First Episode Affective Psychosis: Diagnosis and Treatment

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No conflicts to declare

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- Laboratory for Early Psychosis Research (LEAP) Center - P50MH115846
Outline

• First episode affective psychosis
• Diagnostic issues
  • Prodrome/Transition to first episode
  • Clinical course
• Treatment issues
  • Acute treatment
  • Maintenance
• Conclusions
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• Conclusions
First Episode Affective Psychosis

• Primarily early phase of Bipolar Disorder
  • Common and severe although historically viewed as a more benign condition than non-affective psychosis

• Outcome is mixed, not always associated with full recovery to baseline

• Evidence for early intervention is sparse when compared with non-affective psychosis
  • But evidence for ability to alter long-term trajectory with good treatment (Lithium – e.g. Goodwin 2002; Kessing et al 2014) may be stronger

• Long delay between onset of illness and establishment of diagnosis and delivery of good care (e.g. Baethge et al 2003)
First Episode Affective Psychosis

- Majority of people with Bipolar Disorder have onset with depressive episode
  - Depression is common and prediction of who will develop BD is not robust
- Commonly recognized in a first episode of mania
  - Difficult to hide or fake
    - Euphoria/irritability; reduced need for sleep; goal directed activity; grandiosity; racing thoughts
  - But it can be misinterpreted/missed in the context of psychosis
    - The agitated, pressured, irritable psychotic disorder patient
- Some will ultimately be diagnosed with
  - Schizoaffective disorder (if psychosis persists for significant period outside of mood episodes)
  - Schizophrenia (if mood episodes are isolated and clinically not significant)
First Episode Affective Psychosis

• Composite case vignette from McLean
  • 20 year old college student
  • Increasingly agitated over concern that someone hacked his social media accounts and stole his IT secrets
  • Hears voices telling him to “settle the score”
  • Once hospitalized: sleeping 3-4 hours a night and fully energized during the day; singing songs in the hallways; making sexual advances to female staff
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  • “I know he looks manic to you, but what he really has is schizophrenia” because he is so psychotic
  • Responded well to combination of lithium treatment and second generation antipsychotic in the hospital; returned to school the following semester
Diagnosis in Schizophrenia and Manic-Depressive Illness

A Reassessment of the Specificity of 'Schizophrenic' Symptoms in the Light of Current Research

Harrison G. Pope, Jr, MD, Joseph F. Lipinski, Jr, MD

- Present clinical and research methods of differential diagnosis of schizophrenia and affective psychoses rely very heavily on presenting symptoms and signs, especially in acute psychosis. We have reviewed studies bearing on this issue, including studies of the phenomenology of psychotic illness, outcome, family history, response to treatment with lithium carbonate, and cross-national and historical diagnostic comparisons. We conclude that most so-called schizophrenic symptoms, taken alone and in cross section, have remarkably little, if any, demonstrated validity in determining diagnosis, prognosis, or treatment response in psychosis. In the United States, particularly, overreliance on such symptoms alone results in overdiagnosis of schizophrenia and underdiagnosis of affective illnesses, particularly mania. This compromises both clinical treatment and research.

*(Arch Gen Psychiatry 35:811-828, 1978)*
First Episode Affective Psychosis

• Early manifestations are protean
  • Non-episodic mood symptoms
    • Depressive
    • Manic (more likely to be dysphoric in young people) Wozniak et al 2001
  • Psychosis (>50%; can be mood-incongruent and first-rank) Conus et al 2004
    • Substance use
    • Attentional difficulties

• Onset not always clear cut; slow emergence of cyclic nature
First Episode Affective Psychosis

• What place does it occupy in psychosis early intervention clinics?
Diagnostic Mix at McLean OnTrack

Categories of Psychosis

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<th>Category</th>
<th>All Patients (n=91)</th>
<th>Active Patients (n=69)</th>
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<td>Affective Psychosis</td>
<td>44.0%</td>
<td>46.4%</td>
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<td>Primary Psychosis</td>
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<td>Psychosis NOS</td>
<td>20.9%</td>
<td>14.5%</td>
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<tr>
<td>No Psychosis</td>
<td>2.2%</td>
<td>1.4%</td>
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Shinn et al., *Early Intervention in Psychiatry* 2015
Diagnostic instability in early course psychosis

