Schizophrenia, Bipolar, ASD/Autism, Anxiety/Panic Attacks, OCD/Tourette's, PANS/PANDAS … : Tailored Testing Protocols

Holiday Inn Regents Park, 18th November 2018, London, UK

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Vast number of microbes associated with psychiatric symptoms (*Bransfield 2009; contd. next pg.*) ....

Box 1. Some microbes associated with mental symptoms & mental illness.

Spirochetes

- *Borrelia afzelii* (Lyme disease in the UK and the rest of Europe)
- *Borrelia burgdorferi sensu stricto* (Lyme disease in the USA, UK and rest of Europe)
- *Borrelia garinii* (Lyme disease in the UK and rest of Europe)
- *Borrelia hermsii* (relapsing fever)
- *Borrelia turicatae* (relapsing fever)
- *Leptospira* (Leptospirosis)
- *Treponema pallidum pallidum* (syphilis)

Bacteria

- *Anaplasmas phagocytophilum* (human granulocytic ehrlichiosis)
- *Bartonella henselae* (cat scratch fever)
- *Bartonella quintana* (trench fever)
- *Bartonella rochalimae* (bartonellosis)
- *Chlamydophilia pneumoniae* (chlamydia)
- *Chlamydophila psittaci* (chlamydia)
- *Coxiella burnetti* (Q-fever and post-Q fever fatigue syndrome)
- *Ehrlichia chaffeensis* (human monocytic ehrlichiosis)
- *Francisella tularensis* (rabit fever or tularemia)
- *Haemophilus influenzae* (haemophilus)
- *Listeria*
- *Meningococcus* (meningococcal meningitis)
- *Mycoplasma fermentans*
- *Mycoplasma pneumoniae*
- *Mycobacterium tuberculosis* (tuberculosis)
- *Rickettsia akari* (rickettsialpox)
- *Rickettsia rickettsii* (rocky mountain spotted fever)
- *Rickettsia* species (eastern tick-borne rickettsiosis)
- *Shigella* (shigellosis)
- *Streptococcus pneumoniae* or pneumococcus (pneumonia)
- *Streptococcus* (pediatric autoimmune diseases associated with *Streptococcus*, Sydenham's chorea and St Vitus dance)

Yeast

- *Candida albicans* (candidiasis)
- *Candida dubliniensis*

Source: Bransfield RC. Preventable cases of autism: relationship between chronic infectious diseases and neurological outcome. Ped Health. 2009;3:125–40.

… making it clear that what I present today is just a fraction of what could potentially be tested for

Box 1. Some microbes associated with mental symptoms & mental illness (cont.).

Prion

- Variant Creutzfeldt–Jakob

Viruses

- Borna virus
- *Coltivirus* (Colorado tick fever)
- *Coxsackievirus*
- *Cytomegalovirus*
- *Enterovirus*
- *Flaviviridae* virus (Japanese B encephalitis)
- Hepatitis C virus
- Herpes virus family
- Human endogenous retroviruses
- *Human herpesvirus 4* or Epstein–Barr virus
- HIV
- Influenza A virus subtype H3N2 (Hong Kong flu)
- Influenza virus
- Pandemic influenza of 1918
- *Papopavirus*
- *Paramyxovirus* (measles virus)
- *Parvo B19*
- *Poliovirus*
- Rabies virus
- Rubella
- Toga virus
- Varicella zoster virus (chicken pox)
- Viral meningitis
- West Nile virus

Protozoa

- *Plasmodium* (malaria)
- *Babesia microti* (babesiosis)
- *Babesia duncani* (babesiosis)
- Other *Babesia* species (babesiosis)
- *Toxoplasma gondii* (toxoplasmosis)

Parasites

- *Blastocystis* (blastocystosis)
- *Taenia solium* (neurocysticercosis or cysticercosis)

Fungal

- *Cryptococcoccus*
- Coccidiomycosis
- Histomycosis

Source: Bransfield RC. Preventable cases of autism: relationship between chronic infectious diseases and neurological outcome. Ped Health. 2009;3:125–40.

