

Gluten sensitivity in Multiple Sclerosis

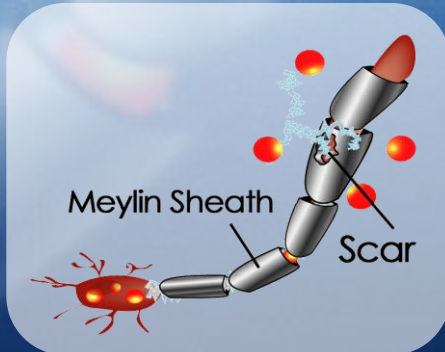
Experimental myth or clinical truth?

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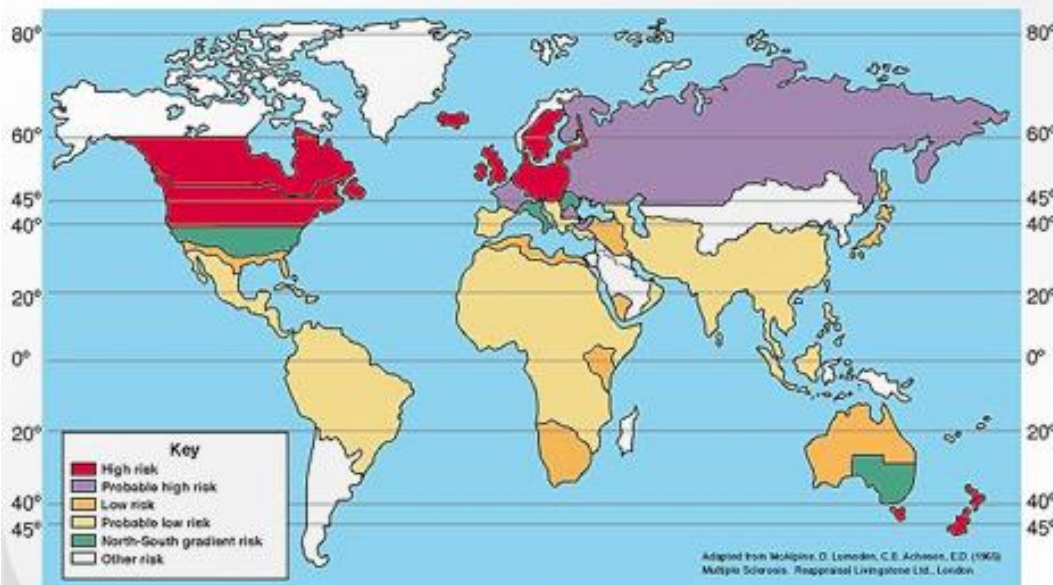
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Multiple Sclerosis (MS) etiology

World Distribution of Multiple Sclerosis



- Environmental factors
 - Nutrition (wheat & rye)?
 - Virus (EBV)?
 - Immunological factors
 - Genetic factors
-
- MS prevalence is higher in areas with predominant use of wheat and rye, as compared to corn and rice growing regions

Anti-gliadin and anti-tissue transglutaminase antibodies in MS

Serum IgA antibody levels in multiple sclerosis (MS) and controls

	Mean	Median	Number	95% CI	P-value
MS					
IgA gliadin	0.327	0.441	38	0.156-0.498	<0.001
IgA gluten	0.249	0.269	38	0.147-0.351	<0.001
IgA casein	0.103	0.159	38	0.041-0.165	0.035
Control					
IgA gliadin	0.061	0.067	27	0.035-0.088	
IgA gluten	0.056	0.051	27	0.035-0.076	
IgA casein	0.039	0.078	27	0.007-0.072	

IgG antibodies level against gluten and gliadin in MS

	Mean	Median	Number	95% CI	P-value
MS					
Gliadin	0.466	0.44	38	0.377-0.556	<0.001
Gluten	0.451	0.4	38	0.358-0.543	<0.001
Control					
Gliadin	0.154	0.1	24	0.073-0.236	
Gluten	0.158	0.1	24	0.066-0.251	

Anti-gliadin and anti-tissue transglutaminase antibodies in MS

Two patients with “atypical” MS-like condition presented with ataxia and other neurological deficits

- **Patient No.1:** IgG AGA, IgA anti tTG, IgA EMA
- **Patient No.2:** IgA EMA

Anti-gliadin and anti-tissue transglutaminase antibodies in MS

- High titers of IgA and IgG AGA and anti tTG antibodies were demonstrated in two patients with neuromyelitis optica syndrome.
- Gluten free diet + methylprednisolone caused a decrease in antibodies levels.

