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RESEARCH

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Analysis of free-living daytime movement in patients with migraine with access to acute treatment

Jonas Van Der Donckt[1*†], Nicolas Vandenbussche[2,3,4†], Mathias De Brouwer[1], Bram Steenwinckel[1], Marija Stojchevska[1], Femke Ongenae[1], Koen Paemeleire[2,3] and Sofie Van Hoecke[1]

Abstract

Background Motion can exacerbate headache during a migraine attack, potentially leading to avoidance of routine physical activity. Advances in wrist-worn actigraphy facilitate objectively analyzing how headache episodes affect physical activity in everyday settings. The primary hypothesis was hypoactivity during daytime headache events. Secondary hypotheses are hypoactivity during the prodromal and postdromal hours closest to the headache event.

Methods During a 90-day prospective observational study, participants diagnosed with migraine wore an actigraphy device on their non-dominant wrist during daily life and work, while also logging migraine-related data in a dedicated smartphone application. There were no restrictions on use of acute and preventive headache treatments. Data from the wrist-worn accelerometer were used to (i) calculate activity energy expenditure, and (ii) predict types of human activities. These metrics were used to compare daytime prodromal, ictal, and postdromal phases of headache events with time-matched intervals during non-headache periods.

Results A significant reduction in daytime physical activity was observed during the ictal phase of headache attacks, as evidenced by decreases in both activity energy expenditure and human activity recognition prediction metrics. A reduction in movement was also observed during evening hours (18:00–24:00) on headache days. However, no significant physical activity changes were noted in the prodromal and postdromal phases. Reduced physical activity was more pronounced during the ictal phase when acute treatments were ineffective.

Conclusions This study is the first to examine the impact of headache on physical activity levels during daytime headache events by assessing changes in daily activities and activity energy expenditure in individuals with migraine, within their habitual environments and without restrictions on acute medication use. Our findings confirm reduced movement during the ictal phase of migraine attacks, supporting the primary hypothesis. Wrist-worn actigraphy further indicated that this reduction is more pronounced when patients experience movement sensitivity. Evening hypoactivity is also observed on headache days. Furthermore, attacks with ineffective acute treatment or moderate-to-high intensity were associated with more pronounced reductions in movement. In contrast, our data did not support the secondary hypothesis that physical activity would decrease during daytime prodromal and postdromal periods.

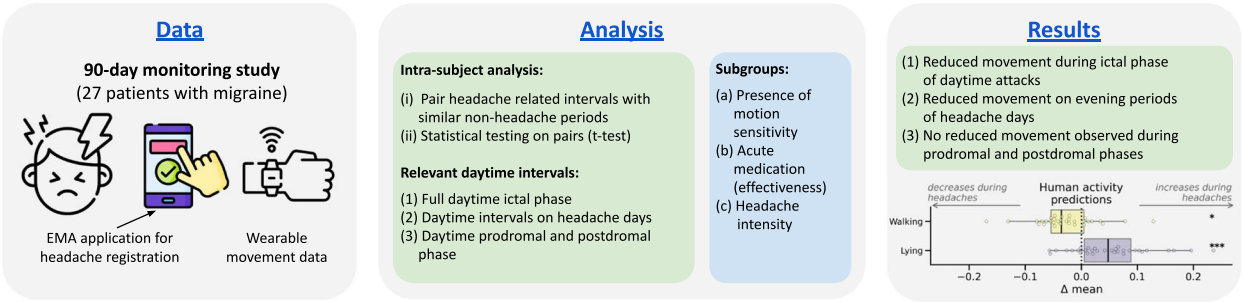
Trial registration NCT04983186 (www.ClinicalTrials.gov).

[†]Jonas Van Der Donckt and Nicolas Vandenbussche contributed equally to this work.

*Correspondence:
Jonas Van Der Donckt
jonvdrdo.vanderdonckt@ugent.be
Full list of author information is available at the end of the article

Keywords Migraine, Actigraphy, Wearable, Movement, Real-world, Activity recognition, Digital biomarker

Graphical Abstract



Background

Migraine is a chronic neurological disorder characterized by recurring headache attacks of moderate to severe intensity, often accompanied by symptoms such as photophobia, phonophobia, nausea or vomiting [1]. Based on scientific knowledge of the disorder, the diagnostic criteria for migraine of the International Classification of Headache Disorders, Third Edition (ICHD-3), stipulate increased mechanosensitivity as one of the accompanying symptoms of untreated migraine attacks. This sensitivity often results in pain exacerbation or avoidance of routine physical activity [1, 2].

Nosological studies investigating migraine have consistently shown that patients exhibit heightened sensitivity to movements throughout the migraine attack [3, 4]. A study based on questionnaires by Pavao Martins et al. reported that trying to sleep and lying down were among the most common reported coping strategies by patients undergoing migraine attacks [5]. Furthermore, physical activity (PA) is frequently identified as a major precipitating or aggravating factor of migraine attacks [6, 7]. Patients with migraine may also experience kinesiophobia [8]. Even during the interictal periods, studies found that patients with migraine tend to be significantly less physically active than controls and that they reported a significantly lower realizable level of activity [9]. The Nord-Trøndelag Health Survey (HUNT) questionnaire study found individuals with migraine and non-migraine headaches to be less physically active compared to those without headaches, possibly due to avoidance behavior [10, 11]. Additionally, this HUNT study observed that the frequency of headaches had a greater impact on physical activity (PA) levels than the type of headache. Conversely, several clinical trials suggest that physical exercise may be beneficial for migraine management, demonstrating a reduction in both the frequency and severity of migraine attacks [12–14]. Pathophysiologically, the heightened sensitivity to movement in migraine sufferers may stem from facilitated activation of nociceptive fibers [15]. Physiological studies from animal experiments show that sensitization of meningeal afferents contributes to intracranial mechanical hypersensitivity, which also explains the clinical observations of exaggerated intracranial mechanosensitivity in humans (e.g. worsening of the pain by coughing, breath-holding, or sudden head movement) [16, 17].

Previous studies already have employed various forms of actigraphy for the study of migraine, with most findings indicating reduced PA during migraine attacks [18–20]. However, these studies often face limitations such as short observation periods, inconsistent methodologies, or insufficient sample sizes, which may impact the generalizability and robustness of their conclusions. For instance, Tulen et al. investigated in total eight migraine episodes of moderate to severe intensity across six female participants, using accelerometers temporarily attached to the trunk and upper legs during an intervention at the onset of each migraine episode. Their findings consistently showed decreased body movement during migraine attacks [18]. Furthermore, the study emphasized that factors such as attack severity, acute treatment efficacy, and the time of day could influence behavioral aspects, including the time spent in various body positions, dynamic activities, and the number of postural transitions. Measurements were conducted in the participants' habitual settings, with a two-day headache-free period serving as baseline [18]. The intervention of approaching patients during migraine episodes, however, could influence their behavior or physical activity patterns, potentially confounding the study results. Similarly, Rogers

et al. analyzed changes in daily, free-living PA during a seven-day monitoring period across university participants, utilizing a migraine cohort of 28 individuals, and 35 non-headache controls. Using pedometers to approximate PA through step counts, they found that individuals with migraine exhibited lower PA levels compared to non-headache controls, noting decreases in the number of steps taken, even on headache-free days [19]. A digital evening questionnaire was utilized to identify headache days. A seven-day monitoring period may however be insufficient to comprehensively assess the influence of migraines on PA levels, as it may fail to capture multiple migraine episodes, their distinct phases (prodrome, attack, postdrome), or the natural variability in PA patterns across different days and contexts, limiting the generalizability of the findings. Lastly, Kikuchi et al. examined the relationship between tension-type headache (TTH) intensity and PA over a seven-day period using momentary headache intensity measures and wrist-worn actigraphy in a cohort of 31 patients with TTH [20]. Their findings revealed a significant negative association between intensity of headache and PA levels.

In summary, many studies have examined PA levels in patients with primary headache disorders, but short monitoring periods and inconsistent findings limit their overall conclusions. For instance, while Rogers et al. observed decreased PA on non-headache days compared to headache days, Tulen et al. found a consistent reduction in PA for their 8 investigated headache episodes. To address these limitations, longitudinal monitoring is needed to enable more granular analyses, such as examining symptom-related effects, medication effectiveness, or headache intensity. Notably, no studies to date have evaluated actigraphy as a tool for quantifying movement-related symptoms like agitation or motion sensitivity in migraine patients.

This study utilizes longitudinal wrist-worn actigraphy to assess PA through two approaches: (i) activity energy expenditure calculated from the accelerometer readings, and (ii) human activity recognition predictions generated by a machine learning (ML) model. The actigraphy data is combined with ecological momentary assessment (EMA) data collected via a dedicated smartphone application, enabling participants to log headache events and their characteristics in real-time. This integration enhances scalability and supports longitudinal monitoring with high temporal granularity [21, 22]. Wrist-worn actigraphy devices have a high acceptance rate by users due to its ease of wear and non-intrusive design, making it well-suited for longitudinal monitoring of PA levels [23]. However, actigraphy devices worn on non-limb locations, such as the hip or chest, are less susceptible to noise and may correlate more strongly with calorimetry, presenting a trade-off between accuracy and user compliance [24].

The primary aim of this observational study is to analyze PA levels in patients with chronic or episodic migraine, as defined by ICHD-3, using wrist-worn accelerometers. The Primary hypothesis is that longitudinal monitored wrist-worn actigraphy data shows reduced PA during the ictal phase of headache events compared to non-migraine periods within the same individuals. Secondary hypotheses propose that PA decreases in the prodromal phase in close relation to the onset of the headache event, and reduced PA in the postdromal phase. This analysis leverages longitudinal actigraphy recordings (± 90 days) and accompanying EMA registrations to capture detailed headache event characteristics. PA changes are assessed by (i) analyzing specific daytime headache events, (ii) performing time-of-day-based analyses on migraine days, and (iii) examining prodromal and postdromal phases of daytime headache events. This work explores the potential of wrist-worn actigraphy as a foundation for developing a digital biomarker for migraine attacks.

Methods

This analysis was part of the mBrain21 study, a comprehensive and longitudinal research initiative as detailed in De Brouwer et al. [22]. The goal of the mBrain21 study was to provide a profound understanding of migraine manifestations within ambulatory environments. To achieve this, study participants were equipped with wrist-worn wearable devices, specifically the Empatica E4®, for on average 90 days, to gather relevant physiological data. The physiological modalities acquired via the E4 device include skin temperature (4 Hz), skin conductance (4 Hz), acceleration (32 Hz), and blood volume pulse (64 Hz) from which the heart rate is derived. The Empatica devices were connected via Bluetooth to a dedicated headache diary smartphone application we developed. Through this application, shown in Fig. 1, participants could log their headache occurrences, characteristics (intensity, location, medication usage and effectiveness), and associated symptoms consistent with ICHD-3 criteria. In addition, specific medication usage, responses to daily morning and evening questionnaires, and behavioral actions including food intake moments are also questioned [22]. Meanwhile, other behaviors, such as physical activities, sleep, and stress-related events, were automatically inferred from the wearable and smartphone sensor data. This integrated setup enabled continuous, real-time, and objective data collection under free-living conditions over an extended period.

