

## Short Report

# Objective digital phenotypes of worry severity, pain severity and pain chronicity in persons living with HIV

Nicholas C. Jacobson and Conall O’Cleirigh

**Summary**

Persons living with HIV report experiencing disproportionately severe and chronic pain and worry. However, no objective biomarkers of these subjective experiences have been developed. To address the lack of objective measures and assist in treatment planning, this study examined whether digital biomarkers of pain severity, pain chronicity and worry could be developed, using passive wearable sensors that continuously monitor movement. Results suggest that digital biomarkers can predict pain severity ( $r[35] = 0.690$ ), pain chronicity (74.63% accuracy) and worry severity ( $r[65] = 0.642$ ) with high precision, suggesting that objective digital biomarkers alone accurately capture internal symptom experiences in persons living with HIV.

**Declaration of interest**

N.C.J. is the owner of a free application published on the Google Play Store entitled ‘Mood Triggers’. He does not receive any direct or indirect revenue from his ownership of the application (i.e. the application is free, there are no advertisements and the data is only being used for research purposes). C.O. has no conflicts to declare.

**Keywords**

Information technologies; anxiety disorders; aetiology; neuroimmunology; neurophysiology.

**Copyright and usage**

© The Royal College of Psychiatrists 2019.

Persons living with HIV report experiencing disproportionately higher rates of severe and chronic pain,<sup>1</sup> as well as mood and anxiety disorders,<sup>2</sup> both of which are under-identified and often untreated in HIV primary care<sup>3</sup> and are associated with medication non-adherence and poorer quality of life.<sup>1,2</sup> To date, these symptoms have only been monitored by subjective patient reports. Although these symptoms inherently involve a subjective perceptible experience, these subjective experiences might be tied to observable and quantifiable alterations in functioning.<sup>4</sup> The present lack of objectively assessed behaviours is highly problematic given that both pain severity and mood and anxiety disorders are associated with substance-use disorders among people living with HIV.<sup>5</sup> In particular, psychiatric comorbidity may alter pain perceptions among those with HIV and consequently fuel prescriptions of opioids, thereby putting people with HIV at an increased risk of opioid substance-use disorders. In addition to the need for objective measures of these symptoms, subjectively monitoring these symptoms requires substantial time and cost for both patients and their medical providers.<sup>6</sup> Thus, sole reliance on subjective reports of pain severity, pain chronicity and mood and anxiety symptoms has many unintended, adverse consequences.

Based on these problems, there is a need to develop objective biomarkers of these symptoms to augment current self-report assessment procedures, and hopefully reduce unnecessary pharmacotherapy for pain due to inaccurate self-reports (i.e. prescriptions for opioids, among others).<sup>7</sup> Just as importantly, objective biomarkers may facilitate timely, cost-effective solutions to monitor pain and worry severity among people living with HIV. Digital phenotyping, the use of passive sensor data (e.g. from smartwatches, smartphones) collected from daily life to make health inferences, presents a viable solution to these notable problems.<sup>6</sup> No research to date has investigated the use of digital phenotyping to assess pain or anxiety symptoms in persons living with HIV. Specifically, psychomotor and sleep disturbances have previously been found to be related to pain severity and can be continuously monitored by using a wearable sensor.<sup>8</sup> Thus, to address the need for continuous, low-cost and objective measures of pain and anxiety severity, we used passive actigraphy data<sup>9</sup> (measuring psychomotor and sleep patterns based on movement recordings) to

