

Running out of Energy: Metabolic Problems in Psychotic Disorders

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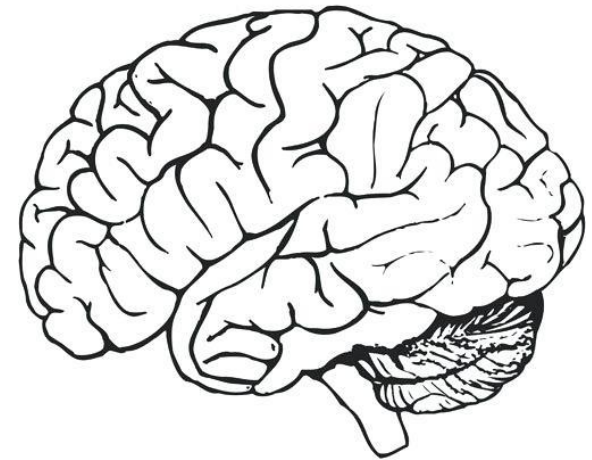
Psychotic Disorders

- Schizophrenia, schizoaffective disorder, bipolar disorder, and related conditions
- Devastating illnesses
 - Common (up to 3% of all people)
 - Strike young (majority are diagnosed 16-25 years old)
 - Chronic relapsing remitting course
 - Can be lethal (suicide)
- Costs to individual and families incalculable
- Costs to society >150 billion dollars/year in US

Psychotic Disorders

- Hallmarks:
 - Delusional thinking
 - Hearing voices
 - Depression and mania
 - Cognitive impairment
 - Inability to care for self, live independently, hold a job, maintain meaningful relationships
- Described since antiquity yet etiology remains enigmatic