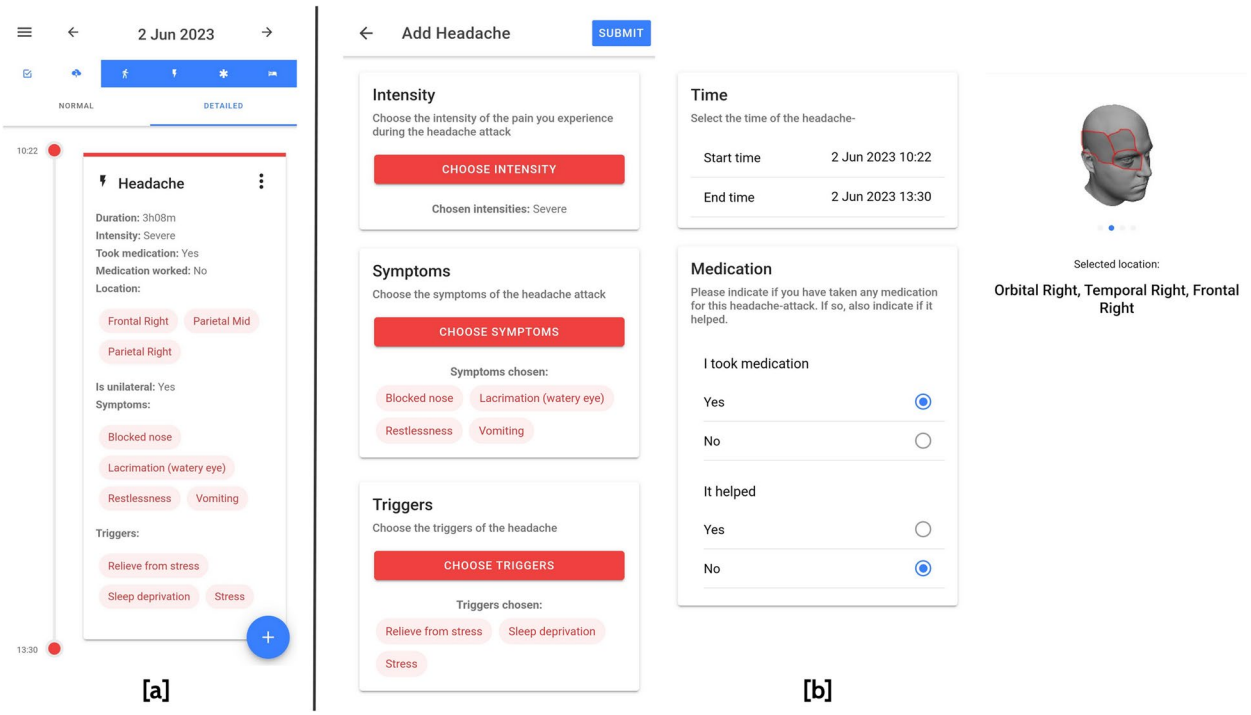


Fig. 1 Headache registration interface of the mBrain21 phone application. Figure 1 [a] shows the overview of headache events registered in the timeline view of the application. Panel [b] visualizes the headache registry module with different steps to be completed

Participants

Study participants were eligible for the study if they were aged 18 to 65, had a migraine history of more than one year as diagnosed by neurologists specializing in headache disorders (NV, KP), and met the ICHD-3 criteria for episodic or chronic migraine. Additional requirements included experiencing at least five days per month free from headaches or related symptoms, migraine onset before age 50, and owning a smartphone with Android Operating System version 8.0 or higher.

Exclusion criteria encompassed any diagnosed headache disorder other than TTH, medication-overuse headaches (as defined by ICHD-3 8.2 and its subsections), daily headaches without pain-free moments, presence of other chronic pain syndromes, significant medical comorbidity that could affect the study outcomes, opioid or barbiturate use, illicit drug or alcohol abuse, or current/planned pregnancy. Participants could also not simultaneously participate in any other academic or commercial medical study.

Study design

Participants were recruited between July 2021 and August 2023. The study involved two in-hospital visits: an initial baseline visit and a final study visit after 90 days. During the baseline visit, all study participants were interviewed by a physician researcher and neurologist with expertise in the field of clinical headache disorders (NV). Participants received instructions on how to wear the Empatica E4® actigraph on their non-dominant wrist, connecting the device to their personal smartphone via Bluetooth, and utilizing the accompanying smartphone application for registering headache events and completing daily morning and evening questionnaires.

During the study period, participants were instructed to wear the device as much as possible (daytime and nighttime), to ensure consistent data collection and minimal disruption to their daily routines. They were also advised to charge the wearable at least once a day, ideally in the evening, before bedtime. Participants were encouraged to perform their regular daily activities during the measurement period. However, they were asked to take off the Empatica E4 device when engaging in activities involving water (e.g., showering and swimming), heat (e.g., barbecuing), or cold (e.g., working in freezers).

Data processing

Wrist-worn accelerometer data processing

In this section, we describe the methodology, illustrated in Fig. 2, for converting raw accelerometer data from the Empatica device (measured in gravitational (g) units) into delta features for our analysis.

The first processing step involves identifying and eliminating periods of wearable non-wear. These are intervals

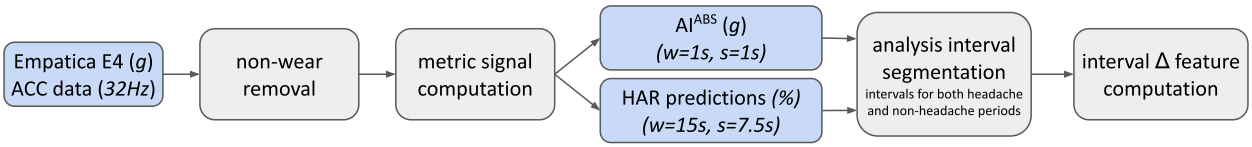


Fig. 2 Flowchart of the wearable data processing pipeline. *Abbreviations: g = gravitational unit, ACC = accelerometer, Hz = Hertz; w = window, s = stride, AI^{ABS} = absolute activity index, Δ = delta*

where the wrist-worn device is not being worn, but continues to record data. Addressing non-wear periods is a recognized challenge in real-world actigraphy research [25]. To address this, a custom algorithm was developed that identifies non-wear periods by analyzing the device's movement, skin-temperature, and skin conductance signals, and combines the signal quality indices (SQIs) of these individual signals to create an on-body status signal. Further details can be found in Van Der Donckt et al. (2024) [26]. Figure 3 provides a visual example of the resulting output of the employed non-wear detection algorithm applied to the physiological signals captured by the wearable.

After excluding non-wear intervals, the remaining accelerometer data is transformed into two distinct signal groups. The first group consists of the Absolute Activity Index (AI^{ABS}), calculated using a 1-s window and 1-s stride, as recommended by Bai et al. [27]. This signal approximates activity energy expenditure (AEE). For a visual overview and further details on the AI^{ABS} transformation, we refer to Fig. 4 and the work of Vandenbussche et al. [28]. The second signal group is derived from a Human Activity Recognition (HAR) ML model, which uses a 15-s window and 7.5-s stride – the default configuration for this model. The utilized HAR ML model was specifically developed for the mBrain21 study, and was trained on an in-house dataset, as described in Van Der Donckt et al. (2022) [29]. At each stride step (7.5 s), the model predicts the probabilities of six distinct activity types: ["Lying", "Sitting", "Standing", "Walking", "Running", "Cycling"], see subplot b (III) of Fig. 4.

The HAR analysis in this work primarily focuses on two key activity classifications: "Lying" and "Walking". These activities were chosen for several reasons (i) the HAR ML demonstrates a high validation accuracy for "Walking", and previous research has identified "Lying" as a common behavioral response during migraine headaches [5], (ii) "Walking" is more commonly performed by the

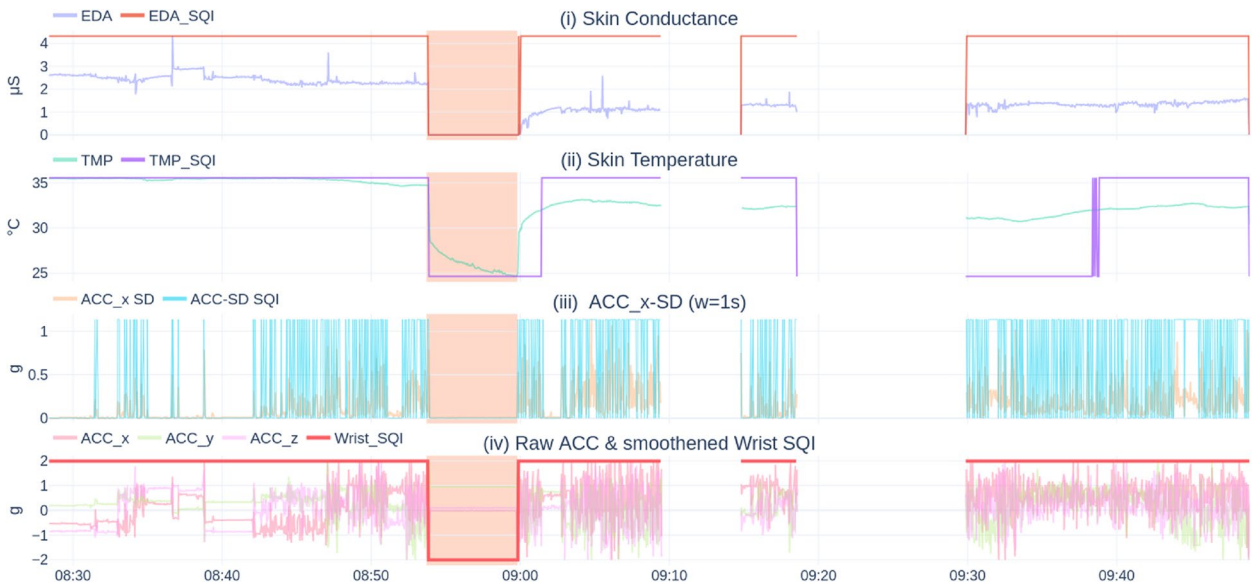


Fig. 3 Visual overview of the non-wear detection algorithm used on an Empatica E4 excerpt, derived from Van Der Donckt et al. [26]. The red-shaded area in each subplot highlights a manually labeled non-wear interval. Subplots (i) and (ii) display signal-specific signal quality indices (SQIs) for the skin conductance ("EDA") and temperature ("TMP"), respectively. Subplot (iii) shows the standard deviation of the ACC x-axis and the corresponding ACC-SD SQI. Subplot (iv) presents the raw three-axis accelerometer data along with the resulting "Wrist_SQI", which combines the signal-specific SQIs from the above subplots. A low Wrist_SQI value between 08:55 and 09:00 denotes non-wear. *Abbreviations*: ACC = accelerometer; SD = standard deviation; SQI = signal quality index, EDA = electrodermal activity, TMP = skin temperature

