
Article:
Marwaha, S., Price, C., Scott, J. et al. (5 more authors) (2018) Affective instability in those with and without mental disorders: A case control study. Journal of Affective Disorders , 241. pp. 492-498. ISSN 0165-0327

https://doi.org/10.1016/j.jad.2018.08.046

Affective instability in those with and without mental disorders: a case control study

[1, 2 *] Steven Marwaha, [3]Charlotte Price, [4]Jan Scott, [5]Scott Weich, [1]Aimee Cairns, [6]Jeremy Dale, [1]Catherine Winsper, [2]Matthew R. Broome

[1]Mental Health and Wellbeing, Division of Health Sciences, University of Warwick CV47AL, UK

[2] Institute for Mental Health, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK

* Corresponding author

[3] Operational Research and Management Sciences Group, Warwick Business School, University of Warwick, CV4 7AL, UK

[4]Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK and IOPPN, Kings College London, UK

[5] Mental Health Research Unit, School of Health and Related Research (ScHARR), University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA, UK

[6] Department of Primary Care, Warwick Medical School, University of Warwick, CV47AL, UK

Word count: 4292

1. Introduction

Affective Instability (AI) is a transdiagnostic symptom (Broome et al., 2015b; Henry et al., 2001b). It has been defined as rapid oscillations of intense affect, with difficulty regulating these or their behavioural consequences (Marwaha, 2013). Multiple strands of evidence have associated AI with suicidal thinking (Palmier-Claus et al., 2012; Yen et al., 2004), health service use (Marwaha et al., 2013c), new onset of depression (Marwaha et al., 2015), psychotic symptoms (Marwaha et al., 2013a), onset of bipolar disorder and increasing time to recovery (Howes et al., 2011; Stange et al., 2016). It is also independently linked to greater medication use and detention under mental health legislation (Patel et al., 2015). It is associated with childhood trauma experiences (including abuse) and it is suggested that it may partly explain the connection between these and psychiatric disorders (Aas et al., 2016; Marwaha et al., 2016; Moffa et al., 2017). The estimated prevalence of AI in the general population is 14%, with levels being higher in younger people and women (Marwaha et al., 2013c; Patel et al., 2015). We (Broome et al., 2015a), and others (Harrison et al., 2017) have suggested that trans-diagnostic investigation of AI is compatible with the NIMH Research Domain Criteria project (Insel, 2014), a framework for understanding mental disorders by study of dysfunction in individual psychological and biological systems.

Through systematically reviewing the literature we have previously identified AI as having three core affect components: intensity, lability, and ability to control the oscillations or their behavioural consequences (Marwaha et al., 2014). The review also identified that comprehensive measurement of all three components is rarely undertaken. The current literature is limited in part by theoretical and methodological heterogeneity in how AI is understood and assessed. This means that studies of AI in different diagnostic groups cannot

be compared, and hence understanding whether AI is similar in different disorders and how it contributes to outcomes such as functioning are hard to ascertain. As such, there is a significant gap in understanding this clinical phenomenon. A second major shortcoming of the current literature is that nearly all studies to date, apart from a few notable exceptions (Ben-Zeev and Young, 2010; Ben-Zeev et al., 2009), have lacked comparisons with individuals without mental disorder. This means it is unclear how far AI represents psychopathology needing intervention or indeed whether it is a core aspect of abnormal mental states, or is a feature of normal mental life.

To our knowledge, only three studies to date have compared AI in different diagnostic groups using the same assessment procedures but limiting assessment of AI to two if its domains. Henry et al. (2001a) examined AI using the Affect Lability Scale (ALS) and Affect Intensity Measure (AIM) in out-patients with Borderline Personality Disorder (BPD) (N=29), bipolar disorder: type II without BPD (N=14), BPD and bipolar disorder: type II (N=12), and no BPD or bipolar disorder but other personality disorders (N=93). Lability scores were significantly ($p< 0.05$) higher in BPD, whilst bipolar patients tended ($p=0.06$) to have higher lability scores than other personality disorders. No differences in affect intensity were observed.

In a similar study those with bipolar disorder had significantly higher scores on the euthymia-elation subscale of the ALS as well as significantly higher scores on affect intensity, whereas those with BPD experienced more shifts between anxiety-depression, euthymia-anger and significantly fewer shifts between euthymia-elation and depression-elation (Reich et al., 2012). Most recently Richard-Lepouriel et al (Richard-Lepouriel et al., 2016) compared ALS and AIM scores in people with bipolar disorder, attention deficit

hyperactivity disorder (ADHD) and controls (dentistry students and doctors). Those with ADHD and bipolar disorder scored higher on ALS than controls, with AIM scores being highest for ADHD. Whilst affective lability appears to be higher in BPD, and people with bipolar disorder, results for affective intensity are discrepant between studies with some evidence that affective intensity may be higher in people with mental disorders than in controls.

Given the paucity of previous research, we aimed to expand the diagnostic groups in which AI is examined (given the suggestion that AI is transdiagnostic), compare these "cases" with psychologically "healthy controls", assess AI more comprehensively, and test whether AI is independently linked to functioning within a clinical population.

