Received: 26 August 2020 | Accepted: 9 October 2020

DOI: 10.1111/head.14028

RESEARCH SUBMISSION

Feasibility of using "SMARTER" methodology for monitoring precipitating conditions of pediatric migraine episodes

Mark A. Connelly PhD[1] | Madeline E. Boorigie BA[2]

[1]Division of Developmental and Behavioral Health, Children's Mercy Kansas City, Kansas City, MO, USA

[2]Division of Neurology, Children's Mercy Kansas City, Kansas City, MO, USA

Correspondence
Mark A. Connelly, Division of Developmental and Behavioral Health, Children's Mercy Kansas City, Kansas City, MO, USA.
Email: mconnelly1@cmh.edu

Funding information
This work was funded in part by an intramural grant from the Marion Merrell Dow Foundation

Abstract

Objective: To evaluate the feasibility in children of an intensive prospective data monitoring methodology for identifying precipitating conditions for migraine occurrence.

Background: Migraine headaches are a common pain condition in childhood and can become increasingly chronic and disabling with repeated episodes. Identifying conditions that forecast when a child's migraine is likely to occur may facilitate next-generation adaptive treatments to prevent future migraine attacks.

Methods: In this cohort study of a sample of 30 youth (ages 10–17) with migraine recruited through a pediatric headache clinic, smartphones supplemented with wearable biosensors were used over a period of 28 days to collect contextual data thought to be potentially relevant to headache occurrence. Self-reported data on headache occurrence, lifestyle, and perceptions of the environment were collected in 4 epochs per day using custom real-time reporting software. Data derived from the wearable biosensor included information on autonomic arousal and physical activity. Built-in sensors on participants' own phones also were used to indicate location and to quantify the sensory environment (e.g., ambient noise and light levels). Data fidelity was monitored to evaluate feasibility of the methods, and participant acceptability was assessed via an end-of-study survey.

Results: Self-report data were obtained on a mean of 88.9% (24.9/28) of assigned days (*SD* = 22.4%) and at a mean of 68.9% (77.2/112) of assigned moments (*SD* = 24.5%). Data from the wearable biosensor were obtained for a mean of 18.7 hours per day worn (*SD* = 2.3 hours), with participants on average wearing the sensor on 20.3 days (*SD* = 9.9). Fidelity of obtaining objective data from phone sensors on the sensory environment and other environmental conditions was highly variable, with these data obtainable from 5 to 22/30 (16.7%–73.3%) of participants' own phones. Most participants (63.3%–100%) responded with at least "somewhat agree" to questions about acceptability of the study methods. However, 5 to 7/30 (16.7%–23.3%) patients indicated difficulties with burden and remembering to wear the sensor. Almost all participants (29/30, 96.7%) agreed that they would want information about when a migraine might occur.

Abbreviations: EDA, electrodermal activity; GPS, global positioning system; ICHD-III, 3rd edition of the International Classification of Headache Disorders; JITAI, just-in-time adaptive intervention; mHealth, mobile health; PedMIDAS, Pediatric Migraine Disability Assessment Scale; SCL, skin conductance level; SMARTER, Sensor-enhanced Mobile Assessment and Real-Time Ecological Reporting.

Conclusions: A contemporary data sampling approach comprising ambulatory sensors and real-time reporting appears to be acceptable to most youth with migraine in this study. Reliability of acquiring some data sources from participants' own phones, however, was suboptimal. Further refining these data sampling methods may enable a novel means of predicting and preventing recurrences of migraine episodes in youth.

KEYWORDS
ecological momentary assessment, feasibility, migraine, pediatric, sensors

INTRODUCTION

Migraine is a common condition in pediatrics and is one of the most prevalent and disabling health conditions worldwide.[1–4] With each recurrence of a migraine headache during childhood, there is a risk that headaches will progress in frequency, severity, and disability.[5–7] Identifying conditions that forecast when a migraine is likely to occur may, therefore, provide a critical window for preemptive medical and/or behavioral management strategies that reduce risk of future morbidity and burden.[8]

Measurable changes in certain internal and environmental states may provide actionable insights into the likelihood of migraine occurrence for children. For example, migraine attacks may be precipitated by changes in stress levels or other so-called trigger variables that provoke the physiological changes underlying a migraine episode.[9,10] Mood changes or enhanced sensory sensitivities also may be early premonitory indicators of an impending migraine headache.[11,12] Although intriguing clinically, identifying variables that reliably precipitate migraine headaches is challenging methodologically.[13,14] Retrospective surveys have been often used to study headache triggers. However, this method assumes a level of self-awareness that may be underdeveloped in children. Such surveys also may identify spurious associations of variables with migraine occurrence due to confirmatory reporting bias.[15–17]

Advances in mobile health (mHealth) offer increasingly sophisticated means of prospectively monitoring an individual's environment and everyday activities. For example, dynamic changes in mood and stress levels can be efficiently monitored using smartphone-based sampling methods.[18,19] Sensors built into smartphones or worn on the body also enable ambulatory monitoring of changes in internal (physiological) and environmental states that may have relevance to migraine, such as changes in autonomic arousal, physical activity, and levels of ambient light and sound.[20–22] Although contemporary mHealth methods may generate unique insights into the context of migraine occurrence, these methods may be overly burdensome for child participants and/or result in low-fidelity data. Thus, prior to development of intelligently timed adaptive headache management interventions for youth, the feasibility needs to be established in this population of implementing contemporary mHealth methods to study migraine precipitants.

