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Exploring actigraphy as a digital phenotyping measure: A study on differentiating psychomotor agitation and retardation in depression

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Abstract

Introduction: Psychomotor activity stands out as a crucial symptom in characterizing behaviors associated with depression. This study aims to explore the potential of actigraphy as a tool for digital phenotyping in characterizing symptoms of psychomotor agitation and retardation, which are clinically challenging dimensions to capture, in patients diagnosed with major depressive episode (MDE) according to DSM-5 criteria.

Methods: We compared rest-activity circadian rhythm biomarkers measured by the Motion Watch 8 actigraphy between 58 (78.4%) patients with MDE and psychomotor retardation (PMR), and 16 (21.6%) patients with MDE and psychomotor agitation (PMA), according to DSM-5 criteria.

Results: Actigraphy allowed to objectively report PMA through heightened activity over a 24-h period, while PMR manifests as reduced activity during the most active 10 h. Lower rest-activity rhythm (RAR) amplitude in PMR was accompanied by increased irregularities in intra- and inter-day rhythms. Interestingly, actigraphy emerges as an objective tool to measure the characteristics of the active and rest periods, free from the confounding effects of sleep disturbances. Indeed, no differences in sleep disturbances were identified between patients exhibiting psychomotor agitation and those displaying PMR.

Conclusion: Digital phenotyping through actigraphy may aid in distinguishing psychomotor retardation and psychomotor agitation allowing for a more precise characterization of the depression phenotype. When integrated with clinical assessment, measurements from actigraphy could offer additional insights into activity rhythms alongside subjective assessments and hold the potential to augment existing clinical decision-making processes in psychiatry.

KEYWORDS

actigraphy, major depressive disorder, rest-activity circadian rhythm, sleep

1 | INTRODUCTION

Depression diagnosis and monitoring predominantly rely on interview-based assessments or self-report scales, incorporating inquiries about current circumstances, personal and family history, and the frequency of depressive symptoms.[1] However, this information is often subjective, based on the patient's report, and influenced by the clinician's judgment, making it susceptible to various biases that can impact the quality of care.[2] Furthermore, the phenotypic diversity present in depressive disorders has led some teams to suggest focusing on more dimensional and objective aspects, such as sleep patterns, and activity rhythms. These aspects are all significant components of depression and are implicated in specific pathophysiological processes.[3] By combining digital measurements with self-reports, clinicians can potentially reduce self-report questionnaire inaccuracies resulting from memory and perception biases. Digital phenotyping, utilizing mobile devices like wearable smartbands and smartphones, involves collecting and analyzing digital data and facilitates data collection in everyday life.[4] It offers the opportunity to capture behavior and symptoms,[4] by enabling passive monitoring of behavioral and physiological factors, providing more frequent and objective measurements that address the limitations of adherence and bias associated with self-reports in depression monitoring.[5,6] Few studies have explored its utility in evaluating 24-hour rest-activity patterns in relation to depression[5,7] while rest-activity rhythm (RAR) measures seem to play a crucial role in characterizing behavior associated with depression.[7–10] Indeed, prior literature has found shorter active periods and later activity rhythm timing objectively mark depression symptoms.[11–13] Moreover, a prior study in depressed patients with comorbid insomnia and excessive daytime sleepiness found delayed activity in the 10 most active hours using actigraphy.[7] Thus, RAR measures may aid in distinguishing psychomotor retardation (PMR) and psychomotor agitation (PMA), which are part of the clinical diagnostic criteria in the DSM-5 for depression, and that pose challenges for objective assessment in clinical practice.[14] Establishing these objective markers could not only assist in distinguishing various patient subtypes, offering insights into underlying pathophysiology but also identify two distinct major clinical therapeutic targets to consider in the development of therapeutic strategies.

One noninvasive digital method for collecting objective activity and sleep–wake rhythms is through actigraphy. Actigraphy can provide reliable estimates of 24-h RAR, using rhythmometric methods like the cosinor model or non-parametric models for quantifying rhythm stability.[7,15] This study aims to conduct an initial psychometric evaluation of actigraphy, a promising passive digital phenotyping measure for psychomotor agitation and retardation during a major depressive episode (MDE). To the best of our knowledge, no study has directly investigated the potential of actigraphy as a tool for assessing RAR in digital phenotyping to characterize symptoms of psychomotor agitation and retardation, which are clinically challenging dimensions to capture, in patients diagnosed with MDE according to DSM-5 criteria. Assessing RAR using actigraphy could offer an objective means of quantifying the behavioral signatures of mood disorders within and across 24-h periods.

Significant outcomes

- Objective actigraphy markers aid in distinguishing depressed patients with psychomotor agitation and retardation allowing for a more precise characterization of the depression phenotype.
- Actigraphy detects psychomotor agitation through heightened activity over a 24-h period and psychomotor retardation through reduced activity during the most active 10 h and irregularities in intra- and inter-day rhythms.
- No significant differences were observed in sleep patterns using subjective assessments and actigraphy between patients with PMR and PMA.