2. Aims

We aimed to answer the following research questions:

1. Does affective instability differ between clinical cases and controls and between diagnostic groups?
2. To what extent are measures of affective lability, intensity and ability to control affect correlated in a trans-diagnostic clinical sample?
3. Is affective instability associated with functioning in a clinical population independent of diagnosis?

3. Methods

We undertook a case-control study among users of secondary care mental health services (cases) and primary care attenders without evidence of current mental disorder (controls). Ethical approval was obtained from the Coventry and Warwickshire Ethics Committee, UK.

Participant consent and data collection was completed by an experienced researcher with a psychology background.

3.1 Participants

Individuals with a range of diagnoses were recruited from secondary care mental health services within Coventry and Warwickshire, UK through convenience sampling. The aim was to include individuals who were representative of the 'typical' case mix of these services, so participants were recruited in out-patient departments, day hospitals, community mental health teams and a specialist personality disorder service. Inclusion criteria were: a] aged 18-65 years; b] capacity to give informed consent; c] the primary reason for attending the mental health service was for management of a clinical diagnosis of BPD, bipolar affective disorder, major depressive episode (moderate or severe depressive episode) or non-affective psychosis as reported by a Consultant Psychiatrist. The researcher confirmed the diagnosis with the Psychiatrist using ICD-10 criteria.

Exclusion criteria were: a] an acute illness episode (sufficient to require urgent or inpatient care) according to the patient's Consultant Psychiatrist; b] unable or unwilling to complete the assessments (e.g. individuals with a clinically assessed learning disability, with insufficient command of the English language to understand and complete questionnaires); or c] individuals with a primary ICD-10 diagnosis of dependency to drugs or alcohol (to avoid confounding by drug or alcohol misuse).

Control participants were recruited from primary care (general practitioner surgeries). Physicians asked patients if they were interested, a researcher in the waiting room then consented the patients and completed the battery of questionnaires. Exclusion criteria for the control group were: a] presence of a current mental disorder (including common mental

disorders such as depression or anxiety disorders); b] dependency on substances or alcohol; c] previous diagnosis of BPD, bipolar disorder, or non-affective psychosis, according to their primary care records.

3.2 Materials

Details were collected on participants' diagnosis (for cases) and confirmed by their Consultant Psychiatrist. Details on duration of illness (cases only) and current medications were identified by a researcher, from clinical records. Medications were grouped as anti-psychotic, anti-depressant, anti-anxiety, mood stabiliser, anti-depressant/mood-stabiliser or 'other' (medication not directly related to the patient's psychiatric diagnosis). Sociodemographic information was collected on age (years), gender, marital status (married/cohabiting, single, separated/widowed), employment (employed, unemployed, other), ethnicity (White British, other), and highest education level (None/GCSE, A Level, Degree/higher degree) (see Table 1).

3.3 Assessment scales

Participants were asked to complete four questionnaires relating to affective / mood instability.

1. The Affective Lability Scale - short form (ALS-18) (Harvey et al., 1989), is a reliable and valid measure comprising 18 items coded 0-3. Overall score is obtained by taking the mean of the scores for each item as indicated by the scale developers. Three subscales can be derived; 'anxiety-depression', 'depression-elation', and 'anger'.
2. The Affective Intensity Measure-20 (AIM) (Larsen et al., 1986a) was used to measure affect intensity. The AIM contains 20 items coded 1 to 6. A person's

overall score is obtained by taking the mean of the scores for each item. The AIM has good internal consistency, test-retest reliability and construct validity (Larsen et al., 1986b).

3. The Affective Control Scale (ACS) (Williams et al., 1997) comprises 42 items, coded 1 to 7 (with some items requiring reverse scoring); it has good psychometric properties including construct validity. A higher ACS score indicates reduced ability to control affect. Four subscales can be derived; 'anger', 'positive affect', 'depressed mood', and 'anxiety'.
4. Mood fluctuation rate: Because of the lack of a previously well validated scale for fluctuation rate (Marwaha, 2013) we used a new bespoke schedule for this study. Mood fluctuation rate was assessed using a question from the Structured Clinical Interview for DSM Disorders (SCID). It asks the respondent to state how often they experienced a sudden marked shift in mood. Study participants rated the number of significant mood fluctuations they experienced over a week. Respondents were asked to consider this for each one of the weeks in the last month prior to assessment, and possible responses were 0, 1-3, 4-7, or >7 mood changes over each week.

Functioning was measured using the WHO Disability Assessment Schedule 2.0 – 12 item version (WHODAS; (Üstün, 2010). This contains 12 items each coded 0 to 4. To obtain a person's final score, the simple version entails summing the scores from each of the 12 items, scores range from 0-48. For consistency in comparing with the other scores above, the mean rather than the sum was used in the current study.

181

182 *3.4 Data analysis*

183

184 Descriptive statistics including means/medians with standard deviations/interquartile ranges,
185 or frequencies with percentages where relevant, were used to investigate participant
186 demographics and characteristics of AI in the different diagnostic groups and controls. There
187 are no clear rules about the acceptable fraction of missing data to justify imputation. As such,
188 we decided on 10%, as a level that would allow imputation, thus enabling us to use as much
189 of the data as possible, whilst also retaining reliability and accuracy (Steyerberg, 2008). As
190 such scores were imputed if the patient had less than 10% missing items. This translates as:
191 AIM: Up to 2 missing values, ALS-18: Up to 2 missing values, ACS: Up to 4 missing values,
192 WHODAS: 1 missing value.