- Diagnosis remained stable: 49%
- Diagnosis changed from referral to most current: 51%

Shinn et al., *Early Intervention in Psychiatry* 2015
Diagnostic Stability of First-Episode Psychotic Disorders and Persistence of Comorbid Psychiatric Disorders Over 1 Year

Table 2: Stability of primary psychotic disorder diagnoses after 1-year of follow-up

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<th>Primary diagnosis at baseline</th>
<th>n</th>
<th>Schizophrenia</th>
<th>Schizophreniform disorder</th>
<th>Schizoaffective disorder</th>
<th>BD*</th>
<th>MDD*</th>
<th>Delusional disorder</th>
<th>Psychotic disorder NOS</th>
<th>Substance-induced psychosis</th>
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<td>29</td>
<td>35</td>
<td>14</td>
<td>1</td>
<td>16</td>
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*BD with psychotic features
*NOS with psychotic features
*Patients with unchanged diagnoses

Figure 1. Diagnostic Stability of Initial ICD-10 Diagnoses (with prevalence [%] from Table 1) in 500 First-Episode Psychotic Disorder Patients at First Lifetime Hospitalization, Ranked by Diagnostic Stability (% remaining unchanged) for the Same Subjects at 24-Month Follow-Up

- Acute schizophrenia-like (28.6%)
- Acute polymorphic psychosis (66.7%)
- Psychosis unspecified, nonorganic (66.7%)
- Depression with psychosis (85.2%)
- Delusional (88.2%)
- Schizophrenia (94.6%)
- Mixed affective episode (94.9%)
- Mania with psychosis (99.0%)
- Schizoaffective (100.0%)

Overall (90.4%)

Proportion of Stable Diagnoses at 2 Years, %

Diagostic stability ranged from 100.0% for schizoaffective disorder (48 cases) to 28.6% for acute schizophrenia-like psychotic disorder (7 cases initially).

Abbreviation: ICD-10 = International Classification of Diseases, Tenth Revision.
Psychotic Major Depression

• First episode depression with psychotic features does exist
• Psychotic MDD accounts for 15-20% of MDD in some studies (Johnson 1992)
• Characterized by:
  • Guilt/worthlessness/feelings of deserved punishment; Fear of physical disease/poverty; Hallucinations of any modality
• Compared to non-psychotic MDD:
  • Lower age at onset
  • Higher recurrence, treatment resistance, likelihood of manic switch, prevalence of substance abuse, family history of mood disorders
  • Higher suicide rates/overall mortality/slower recovery
• Closely related to Bipolar Disorder
  • Family history of BD
  • Subsequent switch to BD diagnosis
Psychotic Major Depression

- Composite case vignette from McLean:
  - 19yo with gradual onset of paranoid psychosis (nihilistic, global conspiracies), depressed mood, severe withdrawal from social activities, psychomotor retardation, cognitive slowing, suicidal ideation
  - Concern for schizophrenia with prominent negative symptoms
  - Treated with antipsychotic and antidepressant combination but very modest response to treatment
  - One year later, had first manic episode – euphoric, flying around the country to find the “perfect college course”, trying to get rich by getting into the gold trade, erotomanic delusion concerning a celebrity
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  • One year later, had first manic episode – euphoric, flying around the country to find the “perfect college course”, trying to get rich by getting into the gold trade, erotomanic delusion concerning a celebrity
  • Mania proved difficult to treat. Repeat hospitalizations; when episode finally broke, he went back into a deep depression. Has not returned to school in 2 years...
First Episode Affective Psychosis

• What’s a clinician to do?
  • Many patients will present with genuinely ambiguous diagnostic pictures
  • Diagnostic categories are not crisp, there is gradations
  • The issue is not mistaking one diagnosis for another. Rather it is being aware of the presence of a second dimension of psychopathology in a sizable number of patients
  • Therapeutic implications
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The Prodrome

• **Summary by:** Howes et al, Psychol Med, 2011

• Attenuated forms of BD symptoms
  • Mood lability; racing thoughts; irritability/agitation

• General symptoms common to a range of psychiatric conditions
  • Depressive mood; anxiety

• Personality traits
  • Cyclothymia

• High sensitivity, low specificity
A positive family history of bipolar disorder, particularly if the parents have early-onset bipolar disorder, is the most significant risk factor for developing a bipolar spectrum disorder.
Staging in Bipolar Disorder

