Research outputs:

**Differences in mood instability in patients with bipolar disorder type I and II: a smartphone-based study**

Background: Mood instability in bipolar disorder is associated with a risk of relapse. This study investigated differences in mood instability between patients with bipolar disorder type I and type II, which previously has been sparingly investigated.

Methods: Patients with bipolar disorder type I (n = 53) and type II (n = 31) used a daily smartphone-based self-monitoring system for 9 months. Data in the present reflect 15,975 observations of daily collected smartphone-based data on patient-evaluated mood.

Results: In models adjusted for age, gender, illness duration and psychopharmacological treatment, patients with bipolar disorder type II experienced more mood instability during depression compared with patients with bipolar disorder type I (B: 0.27, 95% CI 0.007; 0.53, p = 0.044), but lower intensity of manic symptoms. Patients with bipolar disorder type II did not experience lower mean mood or higher intensity of depressive symptoms compared with patients with bipolar disorder type I.

Conclusions: Compared to bipolar disorder type I, patients with bipolar disorder type II had higher mood instability for depression. Clinically it is of importance to identify these inter-episodic symptoms. Future studies investigating the effect of treatment on mood instability measures are warranted. Trial registration NCT02221336.

**Objective smartphone data as a potential diagnostic marker of bipolar disorder**

Currently, the diagnosis in bipolar disorder relies on patient information and careful clinical evaluations and judgements with a lack of objective tests. Core clinical features of bipolar disorder include changes in behaviour. We aimed to investigate objective smartphone data reflecting behavioural activities to classify patients with bipolar disorder compared with healthy individuals. Objective smartphone data were automatically collected from 29 patients with bipolar disorder and 37 healthy individuals. Repeated measurements of objective smartphone data were performed during different affective states in patients with bipolar disorder over 12 weeks and compared with healthy individuals. Overall, the sensitivity of...
objective smartphone data in patients with bipolar disorder versus healthy individuals was 0.92, specificity 0.39, positive predictive value 0.88 and negative predictive value 0.52. In euthymic patients versus healthy individuals, the sensitivity was 0.90, specificity 0.56, positive predictive value 0.85 and negative predictive value 0.67. In mixed models, automatically generated objective smartphone data (the number of text messages/day, the duration of phone calls/day) were increased in patients with bipolar disorder (during euthymia, depressive and manic or mixed states, and overall) compared with healthy individuals. The amount of time the smartphone screen was 'on' per day was decreased in patients with bipolar disorder (during euthymia, depressive state and overall) compared with healthy individuals. Objective smartphone data may represent a potential diagnostic behavioural marker in bipolar disorder and may be a candidate supplementary method to the diagnostic process in the future. Further studies including larger samples, first-degree relatives and patients with other psychiatric disorders are needed.

Reducing the rate and duration of Re-ADMISsions among patients with unipolar disorder and bipolar disorder using smartphone-based monitoring and treatment - the RADMIS trials: Study protocol for two randomized controlled trials
Background: Unipolar and bipolar disorder combined account for nearly half of all morbidity and mortality due to mental and substance use disorders, and burden society with the highest health care costs of all psychiatric and neurological disorders. Among these, costs due to psychiatric hospitalization are a major burden. Smartphones comprise an innovative and unique platform for the monitoring and treatment of depression and mania. No prior trial has investigated whether the use of a smartphone-based system can prevent re-admission among patients discharged from hospital. The present RADMIS trials aim to investigate whether using a smartphone-based monitoring and treatment system, including an integrated clinical feedback loop, reduces the rate and duration of re-admissions more than standard treatment in unipolar disorder and bipolar disorder. Methods: The RADMIS trials use a randomized controlled, single-blind, parallel-group design. Patients with unipolar disorder and patients with bipolar disorder are invited to participate in each trial when discharged from psychiatric hospitals in The Capital Region of Denmark following an affective episode and randomized to either (1) a smartphone-based monitoring system including (a) an integrated feedback loop between patients and clinicians and (b) context-aware cognitive behavioral therapy (CBT) modules (intervention group) or (2) standard treatment (control group) for a 6-month trial period. The trial started in May 2017. The outcomes are (1) number and duration of re-admissions (primary), (2) severity of depressive and manic (only for patients with bipolar disorder) symptoms; psychosocial functioning; number of affective episodes (secondary), and (3) perceived stress, quality of life, self-rated depressive symptoms, self-rated manic symptoms (only for patients with bipolar disorder), recovery, empowerment,
adherence to medication, wellbeing, ruminations, worrying, and satisfaction (tertiary). A total of 400 patients (200 patients with unipolar disorder and 200 patients with bipolar disorder) will be included in the RADMIS trials. Discussion: If the smartphone-based monitoring system proves effective in reducing the rate and duration of readmissions, there will be basis for using a system of this kind in the treatment of unipolar and bipolar disorder in general and on a larger scale.