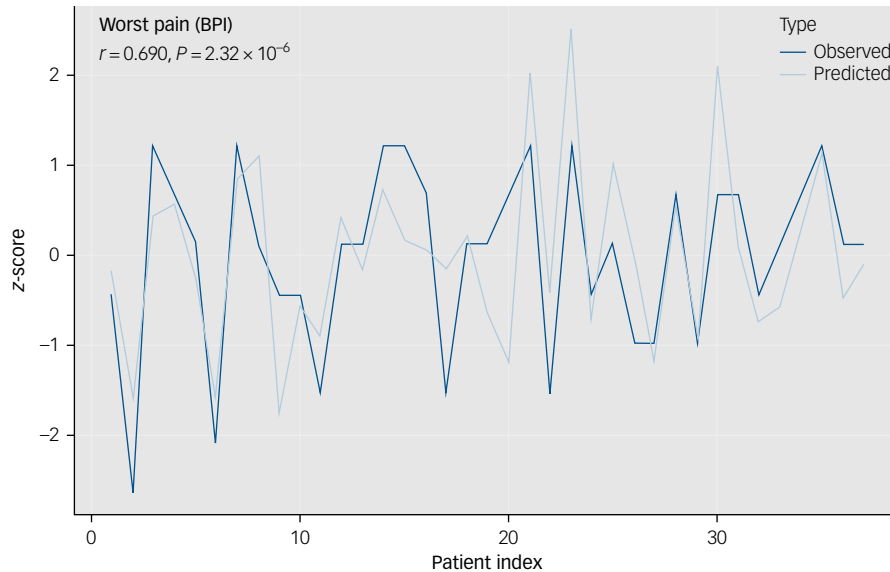
predict pain chronicity, pain severity and worry severity among persons living with HIV. We hypothesised that we could accurately predict these factors by using actigraphy data alone.

**Method****Participants**

A total of 68 patients (70.58% female, 100% Black, Mean<sub>age</sub> = 41.28, s.d.<sub>age</sub> = 8.11, 39.71% unemployed, 19.11% working part time, 41.18% working full time, 54.41% with chronic pain) living with HIV were recruited from Charlotte Maxeke Johannesburg Academic Hospital in South Africa (for more details, see Supplementary Material available at <https://doi.org/10.1192/bjp.2019.168>).<sup>9</sup> All participants had HIV for at least 1 year, but participants had been living with HIV for 7.48 years on average and had been receiving antiretroviral therapy for 5.18 years on average. Regarding the HIV disease severity, 67.64% of the participants had a CD4 (cluster of differentiation 4; a glycoprotein occurring on immune cells) count below 200, suggesting that the participants were likely to experience severe and life-threatening HIV progression.<sup>10</sup> Participants were not eligible for the actigraphy study if they had a physical, neurological or respiratory complaint that impeded their ability to walk, or if they had an infant less than 1 year old as each of these conditions might also alter participants’ natural psychomotor and sleep patterns. Written informed consent was obtained from all patients. The Human Research Ethics Committee (Medical) of the University of the Witwatersrand (clearance no: M140538) approved the following data collection.<sup>9</sup>

**Symptom severity**

Participants completed measures of symptom severity at baseline. To measure chronic pain, participants were asked whether they experienced pain most days over the past 3 months. Those with chronic pain also reported their worst pain severity using the Brief Pain Inventory.<sup>9</sup> This instrument assesses the worst pain severity on an 11-point Likert scale from 0 (‘no pain’) to 10 (‘the



**Fig. 1** This graph depicts the observed and predicted z-scores of patients’ worst pain.

BPI, Brief Pain Inventory.

worst pain you can imagine’). Worry symptom severity was assessed by asking how much participants worried about: (a) health, (b) money, (c) availability of food, (d) pain, (e) their family, and (f) fatigue on a 5-point Likert scale from ‘not at all’ to ‘nearly all the time’.<sup>9</sup> These items were summed to create a dimensional measure of worry severity. All symptom severity data was used for analysis.

### Actigraphy

One week of patient actigraphy data was collected in 1 min epochs, measuring the frequency and intensity of movement during day- and night-times.<sup>9</sup> Actigraphs consist of accelerometers which record acceleration (and are designed to measure movement patterns of the individual). See Supplementary Material for more details.