Toward this end, in this study, we aimed to evaluate the feasibility of using "SMARTER" methodology (Sensor-enhanced Mobile Assessment and Real-Time Ecological Reporting) in children with migraine. We evaluated the extent to which this methodology could be implemented as intended and would be viewed as acceptable to youth with migraine. The study was exploratory, but we hypothesized that data completeness would not systematically vary as a function of participant age, sex, headache status, time of day, or elapsed time in the study. We also hypothesized that ratings of the acceptability of study methods would not covary with age, sex, or headache characteristics.

METHOD

Study design

The study was a single-site prospective cohort study that acquired data using time-contingent ecological momentary assessment methods.[18] Time-contingent ecological momentary assessment involves repeated data sampling at predetermined time intervals throughout the day. The current paper is the first report on the data collected for this study.

Participants

Prescreening and recruitment for the study occurred over an approximate 9-month period (from 2018 to 2019). Participants were recruited from specialty headache clinics associated with a large dedicated pediatric hospital in Kansas City, MO. Patients were eligible to participate if they were between the ages of 10 and 18 years old, were diagnosed with migraine with or without aura based on criteria from the 3rd edition of the International Classification of Headache Disorders,[23] reported an average of at least two migraine episodes per month, and had a smartphone available to use throughout the day. Participants with daily or constant headaches, secondary headaches, significant cognitive impairment or developmental delay, or who were unable to speak and read English were excluded. An a priori enrollment of 30 participants was targeted to establish method feasibility in what we thought to be a minimum representative clinical sample within the study timeframe. This sample size also was derived in part based on recommended minimum sample sizes to use for prediction in multilevel designs.[24] No formal statistical power calculation was conducted prior to the study.

Procedure

Study procedures were approved by the Institutional Review Board of Children's Mercy Kansas City. A research coordinator approached prescreened participants to discuss the study during outpatient visits at a specialty headache clinic. For patients indicating interest in participating in the study, written informed consent was obtained from the patient (if 18 years old) or from a parent or legally authorized representative (for children under 18); written assent also was obtained for children ages 10–17.

Following informed consent procedures, participants completed baseline measures and were trained by the research coordinator in use of a wrist-worn wearable sensor band (Empatica Embrace) and a mobile self-report app (mEMA by ilumivu). Children were asked to wear the sensor band as continuously as possible, removing it only for charging at night and for swimming or bathing/showering. For the daily self-reports, a 4×/day cuing schedule was programed into the mobile app to remind participants to complete measures in the morning, mid-afternoon, evening, and around bedtime. Specific cuing times within these intervals varied by patient to accommodate their requested times to complete the daily self-report items. Children were asked to wear the sensor band and complete daily measures on their phone for a period of 4 weeks (28 days). Raw data from the sensor band and responses to the daily self-report items were automatically wirelessly transferred to a dedicated secure cloud-based study database whenever a cellular or Wi-Fi signal was present. The study data platform was HIPAA-compliant; it contained no identifying data and was accessible only to the study team. All self-report data and sensor data were associated with participant IDs; no identifying data were collected from phones or sensors. Mobile data were encrypted before being pushed to the cloud-based database, and data were always stored within the database and never on the server's file server.

At the completion of the data collection phase, participants received an e-mail link to complete an acceptability survey online and were asked to return the sensor band via a prepaid mailer. Participants received a stipend of $10/week if having completed 90% of daily measures for the given week. Participants also received $5 for completing the baseline survey and the final acceptability survey.

Measures

Baseline measures

All baseline measures were administered to patients electronically via a tablet device in a clinic room. Information on demographic variables (age, sex, grade in school, race, ethnicity, caregiver marital status, caregiver education level, and annual family income) was obtained for the purpose of describing the sample. Information also was obtained at the baseline visit on headache characteristics during the prior month, including the following: frequency of headache episodes, number of headache days, duration of episodes with and without abortive medication, highest/average/lowest headache intensity on a 0–10 numeric rating scale, occurrence of aura symptoms, accompanying symptoms, and perceived triggers. In addition, the PedMIDAS was administered at the baseline visit to quantify level of functional disability.[25,26] The PedMIDAS is a six-item measure evaluating impact of headaches on school, home activities, and social and sports activities. Responses to the items are summed and can be classified as little to no disability (0–10), mild disability (11–30), moderate disability (31–50), and severe disability (>50).

