Mood Instability

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Faculty of Psychiatry of Intellectual Disability Spring Conference 2016

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Royal College of Psychiatrists
Contents of talk

- Mood instability – what is it? Definition
- Epidemiology
- Psychosis and mood instability
- Neurobiology
DSM-5 and RDoC

- Doubts expressed about the validity of diagnoses in DSM-5
- Traditional psychiatric taxonomies may impede translational research in MH.
- Cuthbert & Insel- Research Domain Criteria (RDoC)
- RDoC supports studies of biobehavioural dimensions / clinical phenotypes which cut across existing diagnostic categories.
a) What are the definitions of affective instability in clinical populations, in the scientific literature?

b) What are the available measures of affective instability and how reliable and valid are these?
Methods

- A systematic review using PRISMA guide.
- MEDLINE, EMBASE, PsycINFO, PsychArticles and Web of Science databases were searched. Five journals were hand searched.
- Primary empirical studies included. Studies were selected, data extracted and quality appraised. A narrative synthesis
- Search items in groups: AI terms, emotion terms, mood terms, diagnosis terms, questionnaires eg AIM
- Inclusion criteria were study design, adults and included definition and method of measurement.
11443 abstracts screened for inclusion:

110 papers assessed for inclusion

17 excluded
- Eg non English language
- 5 dissertations
- 7 duplicates

56 excluded
- 28 AI term not defined
- 14 Participant (non-clinical population)
- 12 Study design (letters, review, case studies)
- 2 Measurement

37 included studies in final analysis
Results

- Numbers of definitions for terms in included studies were: affective instability (N=7), affective lability (N=6), affective dysregulation (N=1), emotional dysregulation (N=4), emotion regulation (N=2), emotional lability (N=1), mood instability (N=2), mood lability (N=1) and mood swings (N=1)
- 25 definitions!

- Concepts showed considerable overlap: Affect, Mood vs Emotion
- Terms frequently emphasized significant fluctuations in affect, intensity and control- core features.
- Discrepant in other factors
- Time period poorly specified
- Definitions not disorder specific
Main findings

- Definitions were not specifically linked with conceptualising AI within a particular theoretical framework. Trait vs symptom
- The different terms are used interchangeably because they are largely defined by similar attributes

- The measures assess 3 core attributes: oscillation, intensity, subjective sense of the capacity to control affect and behaviour.
- We propose that AI is defined as “rapid oscillations of intense affect, with a difficulty in regulating these oscillations or their behavioural consequences”.
- No single measure comprehensively assessed AI. Combinations of assessments needed. Eg AIM+ALS+ACS
The prevalence and clinical associations of mood instability in adults living in England: Results from the Adult Psychiatric Morbidity Survey 2007

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Mood instability, mental illness and suicidal ideas: results from a household survey

Steven Marwaha · Nick Parsons · Matthew Broome
Epidemiology of mood instability (i)

- Data from Adult Psychiatric Morbidity Survey (APMS) 2007 (Marwaha et al., 2013).

- Relies on DSMIV Borderline Personality Disorder item: ‘Do you have a lot of sudden mood changes?’

- n=7403

- Prevalence of 13.9%

- It was more common in women than men, peak prevalence was in those aged 16–24, and it gradually declined with age with 7% of 65-to 74-year-olds reporting unstable mood
How common

Overall prevalence 13.9%

Marwaha et al 2013
Epidemiology of Mood Instability (ii)

- Mood instability is reported in 40–60% of those with depression, anxiety disorder, post-traumatic stress disorder and obsessive–compulsive disorder.

- Associated with increased health service use and suicidal ideation, independent of neurotic symptoms, alcohol misuse, borderline personality disorder
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Rates of MI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalised anxiety disorder</td>
<td>49.2</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>56.1</td>
</tr>
<tr>
<td>Depressive episode (any severity)</td>
<td>60.9</td>
</tr>
<tr>
<td>PTSD</td>
<td>63.3</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>67.1</td>
</tr>
</tbody>
</table>
Mood Instability as a Psychopathological Construct: aetiology, prodrome, mediation and prognosis

- Our interest via background in Early Intervention in Psychosis services

- Mood instability as ‘prodrome’ to bipolar?