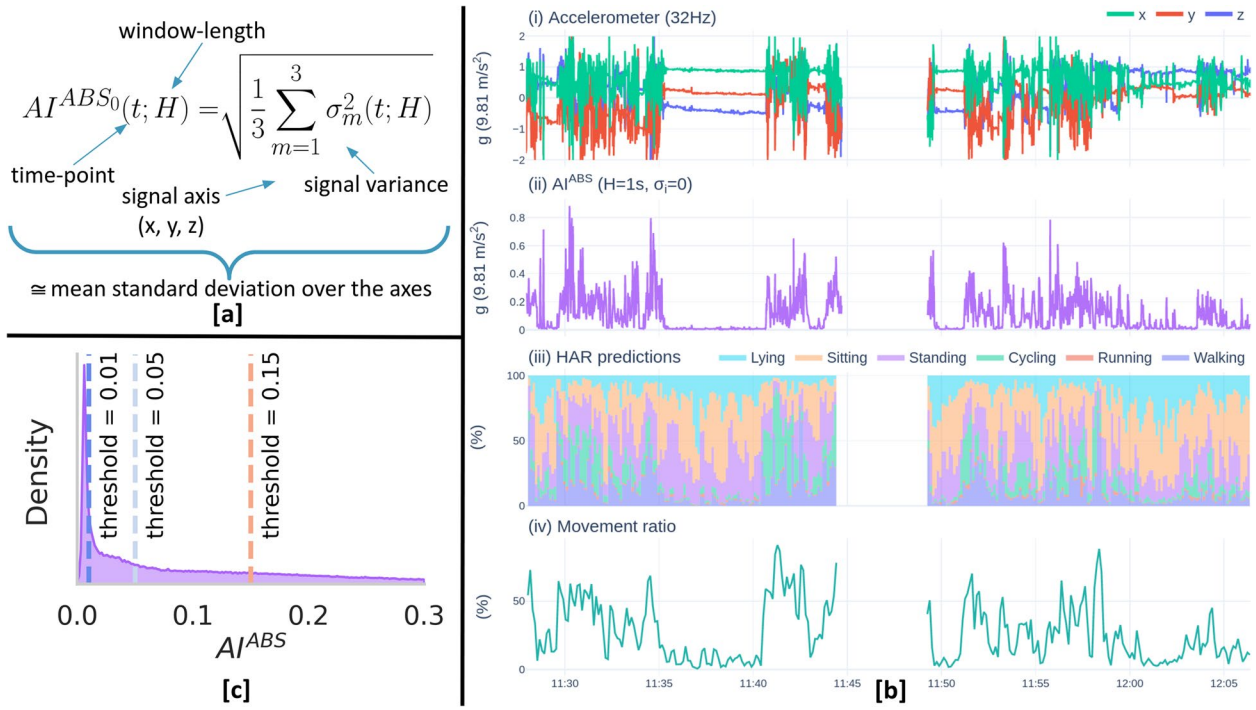


Fig. 4 Detailed overview of AI^{ABS} computation, its distribution characteristics, and HAR predictions with the derived movement ratio. To calculate the AI^{ABS}, the simplified equation given in panel [a] was used, which assumes a systematic noise-variance σ_i of zero. In panel [b] an Empatica E4 accelerometer excerpt of a study participant (i) is transformed into AI^{ABS} values (with window-length $H = 1$ s) (ii). Panel [c] displays the distribution of the AI^{ABS} values of subplot (ii) alongside the threshold values, whose ratio features are utilized for the eventual analysis. In addition, panel [b] demonstrates in subplot (iii) the HAR ML activity prediction probabilities of each class. Lastly, subplot (iv) visualizes the derived "movement ratio" signal from these HAR ML predictions. *Abbreviations*: AI^{ABS} = absolute activity index; H = variance window length; Hz = Hertz, HAR = human activity recognition; ML = machine learning; t = time point; σ_m = signal variance of wrist acceleration over axis x, y or z

general population throughout the day (unlike "Cycling" and "Running"), and (iii) activities such as "Standing" and "Sitting" may cover a wide spectrum of movement intensities and behaviors resulting in varying AEE, which may obscure the results [30]. As such, we hypothesize that differences in movement behavior are most likely to be observed in the "Lying" and "Walking" activities. Additionally, we introduce a "Movement Ratio" signal which aggregates the prediction probabilities for "Walking," "Running," and "Cycling" at each time step, serving as a comprehensive measure of all global body movement activities. Figure 4, panel [b], displays the HAR prediction signals and the "Movement Ratio" signal in subplots (iii) and (iv), respectively.

Eligibility criteria for analysis of headaches and corresponding non-headache periods

To ensure accurate analysis of the registered headache periods, we utilized the entry time metadata—the timestamp when the event was logged in the mobile application—to identify potential reporting biases. Headache events were flagged for a high probability of recall bias if they were logged more than 24 h after the reported end time. Similarly, events were flagged for a high probability of predictive bias if their final update occurred more than two hours before the reported end time. Headache records that were flagged for any of the two criteria were excluded from all subsequent analyses. Table 5. shows the number of remaining bias free headache events after this exclusion process.

For the intervals deemed eligible for analysis, a signal data availability threshold of 95% was applied, which was determined using the methodology outlined in Van Der Donckt et al. (2024) [26]. This threshold strikes a pragmatic balance between metric stability (affected by missing data) and sample retention. Supplementary Fig. 1 provides an overview of the distribution spread of signal metric features across various data retention ratios.

Non-headache periods were matched to each bias-free headache period based on specific criteria. To factor out any implicitness, non-headache periods were selected only from days explicitly reported as headache-free in the following morning's questionnaire. These non-headache periods (i) intersect with the time interval of the corresponding headache period, (ii) must contain wearable data (regardless of the amount as they will be

concatenated further on and the above outlined availability ratio criteria will be applied on that), (iii) occur on the same type of day (i.e., weekday or weekend) as the headache period, and (iv) fall within 14 days before or after of the headache period. This 14-day proximity threshold was chosen to increase the likelihood of similar time-of-day behavior patterns, as movement patterns are typically more consistent on days close to each other [31]. Furthermore, to minimize the impact of prodromal and postdromal symptoms, non-headache periods are required to be at least 24 h distant from the end of previous headaches and the beginning of a future headache. Daytime periods are defined as the interval between 8h30 and 22h30.

We are aware that prodromal or postdromal phases may overlap with our 24-h criterion for non-headache period eligibility, as some studies report prodromal durations of up to 72 h [31, 32]. Conversely, Kelman L. (2004) [33] found that only 13.2% of 893 migraine patients experienced prodromal durations lasting over 12 h. Blau J.N. (1980) [34] noted prodromal phases lasting up to 24 h in a study of 50 participants. Regarding postdrome duration, Kelman L. (2005) [35] observed that 88% of postdromes in 827 headache clinic patients lasted less than 24 h, and Blau J.N. (1991) [36] reported an average postdrome duration of 18 h across 40 patients with migraine. Given these findings, this duration threshold was chosen to ensure a substantial number of closely occurring non-headache periods, making it a pragmatic choice for our study.

Additionally, headache and non-headache periods overlapping with Belgian public holidays were filtered out to avoid the potential impact of atypical behavior during holidays.

When multiple eligible non-headache periods were identified for a single headache period, the metric signals from these intervals were concatenated to create a single non-headache metric distribution. Note that the 95% data availability ratio was applied to the concatenation of the eligible non-headache intervals rather than to each individual interval.

From this concatenated distribution, non-headache features were computed and paired with corresponding features derived from the accompanying headache attacks. Table 1 summarizes the features that are computed for each interval. Supplemental Fig. 2 illustrates the empirically determined AI^{ABS} threshold ratio features, presenting the AI^{ABS} distribution and the threshold ratios across the different activities as predicted by the HAR model.

Lastly, feature deltas (Δ) were computed for each feature by subtracting the corresponding non-headache interval feature from those of the headache interval. Consequently, a positive Δ indicates a higher feature value during the headache period, while a negative Δ indicates a lower value.

Data imputation was not applied; instead, features were computed directly from the metric signals, which may include small bouts of missing data (fewer than 5%). This approach was chosen to avoid further complicating the methodology, especially considering the assumptions required for identifying suitable periods for imputation and aggregation in the context of headache events.

Table 2 provides an overview of all the applied eligibility criteria for headache and non-headache period selection.

Ethics approval and participants' consent

The study was approved by the Ethics Committee of University Hospital Ghent (BC-10031). The study was preregistered at clinicaltrials.gov (NCT04983186). All participants gave informed consent for the collection, analysis, and publication of their data.

Table 1 Overview of utilized features for each metric signal and their descriptions

Metric signal	Feature name	Description
AI^{ABS}	BTR-0.01(*)	Below Threshold Ratio, using a threshold AI^{ABS} value of 0.01 The proportion of the AI^{ABS} signal interval distribution that lies below an AI^{ABS} intensity value of 0.01. This metric range allows us to observe changes in low intensity AEE regions
	TR-0.05–0.15(*)	Between Threshold Ratio, using a lower and upper threshold AI^{ABS} value of 0.05 and 0.15, respectively This metric range allows us to observe changes in moderate to slightly intense AEE regions
	ATR-0.15(*)	Above Threshold Ratio, with a threshold AI^{ABS} value of 0.15 The proportion of the signal interval distribution that lies above an AI^{ABS} value of 0.15. This metric range allows us to observe changes in high intensity AEE regions
Lying **Walking** **Movement ratio**	mean	The activity's average prediction probability for the interval of interest

(*) Given the right-skewed distribution of the AI^{ABS} signal (Fig. 4, panel c), the utilization of threshold ratio-based features facilitates the computation of robust features by effectively accommodating the distribution's asymmetry

Abbreviations: *AEE* Activity energy expenditure, *AI^{ABS}* Absolute activity index, *ATR* Above threshold ratio, *BTR* Below threshold ratio

Table 2 Overview of headache and non-headache interval eligibility criteria

	Headache intervals	Non-headache intervals
Event validity criteria	(i) occur during daytime periods: between 8h30 and 22h30 (ii) Predictive and recall bias filters: retain registrations with increased temporal specificity; Predictive bias: last event interaction must occur later than 2 h before the reported headache end time Recall bias: event must be registered < 24 h after the reported headache end time (iii) no overlap with a Belgian public holiday	(i) occur at the same time of day as the corresponding headache interval (i.e., the same daytime period) (ii) occur at the same type of day as the headache interval (weekday or weekend) (iii) participants explicitly indicated that no headaches occurred on the interval date period through a morning questionnaire response. (iv) non-headache interval boundaries must be > = 24 h distant from headache intervals and be < 14 days from the headache pair (v) no overlap with a Belgian public holiday
Wearable data validity	(iv) > = 95% data availability for the analysis interval	(vi) After stacking all eligible non-headache periods, > = 95% data availability for the analysis interval

As all our analyses are focused on daytime periods, each interval lies within a single day, alleviating the need to check for multiple overlapping dates

Analysis and statistics

Demographic and participant-specific data, including age, sex, duration of headache syndrome, and headache treatment regimens, are provided descriptively as proportions and means with standard deviations (SD). The compliance rate with the daily questionnaire, which serves as an indicator of daily app engagement, is expressed as the percentage of days an individual participant filled out either the morning or evening questionnaire. This rate is reported using the median, along with the first (Q1) and third quartile (Q3). Registered headache episodes are described with average duration (in hours and minutes) and attack intensity, both accompanied by their respective SDs. Lastly, the proportion of attacks treated with acute therapy and the proportion of these acute-treated attacks that were successfully managed are described.

Four main analyses were conducted, each targeting different intervals of the eligible headache events. Table 3 provides an overview of the criteria applied to each analysis.

