

**COULD WE SOMEDAY  
PREVENT SCHIZOPHRENIA  
LIKE WE  
PREVENT CLEFT PALATE?**

---

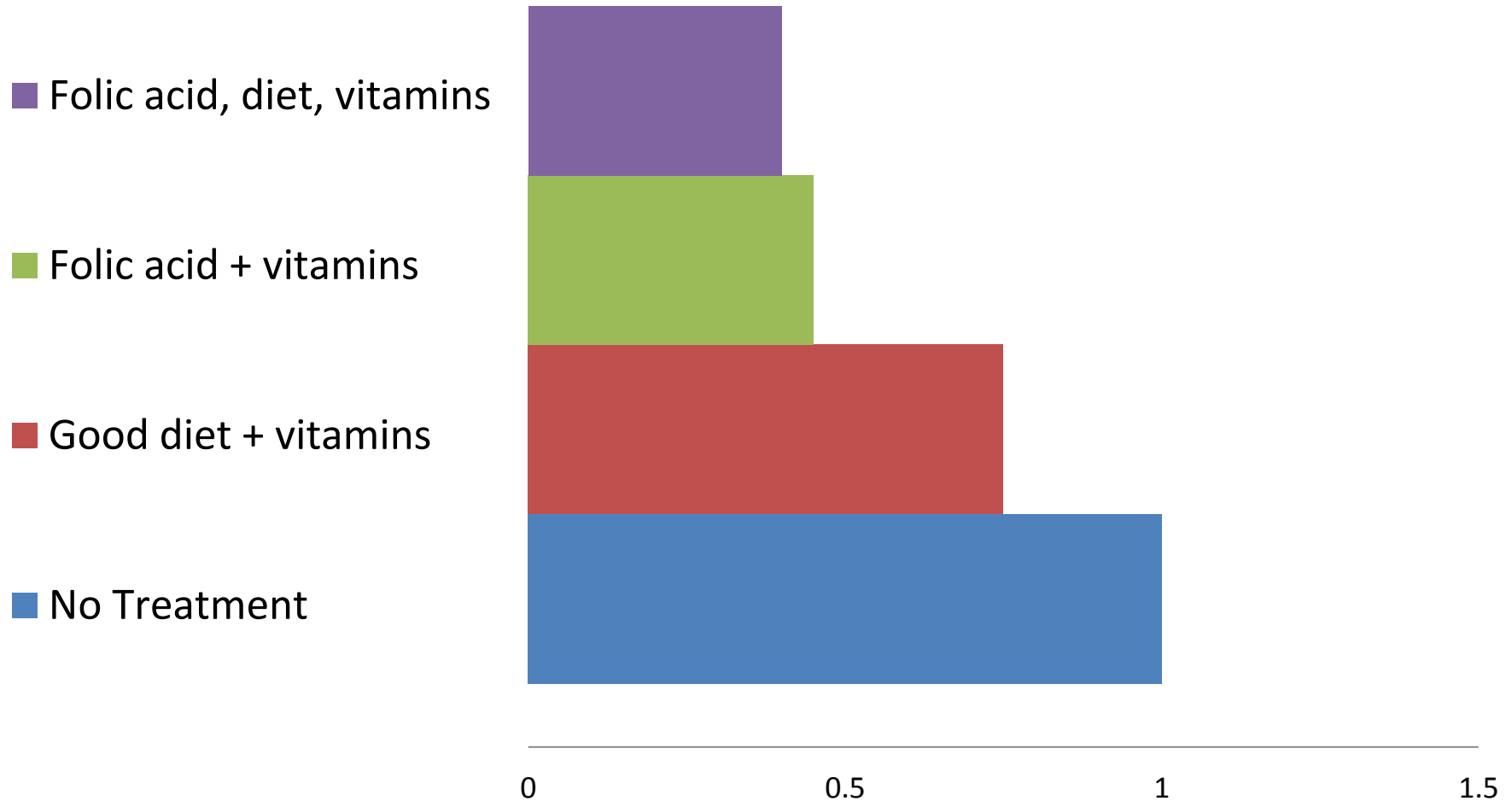
**Robert Freedman, MD**

Professor, Department of Psychiatry

University of Colorado

Editor, American Journal of Psychiatry

# Maternal folic acid supplements prevent developmental abnormalities



# Critical Periods in Development and Schizophrenia—SYMPTOMS

## Fetal and newborn brain formation

- developmental delay



