

Temporal Dynamics of Transdermal Alcohol Concentration Measured via New-Generation Wrist-Worn Biosensor

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Background: The development of a transdermal alcohol biosensor could represent a tremendous advance toward curbing problematic drinking. But several factors limit the usefulness of extant transdermal technology, including relatively lengthy delays between blood alcohol concentration (BAC) and transdermal alcohol concentration (TAC), as well as the large/bulky designs of currently available transdermal sensors (e.g., ankle monitors). The current research examined the lag time between BAC and TAC using a prototype of BACtrack Skyn—a new-generation wrist-worn transdermal sensor featuring a compact design and smartphone integration.

Methods: Participants ($N = 30$) received either a dose of alcohol (target BAC 0.08%) or a nonalcoholic beverage in the laboratory while wearing both the AMS SCRAM ankle monitor and a Skyn prototype. Participants were monitored in the laboratory until breath alcohol concentration (BrAC) dropped below 0.025%.

Results: Device failure rates for Skyn prototypes were relatively high (18 to 38%) compared with nonprototype SCRAM devices (2%). Among participants with usable data, both Skyn- and SCRAM-measured TAC showed strong correlations with BrAC, and both Skyn and SCRAM devices detected alcohol within 30 minutes of first alcohol administration. Skyn-measured TAC peaked over 1 hour earlier than SCRAM-measured TAC (54 versus 120 minutes after peak BrAC, respectively), and time-series models suggested that, on average across all measured portions of the BrAC curve, Skyn TAC lagged behind BrAC by 24 minutes, whereas SCRAM TAC lagged behind BrAC by 69 minutes—all differences statistically significant at $p < 0.001$.

Conclusions: Results provide preliminary evidence for the validity of a new-generation wrist-worn transdermal sensor under controlled laboratory conditions and further suggest favorable properties of this sensor as they pertain to the latency of transdermal alcohol detection. The prototype version of Skyn employed here displayed a higher failure rate compared with SCRAM, and, in future, more reliable and robust Skyn prototypes will be required suitable to field testing across diverse environmental conditions.

Key Words: Alcohol, Biosensor, Transdermal, Blood Alcohol Concentration, Measurement.

THE DEVELOPMENT OF a wearable alcohol biosensor could represent a key advance toward helping people make informed decisions about their drinking and, potentially, toward curbing alcohol-related morbidity and mortality. Devices for the objective quantification of behaviors have long been of interest to researchers and consumers across health domains (e.g., Fitbit for exercise; Haynes and Yoshioka, 2007), but, due to alcohol's neurocognitive effects and also cultural conventions surrounding drinking, the need for a biosensor to measure alcohol

consumption has loomed particularly large. Specifically, drinking at more extreme levels is associated with memory and cognitive disruptions that can impair awareness of the quantity of alcohol consumed (Weissenborn and Duka, 2003; White, 2003). Further, standard drink sizes and quantities can vary widely so that even the cognitively alert drinker may not always be aware of the amount of alcohol she ingests (Barnett et al., 2009; Kerr et al., 2005, 2008). Finally, societal stigma can accompany alcohol consumption for many individuals such that, even given an awareness of their own drinking practices, some might be reluctant to share this information with others, thus interfering with the identification of those in need of alcohol intervention as well as the investigation of drinking behavior via research (Davis et al., 2010; George et al., 1988; Zapolski et al., 2014). A wearable alcohol biosensor might serve health needs across a variety of domains, including aiding prevention of alcohol-related disorders (Fairbairn and Kang, in press), improving outcomes in harm reduction alcohol intervention programs (Barnett, 2015),

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reducing the number of alcohol-related motor vehicle fatalities (Blincoe et al., 2015), and refining outcome assessment in alcohol research (Leffingwell et al., 2013).

Researchers have explored a variety of different methods for the continuous tracking of drinking (Fairbairn and Kang, in press; Swift, 2003), but transdermal devices are currently those with the firmest basis of empirical support for their viability as continuous alcohol biosensors. Approximately 1% of alcohol consumed is diffused transdermally in the form of sweat and insensible perspiration (Swift, 2003; Swift and Swette, 1992). Thus, similar to the manner in which a breathalyzer estimates blood alcohol concentration (BAC) by measuring the quantity of alcohol in expired air, transdermal sensors might estimate BAC by examining alcohol in water vapor emitted from the skin. Measured via a device that rests on the surface of the skin, transdermal assessment is passive and unobtrusive. Correlations between transdermal alcohol concentration (TAC) and BAC tend to be strong (Giles et al., 1987; Luczak and Rosen, 2014; Sakai et al., 2006). Yet, despite their promise, challenges have emerged for transdermal monitors—including challenges associated with the available devices themselves as well as those associated with the data produced by these devices—and these challenges have limited the widespread implementation of transdermal alcohol assessment within research and also everyday drinking contexts.

Concerning challenges associated with the devices themselves, at the present time, the only available transdermal monitors take the form of relatively large/bulky bracelets designed to be worn around the ankle. Although previously some smaller wrist-worn transdermal devices were accessible to researchers (e.g., the WrisTAS device),¹ at the current time, the Secure Continuous Remote Alcohol Monitoring (SCRAM) ankle bracelet is the only widely available wearable alcohol biosensor. SCRAM devices, which weigh about 6 oz and are approximately the dimensions of a large deck of cards, are mainly designed as abstinence monitors for use with criminal justice-involved populations (see Fig. 1). Data from SCRAM have been examined in several dozen studies (Fairbairn et al., 2018; Sirlanci et al., 2018; see Leffingwell et al., 2013 for a review), and associations between SCRAM-measured TAC and BAC have been generally estimated as strong. SCRAM employs fuel cell technology whereby alcohol molecules are translated into a measurable electrical current at the sensor. The large size of these bracelets is partially attributable to the nature of the specific fuel cell employed, which requires a pump to promote the active flow of air across the sensor, a feature that also limits the



Fig. 1. AMS SCRAM ankle bracelet (left) and BACtrack Skyn wrist monitor (right) displayed side by side. The approximate weight of the devices is 6 oz (SCRAM) and 1 oz (Skyn prototype), respectively.