Brain Abnormalities in Psychotic Disorders

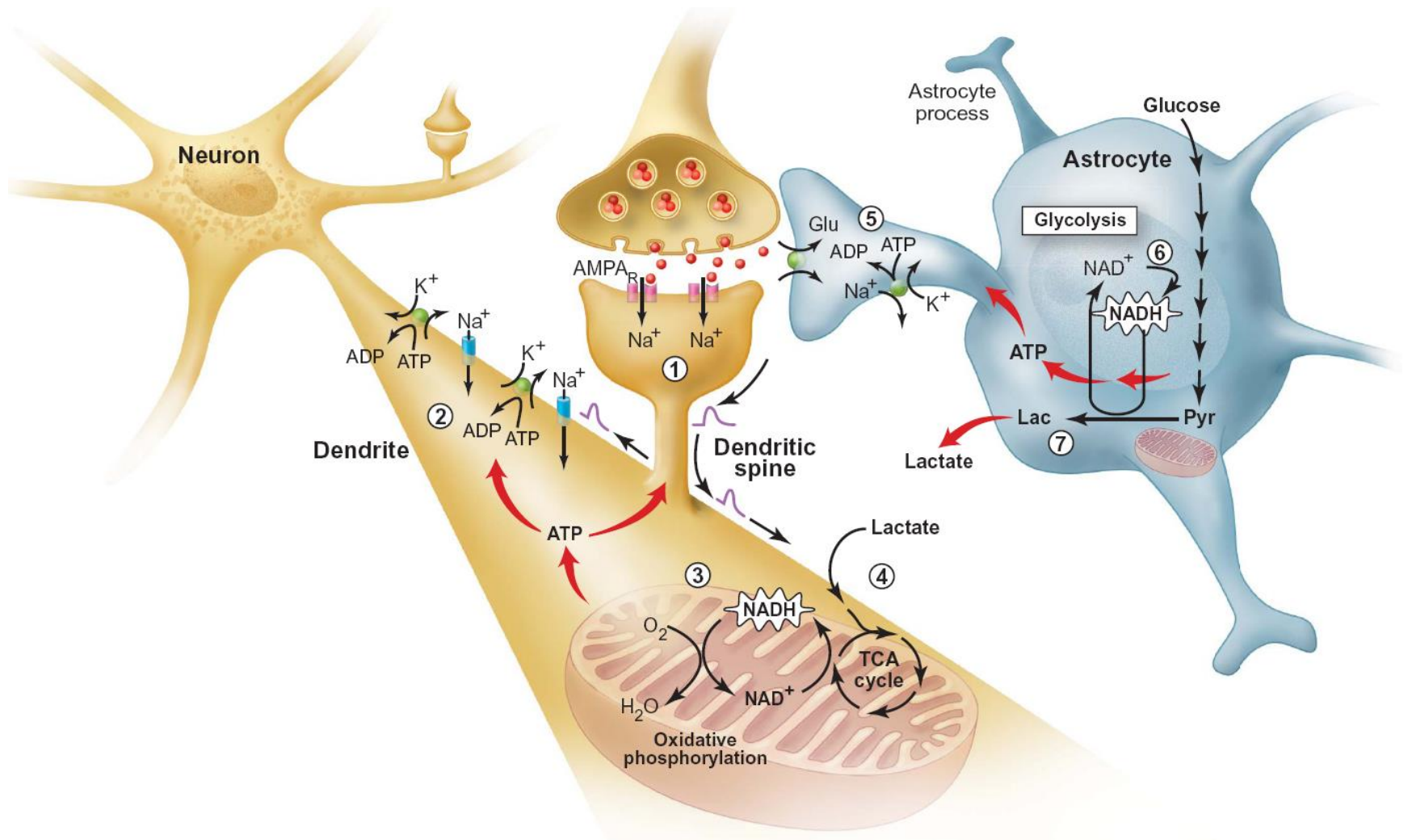




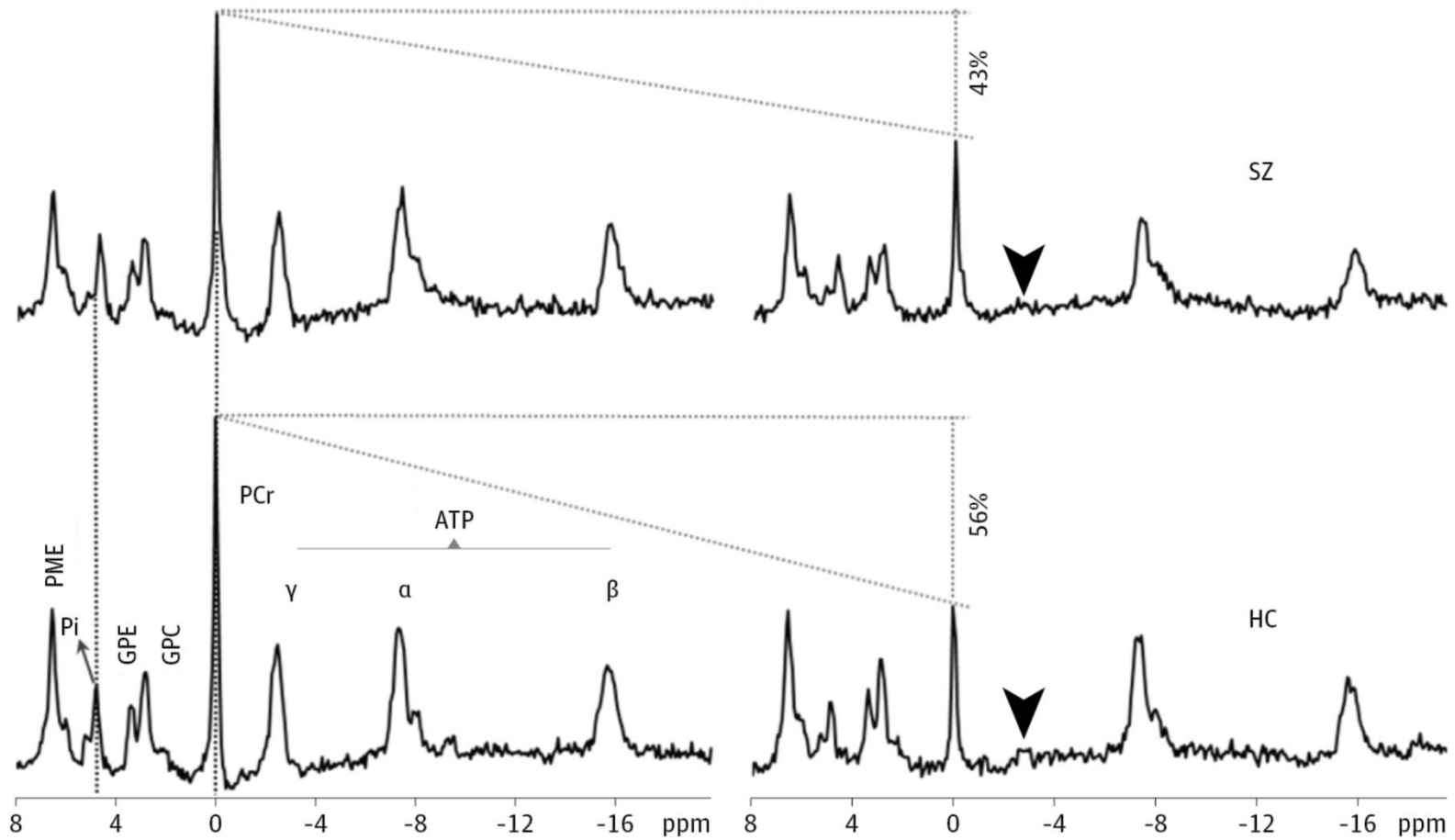
Psychotic Disorders

- Brain illnesses
- Widespread but subtle abnormalities in brain structure, activity, chemistry
- Large number of genetic risk factors
- Abnormalities in nerve cell communication: activity patterns and information processing