Tailored testing protocols for infections that may underlie neuropsychiatric symptoms

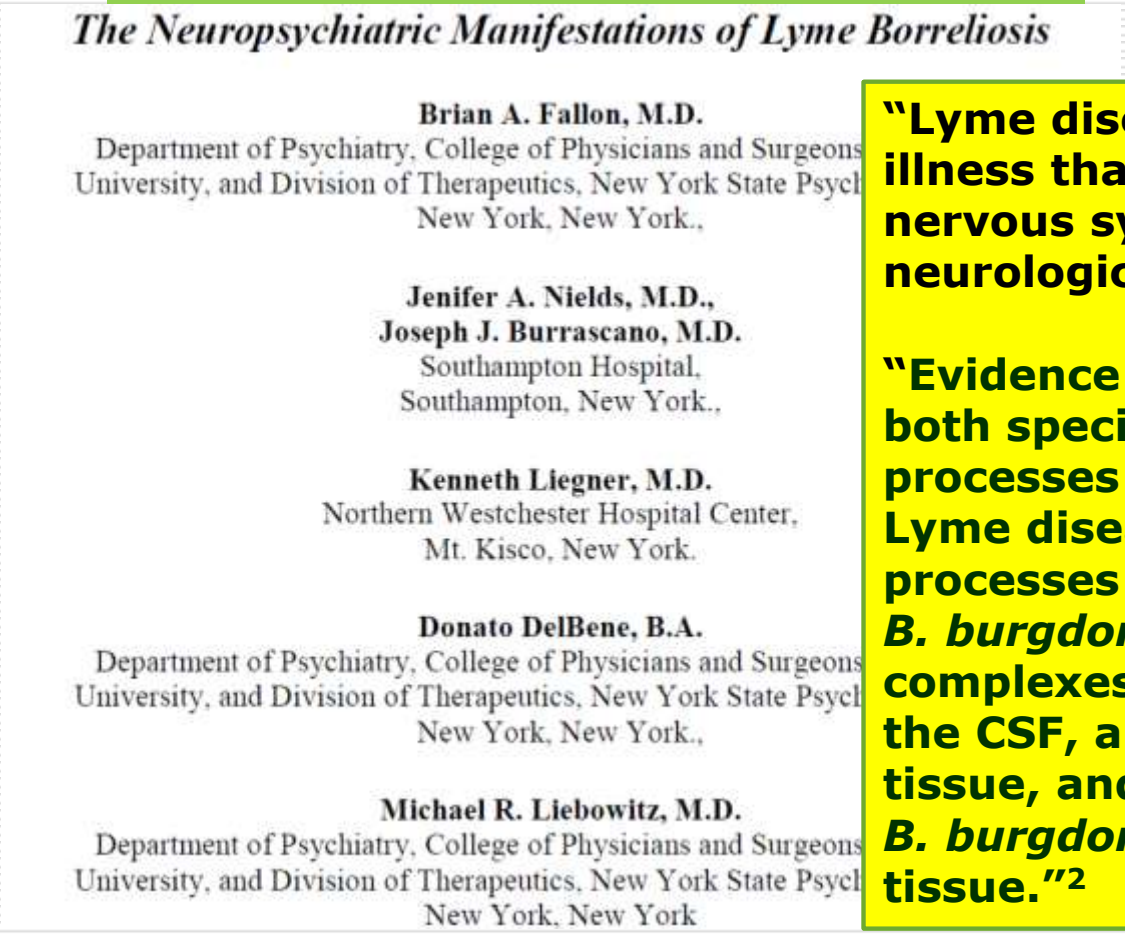
Today we will look at tailored testing protocols for just a select number of conditions, paired with a select number of infections.

Literature is available on many more combinations, so please do not see this as exhaustive in any way. You/your therapist will wish to determine the most likely testing combinations in specific cases by also using checklists and of course – most importantly – by the patient's clinical symptoms.