TAC sampling interval to a relatively extended 30 minutes (Wang et al., in press). The size, ankle positioning, and relatively sparse data produced by these devices appear to be well suited for their application as abstinence monitors with nonvoluntary populations. However, since wearing SCRAM devices can produce discomfort and embarrassment (Barnett et al., 2011), the usefulness of these ankle monitors for voluntary populations (e.g., as health behavior trackers among large populations of consumers) is severely limited.

In addition to challenges associated with the transdermal devices themselves, another important challenge surrounds the nature of the data produced by these devices—in particular, delays between the time that alcohol is ingested and when it can be detected transdermally. TAC is believed to lag behind BAC by a substantial margin, with the extent of this lag being typically estimated as lasting at least 1 hour (Fairbairn and Kang, in press; Leffingwell et al., 2013), and potentially as long as 3 to 4 hours (Marques and McKnight, 2009). Note that several of the more pressing proposed applications of transdermal alcohol biosensors would require real-time or near-real-time estimation of drinking (Fairbairn and Kang, in press; Fairbairn et al., 2018)—for example, researchers aiming to map everyday alcohol use with associated antecedent and/or consequent behaviors in real time. Of note, while it is clear that some delay exists between BAC and TAC, the exact extent of this delay is currently unclear. In estimating this delay, researchers have mainly employed SCRAM ankle monitors and have further examined delays nearly exclusively by examining the relative timing of TAC/BAC peaks (Sakai et al., 2006; Swift et al., 1992). Regarding the former of these issues, since the permeability of the skin and also the density of sweat glands differ on different areas of the body, the relationship between BAC and TAC also differs depending on where on the body TAC is assessed (Swift, 2000). Indeed, a review of the literature

¹One of the first transdermal devices developed was the WrisTAS, marketed by Giner Labs, which was worn around the wrist as a watch (Leffingwell et al., 2013). However, this device was only used for research purposes, to our knowledge, and has not been made available to researchers for several years now.

indicates that the notion that TAC lags behind BAC by a factor of 2 to 4 hours is derived entirely from studies employing ankle monitors (Fairbairn et al., in press; Marques and McKnight, 2009), whereas studies employing wrist sensors (e.g., the early WrisTAS device) have estimated substantially smaller lag times (Swift et al., 1992; see Table 1 for a literature review of studies examining TAC in relation to objectively assessed BAC). In addition, a more nuanced operationalization of lag time—encompassing other portions of the BAC curve beyond TAC/BAC peak—could aid in informing our understanding of the relative timing of TAC versus BAC.

Recently, a new generation of wrist-worn devices has emerged that leverages advances in electronics and wireless communication in order to substantially reduce the size and increase the comfort/attractiveness of transdermal alcohol monitors (Wang et al., in press). One such device is BAC-track Skyn™. Skyn is a small device that includes a transdermal alcohol biosensor, rechargeable battery, and a companion smartphone application. Skyn is worn on the inside of the wrist—a position selected to increase its sensitivity and decrease lag to detected alcohol. Currently in the prototype phase, Skyn is designed to be comfortable, user-friendly, and socially acceptable, similar to a Fitbit or smartwatch (see Fig. 1). Like SCRAM, Skyn uses fuel cell technology in order to assess TAC. Unlike SCRAM, however, Skyn devices do not require a pump to generate airflow across the sensor and instead rely on passive airflow—a feature that reduces the size and dimensions of the device and also facilitates more rapid TAC sampling, with current prototypes allowing for sampling as frequently as every 20 seconds (Wang et al., in press). While the new generation of

transdermal alcohol sensors holds promise for use in research as well as for widespread health behavior monitoring, these devices have not been examined in controlled studies and so the relation of readings produced by these devices to ingested alcohol is unknown.

In the current study, we employ laboratory methods to directly compare data produced by 2 transdermal alcohol monitors—the widely researched SCRAM ankle monitor and the newer wrist-worn Skyn device. This study focuses on an examination of TAC over time among participants administered a single fixed dose of alcohol, although we also include a subsample of participants administered no alcohol by way of control. We used breathalyzer readings to validate TAC measures—chosen as a noninvasive measure with a strong and well-characterized relationship with BAC (Bendtsen et al., 1999; Jones and Andersson, 1996, 2003; Ramchandani et al., 2009). In light of the identified challenges surrounding delays in the detection of alcohol via transdermal monitors (Leffingwell et al., 2013), the primary aim of this research was to examine and quantify lag times between ingested alcohol and TAC, operationalized through a range of metrics intended to capture various positions on the BAC curve.