Mobile self-report measures

Table 1 provides a description of the questions asked each day on the mobile self-report app. Children were asked about the following variables: (a) the occurrence, intensity, and start time of a headache episode; (b) recent activities in which they were engaged (selected from a list and/or generated by the patient); (c) perceived level of stress and "busyness"; (d) perceived level of alertness/sleepiness based on the Faces Sleepiness Scale[27]; and (e) subjective perceptions of the environment (light level, noise level, temperature, and air pressure). Each daily report required up to 3 minutes to complete.

Wearable sensor measures

Table 2 provides a description of the wearable sensor data obtained each day. Sympathetic arousal was monitored using an electrodermal activity (EDA) sensor worn on the nondominant wrist. EDA measured in a naturalistic setting has been shown to reliably increase in response to stressors.[28–31] Continuously sampled EDA data were reduced using Microsoft Excel macros and procedures adapted from Doberenz and colleagues.[29] One-minute epochs containing apparent artifacts or no data recorded were first filtered out. Skin conductance level (SCL), as well as SCL standard deviation (SCLstd) and coefficient of variation (SCL/SCLstd), were computed for each minute epoch. These indices were synchronized with the daily self-report data by averaging them to the hour preceding each self-report. These metrics were selected to quantify both tonic levels and phasic changes of EDA.

Physical activity data were obtained by a wrist-worn microelectromechanical system 3-axis accelerometer contained within the same wearable device as the skin conductance sensor. The accelerometer measures continuous gravitational force (g) applied to side-to-side, forward and backward, and up and down (xyz) dimensions, with a scale range of −2 to +2 g. Indices we chose to derive from the raw accelerometer data included amount of

TABLE 1 Description of items on the daily self-report logs

Variable	Sampling rate	Question text	Response metric
Headache occurrence	4×/day	Do you currently have a headache?	Binary (yes/no)
Headache onset time	Up to 4×/day	What time did your current headache start?	Time of day
Headache intensity	Up to 4×/day	Move the slider to show your current level of headache pain	Electronic VAS from "no pain" to "most pain possible"
Busyness level	4×/day	How busy are you feeling right now	Electronic VAS from "not at all" to "extremely"
Activity engagement	4×/day	What activities have you been doing during the past hour? (select from schoolwork, sport practice or game, club/organized group activity, chores, job, family activity, and/or other)	Binary (yes/no) for each activity
Alertness level	4×/day	Choose the face that best describes how sleepy or alert you are right now.	5-point faces scale
Sleep quality	1×/day (morning only)	Move the slider anywhere along the picture below to show how well you slept last night.	Electronic VAS from "did not sleep well" to "slept very well"
Stress level	4×/day	What is your level of stress right now?	Electronic VAS from "none" to "as bad as it can be"
Perception of light level	4×/day	What is the light level like to you right now?	Electronic VAS from "dark" to "bright"
Perception of sound level	4×/day	What is the sound level like to you right now?	Electronic VAS from "quiet" to "loud"
Perception of temperature	4×/day	What is the temperature like to you right now?	Electronic VAS from "cold" to "hot"
Perception of air pressure	4×/day	What is the pressure in the air like to you right now?	Electronic VAS from "low" to "high"

Note: Headache onset time and intensity were only asked if the participant indicated having a current headache. New headache episodes were defined based on the participant endorsing a current headache and setting the onset time to more than 1-hour difference from a previously endorsed headache. VAS, visual analog scale (coded as ranging from 0–10).

physical activity (sum of acceleration magnitudes calculated for each 2-second epoch) and intensity of physical activity (mean amplitude deviation calculated for each 2-second epoch).[32,33] These metrics of overall level of activity and acute changes in activity level intensities were selected based on their potential relevance to migraine occurrence.[34] The physical activity indices were synchronized with the daily self-report data by averaging each of them to the hour preceding each self-report.

Phone sensor measures

Data on environmental conditions were sought to be monitored using built-in sensors on participants' phones. Table 2 provides a description of the phone sensor data sought to be obtained from participants' phones. Ambient noise level, ambient light level, temperature, and barometric pressure were sampled (if sensors were available on participant phones) and averaged for the 1-hour window preceding each self-report assessment. Location data (latitude/longitude coordinates) from built-in phone global positioning system (GPS) devices also were sampled at the start of each daily self-report.

Figure 1 shows an example of the number of items/data points collected per hour over a 24-hour period across the different measures.

Feasibility measures

Feasibility metrics included both acceptability and implementation, per metrics adapted from Bowen and colleagues.[35] Acceptability was measured at the end of study participation using a questionnaire. The questionnaire contained items asking participants to rate on a 5-point scale ("strongly disagree" to "strongly agree") the extent to which they agreed with statements about the ease of implementation, burden, appropriateness, relevance, and manageability of the data collection procedures. The survey also asked participants about the likelihood of using the methodology in the future and about preferences for receiving individualized information about migraine precipitants. Implementation fidelity was assessed based on level of adherence in completing daily measures and wearing the sensor band.

