The relationship of mood, cognition and physical activity in Depression: Remote symptom monitoring using wearable technology

F Cormack[1,2,7], M McCue[3], C Skirrow[2,4], J Schuster[3*], N Cashdollar[2,5], N Taptiklis[1,2], E Glazer[1,4], E Panagopoulos[1,6], T Van Shaik[1,6], B Fehnert[1,6], J King[1,6], JH Barnett[1,2,7]

[1]Cognition Kit, Cambridge, UK, [2]Cambridge Cognition, Cambridge, UK, [3]Takeda Pharmaceuticals USA, Deerfield, IL, [4]University of Bristol, Department of Psychological Science,[5]Cambridge Cognition, Cambridge MA, USA, [6]CTRL Group, London, UK, [7]University of Cambridge Department of Psychiatry, Cambridge, UK

Background

- Cognitive symptoms are often under-recognised in depression, but can severely impact patients' clinical symptoms, quality of life and risk of relapse.
- Fluctuations of cognitive ability and depressive symptoms are interrelated processes requiring a higher fidelity and frequency of measurement.
- Here we demonstrate the feasibility of remotely collecting cognitive data in individuals suffering from Major Depressive Disorder, as well as the relationship of these high-frequency cognitive assessments with the remote monitoring of depressive symptoms and physical activity.

Aims

1. Demonstrate the feasibility of remotely collecting cognitive data using an Apple Watch in individuals suffering from Major Depressive Disorder
2. Characterise the relationships of high-frequency cognitive assessments with the remote monitoring of depressive symptoms and physical activity.

Methods

Participants

Thirty adults (19 female) with mild-to-moderate Major Depressive Disorder and currently prescribed antidepressant monotherapy.

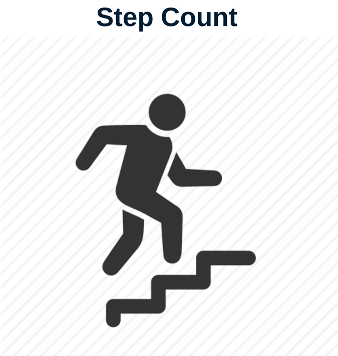
Participant demographic characteristics at baseline

	Mean	SD	Min	Max
Age	37.2	10.4	19	63
Depression symptoms severity (PHQ-9)	9.1	3.1	5	15
Time on medication (months)	9.9	9.5	0.4	94.3
Medication Type		**N**	**(%)**	
Serotonin antagonist and reuptake inhibitor		1/30	3.3%	
Serotonin and norepinephrine reuptake inhibitor		5/30	16.7%	
Selective serotonin reuptake inhibitor		20/30	66.7%	
Tricyclic antidepressants		4/30	13.3%	

Assessments

Mood (PHQ-2)

Step Count



Daily assessments for 6 weeks
Deployed via Apple Watch
- 3x daily N-back brief cognitive assessment (2-Back / ~30sec).
- 1x daily brief self reported mood.
- Daily total step count extracted.

Full-length assessments (weeks 1, 3 and 6)
- CANTAB working memory (SWM) and attention (RVP) tests.
- Depression symptom severity Patient Health Questionnaire (PHQ-9) self-report scale.

