

Behavioral biomarkers for depression drug trials: a pilot study with a novel remote digital monitoring platform

Ahnjili Zhuparris^{1,2}, Ghobad Maleki^{1,2}, Liesbeth van Londen⁵, Ingrid Koopmans^{1,2}, Vincent Aalten^{1,2}, Iris E. Yocarini⁴, Wessel Kraaij⁴, Vasileios Exadaktylos¹, Adam Cohen^{1,2}, Pim Gal¹, Robert-Jan Doll¹, Geert Jan Groeneveld^{1,3}, Albert van Hemert², Gabriël Jacobs^{1,3}

¹Centre for Human Drug Research (CHDR), Leiden, The Netherlands

²Department of Psychiatry, Leiden University Medical Centre (LUMC), Leiden, The Netherlands

³Leiden University Medical Centre (LUMC), Leiden, The Netherlands

⁴Leiden Institute of Advanced Computer Science (LIACS), Leiden, Netherlands

⁵Transparant Centre for Mental Health Care, Leiden, the Netherlands

Introduction

The development of novel antidepressant drugs is hampered by the reliance on in-clinic, interview-based assessments. These reflect periodic, subjective outcomes in contrast to objective assessments in real-time. Drug development for mood disorders is expected to benefit from reliable behavioral biomarkers that quantify drug effects outside the clinic. We used the CHDR Monitoring Remotely Platform (MORE™), to monitor and identify potential digital biomarkers – such as physical activity, social activity, and geolocation-data – for the purpose of future antidepressant drug trials.

Sensor	Feature Category	Features Extracted
Smartphone	Smartphone Use	98% acceleration magnitude
		number of times opening an App(per app category such as social Apps, gaming Apps)
		total duration of App use (per app category such as social Apps, gaming Apps)
Smartphone	Location (GPS/Google places API)	total time spent at a location (per place category, such as home, social locations)
	Social Activity	% of time a voice is present; number of incoming, outgoing and missed calls; number of calls with known and unknown contacts; total and average call duration
Smartwatch	Physical activity	heart rate; steps; exercise duration
	Sleep	total sleep duration; number of times waking up during sleep
Blood Pressure Monitor & Scale	Biometric	blood pressure; weight

Figure 1. Features extracted from the CHDR MORE™ platform. In total 56 features were extracted.

Methods

In this non-interventional pilot study, 30 unipolar depressed outpatients diagnosed with Major Depressive Disorder (MDD) or Persistent Depressive Disorder (PDD), and 29 healthy control subjects were monitored out-of-clinic for 3 weeks. Subjects were tracked with a CHDR MORE™ smartphone app, Withings smartwatch, scale and blood pressure monitor. Fig 1. provides an overview of the features extracted from the MORE platform. A 5-fold cross validated random forest classifier was subsequently used to classify the two populations.

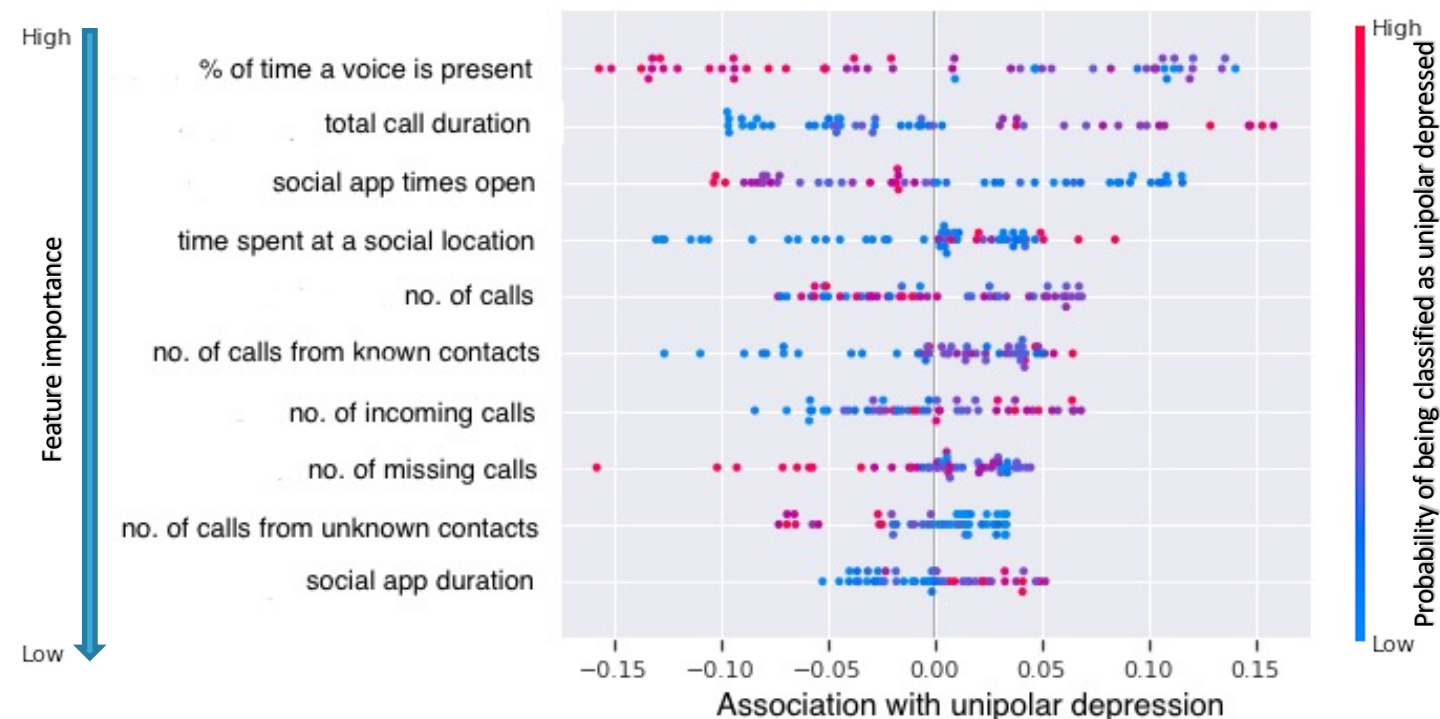


Figure 2. SHAP variable importance plot. The x-axis shows the feature importance, in which the features are ranked in descending order. The y-axis shows the direction of the association between the feature and unipolar depression.

Results

The random forest classifier distinguished depressed patients from healthy volunteers with 69% accuracy, 69% sensitivity and 70% specificity. Fig 2. SHAP (SHapley Additive exPlanations) variable importance plot summarizes the relative contributions of the 10 most predictive features.

Conclusion

A number of digital biomarkers differentiated between unipolar depressed patients and healthy volunteers. Specifically, features related to smartphone use, social activity and mobility performed best in the model. These findings supports further validation of home-based behavioral biomarkers in the development of novel interventions for the treatment of depression.