Analyses

Data from the baseline questionnaires on demographics and headache features were summarized using descriptive statistics (frequencies and percentages, mean [*M*], and standard deviation [*SD*]) for the purpose of describing the sample. Descriptive statistics also were used to summarize the implementation and acceptability data and for summarizing responses for the daily self-report data. For reporting aggregated daily self-report data as a function of moment of the day, medians and

TABLE 2 Description of variables measured by sensors

Data source	Raw sampling rate	Derived variables
Wearable skin conductance sensor	4/minute	• Average skin conductance level (in microsiemens) • Variability of skin conductance (mean of standard deviations, and coefficients of variation)
Wearable accelerometer	32/second	• Average movement intensity (mean amplitude deviation, calculated as the average deviation about the mean in acceleration magnitudes) • Total level of physical activity (calculated as the sum of root mean squares of x, y, x accelerations for each epoch)
Phone global positioning system (GPS) sensor	1/second	• Location (in latitude/longitude) at outset of each daily self-report
Phone sound sensor	2667/second	• Average noise level (root mean square of amplitude) • Variance of noise level • “Social noise” level (frames with voice activity)
Phone light sensor	50/second	Average ambient light level in lux
Phone humidity sensor	50/second	Average relative humidity percentage
Phone temperature sensor	50/second	Average temperature in Celsius
Phone air pressure sensor	50/second	Average air pressure in Hectopascals

Note: Data from wearable sensors were continuously sampled and averaged to 1-hour periods preceding each of the four daily self-report assessments. Data from all phone sensors (except the phone GPS sensor) were sampled only during the 1-hour period preceding each of the four scheduled daily self-report assessments. Location information from the phone GPS unit was recorded only at the time each self-report assessment was due to be completed.

25th/75th percentiles were used. To explore associations between overall data missingness (percent missing data) with age, sex, headache frequency, and averaged headache intensity, Pearson product-moment or point-biserial correlations were used. We used chi-square analysis to evaluate the association between time of day (morning, afternoon, evening, and before bed) and whether data were missing at a given moment. To evaluate whether data missingness differed as a function of elapsed time in the study, we used paired samples *t*-tests to compare proportion of complete data between the first and last 2 weeks of the study. Correlations were used to explore associations between participant acceptability ratings and age, sex, and headache metrics. For correlation and *t*-test analyses, assumptions were first evaluated using histograms, Q–Q plots, and scatterplots as applicable, and a two-tailed significance level was set at $p < 0.05$. Indices used for evaluating overall feasibility of methods were established as follows: (a) proportion of patients with agreement scores on the final acceptability survey of at least 4/5 (agree to strongly agree) for overall satisfaction with the study methods; (b) proportion of patients completing at least 70% of the daily self-report data; and (c) proportion of patients having less than 30% of data missing from the sensor band due to user nonadherence and/or technical failures. All analyses were completed using the Statistical Package for the Social Sciences (IBM, New York).

RESULTS

Participant characteristics

Thirty-six eligible participants were approached for participation in the study, of which 30 (83.3%) agreed to participate. Reasons cited by families for not participating included time constraints (n = 5) or not wanting to participate in research studies (n = 1).

Of the 30 participants enrolled in the study, 25 (83.3%) were female. Ages ranged from 10.3 to 17.8 years (M = 14.0, SD = 2.1). Year in school ranged from grade 5 through grade 12, with a relatively even distribution across years. Twenty-three participants (76.7%) attended public school, with the remainder in private school. Six participants (20.0%) identified as Hispanic ethnicity (three White, two American Indian, and one multiracial). Of the 24 (80.0%) participants identifying as non-Hispanic, most identified as White (n = 20, 83.3%), followed by Black/African American (n = 3, 12.5%) and multiracial (n = 1, 4.2%). Most children (n = 21, 70.0%) had married parents. Eighteen (60.0%) of primary caregivers had a college degree or beyond. Median combined household income for the sample was $90 K.

The mean monthly headache frequency reported on the baseline headache questionnaire was six (SD = 2.8). On average, headache duration with medication was reported to be 9.0 hours (SD = 18.5 hours) and without abortive medication was reported to be 32.9 hours (SD = 43.8 hours). Usual headache intensity was rated on average as 5.9/10 (SD = 1.4); worst headache intensity on average was rated 8.6/10 (SD = 1.3), and lowest headache intensity on average was rated 2.8/10 (SD = 1.7). Average PedMIDAS score at baseline was 13.3 (SD = 14.8), which is in the “mild” range for level of headache-related disability.

Of the 30 participants, 14 (46.7%) reported that they could identify warning signs that a headache was about to start. Blurred vision and sensitivity to lights or sounds were identified most commonly as warning signs (by 4 participants or 13.3% each); other reported warning signs included mood changes (n = 2, 6.7%), dizziness (n = 2, 6.7%), slurred speech (n = 1, 3.3%), and stomach pain (n = 1, 3.3%). The most common perceived headache triggers included loud sounds (n = 21, 70.0%), bright lights (n = 19, 63.3%), worry or stress (n = 18, 60.0%), hunger (n = 16, 53.3%), and too much physical activity (n = 16, 53.3%).