Note that the restricted alcohol dosing procedures employed in this study are well suited to addressing our primary aim of examining comparative lag times across transdermal sensors under controlled conditions, whereas the limited variation in BAC produced by these procedures means that they are less well suited to quantifying the magnitude of BAC-TAC correlations. Nonetheless, given that no prior study has quantified BAC-TAC correlations using this newest generation of transdermal sensors, we also include a

Table 1. Studies Examining Validity of Transdermal Alcohol Sensors Using Objective Assessment Techniques (BrAC/BAC)

Study	N	Type	Device	Locat	Alc Meas	Lag (min)	r's
Giles et al. (1987)	19	Lab	Unspec	Palm	BAC	NR	0.94 to 0.99
Swift and Swette (1992)	15	Lab	WrisTAS	Arm	BrAC	30	0.61 to 0.96
Davidson et al. (1997)	12	Lab	Unspec	Arm	BrAC/BAC	NR	0.52 to 0.70
Dougherty et al. (2012)	22	Lab	SCRAM	Ankle	BrAC	NR	0.70 to 0.99
Hill-Kapturczak et al. (2014)	19	Lab	SCRAM	Ankle	BrAC	NR	NR
Hill-Kapturczak et al. (2015)	21	Lab	SCRAM	Ankle	BrAC	129	0.87
Wang et al. (in press)	2	Lab	Skyn/Tally	Wrist	BrAC	75/55	NR
Sakai et al. (2006)	20	Lab	SCRAM	Ankle	BrAC	150	0.49 to 0.84
Fairbairn et al., 2018 (in press)	48	Lab/Amb	SCRAM	Ankle	BrAC	130	NR
Marques and McKnight (2009)	22	Lab/Amb	WrisTAS/SCRAM	Wrist/Ankle	BrAC	137/270	NR
Sakai et al. (2006)	24	Amb	SCRAM	Ankle	BrAC	NR	NR
Luczak and Rosen (2014)	1	Lab/Amb	WrisTAS	Wrist	BrAC	NR	NR

BAC, blood alcohol concentration; BrAC, breath alcohol concentration; TAC, transdermal alcohol concentration. Lab = laboratory study; Amb = ambulatory study; Unspec = transdermal device not named; Locat = body position of the transdermal device; Alc Meas = How BAC was measured in the study; BAC = direct measure of BAC via blood or plasma; BrAC = breathalyzer; Lag = time (in minutes) between peak BAC and peak TAC; NR = not reported; r's = correlation coefficients between TAC and BAC.

The top section of this table lists studies conducted only in the laboratory, whereas the bottom section lists studies that included an ambulatory (field) assessment arm. Where a study contained both laboratory and ambulatory arms, but examined distinct groups of participants within these arms (e.g., Sakai et al., 2006), the study is listed under both sections of the table.

Note that, in the case of some of the studies listed above, data from the same sample were included in more than 1 publication (e.g., Fairbairn et al., 2018, in press). In such cases, only the citation for the parent (first) publication is listed in the table. Studies featuring devices that were not clearly “wearable” (e.g., Kamei et al., 1998) and also studies featuring sweat patches (e.g., Phillips, 1984) are not included.

preliminary examination of BAC-TAC correlations for both Skyn and SCRAM as a supplemental analysis.

MATERIALS AND METHODS

Participants

A total of 50 young social drinkers underwent experimental procedures. The final sample of participants consisted of the 30 individuals for whom we were able to obtain breathalyzer, SCRAM, and also Skyn readings for the experimental session (see later section on device failures). This final sample of participants consisted of 25 participants assigned to the alcohol condition and 5 participants assigned to the control condition. The average age of participants was 22 years old (range, 21 to 28). Participants were 50% female (15 females and 15 males). Sixty percent of participants identified as White, 23.3% as Asian, and 16.6% as multiracial (3.3% African American/Hispanic, 3.3% Hispanic/Asian, 3.3% White/Asian, and 6.7% White/Hispanic). Participants were required to be at least 21 years of age and no older than 30, to consume alcohol regularly, and report being comfortable with the dose of alcohol administered in the study. Exclusions included taking medications that might interact with alcohol, medical conditions for which alcohol consumption was contraindicated, pregnancy in women, history of severe alcohol use disorder, or especially light drinking practices (see recommendations of the National Advisory Council on Alcohol Abuse and Alcoholism, 1989, for alcohol administration in human subjects). On average, participants reported drinking alcohol on 10.13 days of the past 30 ($SD = 4.73$) and consuming an average of 4.90 drinks per occasion ($SD = 1.83$).

Procedure

Participants who successfully completed a phone screening were invited into the laboratory for a beverage administration session. All participants were required to abstain from drinking alcohol for at least 12 hours prior to their laboratory session, and to refrain from eating for 4 hours. Upon arriving in the laboratory, participants were breathalyzed (Intoximeters Alco-Sensor IV) to ensure a 0.00 breath alcohol concentration (BrAC), and their weight and height were assessed. Pregnancy was assessed in female participants via HCG urine test strip. Participants were then given a light meal that was roughly adjusted for their weight.

Next, SCRAM monitors were positioned on the inside of participants' left ankles, worn high up on the leg, and snug against the calf. Skyn devices were positioned on the inside of participants' left wrists. Both devices were then worn for a no-alcohol baseline period (approximately 1 hour), during which baseline TAC readings were established and participants completed questionnaires unrelated to the current study.

Participants were next administered their study beverages. Beverages were administered in 3 equal parts over the course of 36 minutes, and participants were encouraged to consume their beverages evenly over each of the three 12-minute intervals. Participants assigned to receive alcohol received a dose intended to bring them up to the legal driving limit (0.08%). The precise amount of alcohol administered was adjusted for each individual's body water as calculated based on formulas accounting for gender, height, age, and weight (Curtin and Fairchild, 2003; Watson et al., 1981). Note that this dose of alcohol was originally chosen for the purposes of the parent study investigating alcohol's effects on mood (e.g., Fairbairn et al., 2015, 2018), but it also has utility for the proposed project, given potential applications of wearable biosensors for determining driving safety. Control participants received an isovolumic amount of a nonalcoholic beverage. Assignment to beverage condition was randomly

determined. Beverage intake was monitored via video to validate drink start time (see below) and also to ensure even consumption across the 36-minute drink period.