Limitations

- No specific scales of psychomotor agitation or retardation, designed to evaluate motor disturbances in depressed patients were administered.
- Clinicians may find it valuable to examine patterns of a patient's activity and observe how these patterns evolve over multiple visits and treatments.
- Future studies are needed to measure satisfaction with digital practices

2 | METHODS

2.1 | Study design

This is a naturalistic case–control study conducted in routine care that compares two groups of patients with MDE with psychomotor agitation and with retardation. Consecutive patients presenting at our specialized

university department for the management of sleep disorders and psychiatric conditions, either for scheduled outpatient appointments or hospitalization, were assessed by a psychiatrist. Sleep and circadian rhythms markers were evaluated by subjective (self-report questionnaires) and objective (actigraphy for at least 14 days) measures. Data were collected during routine MDE assessments following DSM-5 criteria.[14,16] While actigraphy was primarily used to examine general activity/rest patterns over a 24-h period, we also analyzed sleep actigraphy variables to ensure that observed differences in activity could not be associated with sleep disorders. Additionally, we conducted an analysis of sleep questionnaires to confirm, first, that patients did report symptoms of PMR and PMA, which are clinically challenging dimensions to capture, and not symptoms related to sleep and wakefulness.

In addition, we collected the patient's medical history (treatments, recurrences, and progression) and through questionnaires the current characteristics of MDE, its comorbidities, as well as sleep and circadian rhythm markers. Psychotropic treatments were also documented. Participants were eligible if they were aged from 18 to 65 years, were affiliated with a social security program, and had been provided with an information sheet. Exclusion criteria included individuals who did not understand or read French, had a medical condition that prevented them from participating in the questionnaire, were unable to provide informed consent due to urgent situations or comprehension difficulties, exhibited behavioral disorders that made assessments unfeasible, worked in shifts or had irregular work hours in the year preceding inclusion and had traveled across more than two time zones in the month before inclusion. Additionally, certain individuals, such as minors and legally protected adults, were also excluded. Further exclusions encompassed individuals under legal guardianship, trusteeship, or curatorship. This project entitled "Study of biomarkers of sleep and circadian rhythms in psychiatric disorders (Som-Psy)" (principal investigator: PA Geoffroy) was conducted in the Department of Psychiatry of Pr Lejoyeux in Bichat-Claude Bernard Hospital (AP-HP, GHU, Paris, France) and at INSERM UMR 1141. It has been ethically approved (No CER-2020-56) by the "Comité d'Évaluation de l'Éthique des projets de Recherche Biomédicale (CEERB) Paris Nord" (Institutional Review Board-IRB 00006477- of the HUPNVS, Université Paris 7, AP-HP). All patients were included between January 2022 and October 2023 at Bichat Claude Bernard hospital (AP-HP, GHU, Paris, France). Patients were given oral information, a written note concerning the study protocol, and each received a no-objection note.

2.2 | Sociodemographic and psychiatric clinical parameters

Sociodemographic characteristics such as gender, age, and body mass index (BMI) were collected. Other clinical parameters were assessed including especially the type of mood disorder (unipolar or bipolar), the age of onset, the number of MDE, the severity of depressive symptoms (using the hetero-questionnaire Montgomery-Asberg Depression Rating Scale [MADRS][17]), the severity of depression and anxiety symptoms (using the self-report questionnaire the Hospital Anxiety and Depression Scale [HADS]).[18] Additionally, the generalized anxiety disorder-7 (GAD-7)[19] were used to assess anxiety symptoms for the past 15 days. Finally, we investigated addictive comorbidities and psychotropic treatments were also documented.

2.3 | Sleep and circadian rhythms measures

2.3.1 | Self-report questionnaires

Patients completed the French versions of the following sleep and circadian rhythms questionnaires: insomnia symptoms in the past month were assessed with the Insomnia Severity Index (ISI)[20] and its subscales (Severity of sleep disturbances, of difficulty staying asleep, of early morning awakenings, of satisfaction with current sleep, of disruption of daily functioning, of apparent difficulties, of concerns regarding sleep disturbances). Scores on the ISI range from 0 to 28, with higher scores indicating greater insomnia symptom severity. Recommended cut-offs on the ISI are: 0–7: no clinically significant insomnia; 8–14: subthreshold insomnia, mild (Category 1); 15–21: clinical insomnia, moderate (Category 2); and 22–28: clinical insomnia, severe (Category 3). All participants were also assessed regarding their sleep quality during the past month with the French version of the 19-item Pittsburgh Sleep Quality Index (PSQI).[21] A total score >5 indicates a significantly disturbed sleep. Hypersomnia symptoms in the past month were assessed with the Hypersomnia Severity Index (HSI) range from 0 to 36, with higher scores indicating greater hypersomnia symptom severity.[22] The excessive daytime sleepiness was evaluated by the Epworth Sleepiness Scale (ESS). The ESS consists of seven situations commonly encountered in daily life, in which patients have to say whether they have more or less chance of falling asleep. The total score ranges from 0 to 24 and high score indicates more sleepiness.[23] The nightmares were assessed with the Nightmare Severity Index (NSI). The NSI encompasses

all main dimensions of nightmare disorder, evaluating four subdimensions: frequency, emotional impact, diurnal impact, and nocturnal impact of nightmares. The total score ranges from 0 to 45, with a higher score indicating greater severity of nightmares.[24] The circadian typology was evaluated by the 19-item Morningness–Eveningness Questionnaire (MEQ) consisting of 19 questions about preferred sleep time and daily performance. The total score ranges from 16 to 86 and a higher score indicates more eveningness.[25]

2.3.2 | Actigraphy

In the context of routine care, all patients were asked to wear an actigraph (MotionWatch 8®) on the wrist of their non-dominant hand for at least 14 consecutive days, as recommended by the American Academy of Sleep Medicine (AASM).[26] Actigraphy has been validated against gold-standard objective sleep measures[27,28] and approved by the AASM Board of Directors for the evaluation of sleep disorders and circadian rhythm sleep–wake disorders.[26]