	6am	7am	8am	9am	10am	11am	12pm	1pm	2pm	3pm	4pm	5pm	6pm	7pm	8pm	9pm	10pm	11pm	12pm	1am	2am	3am	4am	5am
Mobile self-report	--	18	--	--	--	--	17	--	--	--	--	--	--	17	--	--	17	--	--	--	--	--	--	--
Wearable skin conductance sensor	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240
Wearable accelerometer	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200	115,200
GPS sensor on phone	3600	--	--	--	--	3600	--	--	--	--	--	--	3600	--	--	3600	--	--	--	--	--	--	--	--
Sound sensor on phone	9,601,200	--	--	--	--	9,601,200	--	--	--	--	--	--	9,601,200	--	--	9,601,200	--	--	--	--	--	--	--	--
Light sensor on phone	180,000	--	--	--	--	180,000	--	--	--	--	--	--	180,000	--	--	180,000	--	--	--	--	--	--	--	--
Humidity sensor on phone	180,000	--	--	--	--	180,000	--	--	--	--	--	--	180,000	--	--	180,000	--	--	--	--	--	--	--	--
Temperature sensor on phone	180,000	--	--	--	--	180,000	--	--	--	--	--	--	180,000	--	--	180,000	--	--	--	--	--	--	--	--
Air pressure sensor on phone	180,000	--	--	--	--	180,000	--	--	--	--	--	--	180,000	--	--	180,000	--	--	--	--	--	--	--	--

FIGURE 1 Number of potential items or data points sampled per hour over a 24-hour period. Shown in the figure are the number of self-report items and number of sensor raw data points sampled across a 24-hour period, assuming that the wearable sensors were worn the entire day. Phone sensor data were obtained during the hour preceding each of the four daily mobile self-reports. Wearable sensor data were monitored continuously, but indices derived from these data were averaged to the 1-hour period preceding each of the four daily mobile self-reports

Daily self-report data

Participants completed daily self-reports on an average of 88.9% (24.9/28) of the assigned days (SD = 23.4%, range of 31.0%–100%). The percentage of patients completing self-report measures on at least 70% of study days was 83.3% (25/30). Participants completed the self-reports on an average of 68.9% (77.2/112) of the total assigned moments of data collection (SD = 25.1%, range of 14.1%–100%). The proportion of patients completing the self-report measures on at least 70% of all assigned moments was 60.0% (18/30). Percentage of missing moments of self-report data was not statistically significantly associated with participant age ($r = -0.022$, $p = 0.906$), headache frequency ($r = 0.162$, $p = 0.392$), averaged headache intensity ($r = -0.012$, $p = 0.949$), or participant sex ($r_{pb} = 0.039$, $p = 0.839$). There was no association between moments of missing self-report data and time of day, $\chi^2(3) = 3.273$, $p = 0.351$. Self-report data were more frequently completed in the first 2 weeks of the study (M = 80.1%, SD = 18.7%) than the last 2 weeks (M = 60.0%, SD = 35.3%), $t(29) = 3.79$, $p = 0.001$.

Table 3 presents descriptive statistics on participant responses from the daily self-report data. On average, almost nine new headache episodes per participant were captured during the study period (M = 8.8, SD = 7.9). Average duration of new headache episodes was 70.5 minutes (range 21–637 minutes, SD = 87.4). Average headache intensity across participants and days was 4.1/10 (SD = 2.3).

Wearable sensor data

On average across participants, electrodermal activity (EDA) and physical activity data were acquired on 20.3 days (SD = 9.9 days). On days worn, EDA and physical activity data were recorded for a mean of 18.7/24 hours per day (SD = 2.3, participant daily means ranging from 12.4 to 22.2 hours). Reasons for incomplete wearable sensor data comprised both technical issues in data acquisition (e.g., no reading from sensors even though participants reported wearing the sensor band for a given time interval) and participant factors (e.g., removing the device for charging, forgetting to wear it). Nineteen participants (63.3%) had less than 30% of data missing from the sensor band across all hours and days of the study. Missing wearable sensor data were not associated with participant age, sex, headache frequency, headache intensity, time of day, or elapsed time in the study.