Tailored testing protocols

- **Borreliosis and neuropsychiatric disorders: an overview**
- Schizophrenia
- Panic/Anxiety/Cognitive/Mood disorders
- Autism spectrum disorder (ASD)
- Obsessive Compulsive Disorder/Tourette's Syndrome
- PANS/PANDAS

Neuropsychiatric manifestations of Borreliosis were recognised a quarter of a century ago …



The Neuropsychiatric Manifestations of Lyme Borreliosis

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"Lyme disease is a multisystemic illness that can affect the central nervous system (CNS), causing neurologic and psychiatric symptoms."

"Evidence exists to support the role of both specific and nonspecific immune processes in the production of CNS Lyme disease. Evidence of specific processes includes the production of *B. burgdorferi-specific* immune complexes and T cell responses within the CSF, autoantibodies to neural tissue, and cross-reactivity of *B. burgdorferi* antibodies with neural tissue."[2]

Source: 1. Fallon, Brian & Nields, Jenifer & J. Burrascano, Joseph & Liegner, Kenneth & DelBene, Donato & Liebowitz, Michael. (1992). The neuropsychiatric manifestations of Lyme borreliosis. The Psychiatric quarterly. 63. 95-117. 10.1007/BF01064684.Fallon, B. A., & Nields, J. A. (1994). 2. Lyme disease: A neuropsychiatric illness. The American Journal of Psychiatry, 151(11), 1571-1583.

Even back in the 90s, statistics revealed neurological involvement in up to 40% of patients

"Up to 40% of patients with Lyme disease develop neurologic involvement of either the peripheral or central nervous system."

Am J Psychiatry. 1994 Nov;151(11):1571-83.

Lyme disease: a neuropsychiatric illness.

Fallon BA[1], Nields JA.

Author information

Abstract

OBJECTIVE: Lyme disease is a multisystemic illness that can affect the central nervous system (C
symptoms. The goal of this article is to familiarize psychiatrists with this spirochetal illness.

METHOD: Relevant books, articles, and abstracts from academic conferences were perused, and
computerized searches and reference sections from published articles.

RESULTS: Up to 40% of patients with Lyme disease develop neurologic involvement of either the peripheral or central nervous system. Dissemination to the CNS can occur within the first few weeks after skin infection. Like syphilis, Lyme disease may have a latency period of months to years before symptoms of late infection emerge. Early signs include meningitis, encephalitis, cranial neuritis, and radiculoneuropathies. Later, encephalomyelitis and encephalopathy may occur. A broad range of psychiatric reactions have been associated with Lyme disease including paranoia, dementia, schizophrenia, bipolar disorder, panic attacks, major depression, anorexia nervosa, and obsessive-compulsive disorder. Depressive states among patients with late Lyme disease are fairly common, ranging across studies from 26% to 66%. The microbiology of Borrelia burgdorferi sheds light on why Lyme disease can be relapsing and remitting and why it can be refractory to normal immune surveillance and standard antibiotic regimens.

CONCLUSIONS: Psychiatrists who work in endemic areas need to include Lyme disease in the differential diagnosis of any atypical psychiatric disorder. Further research is needed to identify better laboratory tests and to determine the appropriate manner (intravenous or oral) and length (weeks or months) of treatment among patients with neuropsychiatric involvement.

LB can underlie a vast number of neuropsychiatric disorders …

Journal List › Healthcare (Basel) › v.6(3); 2018 Sep › PMC6165408

healthcare MDPI

Healthcare (Basel). 2018 Sep; 6(3): 104.
Published online 2018 Aug 25. doi: 10.3390/healthcare6030104

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Neuropsychiatric Lyme Borreliosis: An Overview with a Focus on a Specialty Psychiatrist's Clinical Practice

Robert C. Bransfield

Author information ► Article notes ► Copyright and License information ► Disclaimer

Abstract

Go to:

There is increasing evidence and recognition that Lyme borreliosis (LB) causes mental symptoms. This article draws from databases, search engines and clinical experience to review current information on LB. LB causes immune and metabolic effects tha… symptoms, usually presenting with significa… autism spectrum disorders, schizoaffective d… disorder, social anxiety disorder, generalized… symptoms), eating disorders, decreased libid… impairments, dementia, seizure disorders, su… episodes, derealization and other impairment… comprehensive psychiatric clinical exam, rev… physical exam relevant to the patient's comp… and knowledgeable interpretation of laborat… may help improve functioning and prevent f… between LB and neuropsychiatric impairmen… conditions can improve understanding of the…