193

194 Two sample t-tests were used to compare means between the cases and controls after
195 verifying that relevant assumptions were valid. Proportions were compared using chi-squared
196 tests. General linear models (GLMs) were used to compare the mean lability (ALS), intensity
197 (AIM), and subjective ability to control affect (ACS) outputs across cases (different
198 diagnostic groups) and the control group. Adjustment was made for age, sex and educational
199 level if necessary. Model assumptions were checked and, in the case of an overall significant
200 difference in mean score across the diagnosis groups, pairwise post-hoc comparisons of
201 adjusted mean scores were performed with a Bonferroni correction. To investigate how far
202 the different aspects of affective instability correlate with each other, the linear association
203 between each pair of measurement scales for the full sample and for the cases only was
204 assessed using Pearson's product moment correlation. Association between each
205 measurement scale and the mood fluctuation rate was assessed using Spearman's rank
206 correlation.

Multiple regression was used to examine the association between affective instability and general assessment of functioning as measured by the WHODAS (Üstün, 2010) in clinical cases, adjusting for diagnosis and other patient characteristics. A purposeful selection approach was used to fit the model. Manual backward elimination was first used to remove variables based on Wald statistics using p = 0.05 as the cut-point for removal. Removed variables were then re-entered into the model one-by-one to check their significance. Variables initially considered in the model included: (a) socio-demographics: age, sex, ethnicity, education level, marital status, (employment status was not considered in the model since the WHODAS incorporates this parameter in ratings), (b) illness characteristics: diagnosis, duration of illness, total number of medications, (c) AI measures: mood fluctuation rate and the mean scores for the ACS, ALS-18 and AIM. All analyses were conducted in IBM SPSS Statistics 24.

4. Results

4.1 Participant characteristics

The initial dataset comprised 101 participants, but 9 individuals were excluded due to missing data (3 bipolar, 2 major depression, and 2 controls). Hence the final sample (N=94) comprised of 69 cases and 25 controls.

Table 1 describes the socio-demographic characteristics of included participants by group (case versus control), and diagnostic subgroups (bipolar disorder (n=11), BPD (n=12), psychosis (n=21), and major depression (n=25)). There was a significant difference between cases and controls in mean age (p=0.001), employment status (p=0.001) and marital status (p<0.001). Age was controlled for during regression analysis as AI is influenced by this

(Marwaha et al., 2013b). Duration of illness was recorded in the dataset for 67 out of the 69 cases and was positively skewed with the sample having been ill for a median duration of 36 months (interquartile range (IQR) 15-156 months). Across the diagnostic groups, participants with depression reported the longest duration of illness (median 120 months, IQR 12-258), followed by participants with BPD (median 36 months, IQR 24-120), psychosis (median 27 months, IQR 20.5-111), and bipolar disorder (median 24 months, IQR 9-36), respectively.

Table 1 about here

The commonest class of medication prescribed was anti-depressants, and most patients reported being prescribed one (25%) or two (25%) medications. Seventeen percent of cases (N=12) were not taking any medication. We did not explore, type of medications and their impact on our results because of the lack of a robust typology of the effectiveness of medications indicated for affective instability (Lieb et al., 2010).

4.2 Comparison of questionnaire scores between cases and controls

Differences in the unadjusted mean scores between cases and the controls for all measures are presented in Table 2. Age and sex were found not to be significant across the sample in the general linear model (GLM) for the ACS, AIM, and WHODAS scores; whilst there was trend towards significance for the effect of age on ALS score (P = 0.068).

Table 2 about here

Affect lability (ALS): When adjusted for age, a statistically overall significant difference was observed in mean ALS-18 scores between cases and controls (F (4,88) =

7.195, $p < 0.001$). Post-hoc pairwise comparisons of mean scores revealed significantly lower mean ALS-18 scores for the control group compared to each diagnosis group but no significant differences between diagnoses.

Affect intensity (AIM): There was little difference in the mean AIM scores between groups, with slightly higher mean scores found for controls compared to cases. These differences were not statistically significant ($p = 0.867$).

Ability to control affect (ACS): An overall significant difference was found between mean ACS scores across the different diagnostic groups, including controls (F (4,89) = 14.520, $p < 0.001$). Post-hoc pairwise comparisons of the mean scores revealed significantly higher mean ACS scores (meaning lower control) for each diagnostic group compared to controls ($p < 0.05$). A significant difference was also found between the mean scores in borderline personality disorder patients and patients with non-affective psychosis ($p = 0.010$).

Mood fluctuations in the last week: Table 2 shows the number of participants (i.e. frequency with percentage) who reported each number of mood fluctuations over the past week prior to assessment. This revealed that cases tended to have more changes in their mood state than controls, although no overall differences were found in rate of mood fluctuation between groups ($p=0.310$). Those with major depression reported the greatest number of mood fluctuations in the last week, followed by non-affective psychosis, borderline personality disorder and then bipolar disorder.