Following beverage administration, participants in the alcohol condition provided breathalyzer readings at approximately 30-minute intervals until they left the laboratory. During this time period, participants engaged in a variety of study tasks, ranging from those requiring a moderate amount of walking (e.g., between rooms in a laboratory) as well as those that were largely stationary (e.g., speaking with another participant while seated). Participants in the control condition were allowed to leave after study tasks were completed (3 to 4 hours after the end of drinking). Participants administered alcohol were required to stay in the laboratory until their BrAC dropped below 0.025%² and also their SCRAM TAC output registered at least 1 descending value (generally between 5 and 7 hours postdrink—average BrAC among alcohol participants at discharge 0.019%).

Data Processing and Analysis

Skyn data were transmitted via Bluetooth from Skyn devices to BACtrack's custom smartphone application, which was installed on our laboratory's iPod touch devices. The application displays TAC readings in graphical form, and the raw data files can be exported in the form of csv files via this application or BACtrack's Internet-based data storage system. SCRAM data were extracted using Direct Connect software and downloaded from SCRAMnet, a cloud-based server.

We analyzed latency of TAC values relative to the onset of drinking and BrAC curves using the following 3 metrics: (i) latency to first transdermally detected alcohol; (ii) time elapsed between peak BrAC and peak TAC; and (iii) latency to maximal cross-correlation across TAC and BrAC curves. As an examination of these latency metrics among control participants would not have been meaningful and, in some cases, would have been impossible (e.g., latency to peak BrAC where BrAC values consist of all 0s), only participants assigned to the alcohol condition were included in latency analyses. Note that data produced by SCRAM are standardized such that it includes a natural zero starting value. In contrast, data produced by the Skyn prototypes used in this study featured no standardized zero point, with baseline values varying across Skyn files. With respect to time to first transdermally detected alcohol, for SCRAM TAC, this was operationalized as the time elapsed from the very beginning of the participant drink period to time of first nonzero SCRAM reading.³ For Skyn TAC (files with no natural zero point—see above), latency to first transdermally detected alcohol was operationalized via a function that systematically tests each point in a series and automatically detects points of change in the trend using a formula that minimizes the sum of the residual error and applies a penalty for each change (MATLAB changepoint function; Killick et al., 2012). Finally, with respect to cross-correlations, these analyses were conducted at the level of the participant and specifically targeted those assigned to receive alcohol (see below). In particular, cross-correlation coefficients indexed the correlation between an individual's BrAC and that individual's TAC (either Skyn or

²In the current study, given the relatively substantial dose of alcohol administered, it was not feasible to keep participants in the laboratory until their BAC reached 0.00. Note that, including the predrink baseline, visits often lasted as long as 9 hours. Using the current procedures, we were able to capture the majority of the descending limb of the BAC curve.

³Note Alcohol Monitoring Systems (AMS) itself uses a much higher threshold (at least 0.02% TAC) when processing SCRAM data files in order to identify alcohol episodes. This relatively high TAC threshold is adopted in order to reduce the risk for false positives, which were not a concern in the current study.

SCRAM) at various lag times (or latencies) over the course of the session.⁴ Since the sampling intervals for BrAC and SCRAM TAC were relatively sparse (~30 minutes) when compared with Skyn (1 minute), BrAC and SCRAM data were interpolated from sampled values such that a file with minute-level estimates of BrAC, SCRAM TAC, and Skyn TAC was produced for each participant spanning the time period from the beginning of the drink period to last BrAC reading (Fritsch and Carlson, 1980; Sidek and Khalil, 2013). Cross-correlation analysis was applied to each participant file, and the lag time that maximized the value of the cross-correlation function between BrAC and TAC (both Skyn and SCRAM) was recorded for each participant (Gottman, 1981). Paired *t*-tests were used to compare lag times for Skyn TAC and SCRAM TAC.

The association between BrAC and transdermally detected alcohol was assessed using the following 3 metrics: (i) correlation in peak BrAC and TAC values across participants; (ii) correlation in area under the curve for BrAC and TAC across participants; and (iii) maximal value of cross-correlation between BrAC and TAC for each participant. For the purposes of calculating peak and area under the curve values, Skyn data were centered and standardized by subtracting the start value (reading taken at the initiation of the drink period) from all subsequent readings. All participants (alcohol and control) were included in the analysis of peak values and area under the curve—which examine variation between participants—whereas only participants in the alcohol condition were included in cross-correlation analyses—which examine variation within participants over time, and so variability at the within-subject level is required. Area under the curve for BrAC, Skyn, and SCRAM data was calculated by summing all data points from the beginning of the drink period to the last moment that a BrAC reading was taken. Pearson's correlation coefficients were used to examine associations between peak values and area under the curve for BrAC and TAC. Maximum cross-correlations between BrAC data and TAC (see above) were calculated for each participant, and then Skyn and SCRAM correlations for each participant were compared using paired *t*-tests.

RESULTS

Descriptive and Device Statistics

Among those assigned to receive alcohol, average peak BrAC was 0.08% (SD = 0.01; Range 0.06 to 0.12). Five different Skyn prototype devices and 13 SCRAM ankle monitors were used for this research. The 5 Skyn devices employed included 3 older generation prototype devices (manufactured in 2016) and 2 newer generation prototype devices with improved Bluetooth connectivity and other additional features (manufactured in 2018). Among alcohol participants, over the course of the entire laboratory session, the average number of BrAC readings collected per participant was 11 (SD = 1.6), the average number of SCRAM

TAC readings was also 11 (SD = 1.4), and the average number of Skyn TAC readings was 309 (SD = 44.3).