The first analysis examines movement differences during headache attacks, focussing on the entire ictal phase. Specifically, AI^{ABS} threshold ratios and average HAR prediction values were calculated for daytime headache intervals and compared with corresponding non-headache daytime data. Importantly, this analysis only included full headache intervals that did not overlap with nighttime hours (22:00 to 10:30), as also assessing movement differences during nighttime periods might skew the results. Consequently, considering the typical duration of (untreated) migraine attacks (i.e. 4–72 h) and the frequent onset of headaches in the early morning (Supplemental Fig. 3), a limited number of headache instances are retained for this analysis ($N = 32$ out of 505 bias-free

Table 3 Summary of criteria applied to different analyses

	(1) Full ictal phase	(2) time-of-day intervals	(3) onset intervals	(4) offset intervals
Headache interval criteria				
(i) daytime criteria	✓	**X**	✓[a]	✓[a]
(ii) headache registration bias:Predictive and recall bias filter	✓	✓	✓	✓
(iii) no Belgian holiday	✓	✓	✓	✓
(iv) >95% data availability	✓	✓[a]	✓[a]	✓[a]
Non-headache interval criteria				
(i) same time as headache interval	✓	✓[a]	✓[a]	✓[a]
(ii) same type of day as headache day	✓	✓	✓	✓
(iii) explicit indication of non-headache day	✓	✓	✓	✓
(iv) interval >24h distant to any headache; <14 day distant to headache event pair	✓	✓[a]	✓[a]	✓[a]
(v) no Belgian holiday	✓	✓	✓	✓
(vi) >95% data after stacking	✓	✓[a]	✓[a]	✓[a]

[a] This criterion is independently validated for each interval within a headache and non-headache interval pair

headache events). In addition, this full daytime headache duration analysis also examines the impact of acute treatment, reported movement sensitivity symptoms, and headache intensity on changes in PA. Acute treatment use and effectiveness was determined by the input of the participant within the headache registration view of the application, as shown in panel [b] of Fig. 1.These variables are visually represented using color hues in three supplementary subplots. Movement sensitivity is identified when either "motion sensitivity" or "pain aggravation during routine activity" was reported.

The second analysis categorizes days as headache or non-headache days based on participants' morning questionnaire responses, which queries whether the previous day was headache-free or not. Eligible headache days were required to also contain the onset of at least one bias-free headache event. Days, marked as headache free by the morning questionnaire, were excluded for analysis if they overlap with a registered headache event or fall on the day before or after a headache event's start or end. No further filtering of the headache days was performed, meaning headache days could include one or multiple headache events, with onset times ranging from early morning or late evening. Each day was segmented into eight two-hour intervals: morning (8–10 h), prenoon (10–12 h), noon (12–14 h), afternoon (14–16 h), early evening (16–18 h), evening (18 h–20 h), late evening (20–22 h), and night (22 h–24 h). For each interval on a headache day, corresponding non-headache intervals are identified using the criteria listed in Table 2, followed by metric feature Δ computation. This independent evaluation leads to a varying number of attack pairs across intervals. Subgroup analyses (e.g., based on acute treatment) were not performed due to the complexity of attributing specific headache events to entire days, such as determining the minimum overlap between an event and a headache day or accounting for multiple events occurring on the same day.

The third and fourth analyses investigate movement differences during specific time intervals around the onset and end of headaches, respectively. These analyses focus on five one-hour intervals: from three hours before headache onset (prodromal phase) to the second hour of the headache (ictal phase), and from the last two hours of the headache (ictal phase) to three hours after its end (postdromal phase). These intervals were chosen in an attempt to capture the most pronounced changes in physical activity, hypothesizing that participants might adjust their behavior, such as increasing activity, during the premonitory phase in anticipation of a headache. Expanding these intervals to encompass the full prodromal and postdromal phases would reduce data availability due to strict inclusion criteria (>95% data coverage and alignment with daytime activity). Similar to the previous analyses, delta features for these periods were computed by subtracting features of non-headache intervals from those of corresponding headache intervals. The number of events considered for each interval may vary, as both headache and non-headache interval pairs must meet the ≥95% data ratio requirement and fall within daytime hours (8h30–22h30). For intervals within the ictal phase (i.e., the one-hour intervals up to 2 h after headache onset or before its end), only those fully contained within the ictal phase of the corresponding headache were included. This excludes intervals of shorter headaches (<2 h) where this condition cannot be met. By independently applying the >=95% data ratio and daytime criteria to each 1-h interval pair (as detailed in Table 3), we retain approximately 2.5 times more pairs than in our first full headache duration analysis ($N=32$), while maintaining the same eligibility criteria for headache and non-headache pairs. In alignment with the first analysis, the second, third, and fourth sub-analyses also examine the presence of motion sensitivity symptoms, acute treatment, and headache intensity.

Statistical testing was performed across all four analyses on the paired signal metric features of headache and their corresponding non-headache intervals. Statistical significance is marked with asterisks (*) in the visualizations. Normality testing, conducted using D'Agostino and Pearson's normality test [37], did not reject the null hypothesis of the samples originating from a normal distribution for the different sample sets. Consequently, we employed the paired sample t-test to determine whether the Δ feature values are symmetrically distributed around zero, considering a two-tailed distribution as the alternative hypothesis. Subsequently, Bonferroni correction was applied for each subplot family to adjust for multiple testing. Reflecting the exploratory nature of this study, both unadjusted and adjusted significance values are presented in the visualizations. Additionally, due to this exploratory nature and the absence of prior data, we did not perform a formal sample size calculation before starting the study.

Data analysis software and visualization tools

All data processing and analysis were conducted using Python version 3.9. Exploratory data analysis of the raw wearable data was performed with Plotly-Resampler [38]. During this exploratory analysis phase, we verified that daytime headaches (adhering to the 22.00–8.30 nighttime filter) did not overlap with participants' typical sleep times, as observed during manual sleep period annotation (see Supplemental Table 1 for sleep period statistics). Statistical testing was conducted using the SciPy library, and the seaborn toolkit was utilized for scientific visualization [39, 40]. To efficiently compute the AI^{ABS},

vectorized numPy functions were leveraged through the tsflex library [41, 42].

Results

Baseline characteristics

In the study, 27 participants out of 30 enrolled participants registered at least one headache event, reporting a total of 572 attacks. The median frequency was 15 attacks per participant, with an interquartile range of 5.5 to 34. After adjusting for headache registration timing bias (i.e., headache criteria (ii) of Table 3), 505 attacks remained for analysis. Table 4 outlines the demographic and baseline characteristics of the 27 participants who reported headaches, while Table 5 details the characteristics of these headaches.

Table 4 Demographics and baseline characteristics of participants, $n = 27$

Age, mean (SD)	37 (13)
Sex, n (%)	Female 21 (78%) / Male 6 (22%)
Average migraine days per month, mean (SD)	7.7 (5.5)
Duration of headache syndrome in years, mean (SD)	18.3 (11.0)
Current use of acute treatment, n (%)	26 (96.3%)
Current use of preventive treatment, n (%)	15 (55.6%)
Days in study, median (Q1-Q3)	91 (83–97)
Days with at least 1 daily questionnaire completed (i.e., compliance rate, %), median (Q1-Q3)	76% (37.2–91.6%)

Analysis 1: full headache duration analysis

Figure 5 presents the feature deltas in full daytime headaches across 32 headache events from 9 participants. Subplot row [a], which does not perform any subgrouping, shows an increase in low-intensity activity periods (AI^{ABS} below threshold 0.01: $p < 0.01$ post-correction) and a decrease in moderate to high intensity periods (AI^{ABS} between 0.05 and 0.15: $p < 0.01$ post-correction) during headache events. This observation is further substantiated by the HAR predictions (row [a], second column), indicating a significant increase in average lying probabilities ($p < 0.001$ post-correction) and a decrease in walking and movement ratio probabilities ($p < 0.05$ and $p < 0.001$ post-correction, respectively). The second subplot row [b] suggests that headache episodes associated with movement sensitivity may correlate with a further reduction in movement, though this observation is based on a small sample size ($N = 5$, 3 participants), limiting its conclusiveness. The third row [c] implies that ineffective acute treatment could result in less intense movements, but this inference is drawn from an even smaller sample

Table 5 Description of headache events

		n	Headache event duration in hours and minutes, mean (SD)	Mean intensity (SD)(*)	Acute treatment use (%)	Acute treatment effectiveness (%)
All events		572	7h09 (8h35) *8h01 (6h22)*	2.96 (0.76) *2.91 (0.43)*	72.0% *72.5%*	69.9% *73.8%*
Bias free events		505	6h42 (8h16) *7h14 (6h01)*	2.96 (0.75) *2.87 (0.45)*	71.7% *71.2%*	71% *73.7%*
Movement sensitivity	No movement sensitivity	404	6h24 (8h13) *7h24 (6h23)*	2.87 (0.61) *2.76 (0.45)*	69.3% *68.8%*	70.0% *69.1%*
	Movement sensitivity	96	7h55 (8h31) *8h57 (6h31)*	3.35 (0.75) *3.47 (0.53)*	83.3% *80.8%*	73.5% *78.2%*
Acute treatment	No treatment	143	5h55 (5h44) *6h42 (5h32)*	2.42 (0.56) *2.30 (0.30)*	0%	/
	Effective treatment	257	6h23 (7h41) *8h12 (7h32)*	3.13 (0.76) *3.14 (0.45)*	100%	100%
	No effective treatment	105	8h34 (11h42) *9h24 (9h17)*	3.24 (0.69) *3.02 (0.51)*	100%	0%
Intensity group	Below moderate	146	5h53 (6h59) *7h24 (11h40)*	1.99 (0.08) *2.00 (0.01)*	41.1% *48.1%*	78.3% 74.3%
	Moderate	241	6h44 (9h15) *7h31 (6h56)*	3 (0) *3 (0)*	78.0% *79.8%*	70.7% *72.9%*
	Above moderate	118	7h37 (7h32) *7h57 (4h44)*	4.05 (0.22) *4.02 (0.05)*	96.6% *96.8%*	67.6% *73.1%*

Remark that upright values indicate average values across the entire population, whereas cursive values indicate the mean of descriptive statistics of per-participant values

Note (*): Intensity levels: 1 = no pain, 2 = light pain, 3 = moderate pain, 4 = severe pain, 5 = very severe pain