General information
State: Published
Organisations: Copenhagen Center for Health Technology, Department of Applied Mathematics and Computer Science, Cognitive Systems, Embedded Systems Engineering, University of Copenhagen, IT University of Copenhagen
Contributors: Faurholt-Jepsen, M., Frost, M., Martiny, K., Tuxen, N., Rosenberg, N., Busk, J., Winther, O., Bardram, J. E., Kessing, L. V.
Number of pages: 13
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: Trials
Volume: 18
Issue number: 1
Article number: 277
ISSN (Print): 1745-6215
Ratings:
BFI (2019): BFI-level 1
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.17 SJR 1.291 SNIP 0.819
Web of Science (2017): Impact factor 2.067
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.04 SJR 1.24 SNIP 0.828
Web of Science (2016): Impact factor 1.969
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 2.09 SJR 1.235 SNIP 0.89
Web of Science (2015): Impact factor 1.859
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 1.96 SJR 1.117 SNIP 0.906
Web of Science (2014): Impact factor 1.731
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 2.38 SJR 1.316 SNIP 1.096
Web of Science (2013): Impact factor 2.117
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 2.68 SJR 1.483 SNIP 1.273
Web of Science (2012): Impact factor 2.206
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 2.64 SJR 1.178 SNIP 1.326
Web of Science (2011): Impact factor 2.496
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.25 SNIP 1.053
Web of Science (2010): Impact factor 2.08
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.088 SNIP 0.988
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.969 SNIP 0.729
Scopus rating (2007): SJR 0.844 SNIP 0.887
Voice analysis as an objective state marker in bipolar disorder

Changes in speech have been suggested as sensitive and valid measures of depression and mania in bipolar disorder. The present study aimed at investigating (1) voice features collected during phone calls as objective markers of affective states in bipolar disorder and (2) if combining voice features with automatically generated objective smartphone data on behavioral activities (for example, number of text messages and phone calls per day) and electronic self-monitored data on illness activity would increase the accuracy as a marker of affective states. Using smartphones, voice features, automatically generated objective smartphone data on behavioral activities and electronic self-monitored data were collected from 28 outpatients with bipolar disorder in naturalistic settings on a daily basis during a period of 12 weeks. Depressive and manic symptoms were assessed using the Hamilton Depression Rating Scale 17-Item and the Young Mania Rating Scale, respectively, by a researcher blinded to smartphone data. Data were analyzed using random forest algorithms. Affective states were classified using voice features extracted during everyday life phone calls. Voice features were found to be more accurate, sensitive and specific in the classification of manic or mixed states with an area under the curve (AUC)=0.89 compared with an AUC=0.78 for the classification of depressive states. Combining voice features with automatically generated objective smartphone data on behavioral activities and electronic self-monitored data increased the accuracy, sensitivity and specificity of classification of affective states slightly. Voice features collected in naturalistic settings using smartphones may be used as objective state markers in patients with bipolar disorder.
Scopus rating (2014): CiteScore 5.74 SJR 3.189 SNIP 1.31
Web of Science (2014): Impact factor 5.62
Scopus rating (2013): CiteScore 4.54 SJR 2.206 SNIP 1.18
Web of Science (2013): Impact factor 4.36
Scopus rating (2012): CiteScore 1.95 SJR 0.718 SNIP 0.479
Original language: English
Electronic versions:
Voice_analysis_as_an_objective_state_marker_in_bipolar_disorder.pdf
DOI:
10.1038/tp.2016.123

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Source: FindIt
Source-ID: 2306668297
Research output: Research - peer-review › Journal article – Annual report year: 2016

Projects:

Machine learning for smartphone-based monitoring and treatment of unipolar and bipolar disorders
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Forskningsrådsfinansiering
01/03/2016 → 15/06/2019
Award relations: Machine learning for smartphone-based monitoring and treatment of unipolar and bipolar disorders
Project: PhD