Integrating Personalized Technology in Toxicology: Sensors, Smart Glass, and Social Media Applications in Toxicology Research

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Abstract Rapid proliferation of mobile technologies in social and healthcare spaces create an opportunity for advancement in research and clinical practice. The application of mobile, personalized technology in healthcare, referred to as mHealth, has not yet become routine in toxicology. However, key features of our practice environment, such as frequent need for remote evaluation, unreliable historical data from patients, and sensitive subject matter, make mHealth tools appealing solutions in comparison to traditional methods that collect retrospective or indirect data. This manuscript describes the features, uses, and costs associated with several of common sectors of mHealth research including wearable biosensors, ingestible biosensors, head-mounted devices, and social media applications. The benefits and novel challenges associated with the study and use of these applications are then discussed. Finally, opportunities for further research and integration are explored with a particular focus on toxicology-based applications.

Keywords mHealth · Drugs of abuse · Biosensors · Smart glass · Social media

Background

With the explosion of digital health tools in both consumer and professional spaces comes the demand for the effective utilization of digital health solutions. Adaptation of common wearable devices, advanced sensors, and social media into healthcare has ushered in the desire for individuals to quantify biometric data and personalize disease management. Advances in biosensor technology, miniaturization of wearable devices, and increased acceptability of connected devices create the opportunity for clinicians to gather data and develop interventions in novel spaces [1]. Defined by the World Health Organization as “the use of mobile and wireless technology to support medicine and public health objectives” [2], mobile health (mHealth) is a burgeoning field with immense potential for both research and clinical applications. The ultimate goal is to develop a suite of technology that provides convenient, real-time, accurate evaluation of health-related problems with rapid, effective technology-driven solutions to allow clinicians to treat patients at the moment of greatest need without the restrictions of physical and temporal proximity required in the traditional interventional models. mHealth tools are even now more common and more flexible than traditional health care tools.

The availability of almost a hundred thousand health-related consumer applications on the market in 2016 [3] clearly demonstrates both demand for and access to mHealth tools. Despite the widespread availability and patient acceptance of mobile technology, research demonstrating clear outcome-related benefits is generally lacking in the current literature. Many fields in medicine, such as behavioral health, and cardiology are rapidly adopting technology-based interventions [4, 5]. Although mHealth applications are not yet widely used in toxicology research, our specialty faces unique challenges that make mHealth exceptionally advantageous. Particular

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benefits for toxicologists include the ability to interface with difficult to reach patient populations, study behaviors that are difficult to quantify, explore sensitive topics that less likely to be disclosed, and evaluate patients remotely [1, 6–9].

This manuscript will review the current knowledge and promising future applications of several popular areas of mHealth research (Table 1) with a focus on those especially pertinent to medical toxicology. We will then review the advantages and challenges unique to this line of research and finally will propose ways which toxicologists can leverage the mHealth movement and integrate these technologies to advance our specialty and improve patient outcomes.

mHealth Sectors

Wearable Biosensors

Integral to the concept of the quantified self, or the practice of measuring daily activities for health improvement [21], wearable devices (or wearables) have become pervasive in everyday life. Watch-style trackers that monitor sleep and activity are among the most commonly used by consumers. Wearable devices come in multiple other form factors including pendants, vests, shoes, and clothing items. Wearables measure multiple physiologic and physical parameters in a continuous fashion such as heart rate, skin temperature, accelerometry, skin conductance, geolocation (via GPS), altitude, electrocardiogram (ECG), respiratory rate, and oxygen saturations. Commercial devices keep simple logs enabling users to track progress (e.g., steps taken, calories burned, and heart rate trends) whereas research grade devices such as the Empatica E4 (Fig. 1a, b) store tremendous amounts of raw data to be

analyzed in a more robust fashion. These data can then be used to identify patterns that correlate with behaviors or events of interest [9, 22]. Newer generations of wearable sensors boast improvement in noise cancellation mechanisms, wireless transmission to phone and/or cloud-based interface, improved battery life, and even the potential to be powered by the human body [23], all of which make sensors more efficient and user-friendly. Cost of wearable devices varies with relatively inexpensive consumer devices ranging from \$30 to several hundred dollars, where research grade wearable devices can exceed several thousand dollars each depending on the device and capabilities.