## Childhood— 3-5-12 years

- ADD, social isolation



## Adolescence— 13-18 years

- Anxiety, depression, OCD, school failure, concealed hallucinations, suicide



## Early Adulthood— 18-30 years

- Chronic symptoms and disability

First Connections

Connections Bloom

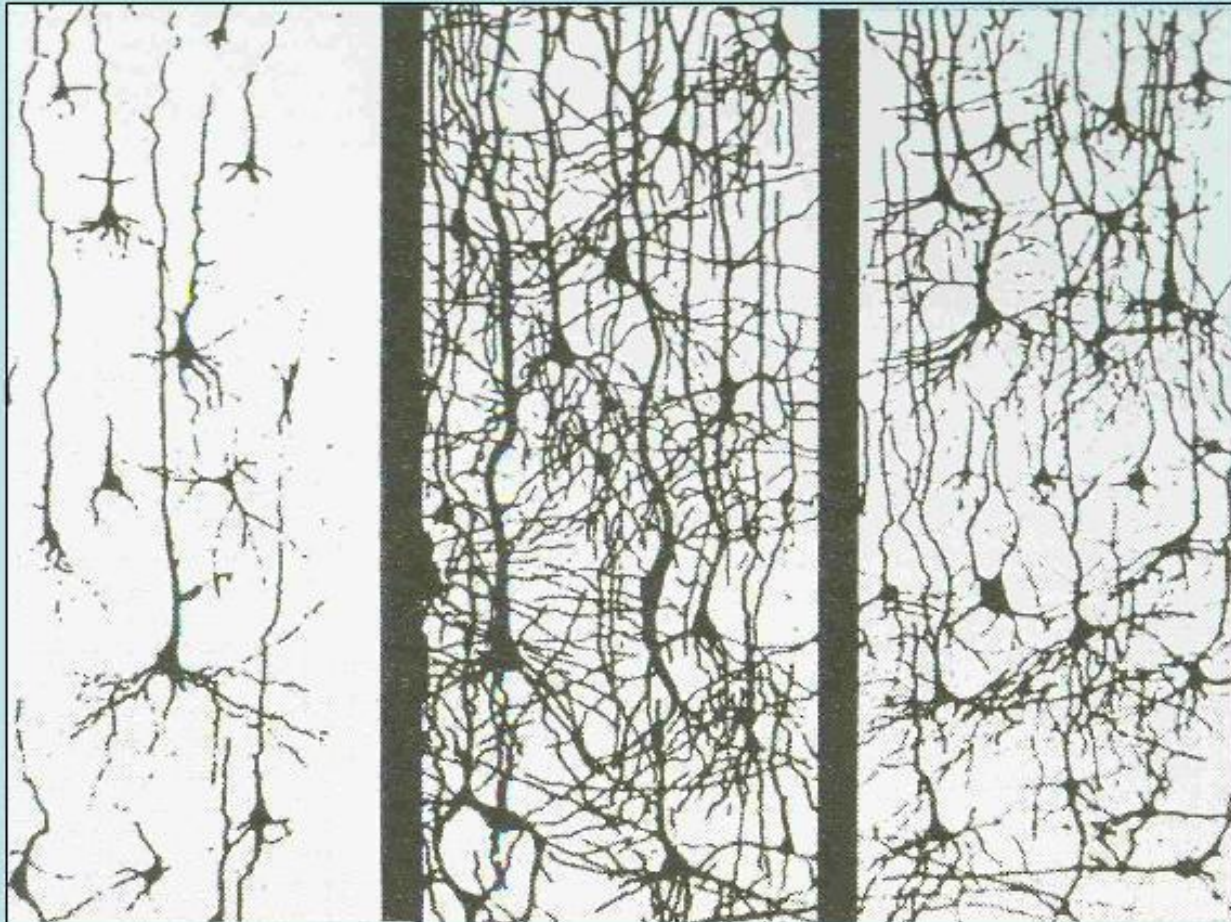
Pruning to Precision

**Synaptic Density**

At birth

6 years old

14 years old



Source: Rethinking the Brain, Families and Work Institute, Rima Shore, 1997; Founders Network slide