Abbreviations: *n*, *N* Number, *SD* Standard deviation

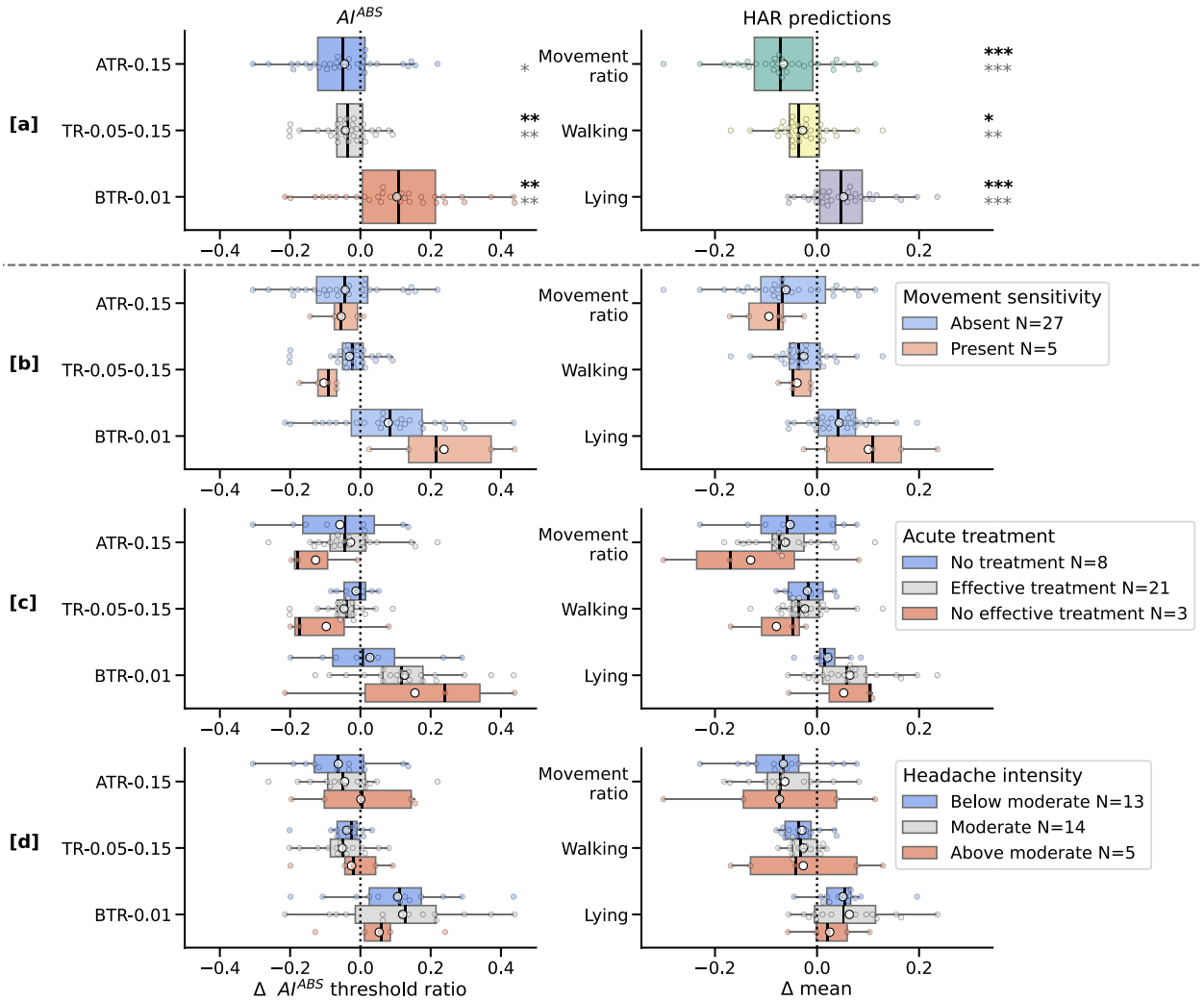


Fig. 5 Analysis of daytime full headache duration feature deltas, subtracting the values from a corresponding non-headache period from those of the headache period (32 headache events across 9 patients). Each subplot row presents the same data, differentiated by color-coding for various aspects. The first row [a] is color-coded by metric signal feature, row [b] indicates the presence of the movement sensitivity symptom during headache registration, row [c] shows whether acute treatment was used and whether it was effective, and row [d] is color coded based on experienced headache intensity. Large o-shaped markers in the box plots signify the mean values. Row [a] presents both uncorrected and corrected p-values, displayed with dim gray and bold black asterisks (*), respectively. No statistical testing was performed for row [b], [c], and [d] due to reduced sample size for the subgroups. *Note: P-values: ****=$p<0.0001$, ***=$p<0.001$, **=$p<0.01$, *=$p<0.05$. Abbreviations: AI^{ABS}: absolute activity index; ATR = above threshold ratio; BTR = below threshold ratio; HAR = human activity recognition; TR = threshold ratio; Δ = feature delta*

($N=3$, 1 participant). Subplot row [d] does not exhibit a clear trend in relation to headache intensity, and the small sample size ($N=5$, 3 participants) for "above moderate" intensity precludes any firm conclusions.

Analysis 2: time-of-day based analysis

Figure 6 examines differences in PA across eight two-hour intervals using six signal metric features. From morning to late afternoon (i.e., 8–10 h, 10–12 h, 12–14 h, 14–16 h, 16 h-18 h), no consistent changes in movement are observed. However, during the early evening interval, ("18–20 h") a significant decrease is noted in movement ratio probabilities ($p<0.01$ post-correction). The late evening interval of "20–22 h" shows significant reductions in both movement ratio and walking metrics ($p<0.01$ post-correction). Visually, the "18–20 h", "20–22 h", and "22–24 h" intervals display a consistent trend of decreased movement in AI^{ABS} (row 1) and HAR probability (row 2) features, though not always statistically significant.

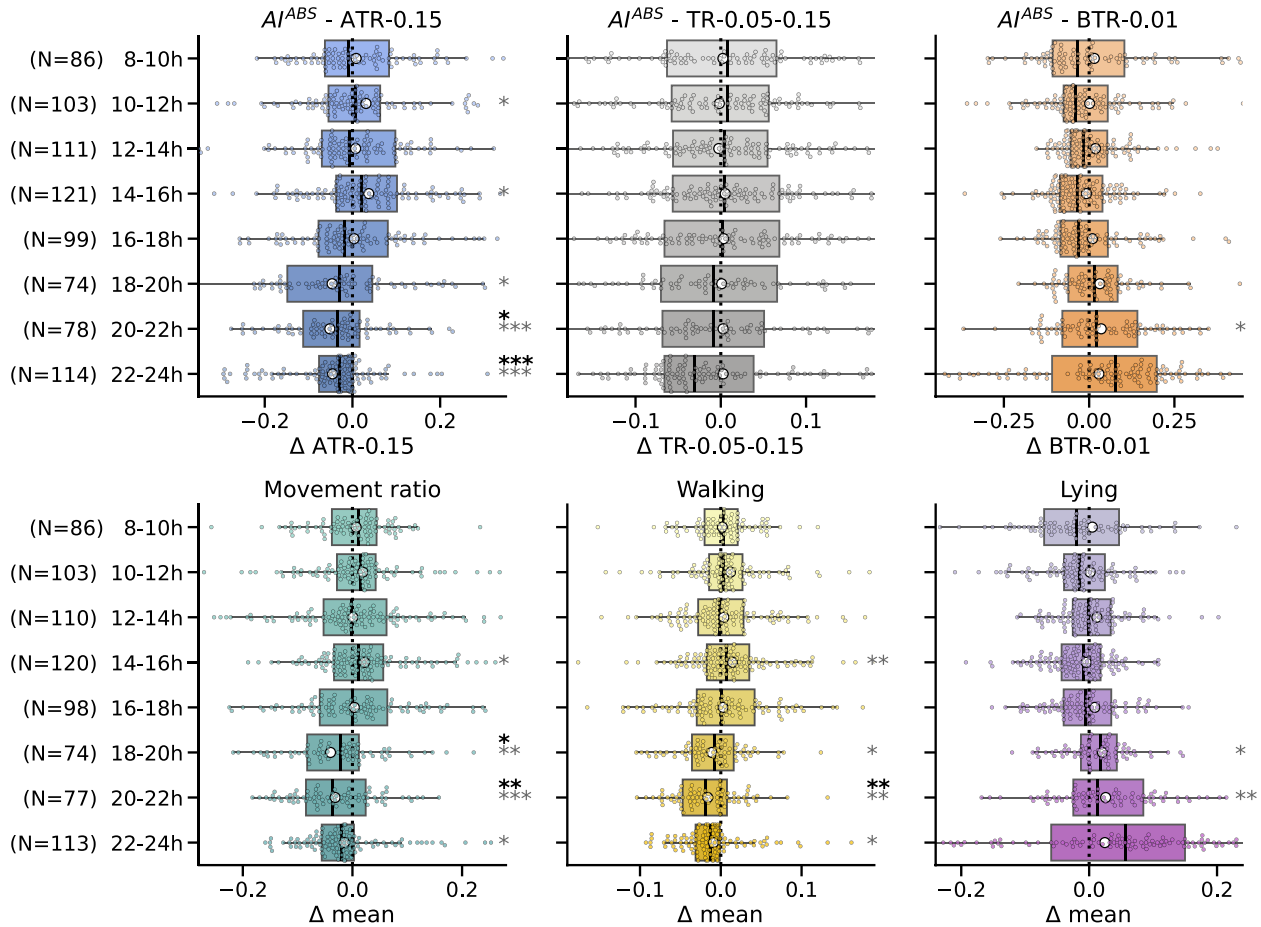


Fig. 6 Time-of-day interval analysis for AI^{ABS} (row 1) and HAR prediction (row 2) feature *Δs*, subtracting the values from a corresponding non-headache day from those of the headache day. Both subplot rows utilize identical interval data. Large o-shaped markers in the box plots signify the mean values. The (*N* = #) prefix for each y-axis label indicates the number of attack pairs for the corresponding interval. Uncorrected and corrected *p*-values are represented with dim gray and bold black asterisks, respectively. *Note: P-values: **** = p < 0.0001, *** = p < 0.001, ** = p < 0.01, * = p < 0.05. Abbreviations: AI^{ABS}: absolute activity index; ATR = above threshold ratio; BTR = below threshold ratio; TR = threshold ratio;; Δ = feature delta*

Analysis 3: fixed intervals relative to headache onset

Figures 7 and 8 display the feature deltas for 1-h intervals around headache onset, using AI^{ABS} and HAR prediction signal metrics, respectively.

In subplot row [a] of both figures, no clear trends are observed in the prodromal phase, aside from a slight, non-significant increase in lying probabilities during the "−2 h to −1 h" and "−1 h to onset" intervals. During the first hour of the ictal phase ("onset to 1 h"), a significant decrease in movement intensity is observed (AI^{ABS} below threshold 0.01: $p < 0.05$ post-correction). This decrease is also significant for the movement ratio and lying HAR predictions ($p < 0.05$ after correction for both) during the same interval, as shown in Fig. 8. No significant changes are observed for the "1 h to 2 h" interval of the ictal phase in either figure.

Subplot row [b] categorizes headache event pairs based on the presence of motion sensitivity as reported symptom. In the movement sensitivity subgroup, both AI^{ABS} (Fig. 7) and HAR predictions (Fig. 8) suggest increased movement during the prodromal phase (i.e., "−3 h to −2 h", "−2 h to −1 h", and "−1 h to onset"), followed by decreased movement during the ictal phase. This decrease during the headache phase aligns with findings from the daytime ictal interval analysis in Fig. 5. Supplemental Fig. 5 provides additional analysis for the motion sensitivity subgroup, showing non-corrected statistical significance for increased movement during the prodromal "−1 h to onset" phase.

In subplot row [c] of both figures, medication effectiveness is color-coded. No distinct trends are observed during the prodromal phase, except for a slight reduction in movement ratio for non-effectively treated attacks.