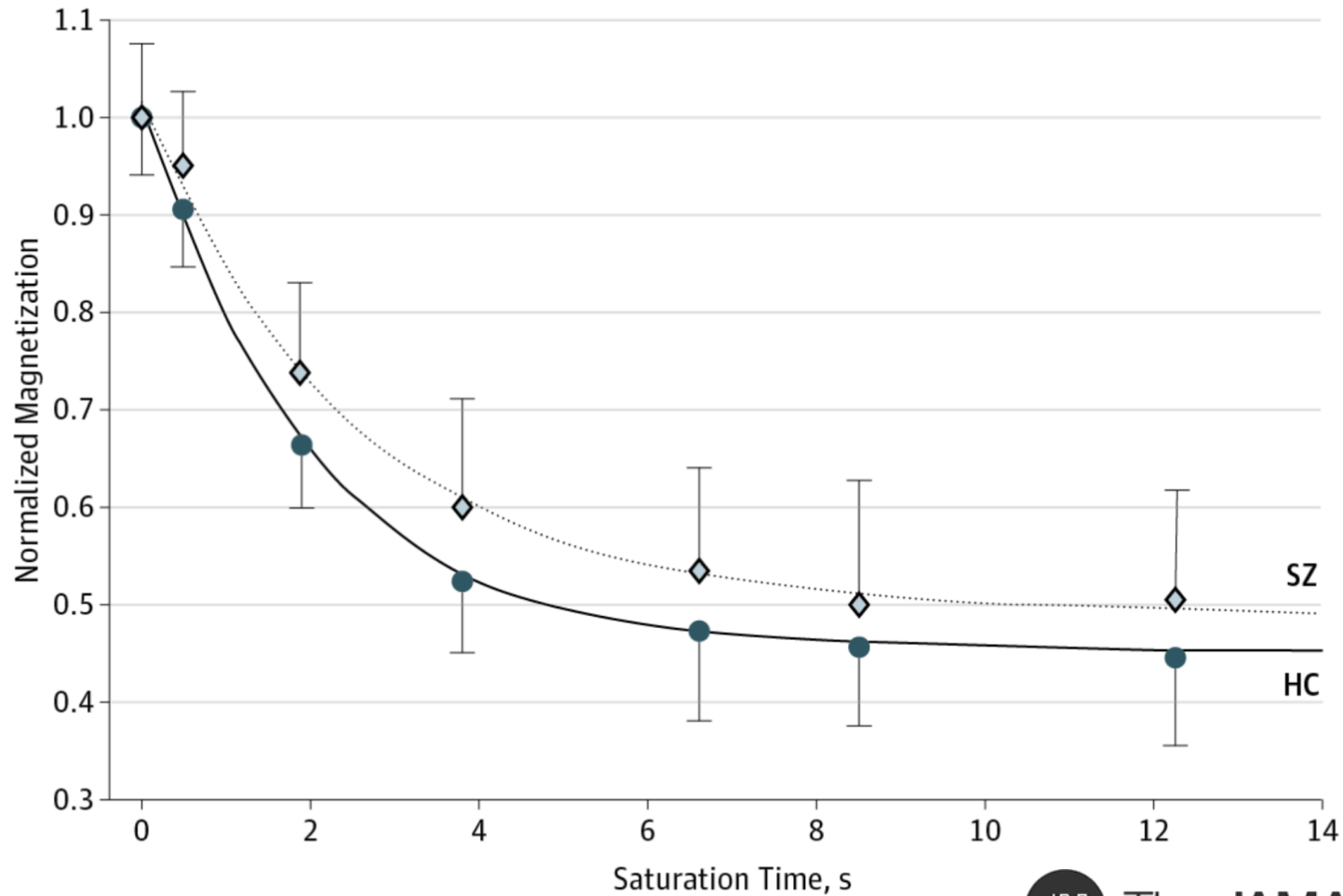
Nerve Cell Communication



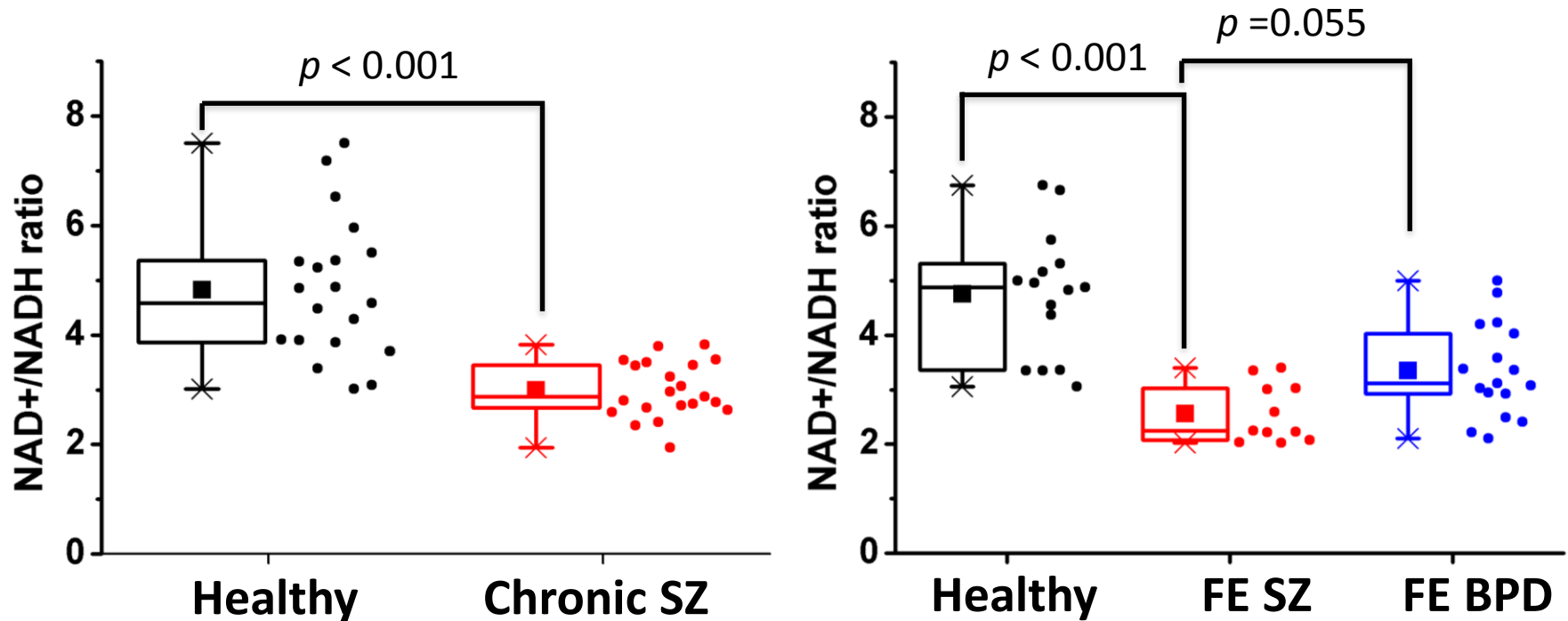
From: In Vivo Evidence for Cerebral Bioenergetic Abnormalities in Schizophrenia Measured Using ³¹P Magnetization Transfer Spectroscopy
JAMA Psychiatry. 2014;71(1):19-27. doi:10.1001/jamapsychiatry.2013.2287