Patients began to wear the actigraph on the days for which they completed self-assessment questionnaires of sleep and circadian profile. The MotionWatch 8 actigraph (CamNTech®) is an accelerometer that detects the intensity and the amount of movement as a function of time. For this study, data were sampled in 30-s epochs and participants were instructed to press the event-marker when they went to bed to go to sleep and when they got out of bed at the start of the next day. They also completed at the same time a sleep diary (as previously detailed in Reference 9). Other requirements were kept to a minimum to try to minimize intrusion into sleep/activity routines. Recording was made during periods when the participants were not on vacation and not involved in unusual activities. MotionWare 8 software (version 1.3.17) was used to collect, score, and analyze data. MotionWare 8 software includes sleep–wake rhythm analysis and Non-Parametric Circadian Rhythm Analysis (NPCRA).

Experienced psychiatrists and sleep physicians (JM and PAG) analyzed all the actigraphy records of patients using the sleep detection algorithm provided by Actiwatch and any incongruences between the sleep diary and actigraphy rest periods were clarified prior to statistical analyses.[29]

Sleep variables

The sleep biomarkers explored primarily by the MotionWatch 8® actigraphy between patients with PMA and PMR include (1) total night sleep time (TST) which reflects total time effectively spent asleep (in hours), (2) sleep onset latency representing the difference between bedtime and sleep (in minutes), (3) wake after sleep onset or nocturnal awakenings (WASO) indicating the period of wake time in sleep period (in hours), (4) actual wake representing the period of wake time during sleep period (in percentage), (5) actual sleep representing the period of sleep time during the sleep period (in percentage), (6) rest per 24 h representing the percentage of epochs in 24 h period which could be counted as sleep, if the whole period where analyzed as night time, (7) sleep fragmentation index indicating the degree of fragmentation of the sleep period, and (8) sleep efficiency (SE) representing the total sleep time (TST) divided by the time in bed (in percentage).

Rest-activity circadian rhythms

The RAR biomarkers measured by the Motion Watch 8 actigraphy (CamNTech) compared between the two groups over the entire 14-day period include: (1) measures of activity: the actigraphy markers of phase with the L5 onset which is the onset of the 5 h the least active and the M10 onset which is the onset of the 10 h the most active. The M10 reflects how active the wake periods are and the L5 reflects resting levels during the night and a lower L5 indicates less more restful sleep; (2) measures of variability (day-to-day stability of the sleep–wake rhythm and intra-day sleep–wake rhythm variability).[30,31] Intradaily variability (IV) is defined as the ratio of the hour-to-hour activity variability to the overall activity variability (Values between 0 and 2, higher values reflect more fragmented rhythms, e.g., due to frequent daytime napping or night-time awakenings). The IV provides an estimate of the fragmentation of the 24-h RAR. Interdaily stability (IS) is defined as the ratio of variability within the mean 24-h activity profile to the overall activity variability (higher values indicate the typical 24-h profile accounts for a greater degree of the overall variability in the time series recording, reflecting greater stability of the mean 24-h profile across days). The IS provides an estimate of how closely the 24-h RAR follows the 24-h light–dark cycle (IS = 0 for Gaussian noise, IS = 1 for perfect stability). As such, a higher IS indicates good synchronization to light and other environmental cues that regulate the biological clock; (3) measure of rhythm amplitude: the relative amplitude is the difference between M10 and L5 in the average 24-h pattern, normalized by their sum; higher relative amplitudes therefore indicate a more robust 24-h RAR, reflecting both relatively lower activity during the night and higher activity when awake.

2.4 | Statistical analysis

Each categorical variable was described with a number and percentage, while each continuous variable was described with a mean and standard deviation (SD). The normality of the continuous variables' distribution was assessed with visual inspection of histograms and with the statistical test of normality (Shapiro–Wilk test $p > 0.05$), and we looked at the equality of variances between the two groups for the measured variable (Levene test $p > 0.05$). We compared the two groups using parametric or non-parametric tests in case of non-normal distribution. Non-parametric tests were used for variables showing non-normal distributions (Wilcoxon-Mann–Whitney test, "U test"). When normal distribution was confirmed, a parametric test was used (*t*-test), with the chi-squared tests used to compare categorical variables. Univariate two-sided analyses were performed on the total sample of 74 participants. To account for the potential confounding factors, any variables that were significantly different ($p < 0.05$) between groups were then entered into a binomial logistic regression analysis. Significance after regression is annotated by p* in all our tables. Analyses were performed using JAMOVI software (2.3.26). For all tests, a value of $p < 0.05$ was considered significant.

3 | RESULTS

3.1 | Sample characteristics

Seventy-four patients with MDE were assessed (Table 1). Among those patients, 58 (78.4%) reported MDE with PMR and 16 (21.6%) reported MDE with PMA. Table 1 summarizes clinical and sociodemographic variables for these two groups. Compared with patients with PMA, patients with PMR reported more frequently current tobacco smoking (29.8% vs. 0%, $p = 0.013$).

While patients with PMA reported more frequently alcohol use disorder (25% vs. 5.2%, $p = 0.016$), there were no statistically significant differences between the two groups regarding age, gender, BMI, unipolar or bipolar subtype of MDE, age of onset of the mood disorder, severity of MDE, number of MDE, other addictive comorbidities, and treatments.