Source: Bransfield RC. Neuropsychiatric Lyme… a Focus on a Specialty Psychiatrist's Clinical P…

"LB causes immune and metabolic effects that result in a gradually developing spectrum of neuropsychiatric symptoms, usually presenting with significant comorbidity which may include **developmental disorders, autism spectrum disorders, schizoaffective disorders, bipolar disorder, depression, anxiety disorders (panic disorder, social anxiety disorder, generalized anxiety disorder, posttraumatic stress disorder, intrusive symptoms), eating disorders, decreased libido, sleep disorders, addiction, opioid addiction, cognitive impairments, dementia, seizure disorders, suicide, violence, anhedonia, depersonalization, dissociative episodes, derealization and other impairments**."

… in children as well as adults …

Unraveling Diagnostic Uncertainty Surrounding Lyme Disease in Children with Neuropsychiatric Illness

Michael P. Koster, MD[a,*], Aris Garro, MD, MPH[b]

Case reports of neuropsychological manifestations of Lyme disease that are of special interest to psychiatrists include: Alice in Wonderland syndrome (sensation that things are getting larger and smaller), Tourette syndrome, acute delirium, catatonia, psychosis, and stroke mimics such as aphasia.[5–9] Although these case reports demonstrate that Lyme disease can present with atypical neuropsychiatric manifestations, it is important to note they
signs and symptoms of Lyme dis
tionally, objective findings can he
positive Lyme serology with lym
intrathecal production of Lyme a
changes with increased signal on

"Case reports of neuropsychological manifestations of Lyme disease … include … Tourette syndrome, acute delirium, catatonia, psychosis …"

NEUROPSYCHIATRIC AND CLINICAL OUTCOMES IN CHILDREN WITH LYME DISEASE

Given the neurotropism of *Borrelia burgdorferi,* it is not surprising that patients could experience neuropsychiatric symptoms after infection including sleep disturbance, memory problems, and mood changes. What is difficult to determine is whether these

Source: Unraveling Diagnostic Uncertainty Surrounding Lyme Disease in Children with Neuropsychiatric Illness Koster, Michael P. et al. Child and Adolescent Psychiatric Clinics , Volume 27 , Issue 1 , 27 - 36

Basic testing panel for Borreliosis

1. Borrelia SeraSpot (modern Western blot)
2. Borrelia-EliSpot (current T-cell activity)
3. CD57-cells (chronic immune suppression)
4. New option: Tickplex Basic, includes round bodies (persisters)

Tailored testing protocols

- Borreliosis and neuropsychiatric disorders: an overview
- **Schizophrenia**
- Panic/Anxiety/Cognitive/Mood disorders
- Autism spectrum disorder (ASD)
- Obsessive Compulsive Disorder/Tourette's Syndrome
- PANS/PANDAS

Many sources on Borreliosis-associated schizophrenia and schizoaffective-conditions

Hess, A., Buchmann, J., Zettl, U.K., Henschel, S., Schlaefke, D., Grau, G., & Benecke, R. (1999). Borrelia burgdorferi central nervous system infection presenting as an organic schizophrenia-like disorder. *Biol Psychiatry45*(6):795.

Brown, J.S. Jr. (1994). Geographic correlation of schizophrenia to ticks and tick-borne encephalitis. *Schizophr Bull*; 20(4):755-75

Nicolson G., & Haier, J. (2009). Role of chronic bacterial and viral infections in neurodegenerative, neurobehavioral, psychiatric, autoimmune and fatiguing illnesses: Part I. *BJMP 2*(4) 20-28.

.Frykholm BO. On the question of infectious aetiologies for multiple sclerosis, schizophrenia and the chronic fatigue syndrome and the treatment with antibiotics. Med Hypotheses 2009; 72: 736-739.8

Roelcke, U., Barnett, W., Wilder-Smith, E., Sigmund, D., Hacke, W., 1992. Untreated neuroborreliosis: Bannwarth's syndrome evolving into acute schizophrenia-like psychosis. A case report. J. Neurol. 239 (3), 129–131.

