComp), 2015, pp. 493–504.

[8] N. Saleheen, A.A. Ali, S.M. Hossain, et al., 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, (UbiComp), 2015, pp. 999–1010.

[9] S.M. Hossain, T. Hnat, N. Saleheen, et al., mCerebrum: a mobile sensing software platform for development and validation of digital biomarkers and interventions, Proceedings of the 15th ACM Conference on Embedded Networked Sensor Systems (SenSys), 2017, pp. 1–14.