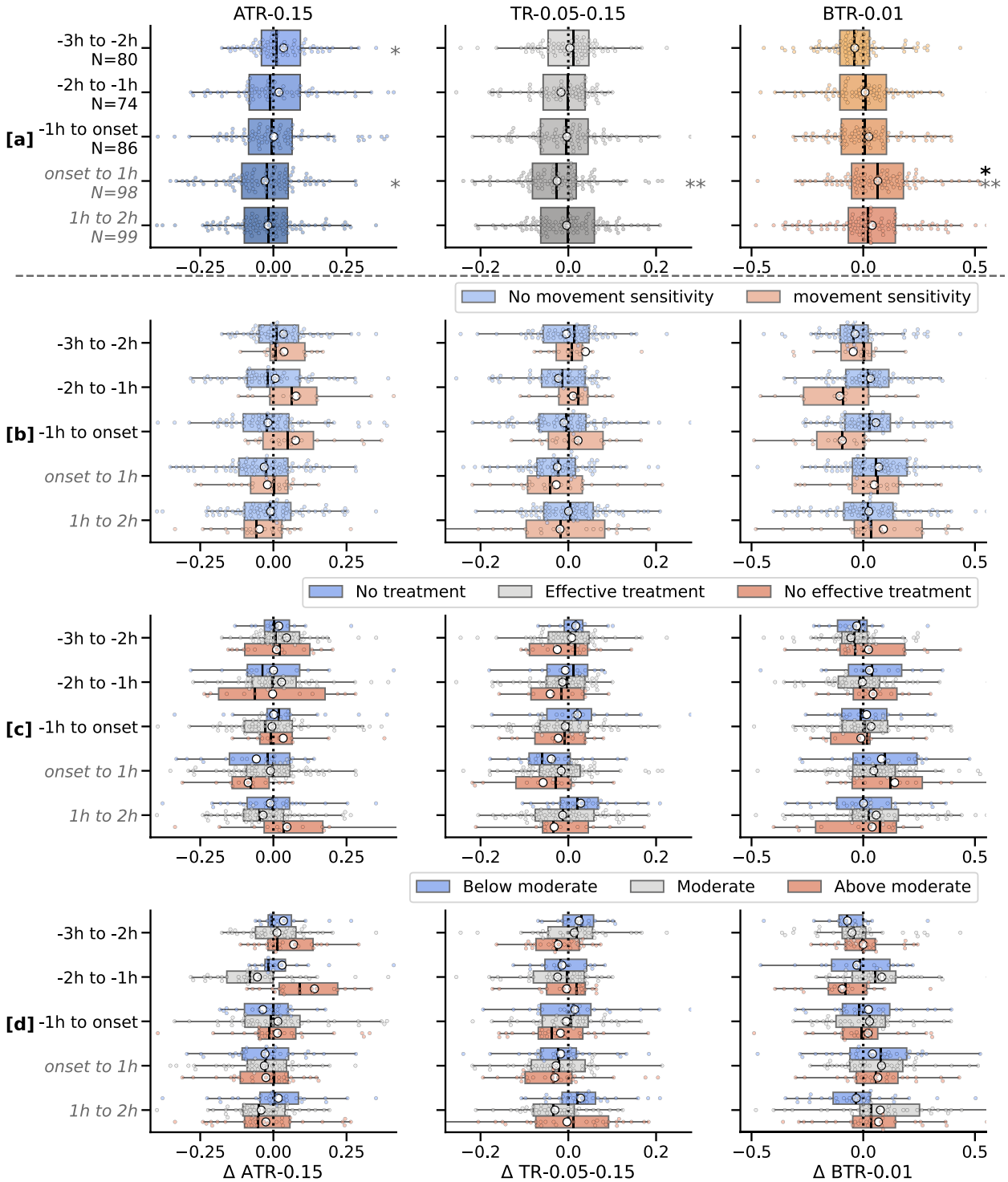


Fig. 7 Daytime AI^{ABS} Δ plots for intervals relative to headache onset, subtracting the values from a corresponding non-headache period from those of the headache period. Each subplot row displays identical data, color-coded by metric signal feature [a], presence of movement sensitivity as a symptom during headache registration [b], acute treatment use and its effectiveness [c], and headache intensity [d]. Large o-shaped markers in the box plots signify the mean values. The first row presents both uncorrected and corrected p-values, displayed with dim gray and bold black asterisks, respectively. Ictal intervals are marked by gray italic y-axis labels. No statistical testing was performed for row [b], [c], and [d] due to reduced sample size for the subgroups. *Note: P-values: **** = p < 0.0001, *** = p < 0.001, ** = p < 0.01, * = p < 0.05. Abbreviations:* AI^{ABS}*: absolute activity index; ATR = above threshold ratio; BTR = below threshold ratio; TR = threshold ratio; Δ = feature delta*

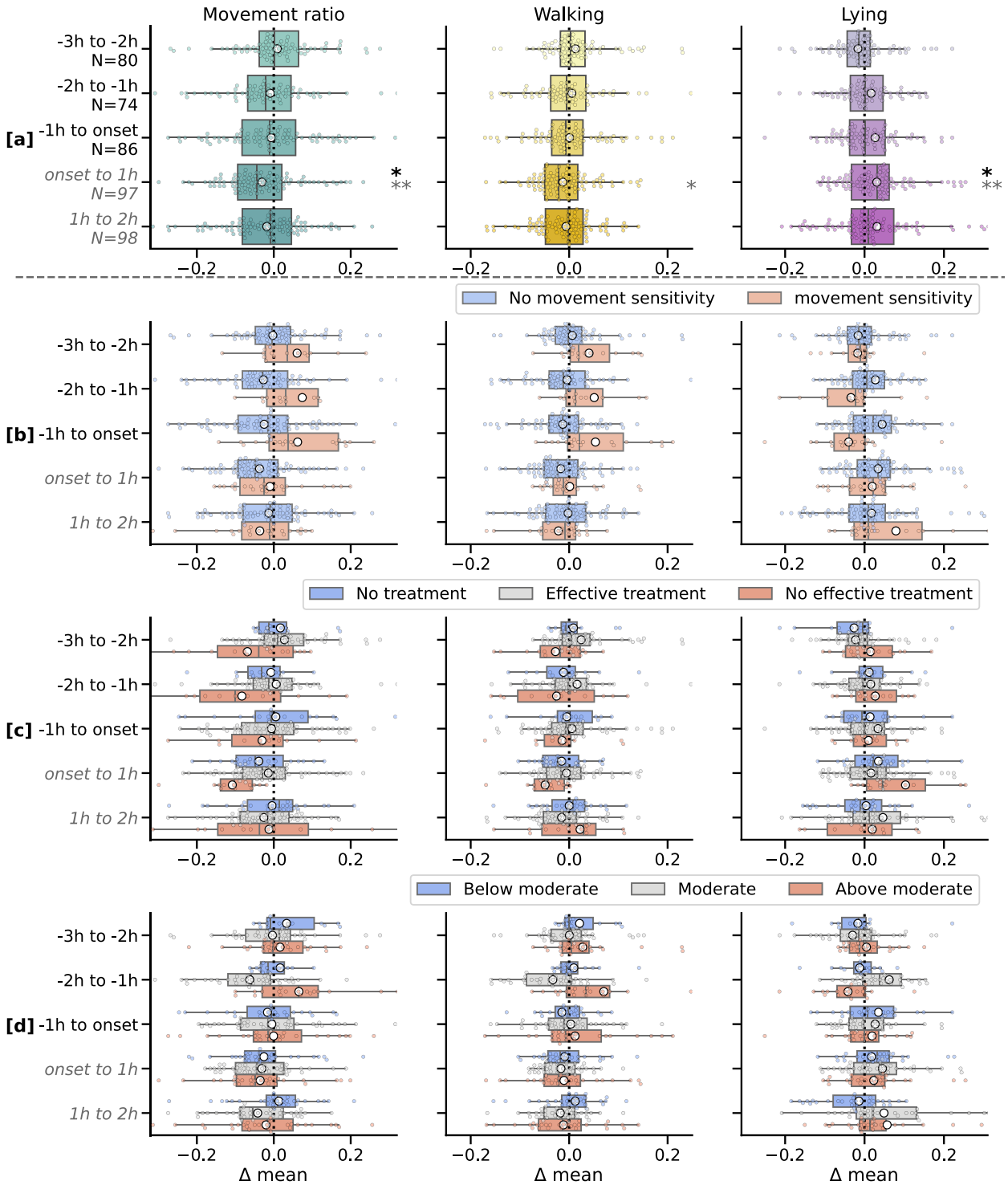


Fig. 8 Daytime HAR Δ plots for intervals relative to headache onset, subtracting the values from a corresponding non-headache period from those of the headache period. Each subplot row displays identical data, color-coded by [a] metric signal feature, [b] presence of movement sensitivity as a symptom during headache registration, [c] acute treatment use and its effectiveness, and [d] headache intensity. Large o-shaped markers in the box plots signify the mean values. The first row presents both uncorrected and corrected p-values, displayed with dim gray and bold black asterisks, respectively. Ictal intervals are marked with gray italic y-axis labels. No statistical testing was performed for row [b], [c], and [d] due to reduced sample size for the subgroups. *Note: P-values: **** = $p < 0.0001$, *** = $p < 0.001$, ** = $p < 0.01$, * = $p < 0.05$. Abbreviations: HAR = human activity recognition; Δ = feature delta*

However, during the "onset to 1 h" interval of the ictal phase, non-effectively treated attacks show a significant decrease in movement intensity, as detailed by Supplemental Fig. 6.

Lastly, subplot row [d] in Figs. 7 and 8 shows an increase in movement for above-moderate intensity attacks during the "−3 h to −2 h" and "−2 h to −1 h" intervals. This is supported by a significant increase of AI^{ABS} (above threshold 0.15: $p < 0.05$ post-correction) features for the "−2 h to −1 h" interval, as depicted by Supplementary Fig. 7. For the ictal phase, below-moderate intensity attacks exhibit a slightly smaller decrease in movement compared to the moderate and above moderate intensity subgroups.

Analysis 4: fixed intervals relative to headache end

Figures 9 and 10 continue the analysis of feature Δs for 1-h intervals, this time focussing on periods relative to the end of the headache.

Subplot row [a] in both figures highlights a significant reduction in movement during the ictal phase ("−2 h to −1 h", "−1 h to end"). In the postdromal phase, AI^{ABS} features do not indicate significant movement changes, while HAR prediction features indicate a slight decrease in PA. This is reflected by a significant decrease in walking probabilities and an increase in lying probabilities for the "end to 1 h" interval ($p < 0.05$ for both post-correction).

Subplot row [b] categorizes the event pairs of [a] based on the presence of motion sensitivity symptoms. In alignment with earlier findings, the motion sensitivity subgroup shows a greater reduction in PA during the ictal phase. Furthermore, this PA reduction for the motion sensitivity subgroup appears to intensify as the phase progresses towards the headache end, as visually highlighted in Supplemental Fig. 8. In the postdromal phase, no significant movement differences are observed for either subgroup, except for a minor increase in movement in the "2 h to 3 h" interval for the movement sensitivity category.

Subplot Row [c] of Figs. 9 and 10 groups delta features by the effectiveness of acute treatment. The trend remains the same for the subgroup receiving ineffective treatment, showing movement reduction during the ictal phase, with a greater reduction for the non-effective treated subgroups, but no significant PA changes for the groups during the postdromal phase. Supplemental Fig. 9 provides a visualization of the ineffective acute treatment group.