In Fig. 2, we provide visualizations of data from all alcohol (P1-P25) and control participants (P26-30) during the laboratory session. In line with data produced in prior studies, visual inspection of these data suggests that there exists variability in both Skyn- and SCRAM-measured TAC that appears to be unconnected with alcohol consumption. Nonetheless, among participants assigned to receive alcohol, TAC broadly mirrors the characteristic BAC curve, ascending with alcohol ingestion and then descending with the passage of time following ingestion.

Device Failure Rate

Note that Skyn devices used in this study were prototypes, and rates of failure of both the devices and the accompanying smartphone application were relatively high. A total of 9 Skyn files were either incomplete, blank, or unusable due to device failure (3 files were completely blank for unknown reasons, 3 files consisted of an entirely flat line with no oscillation, and 3 files were blank or severely truncated due to battery failure). An additional 10 Skyn files were lost during the initial stages of this project as our team learned to work with these delicate prototypes.⁵ In contrast, SCRAM devices, which are not in the prototype phase, produced only 1 unusable (flat line) file within the conduct of this research. In sum, failure rates for Skyn prototypes ranged from 18% to 38% (depending on metric), whereas the failure rate for SCRAM was 2%. Data presented in the results below reflect that derived from our final sample of participants—individuals for whom we were able to obtain BrAC, SCRAM, and also Skyn data (see the Methods section).

TAC Latency

With respect to latency to first detected alcohol, both Skyn TAC and SCRAM TAC appeared to perform relatively well, detecting alcohol within 30 minutes of the initiation of the drink period. Time to first detected alcohol via Skyn was 22.08 (SD = 12.38) minutes⁶ and was very similar for SCRAM at 22.52 (SD = 13.03) minutes. The difference

⁴Cross-correlation is a metric for assessing the similarity of 2 time series as a function of the level of displacement between the series. A cross-correlation analysis will produce the value of the correlation of 2 time series across multiple different "lags" or displacement levels—for example, Skyn value at time *t* with BrAC at *t* - 1, Skyn value at time *t* with BrAC at *t* + 1, and contemporaneous Skyn and BrAC. The maximal cross-correlation—or the time lag at which the correlation between the time series is at its peak—can be used to assess the level of displacement between the time series.[

⁵The Bluetooth connection feature of the Skyn devices naturally disconnected from the accompanying smartphone application throughout the visit as participants moved from room to room. In order to reconnect and generate a data file for some of these Skyn prototypes, it was necessary to first close and then re-open the accompanying smartphone application and also disconnect/reconnect the device from Bluetooth—a quirk we discovered only with trial and error after experiencing some data loss.

⁶In addition to the MATLAB changepoint function, we also attempted this analysis using one additional operationalization—defining time to first detected alcohol as 10 consecutive Skyn readings above the initial baseline value. Using this alternative operationalization, the average time to first detected alcohol via Skyn was 17.72 minutes (SD = 11.51). However, given that the choice of "10 values" was somewhat arbitrary, we present the automated MATLAB approach (above) for the purposes of final analyses.