# Developmental Illnesses— Two Models

- Unfolding—hidden defects from before birth that do not emerge until the person develops full brain capacity
- Multiple insults—two and three hit models, first hit creates vulnerability, and second hit then becomes devastating
- Either way, persons who will develop schizophrenia cannot be identified until they actually have it, ? too late to prevent it

# Prevention of Schizophrenia

## PRIMARY

- **intervention during fetal brain development**

## SECONDARY

- intervention during the prodrome of schizophrenia in adolescence

## TERTIARY

- enhanced early treatment of first and second episodes

# Primary Prevention

**Universal treatment directed to the whole population.**

Model is folic acid in pregnancy to prevent spina bifida and cleft palate.

**Obstacles: Intervention must be simple, safe, and acceptable universally.**

**Waiting two to three decades for confirmation is daunting.**

**Where to do we start?**

# Early brain dysfunction in newborns who will later develop schizophrenia has long been known

VOL. 20, No. 3, 1994

## Neuromotor Precursors of Schizophrenia

441

---

by *Elaine F. Walker, Tammy Savole, and Dana Davls*

Abstract

also discussed.  
*Schizophrenia Bulletin*, 20(3):







Many of the same genes that will later malfunction in schizophrenia are also responsible for the development of the brain before birth.

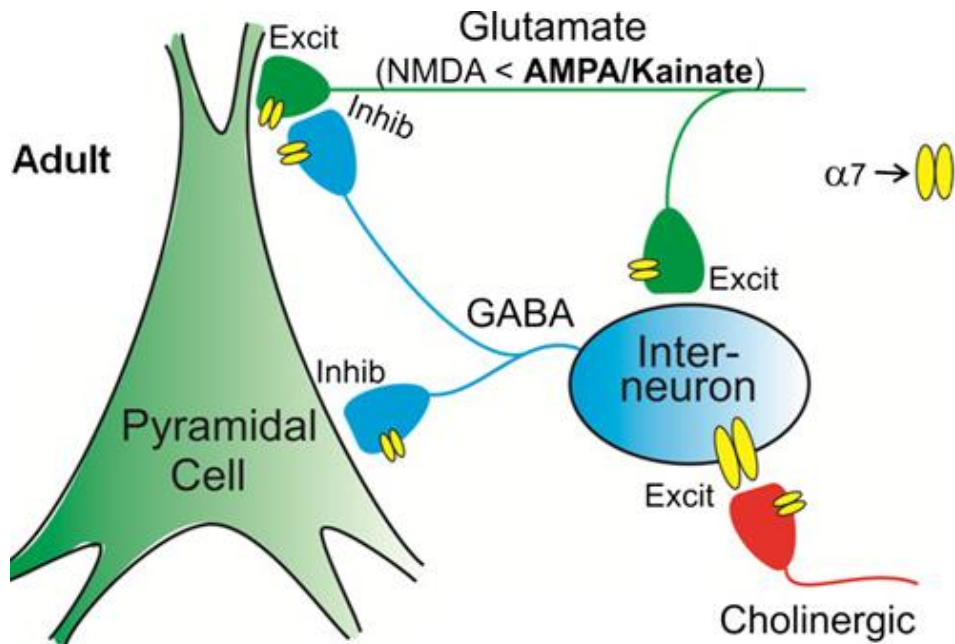
## A gene clue: People with schizophrenia smoke more heavily than any other group.

They activate alpha 7 nicotinic receptors, which are genetically abnormal in schizophrenia. How can we do better than give patients cigarettes?

