

# **The Gluten Link: The Connection between Schizophrenia and Celiac Disease**

**Bushra Bhatti<sup>1,2</sup>, Craig Sturgeon<sup>1,2</sup>, Debby Kryszak<sup>1,2</sup>,  
Patricia Gregory<sup>3</sup>, William W Eaton<sup>3</sup>, Nicola Cascella<sup>4</sup>,  
Alessio Fasano<sup>1,2</sup>**

- 1. Center for Celiac Research, University of Maryland, School of Medicine**
- 2. Mucosal Biology Research Center, University of Maryland, School of Medicine**
- 3. Department of Mental Health, Johns Hopkins Bloomberg School of Public Health**
- 4. Department of Psychiatry, Johns Hopkins School of Medicine**

# Abstract

**Background:** Celiac disease is an immune-mediated reaction to gluten, presenting with diarrhea, weight loss, abdominal complaints and a range of less common associated neurologic and psychiatric symptoms. Evidence of a link between schizophrenia and celiac disease dates back as far as 1961. A theory for this association presented by Dohan was that gluten serves as an environmental trigger in individuals predisposed to schizophrenia. This theory was supported by two series of ecologic data: the first showing that the prevalence of schizophrenia was decreased in time periods of low grain consumption and the second comparative study showing that the prevalence of schizophrenia was lower in geographic areas of low grain consumption. Recent data from Denmark show elevated prevalence of celiac disease in cases of schizophrenia and in their relatives. **Aims:** To evaluate the prevalence of celiac disease and gluten-sensitivity in subjects with schizophrenia. **Methods:** A series of 1419 blood samples of subjects with schizophrenia from The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Project were studied. All samples were screened with: tTG-IgA and AGA-IgA, AGA-IgG. All positive tTG-IgA samples were confirmed with EMA. **Results:** The serological test combination used to detect celiac disease (EMA positive and/or tTG-IgA and AGA IgA positive) identified 24 positive subjects, suggesting that the prevalence of celiac disease among schizophrenic patients is double (1:59) when compared to that reported in healthy individuals (1:133). Our screening revealed also an extremely elevated number of AGA IgA-positive subjects (280) and an unusually low AGA IgG positive subjects (6). The number of subjects exclusively positive for AGA IgA, a potential marker of gluten sensitivity, suggests a high prevalence of this condition (1:5) among the CATIE cohort. **Conclusions:** These preliminary observations suggest that within the CATIE subjects with schizophrenia there is a mixture of two populations: celiac patients (1:59) and gluten-sensitive patients (1:5). Since changes in behavior have been described both in celiac disease and gluten sensitivity, we conclude that 1 out of 5 schizophrenic patients in this cohort could potentially benefit from a gluten free diet.

# Background

Celiac disease is an immune-mediated reaction to gluten, presenting with diarrhea, weight loss, abdominal complaints and a range of less common associated neurologic and psychiatric symptoms. Evidence of a link between schizophrenia and celiac disease dates back as far as 1961. A theory for this association presented by Dohan was that gluten serves as an environmental trigger in individuals predisposed to schizophrenia. This theory was supported by two series of ecologic data: the first showing that the prevalence of schizophrenia was decreased in time periods of low grain consumption and the second comparative study showing that the prevalence of schizophrenia was lower in geographic areas of low grain consumption. Recent data from Denmark show elevated prevalence of celiac disease in cases of schizophrenia and in their relatives.

# Background

- Celiac Disease CD and schizophrenia (SZ) have approximately the same prevalence but epidemiologic data show higher prevalence of CD among SZ patients.
- The reason for this higher co-occurrence is not known but the clinical knowledge about the presence of immunologic markers for CD or gluten intolerance in SZ patients may have profound implication for treatment.