Response of gluten antibodies to treatment

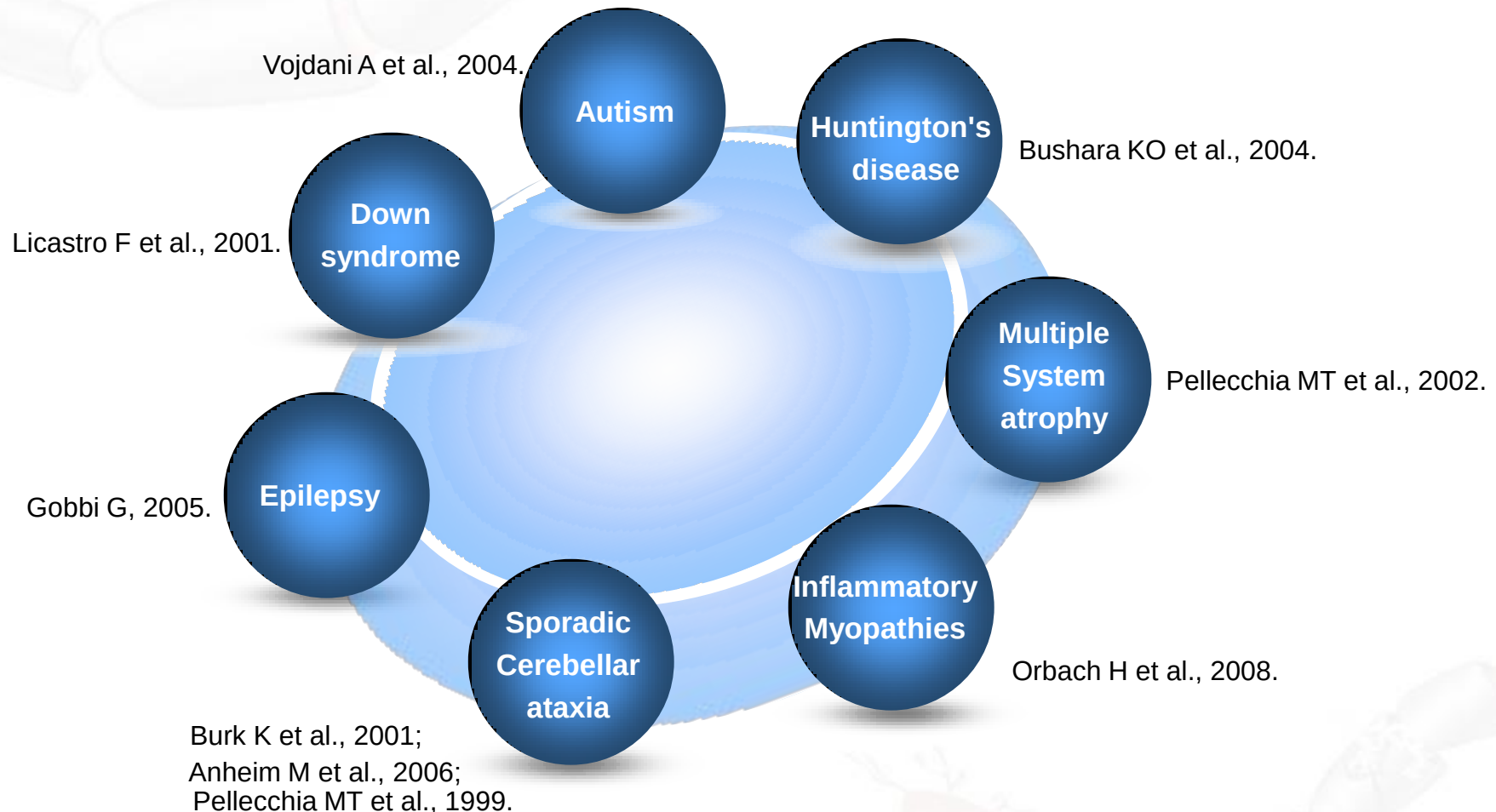
	Case 1				Case 2		
	Week 1	Week 2	Week 12	Relapse	Week 1	Week 4	Week 8
AGA, IU/l	55.3	42.5	16.3	30.1	143	64	7
GGA, IU/l	27.4	11.8	8	10.3	9	8	8
TTG, IU/l	28.6	27.2	9.6	13.6	100	59	3

AGA, IgA anti-gliadin antibodies (normal value <11 IU/l); GGA, IgG anti-gliadin antibodies (normal value <11 IU/l); TTG, tissue transglutaminase (normal value <5 IU/l).