Phone sensor data

Eighteen participants had iPhones (iOS) and 12 participants had phones with Android operating systems (Samsung, LG) available to use during the study. Participant location data acquired from phone GPS units were recorded at 100% of measurement occasions. All other data varied widely in ability to be sampled from phone sensors. Information from sensors recording air pressure and precipitation was only available on 5/30 participants' phones (17%) and for an average of 5% (6/112) of measurement occasions (SD = 14%, range across participants of 0–59%). Data on ambient light could be recorded at least once for 22/30 participants (73%) but were only captured on average for 32% (36/112) of measurement occasions (SD = 23%, range across participants of 0–80%). Information on ambient sound level and voice activity were only captured for an average of 20% (22/112) of measurement occasions (SD = 20%, range across participants of 0–90%). Missing data either were a result of a specific sensor not being available on a given participant's phone or technical unreliability in acquiring and synchronizing phone sensor data with the self-report measurement

TABLE 3 Aggregate descriptive statistics for responses to daily self-report items

Variable	Range of participant means	Grand mean ± standard deviation	Moment 1 median [25th percentile, 75th percentile)	Moment 2 median [25th percentile, 75th percentile)	Moment 3 median [25th percentile, 75th percentile)	Moment 4 median [25th percentile, 75th percentile)
Number of new headache episodes	N/A	8.8 ± 7.9	N/A	N/A	N/A	N/A
Intensity level of new headache episodes (0–10 VAS)	0.6–7.0	4.4 ± 1.8	5.0 [2.0, 6.0]	4.0 [2.0, 6.0]	3.0 [1.7, 6.0]	4.0 [2.0, 6.0]
Busyness level (0–10 VAS)	1–6	3.6 ± 2.5	3.0 [1.0, 6.0]	3.0 [1.0, 6.0]	3.0 [1.0, 6.0]	2.0 [1.0, 5.0]
Activity engagement (% of moments endorsing recent involvement in this activity)						
Schoolwork	0–60%	27.6% ± 15.0%	10.5% [0.0, 56.2%]	50.9% [24.1, 62.8%]	31.3% [7.9, 50.5%]	12.1% [3.8, 29.8%]
Sport	0%–30%	6.5% ± 7.6%	0.0% [0.0, 0.0%]	0.0% [0.0, 6.9%]	0.0% [0.0, 14.0%]	3.8% [0.0, 19.1%]
Club activity	0%–25%	4.0% ± 6.5%	0.0% [0.0, 0.0%]	0.0% [0.0, 10.1%]	0.0% [0.0, 6.4%]	0.0% [0.0, 7.4%]
Chores	0%–26%	9.0% ± 7.9%	0.0% [0.0, 19.2%]	7.3% [0.0, 18.3%]	7.6% [0.0, 18.9%]	6.7% [0.0, 14.9%]
Job	0%–22%	1.8% ± 4.4%	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]
Family activity	2%–92%	29.6% ± 22.3%	11.1% [1.7, 23.6%]	21.8% [12.4, 38.0%]	30.0% [14.9, 62.1%]	43.9% [21.2, 65.1%]
Activity with peers	0%–74%	17.8% ± 16.6%	3.7% [0.0, 12.0%]	15.4% [3.7, 33.9%]	15.0% [9.2, 31.7%]	21.1% [10.1, 40.7%]
Sleeping	0%–29%	10.7% ± 8.9%	23.7% [8.5, 56.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 3.4%]
Watching TV	0%–22%	2.5% ± 5.0%	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 0.0%]	0.0% [0.0, 0.8%]
Other	1%–57%	14.4% ± 12.6%	12.0% [3.0, 40.6%]	9.7% [3.0, 21.9%]	12.7% [4.8, 32.1%]	12.9% [4.8, 31.6%]
Alertness level (0–10 VAS)	1.1–3.4	2.0 ± 0.6	2.0 [1.0, 4.0]	1.0 [1.0–2.0]	1.0 [1.0–2.0]	2.0 [1.0–3.0]
Sleep quality (0–10 VAS)	2.2–9.2	5.5 ± 1.7	6.0 [3.0, 8.0]	N/A	N/A	N/A
Stress level (0–10 VAS)	0.1–6.3	3.3 ± 2.0	3.0 [0.0, 6.0]	3.0 [0, 6.0]	3.0 [0, 5.0]	2.0 [0.0–5.0]
Perception of light level (0–10 VAS)	3.6–7.1	5.1 ± 0.9	5.0 [2.0, 6.0]	6.0 [5.0, 8.0]	5.0 [4.0, 7.0]	5.0 [2.0, 7.0]
Perception of sound level (0–10 VAS)	1.3–8.0	4.1 ± 1.4	3.0 [1.0, 5.0]	5.0 [3.0, 7.0]	5.0 [2.0, 6.0]	4.0 [2.0, 6.0]
Perception of temperature (0–10 VAS)	2.7–6.8	4.6 ± 0.9	5.0 [3.0, 6.0]	5.0 [3.0, 6.0]	5.0 [3.0, 6.0]	5.0 [3.0, 6.0]
Perception of air pressure (0–10 VAS)	0.2–8.6	3.7 ± 1.6	4.0 [2.0, 5.0]	4.0 [2.0, 5.0]	4.0 [2.0, 5.0]	4.0 [2.0, 5.0]

Note: The range of participant means represents the highest and lowest participant means across all occasions of measurement. The grand mean is the mean across all participants and measurement occasions. Values reported for Moment 1 through Moment 4 correspond to medians and 25th and 75th percentiles aggregated over the daily sampling intervals; Moment 1, morning; Moment 2, mid-afternoon; Moment 3, evening; Moment 4 = bedtime; VAS, visual analog scale.

occasions. Missing phone sensor data were not associated with participant age, sex, headache frequency, headache intensity, or elapsed time in the study. There was an association between time of day and missing phone sensor data, with phone sensor data relatively more often missing for the morning assessments, χ^2 (3) = 12.854, p = 0.005.