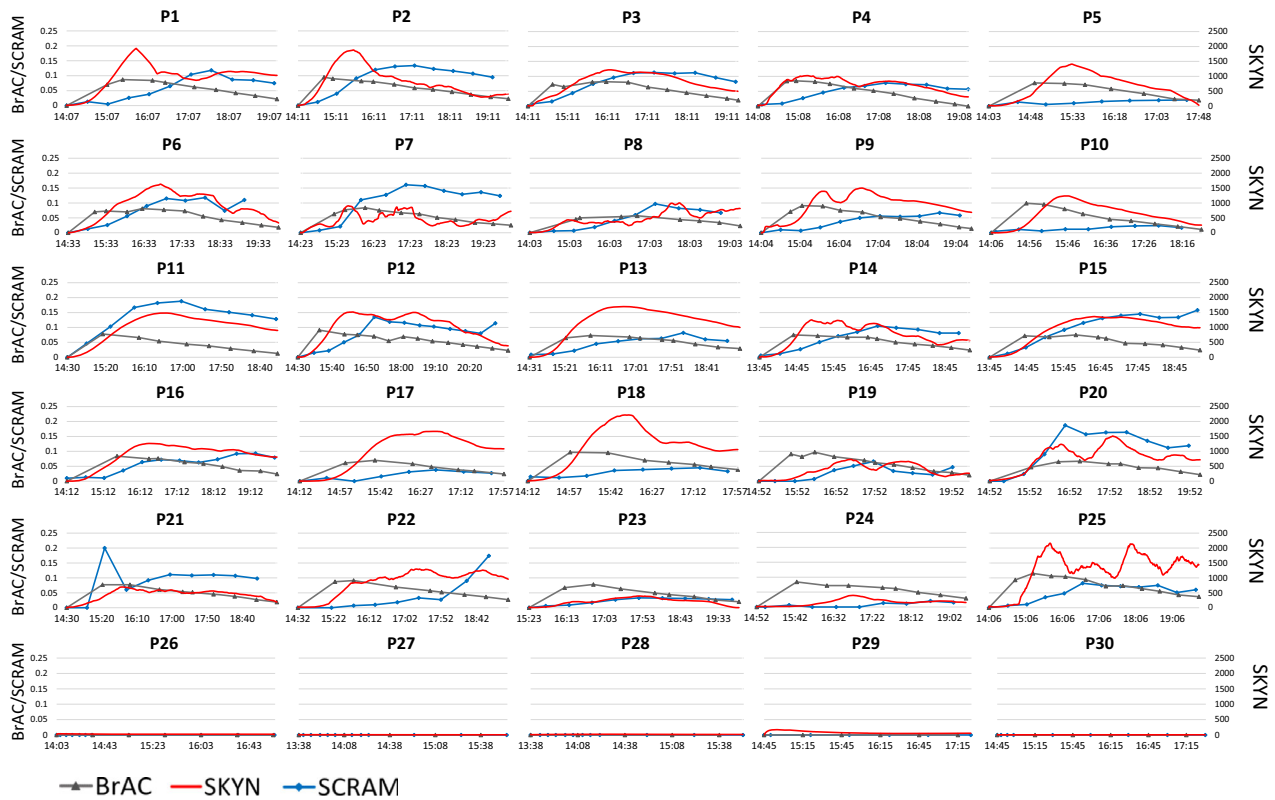


Fig. 2. Skyn prototype, SCRAM, and breath alcohol concentration (BrAC) data for each of the 25 participants assigned to receive alcohol (P1-P25) as well as the 5 no-alcohol control participants (P26-P30). Data reflect the entire period of assessment, beginning from the moment just prior to first alcohol consumption (beginning of the drink period) to the final BrAC reading. For this visualization of Skyn data, data were standardized by subtracting the lowest value for each participant file, and a 30-minute moving average window was also applied.

Table 2. Latency to Transdermal Detection of Alcohol

	Mean minutes (SD)	Paired <i>t</i> -test (Skyn vs. SCRAM)
Latency to first detection		
SCRAM TAC	22.52 (13.03)	
Skyn TAC	22.08 (12.38)	$t(24) = 0.14, p = 0.891$
Latency to peak		
BrAC	77.28 (30.34)	
SCRAM TAC	197.20 (42.60)	
Skyn TAC	131.52 (32.90)	$t(24) = 6.41, p < 0.001$
Max cross-correlation Lag		
BrAC and SCRAM TAC	68.56 (36.83)	
BrAC and Skyn TAC	23.88 (26.11)	$t(24) = 5.18, p < 0.001$

BrAC, breath alcohol concentration; SD, standard deviation; TAC, transdermal alcohol concentration.

All latency values above are calculated with respect to the beginning of the drink period for alcohol participants ($N = 25$). Cross-correlations were calculated based on data collected from the beginning of the drink period until discharge, which occurred once BrAC had dropped below 0.025% and TAC had also begun to descend (average BrAC at discharge 0.019%).

between these values was nonsignificant, $t(24) = 0.14$, $p = 0.891$. See also Table 2.

BrAC readings reached their peak an average of 77.28 (SD = 30.34) minutes after the start of drinking. Skyn TAC readings peaked an average of 131.52 (SD = 32.90) minutes

after the start of drinking (54 minutes after peak BrAC), and SCRAM TAC readings peaked an average of 197.20 (SD = 42.60) minutes after the start of drinking (120 minutes after peak BrAC). The difference in lag time between peak Skyn TAC and peak SCRAM TAC emerged as highly significant: $M_{\text{diff}} = 65.68$ minutes (SD = 51.27), $t(24) = 6.41$, $p < 0.001$.

Finally, when cross-correlation coefficients were examined, the average latency of maximal cross-correlation between BrAC and Skyn TAC was 23.88 (SD = 26.11) minutes. The average latency of maximal cross-correlation between BrAC and SCRAM TAC was 68.56 (SD = 36.83) minutes. The difference in lag time between peak Skyn TAC and peak SCRAM TAC emerged as highly significant: $M_{\text{diff}} = 44.68$ minutes (SD = 43.09), $t(24) = 5.18$, $p < 0.001$. Note that these values reflect the average lag time across all portions of the BAC curve measured in the current research—representing the majority, although not the entirety, of BAC/TAC curves (see Methods). See Table 3 for cross-correlation lag times presented at the level of the device.

TAC-BrAC Associations

Here, we provide preliminary information concerning the association between BrAC, Skyn TAC, and SCRAM TAC

Table 3. Device-Level Maximal Cross-Correlation Values and Lag Times Between BrAC and TAC

	Device ID	N	Mean Max Cross-correlation (SD)	Mean Max Cross-correlation Lag (SD)
Device-level	7AB3	8	0.66 (0.16)	17.75 (10.98)
Cross-correlations for Skyn	B6B3	2	0.40 (0.18)	32.50 (7.78)
	18	3	0.58 (0.03)	22.00 (14.18)
	9	2	0.50 (0.26)	16.50 (23.34)
	0DB5	10	0.62 (0.12)	29.10 (38.98)
Device-level	24141	2	0.50 (0.05)	26 (31.11)
Cross-correlations for SCRAM	80002	1	0.42	57
	114798	2	0.47 (0.01)	72 (11.31)
	114888	4	0.43 (0.08)	67 (25.81)
	115307	4	0.53 (0.16)	64.50 (24.37)
	115411	1	0.69	48
	115503	1	0.52	180
	115887	1	0.57	93
	117117	1	0.56	71
	126571	1	0.61	118
	127392	4	0.52 (0.21)	48.75 (33.08)
	127453	1	0.50	49
	127773	2	0.51 (0.06)	90.50 (41.72)

BrAC, breath alcohol concentration; N, number of participants who wore this device; SD, standard deviation; TAC, transdermal alcohol concentration.

Mean Max Cross-correlation Lag is presented in minutes. Devices worn by only 1 participant list no standard deviation.