### Analyses

Digital biomarkers were created from the actigraphy data, using idiographic results from the Differential Time-Varying Effect Model (which measured lagged autoregressive relationships overall, as well as during day- and night-times), spectral analysis (which measured oscillation patterns overall, as well as during day- and night-times) and the distributions of the movements (i.e. mean, median, mode, skewness, kurtosis and quantiles of movement intensity overall, as well as during day- and night-times).<sup>4,11</sup> Psychomotor patterns are thought to reflect movements predominantly during daytime periods or patterns consistent across both day- and night-time, whereas sleep patterns were thought to be measured specifically to night-time periods. Biomarkers were not tied to the specific study protocol (i.e. not related to the study day, day of the week or day of the year), increasing the likelihood that these measurements would be more broadly generalisable. Extreme gradient boosting (a machine learning method) with an ensemble approach was used to analyse the data. Leave-one-out cross-validation was used to control for over-fitting. Primary outcomes were the correlations between predicted and observed worry and pain severity scores, and the kappa agreement between the predicted versus observed chronic pain status.

### Results

The correlation between predicted and observed values was strong for both the worst pain severity ( $r[35] = 0.690$ , 95% CI 0.472–0.828,  $P < 0.001$ ) and worry symptom severity ( $r[65] = 0.642$ , 95% CI 0.476–0.764,  $P < 0.001$ ) (Fig. 1). Predicted and observed pain remained strong when predicted worry severity was controlled ( $r[35] = 0.640$ , 95% CI 0.399–0.798,  $P < 0.001$ ). The kappa agreement of predicted versus observed patients with chronic pain was moderate (kappa 0.485, accuracy 74.63%,  $P < 0.001$ , sensitivity 0.700, specificity 0.784).

### Discussion

These findings demonstrate that objective passive movement data can be used to accurately detect pain symptom severity, pain chronicity and worry severity among persons living with HIV. These results suggest that objective psychomotor and sleep patterns may be used to accurately and objectively detect pain and worry severity and chronicity. These results are particularly notable given that symptom monitoring is important in delivering optimal care to this patient population. As anxiety and mood are centrally important in HIV disease management,<sup>2</sup> these results may have important implications towards pain management and care in this patient population. Nevertheless, the current work has limitations: we were unable to assess symptom changes across time (given the cross-sectional nature of the self-report measures) and we do not know if changes in treatment planning may result if medical providers are provided with this information (i.e. reduce unnecessary increases in opioid dosages and ultimately limit opioid-use disorders among people with HIV).<sup>6</sup> Future work should conduct randomised controlled trials to determine whether using these objective digital biomarkers could effectively direct persons living with HIV to specific psychopharmacological therapies or supportive psychotherapies instead of opioid treatments, compared with more traditional self-report methods alone (i.e. a checklist including symptoms of pain severity, depression, anxiety and substance use). Moreover, remote symptom monitoring based on objective digital biomarkers may support

patient-centred outcomes by facilitating more timely intervention and allowing for more efficient use of HIV and other healthcare services in resource-limited settings.

**Nicholas C. Jacobson** , MS, Clinical Fellow of Psychology, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, USA; **Conall O'Cleirigh**, PhD, Associate Professor of Psychology, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, USA

**Correspondence:** Nicholas C. Jacobson, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Suite 2000, 185 Cambridge Street, Boston, MA 02114, USA. Email: [ncjacobson@mgh.harvard.edu](mailto:ncjacobson@mgh.harvard.edu)

First received 1 Feb 2019, accepted 3 Jun 2019

### Supplementary material

Supplementary material is available online at <https://doi.org/10.1192/bjp.2019.168>.

### Acknowledgements

The current manuscript uses public-use data made available from A. L. Wadley, D. Mitchell and P. R. Kamerman.

### References

- 1 Miaskowski C, Penko JM, Guzman D, Mattson JE, Bangsberg DR, Kushel MB. Occurrence and characteristics of chronic pain in a

community-based cohort of indigent adults living with HIV infection. *J Pain* 2011; **12**: 1004–16.