Acceptability survey results

Descriptive statistics for responses to the acceptability survey are shown in Table 4. Most participants agreed or strongly agreed that the daily self-report methods were not overly burdensome (26/30, 86.7%), easy to use (22/30, 73.3%), and something they would be willing to continue to do if it could help inform management of their headaches (26/30, 86.7%).

Most participants also agreed or strongly agreed that the wearable sensor band was easy to use (25/30, 83.3%) and agreed they would be willing to continue to use the band if it could help them manage their headaches (26/30, 86.7%). Eighty-seven percent of participants (26/30) agreed that they were satisfied overall with the data monitoring methods. However, nearly half (14/30, 46.7%) of participants at least partly agreed that wearing the sensor band sometimes interfered with daily life, and 8/30 (26.7%) of respondents agreed that they "often forgot to put on the band." Responses to the acceptability survey questions were not significantly correlated with participant age, sex, or with headache frequency or intensity.

Regarding participant preferences for reporting of information on headache precipitants, 59% responded that they would rather see a report on a phone app then meet with a doctor or nurse to review data. All but one participant reported a desire to be warned about when their migraine could occur. Eighty-two percent of participants reported a preference to receive information both about their migraine predictors and about things that might help prevent their migraine from occurring.

TABLE 4 Descriptive statistics for responses to the acceptability survey

Item	Mean ± standard deviation	Range of responses
The daily questions were easy for me to understand	4.6 ± 0.5	4–5
It took too long to answer the daily questions	1.7 ± 0.9	1–4
It was easy to use my phone to answer the daily questions	4.1 ± 1.1	1–5
Overall, I was satisfied with using the mobile app to answer the daily questions	4.5 ± 0.9	2–5
I would be willing to continue to answer the daily questions if it would help my headaches	4.1 ± 1.0	2–5
The sensor band was easy to use	4.3 ± 1.1	1–5
I often forget to put on the sensor band	2.8 ± 1.4	1–5
Using the sensor band interfered too much with my life	2.3 ± 1.2	1–4
I would be willing to continue to use a sensor band like this if it would help my headaches	3.9 ± 1.3	1–5

Note: The response metric for the acceptability questions ranged from 1 ("strongly disagree") through 5 ("strongly agree"), with the midpoint option being "neither agree nor disagree."

DISCUSSION

Advances in mobile technology and data science are enabling a capacity to inform the timing of health interventions. Treatment options may be suggested to an individual when the risk of an event, such as a migraine headache, is predicted to be increasing based on monitored data and advanced analytic techniques (e.g., machine learning). However, the feasibility of initially acquiring sufficient naturalistic self-report and other data required to "teach" these adaptive treatments when to intervene is largely unknown in pediatric samples. We found that most children with migraine in the current study could use their smartphones to routinely report on their headaches and daily activities over a period of 4 weeks. Fewer children were adherent in completing multiple self-reports per day. We also found that passive data monitoring using wearable sensors resulted in data on autonomic arousal and physical activity for the majority of the day and on most days sampled. However, technical reliability and adherence with wearable sensors were variable across child participants. Additionally, passive monitoring of the immediate environment (e.g., intensity of noise and light) using built-in sensors on children's phones could only be completed for a minority of participants and sampling epochs. Participants generally rated the data sampling methods as acceptable, and they expressed interest in using methods like these to receive information about when a migraine is likely to occur. Levels of adherence with, and acceptability of, the study methods were found to be statistically unrelated to participant age, sex, or the frequency or intensity of headaches.

The promises and limitations of forecasting migraine attacks has been debated in the adult literature. The importance of adequate data calibration for developing predictive models has been especially emphasized.[14,36,37] Data calibration in turn requires reliable prospective data sampling and, at least initially, participant labeling of the outcome (headache occurrence) and of the activities/experiences that may be relevant in predicting that outcome. Given that the accuracy of event reporting improves with closer temporal proximity to the actual occurrence of the events being reported,[16,38–40] acquiring multiple self-reports per day is optimal. The current study suggests that most children with migraine are able to label headache occurrence and daily activities using mobile self-report for an average of 2–3 times per day over a 4-week period. This level of reliability is comparable to that observed in other pediatric studies.[39,41,42]

In a meta-analysis of studies using multiple within-day electronic reporting (ecological momentary assessment) with youth, an average compliance rate of 66.9% was observed for studies that used 4–5 self-report prompts per day. Protocols included in the meta-analysis varied from 2 to 9 self-reporting prompts per day (M = 4.2/day) over a period of 2–42 days (M = 13.3 days). Interestingly, daily self-report compliance for youth appears to be highest for studies prompting for self-report less than four times per day *and* for studies with six or more prompts per day. Adherence with daily self-report has generally been found to be unrelated to the time of day, age, sex, and disease status[42]; this was the case for the current study as well. Minimum completeness thresholds for prospective self-report to be informative for predictive models depend on several factors, including frequency of outcome occurrence, variability of the monitored variables, and choice of analytic approach. However, the results of the current study for intensive self-report sampling in youth with migraine over a plausibly representative time frame are promising for being able to "train" future headache prediction models.