3.2 | Sleep and circadian rhythm subjective assessments

There were no significant differences in terms of subjective assessments between patients with PMR and PMA (Table 2). This concerned insomnia severity as measured by the ISI total score, sleep quality measured by the PSQI total score, hypersomnia severity as measured by the HSI total score, daytime sleepiness as assessed by ESS, nightmares severity as measured by the NSI, chronotype as evaluated by Horne and Östberg, and subjective sleep quality as measured by the PSQI.

3.3 | Actigraphy

All patients wore the actiwatch for at least 14 days. Patients with PMR, compared with patients with PMA, had a lower average IS (0.36 [±0.12] vs. 0.48 [±0.09], $p < 0.001$ and $p^* = 0.006$) and a higher IV (0.91 [±0.17] vs. 0.75 [±0.14], $p = 0.004$ and $p^* = 0.0012$), (Tables 3 and 4). The M10, reflecting the activity level during wake periods, was significantly lower among patient with PMR (10463.26 [±4069.59] vs. 15046.75 [±3425.03], $p < 0.001$ and $p^* = 0.002$). The relative amplitude, reflecting activity over a 24-h period, was significantly higher among patients with PMA (0.80 [±0.13] vs. 0.89 [±0.05], $p = 0.014$ and $p^* = 0.027$). Additionally, in multivariate analysis, no significant differences were observed in the percentage of rest per 24 h, indicating no significant differences in the percentage of the sleep period within a 24-h period, between the two groups (46.62 [±9.13] vs. 41.61 [±6.88], $p^* = 0.069$). No significant differences were observed in other RAR actigraphy variables between the groups.

4 | DISCUSSION

Our study provides compelling evidence supporting actigraphy as a potent tool for objectively characterizing psychomotor activity in individuals with depression and distinguishing between psychomotor agitation and retardation. These clinical dimensions are challenging to capture clinically because they are multidimensional encompassing both mental and motor aspects and may fluctuate over time. Actigraphy emerges as an objective tool to measure the characteristics of the active and rest periods, free from the confounding effects of sleep disturbances, in patients meeting DSM-5 diagnostic criteria for psychomotor agitation or retardation. Specifically, actigraphy detects psychomotor agitation through increased activity levels over a 24-h period, while psychomotor retardation is characterized by decreased activity during the most active 10 h, along with irregularities in intra- and inter-day rhythms. Notably, it does so without identifying differences in sleep disturbances between patients exhibiting psychomotor agitation and those displaying

TABLE 1 Sociodemographic and clinical characteristics of patients with major depressive episode (MDE) and psychomotor retardation (PMR) or agitation (PMA).

	Groups mean (SD) or *n* (%)		Comparison PMR versus PMA	
Variables	**PMR (*n* = 58; 78.4%)**	**PMA (*n* = 16; 21.6%)**	**Chi-square test, *t*-Student, Mann–Whitney *U***	***p***
Age (years)	41.13 (±13.8)	34.4 (±11.6)	330.5	0.28
BMI (kg/m^2)	25.5 (±8.5)	25.2 (±7.5)	360.0	0.27
Gender				
Female	9 (56.3%)	41 (29.3%)	1.19	0.27
Male	7 (43.8%)	17 (70.7%)		
Subtype				
Unipolar	14 (87.5%)	39 (67.2%)	2.53	0.11
Bipolar	2 (12.5%)	19 (32.8%)		
Age of onset (years)	25.2 (±12.1)	26.2 (±14.4)	384	0.91
Number of depressive episodes	2.8 (±2.38)	4.4 (±5.7)	331	0.54
Number of (hypo)manias	0.85 (±4.24)	0.13 (±0.51)	394	0.63
Number of manias	0.65 (±4.042)	0.00 (±0.00)	384	0.14
Number of hospitalizations	2.13 (±4.53)	1.06 (±0.99)	405	0.63
Antidepressants			1.71	0.19
Yes	44 (78.6%)	10 (62.5%)		
No	12 (21.4%)	6 (37.5%)		
Hypnotics			0.004	0.95
Yes	25 (55.4%)	7 (43.8%)		
No	31 (44.6%)	9 (56.3%)		
Anxiolytics			2.0	0.16
Yes	25 (44.6%)	4 (25%)		
No	31 (55.4%)	12 (75%)		
Mood stabilizers			3.33	0.068
Yes	25 (43.9%)	3 (18.8%)		
No	32 (56.1%)	13 (18.3%)		
Antipsychotics			0.983	0.322
Yes	3 (94.6%)	2 (12.5%)		
No	53 (5.4%)	14 (87.5%)		
MADRS score	25.42 (±7.95)	24.81 (±7.49)	−0.27	0.79
YMRS score	1.44 (1.37)	1.30 (1.61)	381.5	0.527
HAD-total	22.12 (±6.75)	22.75 (±6.81)	0.33	0.75
GAD-7	13,875 (±5.13)	12.3 (±4.61)	1619	0.45
Current tobacco smoking				
Yes	17 (29.8%)	0 (0%)	6.22	**0.013**
No	40 (70.2%)	16 (100%)		
Current coffee use			3.09	0.079
Yes	38 (67.9%)	7 (43.8%)		
No	18 (32.1%)	9 (56.3%)		
Current tea use			0.29	0.59
Yes	20 (36.4%)	7 (43.8%)		
No	35 (63.6%)	9 (56.3%)		

TABLE 1 (Continued)