Dramatic physiologic changes that occur with substance abuse, coupled with the current lack of accurate or real-time detection methods, create a unique opportunity for toxicologists to develop lines of investigation in wearable technology. Whereas our current practice allows us to react only after a problematic behavior (i.e., drug abuse) or dangerous effect (drug toxicity) has occurred, detection of physiologic changes that herald substance abuse as they occur provides an opportunity for real-time intervention. Wrist-mounted wearable biosensors can detect cocaine and opioid use based on characteristic changes in movement, skin conductance, and skin temperature and may be able to identify the development of drug tolerance [9, 22]. Future research should explore the use of wearables in identifying periods of vulnerability (and opportunities for intervention) across the spectrum of substance abuse disorders.

Ingestible Sensors

Optimal methods for monitoring medication adherence during disease therapy and understanding circumstances in which

Table 1 mHealth sectors, example devices and platforms, and evidence-based applications

mHealth sector	Example devices/platforms	Applications
Wearable biosensors	Empatica E4	Detection of cocaine and opioid use [9]
	Philips biosensor	Fitbit for stroke/cardiac rehab [10, 11]
	Fitbit	
Ingestible sensors	Scanadu	
	eTectRx ID Cap	Detection of opioid ingestion [7]
	Proteus Digital Health	Diabetes management [12]
Head-mounted devices	GI sensor	DOT in schizophrenics [13]
	Google Glass	Low intensity teledermatology [14]
	Vuzix Smart Glasses	ED-based toxicology consults [15]
	ODG	ICU-based toxicology consults [8]
Social media	Twitter	Emerging drug trends [16]
	Instagram	Twitter trends for novel drugs [17]
	Facebook	Social media and suicide detection [18]
	Tumblr	Twitter-based focus groups for crowd sourcing [19] Twitter for weight loss [20]

Fig. 1 **a, b** Empatica E4 Wearable Biosensor. **c** Ingestible Sensor Capsule with radiofrequency emitter. **d** Medication inserted into capsule. **e** Complete Digital Pill. **f, g** Head-mounted Smart Glass

adverse drug events occur remain elusive for toxicologists [24]. Outpatient substance abuse treatment monitoring and high-risk medication monitoring rely on indirect measures of ingestion, such as patient self-report, pharmacy refill history, or smart pill caps, all of which are marred by inconsistencies or easily thwarted technology [25, 26]. Similarly, clinical presentation of the poisoned patient is frequently clouded in ambiguity—unconfirmed ingestion time, unconfirmed xenobiotic formulation, and unconfirmed dose.

Ingestible biosensor systems directly measure medication ingestion events [13, 26]. These systems are comprised of an inert radiofrequency emitter (Fig. 1c) coupled with the desired medication forming a digital pill (Fig. 1d, e) [13, 27]. As the digital pill is ingested, it is energized by chloride ions in stomach acid, emitting a preset radiofrequency signal, which is captured by a wearable device. The wearable device relays ingestion data (pill identification and ingestion time) to a cloud-based server that is able to display customized ingestion data to patients and physicians. Behavioral interventions and messages can be triggered in response to adherence (or nonadherence) and can occur in real time [24].

Knowledge of precisely when medications are ingested, how many pills are ingested, and patterns of ingestion are important details for medical toxicologists that may assist in decision-making adverse drug events and adherence monitoring. Ingestible biosensor systems show promise in replacing directly observed therapies for tuberculosis, adherence monitoring in individuals with psychiatric illness, and monitoring adherence in high-risk patients and expensive medication regimens [12, 13, 28]. Acceptance of ingestible biosensors in individuals is high, with over 90% of emergency department-based patients with chronic medical problems reporting willingness to utilize an ingestible biosensor to monitor medication adherence [29]. An ingestible biosensor system has been used successfully to monitor outpatient opioid

therapy, with 87% accuracy and 80% patient acceptance [7]. With expertise in pharmacokinetics/pharmacodynamics and experience with a broad range of adverse drug effects, toxicologists are primed to play a leading role in medication adherence monitoring with ingestible biosensors to monitor diseases like human immunodeficiency virus, hepatitis C, and congestive heart failure [26].

