Research Update on Schizophrenia

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Two themes of research in schizophrenia

• The course of schizophrenia in the first ten years: the benefits of treatment, changes in diagnosis and the effects of marijuana.

• The prevention of schizophrenia in future generations: can you protect your grandchildren?
What effect does marijuana have?

Accelerated loss of brain volume in patients who use cannabis.

(From Am J Psychiatry 2008; 165:490–496)
Myth—The first doctor told me that my son had schizoaffective disorder, but the new doctors think it’s schizophrenia.
How much difference do services in the community make?

Better participation leads to better compliance with medication and lower doses.
Will there be a job?

Figure 1. Percentage of individuals with psychiatric disabilities who received or did not receive supported employment services who had any earned income (2000–2012).

- Supported employment group (N=234)
- Control group (N=215)

In multivariable longitudinal random logistic regression models, supported employment participants were significantly more likely to have any earned income than control group participants (odds ratio = 2.89, p = 0.022).

Cook JA AJP 2016, in press
Are the newest drugs the best drugs?

Myth: My doctor tried everything, but then she finally found something that works.
Schizophrenia 2016: Summary

1. People are getting better.
2. Diagnoses are not the issue they seem to be.
3. New medications are not improving outcome (although they decrease side effects).
4. There are benefits of early treatment: better outcomes and fewer suicides.
5. Marijuana adds to the loss of cognitive function.
6. Fewer than 1 of 10 people return to long term, full time employment.
7. Don’t overlook clozapine.
Schizophrenia 2016: Summary: A Ceiling on Effectiveness

1. New medications are not improving outcome.
2. There are some benefits of early treatment: better outcomes and fewer suicides, but these benefits are small.
3. Marijuana adds to the loss of cognitive function.
4. Fewer than 1 of 10 people return to long term, full time employment.
5. 10% commit suicide or other violent acts, including mass shootings.
Are we seeing the real problem? James Craik MD worries about his fatal bleeding of Washington for a sore throat in 1799, a condition that has been routinely cured by penicillin since 1950.
A clue: People with schizophrenia smoke more heavily than any other group. They activate alpha 7 nicotinic receptors, which are genetically abnormal in schizophrenia. How can we do better than give patients cigarettes?

“Very soon, being without a pack of cigarettes made me very uneasy.”

If schizophrenia is a genetic illness, and... genes are the blueprint that builds the brain before birth, why don’t we intervene then?
Early brain dysfunction in newborns who will later develop schizophrenia has long been known.
The brain develops before birth using a series of neurotransmitter “operating systems.”

Alpha7 nicotinic receptors, one of the receptors abnormal in schizophrenia, help install the new systems.
In the fetal brain, alpha 7 nicotinic receptors are more widely distributed than in adults, consistent with their greater activity then.
In the fetal hippocampus, alpha 7 nicotinic receptors are more widely distributed. ....but how are they activated?
Choline activates nicotinic receptors before birth

- Normal ingredient in liver, eggs, and meats.
- Pregnant women often cannot keep up with the demands of the baby.
- Stress, anxiety, depression, infection, and nicotine use during pregnancy all increase the risk for mental illness in the baby and may be overcome by increasing choline.
- The single greatest risk factor, genetic risk, may be overcome by increasing choline as well. Phosphatidylcholine is available as a natural vitamin.
Normal genes and nutrition

Genetic and nutritional deficiencies

Can choline supplements overcome deficiencies?
Choline prevents the childhood behavioral difficulties that people with schizophrenia had in their childhoods. It moves the needle of risk back.

- Social Withdrawal
- Attention Problems

Perinatal choline

3-4 year old

Adult Schizophrenia

Folic acid is an example of a nutrient that prevents the developmental abnormality cleft palate before birth (Wilcox 2007)
Like folic acid, choline is effective only before birth; you cannot wait until later when you are already ill.
Fetal life is only Step 1 in brain development. Each step is part of the risk for future mental illness.

<table>
<thead>
<tr>
<th>Synaptic Density</th>
<th>At birth</th>
<th>6 years old</th>
<th>14 years old</th>
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Source: Rethinking the Brain, Families and Work Institute, Rima Shore, 1997; Founders Network slide
Better treatment for schizophrenia now and in the future

• Now: Maximize support services in the community, try clozapine before switching to newer drugs (it’s more effective), and avoid marijuana (easier said than done).

• In the future: Interventions from before birth to prevent the illness.