Variables	Groups mean (SD) or *n* (%)		Comparison PMR versus PMA	
	PMR (*n* = 58; 78.4%)	PMA (*n* = 16; 21.6%)	Chi-square test, *t*-Student, Mann–Whitney *U*	*p*
Current alcohol use disorder			5.76	**0.016**
Yes	3 (5.2%)	4 (25%)		
No	55 (94.8%)	12 (75%)		
Current cannabis use disorder			0.246	0.62
Yes	6 (10.3%)	1 (6.3%)		
No	52 (89.7%)	15 (93.8%)		
Current stimulant use disorder			2.01	0.15
Yes	2 (3.4%)	2 (12.5%)		
No	56 (96.6%)	14 (87.5%)		
Current opiate use disorder			3.74	0.053
Yes	1 (1.7%)	2 (12.5%)		
No	57 (98.3%)	14 (87.5%)		

Note: Bold values indicate a statistically significant difference with a *p*-value less than 0.05.
Abbreviations: GAD-7, generalized anxiety disorder-7; HAD-A/D, hospital anxiety and depression scale-anxiety/depression; Hx, history; MADRS, Montgomery-Asberg Depression Rating Scale.

TABLE 2 Comparison of patients with major depressive episode (MDE) and psychomotor retardation (PMR) or agitation (PMA) regarding subjective sleep and circadian rhythm markers.

Variables	Groups mean (SD) or *n* (%)		Comparison PMR versus PMA	
	PMR (*n* = 58; 78.4%)	PMA (*n* = 16; 21.6%)	Chi-square test, *t*-Student, Mann–Whitney U	*p*
Insomnia severity (ISI total score)	17.93 (±6.66)	18.25 (±3.066)	0.184	0.85
Sleep quality (PSQI total score)	12.38 (±4.40)	12.63 (±3.89)	0.202	0.84
Excessive daytime sleepiness (ESS)	8.87 (±6.2)	10.75 (±3.9)	318.5	0.16
Hypersomnia severity (HSI total score)	17.65 (±6.42)	17.92 (±5.25)	284.5	0.79
Nightmare severity index (NSI)	8.12 (±6.4)	11.67 (±7.7)	185	0.13
Morningness–Eveningness Questionnaire (MEQ)	46.53 (±13.024)	45.63 (±10.67)	−0.25	0.8

Abbreviations: ESS, Epworth Sleepiness Scale; H&O, Horne and Östberg Questionnaire; HSI, Hypersomnia Severity Index; ISI, Insomnia Severity Index; PSQI, Pittsburg Sleep Quality Index; NSI, Nightmare Severity Index; MEQ, Morningness–Eveningness Questionnaire.

psychomotor retardation, as confirmed by the absence of variation in reported sleep complaints measured by scales.

RARS are the most commonly used metrics to measure the characteristics of the active and rest periods, as well as how these periods, occurred throughout the day or night. Moreover, RARs capture unique phenomena only assessable over 24-h intervals, such as the stability of activity patterns across days and the duration of the active period relative to the resting period.

Our study demonstrates that RARs measures provide a comprehensive and objective assessment of depression's behavioral manifestations. These manifestations otherwise are challenging to assess and also lack distinction in the DSM-5. PMR, characterized by a diminished and less consistently patterned activity level, is a pivotal aspect. RARs can serve as a tool for monitoring individual patients, offering additional insights to assist clinicians in tailoring behavioral treatments to specific patients. Actigraphy markers enable the identification of two distinct major clinical therapeutic targets, facilitating the development of therapeutic strategies while considering the subtype of bipolar or unipolar mood disorder to guide treatment selection.

TABLE 3 Comparison of patients with major depressive episode (MDE) and psychomotor retardation (PMR) or agitation (PMA) regarding objective sleep and circadian rhythm markers assessed with actigraphy.

	Groups mean (SD) or *n* (%)		Comparison PMR versus PMA	
Variables	**PMR (*n* = 58; 78.4%)**	**PMA (*n* = 16; 21.6%)**	***t*-Student, Mann–Whitney *U***	***p***
L5 onset (hh:mm:ss)	03:03:00 (±04:34:31)	05:52:30 (±08:38:24)	387	0.39
L5 average	1140.55 (±957.22)	808.25 (±470.28)	389	0.33
M10 onset (hh:mm:ss)	10:00:60 (±02:22:13)	10:18:45 (±02:33:36)	436	0.79
M10 average	10463.26 (±4069,59)	15046.75 (±3425.03)	4.12	**<0.001**
Relative amplitude	0.80 (±0.13)	0.89 (±0.05)	277	**0.014**
Rest per 24 h%	46.62 (±9.13)	41.61 (±6.88)	−2.03	**0.045**
Fragmentation index	33.012 (±13.18)	28.54 (±7.26)	−1.3	0.19
Interdaily stability	0.36 (±0.12)	0.48 (±0.09)	3.67	**<0.001**
Intradaily variability	0.91 (±0.17)	0.75 (±0.14)	−2.94	**0.004**
Time in bed	08:43:20 (±01:23:07)	08:57:43 (±01:14:58)	0.63	0.53
Actual sleep time (hh:mm:ss) (TST)	07:03:21 (±01:26:36)	07:20.03 (±00:53:58)	386	0.31
WASO (hh:mm:ss)	01:16:15 (±01:26:24)	01:21:52 (±01:21:18)	−0.003	0.99
Sleep onset latency (mm:ss)	13:13 (±10:30)	10:55 (±14:32)	358	0.166
Sleep efficiency (%)	80.67 (±7.09)	82.20 (±5.53)	0.79	0.42
Actual wake %	16.21 (±6.12)	15.41 (±4.9)	−0.48	0.63
Actual sleep %	84.79 (±6.12)	84.59 (±4.9)	0.73	0.47

Bold values indicate a statistically significant difference with a p-value less than 0.05.
Abbreviations: L5, least five; M10, most ten; TST, total sleep time; WASO, wake after sleep onset.