4.3 Correlations between different components of AI, mood fluctuation rate and functioning

Correlations are shown in table 3. Strong positive correlations were found between the ALS and the ACS in the full and cases only analysis. Weak to moderate correlations were found between the AIM and the ALS. When assessing the association between each measurement scale and mood fluctuation rate 'last week', moderate to strong positive correlations were found between mood fluctuation and ALS and ACS. There was a weak correlation between AIM and mood fluctuation rate. All correlations were weaker when focusing on the cases only.

Table 3 about here

4.4 AI and functioning

In the clinical sample, an overall significant difference was observed between mean WHODAS scores across the different diagnosis groups, F (4,89) = 11.454, $p < 0.001$ ($p < 0.05$ for bipolar disorder). Post-hoc pairwise comparisons revealed significantly lower mean WHODAS scores for the control group compared to each diagnosis group, as might be expected, but differences between diagnostic groups were not significant.

A multiple regression model investigating factors associated with the WHODAS score, demonstrated that both ALS-18 and ACS scores were significantly associated with current level of functioning. After correcting for multicollinearity, ALS-18 score was retained in the final model (beta=0.845, $p<0.001$), along with the total number of medications (beta=0.107, $p<0.046$). All other variables considered, including diagnosis, were not significantly associated with WHODAS score in the final model.

5. Discussion

5.1 Main findings

This is the first study, to our knowledge, that has comprehensively assessed the core components of affective instability in a trans-diagnostic clinical population and compared clinical cases with a control group without mental disorder. We found only affective lability and affective control is significantly different in people with a range of mental disorders in comparison to those without. No differences were observed between people with and without mental disorder in the intensity of affect experienced or the rate of mood fluctuation in the last week. Two of the three components of affective instability (lability and intensity) did not differ significantly between individuals with different psychiatric diagnoses, although ability to control affect was significantly different in individuals with BPD in comparison to non-affective psychosis. Whilst the small numbers within each diagnostic group mean that interpretation can only be exploratory, contrary to expectation, we found that the greatest number of mood changes in a week was experienced by people with major depression, followed by non-affective psychosis, BPD and then bipolar disorder.

In terms of the affective instability construct, the strongest inter-correlation was found between lability and ability to control affect, with much weaker (modest) correlations between affective intensity and ability to control affect (or lability and control). Finally, only affective lability, but not affective intensity, ability to control affect or mood fluctuation rate was associated within functioning independent of diagnosis and other important confounders.

5.2 Limitations

Our sample size was relatively modest (just under 100). This limited the statistical power of our analyses and increased the risk that our results might be due to type II error. This means that comparisons of affective instability between diagnostic groups in particular,

should be considered entirely exploratory, and other interpretations tentative. Another caveat to comparisons between diagnoses is that we did not complete inter-rater reliability assessments. However, this is the largest study to date exploring our questions.

Our observations related to affective instability are limited to the four mental disorders that we sampled. We cannot therefore generalize our findings to other disorders, where affective instability is known to be important such as OCD (Bowen et al., 2015) or ADHD (Asherson et al., 2007). Furthermore, we could not take into account the contribution made by mental or physical comorbidities in our sample. However, given our sample of cases were those in contact with secondary mental health services there are likely to be high levels of comorbidity. Therefore, it is possible that high levels of affective lability and problems with affective control are linked to comorbidity and this should be the focus of future studies. In our regression modelling we were not able to control for some factors known to impact functioning such as cognition, illness severity, premorbid functioning and depressive symptoms.

The cases sampled were not in an acute illness episode and it is conceivable that this biased estimate of group difference towards the null, that is, there is no difference between the cases and controls on affective instability measures. Affect intensity (and possibly instability) might vary with illness acuity, which might explain why differences between cases and controls in the present study were smaller than those reported in an in-patient sample (Henry et al., 2008; Reich et al., 2012). Whilst we did not assess illness severity, we adjusted for illness duration and number of medications, both of which might be expected to be associated with illness severity. More specifically, we also did not assess current mood state using standardised measures and therefore do not know how far the severity of current

362 mood (e.g depth of depression) could have impacted on our results. There is little current
363 evidence on how far AI changes, as mood becomes lower or more elated to guide how this
364 could have influenced out main findings. Indeed, in bipolar disorder, AI is found in both
365 euthymic and periods of acute illness (Harvey, 2008). We explored whether AI is different
366 between cases and controls. Future studies should also aim to explain the differences between
367 affective instability in people with mental disorders and without.
368
369 We used assessment measures which require recall of affective experiences. These
370 may be prone to bias, particularly when compared to ecological momentary assessments
371 (EMA) (Broome et al., 2015b). How accurately people with mental disorders recall their
372 affective experiences might differ depending on diagnosis. The ratings themselves at an
373 individual level may also be dependent on an initial calibration to understand what is meant
374 by a "marked" shift in mood (Holmes et al., 2016). Therefore, paradoxically individuals with
375 fewer mood fluctuations may better report retrospective fluctuations as they would have
376 stood out in their experience, whilst those with more frequent fluctuations may only report
377 "marked" ones, as small fluctuations were perhaps normalised by their experience. This is
378 one potential explanation of why depressed patients reported more fluctuations than other
379 groups, though this was not statistically significant. The question used to assess mood
380 fluctuation didn't specify type of affect and therefore could have excluded swings in anger
381 and irritability, which have been shown to differentiate between diagnosis (Tsanas et al.,
382 2016). We also recognise that current mood state may have impacted on assessment.
383
384 Whilst momentary assessment of psychopathology appears feasible using
385 smartphones (Tsanas et al., 2016), it is as yet unclear whether retrospective affective
386 assessments and EMA relate to the same underlying psychological or biological processes,