Head-Mounted Devices for Teletoxicology

Bedside evaluation of poisoned patients reveals pertinent details that may alter the course of diagnostic testing and treatment including antidotal therapy [30]. Toxicologists frequently rely upon phone-based communication to help manage poisoned patient remote from their physical location [31]. Advances in audio-visual technology and wireless streaming have imparted the capability to virtually examine and even make personalized recommendations to remote providers. Similar to telestroke and tetrauma systems, remote audiovisual management of toxicology patients—teletoxicology—is a feasible and valuable option for the toxicologist who is required to remotely evaluate and manage severely poisoned individuals [6, 15].

Head-mounted computers (e.g., smart glasses, Fig. 1f, g) that project first person viewpoints through an integrated video camera and multimedia software backbone can provide a remote toxicologist with a unique and pertinent assessment of the poisoned patient from the consulting physician's point of view. These commercial smart glass devices are intuitive and unobtrusive, requiring minimal training for physicians, and provide the benefits of telemedical consultation without the burden of expensive hardware and information technology setup. In a busy emergency department where the majority of toxicology consults tend to occur, a head-mounted device

integrated into the emergency medicine physician's workflow permits a bedside subspecialty consultation in real time with minimal interruption. Physical exam findings such as pupil size, the presence of clonus, and the character of altered mental status can be validated and agreed upon while advanced data including ECG findings, imaging studies, and laboratory values can be viewed in real time with the consulting provider, improving confidence in the toxicology consultation [15, 32]. The cost of smart glasses ranges from \$300 to \$1500 per unit with associated cost for secure software and data storage. The appeal of smart glass technology for telemedicine lies in its portability; a single unit allows the user to transform their space into a telemedicine suite without the need to invest in the significant infrastructure required to support traditional telemedicine services. Teletoxicology-based consultations also have the potential to decrease admissions/transfers and improve recommendations for antidotal therapy compared to phone consultations alone [15].

Smart glass and other advanced audiovisual communication technologies provide a feasible solution enabling toxicologists to access critical components of a physical exam in order to provide improved triage and management decisions. Although proven to be valuable, teletoxicology continues to face barriers to reimbursement similar to other remote consultations. Understanding the state-dependent milieu of reimbursement will be critical to toxicologists who wish to deploy an advanced teletoxicology service. Future research should be directed toward demonstrating the benefits of teletoxicology service integrated into a toxicology practice from both cost saving and clinical outcome perspectives.

Social Media

The popularity of social media has been steeply rising over the past two decades; it is a continuously evolving form of communication via various public and private platforms. The availability of mobile devices, in particular smartphones, has accelerated the growth of social media and its platforms. According to the Pew Report, 65% of adults were using social media networking sites in 2015, an increase from just 7% in 2005 [33]. Across age groups, 59% of seniors report going online, with 46% of online seniors using social media [34]. Among teens, 92% report going online daily, with 76% reporting that they use social media [35]. Facebook, YouTube, and Twitter are ranked the most popular social networking sites in the USA.

Given the overwhelming use of social media, it has emerged as an important avenue for investigation although social media research is still in its infancy. There are many opportunities for social media-based research in medicine, in particular behavioral science topics. Many researchers have used social media for informational and intervention-based

approaches to weight loss, smoking cessation, alcohol reduction, and substance abuse [19, 20].

A major benefit to social media-based research studies is the relatively low overall cost, with the major expense being data storage space. Fees are varied and depend on size of storage, computer utilization, and memory size. Amazon Web Services is one such service available with a free tier followed by a fee. Katsuki et al. report paying US \$17 per instance with 40GB of storage space [36].

