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Peripheral skin temperature differentiates unipolar and bipolar depression

Dear Editor,

We read with interest the recent study by Valenzuela-Pascual et al. reporting an increase in peripheral skin temperature during manic episodes compared to depressive episodes in patients with bipolar disorder (Valenzuela-Pascual et al., 2025). Their results suggest that skin temperature, passively recorded by wearable sensors, could serve as a state-dependent physiological marker of manic versus depressive phases. This aligns with recent efforts to identify objective physiological correlates of psychiatric symptoms using unobtrusive, ecological tools. We would like to offer a complementary perspective based on data from the CALYPSO study, in which peripheral skin temperature was used to explore trait-level physiological differences between unipolar and bipolar depression.

CALYPSO (in French, Clinique et Analyses Psychiatriques Objectives) is a multimodal ongoing study designed to identify objective behavioural and physiological markers of depression subtypes, using structured clinical interviews, synchronized video recordings analysed by computer vision, and data collected from wearable sensors. All participants are adults (≥18 years), hospitalized for a major depressive episode, with diagnoses established according to DSM-5 criteria and confirmed through the MINI and the Mood Disorder Questionnaire (MDQ) to assess lifetime manic or hypomanic features. All participants provided written informed consent prior to inclusion in the study. The CALYPSO clinical protocol was reviewed and approved by the appropriate ethics committee (Comité de Protection des Personnes Nord Ouest IV), under reference number 2022-A01160-43, in accordance with the Declaration of Helsinki and relevant national regulations. In the present subsample, we included 31 patients, whom 18 met criteria for unipolar depression and 13 for bipolar depression. All patients were assessed during a current depressive episode, providing a uniform clinical state for between-diagnosis comparisons. Each participant underwent a video-recorded standardized psychiatric interview, during which peripheral skin temperature and other physiological signals (electrodermal activity, heart rate, accelerometry) were recorded using the Empatica E4 wristband. In contrast to Valenzuela-Pascual et al., who compared mood phases within a bipolar sample, our analysis focused on whether inter-individual diagnostic differences could be detected from short-duration clinical assessments during the same mood state (Fig. 1).

Using supervised machine learning models trained on skin temperature, we achieved a classification performance reaching an accuracy of 93.55 %.in distinguishing bipolar from unipolar depression (Ouzar et al., 2025). These results suggest that skin temperature is not only sensitive to mood phase transitions, as shown by Valenzuela-Pascual et al., but may also carry trait-like signals linked to diagnostic subtype, even in the absence of phase variation. We agree with Valenzuela-Pascual et al. that skin temperature likely reflects central autonomic regulation, possibly linked to sympathetic–parasympathetic shifts during mood fluctuations. However, our findings suggest that these thermal dynamics may also reflect constitutional features of mood disorder subtypes, beyond the transient mood state. In particular, the distinctiveness of the bipolar temperature profile during depression may reflect persistent autonomic imbalance, altered peripheral vasomotor control, or dysregulated thermoregulatory set-points involving hypothalamic–brainstem circuits. These mechanisms could result in subthreshold sympathetic overactivation, blunted circadian modulation (Geoffroy and Maruani, 2025), which remain invisible to classical clinical scales but may be captured through wearable sensor data. This diagnostic perspective complements the state-based findings of Valenzuela-Pascual et al., and we believe both approaches—phase comparison and subtype differentiation—are crucial to move toward precision psychiatry. While the former captures intra-individual variation, the latter targets inter-individual diagnosis, and both are necessary for developing stratified interventions.

Beyond its predictive performance, the temperature signal was integrated in CALYPSO into a broader effort to capture layered phenotypes using computational psychiatry approaches. Our study combined behavioural features extracted via computer vision from video interviews with physiological and motor data from wearables, allowing for multimodal modelling of psychiatric subtypes. The inclusion of skin temperature among the most predictive variables for bipolar depression highlights its diagnostic relevance within this layered framework.

Our results also reinforce the notion that wearables, when embedded in structured clinical paradigms, can support decision-making beyond symptom self-report, by revealing latent biological signatures. Importantly, unlike Valenzuela-Pascual et al., these differences emerged from brief, controlled clinical interviews, and not from prolonged ambulatory recordings. This indicates the potential utility of structured sensor-assisted assessments in inpatient settings, where extended ecological monitoring may not be feasible.