Energy Deficiency in Schizophrenia



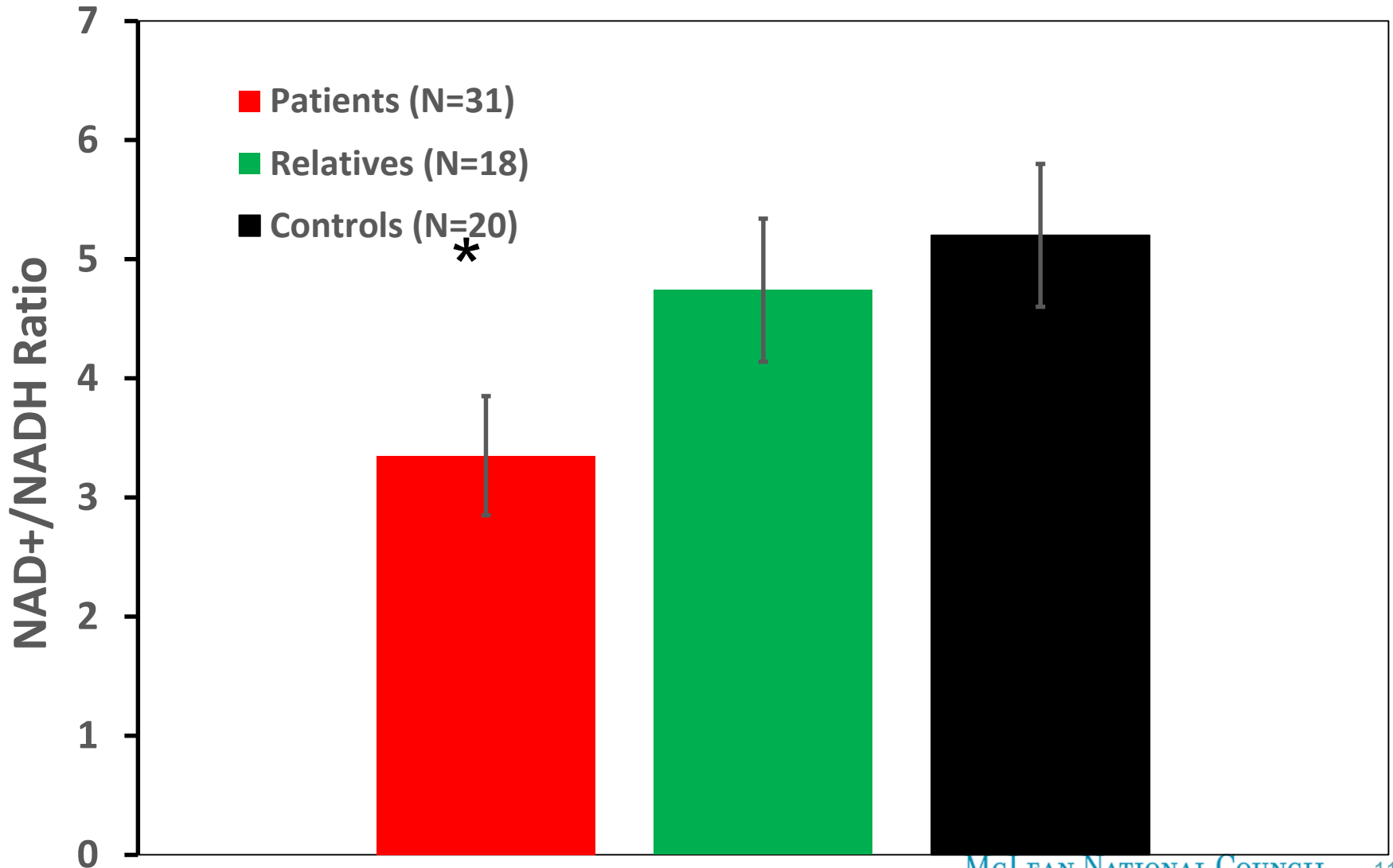
Low Energy Production Associated with Greater Brain Damage



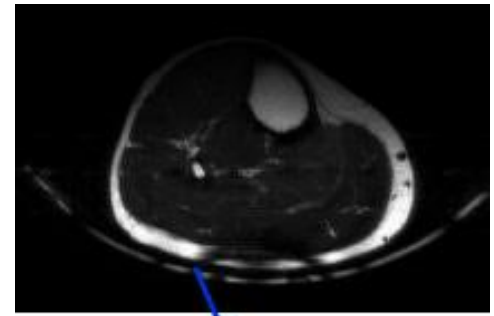
FE: First episode; SZ: Schizophrenia; BPD: Bipolar Disorder

NAD⁺/NADH ratio: a key player in managing harmful by-products of energy production