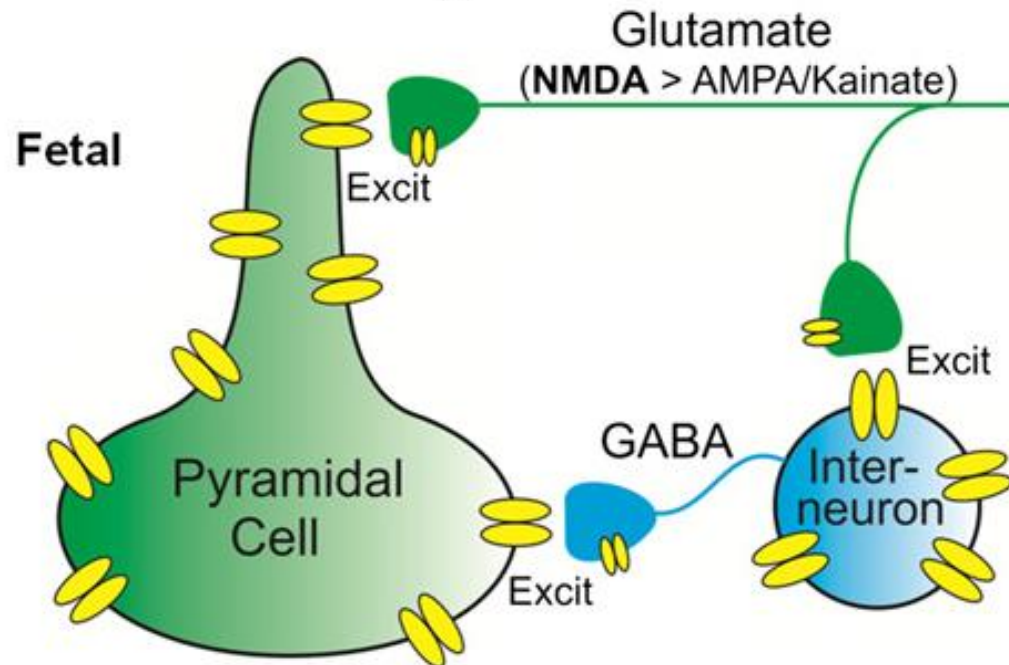


*"Very soon, being without a pack of cigarettes made me very uneasy."*

Elyn R. Saks, *The Center Cannot Hold*. 2007.



In the fetal **brain**, alpha 7 nicotinic receptors are more widely distributed than in adults.