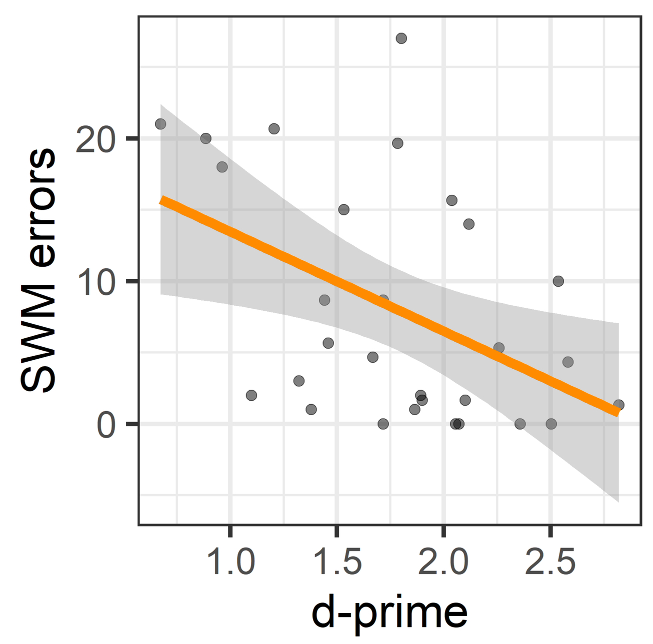
Analysis

- Bivariate (Pearson) correlations between mean full-length and daily assessments.
- Longitudinal mixed effects models: Fixed effect of time, random effect of participant with random intercept and random slope. Linear, quadratic and cubic time-effects compared. Diurnal and weekday effects examined in each best fitting model. Response variables:
  - Mean n-back score (d-prime) for each daily testing session, daily mood (average of 3 daily self-report items), and total daily step count
- Non-linear model: $Y = a - (b/X)$; yielding a = asymptote, b=slope, for Y=baseline adjusted d-prime, X=test session. 90% learning at: X=10*b/a [1]
- Fluctuations are defined as random effects residuals of best fitting mixed models.
- Mixed models examine if fluctuations in mood were predicted by fluctuations in d-prime and step count
  - Where significant concurrent variation found, lagged associations examined
  - Analysis repeated after removing data prior to 90% learning level

Results

Validation

- Excellent adherence: days with ≥1 assessment 96% cognition, 94% mood [2].
- Correlations of full-length cognitive tests with mean daily d-prime: SWM errors: R=-0.45, p≤0.01, RVP A': R=.50, p≤0.01 [2]
- Correlations of mean daily self-reported mood score with full-length PHQ-9: R=0.69, p ≤0.01 [2]