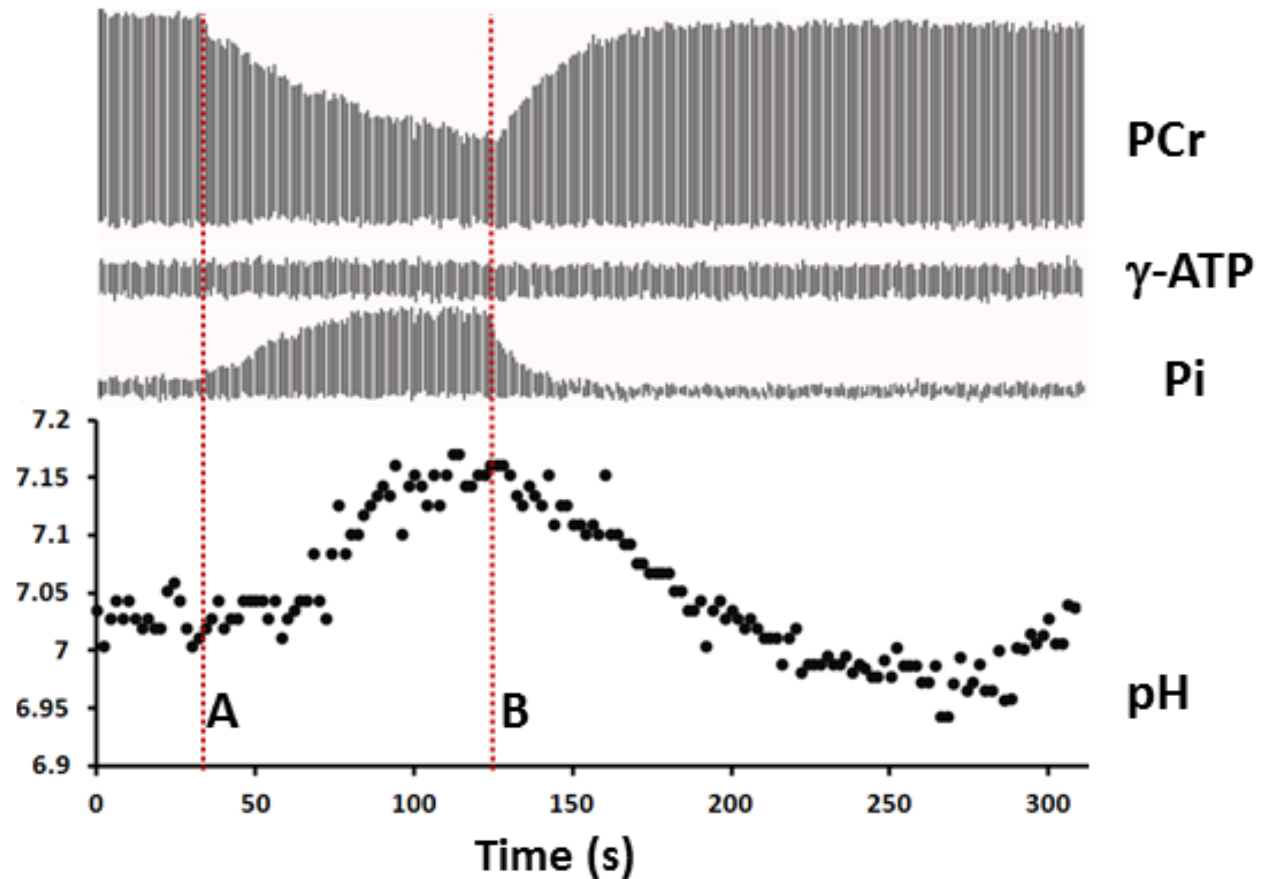
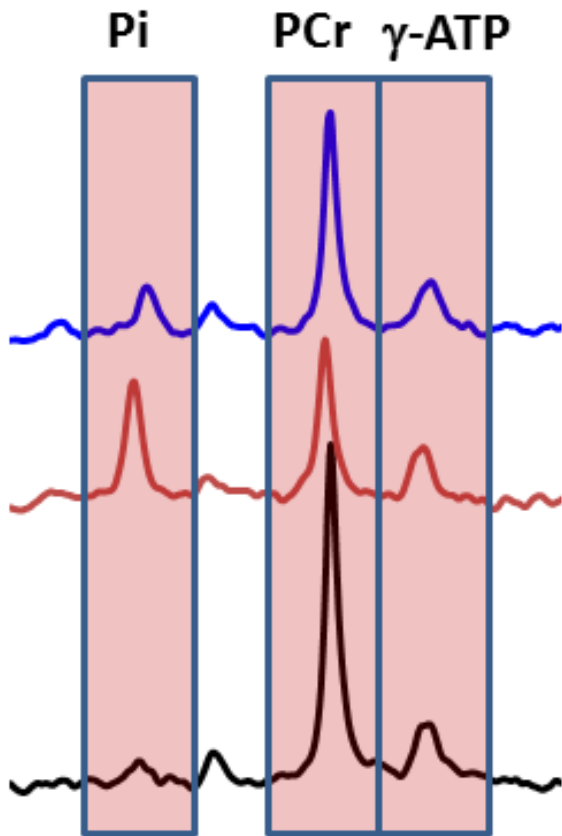
Evidence for Genetic Factors Underlying Brain Abnormality in Unaffected Siblings of People with Psychotic Disorders



