

Association of Group A *Streptococcus* Exposure and Exacerbations of Chronic Tic Disorders

A Multinational Prospective Cohort Study

Davide Martino, MD, PhD, Anette Schrag, MD, PhD, Zacharias Anastasiou, PhD, et al., on behalf of the EMTICS Collaborative Group

Cite as: *Neurology*® 2021;96:e1680-e1693. doi:10.1212/WNL.0000000000011610

Correspondence

Dr. Martino
davide.martino@ucalgary.ca

Study Question

Does exposure to Group A *Streptococcus* (GAS) exacerbate tics in young people with chronic tic disorders (CTD)?

What Is Known and What This Paper Adds

The clinical description of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection has prompted interest in potential associations between GAS exposure and tic severities, but the existing literature does not offer clear support for such an association. This investigation's results provide further evidence against an association.

Methods

For these longitudinal analyses, the investigators recruited 715 children with CTD (77% male; mean age, 10.7 ± 2.8 years) through 16 specialized clinics in Italy, Spain, Switzerland, Germany, the UK, Israel, the Netherlands, Hungary, and Denmark between 2013 and 2016. These participants underwent tic severity assessments during quarterly in-person clinical visits and telephone interviews conducted over 16–18 months. The investigators defined tic exacerbation as a ≥6-point increase in a participant's Yale Global Tic Severity Scale–Total Tic Severity Score since the previous assessment. During the clinical visits, clinical personnel collected pharyngeal swabs and serum samples, and laboratory personnel tested those samples for markers of GAS infection. The investigators used multivariate logistic regression models to test for associations between GAS exposure and tic exacerbation.

Results and Study Limitations

In total, 308 participants (43%) collectively experienced 405 tic exacerbation events. The percentage of exacerbations

Table Associations Between GAS Exposure and Tic Exacerbation for Different Definitions of GAS Exposure

Definition of GAS exposure	Odds ratio (95% confidence interval) for tic exacerbation
New definite exposure	1.34 (0.64–2.80)
As above or new possible exposure	0.97 (0.50–1.88)
As above or ongoing definite exposure	1.34 (0.87–2.08)
As above or ongoing possible exposure	1.10 (0.74–1.65)

temporally associated with GAS exposure ranged from 5.5% to 12.9% depending on how the investigators defined GAS exposure. Regardless of the definition used, the regression analyses did not reveal any associations between GAS exposure and tic exacerbation. The present study's limitations include possible between-center differences in clinical and microbiological assessment procedures.

Study Funding and Competing Interests

This study was funded by the EU. Some authors report receiving personal fees and funding from foundations, the University of Calgary, healthcare companies, and the Canadian, German, Swiss, and UK governments; receiving publishing royalties; and working on industry-sponsored clinical trials. Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

Neurology[®]

Association of Group A *Streptococcus* Exposure and Exacerbations of Chronic Tic Disorders: A Multinational Prospective Cohort Study

Davide Martino, Anette Schrag, Zacharias Anastasiou, et al.

Neurology 2021;96:e1680-e1693 Published Online before print February 10, 2021

DOI 10.1212/WNL.0000000000011610

This information is current as of February 10, 2021

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/96/12/e1680.full
References	This article cites 46 articles, 2 of which you can access for free at: http://n.neurology.org/content/96/12/e1680.full#ref-list-1
Citations	This article has been cited by 4 HighWire-hosted articles: http://n.neurology.org/content/96/12/e1680.full##otherarticles
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): ADHD http://n.neurology.org/cgi/collection/adhd All CBMRT/Null Hypothesis http://n.neurology.org/cgi/collection/all_cbmrt_null_hypothesis Bacterial infections http://n.neurology.org/cgi/collection/bacterial_infections Tics http://n.neurology.org/cgi/collection/tics Tourette syndrome http://n.neurology.org/cgi/collection/tourette_syndrome
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2021 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