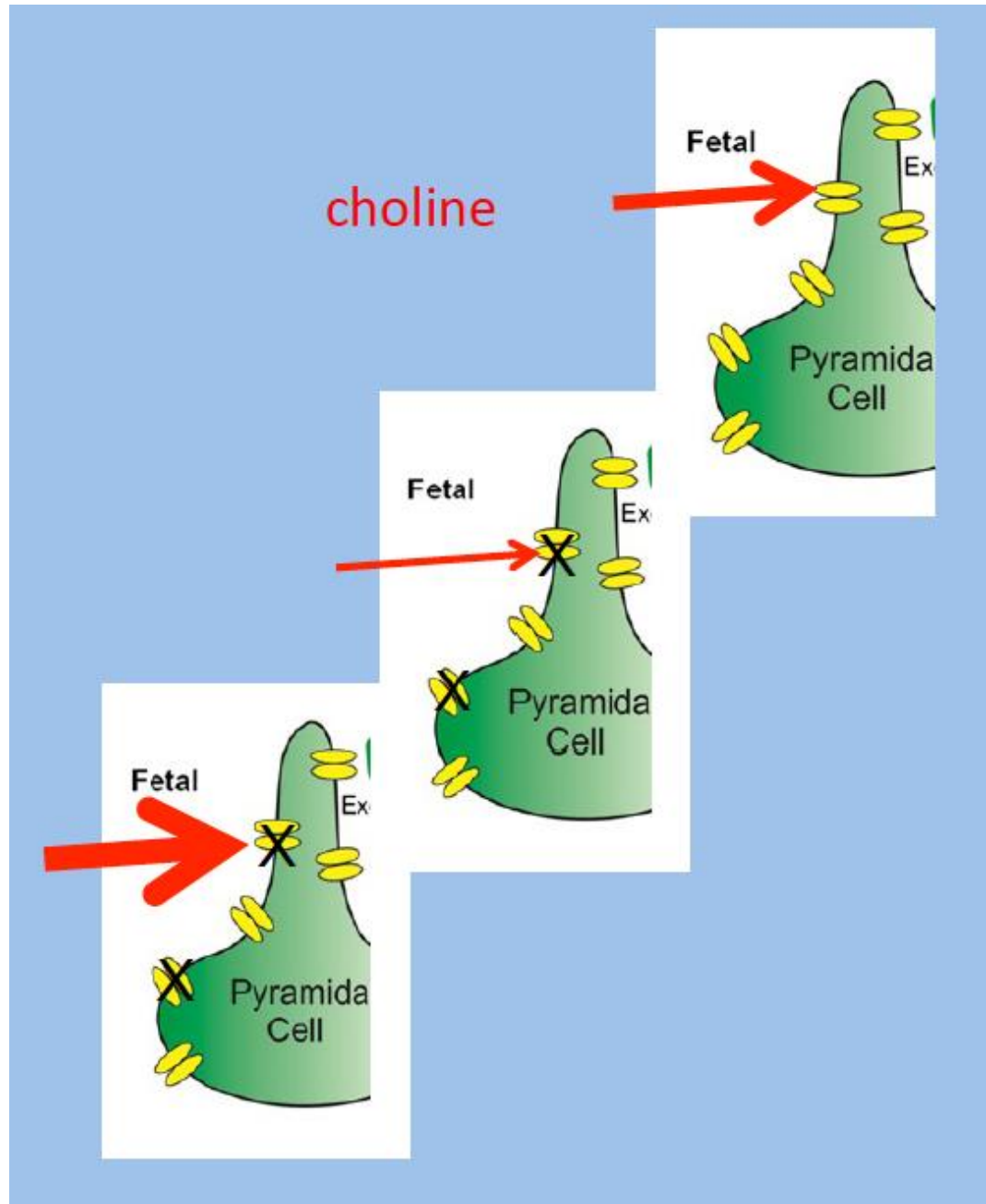
# Choline activates nicotinic receptors before birth

- 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?

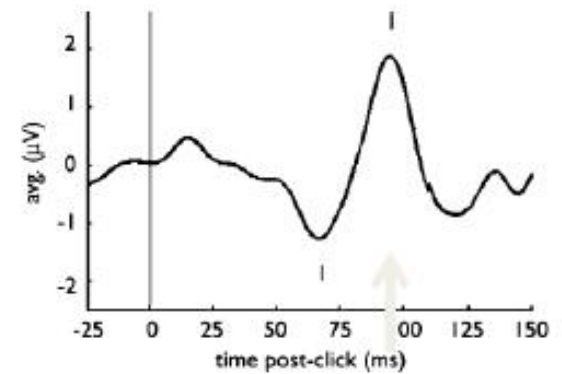
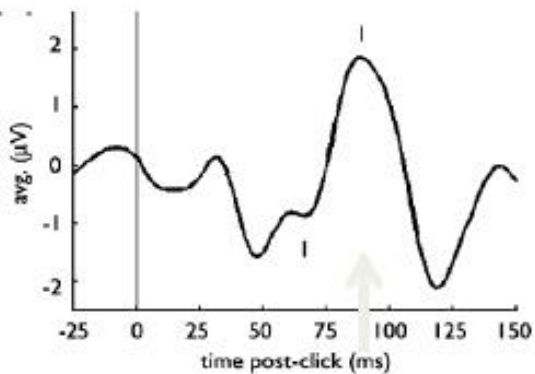