31P MRS Studies in Calf Muscle



31P surface RF coil



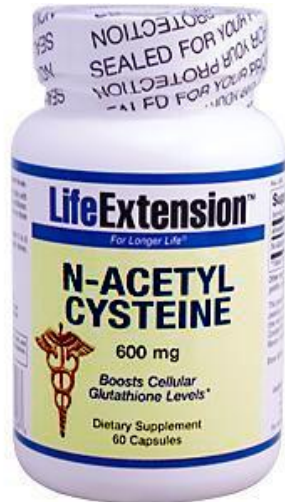
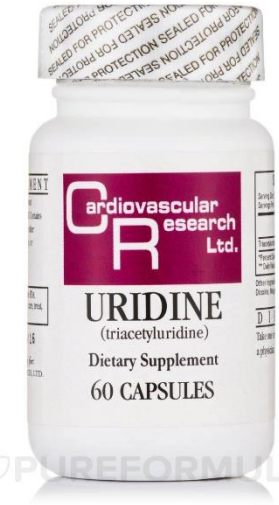
Implications

- Major abnormalities in brain bioenergetics in psychotic disorders
- Abnormalities are present at disease onset and in unaffected first-degree relatives
 - Support for ongoing genetic studies (collaboration with the Broad Institute)

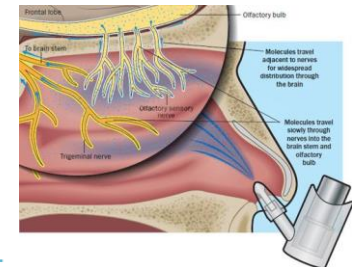


THE CHARLIE FOUNDATION

for Ketogenic Therapies



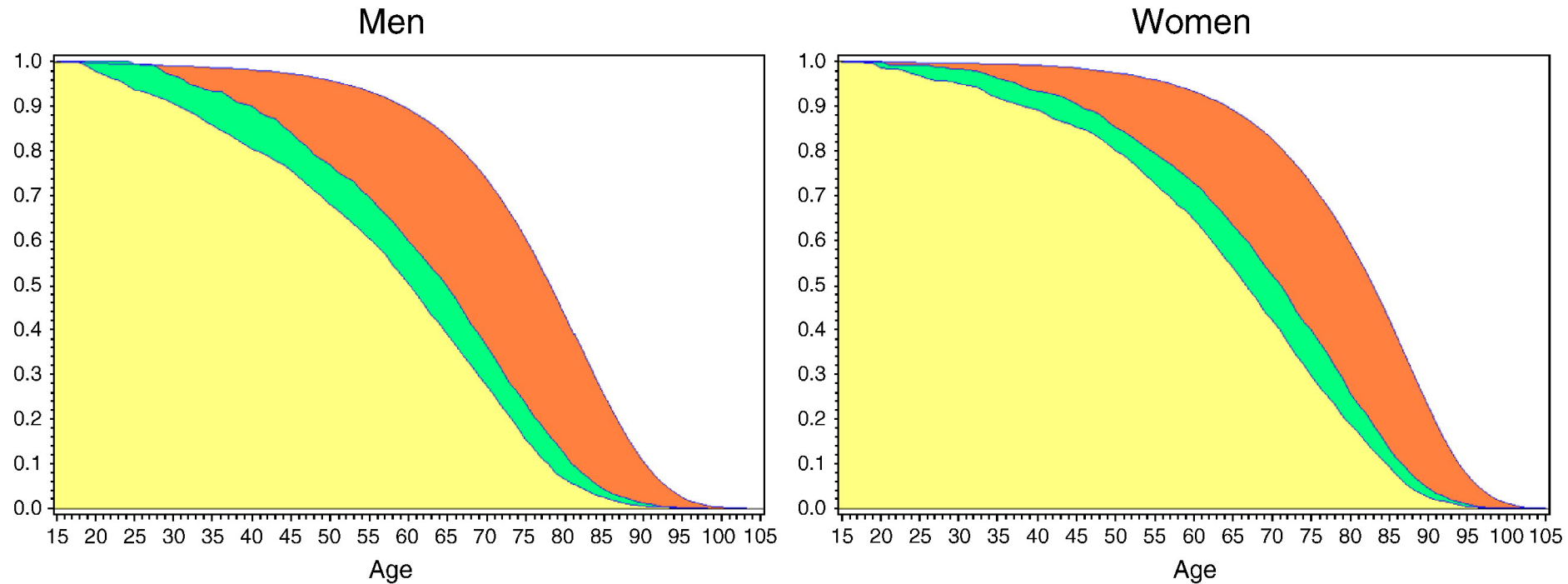
Study of Nasal Insulin to Fight Forgetfulness (SNIFF)





Cardiometabolic Mortality in Psychotic Disorders

Premature mortality in Schizophrenia (Yellow) and Bipolar Disorder (Green) compared with the general population



Life expectancy and cardiovascular mortality in persons with schizophrenia

Thomas M. Laursen^a, Trine Munk-Olsen^a, and Mogens Vestergaard^b

Purpose of review

To assess the impact of cardiovascular disease on the excess mortality and shortened life expectancy in schizophrenic patients.

Recent findings

Patients with schizophrenia have two-fold to three-fold higher mortality rates compared with the general population, corresponding to a 10–25-year reduction in life expectancy. Although the mortality rate from suicide is high, natural causes of death account for a greater part of the reduction in life expectancy. The reviewed studies suggest four main reasons for the excess mortality and reduced life expectancy. First, persons with schizophrenia tend to have suboptimal lifestyles including unhealthy diets, excessive smoking and alcohol use, and lack of exercise. Second, antipsychotic drugs may have adverse effects. Third, physical illnesses in persons with schizophrenia are common, but diagnosed late and treated insufficiently. Lastly, the risk of suicide and accidents among schizophrenic patients is high.