- However, more complex - can occur in the earliest phases of attention-deficit hyperactivity disorder and depressive disorder.

- Mediating factor in the pathway from trauma to emerging borderline personality disorder and in the genesis of hallucinations, paranoia and psychotic disorders.

- Mood instability independently predicts worse long-term outcome in euthymic patients with bipolar disorder.
Patient experience

- Bilderbeck et al 2014. 28 people with MI referred to secondary MHS received qualitative interviews.

- Themes:
  - People want an explanation and help
  - Want consistent and continuous care
  - Struggle to communicate and be understood: need to convince clinicians of the legitimacy of symptoms
  - Often feeling dismissed and discredited
Did Kraepelin endorse the Kraepelinian dichotomy?

‘No expert will deny that cases which cannot be classified safely are disturbingly frequent … We will have to get used to the idea that all signs are insufficient to delineate manic-depressive insanity from schizophrenia and … that overlap occurs’ (Kraepelin, 1920).
Why are mood symptoms relevant in psychosis aetiology? [1/2]

- Persistence of symptoms: co-existence of affective disturbance is a major factor in determining whether young people who experience minor psychotic symptoms will progress to psychotic disorder that requires care.

- Cohort studies have consistently shown that preschizophrenic children have an excess of depression and social anxiety.

- Retrospective studies show that the first noticeable psychological disturbances in individuals who later become psychotic include depression and anxiety.
Why are mood symptoms relevant in psychosis aetiology? [2/2]

- Most patients with a first-episode of schizophrenia will have had a depressed mood, and at least one frank episode of depression, in the year prior to hospitalisation.

- From studies of those with the at risk mental state for psychosis (ARMS), it is clear that prior to the onset of frank psychosis there are prominent mood and anxiety symptoms, many of which reach DSM diagnostic criteria.

- Affective symptomatology may play a role in the genesis of positive symptoms such as hallucinations and delusions.

- Anxiety facilitates the development of aberrant cognitive schema and beliefs, and influences the generation of anomalous experiences and then the maintenance of delusions once formed.
Shared risk

- Commonalities in developmental, genetic, epidemiological, outcome studies between Sz and affective disorder.

- Genes: inherited predisposition to psychosis in general + specific factors that modulate precise form (e.g. contribute to positive, negative, manic, and depressive symptoms).

- Shared developmental risk factors: difficult labour, winter birth, urban birth, motor milestones.

- Imaging: structural abnormalities in both BPAD and Sz: increased ventricular volume however more marked in Sz. Other wider changes in Sz.
Fig. 1 Salience dysregulation syndrome. Six dimensions that tend to co-occur make up the salience dysregulation syndrome. Individuals may make the transition from 'risk' to 'need for care' if they pass the threshold on one or more dimensions, and accordingly may fit sub-categories 'with affective expression', 'with developmental expression' and 'not otherwise specified'. Patient A: 'typical' salience dysregulation syndrome with developmental expression; Patient B: 'typical' salience dysregulation syndrome with affective expression; Patient C: salience dysregulation syndrome not otherwise specified. Position of subcategories and dimensions with respect to each other is arbitrary.
Mood Instability and Psychosis: Analyses of British National Survey Data

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Mood instability and psychosis

- Affective disorders and psychosis linked
- Psychosis fluctuates and may be consequent to a change in affect
- MI in psychosis a neglected area
- Evidence that mood dysregulation links CSA to personality disorder
- CSA also linked to psychosis and could this connection be mediated by MI too?
Hypotheses

1) Mood instability is associated with psychosis and individual psychotic phenomena.

2) MI predicts the later emergence of auditory hallucinations and paranoid ideation.

3) MI mediates the link between child sexual abuse and psychosis.
Methods

- Analyses of British national surveys of psychiatric morbidity in 2000 and 2007.
- Participants selected using population-based multi-phase probability sampling.
- Age range 16–74 in the 2000 National survey (N=8580, response rate 70%), and 16+ in 2007 (N=7403, response rate 57%).
- Full details in McManus et al 2007
- 18 month follow up of a subsample (N=2406) of the 2000 survey.
- Analyses were separate
Measures

- Psychosis: 3 ways, a diagnosis of probable psychosis, ratings of paranoia and auditory hallucinations (PSQ), and dimensional score of paranoia.