Adding in ambulatory sensors to migraine research may uniquely offer a potential to identify behavioral phenotypes. For example, individual children or subgroups may be particularly susceptible to developing migraine with exposure to environmental irritants; others instead may be especially sensitive to relative increases in physical exertion or autonomic arousal. In turn, different treatments might then be selected and personalized based on the detected phenotypes. In pediatric patients especially, passive monitoring with sensors may also help overcome limitations in children's awareness of, or reporting about, early stages of migraine or putative trigger variables such as stress. Sensors, in combination with machine learning algorithms, have been explored in an increasing variety of applications. For example, they have been shown to validly identify periods of high stress in some samples, to accurately recognize types of physical activities, and to be potentially useful for identifying episodes of anxiety and depression in youth.[43–46] Wearable physiological and other sensors are relatively new to pediatric research, however, and feasibility and acceptability data are somewhat scant. In the current study, most youth with migraine rated the study methods involving sensors to be acceptable and generally low burden. The majority of participants also wore the physiological and activity sensor for the majority of the day on days worn, and for more days than not during the sampling period. As such, we likely captured representative information on physical activity and autonomic arousal for many, though not all, participants. These acceptability and reliability results are comparable to those from other pediatric studies in which sensors have been employed.[21] However, we also found that the reliability of sensor data acquisition was quite low in some cases. This was especially true if relying on sensors in participants' own phones to monitor environmental data such as amount of noise exposure. Given the ubiquity of smartphone use in youth, use of built-in phone sensors for monitoring potential precipitants of headaches has the advantage of being low burden but seemingly at the expense of data fidelity. Conversely, use of additional wearable sensors for monitoring environmental or other types of data in youth with migraine may be more informative for future studies but at the expense of additional participant burden.

Almost all participants in the current study reported strong interest in identifying migraine predictors and being notified about when a migraine might occur. These data are promising for development of just-in-tine adaptive interventions (JITAIs). Just-in-time adaptive interventions involve suggesting one or more selected treatment strategies, typically via mobile devices, at moments of clinically important changes in monitored contextual data.[8] This approach contrasts with typical clinical practice in which behavioral recommendations for migraine (e.g., lifestyle changes) are made at a static point in time with the expectation that they will be recalled and reliably implemented. JITAIs thus far have been primarily developed for adult populations and have mostly focused on increasing physical activity and reducing substance abuse.[8] Based on the acceptability findings of the current study, more research seems warranted to directly evaluate feasibility and efficacy of JITAIs using monitored data for pediatric migraine.

Our study had several limitations that should be considered when interpreting results. Our study sample is small and was selected from a subspecialty headache clinic. Thus, results for adherence and acceptability may not be generalizable to a community population of youth with migraine. We also selected a small subset of variables to monitor in this feasibility study relative to the wide spectrum of migraine triggers that have been reported in the literature. The balance between informative data monitoring and participant burden needs further exploration in future research with pediatric samples. Moreover, monitoring variables with the intent of eventually modifying them (or the response to them) assumes that the monitored variables (or responses to them) are indeed modifiable; this may not be the case across the data monitored in the current study. Our study results also are likely partly a function of the choice of technology, software, and type of data sampling scheme we used; different results may have been obtained if alternative technologies or methods (e.g., variable interval sampling) were selected. Further work is needed to identify the most suitable and sustainable technologies and methods for identifying and intervening on headache precipitants in youth.

In conclusion, a contemporary data sampling approach comprising ambulatory sensors and real-time reporting appears to be acceptable to most youth with migraine. This approach may enable novel methods of predicting and preventing migraine headache occurrence. A planned future study from the data acquired herein centers on evaluating the extent to which idiographic machine learning methods can be used to predict the probability of a child's migraine attacks from variably complete data derived from sensors. Additional future studies are needed to determine minimum requirements for data completeness and to determine best practices for enhancing adherence with data monitoring protocols for children and adolescents.

CONFLICT OF INTEREST

Authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Mark Connelly: Conceptualization, data curation, formal analysis, funding acquisition, methodology; project administration, resources, software, supervision, visualizations, writing - original draft, and writing – review and editing. Madeline Boorigie: Data curation, investigation, project administration, software, writing – review and editing.

ORCID

Mark A. Connelly https://orcid.org/0000-0001-8157-8901

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How to cite this article: Connelly MA, Boorigie ME. Feasibility of using "SMARTER" methodology for monitoring precipitating conditions of pediatric migraine episodes. *Headache*. 2021;61:500–510. https://doi.org/10.1111/head.14028