

Untangling complexity: Identifying early markers of depression

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Major depressive disorder is a mental disorder thought to affect at least 5% of the global population, placing significant burden on healthcare resources worldwide. While depressive episodes may appear gradually over the course of several weeks, they may also occur abruptly, leading to sudden transitions. Predicting the latter could lead to timely interventions that could prevent the episode or mitigate its effects. Here I briefly describe how nonlinear time series analysis (NLTA) has been used to do this in the Transitions in Depression (TRANS-ID) project.

Measurements: In the context of exploring depression dynamics, nonlinear time series analysis (NLTA) can be used to analyze different types of time series such as like ecological momentary assessments (EMA), physical activity measures, and electrocardiogram (ECG) recordings. In the former an individual is asked to report their emotions, behavior etc multiple times a day on a quantitative scale. The latter two are also known to be linked closely to depression. Depression itself is quantitatively measured using a symptom checklist (SCL-90-R depression subscale), which is then confirmed through a clinical diagnosis. In the TRANS-ID project had 56 participants who were tapering their anti-depressant medication and hence at risk for a recurrence of depression. For 4 months they self-reported EMA 5 times a day through a smartphone, physical activity every minute through a wrist worn actigraph (MotionWatch 8) and ECG every morning and evening for 5 minutes through an ECG monitor (Cortrium ECG, sampled 250 Hz). The SCL-90 depression subscale was filled out weekly, along with assessments by clinicians. A little over 50% of participants experienced transitions towards higher depressive symptoms in the assessment period.

EMA and critical slowing down: Since depressive transitions can be sudden, it has been speculated that its onset can be considered as a critical transition to a different dynamical state. In dynamical systems, critical transitions are often preceded by early warning signals (EWS), i.e. an increase in the autocorrelation and variance, leading up to the transition. Such EWS were initially observed in the EMA data of a single individual prior to a transition towards depression. When examining a larger group in the TRANS-ID project, those experiencing depressive episodes had about 3 times more EWS than those who did not. However false positives and negatives were high, limiting immediate clinical utility[1].

Physical activity: Depression is linked to decreased physical activity and disturbed circadian rhythms. In an

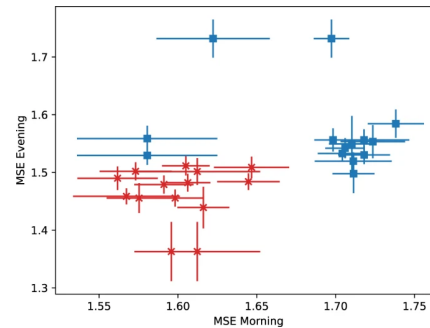


Figure 1: MSE of IBI time series measured in the morning and evening for depressed (red crosses) and non-depressed (blue boxes).

initial study, a sample of physical activities of 21 currently depressed and 25 non-depressed individuals were analysed using recurrence quantification analysis (RQA). Metrics derived from these showed a higher relation to depression than conventionally derived metrics from actigraphy[2]. In the TRANS-ID sample, physical activity data in the 4 weeks prior to a depressive transition were studied using RQA. Various RQA metrics showed accuracies between .5 to .62, again indicating predictions above chance, but of limited immediate clinical utility.

Heart rate: The complexity of the heart response reduces when individuals are depressed, but it is not clear whether this is an effect of depression or precedes it. In the TRANS-ID sample 2 metrics of complexity, the multiscale entropy (MSE, see Fig. 1) and Higuchi dimension (HD), were estimated from inter R peak intervals (IBI) which were extracted from ECG data. A logistic regression model could correctly identify individuals who experienced transitions in 67 to 97% cases, from the first 4 weeks of data, before the transitions had occurred[3]. If validated through further research this could be a digital biomarker that could potentially lead to early detection.

References

- [1] Smit, A., et al. *Critical slowing down in momentary affect as early warning signal of impending transitions in depression*, Psyarxiv (2022): osf.io/lu6vdlg
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