Summary

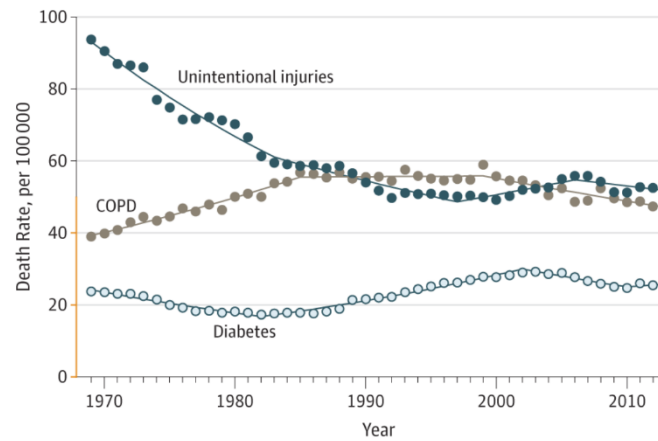
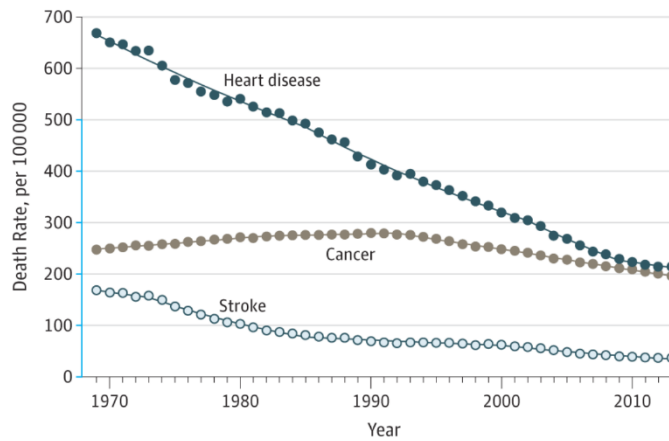
Schizophrenia is associated with a substantially higher mortality and curtailed life expectancy partly caused by modifiable risk factors.

Keywords

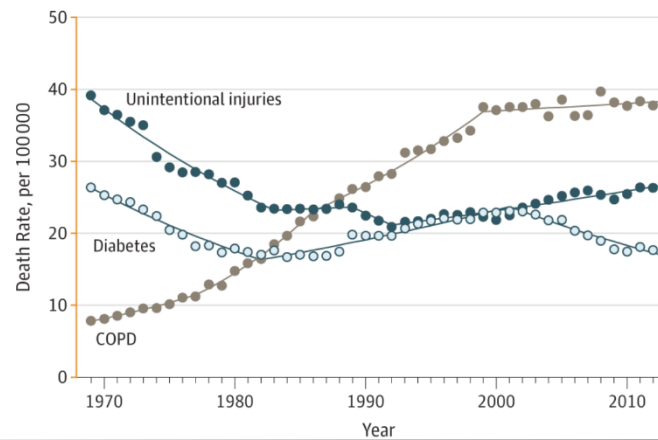
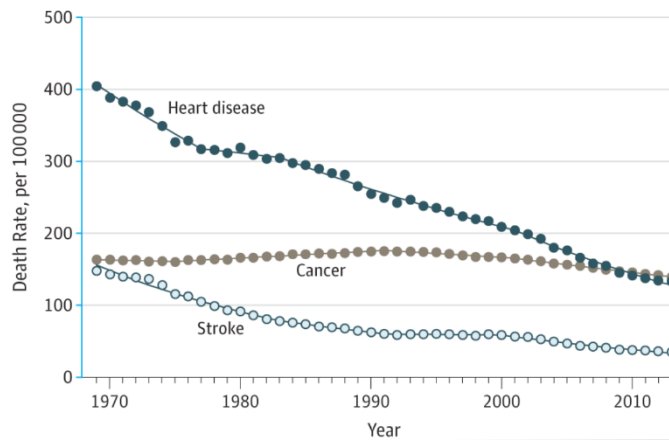
cardiovascular disease, life expectancy, mortality, physical illness, schizophrenia


From: Temporal Trends in Mortality in the United States, 1969-2013
 JAMA. 2015;314(16):1731-1739. doi:10.1001/jama.2015.12319