Topics pertaining to medical toxicology have emerged as important areas for social media-based research. Because online forums and social media allow for anonymous dissemination of information such as drug diversion, illicit drug use, and innovate drug use [16], social media monitoring is useful for researchers and clinicians to understand emerging drug trends. The Psychonaut Web Mapping Project used social media, in part, to develop an integrated mapping and monitoring system to allow for the early identification of emerging trends in recreational drug use [37]. The publicly available platform Twitter, which has 313 million active users, has also become a popular source of data for social media researchers to collect data on a variety of topics, including prescription medication use and abuse. In one study, representative tweets using the terms "Percocet," "Percs," "Oxycontin," "Oxys," "Vicodin," and "Hydros" were collected over 11 days using an automated Twitter Archiving Google Spreadsheet® (TAGS) platform to search Twitter. In total, 2100 original tweets were manually reviewed by investigators and found that these substances are frequently the subject of user tweets [17]. In a separate study using machine learning rather than manual review of content, 11 million tweets were collected and searched specifically for mentions of Percocet, OxyContin, or oxycodone. 2.3 million tweets were found, analyzed by theme, finding that most common theme to be polypharmacy and drug abuse [38]. Another study reviewed over 2 million tweets regarding nonmedical use of commonly abused prescription medications; they found that users were providing resources to obtain medications, with hyperlinks to online pharmacies that sold prescription medications without a prescription. Results were also geocoded to show the location of origin [36]. Other studies have focused on a single medication with abuse potential; Adderall. Tweets from 132,099 unique users found that the number of tweets regarding Adderall peaked during traditional college and university final exam periods, with 12.9% of tweets identified using it as a study aid [39].

The US Food and Drug Administration (FDA) has also taken steps toward using social media as a depot for drug safety information. The FDA collaborated with Epidemico, a health informatics company, to develop the digital data-mining platform MedWatcher Social. This platform was developed to collect publicly available posts from Twitter and Facebook about drug safety events and experiences with medical products to identify potential adverse events [40, 41].

Other groups have also investigated the use of social media to aid to earlier detection of drug-related adverse events [42, 43]. While this technology is still in development, it appears to be an important source of information with regards to patient safety.

Social media-based research allows rapid access to a large amount of publically available data, and the ability to reach out to a large, diverse group of users or to a targeted subset of the users as needed. As research in this area is in early stages of growth, a constant outpouring of new methods creates many opportunities for toxicology research. Toxicologists can use social media to play a key role in research on drug surveillance, medication safety, drug abuse, and drug-related behavioral trends.

Benefits Unique to mHealth Approaches

The inherent portability and personal nature of mHealth devices and social media platforms provides researchers and clinicians the opportunity to interact and respond to previously undiscovered information (e.g., real-time contextualized biometric data, medication ingestion events) in patient populations. We can use wearables to gather data on and respond to events as they occur in daily life, telemedicine to bring a remote specialist to the bedside, ingestible sensors to understand exactly when and how patients are taking medicine and social media to understand how drugs are affecting the population. mHealth can also reduce socioeconomic disparities [4] by providing expanded access to care in populations that may lack resources to utilize the healthcare system. Overall, mHealth interventions can provide lower cost solutions with improved efficiency [44]. mHealth approaches can also enhance the patient experience by using a familiar format to encourage patient engagement and to empower patients to be active participants in their own care.

Even more powerful than the use of an individual mHealth device or platform alone is the potential for integration across

devices to create the ultimate connected patient experience. Ingestible sensors can confirm ingestion of medications while wearable biosensors record and trend the physiologic response to them. Wearable sensor data can be transmitted via Bluetooth connectivity to the cloud, reviewed by a physician who can then use a smart glass device to check in on a patient. Wearable and ingestible sensor data can be used in social media support groups to promote health behaviors among members. Disparate data streams from multiple devices can give toxicologists a more complete assessment of an individual's health and lifestyle, ultimately allowing for a personalized approach to reinforce healthy behaviors and curtail detrimental ones.

Research Challenges

While mHealth promises to revolutionize healthcare with its novel solutions, it also presents novel challenges in research applications that require consideration. The acquisition of continuous, real-time health-related information poses many unique hurdles that have yet to be conquered. Compared to traditional basic science or epidemiological research, mHealth approaches present a particular challenge when it comes to accuracy, security, privacy, investigator practices, and patient responses (Table 2).