We emphasize that CALYPSO is a work in progress: further data collection and validation in larger samples are ongoing. Future analyses will explore whether combining temperature with other signals (e.g., facial emotion, posture, voice, gait) may further improve classification and support longitudinal monitoring. Importantly, the CALYPSO framework is openly designed to bridge clinical psychiatry and real-world data science and may serve as a model for integrating sensor technologies into inpatient care.

This study is part of the ongoing CALYPSO programme, which combines wearable physiological monitoring, computer vision techniques, and multimodal behavioural signal extraction in a naturalistic clinical setting. Participants were rigorously phenotyped using validated tools (DSM-5, MINI, MDQ), allowing for reliable diagnostic stratification. Nonetheless, some limitations must be acknowledged: the influence of ongoing treatments was not controlled, the analysis focused solely on the unstructured segment of the interview, and the sample size

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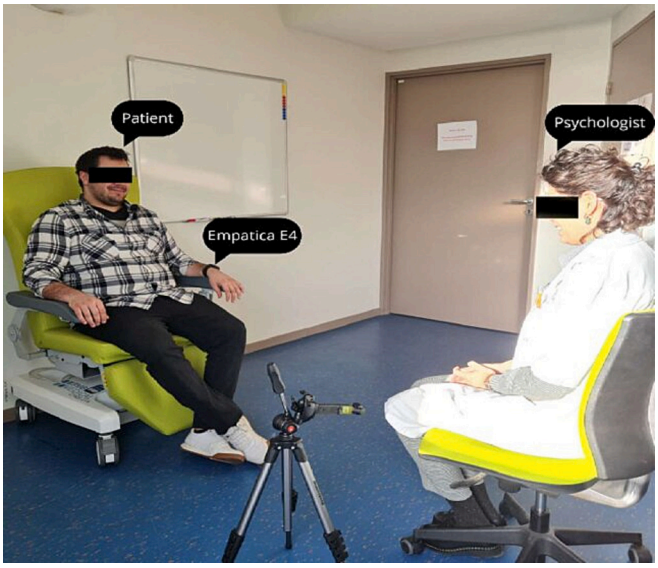

Fig. 1. CALYPSO experimental setup.
Standardized clinical interviews are conducted between a psychologist and a participant, with fixed positions for all equipment and personnel. For illustrative purposes, the role of the patient is played here by an engineer from the CALYPSO team. A tripod-mounted camera records the session, while the Empatica E4 wristband collects physiological signals including skin temperature. All recordings follow a strictly uniform protocol to ensure reproducibility across participants.

remains limited. Future work should aim to replicate these findings in larger and more diverse populations, and to link these objective behavioural features with underlying pathophysiological mechanisms.

In conclusion, while Valenzuela-Pascual et al. convincingly demonstrate that peripheral skin temperature varies across manic and depressive phases in bipolar disorder, our data suggest that temperature may also encode trait-level differences between mood disorder subtypes. These findings highlight the potential of wearable-derived temperature as a bimodal marker, both state- and trait-sensitive, with implications for diagnosis, prognosis, and treatment personalization in mood disorders (McIntyre et al., 2020).

Contributors

All authors participated in the writing and revision of the successive drafts of the manuscript and approved the final version. The study design and conceptual framework were jointly secured by the senior investigators (AA, MD, FD). Data collection was coordinated by the clinical research team (AA, CN). The analyses were conducted by the computer science team (YO, FB, EP, MD).

CRediT authorship contribution statement

Ali Amad: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Funding acquisition, Data curation, Conceptualization. **Yassine Ouzar:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Clémence Nineuil:** Writing – review & editing, Writing – original draft, Project administration, Data curation. **Fouad Boutaleb:** Writing – review & editing, Formal analysis, Data curation. **Emery Pierson:** Writing – review & editing, Formal analysis. **Fabien D'Hondt:** Writing – review & editing, Resources, Funding acquisition. **Mohamed Daoudi:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

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Declaration of competing interest

The authors declare no conflicts of interest related to this work.

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