# Two ways to study choline

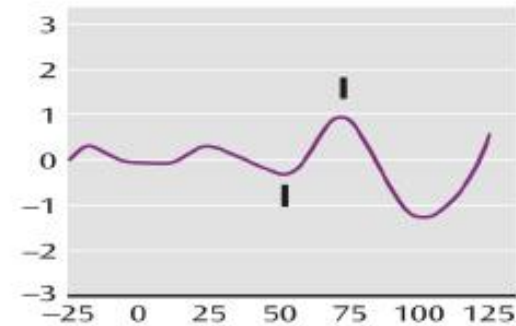
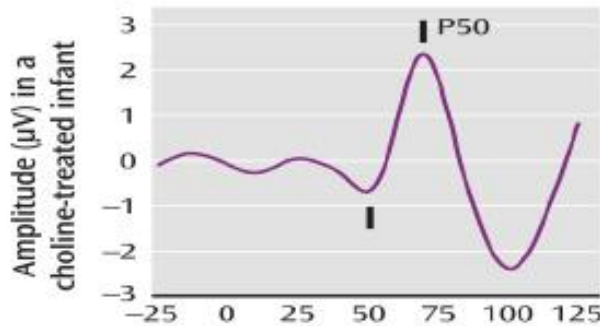
- **Measure** choline levels in mothers during pregnancy and wait 25 years to see if their children become ill.
- **A clinical trial.** All mothers receive dietary advice but half receive choline supplements and half receive placebo. The baby's brain development is assessed at birth and then throughout childhood.



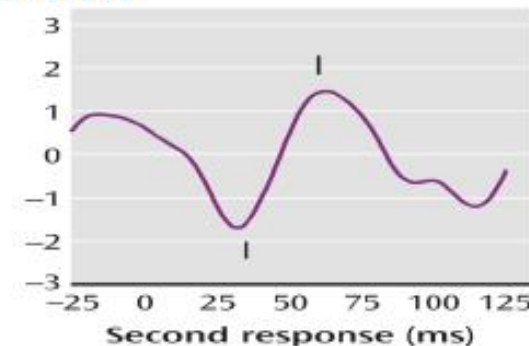
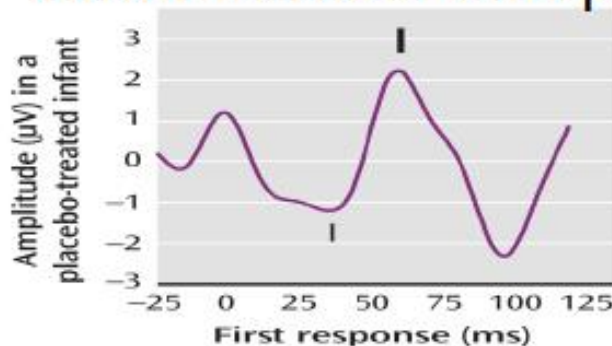
## Infant of a psychotic mother