especially as the former will be subject to important cognitive processes (e.g contextual processing), which control how mood is experienced (Dubad et al., 2018). There is also the issue of how far individuals recognize and name affective states in the same way.

5.3 Theoretical and clinical implications

Our findings only partly validated our original definition of affective instability as a trans-diagnostic parameter incorporating affect lability, ability to control and intensity (Marwaha et al., 2014). Affect lability and the ability to control these were indeed found to occur at higher levels than in controls and at similar levels across the different diagnostic groups. Scores on both measures were also relatively strongly correlated with each other re-enforcing the notion that they are facets of the same or similar underlying latent construct. Affective intensity was only relatively weakly associated with other affective instability measures. Replication in a much larger sample is required to understand how far this pattern holds true. In the current study affective intensity was no different between cases and controls or between the cases themselves consistent with previous literature (Henry et al., 2001b). Whilst caution is necessary in interpretation, this does suggest that intensity of affect may not be a feature that may help delineate the boundaries of "normal" or "abnormal" affective experience, or at least in the way that it was measured here. Again, a study with a larger sample size is required.

Mood fluctuation rate (as measured by our bespoke instrument) showed some concurrent validity with two measures of affective instability, and surprisingly, fluctuation rate was no different between cases and controls. This may be a function of our sample size, but this finding should prompt larger studies, with more comprehensive fluctuation change

413 assessments to investigate this area. Crucially, these studies need to include people without
414 mental disorders as controls.
415
416 We used a comprehensive way to measure affective instability in people with
417 different diagnoses and the current results as well as previous research provides some
418 counterbalance to the notion that affective instability is specific to or more severe in people
419 with bipolar disorder or borderline personality disorder. The challenge now is to understand
420 whether more subtle differences exist that may be clinically useful, such as whether a
421 particular valence change is more or less common in different disorders (Reich et al., 2012)
422 or whether richer, digitally captured mood data is helpful in differentiating disorders. Current
423 evidence indicates clinicians do not use diagnostic criteria effectively to distinguish disorders
424 such as BPD and bipolar disorder in which affective instability symptoms are seen to overlap
425 (Saunders et al., 2015). Further research into common and uncommon valence changes in the
426 disorders, perhaps incorporating digital mood monitoring, may help to resolve this clinical
427 difficulty.
428
429 Finally, we demonstrate that affective instability independently adversely impacts
430 functioning in people with mental disorders, and this is independent of diagnosis. The
431 measure of functioning that we used suggests the impact could be on multiple domains
432 including learning new tasks, joining in community activities, day to day work and
433 maintaining friendships. We have previously found that interpersonal conflict is part of the
434 pathway from affective instability and incident depression (Marwaha et al., 2015) and the
435 current study is also consistent with other work highlighting the impact of affective instability
436 on functioning in bipolar and transdiagnostically (Patel et al., 2015; Strejilevich et al., 2013).

We extend these previous findings by identifying that affective lability, as opposed to other aspects of AI such as ability to control affect or intensity, has the greatest impact.

As such affective lability has the potential for being a therapeutic target that could improve functional outcomes in mental disorders. Pharmacological interventions that are widely used (e.g mood stabilising antipsychotics) and emotional regulation training (Berking et al., 2008) need more robust trial evidence, but could have a significant impact on distress and outcomes.

References

1. Aas, M., Henry, C., Bellivier, F., Lajnef, M., Gard, S., Kahn, J.-P., Lagerberg, T., Aminoff, S., Bjella, T., Leboyer, M., 2016. Affective lability mediates the association between childhood trauma and suicide attempts, mixed episodes and co-morbid anxiety disorders in bipolar disorders. Psychological Medicine, 1-11.

2. Asherson, P., Chen, W., Craddock, B., Taylor, E., 2007. Adult attention-deficit hyperactivity disorder: recognition and treatment in general adult psychiatry. The British Journal of Psychiatry 190, 4-5.

3. Ben-Zeev, D., Young, M.A., 2010. Accuracy of hospitalized depressed patients' and healthy controls' retrospective symptom reports: an experience sampling study. The Journal of nervous and mental disease 198, 280-285.

4. Ben-Zeev, D., Young, M.A., Madsen, J.W., 2009. Retrospective recall of affect in clinically depressed individuals and controls. Cognition and Emotion 23, 1021-1040.

5. Berking, M., Wupperman, P., Reichardt, A., Pejic, T., Dippel, A., Znoj, H., 2008. Emotion-regulation skills as a treatment target in psychotherapy. Behaviour research and therapy 46, 1230-1237.