TABLE 4 Multivariate analysis—Comparison of patients with major depressive episode (MDE) and psychomotor retardation (PMR) or agitation (PMA) regarding objective sleep and circadian rhythm markers assessed with actigraphy.

	Groups mean (SD) or n (%)		Comparison PMR vs PMA	
Variables	**PMR (*n* = 58; 78.4%)**	**PMA (*n* = 16; 21.6%)**	**Z-score**	***p****
M10 average	10463.26 (±4069,59)	15046.75 (±3425.03)	4.12	**0.002**
Relative amplitude	0.80 (±0.13)	0.89 (±0.05)	277	**0.027**
Rest per 24 h%	46.62 (±9.13)	41.61 (±6.88)	−2.03	0.069
Interdaily stability	0.36 (±0.12)	0.48 (±0.09)	3.67	**0.006**
Intradaily variability	0.91 (±0.17)	0.75 (±0.14)	−2.94	**0.012**

Note: Bold values indicate a statistically significant difference with a *p*-value less than 0.05.
**p*-value adjusted for current tobacco smoking and current alcohol use disorder.

Previous studies have provided evidence supporting RARs as markers of depression.[32] Some research suggested that individuals with depression manifested less robust or regularly patterned RARs, while others observed a correlation between depression and low RAR amplitude.[11,32,33] Additionally, prior investigations revealed that participants with higher levels of depressive symptoms tended to show lower interdaily stability and higher intradaily variability.[34] Our study highlighted that the specific characteristics of RARs associated with depression are not uniform and vary based on the behavioral phenotype of depression. Furthermore, contrary to previous studies, our findings indicated that the association between behavioral phenotype and RARs remained independent of depression severity, depression characteristics, the type of mood disorder, and its comorbidities.

This study aims to explore the potential of actigraphy as a tool for digital phenotyping in characterizing symptoms of psychomotor agitation and retardation, which pose clinical challenges, in patients diagnosed with MDE according to DSM-5 criteria. As suggested by our study

and supported by previous research, actigraphy seems to serve as a valuable tool for elucidating the motor activity of patients experiencing psychomotor agitation or retardation, surpassing the scope of simple clinical evaluation as outlined in DSM-5. Unlike subjective scales, actigraphy provides an objective snapshot of patients' activity characteristics over a 14-day period. The next step will involve administering subjective scales to provide further details, particularly regarding ideation with accelerated or slowed cognitive processes. Incorporating data from wearables will contribute to a more comprehensive characterization of the depression phenotype and significantly enhance clinicians' understanding of a patient's condition. Another next step of the digital phenotyping approach will involve using RARs data from actigraphy to identify different types of depression, rather than just comparing actigraphy data between two predefined groups.

Moreover, MDE exhibits a wide array of manifestations, resulting in difficulties in forecasting the trajectory of the illness and in effectively monitoring patients. These results pave the way for exploring longitudinal multimodal approaches and digital strategies, with a specific emphasis on integrating actigraphy into machine learning algorithms that incorporate individual physiological data to discern a distinctive biosignature. Such approaches could assist in better predicting the evolution of individual symptoms using machine learning or other AI techniques.[4] The concept of digital phenotype could encompass a broader range of phenotypic markers than clinicians typically gather, thus enhancing treatment selection and mitigating the influence of cognitive bias on decision-making. This area of research appears to be highly active, with actigraphy potentially contributing to predicting the progression of mood disorders, identifying biosignatures, and evaluating treatment responses.[4]

Our study has some limitations that should be commented. First, we did not administer specific scales of psychomotor agitation or retardation to our patients, such as the Motor Agitation and Retardation Scale (MARS) or the Depressive Retard Rating Scale (DRRS), designed to evaluate motor disturbances in depressed patients.[35,36] It would have been interesting to compare the results with actigraphy outcomes to conclude the validity and reliability of actigraphy in discriminating between PMR and PMA. Even though, the primary aim of actigraphy is to provide additional insights into activity rhythms alongside subjective assessments using digital phenotyping. This holistic approach holds the potential to better characterize the depression phenotype and augment existing clinical decision-making processes in psychiatry. By combining patient self-reports and actigraphy outcomes, these measurements may contribute to a more nuanced characterization of the depression phenotype.