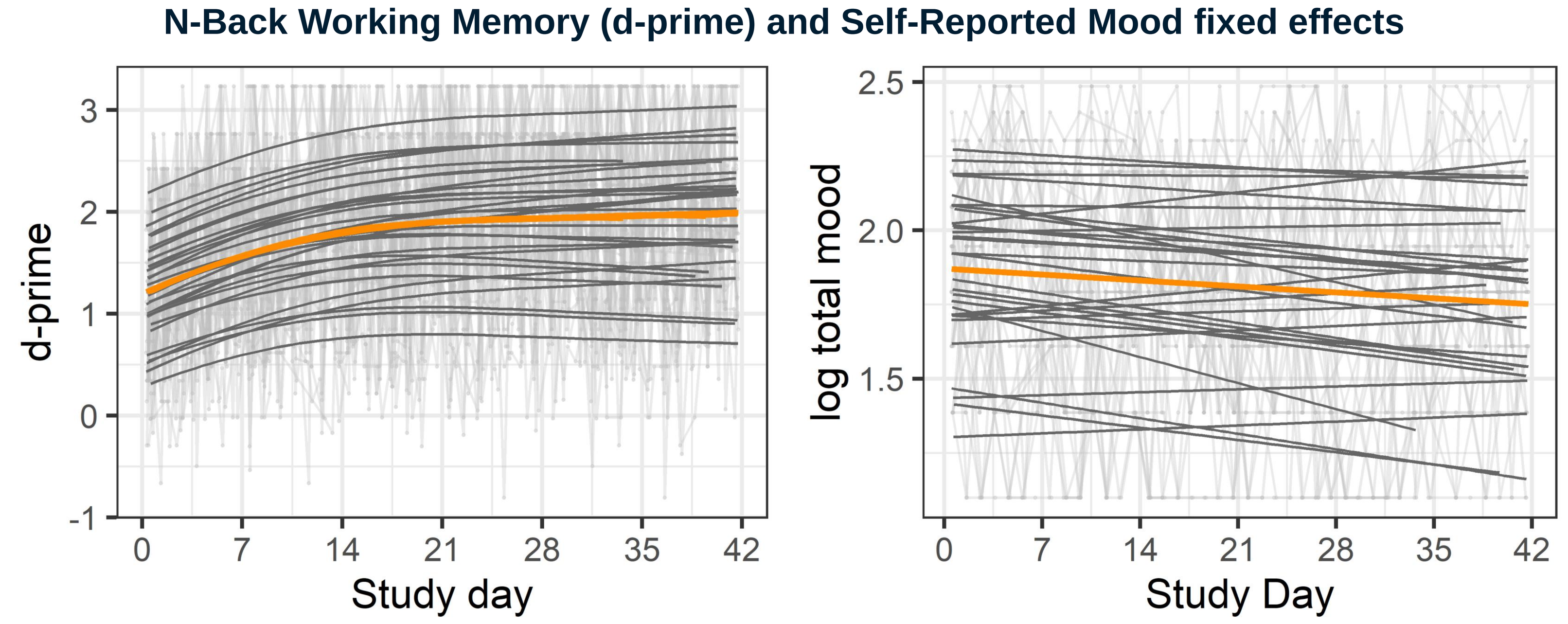


Mean N-Back Performance (d-prime) & Full Length Working Memory assessment

Longitudinal change

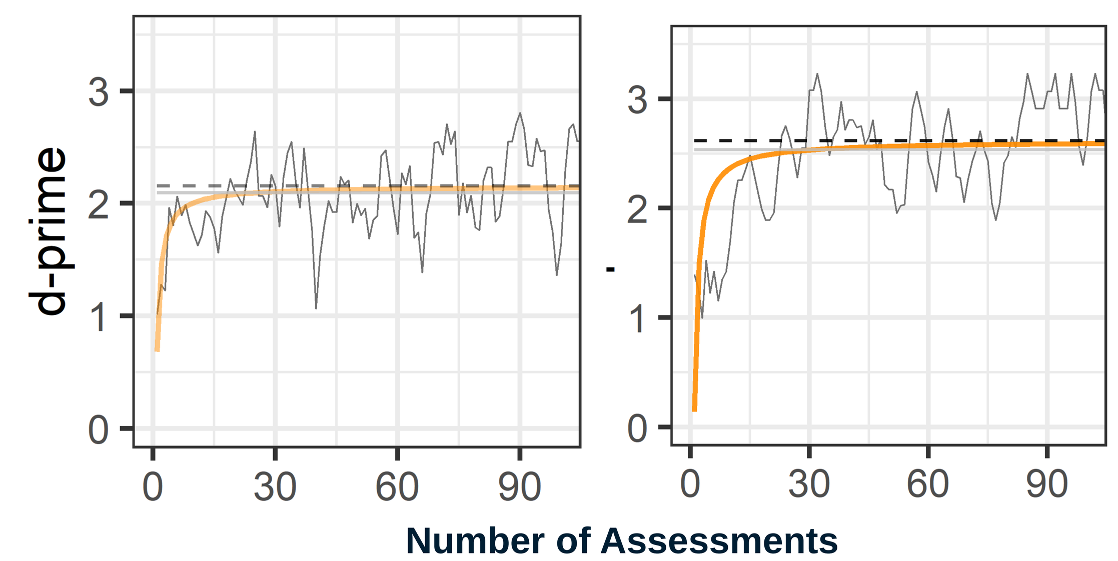
- Cubic change in n-back is best fit (p<0.001) representing a learning period and subsequent plateau.
- Linear change in mood is best fit (p<0.02). Modest improvement during study
- No significant time-trends in step count activity

N-Back Working Memory (d-prime) and Self-Reported Mood fixed effects



Random effect (dark grey), Fixed effect (orange) model fits & individual scores (pale grey)