6. Bowen, R., Balbuena, L., Baetz, M., Marwaha, S., 2015. Mood instability in people with obsessive compulsive disorder and obsessive-compulsive personality traits. Journal of Obsessive-Compulsive and Related Disorders 6, 108-113.

7. Broome, M.R., He, Z., Iftikhar, M., Eyden, J., Marwaha, S., 2015a. Neurobiological and behavioural studies of affective instability in clinical populations: a systematic review. Neuroscience & Biobehavioral Reviews 51, 243-254.

8. Broome, M.R., Saunders, K., Harrison, P., Marwaha, S., 2015b. Mood instability: significance, definition and measurement. The British Journal of Psychiatry 207, 283-285.

9. Dubad, M., Winsper, C., Meyer, C., Livanou, M., Marwaha, S., 2018. A systematic review of the psychometric properties, usability and clinical impacts of mobile mood-monitoring applications in young people. Psychological medicine 48, 208-228.

10. Harrison, P.J., Geddes, J.R., Tunbridge, E.M., 2017. The Emerging Neurobiology of Bipolar Disorder. Trends in neurosciences.

11. Harvey, A.G., 2008. Sleep and circadian rhythms in bipolar disorder: seeking synchrony, harmony, and regulation. American journal of psychiatry 165, 820-829.

12. Harvey, P.D., Greenberg, B.R., Serper, M.R., 1989. The affective lability scales: development, reliability, and validity. Journal of clinical psychology 45, 786-793.

13. Henry, C., Mitropoulou, V., New, A.S., Koenigsberg, H.W., Silverman, J., Siever, L.J., 2001a. Affective instability and impulsivity in borderline personality and bipolar II disorders: similarities and differences. Journal of psychiatric research 35, 307-312.

14. Henry, C., Mitropoulou, V., New, A.S., Koenigsberg, H.W., Silverman, J., Siever, L.J., 2001b. Affective instability and impulsivity in borderline personality and bipolar II disorders: similarities and differences. Journal of Psychiatric Research 35, 307-312.

15. Henry, C., Van den Bulke, D., Bellivier, F., Roy, I., Swendsen, J., M'Baïlara, K., Siever, L.J., Leboyer, M., 2008. Affective lability and affect intensity as core dimensions of bipolar disorders during euthymic period. Psychiatry Research 159, 1-6.

16. Holmes, E.A., Bonsall, M.B., Hales, S.A., Mitchell, H., Renner, F., Blackwell, S.E., Watson, P., Goodwin, G.M., Di Simplicio, M., 2016. Applications of time-series analysis to mood fluctuations in bipolar disorder to promote treatment innovation: a case series. Translational Psychiatry 6, e720.

17. Howes, O.D., Lim, S., Theologos, G., Yung, A.R., Goodwin, G.M., McGuire, P., 2011. A comprehensive review and model of putative prodromal features of bipolar affective disorder. Psychological Medicine 41, 1567-1577.

18. Insel, T.R., 2014. The NIMH research domain criteria (RDoC) project: precision medicine for psychiatry. American Journal of Psychiatry 171, 395-397.

19. Larsen, R.J., Diener, E., Emmons, R.A., 1986a. Affect intensity and reactions to daily life events. Journal of personality and social psychology 51, 803.

20. Larsen, R.J., Diener, E., Emmons, R.A., 1986b. Affect Intensity And Reactions To Daily Life Events. Journal of Personality and Social Psychology 51, 803-814.

21. Lieb, K., Völlm, B., Rücker, G., Timmer, A., Stoffers, J.M., 2010. Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. British Journal of Psychiatry 196, 4-12.

22. Marwaha, S., Balbuena, L., Winsper, C., Bowen, R., 2015. Mood instability as a precursor to depressive illness: A prospective and mediational analysis. Australian and New Zealand Journal of Psychiatry, 0004867415579920.

23. Marwaha, S., Broome, M., Bebbington, P., Kuipers, E., Freeman, D., 2013a. Mood instability and Psychosis: findings from British national surveys. Schizophrenia Bulletin.

24. Marwaha, S., Gordon-Smith, K., Broome, M., Briley, P., Perry, A., Forty, L., Craddock, N., Jones, I., Jones, L., 2016. Affective instability, childhood trauma and major affective disorders. Journal of affective disorders 190, 764-771.

25. Marwaha, S., He, Z., Broome, M., Singh, S.P., Scott, J., Eyden, J., Wolke, D., 2014. How is affective instability defined and measured? A systematic review. Psychol Med 44, 1793-1808.

26. Marwaha, S., He, Z., Broome, M. Singh, S.P., Scott, J., Eyden, J., Wolke, D., 2013. How is affective instability defined and measured. A systemtaic review. Psychological medicine.

27. Marwaha, S., Parsons, N., Flanagan, S., Broome, M., 2013b. The prevalence and clinical associations of mood instability in adults living in England: results from the Adult Psychiatric Morbidity Survey 2007. Psychiatry research 205, 262-268.