Second, clinicians may find it valuable to examine patterns of a patient's activity and observe how these patterns evolve over multiple visits and treatments. In addition, within our depressed patient population, we did not measure satisfaction or acceptability regarding wearing the watch for 14 days to digital practices. Satisfaction is a challenge for longitudinal monitoring. Third, we investigated whether actigraphy could serve as a device to objectively assess two criteria from the DSM-5 for depression, psychomotor agitation and psychomotor retardation, which are variables encompassing both the psychic and motor spheres. Actigraphy primarily managed to objectify motor behavior, activity level, rest, and rhythm. It will be necessary to separately compare psychic agitation and retardation and motor agitation and retardation, which are likely different dimensions to capture using wearables. While the measurement of psychic agitation using wearables is a concept that requires further exploration and development, it could potentially involve the analysis of various physiological and behavioral parameters. For example, wearable devices equipped with sensors capable of monitoring heart rate variability, skin conductance, or even voice analysis could provide insights into the physiological manifestations of psychic agitation. Additionally, the electroencephalogram (EEG) could also be considered as a potential tool for measuring "psychic agitation" using wearables. Fourthly, we did not conduct a priori power calculations for this study. However, based on the outcome criterion "M10," which reflects the activity level during wake periods with a first-degree risk (alpha) of 5%, and with a total of 74 patients (58 in the PMR group and 16 in the PMA group), we estimated the a posteriori power of the study to be 99%. This outcome is clinically relevant because it is a principal actigraphy marker for characterizing psychomotor activity in individuals with depression and distinguishing between psychomotor agitation and retardation. Thus, it was a suitable criterion to estimate the expected effect between the two groups. The final limitation of our article concerned multiple comparison tests, as many factors were analyzed. Applying a Bonferroni correction to the actigraphy data would have reduced the alpha level to 0.003; however, some criteria, such as M10, remained significantly associated with the outcome. Moreover, variables with an alpha <0.05, such as measures of variability or rhythm amplitude, were clinically relevant for characterizing psychomotor activity in individuals with depression and distinguishing between psychomotor agitation and retardation, despite the risk of statistical errors in hypothesis testing.

To conclude data from actigraphy wearables can aid clinicians in forming a more comprehensive understanding of a patient's psychomotor manifestations. RAR measures provided by actigraphy play a significant role in characterizing the behavioral associated with depression and could be integrated into more multimodal and longitudinal approaches to predict clinical evolutions or treatment responses in patients, thereby aiding clinical practice.

AUTHOR CONTRIBUTIONS

J. Maruani and P. A. Geoffroy: Writing—original draft and making the statistical analyses. All other authors: Conceptualization, Investigation, Methodology, Supervision, Validation, Visualization, Writing—review and editing. All authors contributed to the article and approved the submitted version.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data belongs to the project entitled "Study of biomarkers of sleep and circadian rhythms in psychiatric disorders (Som-Psy)" (principal investigator: PA Geoffroy) conducted at the Department of Psychiatry of Pr Lejoyeux in Bichat Claude Bernard Hospital (AP-HP, GHU, Paris, France) and at INSERM UMR 1141. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

INFORMED CONSENT

Patients were provided with oral information, a written note detailing the study protocol, and each received a no-objection note. The consent given by the participants does not permit the storage of data at an individual level in repositories or journals.

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REFERENCES

1. Fortney JC, Unützer J, Wrenn G, et al. A tipping point for measurement-based care. *Psychiatr Serv*. 2017;68(2):179-188. doi:10.1176/appi.ps.201500439
2. Falvey JE. Science or serendipity? What we know about clinical judgment in mental health. *J Ment Health Couns*. 1992;14:458-470.
3. Geoffroy PA, Gottlieb J. Activity, cognition, and emotion: three dimensional pillars of the natural presentations of mood disorders enriched by the "sleep" fourth dimension (ACES). *Bipolar Disord*. 2020;22(6):631-632. doi:10.1111/bdi.12957
4. Ricka N, Pellegrin G, Fompeyrine DA, Lahutte B, Geoffroy PA. Predictive biosignature of major depressive disorder derived from physiological measurements of outpatients using machine learning. *Sci Rep*. 2023;13(1):6332. doi:10.1038/s41598-023-33359-w
5. Stern E, Micoulaud Franchi JA, Dumas G, et al. How can digital mental health enhance psychiatry? *Neurosci Rev J Bringing Neurobiol Neurol Psychiatry*. 2023;29(6):681-693. doi:10.1177/10738584221098603
6. Fedor S, Lewis R, Pedrelli P, Mischoulon D, Curtiss J, Picard RW. Wearable Technology in Clinical Practice for depressive disorder. *N Engl J Med*. 2023;389(26):2457-2466. doi:10.1056/NEJMra2215898
7. Maruani J, Boiret C, Leseur J, et al. Major depressive episode with insomnia and excessive daytime sleepiness: a more homogeneous and severe subtype of depression. *Psychiatry Res*. 2023;330:115603. doi:10.1016/j.psychres.2023.115603
8. Romier A, Maruani J, Lopez-Castroman J, et al. Objective sleep markers of suicidal behaviors in patients with psychiatric disorders: a systematic review and meta-analysis. *Sleep Med Rev*. 2023;68:101760. doi:10.1016/j.smrv.2023.101760
9. Geoffroy PA, Boudebesse C, Bellivier F, et al. Sleep in remitted bipolar disorder: a naturalistic case-control study using actigraphy. *J Affect Disord*. 2014;158:1-7. doi:10.1016/j.jad.2014.01.012
10. Murray G, Gottlieb J, Hidalgo MP, et al. Measuring circadian function in bipolar disorders: empirical and conceptual review of physiological, actigraphic, and self-report approaches. *Bipolar Disord*. 2020;22(7):693-710. doi:10.1111/bdi.12963
11. Smagula SF, Ancoli-Israel S, Blackwell T, et al. Circadian rest-activity rhythms predict future increases in depressive symptoms among community-dwelling older men. *Am J Geriatr Psychiatry*. 2015;23(5):495-505. doi:10.1016/j.jagp.2014.06.007
12. Smagula SF, Boudreau RM, Stone K, et al. Latent activity rhythm disturbance sub-groups and longitudinal change in depression symptoms among older men. *Chronobiol Int*. 2015;32(10):1427-1437. doi:10.3109/07420528.2015.1102925
13. Smagula SF, Krafty RT, Taylor BJ, Martire LM, Schulz R, Hall MH. Rest-activity rhythm and sleep characteristics associated with depression symptom severity in strained dementia caregivers. *J Sleep Res*. 2017;26(6):718-725. doi:10.1111/jsr.12549
14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. Amer Psychiatric Pub Incorporated; 2013:947.
15. Luik AI, Zuurbier LA, Hofman A, Van Someren EJW, Tiemeier H. Stability and fragmentation of the activity rhythm across the sleep-wake cycle: the importance of age, lifestyle, and mental health. *Chronobiol Int*. 2013;30(10):1223-1230. doi:10.3109/07420528.2013.813528
16. Geoffroy PA, Bellivier F, Scott J, et al. Bipolar disorder with seasonal pattern: clinical characteristics and gender influences. *Chronobiol Int*. 2013;30(9):1101-1107. doi:10.3109/07420528.2013.800091
17. Blum L. *Montgomery Asberg Depression Rating Scale (MADRS)*. Strokengine; 2023 Accessed July 6, 2023. https://strokengine.