Earl AK, Sullivan KM, Warfel D, Feldman SM, Richardson CM, Vyas G, et al. Lyme disease and schizophrenia: Case studies from an adjunctive minocycline study. Schizophr Bull. 2013;39(Suppl 1):62–

German Title: [Endogenous paranoid-hallucinatory syndrome caused by Borrelia encephalitis]

Authors: Barnett W, Sigmund D, Roelcke U, Mundt C Source: Nervenarzt 1991 Jul;62(7):445-7

Undiagnosed Lyme disease in adults with schizophrenia

Koola, Maju Mathew et al. Schizophrenia Research , Volume 168 , Issue 1 , 579 - 580

A number of patients with schizophrenia (2015 study) were found to have LD & improved on appropriate therapy

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Schizophr Res. 2015 Oct; 168(1-2): 579–580.
doi: [10.1016/j.schres.2015.06.029]

PMCID: PMC5493317
NIHMSID: NIHMS869790
PMID: 26255567

Undiagnosed Lyme disease in adults with schizophrenia

Maju Mathew Koola, Kelli M. Sullivan, Amber K. Earl, Stephanie M. Feldman, Charles Richardson, Gopal R. Vy
Heidi J. Wehring, and Deanna L. Kelly*

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Dear Editors

Lyme disease (LD) is the world's leading tick borne infection caused by the spirochete, *Borrelia burgdorferi* (Bb). This infection is a global health concern and is associated with numerous cardiolo dermatologic, rheumatologic neurologic, and psychiatric manifestations (Bratton et al., 2008). Only epidemiologic studies have evaluated the frequency of antibodies to Bb in psychiatric patients; one study found only 1/517 (0.2%) of all adult psychiatric patients had Lyme titer seropositivity (Nadelman et al., 1997) and the other larger study found that 322/926 (35%) of psychiatric inpatients had seropositivity to antibodies to Bb (Hajek et al., 2002). While a few cases have been reported (Hess et al., 1999; Mattingley and Koola, 2015; Roelcke et al., 1992) no studies to our knowledge have examined Lyme disease prevalence in patients with psychosis or schizophrenia or from a population of those being treated in the outpatient setting where infection may be more likely. It is interesting to note that seasonal (March to April) distribution of increased LD infection risk corresponds with the birth excess for schizophrenia in the winter months (Tochigi et al., 2004). Also, areas of the world non-endemic for LD have a low prevalence of schizophrenia (Fritzsche, 2002).

We examined the presence of positive Lyme titers during routine screening in 52 potential research candidates (outpatient and inpatient) in Baltimore, MD. All were between the ages of 18 and 64 years and were on a stable dose of clozapine for at least six months. The Lyme titer was performed by Lab Corp ® by

"Clinicians working in endemic, high-risk areas should consider LD in the differential diagnosis of any atypical psychiatric presentation."

Source: Koola MM, Sullivan KM, Earl AK, et al. Undiagnosed Lyme disease in adults with schizophrenia. Schizophr Res. 2015;168(1-2):579-80.

"Lyme Disease can present with symptoms similar to bipolar disorder"

Indian Journal of Psychological Medicine
Official publication of the South zone branch of the Indian psychiatric society
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Indian J Psychol Med. 2015 Apr-Jun; 37(2): 243–246.
doi: 10.4103/0253-7176.155660
PMCID: PMC4418265
PMID: 25969618

Association of Lyme Disease and Schizoaffective Disorder, Bipolar Type: Is it Inflammation Mediated?