• Organizes well-known observations and concepts
  • Common, non-specific, and milder early presentations
  • Some individuals progress over time to more specific syndromes
  • Differential pace and details of progress across individuals

• Explicit parallel to other fields of medicine, e.g. cancer
  • But with no underlying biology to stages in psychiatry

• Does not address whether earlier stages contain individuals with:
  • Genuinely pluripotent conditions, or
  • Specific future trajectories mixed together because early presentations are similar
Stage 0
Asymptomatic

Stage 1a
Non-specific distress

Stage 1b
Sub-threshold high-risk

Stage 2
First episode

Stage 3a
Recurrence/persistence

Stage 3b
First threshold relapse

Stage 3c
Multiple relapses

Stage 4
Treatment resistance

Kindling Allostatic load

Treatment response

Functional impairment

Prognosis

Cognition and imaging changes Neuroprogression

Potential therapeutic interventions

Mental health literacy, self-help, lifestyle (diet, smoking)

Lifestyle modification, substance abuse reduction, CBT, supportive counselling, nutraceuticals

1a plus pharmacotherapy

1b plus phase-specific drug or mood stabilizer, case management, engagement, psychoeducation, psychotherapy

2 plus emphasis on maintenance medication and psychosocial strategies for full remission

2a plus relapse prevention strategies

3b plus combination of mood stabilizers

3c plus clozapine, functional/cognitive remediation, ACT

Berk et al 2017
Psychosis with Methylphenidate or Amphetamine in Patients with ADHD


“Among 221,846 young adults who received a stimulant for attention deficit–hyperactivity disorder, the percentage of patients who had an episode of psychosis within 60 days after starting the medication was higher among amphetamine users (0.21%) than among methylphenidate users (0.10%).”
Focus on cannabis use in early psychosis

Shinn et al., Early Intervention in Psychiatry 2015
First Episode Affective Psychosis

• What happens during/after a first episode of mania?
First Episode Affective Psychosis

• Great deal of psychic/behavioral disruption
  • Damage to personal relationships
  • Deviation from work/school trajectory

• Progressive loss of insight

• Generally treatment responsive and relatively quick return of individual agency/self efficacy

• Followed by regained insight/alliance

• Metabolizing episode is challenging – guilt/shame, rebuilding relationships, return to functioning
Progression of Recovery

- Progression of recovery after first episode mania (Tohen et al, AJP, 2003):
  - Syndromal - rapid and common (98%)
    - No longer meeting criteria for manic/mixed/depressive episode
  - Symptomatic - slower and not universal (75%)
    - Symptom levels below some low threshold
  - Functional - slowest and occurs in about 50%
    - Return to premorbid occupational/residential status
Recovery and Recurrence Following a First Episode of Mania: A Systematic Review and Meta-Analysis of Prospectively Characterized Cohorts

Andréeanne Gignac, MD; Alexander McGirr, MD, MSc; Raymond W. Lam, MD; and Lakshmi N. Yatham, MBBS

Results: We identified 8 studies representing a total of 734 first-episode patients. The syndromal recovery rates were 77.4% at 6 months and 84.2% at 1 year. Only 62.1% of patients had achieved a period of symptomatic recovery within 1 year. Recurrence rates were 25.7% within 6 months, 41.0% by 1 year, and 39.7% by 4 years. Younger age at first episode was associated with risk of recurrence after 1 year.

Conclusions: The majority of patients with first-episode mania exhibit syndromal recovery and, to a lesser extent, symptomatic recovery. The risk of recurrence is high, although the rates are slightly lower than those in mixed cohorts, with greater risk of recurrence associated with younger age at onset. Given lower recurrence than among mixed cohorts, there may be a window of opportunity to provide optimal treatment early and alter disease progression.