- Depression / anxiety: 4 levels of severity obtained from the CIS–R.

- Hypomanic mood in past year: PSQ.

- PTSD: Trauma Screening Questionnaire

- MI: item from the DSM-IV BPD SCID-II. “In relation to the last several years do you have a lot of sudden mood changes?” yes / no.

- CSA: (<16) sexual intercourse / molestation
Key results i) cross-sectional

- MI was a very common concomitant of psychosis, being present in 53% of people with psychosis in 2000 and in 77% in 2007.

- In both surveys, the equivalent general population rate was around 14%.

- The corresponding ORs were large and highly significant in each year (7.5 CI: 4.1–13.8) and 21.4 (CI: 9.7–47.2), respectively), and remained so 6.4 (CI 3.4–11.9) and 16.2 (CI 7.4–35.6), respectively) after adjustment for age, sex, marital status, employment status, and ethnicity.

- Adjustment for current affective state as indicated by the CIS-R total score reduced but did not eliminate the extent and significance of the association. Further controlling for hypompanic mood in the 2000 data set, and for hypompanic mood and PTSD screen status in the 2007 data set, had little additional effect on the ORs linking instability and psychosis.
Figure 1 The cross-sectional associations of mood instability and psychosis with paranoia

- Total population
- Mood instability +ve
- Psychosis +ve

Paranoia score

Percentage (weighted)
Key results – ii) longitudinal

- In people who were not initially paranoid, baseline MI predicted the development of paranoid ideation over the 18-month follow-up period. If the baseline CIS-R score was controlled, the OR reduced from 2.3 (CI: 1.6–3.3) to 1.6 (CI: 1.1–2.4) but remained significant. In participants who initially acknowledged paranoid ideas, baseline endorsement of MI predicted the maintenance of paranoia at follow-up (OR: 2.45; CI: 1.8–3.3). Again this was little affected by controlling for initial CIS-R score.

- The emergence of auditory hallucinations appeared to be predicted by MI in the same way, although controlling for baseline CIS-R score reduced the OR, from a highly significant 2.6 (CI: 1.5–4.4) to 1.7 (CI: 0.97–2.9): the P value then fell short of conventional significance, at 0.063. However, MI did not predict the maintenance of auditory hallucinations. It is possible that hallucinations are more sporadic than paranoid ideation; if so, this would reduce the ability to predict their emergence and maintenance.
Key results – iii) mediation analysis

- Data only available in the 2007 survey to analyze the extent to which MI might mediate the associations of CSA with psychosis, paranoid ideation, and auditory hallucinations.

- The indirect route via MI was highly significant, accounting for over a third of the total effect for psychosis and persecutory ideation, and a quarter of that for auditory hallucinations.
### MI as a mediator of the link between CSA

| Probable Psychosis       | Effect | OR   | Robust standard error | P>|z| |
|--------------------------|--------|------|-----------------------|-----|
| Reduced                  |        | 11.09| 4.95                  | 0.0001 |
| Full                     |        | 4.83 | 2.22                  | 0.001  |
| Difference               |        | 2.30 | 0.42                  | 0.0001 |

**34.6% of the link is mediated by mood instability.**

<table>
<thead>
<tr>
<th>Paranoid ideation</th>
<th>Reduced</th>
<th>4.10</th>
<th>0.80</th>
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<tbody>
<tr>
<td>Full</td>
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<td>2.52</td>
<td>0.50</td>
</tr>
<tr>
<td>Difference</td>
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<td>1.63</td>
<td>0.14</td>
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**34.5% of the link is mediated by mood instability.**

<table>
<thead>
<tr>
<th>Auditory hallucinations</th>
<th>Reduced</th>
<th>3.94</th>
<th>1.24</th>
<th>0.0001</th>
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<tbody>
<tr>
<td>Full</td>
<td></td>
<td>2.79</td>
<td>0.87</td>
<td>0.001</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
<td>1.41</td>
<td>0.10</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**25.3% of the link is mediated by mood instability.**
Summary of findings

- MI was strongly associated in cross-sectional analyses with all of our chosen measures, remaining so after adjustment for sociodemographic variables and for current mood state. This implied a contribution from MI independent of the mere presence of anxiety, depression, and hypomania.