- 2 Brandt C, Zvolensky MJ, Woods SP, Gonzalez A, Safren SA, O'Cleirigh CM. Anxiety symptoms and disorders among adults living with HIV and AIDS: A critical review and integrative synthesis of the empirical literature. *Clin Psychol Rev* 2017; **51**: 164–84.
- 3 O'Cleirigh C, Magidson JF, Skeer MR, Mayer KH, Safren SA. Prevalence of psychiatric and substance abuse symptomatology among HIV-infected gay and bisexual men in HIV primary care. *Psychosomatics* 2015; **56**: 470–8.
- 4 Jacobson NC, Weingarden H, Wilhelm S. Digital biomarkers of mood disorders and symptom change. *NPJ Digit Med* 2019; **2**: 3.
- 5 Tsao JCI, Soto T. Pain in persons living with HIV and comorbid psychological and substance use disorders. *Clin J Pain* 2009; **25**: 307–12.
- 6 Insel TR. Digital phenotyping: Technology for a new science of behavior. *JAMA* 2017; **318**: 1215–6.
- 7 Cunningham CO. Opioids and HIV infection: From pain management to addiction treatment. *Top Antivir Med* 2018; **25**: 143–6.
- 8 Long AC, Palermo TM, Manees AM. Brief report: Using actigraphy to compare physical activity levels in adolescents with chronic pain and healthy adolescents. *J Pediatr Psychol* 2008; **33**: 660–5.
- 9 Wadley AL, Mitchell D, Kamerman PR. Resilience does not explain the dissociation between chronic pain and physical activity in South Africans living with HIV. *PeerJ* 2016; **4**: e2464.
- 10 Post FA, Wood R, Maartens G. CD4 and total lymphocyte counts as predictors of HIV disease progression. *QJM: Int J Med* 1996; **89**: 505–8.
- 11 Jacobson NC, Chow SM, Newman MG. The Differential Time-Varying Effect Model (DTVEM): A tool for diagnosing and modeling time lags in intensive longitudinal data. *Behav Res Methods* 2019; **51**: 295–315.



## psychiatry in music

### Triskaidekaphobia and Schoenberg: musical expressionism or psychiatric consequence?

Jack Wellington \* and Alexander Wellington\*

When listening to classical music, one must consider the motives, aims and details a composer would have considered when constructing the very melodies and accompaniments we still hear to this day. Take for example *Verklärte Nacht*, a one movement piece dedicated for string sextet composed by Arnold Schoenberg. Schoenberg, the Austrian-born composer who founded the Second Viennese School, was a master of atonality and pioneer of the expressionist movement of 20th-century music. His compositions consisted of the 12-tone row, a static, ordered selection of 12 chromatic notes within an octave accompanied by admissible permutations that derive the harmonic and melodic content of a serial work of music. The significance lies in the number of tones, as Schoenberg was believed to be afflicted with triskaidekaphobia, the irrational fear of and aversion to the number 13. Thus, various opuses of Schoenberg, most famously *Moses und Aron*, had to abide by his inexplicable phobia of the number 13 – the original title of this work was *Moses und Aaron*, which consisted of 13 letters. Again, the last of Schoenberg's creations, entitled *Das Buch der hängenden Gärten*, substituted the 13th poem of his 15-part song cycle for a poem labelled '12a', altering the systematic numeric structure to incorporate his fear of the 'unlucky number 13'. Therefore, was Schoenberg's nonsensical fear of the number 13 in fact responsible for the development of the 12-tone row and, thus, was a psychiatric anxiety disorder the root of musical expressionism? We will never know.

© The Author(s), 2021. Published by Cambridge University Press on behalf of the Royal College of Psychiatrists

The British Journal of Psychiatry (2021)  
218, 167. doi: 10.1192/bjp.2020.221

\* Both authors contributed equally and therefore are considered joint first authors.