Anti-gliadin and anti-tissue transglutaminase antibodies in MS

- Normal AGA titers were reported in 14 MS patients
Jones PE et al., 1979
- The level of AGA was studied in plasma samples from 36 patients with MS, and only one of the patients had a positive result
Hunter AL et al., 1984
- Forty-nine MS patients were examined for serologic evidence of AGA, anti-tTG and EMA. No significant difference was found between the MS patients and the control group
Pengiran Tengah CD et al., 2004
- IgA tTG antibodies were measured in an unselected group of 95 adults with MS. All patients presented normal values of tTG and total serum IgA
Salvatore S et al., 2004

Anti-gliadin antibodies in other neurologic diseases

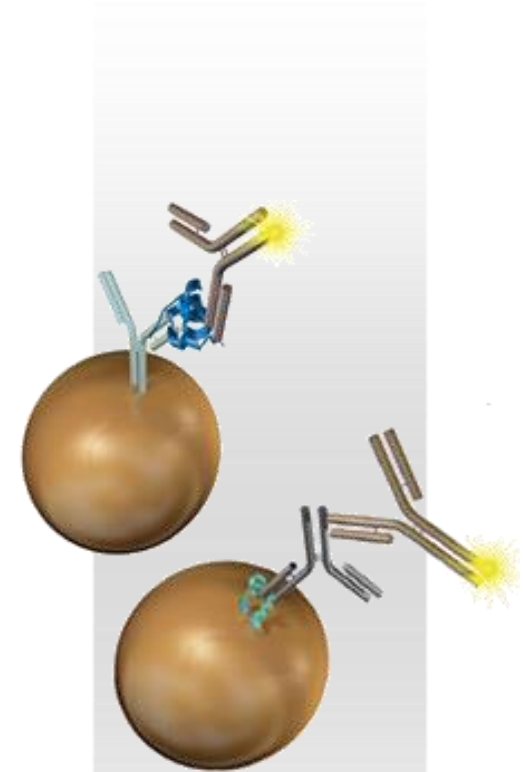


Study objective

To determine the association of AGA and anti-tTG antibodies with MS in order to verify the possible usefulness of these antibodies in managing neurological progression in patients with MS

Patients and methods

- Ninety eight Colombian patients with MS were included in a cross-sectional study
- All the patients met the Poser criteria
- There were 23 males and 75 females with MS
- Mean age of 45.1 ± 10.3 years
- Mean duration of disease of 12.4 ± 8 years
- 47% had a relapsing-remitting course of disease
- 140 Colombian individuals were included as a control population, their mean age was 41 ± 9.4 years and 7% of controls were males
- Bio-Rad BioPlex 2200 Multiplexed Immunoassay
- Pearson Chi-Square test and the two-sided Fisher's Exact test

