

# **Elevated levels of Neuronal Tissue Transglutaminase (tTG) 6 in tTG 2 positive Schizophrenic Subjects**

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# 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 showed that the prevalence of schizophrenia was decreased during 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 antibodies against neuronal transglutaminase (tTG)6 in tTG2 positive schizophrenia subjects. **Methods:** Intestinal anti-tTG 2, anti-gliadin IgA, anti-gliadin IgG and anti-endomysium antibodies (EMA) were assayed in 1401 schizophrenic patients who were part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study and 900 controls. Neuronal anti-tTG6 antibodies were tested in those schizophrenic patients that were positive for anti-tTG2 antibodies and in matched controls with a ratio 1 patient: 2 controls. **Results:** Prevalence of EMA-positive schizophrenia subjects was much lower (1:280) compared to the prevalence of anti-tTG2 antibodies (1:19). Of the 74 schizophrenic subjects that tested positive for anti-tTG2 antibodies, 36 tested positive for anti-tTG6 antibodies as well (prevalence 1:2), compared to 7 tTG6 positive subjects among the 148 controls (prevalence 1:21). **Conclusions:** Our preliminary observations suggest that the discrepancy between positive EMA and tTG2 antibodies that we observed among schizophrenic patients can be related to the concomitant presence of neuronal anti-tTG6 antibodies. Schizophrenic patients with elevated tTG2 are 10 times more likely to test positive for tTG6 as compared to age and gender matched controls. These results point to a possible role of tTG6 as a biomarker of gluten sensitivity among schizophrenic patients.

# 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 showed that the prevalence of schizophrenia was decreased during 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 antibodies against neuronal transglutaminase (tTG)-6 in tTG-2 positive schizophrenia subjects

# Methods

- Intestinal anti-tTG 2, anti-gliadin IgA, anti-gliadin IgG and anti-endomysium antibodies (EMA) were assayed in 1401 schizophrenic patients who were part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study and 900 controls.
- Neuronal anti-tTG6 antibodies were tested in those schizophrenic patients that were positive for anti-tTG2 antibodies and in matched controls with a ratio 1 patient: 2 controls.

# Results

**1,401**  
**Schizophrenic subjects**  
**from The CATIE Project**

**tTG-IgA-2 +**  
**74**

**tTG-IgA-6 +**  
**36**



**Age and Gender**  
**Matched Controls**  
**148**

**tTG-IgA-6 +**  
**6**

**tTG-IgA +**  
**and EMA-IgA +**  
**5**

Prevalence of tTG-IgA-6 Positivity  
among Schizophrenic Subjects  
with a positive tTg-IgA-2

(N=74):

1:2

Prevalence of tTG-IgA-6  
positivity among age/  
gender matched controls

(N=148):

1:21

Prevalence of EMA positive  
schizophrenic subjects

(N=5)

1:280

# Conclusions

- Our preliminary observations suggest that the discrepancy between positive EMA and tTG-2 antibodies that we observed among schizophrenic patients can be related to the concomitant presence of neuronal anti-tTG-6 antibodies.
- Schizophrenic patients with elevated tTG2 are 10 times more likely to test positive for tTG-6 as compared to age and gender matched controls.
- These results point to a possible role of tTG-6 as a biomarker of gluten sensitivity among schizophrenic patients.