The final subplot row [d] provides an overview of the headache intensity categories, revealing a more pronounced reduction in movement during the ictal phase for the above-moderate intensity subgroup, aligning with prior observations. This trend is further detailed in Supplemental Fig. 10. The below-moderate subgroup does not show a decrease during the ictal phase. No discernible movement differences are noted in the postdromal phase across intensity subgroups.

Discussion

Only a few prior actigraphy studies have examined PA levels in patients with headache disorders in free living ambulatory environments [18, 20]. These studies were often limited by short observation periods or inconsistent methodologies, which affected the robustness and generalizability of their findings. Our study addresses these gaps by conducting a longitudinal analysis of daytime PA, evaluating AEE and movement behaviors, in patients with migraine within their natural settings, including their habitual use of acute treatments. Using wrist-worn actigraphy combined with a smartphone-based ecological momentary assessment (EMA), we captured high-resolution headache registration data alongside covariates such as movement sensitivity, acute medication usage, and headache intensity over a median duration of 91 days. A dual analytical approach integrated raw accelerometer data (AI^{ABS}) and ML predictions (movement ratio, walking, lying) derived from a HAR algorithm.

The study results demonstrate high consistency between both AI^{ABS} and HAR prediction signal metrics, suggesting that for the tasks presented in the results section, processed data from HAR algorithms may suffice when raw actigraphy data is not available. This reduces the dependence on specialized actigraphy sensors and raw data, potentially lowering costs, enhancing accessibility, and enabling activity monitoring in broader settings, including resource-constrained environments or retrospective studies utilizing existing HAR data.

More importantly, our findings support the primary hypothesis that the daytime ictal phase of migraine attacks are characterized by a significant reduction in intense movement and an increase in low-intensity activities, such as lying down, see Fig. 5 [a]. However, our secondary hypotheses regarding hypoactivity during the prodromal and the postdromal phase were not supported by the data (Figs. 7, 8, 9 and 10). Notably, our interval-based analysis in Fig. 9 [a] and 10 [a] highlighted a progressively declining trend in AEE and movement during the ictal phase, with the largest reduction in the "−1 h to end" interval.

Several potential explanations may account for the absence of reduced movement during the prodromal and postdromal phases. One possibility is that participants had difficulty distinguishing the prodromal and postdromal phases from the headache phase, which may have led to misclassification or overlap. Additionally, postdromal

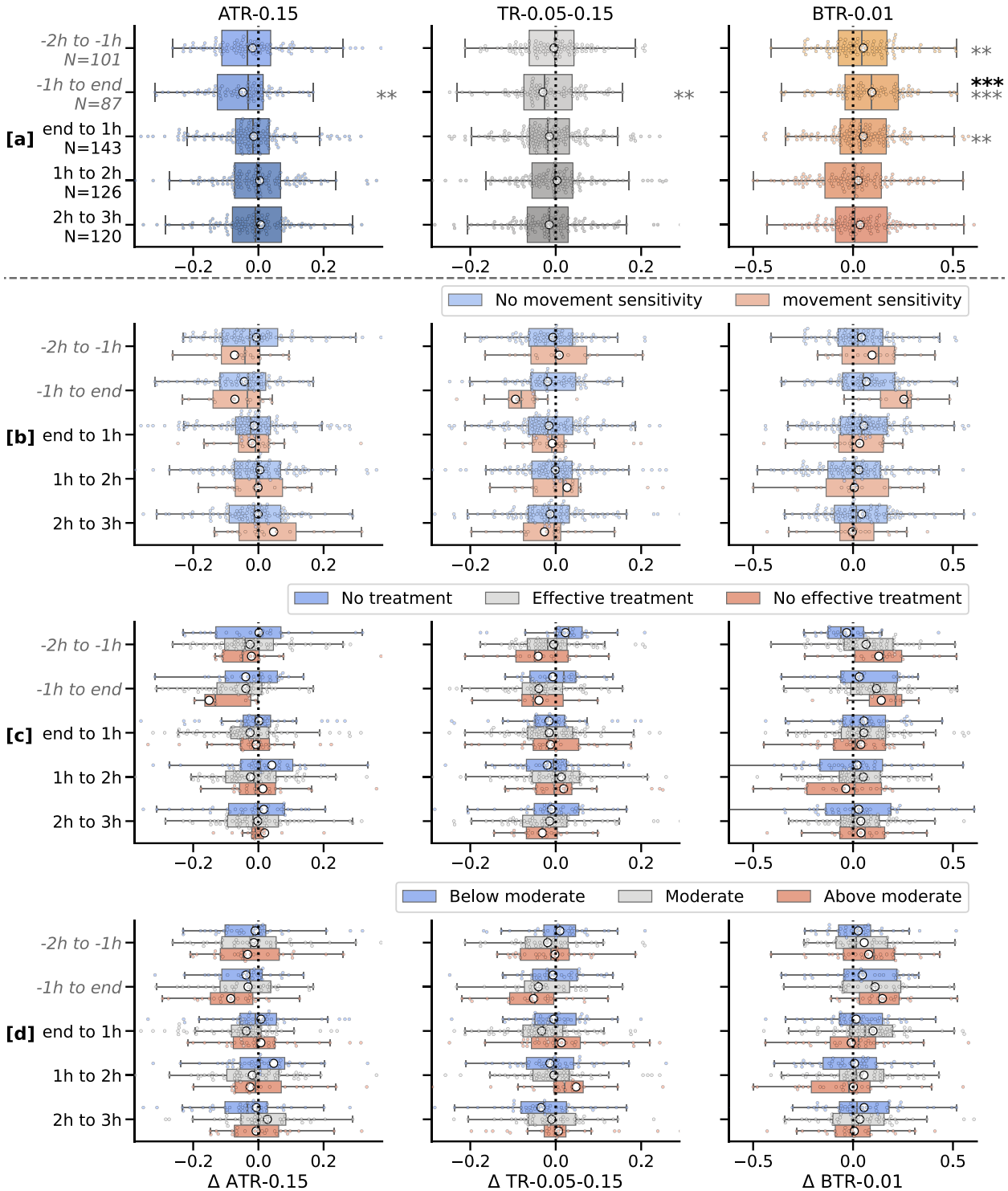


Fig. 9 Daytime AI^{ABS} Δ plots for intervals relative to headache end, subtracting the values from a corresponding non-headache period from those of the headache period. Each subplot row displays identical data, color-coded by metric signal feature (row [a]), presence of movement sensitivity as a symptom during headache registration (row [b]), acute treatment (row [c]) and headache intensity (row [d]). Large o-shaped markers in the box plots signify the mean values. The first row presents both uncorrected and corrected p-values, displayed with dim gray and bold black asterisks, respectively. Ictal intervals are marked with gray italic y-axis labels. No statistical testing was performed for row [b], [c], and [d] due to reduced sample size for the subgroups. *Note: P-values: **** = p < 0.0001, *** = p < 0.001, ** = p < 0.01, * = p < 0.05. Abbreviations:* AI^{ABS}*: absolute activity index; ATR = above threshold ratio; BTR = below threshold ratio; TR = threshold ratio; Δ = feature delta*

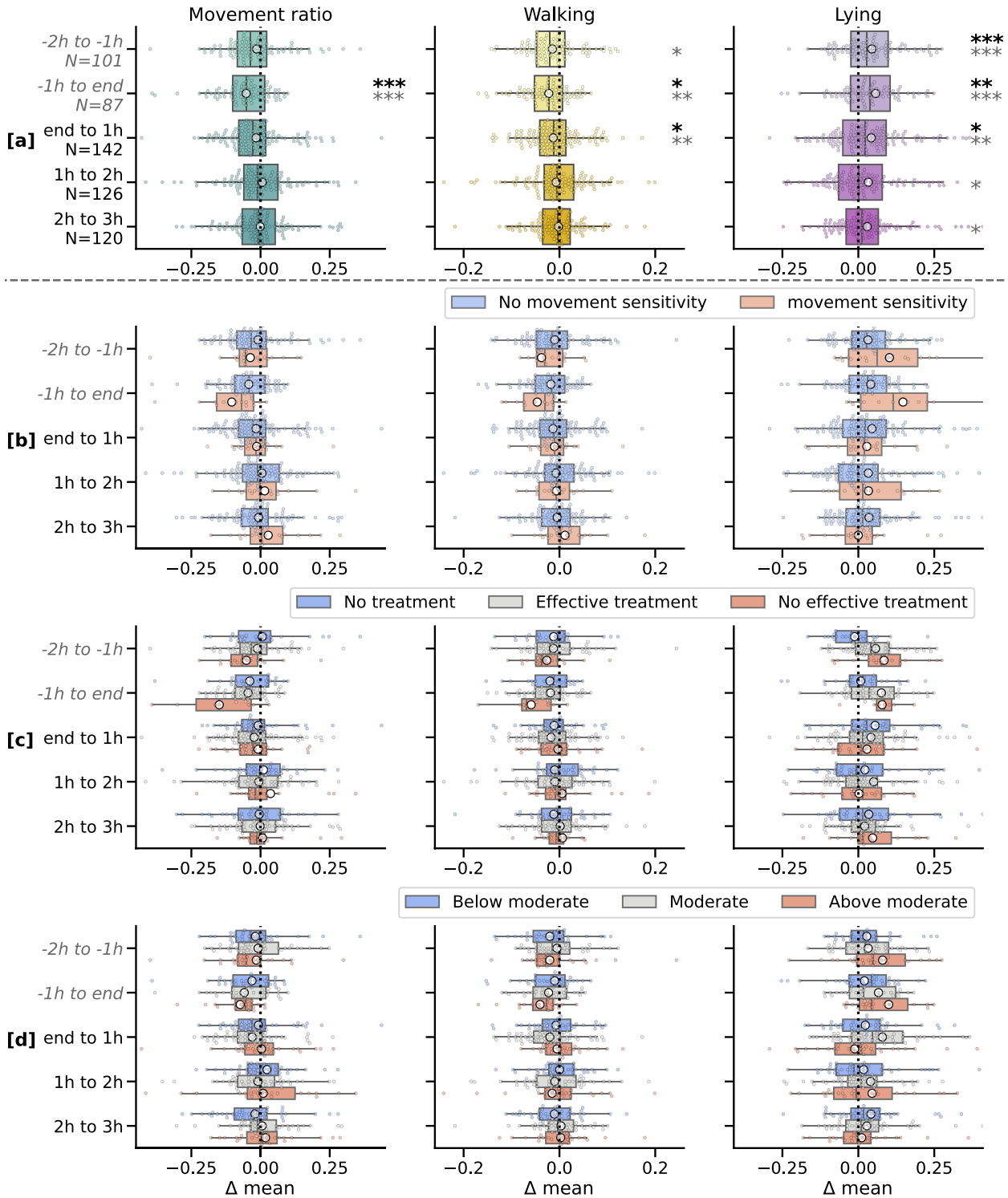


Fig. 10 Daytime HAR predictions *Δ* plots for intervals relative to headache end, subtracting the values from a corresponding non-headache period from those of the headache period. Each subplot row displays identical data, color-coded by metric signal feature (row [a]), presence of movement sensitivity as a symptom during headache registration (row [b]), acute treatment (row [c]) and pain intensity (row [d]). Large o-shaped markers in the box plots signify the mean values. The first row presents both uncorrected and corrected p-values, displayed with dim gray and bold black asterisks, respectively. Ictal intervals are marked with gray italic y-axis labels. No statistical testing was performed for row [b], [c], and [d] due to reduced sample size for the subgroups. *Note: P-values: **** = p < 0.0001, *** = p < 0.001, ** = p < 0.01, * = p < 0.05. Abbreviations: HAR = human activity recognition; Δ = feature delta*

fatigue could manifest in forms unrelated to gross motor activity, such as cognitive or emotional fatigue, which would not be captured by physical activity metrics. By reviewing the literature, it can also be concluded that either movement sensitivity is an understudied symptom of the premonitory and postdromal phase, or the symptom by nature of the disorder is very infrequently present during these phases [43, 44].