576 28. Marwaha, S., Parsons, N., Flanagan, S., Broome, M., 2013c. The prevalence and clinical
577 associations of mood instability in adults living in England: results from the Adult Psychiatric
578 Morbidity Survey 2007. Psychiatry research 205, 262-268.
579
580 29. Moffa, G., Catone, G., Kuipers, J., Kuipers, E., Freeman, D., Marwaha, S., Lennox, B.R., Broome,
581 M.R., Bebbington, P., 2017. Using directed acyclic graphs in epidemiological research in psychosis: an
582 analysis of the role of bullying in psychosis. Schizophrenia bulletin 43, 1273-1279.
583
584 30. Palmier-Claus, J.E., Taylor, P.J., Gooding, P., Dunn, G., Lewis, S.W., 2012. Affective variability
585 predicts suicidal ideation in individuals at ultra-high risk of developing psychosis: An experience
586 sampling study. British Journal of Clinical Psychology 51, 72-83.
587
588 31. Patel, R., Lloyd, T., Jackson, R., Ball, M., Shetty, H., Broadbent, M., Geddes, J.R., Stewart, R.,
589 McGuire, P., Taylor, M., 2015. Mood instability is a common feature of mental health disorders and
590 is associated with poor clinical outcomes. BMJ Open 5, e007504.
591
592 32. Reich, D.B., Zanarini, M.C., Fitzmaurice, G., 2012. Affective lability in bipolar disorder and
593 borderline personality disorder. Comprehensive Psychiatry 53, 230-237.
594
595 33. Richard-Lepouriel, H., Etain, B., Hasler, R., Bellivier, F., Gard, S., Kahn, J.-P., Prada, P., Nicastro, R.,
596 Ardu, S., Dayer, A., 2016. Similarities between emotional dysregulation in adults suffering from
597 ADHD and bipolar patients. Journal of affective disorders 198, 230-236.
598
599 34. Saunders, K., Bilderbeck, A., Price, J., Goodwin, G., 2015. Distinguishing bipolar disorder from
600 borderline personality disorder: A study of current clinical practice. European Psychiatry 30, 965-
601 974.
602
603 35. Stange, J.P., Sylvia, L.G., da Silva Magalhães, P.V., Miklowitz, D.J., Otto, M.W., Frank, E., Yim, C.,
604 Berk, M., Dougherty, D.D., Nierenberg, A.A., 2016. Affective instability and the course of bipolar
605 depression: results from the STEP-BD randomised controlled trial of psychosocial treatment. The
606 British Journal of Psychiatry 208, 352-358.
607
608 36. Steyerberg, E.W., 2008. Clinical prediction models: a practical approach to development,
609 validation, and updating. Springer Science & Business Media.
610
611 37. Strejilevich, S., Martino, D., Murru, A., Teitelbaum, J., Fassi, G., Marengo, E., Igoa, A., Colom, F.,
612 2013. Mood instability and functional recovery in bipolar disorders. Acta Psychiatrica Scandinavica
613 128, 194-202.
614
615 38. Tsanas, A., Saunders, K., Bilderbeck, A., Palmius, N., Osipov, M., Clifford, G., Goodwin, G., De Vos,
616 M., 2016. Daily longitudinal self-monitoring of mood variability in bipolar disorder and borderline
617 personality disorder. Journal of affective disorders 205, 225-233.
618
619 39. Üstün, T.B., 2010. Measuring health and disability: Manual for WHO disability assessment
620 schedule WHODAS 2.0. World Health Organization.
621
622 40. Williams, K.E., Chambless, D.L., Ahrens, A., 1997. Are emotions frightening? An extension of the
623 fear of fear construct. Behaviour research and therapy 35, 239-248.
624

41. Yen, S., Shea, M.T., Sanislow, C.A., Grilo, C.M., Skodol, A.E., Gunderson, J.G., McGlashan, T.H., Zanarini, M.C., Morey, L.C., 2004. Borderline personality disorder criteria associated with prospectively observed suicidal behavior. The American journal of psychiatry 161, 1296-1298.

Table 1: **Descriptive statistics by group; case versus control and diagnosis subgroups (n = 94)**

Characteristic	Control (n = 25)	Case (n = 69)	Cases by diagnosis				Total (n = 94)	Case versus control	
			Bipolar (n = 11)	Borderline (n = 12)	Psychosis (n = 21)	Depression (n = 25)		P value	Test
Age (years); mean (SD)	48.5 (10.8)	38.2 (12.8)	35.6 (13.3)	33.9 (11.0)	34.9 (9.8)	44.2 (14.1)	41.0 (13.1)	0.001	t test
Male; n (%)	9 (36.0%)	36 (52.2%)	6 (54.5%)	2 (16.7%)	12 (57.1%)	16 (64.0%)	45 (47.9%)	0.165	Chi square test
Employment; n (%):									
– Employed	19 (76.0%)	26 (37.7%)	5 (45.5%)	4 (33.3%)	6 (28.6%)	11 (44.0%)	45 (47.9%)	0.001	Chi Square test (employed vs unemployed, n = 90)
– Unemployed	5 (20.0%)	40 (58.0%)	6 (54.5%)	8 (66.7%)	14 (66.7%)	12 (48.0%)	45 (47.9%)		
– Other	1 (4.0%)	3 (4.3%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	2 (8.0%)	4 (4.3%)		
Ethnicity; n (%)									Chi square test
– White British	18 (72.0%)	57 (82.6%)	9 (81.8%)	10 (83.3%)	14 (66.7%)	24 (96.0%)	75 (79.8%)	0.259	
– Other	7 (28.0%)	12 (17.4%)	2 (18.2%)	2 (16.7%)	7 (33.3%)	1 (4.0%)	19 (20.2%)		
Education; n (%)									Chi square test (n = 89)
– None/GCSE	7 (28.0%)	35 (50.7%)	5 (45.5%)	5 (41.7%)	12 (57.1%)	13 (52.0%)	42 (44.7%)	0.061	
– A level	3 (12.0%)	16 (23.2%)	4(36.4%)	2 (16.7%)	5 (23.8%)	5 (20.0%)	19 (20.2%)		
– Degree/higher degree	11 (44.0%)	17 (24.6%)	2 (18.2%)	5 (41.7%)	3 (14.3%)	7 (28.0%)	28 (29.8%)		
– *[Missing]*	*4 (16.0%)*	*1 (1.4%)*	-	-	*1 (4.8%)*	-	*5 (5.3%)*		