- MI significantly predicted new inceptions of both paranoid ideation and auditory hallucinations though the finding for the latter was reduced to trend level after controlling for baseline CIS-R score. MI also predicted the maintenance of paranoid ideation, but not of auditory hallucinations.

- Hypothesis that MI substantially mediates the association of CSA with psychosis, paranoid ideation, and auditory hallucinations was also supported.
Implications

- Repetition of dysphoric mood - unsettling belief that equanimity can never be relied upon.

- Bursts of anxiety - world persistently unsafe.

- Sense of loss of control may prompt explanations in terms of external influence.

- MI as a target for treatment to prevent emergence of psychosis.

- Effect of MI may relate to neurobiological changes making people vulnerable to psychotic experiences. e.g. dysregulation in BPD linked to changed central dopaminergic and serotonergic functioning.
Review

Neurobiological and behavioural studies of affective instability in clinical populations: A systematic review

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RDoC

\section*{ABSTRACT}

\textbf{Objectives:} To evaluate the neurobiological, psychophysical and behavioural measures of affective instability in clinical populations.

\textbf{Data sources:} A range of medical and psychological science electronic databases were searched (including MEDLINE, EMBASE, and PsycINFO). Hand searching and reference checking are also included.

\textbf{Review methods:} Reviews, systematic reviews, experimental and cross-sectional studies, providing affective instability in neurobiological and behavioural measurements in clinical populations. Studies were selected, data were extracted and quality was appraised.

\textbf{Results:} Twenty-nine studies were included, 6 of which were review studies (one a meta-analysis) and 23 of which were primary studies, across a wide variety of disorders including ADHD, bipolar affective disorder, schizophrenia, severe mood dysregulation, major depression, and borderline personality disorder.

\textbf{Conclusions:} The bulk of the studies converge on the role of the amygdala, particularly in borderline personality disorders, and how it connects with other areas of the brain. Future research needs to extend these findings across diagnoses and development.

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Intro and rationale

- Little research studying neurobiological and behavioural measurements of affective instability in clinical populations. Systematic review aims to collate evidence on the neurobiological and behavioural measurement for affective instability in clinical populations, across the diagnostic spectrum.

- Goal to consider whether MI meets the ideal expressed in the Research Domain Criteria (RDoC). RDoC supports research that studies biobehavioral dimensions, which cut across existing diagnostic categories, with the key idea being that advances in genetics, systems neuroscience and behavioral science are not wholly consistent with the existing categories of mental disorder as defined in both the ICD and DSM. Hence, traditional psychiatric taxonomies may be an impediment to translational research.

- Given that MI manifests developmentally, neuroscientific, behavioral & psychometric strategies, may allow mechanisms underpinning AI to be detected prior to the problems associated with it developing, and hence offer a window for early detection, intervention and prevention of harms.
Methods – (i)

- PRISMA guidelines

2.1. Eligibility criteria

Studies were included if they met the following criteria:

a) Study design: for primary studies, experimental studies (randomised controlled trials, nonrandomized controlled trials, controlled before-and-after studies, and cross-sectional studies); as well as reviews.

b) Participants: we defined clinical population as subjects meeting the diagnostic criteria of DSM-IV or ICD-10.

c) Neurobiological and behavioural measurements: we defined neurobiological measurements as including any affective neuroscience paradigm, for example, fMRI, EEG and PET; behavioural measurements as any format of cognitive and behavioural test/task, for example: the Attention Network Test (ANT).

d) Comparison: we did not have restrictions for the comparator characteristics.

e) Outcomes: we included studies that reported outcomes relating to neurobiological and behavioural measurements for affective instability.
Methods (ii)

- MEDLINE, EMBASE, PsycINFO, PsycArticles and Web of Science. The main search was from the date of inception of each database to February 2012, and was then updated till January 2014.