## Infant treated with choline at 1 month

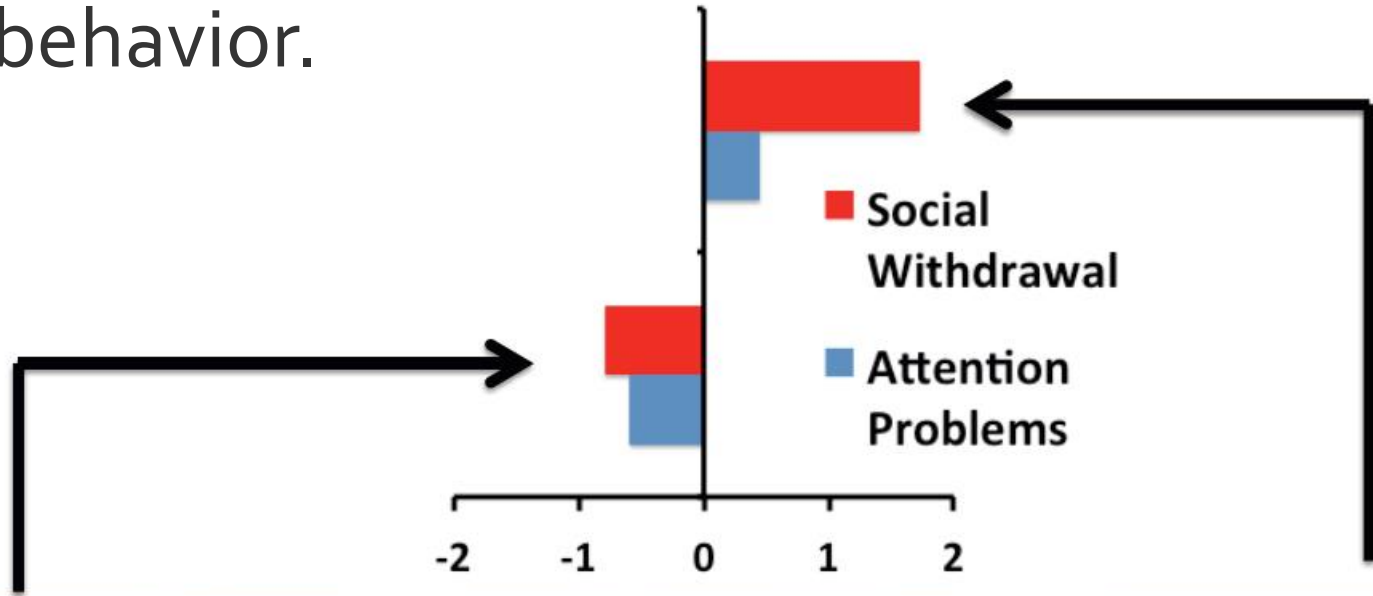


## Infant treated with placebo



The brain needs to inhibit responses to repeated sounds. This function develops just before birth and requires the effect of choline on nicotinic receptors. People with schizophrenia generally do not develop this capability.

At 30 months of age parents can reliably rate their child's behavior.