Marital status; n (%) – Married/cohabiting	20 (80.0%)	22 (31.9%)	1 (9.1%)	6 (50.0%)	5 (23.8%)	10 (40.0%)	42 (44.7%)	< 0.001	Chi square test
– Single/separated/ widowed	5 (20.0%)	47 (68.1%)	10 (90.9%)	6 (50.0%)	16 (76.2%)	15 (60.0%)	52 (55.3%)		

Table 2: **Unadjusted mean scores (with standard deviation) and count (%) for each measurement scale and subscales**

Measurement scale	Controls (n = 25)	Cases (n = 69)				All (n = 94)	Case versus control (General linear models, F test)
		Bipolar (n = 11)	Borderline (n = 12)	Psychosis (n = 21)	Depression (n = 25)		
ACS (scale 1-7)	3.36 (0.56)	4.39 (0.66)	5.14 (0.58)	4.23 (0.86)	4.52 (0.86)	4.21 (0.92)	p<0.001
ACS: Anger	3.06 (0.60)	4.31 (0.83)	5.21 (0.96)	4.07 (0.89)	4.08 (1.15)	3.97 (1.11)	
ACS: Positive-affect	3.48 (0.63)	4.17 (0.73)	4.12 (1.02)	4.05 (0.89)	3.87 (1.03)	3.88 (0.89)	
ACS: Depressed	3.36 (0.75)	4.96 (0.88)	5.92 (0.72)	4.40 (1.01)	5.38 (1.04)	4.64 (1.27)	
ACS: Anxiety	3.42 (0.57)	4.31 (0.84)	5.63 (0.60)	4.42 (1.23)	4.93 (0.95)	4.43 (1.13)	
ALS-18 (scale 0-3)	0.64 (0.58)	1.47 (0.62)	1.66 (0.49)	1.53 (0.67)	1.50 (0.62)	1.29 (0.71)	p<0.001[1]
ALS-18: Anxiety/Depression	0.55 (0.65)	1.49 (0.69)	2.23 (0.79)	1.60 (1.01)	1.88 (0.87)	1.46 (1.00)	
ALS-18: Depression/Elation	0.86 (0.70)	1.66 (0.57)	1.45 (0.58)	1.65 (0.73)	1.52 (0.53)	1.38 (0.70)	
ALS-18: Anger	0.38 (0.48)	1.16 (0.95)	1.42 (0.96)	1.27 (0.88)	1.08 (1.03)	0.99 (0.92)	
AIM (scale 1-6)	3.50 (0.48)	3.45 (0.37)	3.37 (0.44)	3.42 (0.56)	3.37 (0.39)	3.42 (0.45)	p=0.867
Number of mood fluctuations reported in the last week							P=0.310
0	13 (52%)	2 (18.2%)	0 (0%)	5(23.8%)	2 (8%)	22 (23.4%)	
1-3	10 (40%)	5 (45.5%)	3 (25%)	4 (19%)	8 (32%)	30 (31.9%)	
4-7	2 (8%)	3 (27.3%)	7 (58.3%)	7 (33.3%)	7 (28%)	26 (27.7%)	
>7	0 (0%)	1 (9.1%)	2 (16.7%)	5 (23.8%)	8 (32%)	16 (17.0%)	
WHODAS[2] (scale 0-4)	0.54 (0.11)	1.43 (0.61)	1.83 (0.69)	1.75 (1.00)	1.89 (0.91)	1.44 (0.96)	p<0.001

[1] Adjusted for age.

Table 3: Correlation coefficients between each pair of measurement scales

Full -sample (N=94)					
		AIM	**ALS-18**	**ACS**	**Mood fluctuation (last week)**
AIM		1	0.210	0.188	0.12
ALS-18			1	0.776	0.61
ACS				1	0.53
Mood fluctuation (last week)					1
Cases only (N=69)					
		AIM	**ALS-18**	**ACS**	**Mood fluctuation (last week)**
AIM		1	0.322	0.265	0.157
ALS-18			1	0.666	0.45
ACS				1	0.29
Mood fluctuation (last week)					1