A Male



B Female



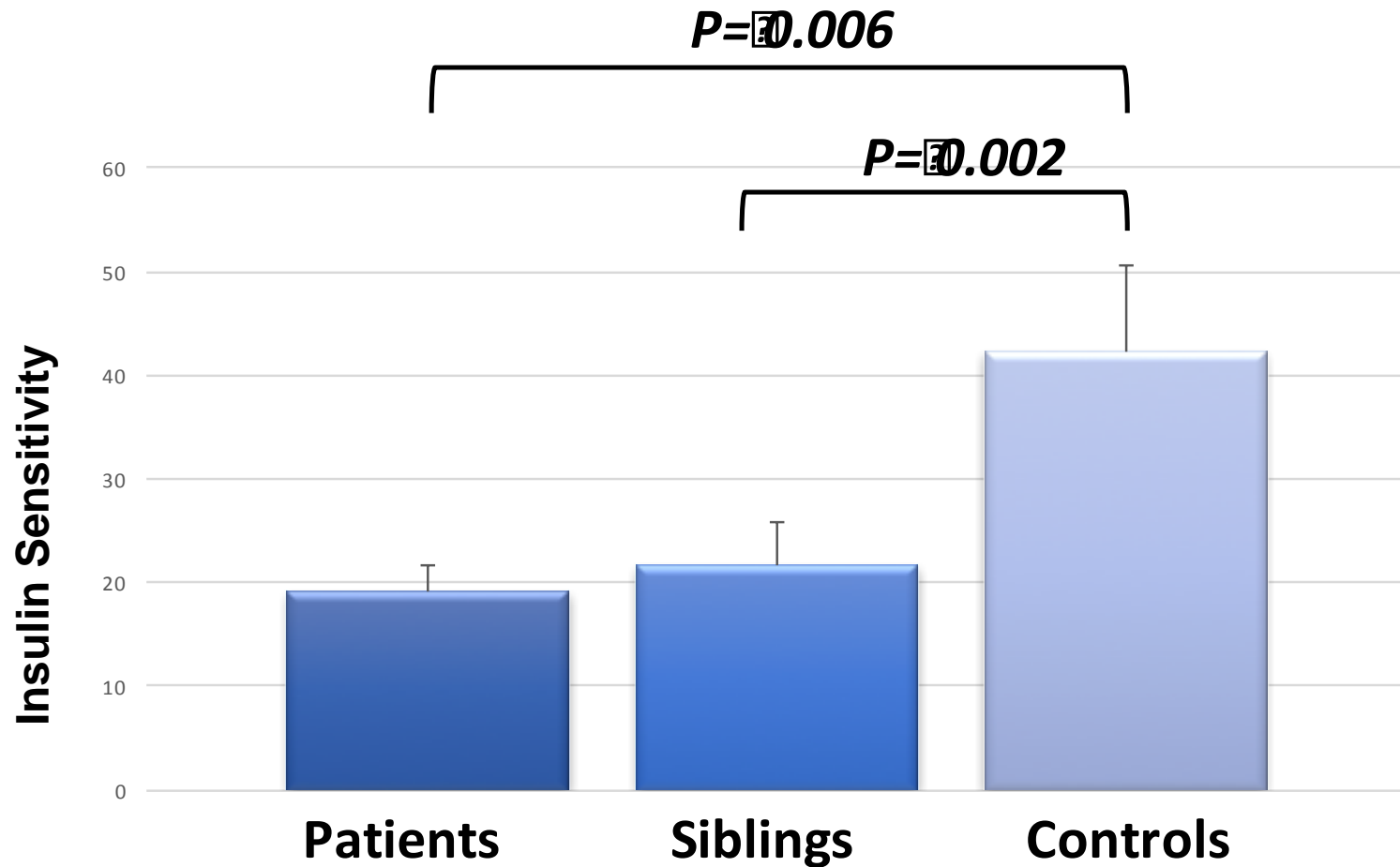
- 
- Fragmentation of care
 - Diffusion of responsibility
 - Lack of interest from psychiatrists
 - Reimbursement and time management issues
 - Adherence
 - Complex regimens
 - Side effects and adverse events
 - Cost
 - Illness-specific factors – symptoms, cognition etc.

Risk Factors

- Sedentary lifestyle
- Tobacco smoking
- Antipsychotic medication exposure
- Poor medical care: access, stigma, adherence
- Disease-specific metabolic vulnerability:
 - Weight gain, insulin sensitivity, diabetes mellitus



Disease-Specific Metabolic Vulnerability



- Lower insulin sensitivity is a forerunner to diabetes
- Correlated with cognitive function



Bending the Mortality Curve?

- Treat underlying biological vulnerability
- Improve primary care interventions
- Support healthier lifestyle for patients
- Develop innovative tools to reach patients and enhance behavior change

Goings-on at McLean Hospital

FITNESS – Fixed Dose Intervention Trial of New England Enhancing Survival in Serious Mental Illness Patients



Presenting the 2017

Technology in Psychiatry Summit

Building a More Accessible Future



November 6-7, 2017
Harvard Medical School
Boston, MA



FITNESS – Fixed Dose Intervention Trial of New England Enhancing Survival in SMI Patients

- Started 9/15/2014; enrolled first participant Jan 2015; 4 year study
- 300 patients randomized to:
 - Fixed low dose combination of a cholesterol lowering agent and an angiotensin drug
 - Or treatment as usual
- Intervention: Simvastatin PO 20mg daily and Losartan PO 25mg daily
- Open-label; there is no placebo
- Total compensation for completing all study visits: \$420
- Sites: McLean Hospital; MGH Bipolar Clinic; MMHC; BayCove Gill Clinic

FITNESS – Fixed Dose Intervention Trial of New England Enhancing Survival in SMI Patients

- “Population-based” approach
 - Low-cost medication; fixed low dose; based in MH clinic
- APRNs follow patients in mental health clinics for 12 months
 - “Primary care” intervention embedded within mental health care
- Primary outcome measure: **adherence**
- Secondary measures:
 - Can we modify cardiovascular risk profile?
 - Many other variables will be measured
 - Symptoms, cognition, perceptions of care
- Experience so far:
 - Enrollment at 240 patients
 - Good acceptability/tolerability of intervention

Acknowledgments

- McLean Hospital Center of Excellence in Psychotic Disorders team
- McLean-MGH-HSPH FITNESS study team
- McLean Hospital leadership
- Our patients and their families!



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Questions and Discussion