Bipolar implies two poles: two possibilities. Opposites. However, this term could lead to reductionist thinking.

Concept of dysphoria becomes most relevant when considering the mixed states of Bipolar Disorder.

Dysphoria - conflated with the idea of depressive symptoms occurring in mania “dysphoric mania” though use and interpretation of the term has varied.

Irritable Mood - considered an alternative mood expression in a manic episode
Mixed States: Current and Past Definitions

- DSM 5
  - Mixed State is denoted by the specifier “with mixed features”
  - For mixed mania/hypomania: at least 3 of (for majority of days):
    1. Prominent dysphoria or depressed mood
    2. Diminished interest or pleasure
    3. Psychomotor Retardation
    4. Fatigue or loss of energy
    5. Worthlessness/guilt
    6. Thoughts of death/suicide
Mixed States: Current and Past Definitions

- DSM 5
  - For mixed depression: at least 3 of (for majority of days):
    - Elevated/expansive mood
    - Inflated self-esteem/grandiosity
    - Talkativeness/pressure
    - Flight of ideas/subjectively racing thoughts
    - Increase in energy/goal-directed activity
    - Involvement in activities with high potential for painful consequences
    - Decreased need for sleep
Criteria met for both a Manic Episode and a Major Depressive Episode

Nearly every day

For at least 1 week

The individual experiences rapidly alternating moods (sadness, irritability, euphoria) accompanied by symptoms of both a manic and a depressive episode.

Excludes states induced by "substances", including antidepressants, ECT, light therapy or other medications.
Mixed States: DSM-III-R

- Criteria met for both a Manic Episode and a Major Depressive Episode
- Intermixed, or rapidly alternating every few days

And:

- Prominent depressive symptoms lasting at least a full day
Mixed States ICD-10

- Episode characterized by either a mixture or a rapid alternation (i.e. within a few hours) of hypomanic, manic and depressive symptoms

- Both manic and depressive symptoms must be prominent most of the time during a period of at least 2 weeks.
Kraeplin’s conception of mood states

(in Dayer et al. Bipolar Disorders 2000)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mood</th>
<th>Thought</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure Depression</td>
<td>I</td>
<td>I</td>
<td>I</td>
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<tr>
<td>Depressive/anxious Mania</td>
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<tr>
<td>Agitated depression</td>
<td>I</td>
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<tr>
<td>Depression with flight of ideas</td>
<td>I</td>
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<tr>
<td>Mania with poverty of thought</td>
<td>E</td>
<td>I</td>
<td>E</td>
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<tr>
<td>Manic stupor</td>
<td>E</td>
<td>I</td>
<td>I</td>
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<tr>
<td>Inhibited mania</td>
<td>E</td>
<td>E</td>
<td>I</td>
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<tr>
<td>Pure Mania</td>
<td>E</td>
<td>E</td>
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</tr>
</tbody>
</table>
The nature of Mixed States/Dysphoric Mania:

- Stage-related (peak mania), or severe form of mania
- Transitional state between manic and depressive episodes
- Independent mood state
- A typical form of mania
Dysphoria as a third dimension

- Proposed that mixed states consist of combinations of 3 dimensions: depressive syndrome; manic syndrome and dysphoric syndrome.

- Evidence suggesting the validity of a third dimension:
  - Three factor analyses of mania demonstrated the existence of a factor corresponding to irritability/aggression or irritability/paranoia or irritability.
  - Nosology of depression throughout psychiatric history – hostile or angry depression often suggested. Suggests a separate dimension, usefully separated as per anxiety in depression.
  - Psychic inner agitation in mixed depressive states (Koukoupoulis)
Dysphoria as a third dimension

Dayer et al proposed the dysphoric syndrome as:

- The presence during at least 24 hours of overt irritability including two of the following criteria:
  - Expressed (subjective) internal tension
  - Expressed (subjective) irritability or feelings of hostility in reaction to external stimuli
  - Aggressiveness or destructive behaviours
  - Suspiciousness
Dysphoria as a third dimension

Dayer A et al. Bipolar Disorders 2000: 2: 316-324
Treatment of Mixed Mood States

- Earlier opinion that mixed states predicted non-response to lithium, and should be treated with an antiepileptic e.g. carbamazepine or valproate.

- Evidence supporting this was somewhat limited.

- Differing definitions of mixed states over time (DSM III, IV, 5 and ICD) have somewhat hampered studies. Criteria can be too narrow or too broad. Some researchers used own criteria.
Treatment of Mixed States
(Parker & Ricciardi 2018)

- Recent review in Australasian Psychiatry, as to whether consensus exists around the treatment of mixed states.
- Notes that rates of mixed states reported to occur in 10-70% of manic patients, depending on criteria used.
- Mixed states tend to show variability and lability of mood, a slight female preponderance and increase the risk of suicide.
- May also have younger age at onset and more episode recurrences.
Treatment of Mixed States
(Parker & Ricciardi 2018)

- CANMAT (Canadian) guidelines recommend avoiding antidepressants in bipolar patients with mixed features
- Support for several atypical antipsychotics e.g. olanzapine-fluoxetine, asenapine, lurasidone for bipolar depression
- Support for asenapine, aripiprazole, olanzapine, ziprasidone and valproate for mania with mixed features

- World Federation of Societies of Biological Psychiatry (WFSBP)
- Avoid antidepressants in bipolar patients with a mixed state (olanzapine + fluoxetine did not worsen outcome)
- Olanzapine, Paliperidone, Aripiprazole for acute mixed manic states
Treatment of Mixed States

(Parker & Ricciardi 2018)

- WFSBP recommendations cont...
- Ziprasidone, carbamazepine, lurasidone, olanzapine and ECT for bipolar depressed mixed states
- Quetiapine, lithium and olanzapine (either as monotherapy or combined) best choice for preventing a new mixed episode
- Valproate, olanzapine and lithium might be best for preventing a mixed episode after any mixed index episode.

- WFSBP guidelines note numerous problems in the definition and measurement of mixed states, and recommendations should be viewed with caution. Most studies underpowered.