Cross-correlations refer to within-subject correlations between TAC (measured either using Skyn or SCRAM devices) and BrAC for alcohol participants ($N = 25$) measured over time during the course of the laboratory session. Cross-correlations were calculated based on data collected from the beginning of the drink period until discharge, which occurred once BrAC had dropped below 0.025% and TAC had also begun to descend (average BrAC at discharge 0.019%). Cross-correlations listed under Skyn devices represent associations between BrAC and Skyn-measured TAC, and cross-correlations listed under SCRAM devices represent associations between BrAC and SCRAM-measured TAC.

Of the Skyn devices listed above, 7AB3, B6B3, and 0DB5 represent older generation Skyn prototypes (2016), whereas devices 18 and 9 represent newer generation prototypes (2018).

when dosing range in the alcohol condition is highly restricted (see above). Across all 30 participants, there was a strong and significant positive correlation between peak BrAC and peak Skyn TAC values, $r = 0.77$, $n = 30$, $p < 0.001$. There was also a strong significant correlation between peak BrAC and peak SCRAM TAC, $r = 0.56$, $n = 30$, $p = 0.001$. Participants who reached a higher peak BrAC also had higher peak TAC values, as measured using Skyn and also SCRAM. Concerning area under the curve, there was a strong and significant positive correlation for BrAC and Skyn TAC, $r = 0.79$, $n = 30$, $p < 0.001$, as well as for BrAC and SCRAM TAC, $r = 0.60$, $n = 30$, $p < 0.001$. Finally, in cross-correlation analyses examining within-participant change over time among alcohol participants examined as time series (see above), the average maximal cross-correlation between BrAC and Skyn TAC was 0.60 ($SD = 0.15$). The average maximal cross-correlation between BrAC and SCRAM TAC was 0.51 ($SD = 0.12$). The difference between these correlations emerged as statistically significant: $M_{\text{diff}} = 0.09$ ($SD = 0.20$), $t(24) = 2.38$, $p = 0.026$,

with cross-correlations being higher for Skyn versus SCRAM. Note that results of analyses examining area under the curve and also cross-correlations (although not peak values) should be interpreted with incomplete TAC/BAC trajectories and also differential lag times for Skyn versus SCRAM in mind. See Table 3 for cross-correlations at the level of the device.

DISCUSSION

Transdermal alcohol sensors represent a promising method for continuous, unobtrusive measurement of alcohol consumption. But the measurement of alcohol consumption transdermally has been associated with significant challenges, including those associated with devices themselves as well as the delay in data produced by these devices. The current research represents the first systematic examination of data produced via a new-generation transdermal device that features a compact, wrist-worn design, relatively rapid TAC sampling, and smartphone connectivity. Specifically, using data derived from a controlled dosing context and varied metrics for capturing TAC latency, we examined lag times between ingested alcohol and transdermally detected alcohol among participants wearing both the SCRAM ankle monitor and a prototype of the newer wrist-worn Skyn device. Both Skyn and SCRAM showed initial temporal sensitivity to ingestion of a moderate dose of alcohol, detecting alcohol within 30 minutes of first consumption. As time progressed across the drinking episode, the wrist-worn Skyn device emerged as generally faster in its response to alcohol ingestion compared with the ankle-worn SCRAM. Specifically, TAC measured using Skyn reached its peak over an hour prior to TAC measured using SCRAM (54 minutes after peak BrAC for Skyn versus 120 minutes after peak BrAC for SCRAM). On average, when all measured portions of the BAC curve were considered via time-series models, Skyn lagged behind BrAC by approximately 24 minutes, whereas the average lag between BAC and SCRAM was significantly longer at 69 minutes. In other words, in time-series models, the lag time between Skyn and SCRAM emerged as nearly double the duration of lag time between Skyn and actual BrAC. Finally, this study also provides some information on the validity of the wrist-worn prototype in terms of dose-response—although associations captured within this study should be considered preliminary (likely dampened) due to the restricted dosing range as well as the slightly truncated TAC/BAC trajectories captured in our laboratory session. Note that Skyn devices used in this study were prototypes, and data captured with both Skyn and SCRAM devices demonstrated variability in TAC that appeared to be unrelated to BrAC. Nonetheless, correlations between Skyn TAC and BrAC captured within this study were large in magnitude and tended to exceed correlations between BrAC and SCRAM TAC.

The lag time between ingested alcohol and transdermally detected alcohol is typically estimated as being at least

1 hour in duration (Leffingwell et al., 2013), with some studies estimating this delay as lasting up to 4 hours (Marques and McKnight, 2009). Note that these lengthier delay estimates have been derived from studies employing the SCRAM ankle monitor and have further not typically examined lag times at points on the BAC curve beyond peak values (Marques and McKnight, 2009; Sakai et al., 2006; Fairbairn and Kang, in press; See Table 1 for a review). The prolonged nature of such delays might preclude certain real-world applications of transdermal alcohol sensors—for example, a drinker wishing to assess his/her safety for operating a motor vehicle. As with past research, data from the current study continued to provide evidence for a delay in the transdermal detection of alcohol when compared with BrAC. However, here, when examined across the entire sampling interval investigated in this research—which encompassed the majority (although not the entirety) of the BAC curve—the average lag time between Skyn-estimated TAC and BrAC was <30 minutes, significantly smaller than that estimated via SCRAM. In the future, applications of advanced machine learning algorithms—with the ability to predict future values based on sequences of current values—might ultimately be applied to TAC data to further reduce the extent of this lag (Mandic and Chambers, 2001).

