



## *Mycoplasma pneumoniae* infection and Tourette's syndrome

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### Abstract

An association between infection and Tourette's syndrome (TS) has been described repeatedly. A role for streptococcal infection (PANDAS) has been established for several years, but the involvement of other infectious agents such as *Borrelia burgdorferi* or *Mycoplasma pneumoniae* has only been described in single case reports. We examined antibody titers against *M. pneumoniae* and various types of antibodies by immunoblot in patients and in a sex- and age-matched comparison group. Participants comprised 29 TS patients and 29 controls. Antibody titers against *M. pneumoniae* were determined by microparticle agglutination (MAG) assay and confirmed by immunoblot. Elevated titers were found in significantly more TS patients than controls (17 vs. 1). Additionally, the number of IgA positive patients was significantly higher in the TS group than in the control group (9 vs. 1). A higher proportion of increased serum titers and especially of IgA antibodies suggests a role for *M. pneumoniae* in a subgroup of patients with TS and supports the finding of case reports implicating an acute or chronic infection with *M. pneumoniae* as one etiological agent for tics. An autoimmune reaction, however, has to be taken into account. In predisposed persons, infection with various agents including *M. pneumoniae* should be considered as at least an aggravating factor in TS.

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### 1. Introduction

Tourette's syndrome (TS) is characterized by childhood and adolescent onset of simple or complex motor and vocal tics including echolalia and echopraxia (American Psychiatric Association, 1994; Müller et al., 1997a). The pathophysiological mechanisms underlying the disease are still unknown.

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However, there is no doubt that dopaminergic neurotransmission and genetic factors play a role (Pauls and Leckman, 1996; Hebebrand et al., 1997; Müller et al., 2002) and that a functional defect in the basal ganglia is involved (Kurlan, 1992; Peterson et al., 1993).

Recent reports suggest that an infectious or post-infectious process may be an important environmental factor in the pathogenesis of at least a subgroup of TS patients. In the meantime, the PANDAS syndrome for children and adolescents (*Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections*) (Swedo et al., 1997) has been proposed, and successful experimental immune therapies have been described (Müller et al., 1997b; Perlmutter et al., 1999), although methodological and conceptual shortcomings of the PANDAS concept are still under discussion (Hoekstra et al., 2002). Similar associations between infection, postinfectious phenomena, and tics as in children/adolescents, however, have also been observed in adult TS patients (Greenberg et al., 1998; Müller et al., 2000a; Müller et al., 2001).

Streptococci are not the only infectious agents that may play a role in TS (Riedel et al., 1998). After observing that infection with *M. pneumoniae* worsened the clinical symptoms of TS patients (Müller et al., 2000b), we determined antibody titers against *M. pneumoniae* in TS patients and compared them with those of controls. *M. pneumoniae* is a common cause of upper and lower respiratory tract infection (Clyde, 1993) and also affects other organ systems. *M. pneumoniae* is known to cause extrapulmonary affections including central nervous system (CNS) manifestations in up to 10% of infected persons. The CNS complications are often seen without preceding or associated pulmonary symptoms (Hagelskjaer and Hansen, 1993). Reports of successful cultivation and the positive PCR from CSF indicate that *M. pneumoniae* is able to penetrate the blood–CSF barrier. One of the most common extrapulmonary manifestations is a disorder of the central or peripheral nervous system (Pfausler et al., 2002; Socan et al., 2001). In particular, involvement of the basal ganglia has been described repeatedly, resulting in motor symptoms such as dystonia or parkinsonism (Al-Mateen et al., 1988; Saitoh et al., 1993; Kim et al., 1995; Brandel et al., 1996; Larsen and Crisp, 1996; Zambrino et al., 2000; Green and Riley, 2002).

The aim of this study was to examine whether patients with TS had higher serum antibody titers against *M. pneumoniae* than the comparison group.

## 2. Methods

### 2.1. Patients

Twenty-nine outpatients with TS (7 females/22 males) ranging from 6 to 60 years of age (mean  $21.6 \pm 13.3$  years) entered the study, which was performed between August and December of 1 year. TS patients and controls came from the region of upper Bavaria and Swabia. The broad age range reflects the fact that TS starts in childhood/adolescence but often persists during adulthood.

All patients fulfilled the diagnostic criteria for TS according to DSM-IV (American Psychiatric Association, 1994). The diagnosis was made by two experienced independent psychiatrists. Since the gender ratio for TS is about one female to four males, the ratio in this study met our expectations.

The symptoms of TS were assessed with the Tourette's Syndrome Global Scale (TSGS) (Leckman et al., 1988). Patients' scores on the TSGS ranged between 8 and 53.5 points (mean =  $29.2 \pm$  S.D. 15.2 points). The duration of the disease ranged from 1 year to 45 years (mean =  $13.0 \pm$  S.D. 12.5 years). Eight of the patients (3 females, 5 males) had comorbid obsessive-compulsive disorder. All patients and controls underwent a clinical and laboratory examination (blood analysis, C-reactive protein) for signs of inflammation or infection.

Twenty-nine sex- and age-matched healthy control subjects had been admitted to a Munich outpatient day hospital for an elective surgical intervention (7 females, 22 males) between August and December of the same year. They ranged in age from 6 to 59 years (mean age =  $21.2 \pm$  S.D. 13.6 years). The controls underwent a medical and laboratory examination by experienced medical doctors with a special focus on movement disorders and tics. A history regarding movement disorders or obsessive-compulsive symptoms was obtained by interview. None of the TS patients had clinical or laboratory signs of a current infection. Controls with respiratory tract infections, signs of systemic infections or tics were excluded

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