ca/en/assessments/montgomery-asberg-depression-rating-scale-madrs/
18. Barczak P, Kane N, Andrews S, Congdon AM, Clay JC, Betts T. Patterns of psychiatric morbidity in a genito-urinary clinic. A validation of the hospital anxiety depression scale (HAD). *Br J Psychiatry*. 1988;152:698-700. doi:10.1192/bjp.152.5.698
19. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. doi:10.1001/archinte.166.10.1092
20. Bastien CH, Vallières A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med*. 2001;2(4):297-307. doi:10.1016/s1389-9457(00)00065-4
21. Ait-Aoudia M, Levy PP, Bui E, et al. Validation of the French version of the Pittsburgh sleep quality index addendum for posttraumatic stress disorder. *Eur J Psychotraumatol*. 2013;4:19298. doi: 10.3402/ejpt.v4i0.19298
22. Kaplan KA, Plante DT, Cook JD, Harvey AG. Development and validation of the hypersomnia severity index (HSI): a measure to assess hypersomnia severity and impairment in psychiatric disorders. *Psychiatry Res*. 2019;281:112547. doi:10.1016/j.psychres.2019.112547
23. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14(6):540-545. doi:10.1093/sleep/14.6.540
24. Geoffroy PA, Stern E, Maruani J, et al. The nightmare severity index (NSI): a short new multidimensional tool for assessing nightmares. *J Sleep Res*. 2023;33:e14065. doi:10.1111/jsr.14065
25. Taillard J, Philip P, Chastang JF, Bioulac B. Validation of Horne and Ostberg morningness-eveningness questionnaire in a middle-aged population of French workers. *J Biol Rhythm*. 2004;19(1):76-86. doi:10.1177/0748730403259849
26. Smith MT, McCrae CS, Cheung J, et al. Use of Actigraphy for the evaluation of sleep disorders and circadian rhythm sleep-wake disorders: an American Academy of sleep medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med*. 2018;14(7):1209-1230. doi:10.5664/jcsm.7228
27. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*. 2003;26(3):342-392. doi:10.1093/sleep/26.3.342
28. Martoni M, Bayon V, Elbaz M, Léger D. Using actigraphy versus polysomnography in the clinical assessment of chronic insomnia (retrospective analysis of 27 patients). *Presse Med*. 2012;41(3 Pt 1):e95-e100. doi:10.1016/j.lpm.2011.07.019
29. Geoffroy PA, Scott J, Boudebesse C, et al. Sleep in patients with remitted bipolar disorders: a meta-analysis of actigraphy studies. *Acta Psychiatr Scand*. 2015;131(2):89-99. doi:10.1111/acps.12367
30. Wescott DL, Franzen PL, Hasler BP, et al. Elusive hypersomnolence in seasonal affective disorder: actigraphic and self-reported sleep in and out of depressive episodes. *Psychol Med*. 2023;53(4):1313-1322. doi:10.1017/S003329172100283X
31. Wescott DL, Wallace ML, Hasler BP, et al. Sleep and circadian rhythm profiles in seasonal depression. *J Psychiatr Res*. 2022;156:114-121. doi:10.1016/j.jpsychires.2022.10.019
32. Robillard R, Naismith SL, Smith KL, et al. Sleep-wake cycle in young and older persons with a lifetime history of mood disorders. *PLoS One*. 2014;9(2):e87763. doi:10.1371/journal.pone.0087763
33. Maglione JE, Ancoli-Israel S, Peters KW, et al. Depressive symptoms and circadian activity rhythm disturbances in community-dwelling older women. *Am J Geriatr Psychiatry*. 2014;22(4):349-361. doi:10.1016/j.jagp.2012.09.003
34. Luik AI, Zuurbier LA, Direk N, Hofman A, Van Someren EJW, Tiemeier H. 24-hour activity rhythm and sleep disturbances in depression and anxiety: a population-based study of middle-aged and older persons. *Depress Anxiety*. 2015;32(9):684-692. doi:10.1002/da.22355
35. Sobin C, Mayer L, Endicott J. The motor agitation and retardation scale: a scale for the assessment of motor abnormalities in depressed patients. *J Neuropsychiatry Clin Neurosci*. 1998;10(1):85-92. doi:10.1176/jnp.10.1.85
36. Pier MPBI, Hulstijn W, Sabbe BGC. No psychomotor slowing in fine motor tasks in dysthymia. *J Affect Disord*. 2004;83(2–3):109-120. doi:10.1016/j.jad.2004.05.002

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