David William Mattingley and Maju Mathew Koola[1]

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Abstract

Go to

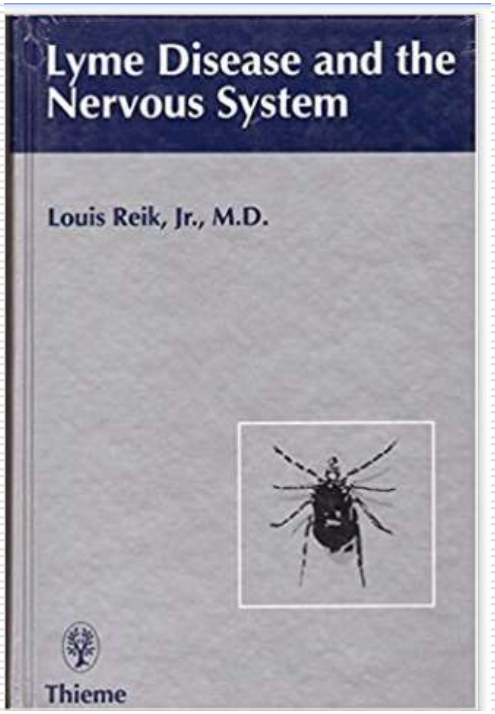
Lyme disease has been reported to be associated with various psychiatric presentations. *Borreliaburgdorferi* (Bb) can present with symptoms similar to schizophrenia and bipolar disorder. It has been suggested that inflammation incurred during the Bb infection leads to neurodegenerative changes that result in schizophrenia-like presentations. We report a case of a 41-year-old male with a past history of Bb infection who presents with psychosis. Later in the course of his hospitalization, he developed mood symptoms and was diagnosed with schizoaffective disorder, bipolar type. This case highlights the diagnosis and treatment of a patient with the unique presentation of schizoaffective disorder, bipolar type in the setting of previous Bb infection.

Keywords: *Inflammation, lyme disease, psychosis, schizoaffective disorder*

INTRODUCTION

Go to

Lyme disease is highly prevalent across Europe and the eastern parts of North America.[1] In 2011, the Centers for Disease Control reported that 96% of the reported cases of lyme disease occurred in 13 US



Source: Mattingley DW, Koola MM. Association of Lyme Disease and Schizoaffective Disorder, Bipolar Type: Is it Inflammation Mediated? Indian Journal of Psychological Medicine. 2015;37(2):243-246. doi:10.4103/0253-7176.155660.

Chlamydia pneumoniae has also been documented in schizophrenia, and its suspected mechanism of action

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Increased prevalence of *Chlamydophila* DNA in post-mortem brain frontal cortex from patients with schizophrenia

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Stanley Medical Research Institute (SMRI)

ABSTRACT

Infection can initiate symptoms of mental illness. It has been shown previously that *Chlamydophila* DNA is present six times more often in the blood of patients with schizophrenia than in the blood of control individuals. Monocytes, the main targets of *Chlamydiaceae* infection, are microglia precursors. We identified *Chlamydiaceae* infection using blinded brain DNA samples derived from the frontal cortex. Using PCR and sequence analysis, we found *Chlamydophila* DNA to be four times greater in patients with schizophrenia than in controls (schizophrenia: N=34, microbial DNA frequency 23.5%; controls: N=35, microbial DNA frequency 5.7%; P=0.045, OR=5.08). Persistent *Chlamydophila*-infected microglia or neuronal cells may impair neuronal circuits and thus be a mechanism for causing psychiatric illness in these patients.

1. Introduction

levels of several cytokines have been shown to be associated with schizophrenia (Drexhage et al., 2010).

"Using PCR and sequence analysis, we found *Chlamydophila* DNA to be four times greater in patients with schizophrenia than in controls … Persistent *Chlamydophila*-infected microglia or neuronal cells may impair neuronal circuits and thus be a mechanism for causing psychiatric illness in these patients."

Stanley Medical Institute dedicated to toxoplasmosis-schizophrenia research

"More than 80 studies have reported increased antibody levels to *T. gondii* in individuals with schizophrenia and related psychoses."

*(Last updated **September 2018**)*

Torrey et al. found that cat ownership before age 13 was a risk factor for the later development of psychoses

Schizophrenia Research 165 (2015) 1–2

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

ELSEVIER

Is childhood cat ownership a risk factor for schizophrenia later in life?