Migrating from controlled settings to natural environments puts the validity and authenticity of data into question. Factors influencing variables of interest (such as medications and comorbidities) pose a particular concern among physicians and researchers [45]. Contextual information, such as wearable device positioning and ambient conditions, have the ability to alter readings but are difficult to define and collect [9, 45]. Wide variability among user physiology based on demographic characteristics and health status challenges the concept of universal baselines and “gold standards” [9, 46]. Discontinuous data streams due to device failures and non-compliant users may result in increased risk for missed events

Table 2 mHealth challenges and solutions

Challenge	Example	Potential solution
Accuracy	No universal baseline	Compare patients to themselves over time as oppose to preset standards
Security	Signal eavesdropping/hacking	Higher level encryption, identification based on personalized physiology parameters (such ECG waveform matching)
Privacy	Loss of confidential data	Restriction to de-identified data to cloud, or use of HITECH/HIPAA compliant cloud server
Investigator practices	Need for expertise from various scientific displaces (medicine, behavioral science, engineering, computer science)	“Team Science” approach, specific focus on interdisciplinary communication strategies
Patient responses	Behavior modification due to the presence of tech	Ecological momentary assessment, placebo controlled clinical trials

of interest [5, 9, 45]. Cloud computing, which allows visualization, real-time processing, and storage of large quantities of data [47], opens the door to signal manipulation and data tampering.

Once data collection moves outside the isolation of the healthcare facility, geographic boundaries cease to exist [45] and research is happening in a world of unencrypted guest networks, hackers, and forgetful users who lose devices [47, 48]. The quantity and quality of data collected is much wider than what is typically obtained in traditional clinical settings, but regulations and guidelines related to the sharing of information and data ownership have not evolved at the same pace. Current privacy laws are variable and contain gray areas that allow for developer interpretation, leaving unaware users at risk of exposure [47, 48].

Due to its multifaceted nature and enormous volumes of data output, the success of mHealth interventions heavily relies on collaborations of multidisciplinary teams, such as clinicians, engineers, software developers, and statisticians. Being able to facilitate successful “team science” throughout entire project periods does not come without obstacles, as interests and methodologies vary among fields. Work styles also tend to fluctuate—clinical researchers focus on long-term projects that start with an idea and end with a deployed intervention while technologists work in a fast-paced “roll out and update” fashion [5].

mHealth research not only requires study teams to identify and resolve a plethora of unfamiliar challenges, but they must do so in a timely manner due to rapid and consistently evolving technologies that result in obsolete interventions [5]. With 5.5 years being the average lag time between initiation of subject recruitment to outcome publication for randomized control trials, this gold standard testing of efficacy and effectiveness is no longer feasible [9]. Interventions must be able to maintain some degree of flexibility and continuously improve. Some aspects, such as maintaining compatibility with new and updated operating systems, are beyond control of the study team.

Finally, mHealth applications can have unintended behavioral modifications, calling into question whether interventions are effective or the mere constant presence of a device is generating change. Without gold standards to test effectiveness and usability, it is difficult for researchers (or clinicians) to generate evidence-based recommendations to guide best practice.

Conclusion

The yet unrecognized potential of mobile health solutions lies in the ever-increasing availability, portability, familiarity, and affordability of mobile devices combined with our society’s increasing tendency toward connected living. Wearable

devices, ingestible sensors, teletoxicology devices, and social media platforms are just a few of tools that innovative toxicologists can use to improve our patient care. mHealth can facilitate better and more affordable care but requires more research to drive effective implementation. mHealth presents a set of unique challenges to researchers, clinicians, and patients. This line of research utilizes novel approaches compared to traditional basic science research; however, it must be done in a systematic and rigorous fashion to ensure scientific integrity. Given that this research is in its infancy, major gaps exist in delineating the efficacy and outcome-based benefit of mHealth interventions. Toxicologists should consider mHealth applications for investigations in areas such as substance abuse tracking, medication adherence, consultation services, and surveillance for drug use trends.

Compliance with Ethical Standards

Conflicts of Interest None.

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