Risk of recurrence after a single manic or mixed episode – a systematic review and meta-analysis

Lars Vedel Kessing1,2 | Per Kragh Andersen3 | Maj Vinberg1,2

respectively. Results from meta-analyses showed a 1-year rate of recurrence of 35% (95% confidence interval [CI]: 30-41%) in adults, and in adolescents/children, a 1-year rate of recurrence of 48% (95% CI: 38-58%), a 2-year rate of 46% (95% CI: 33-60%) and a 4-5-year rate of recurrence of 65% (95% CI: 52-77%; as data from different
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Treatment in First Episode Affective Psychosis

• No equivalent of RAISE/NAVIGATE in affective psychosis
• Only two randomized clinical trials testing generic bipolar disorder pharmacotherapy recommendations in first episode:
  • Conus et al 2015 – lithium+olanzapine vs. lithium+chlorpromazine
  • Berk et al 2017 – lithium vs. quetiapine showed mixed results over 12 months following first episode mania
    • Possible benefit for lithium
• Role of IPSRT, CBT, FFT
Treatment in First Episode Affective Psychosis

- In clinical experience, interventions from FEP literature show great benefit
  - Recovery-oriented person-centered care
  - Harm reduction through reduction of substance use
  - Supported employment/education
  - Family psychoeducation
Highlights of Bipolar Disorder Pharmacotherapy

• Treat acute mania with mood stabilizer + antipsychotic
  • Lithium is the first line mood stabilizer
  • Antipsychotics are strongly antimanic but taper off 6-12 months after episode

• Treatment of acute depression (major unmet need)
  • Ensure patient adequately mood stabilized
  • Consider Lamotrigine/Quetiapine/Aripiprazole/Lurasidone
  • Use antidepressants sparingly, and never without mood stabilizer on board

• Maintenance treatment
  • Long term Lithium treatment associated with salutary prophylactic effect
Starting lithium prophylaxis early v. late in bipolar disorder

Lars Vedel Kessing, Eleni Vradi and Per Kragh Andersen

Overview of international and national guidelines for bipolar disorder.

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Author(s)</th>
<th>Year</th>
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<th>Adolescents</th>
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<td>(Early Psychosis Guidelines Writing Group and EPPIC National Support Program, 2016)</td>
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<td>National Institute of Health and Care Excellence (NICE) (National Collaborating Centre for Mental Health (UK), 2014)</td>
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+ One to two sentences relevant to early stage BD or adolescents.
+ + More than two sentences relevant to early stage BD or adolescents.
+ + + More than one paragraph relevant to early stage BD or adolescents.
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Table 2: Recommended interventions for first-episode mania from current clinical guidelines
Treatment in First Episode Affective Psychosis

- Major unresolved question: when is maintenance pharmacotherapy indicated?
  - I.e. do we continue Lithium indefinitely in someone who had excellent recovery from first episode mania?
- McLean experience: many individuals can tolerate cross-taper to Lamotrigine monotherapy
  - Not routine discontinuation of all pharmacotherapy
- What is the risk/benefit calculus for long-term treatment?
The case for improved care and provision of treatment for people with first-episode mania

Sameer Jauhar*, Aswin Ratheesh*, Christopher Davey, Lakshmi N Yatham, Patrick D McGorry, Phillip McGuire, Michael Berk, Allan H Young

The care of people with first-episode mania has been overlooked in comparison with the care of patients with other non-affective psychoses, despite evidence suggesting targeted treatments might be of benefit for this patient group. In this Personal View, we outline the general epidemiology of first-episode mania in the context of bipolar disorder, the natural history of mania (with an emphasis on its recurrent nature), current evidence for pharmacological, psychological, and service-level interventions, current guidelines for the treatment of first-episode mania, and provide a patient’s point of view of the care pathway (appendix). We note the paucity of high-quality evidence for interventions in first-episode mania and the lack of agreement among treatment guidelines in relation to treatment, especially maintenance treatment. We suggest that, based on high morbidity and clinical need, research evidence to inform guideline development is necessary, and in the interim, clearer guidance on treatment and diagnosis should be given; specifically, we have suggested that patients should be cared for within a first-episode psychosis service, when such a service exists.

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Clinical Experience in First Episode Affective Psychosis

• Deep depression commonly seen following first episode mania
  • Implications for self-image and treatment alliance
• Good alliance and adherence to treatment are common
• Cannabis/Psychostimulants become points of contention
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Conclusions

• Affective psychosis is commonly seen in early psychosis services
  • Don’t miss mania!

• These young people belong in our services
  • Diagnostic fluidity in early phase
  • Evidence slim but likely benefit
  • Many needs similar, some divergent

• Great need for additional research and treatment development for this population
Thank you!