- Search terms

<table>
<thead>
<tr>
<th>Group 1 (affective)</th>
<th>Group 2 (mood)</th>
<th>Group 3 (emotion)</th>
<th>Group 4 (disorder)</th>
<th>Group 5 (established measures)</th>
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</thead>
<tbody>
<tr>
<td>Affective instability</td>
<td>Mood instability</td>
<td>Emotion instability</td>
<td>Borderline personality disorder (BPD)</td>
<td>Mood Disorder Questionnaire</td>
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<tr>
<td>Affective dysregulation</td>
<td>Mood dysregulation</td>
<td>Emotion dysregulation</td>
<td>Bipolar disorders (BP)</td>
<td>Short Mood and Feelings Questionnaire</td>
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<tr>
<td>Affective lability</td>
<td>Mood lability</td>
<td>Emotion lability</td>
<td>Post-traumatic stress disorder (PTSD)</td>
<td>Affective Liability Scale</td>
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<td></td>
<td>Mood swings</td>
<td></td>
<td>Attention deficit hyperactivity disorder (ADHD)</td>
<td>Affect Intensity Measure</td>
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<td></td>
<td></td>
<td></td>
<td>Unstable personality traits</td>
<td>Strengths and Difficulties Questionnaire</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Child Behaviour Checklist</td>
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</table>
Results (i)

Fig. 1. PRISMA flow chart.
Results (ii)

- Papers found above cover a wide range of affective psychopathology including within disorders such as ADHD, bipolar affective disorder, schizophrenia, severe mood dysregulation, major depression, and borderline personality disorder. No primary studies were found in this systematic search which examined affective instability in PTSD.

- Measures to determine affective instability and mood dysregulation in the studies differ: some studies assume that such dysregulation exists due a given diagnosis being present, others assess mood dysregulation with a specific measure such as the MDQ, DERS, and PAI-BOR as well as bespoke measures.

- Techniques employed to study mood dysregulation have used emotionally salient stimuli (faces) in fMRI, and those that induce certain emotional states – in this review we found use of both narrative- based mood induction (via reading a story) as well as a task-evoked frustration based upon performance of a task.
Conclusions (i)

- The majority of the functional neuroimaging studies found examined affective instability within borderline personality disorder. Despite a variety of different tasks, there seems some convergence in that alterations in amygdala activation are found and interpreted to reflect problems in emotional processing, salience to emotional stimuli, and the individual’s behavioural response to such stimuli.

- Functional connectivity analysis suggests a change in connectivity between regions such that the salience network may become more connected than the central executive network, and increased connectivity between the ventromedial prefrontal cortex and the amygdala, and decreased between areas of the anterior cingulate.

- In addition, the anterior cingulate cortex may have a role in behavioural compensation in mood instability in BPD, and the limbic system (specifically, amygdala, insula, and DLPFC) in modulating the impact of emotional distraction on working memory in those with BPD.
Fig. 2. Schematic of anatomical areas linked to affective instability.
Conclusions (ii)

- Based on these studies, the amygdala is a key area to understand affective instability in those with BPD, with connectivity between the salience network and other regions possibly being relevant transdiagnostically. The precise nature and location of this changed connectivity appears to be more diagnostically specific.

- Further imaging studies should examine the role of the amygdala in affective instability transdiagnostically to determine whether the findings for BPD are present in other disorders, and whether any other changes are present that may be disorder specific, such as the connectivity of the salience network.

- We would suggest that AI would meet the requirements of RDoC – it is likely to reflect problems in a core behavioural function of the brain, seems likely to be related to a dysfunction in neural circuits, and is dimensional (or rather, may have a few dimensions).
Points to end

- Mood instability has been assessed in different ways. Multiple but overlapping definitions
- It is a precursor of a range of disorders
- It may be a mediating link between an exposure and a clinical outcome
- It is transdiagnostic
- Important in prognosis
- Clinical associations with suicidality, functional impacts, hospitalisation, anti-psychotic and mood stabiliser use and health service use
- It is important in patient experience
Future directions

- Role of mood instability in mediating connection between bullying and psychosis.

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Bullying victimisation and risk of psychotic phenomena: analyses of British national survey data

Gennaro Catone, Steven Marwaha, Elizabeth Kuipers, Belinda Lennox, Daniel Freeman, Paul Bebbington, Matthew Broome

- CONBRIO

- Experimental medicine paradigm – MI as screen for medication

- Automated monitoring of mood

- Assessing dimensions of mood instability in clinical populations

- Prediction of relapse and stratification of risk

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