Nonlinear model of N-Back learning

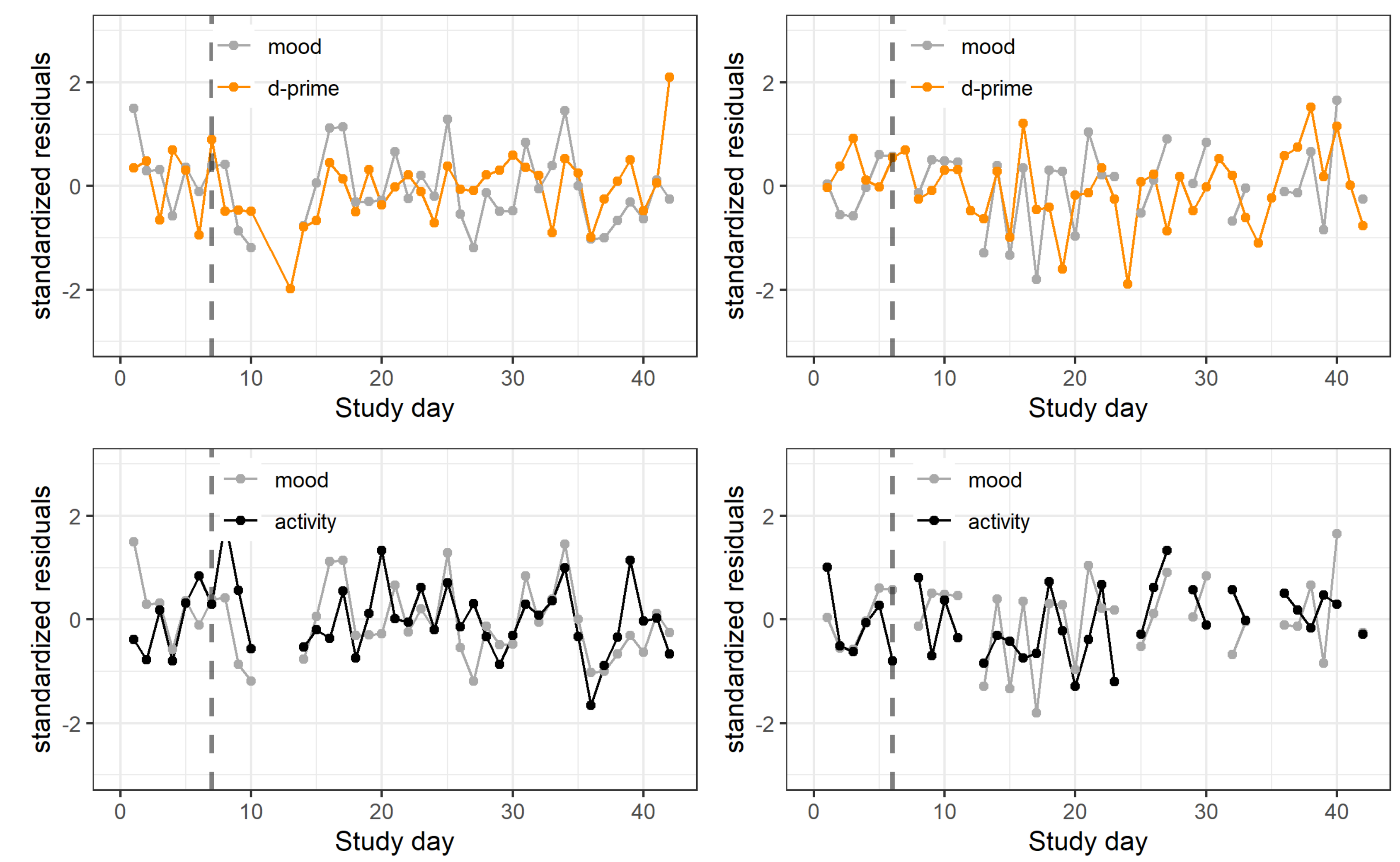


N-Back Learning Curve with performance relative to baseline against aassessment number (3 session moving average). For two participants showing Learning curve (orange), Asymptote (dashed line)

- Non-linear analysis shows good model fit for 28/30 participants.
- 90% learning level reached at mean 10 days (range 6-24).
- Slope and asymptote correlated with mean activity (slope: Rho=0.44 [0.05-0.75], p=0.02; asymptote: Rho=0.45 [0.08-0.68], p=0.02).
- No significant correlations for mood.

Covariation between Mood, Cognition and Activity

- After excluding learning period we observed covariation of Daily Mood & d-prime (p=0.01) and covariation of Daily Mood & Step Count (p=0.0001)
- Lagged analysis showed that increased step count was associated with better mood on the following day(p=0.05)



Model residuals for Mood & N-back and Mood & Activity in two participants, before and after 90% learning (dashed line).

Conclusions

- These data support the feasibility of deploying remote symptom monitoring techniques via wearable technology in psychiatric populations, such as Major Depressive Disorder.
- This work establishes methods for synthesizing high-frequency cognitive data, brief mood and biometric data in order to create sensitive digital profiles of an individuals' clinical symptoms.

References:
[1] Feldman LS, Cao J, Andalib A, Fraser S, Fried GM (2009). A method to characterize the learning curve for performance of a fundamental laparoscopic simulator task: Defining '"learning plateau"' and '"learning rate"'. *Surgery* 146, 381–386.
[2] Cormack, F., McCue, M., Taptiklis, N., Skirrow, C., Glazer, E., Panagopoulos, E., van Schiak, TA., Fehnert, B., King, J., & Barnett, JH. (2019) Wearable Technology for High-Frequency Cognitive and Mood Assessment in Major Depressive Disorder: Longitudinal Observational Study. *JMIR Ment Health*. 6(11), e12814.

Contacts Dr Francesca Cormack **Email:** fc@cognitionkit.com, **Cognition Kit Ltd** Tunbridge Court, Tunbridge Lane, Bottisham, Cambridge, CB25 9TU, UK. FC, CS, NC, NT and JB are employees of Cambridge Cognition. TvS, EG, BF and JK are employees of Ctrl Group. MM is a current employee of Takeda Pharmaceuticals and receives stock options. JS* is a former employee of Takeda Pharmaceuticals. The authors report no conflict of interest for this work.

This work was sponsored and funded by Takeda Pharmaceuticals.

Cog Kit · Takeda · Cambridge Cognition · Ctrl Group · University of Cambridge