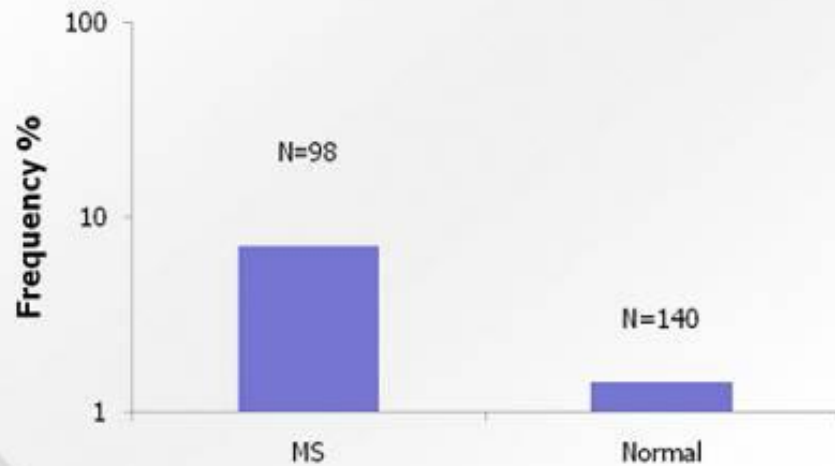


Results

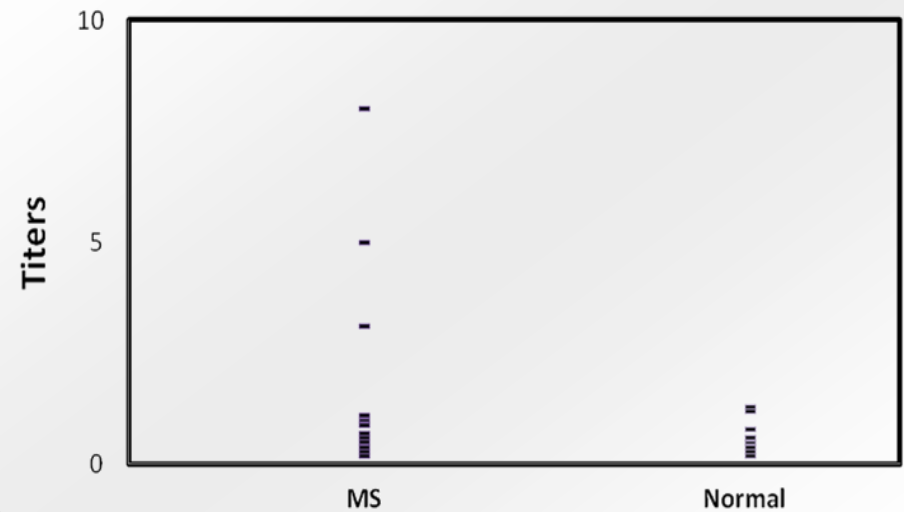
Elevated titers of IgG AGA in MS

IgG AGA Frequency %

$P < 0.05$

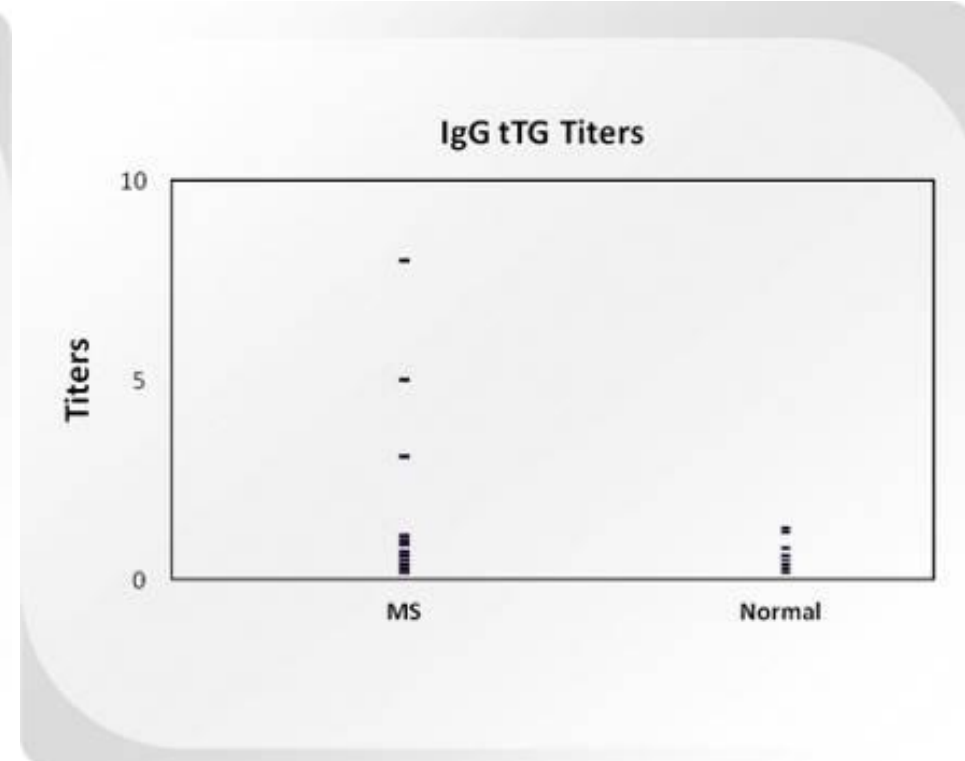
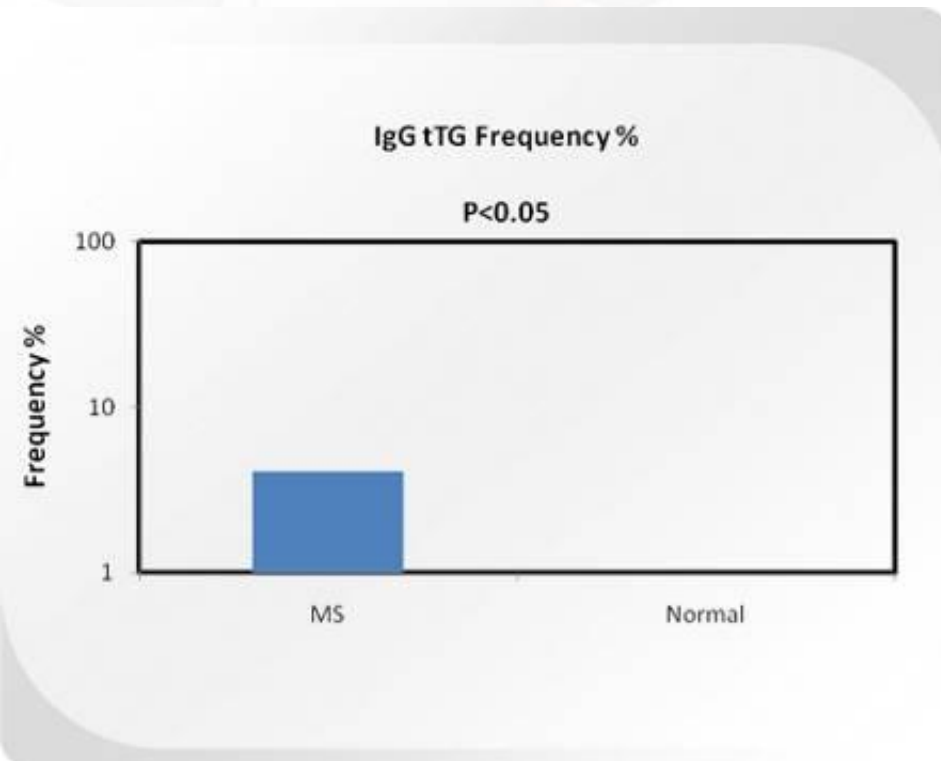