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Schizophrenia
Bipolar disorder
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Toxoplasmosis
Toxoplasma gondii

ABSTRACT

Two previous studies suggested that childhood cat ownership is a possible risk factor for later developing schizophrenia or other serious mental illness. We therefore used an earlier, large NAMI questionnaire to try and replicate this finding. The results were the same, suggesting that cat ownership in childhood is significantly more common in families in which the child later becomes seriously mentally ill. If true, an explanatory mechanism may be *Toxoplasma gondii*. We urge our colleagues to tr... whether childhood cat ownership is truly a risk factor for later schizop...

1. Introduction

In 1995 a study suggested that cat ownership during childhood ... list; the refusal rate was 9%. Two ... without any serious mental illn... telephone exchange as the subject...

Researchers have found that cat ownership in youth is a risk factor for the development of psychoses: speculation that the transmission of a zoonotic agent such as T. gondii could be a mechanism for schizophrenia

"T. gondii gets into the brain and forms microscopic cysts. … it then becomes activated in late adolescence and causes disease, probably by affecting the neurotransmitters."
E. Fuller Torrey

Toxoplasma seropositivity among patients with schizophrenia in a 2011 study (62 PX) was 67.7%

al List › Iran J Parasitol › v.6(2); 2011 Jun › PMC3279881

Iranian Journal of Parasitology

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Iran J Parasitol. 2011 Jun; 6(2): 31–37.

PMCID: PMC3279881
PMID: 22347285

Toxoplasma Infection in Schizophrenia Patients: A Comparative Study with Control Group

A Alipour,[1,2] S Shojaee,[1,2] M Mohebali,[1,2] M Tehranidoost,[3] F Abdi Masoleh,[3] and H Keshavarz[1,2,*]

Author information ► Article notes ► Copyright and License information ► Disclaimer

Abstract

Go to:

Background

Schizophrenia is a serious, chronic, and often debilitating neuropsychiatric disorder. Its causes are still poorly understood. Besides genetic and non-genetic (environmental) factors are thought to be important as the cause of the structural and functional deficits that characterize schizophrenia. This study aimed to compare *Toxoplasma gondii* infection between schizophrenia patients and non-schizophrenia individuals as control group.

Methods

A case-control study was designed in Tehran, Iran during 2009-2010. Sixty-two patients with schizophrenia and 62 non-schizophrenia volunteers were selected. To ascertain a possible relationship between *T. gondii* infection and schizophrenia, anti-*Toxoplasma* IgG antibodies were detected by indirect-ELISA. Data were statistically analyzed by chi- square at a confidence level of 99%.

Results

The sero-positivity rate among patients with schizophrenia (67.7%) was significantly higher than control group (37.1) (P <0. 01).

Conclusion

A significant correlation between *Toxoplasma* infection and schizophrenia might be expected.

Seropositivity for toxoplasma 67.7% - "significantly higher than the control group"

Association found between bipolar disorder and CMV/HSV2

ELSEVIER

Neuroscience Research

Volume 115, February 2017, Pages 59-63

Short communication

Infection and inflammation in schizophrenia and bipolar disorder

Teppei Tanaka [a, 1], Taro Matsuda [b, 1], Lindsay N. Hayes [a, 1], Shuojia Yang [c], Katrina Rodriguez [b], Emily G. Severance [c], Robert H. Yolken [a, c], Akira Sawa [a, b], William W. Eaton [b]

Abstract

The present study investigated the relationship between exposure to infectious agents and inflammation markers in individuals with schizophrenia (SZ), bipolar disorder (BP), and controls without a psychiatric disorder. We measured plasma levels of antibodies and innate immune markers and correlated them with clinical symptoms and cognitive function. In both SZ and BP, we found an increase in soluble CD14, and in BP an increase in C-reactive protein, IgM class antibodies against cytomegalovirus (CMV), and IgG class antibodies against herpes simplex virus 2. Furthermore in BP, we observed a negative relationship between IgG antibodies against CMV and scores for cognitive function.