The time of day interval analysis (Fig. 6) revealed that participants exhibited reduced movement during evening hours (i.e., 18–20 h, 20–22 h, and 22–24 h) on headache days. This outcome aligns with existing evidence that suggesting fatigue or a worn-out effect leads patients to be less active at the end of a headache day. However, considering that the majority of ictal phases conclude in the evening (Supplemental Fig. 3) and the most substantial movement reduction is observed during the "−1 h to end" interval (Figs. 9 and 10), these findings likely share a period overlap. The insights from Fig. 6, coupled with the observation that most migraine attacks end in the evening, suggest a potential focus for future research on evening data to enhance headache day detection.

In the subgroup analyses, we discovered that wrist-worn activity devices can detect changes in activity levels for headache events characterized by movement sensitivity (Fig. 5 [b]). Specifically, during the ictal phase, headaches characterized by motion sensitivity demonstrate a more pronounced decrease in activity compared to those without this symptom (row [b] of Figs. 9 and 10). Intriguingly, headaches associated with either motion sensitivity or an above moderate intensity exhibit increased activity during the prodromal phase (row [b] of Figs. 7 and 8). Interpretation of this finding is challenging, but several hypotheses arise: 1) a subconscious increase in movement during the prodromal phase, 2) a deliberate increase in activity destined to complete daily tasks before headache onset, or 3) hyperactivity as a trigger for headache events with movement sensitivity. Notably, episodes without motion sensitivity symptom also exhibited reduced PA during the ictal phase (Fig. 5 [b]). This hypoactivity could be attributed to other migraine-related symptoms, such as fatigue or cognitive disturbances, or it might result from patients' deliberate avoidance of stimulus-rich environments.

Although pain may contribute to reduced activity, we found that the majority of successfully treated headaches still led to reduced activity levels in the ictal phase (row [c] of Figs. 9 and 10, intervals "−2 h to end" and "−1 h to end"). However, attacks of below moderate intensity show less significant reductions in PA during the ictal phase (row [d] of Figs. 7, 8, 9 and 10). Analysis of the headache intensity levels in Table 5. reveals an average intensity of 3.13 (suggesting moderate pain) for the effective treatment group, compared to an average intensity 1.99 (suggesting light pain) for the below moderate subgroup. This suggests that while treatment effectiveness may aid in alleviating the pain (momentarily), perceived headache intensity may be a more primary driver for activity level changes. Additionally, significantly higher headache intensity levels are observed for events associated with movement sensitivity (Mann-Whitney u-test on bias-free headache events, $p < 0.001$, $N = 505$). Specifically, events with movement sensitivity had an average intensity of 3.35 (moderate-to-severe pain) compared to 2.87 (light-to-moderate pain) for those without this symptom. This heightened intensity may contribute to the increased hypoactivity observed in the motion sensitivity group during the ictal phase.

Headache attacks that were not treated effectively showed a statistically supported reduction in movement during the ictal phase (row [c] of Figs. 7, 8, 9 and 10), particularly in the intervals immediately preceding the end of the ictal phase (e.g., "−2 h to end" and "−1 h to end", see Supplemental Fig. 9—"Lying"). While similar trends are visually apparent across other metric signals, the small sample size for this subgroup limits broader generalization. This trend of decreasing PA when nearing the end of the ictal phase may correspond with the buildup of headache pain throughout the ictal phase [15].

Certain interesting sub analyses, such as grouping attacks based on ICHD-3 migraine criteria, were deliberately not performed. The ICHD-3 diagnostic criteria focus on untreated attacks, which we confound by allowing acute and preventive treatments. Additionally, our focus on daytime intervals and the 95% data availability threshold further reduce the number of attacks qualifying as migraines. Therefore, we refrained from conducting this analysis.

As migraine is a disorder of sensory processing – particularly involving mechanosensitive pain fibers of the trigeminovascular system [45, 46]— the reduced PA observed during the various phases of a migraine attack may stem from several overlapping factors. First example, patients may experience movement sensitivity, which is the aggravation of pain due to otherwise non-painful activity or routine activities. Second, they may withdraw themselves from physically or cognitively demanding tasks to minimize external stimuli. Additionally, rest and sleep are therapeutic for migraine relief, leading to spontaneous hypoactivity as an adaptive behavior. This may be reflected in the hypoactivity seen during the time blocks between 18.00 to 22.00, when fatigue is already building during the evening but is exacerbated by the ictal or postdromal effects of headache attacks (Figs. 6 and 7).

Key strengths of our study include the consistency observed between the AI^{ABS} and HAR analyses, offering

diverse methodological approaches towards actigraphy analysis in headache disorders. Moreover, the study's rigorous methodology—characterized by precise definitions of headache episodes and strict data validity criteria—aims to improve the reliability of our findings, while addressing the inherent challenges of monitoring migraines in real-world contexts. The outlined intra-subject analysis framework is widely applicable to other event-based wearable monitoring studies, such as those investigating epilepsy or mood disorders, as well as studies exploring disorder-related factors like the impact of preventive treatments (see Supplemental Fig. 11 for preliminary analysis). These studies help evaluate whether certain symptoms or disorders do have an impact on daily life quality or behavior (such as activity levels). Moreover, with large sample sizes, these studies could analyze extensive datastreams to determine the feasibility of detecting these events in real-world conditions.

Limitations to the study should also be addressed. First, the most important limitation to the study is its exploratory nature with no pre-specified sample size. Given the low sample size and the rigorous preprocessing done to access the most robust parts of the dataset, thereby losing multiple data points during the process (e.g. due to missing data, non-wear periods, connectivity problems etc.), the results of this study should be interpreted as hypothesis-generating rather than directly inferential. Additionally, the cohort was limited to Android users with sufficient technical skills, introducing potential selection bias. Moreover, the study design and inclusion criteria implicitly resulted in the majority of participants being white-collar workers. Second, throughout the data processing methodology, we established our own set of rules and thresholds to ensure data validity and determine eligibility for headache and non-headache intervals. The majority of these values were validated during exploratory analysis and optimized to balance data availability with theoretical validity. While these custom rules were tailored to the study's specific needs, they should be considered when interpreting the results. Third, our non-headache selection procedure allows pairing overlapping non-headache intervals for multiple headache periods. Fourth, it has been demonstrated that wrist-worn actigraphy devices are less representative of global body movements and, consequently, AEE [24]. Although we partially mitigate this limitation by employing a dual metric signal approach, for which the HAR ML predictions estimate global body activities, no direct extrapolation of the results presented above can be made in regard to accelerometers placed anywhere else on the body. Fifth, although our analysis tried to minimize potential recall bias, the start and end times of headache events were collected through self-reporting in the smartphone application, meaning no real-time registration (e.g. via button or command) was utilized. We acknowledge the fact that pain from migraine attacks builds up over time, and so a precise starting point is often obscured. Therefore, the exact start of a headache event is hard to determine with a high temporal accuracy. Moreover, the EMA headache registration requires participants to report a single headache intensity level. This can be problematic as headache intensity may change throughout the ictal phase or due to medication use. Differences in interpretation, with some reporting their average intensity while others record their peak intensity, could further complicate the data. Furthermore, timestamps for the exact time of intake of acute treatment were also unavailable, making analyses on the effect of acute medication on AEE currently impossible. Additionally, the study lacked information whether participants experienced episodic or chronic migraine, possibly confounding the results. Last, we need to consider the effect of wearable wear bias, implying that participants may tend to wear the wearable less during certain types of activity, potentially skewing the findings. Specifically, since the Empatica E4 device is not waterproof, it cannot be worn during water-related activities, resulting in an incomplete capture of overall behavior.

Conclusions

This study is one of the first and largest exploratory investigations to objectively analyze daytime movement behavior in patients with migraine within their habitual environments. Our findings demonstrate the feasibility of wrist-worn actigraphy to detect changes in physical activity (PA) during headache events. Specifically, the results support our primary hypothesis of reduced PA during the ictal phase, particularly in cases of unsuccessfully treated headaches and those with reported movement sensitivity. Additionally, we observed decreased PA during evening hours on headache days compared to non-headache days. However, our secondary hypothesis of reduced activity during the prodromal and postdromal periods was not supported by the data. Overall, this study highlights a robust methodological framework for analyzing objective movement data and underscores the potential of wrist-worn actigraphy as a promising digital biomarker for migraine attacks.

Abbreviations

ICHD-3	International Classification of Headache Disorders, Third Edition
PA	Physical Activity
TTH	Tension-type headache
EMA	Ecological momentary assessments
SQI	Signal quality index
AI^{ABS}	Absolute activity index
Σ_m	Signal variance of wrist acceleration over axis x, y or z
AEE	Activity energy expenditure
HAR	Human Activity Recognition

ML	Machine Learning
ACC	Accelerometer
SD	Standard deviation
EDA	Electrodermal activity
TMP	Skin temperature
TR	Threshold ratio
ATR	Above threshold ratio
BTR	Below threshold ratio
Δ	Feature deltas
Q1	First quartile
Q3	Third quartile

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
Study concept and design: all authors. Acquisition of data: NV, KP. Analysis and interpretation of data: JVDD, NV, KP. Drafting of the manuscript: JVDD, NV. Revising it for intellectual content: all authors. Final approval of the completed manuscript: all authors.

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Data availability
The data supporting the findings of this study are not publicly available due to ethical and participant privacy concerns. Data sharing is restricted to comply with the confidentiality agreements made with participants. Researchers requiring access to specific aspects of the data may contact the corresponding author for further discussion. The majority of code and methodology align with examples provided in the authors' analysis methodology paper: https://github.com/predict-idlab/data-quality-challenges-wearables.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of University Hospital Ghent (BC-10031). The study was preregistered at clinicaltrials.gov (NCT04983186). All patients gave written informed consent at the beginning of the study for the collection, analysis and publication of their data.

Consent for publication
All patients gave written informed consent at the beginning of the study for the collection, analysis and publication of their data.

Competing interests
The authors declare no competing interests.

Author details
[1]IDLab, Ghent University - imec, Technologiepark-Zwijnaarde 126, Ghent B-9052, Belgium. [2]Department of Neurology, Ghent University Hospital, Corneel Heymanslaan 10, Ghent B-9000, Belgium. [3]Department of Basic and Applied Medical Sciences, Faculty of Medicine and Health Sciences, Ghent University, Corneel Heymanslaan 10, Ghent B-9000, Belgium. [4]Department of Neurology, AZ Sint-Jan Bruges, Ruddershove 10, Bruges 8000, Belgium.

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