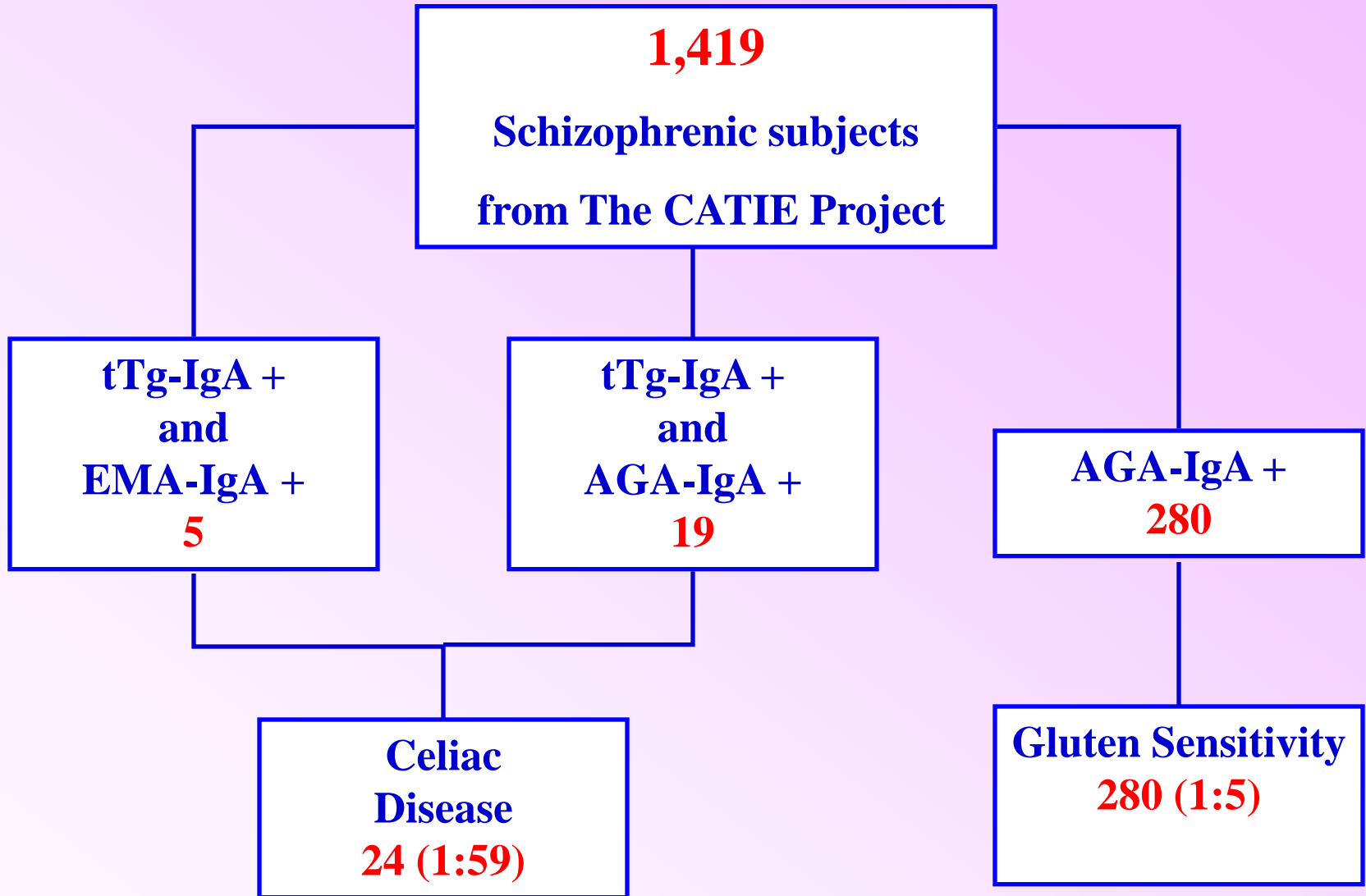
# Aims

- To evaluate the prevalence of celiac disease and gluten sensitivity in subjects with schizophrenia.

# Methods

- A series of 1,419 blood samples of subjects with schizophrenia from The National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Project were studied.
- Samples were initially screened for human anti-tissue transglutaminase-IgA (tTg-IgA), anti-gliadin-IgA (AGA-IgA) and anti-gliadin-IgG (AGA-IgG) antibodies.
- All positive tTg-IgA samples were screened for anti-endomysial antibodies (EMA)

# Results



**Prevalence of CD in the General  
Population (N= 4,126): 1:105**

**Prevalence of GS in the General  
Population (N=12,594): 1:27**

# Results

	Assay Combinations	Schizophrenia Prevalence (N=1419)		General Population Prevalence
<b>Celiac Disease</b>	tTG-IgA + & EMA +  and/or  tTG-IgA + & AGA-IgA +	24 (2%)	<b>1:59</b>	<b>1:105</b>
<b>Gluten Sensitivity</b>	AGA-IgA +	280 (20%)	<b>1:5</b>	<b>1:27</b>



# Definitions

- **Celiac Disease:** is a genetic disorder affecting children and adults. People with Celiac Disease are unable to eat foods that contain gluten, which is found in wheat and other grains. In people with Celiac Disease, gluten sets off an autoimmune reaction that causes the destruction of the villi in the small intestine.
- **Gluten Sensitivity:** the genetic component regarding Gluten Sensitivity is questionable. People with Gluten sensitivity experience distress/symptoms similar to Celiac Disease when eating gluten containing products and show improvement of symptoms when they follow a gluten free diet. There is no indication the gluten consumption caused destruction of the villi in the small intestine.

	<b>Celiac Disease</b>	<b>Gluten Sensitivity</b>
<b>Gluten free diet beneficial</b>	Yes	Yes
<b>(tTg-IgA and EMA) Positive</b>	Positive	Negative
<b>AGA-IgA &amp;/or AGA-IgG antibodies</b>	Positive and/or Negative	Positive
<b>Damage to intestinal villi</b>	Yes	No
<b>Auto-Immune Disorder</b>	Yes	No
<b>Genetic Disorder</b>	Yes	?

# Conclusions

These preliminary observations suggest that within the CATIE subjects with schizophrenia there is a mixture of two populations:

**Celiac patients: N=24 (1:59)**

**Gluten-sensitive patients N=280 (1:5)**

Since changes in behavior have been described both in celiac disease and gluten sensitivity, we conclude that:

- **1 out of 5 schizophrenic patients in this cohort could potentially benefit from a gluten free diet.**