Perinatal  
choline



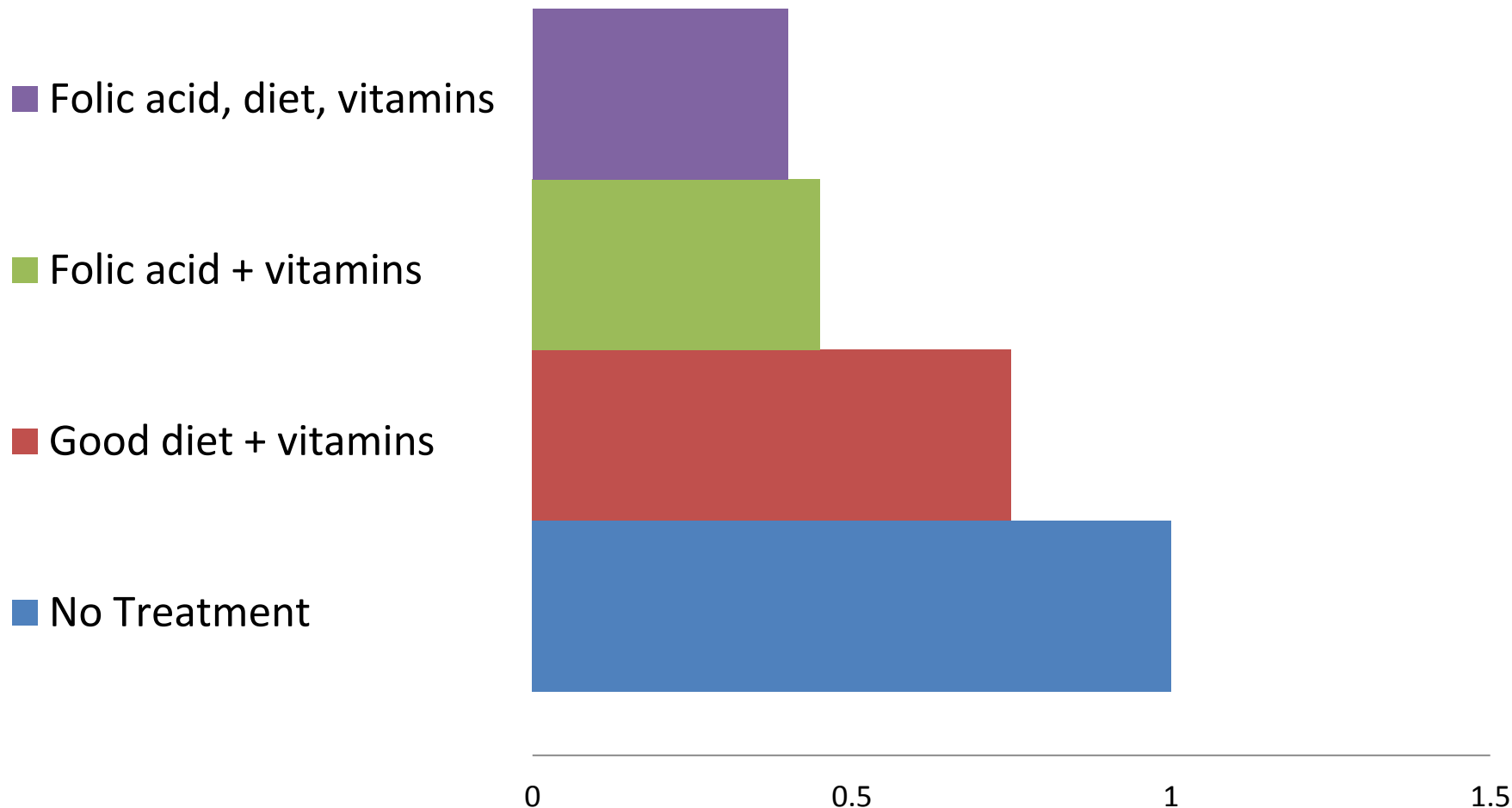
3-4 year  
old



Adult  
Schizophrenia

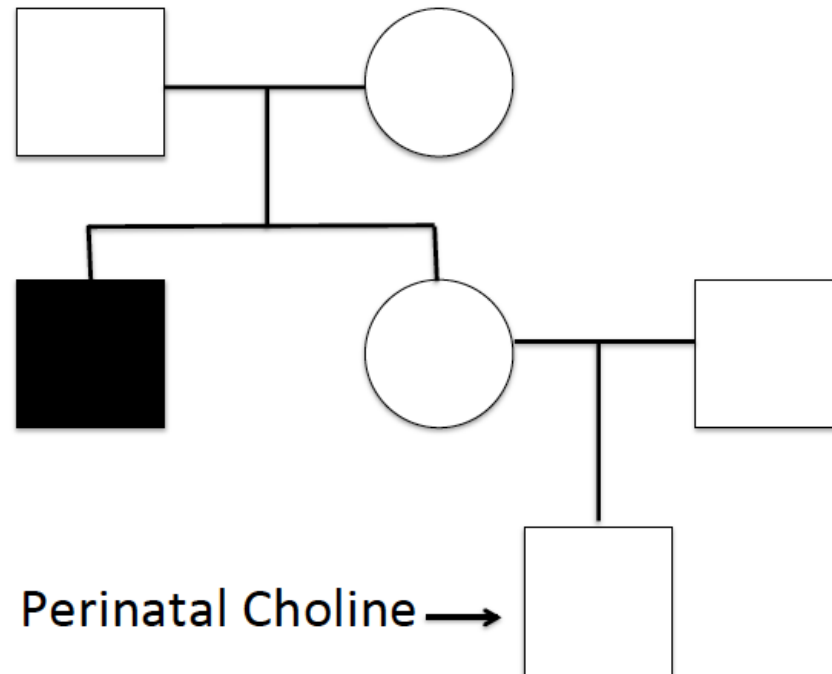


# Good diet alone does not prevent cleft palate and it will not prevent mental illness



*Like folic acid, choline is effective only before birth;*  
you cannot wait until later when you are already ill.

Folic acid prevents spina bifida, cleft palate and even microcephaly. Choline may have similar broad effect.



# What is the Goal?

## Prevention of Heart Disease as a Model

### Primary prevention

- better diets, exercise, smoking restrictions.

### Secondary prevention

- statins, antihypertensives, weight loss programs

### Tertiary prevention

- AED's, stents

The **combined** result is that deaths from heart disease have decreased significantly in the U.S.

We need to do the same for schizophrenia.



**For the child waiting  
to be born tomorrow,  
someday is NOW.**

**For more  
information:**

**[PrenatalDoctorAdvice.com](http://PrenatalDoctorAdvice.com)**