In addition to its implications for the understanding of lag times between BAC and TAC, this research also contributes to the literature by providing preliminary information on the validity of a relatively compact, wrist-worn sensor. To date, a barrier to the widespread implementation of transdermal biosensors has been the relatively large/bulky nature of extant transdermal devices. At the present time, the SCRAM ankle monitor is the only readily available transdermal sensor. SCRAM, and similar devices, will likely continue to have an important place in assessing drinking among criminal justice-involved populations and for some research and clinical applications, and, at the current time, SCRAM remains the most reliable available transdermal sensor. However, the relatively bulky design and ankle positioning of this device limit its usefulness outside of specific clinical, criminal justice, and research applications and preclude its implementation among broad populations of drinkers interested in tracking their health behaviors. Thus, although approximately half of the world's population drinks alcohol (WHO, 2014), with 27% of US adults reporting at least 1 episode of binge drinking in the past month (SAMHSA, 2015), only a subsample of these individuals are served by current transdermal technology. Note that the current study examined TAC data in response to a fixed dose of alcohol, restricting the range of BACs and so likely leading to attenuated estimates of the associations between TAC and BAC. Nonetheless, despite the fixed dosing procedures, associations between Skyn TAC and BAC emerged as strong. Thus, by providing initial data for the validity of a compact, wrist-worn sensor, the current study takes an important first step toward

providing an attractive, wearable device for everyday drinkers seeking to monitor their alcohol consumption.

Although the current project represents an important first step to addressing specific challenges associated with the transdermal detection of alcohol, many other key challenges lie ahead before these devices are ready for real-world implementation. As noted above, similar to data produced by prior studies (Leffingwell et al., 2013), data from the current study indicate that the BAC-TAC correlation is strong, but yet this correlation is not a perfect one and so some portion of the variation in TAC remains as yet unexplained. As it pertains to Skyn data, some of this unexplained variability is likely attributable to the fact that the devices used in this study were hand-assembled prototypes, and so, this variability may diminish with device development as prototypes improve and machine-made devices become available. It is also possible that some of this unexplained variability may simply be a characteristic intrinsic to transdermal alcohol measurement. Note that current Skyn prototypes collect data on not only TAC, but also include temperature and accelerometer gauges—measures that may account for some portion of the variability in the BAC-TAC relationship—and algorithms that incorporate information from all of these gauges simultaneously may ultimately be able to provide a closer approximation of exact BAC values. Further, the relationship between TAC and BAC is believed to vary depending on both individual-level factors (e.g., the thickness of an individual's skin) as well as situation-level factors (e.g., degree of ambient humidity). Note that it is possible that the extent of variation in the BAC-TAC relationship has been overestimated due to a tendency of prior studies to rely on data from the SCRAM monitor, the ankle positioning of which might lead to increased variation in the distance between sensor and skin (e.g., sliding from sitting snug against the calf to hanging loosely around the ankle bone as participants walk)—a factor that has been theorized to have an important impact on the BAC-TAC relationship (see Anderson and Hlastala, 2006). Nonetheless, it will be critical to conduct research examining large and diverse samples of participants, in addition to extensive research in real-world contexts featuring fluctuation in ambient conditions, in order to further disentangle the relationship between TAC and BAC. These future studies will also need to address the issue of potential “false positive” TAC values produced by environmental alcohol, considering sensitivity and specificity as well as the reliability of the Skyn over time and across devices. Relatedly, data from the current Skyn prototype represent a raw value reflecting electrical current detected at the transdermal sensor and has not been standardized to include a meaningful zero metric or reflect a scale comparable to BAC. Thus, in the current study, we examine correlations between Skyn TAC and BAC, rather than estimating the accuracy of measurements produced from the Skyn device. Skyn data in the current study were standardized for each individual/device combination by subtracting out the baseline value. Translating Skyn data into estimates along a

standardized metric—and accounting for factors that might lead to differential baseline values across different device/individual combinations—is a task for future research.

Although the current study does suggest that the lag time between BAC and TAC diminishes when TAC is measured using Skyn, the question of mechanism is unaddressed. The extent to which this effect is explained by characteristics of the device (e.g., method of measurement and sampling interval) or by the body positioning of the device (e.g., relative distribution of sweat glands and permeability of skin) is left for future research to explore. It is also worth noting that the hand-assembled Skyn prototypes employed in this study yielded a relatively high failure rate (18 to 38% versus 2% for SCRAM). More durable and reliable prototypes will likely be required before extensive field testing is feasible. Thus, at the current time, SCRAM is still the most reliable transdermal alcohol sensor.

Finally, note that participants in the current study left the laboratory once their BrAC had descended below 0.025% and their TAC had also begun to descend (see Methods). Thus, although these methods did capture the majority of BAC and TAC curves for participants enrolled, these curves were not complete. Thus, analyses presented here that might be impacted by such incomplete curves—area under the curve calculations and also cross-correlation analyses—should be interpreted with these truncated curves in mind. Future research should examine complete TAC/BAC curves when feasible.

CONCLUSION

A wearable alcohol biosensor has the potential to fill a tremendous public health gap. The path toward developing such a biosensor has been lengthy and involved formidable challenges. Recent devices have been developed that leverage advances in miniaturization and electronics, and rigorous research of such devices, employing multiple methods and large human samples, offers the possibility of at last producing a viable alcohol biosensor and, importantly, clarifying its potential place in the arsenal of techniques aimed at better researching, preventing, and treating alcohol use disorders.

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CONFLICT OF INTEREST

BACtrack Skyn devices used in this research were issued free of charge from the company BACtrack. At the time this research was conducted, no price was associated with the

BACtrack Skyn, and to our knowledge, all researchers who requested them were provided with a complementary Skyn device.

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