IgG AGA Titers



Results

Elevated titers of IgG antibodies against tTG in MS



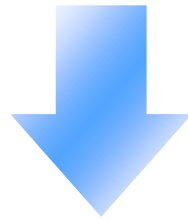
Results

	Mean	Median	Number	Percentage	P-value
MS (98)					
IgA AGA	0.32	0.2	7	7.2%	0.238
IgA tTG	0.2	0.2	0	0	
IgG AGA	0.52	0.2	7	7.1%	0.035
IgG tTG	0.35	0.3	4	4.1%	0.028
Control (140)					
IgA AGA	0.34	0.2	5	3.6%	
IgA tTG	0.2	0.2	0	0	
IgG AGA	0.25	0.2	2	1.4%	
IgG tTG	0.33	0.3	0	0	

What is the correlation between AGA and neurological dysfunction?

Several theories try to explain this correlation:

Over expression of myelin epitopes



Hyperactive response of the immune system

Molecular mimicry with cross-reactivity of the AGA –
myelin epitopes

What is the correlation between AGA and neurological dysfunction?

- Synapsins are multifunctional cytosolic phosphoproteins which are involved in the regulation of neurotransmitter release
- Synapsins were found to be related to the pathogenesis of the neurological dysfunction in experimental allergic encephalitis (EAE) animal model
De Santis ML et al., 1992
- **A cross-reactivity between both animal and human AGA with synapsin I was identified**

Alaedini A et al., 2007

Conclusions

In this study we found significant increased IgG AGA (7.1%, $p=0.035$) and anti tTG titers (4.1%, $p=0.028$) in MS patients, thus establishing the association between these antibodies and MS patients. The specific role of these antibodies in multiple sclerosis requires additional research.

A gluten-free diet as a treatment in MS: Anecdotal reports



- **Efficient:** MacDougall R, 1973; Matheson NA, 1974;
- **Non-Efficient:** Liversedge LA, 1977; Franklin GM et al, 2003.



Thank You!

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