Elucidating Predictors and Mechanisms of the Onset of Psychosis, Using the Clinical High Risk Strategy

• Increased risk of developing schizophrenia:
  – Accelerated loss of gray matter, especially in prefrontal cortical regions
  – Factors related to stress reactivity, especially elevations in cortisol
  – Factors associated with impaired brain plasticity measured by electrophysiology
  – Peripheral biomarkers of inflammation
  – Clinical criteria related to altered thought process

Mechanisms of Anti-inflammatory Treatment in Schizophrenia

• Persistent infection and neuroinflammation is potentially etiologic in schizophrenia
• Biomarkers for schizophrenia are emerging, including elevations in pro-inflammatory cytokines.
• Efficacy of anti-inflammatory medications as adjunctive treatment for schizophrenia.
  – Aspirin, other NSAIDs, minocycline, antiviral agents

Genetics and Genomics in Psychiatry: Implications for Biology, Diagnosis and Treatment

- Schizophrenia and other psychiatric disorders
  - Multiple genetic vulnerability factors
    - Common polymorphisms – alterations that are widely shared
    - Rare polymorphisms – i.e. that impact schizophrenia risk
    - Few have significant impact on risk

- Genomic landscape has greater impact than previously realized

- Neurobiology of the illness more challenging to understand

Changes to DSM 5: Schizophrenia

- At least one core psychotic symptom required for diagnosis
  - Delusions, hallucinations, disorganized speech
- Differentiation between core features and accompanying features, which will help in differential diagnosis
- Introduction of dimensions of psychotic disorders
- Eliminate current subtypes
- Include diagnosis of “attenuated psychosis syndrome” as condition for further study
- Modify criteria for schizoaffective disorder
- Treat catatonia uniformly across manual
Dimensions of Schizophrenia in DSM 5:

- Reality distortion – Delusions
- Reality distortion – Hallucinations
- Depression
- Mania
- Negative symptoms
- Disorganization
- Psychomotor symptoms, including catatonia
- Impaired cognition

(To be rated on 0-4 scale: 0 – not present; 1 – equivocal; 2 – mild; 3 – moderate; 4 – severe)
Summary of Changes from ICD-10 to ICD-11

- Introduction of **symptom** specifiers and new **course** specifiers
- Schizophrenia **subtypes** will be **omitted**
- Schizophrenia **first-rank symptoms** will be **deemphasized**
- **Symptom criteria** of schizophrenia and mood disorder of moderate or severe degree are required for diagnosis of schizoaffective disorder
- Major restructuring of **ATPD** and **delusional disorders**
- **Attenuated psychosis syndrome** not a separate mental disorder
• 444 schizophrenic patients treated over 15 months
  – Selected patients who had been incarcerated
  – Patients given prescription, not drug, to monitor adherence
  – Non-adherent patients continued in study
• Primary Endpoint: treatment failure (arrest/incarceration, psychiatric hospitalization, suicide, treatment stoppage or supplementation due to inadequate safety, efficacy, tolerability, increased psychiatric services)

Trajectories of Antipsychotic Response in Drug-naive Schizophrenia Patients: Results from the 6-month ESPASS Follow-up Study

• Retrospective review of pharmacy records in 467 treatment-naïve schizophrenic patients in France
• Subgroup analysis of larger study started in 2005-2006
• Primary outcome: CGI severity
  – Most patients very symptomatic at baseline

Responses to Therapy in Schizophrenia

Subgroups:

• Rapid response, decline from moderately severe to minimal
  – Still moderately ill at 1 month; symptom free to 6 months
  – 10% of patients

• Gradual response
  – Marked to mild-moderate over 6 months
  – 44% of group

• Remained mildly ill
  – Markedly symptomatic at 6 months
  – 28% of group

• Unsustained clinical improvement
  – Started at mild; Stayed at mild
  – 13% of group

• Remained very ill
  – Started at severe; stayed at marked to severe
  – 5% of group

Early Improvement Predicts Endpoint Response to Lurasidone in Schizophrenia: Pooled Analysis of Five Double-blind Trials

- 5 similar 6-week trials
- Approximately 1000 patients
- Acute exacerbation of schizophrenia
- Lack of PANSS improvement at week 3 was highly predictive of non-response at week 6

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