"We found … in bipolar disorder an increase in C-reactive protein, **IgM class antibodies against cytomegalovirus (CMV), and IgG class antibodies against herpes simplex virus 2.**
… we observed a negative relationship between IgG antibodies against CMV and scores for cognitive function."

Source: T Tanaka, T Matsuda, LN Hayes, S Yang, K Rodriguez, EG Severance et al. Infection and inflammation in schizophrenia and bipolar disorder. Neuroscience Research Feb. 2017 115, 59-63

HSV1 and HHV6 also associated with schizophrenia risk

PLOS ONE A Peer-Reviewed, Open Access Journal

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PLoS One. 2015; 10(3): e0116696.
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PMCID: PMC4363491
PMID: 25781172

Infection and Inflammation in Schizophrenia and Bipolar Disorder: A Genome Wide Study for Interactions with Genetic Variation

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Abstract

Go to:

Inflammation and maternal or fetal infections have been suggested as risk factors for schizophrenia (SZ) and bipolar disorder (BP). It is likely that such environmental effects are contingent on genetic background. Here, in a genome-wide approach, we test the hypothesis that such exposures increase the risk for SZ and BP and that the increase is dependent on genetic variants. We use genome-wide genotype data, plasma IgG antibody measurements against *Toxoplasma gondii,* Herpes simplex virus type 1, Cytomegalovirus, Human Herpes Virus 6 and the food antigen gliadin as well as measurements of C-reactive protein (CRP), a peripheral marker of inflammation. The subjects are SZ cases, BP cases, parents of cases and screened controls. We look for higher levels of our immunity/infection variables and interactions between them and common genetic variation genome-wide. We find many of the antibody measurements higher in both disorders. While individual tests do not withstand correction for multiple comparisons, the number of nominally significant tests and the comparisons showing the expected direction are in significant excess (permutation p=0.019 and 0.004 respectively). We also find CRP levels highly elevated in SZ, BP and the mothers of BP cases, in agreement with existing literature, but possibly confounded by our inability to correct for smoking or body mass index. In our genome-wide interaction analysis no signal reached genome-wide significance, yet many plausible candidate genes emerged. In a hypothesis driven test, we found multiple interactions among SZ-associated SNPs in the HLA region on chromosome 6 and replicated an interaction between CMV infection and genotypes near the *CTNNA3* gene reported by a recent GWAS. Our results support that inflammatory processes and infection may modify the risk for psychosis and suggest that the genotype at SZ-associated HLA loci modifies the effect of these variables on the risk to develop SZ.

"Many infectious agents have been associated with SZ risk [12], including *Toxoplasma gondii* (TOXO), **Herpes simplex virus type 1 (HSV1)**, cytomegalovirus (CMV) and **human herpes virus 6 (HHV6)** [13]."

Schizophrenia/Bipolar disorder

1. Borrelia SeraSpot + Borrelia-EliSpot + CD57-cells + Tickplex Basic
2. Chlamydia pneumoniae IgG/IgA antibodies + Chlamydia pneumoniae EliSpot
3. Bartonella IgG/IgM antibodies + Bartonella EliSpot
4. Toxoplasma IgG/IgM antibodies
5. CMV EliSpot
6. HSV1 and HSV2 Elispot
7. HHV-6 IgG/IgM antibodies

Tailored testing protocols

- Borreliosis and neuropsychiatric disorders: an overview
- Schizophrenia
- **Panic/Anxiety/Cognitive/Mood disorders**
- Autism spectrum disorder (ASD)
- Obsessive Compulsive Disorder/Tourette's Syndrome
- PANS/PANDAS

Panic attacks/disorders can have an infectious driver …

J Psychiatr Pract. 2000 Nov;6(5):352-6.

Panic attacks may reveal previously unsuspected chronic disseminated lyme disease.

Sherr VT

Abstract

The author describes the histories of three patients with panic-like episodes that turned out to be related to underlying, previously unsuspected tick-borne diseases. Each woman experienced symptoms that are not usual in panic disorder but are typical of neurological Lyme disease, including exquisite sensitivity to light, touch, and sounds, joint pain often in combination with cognitive changes including mental fogginess and loss of recent memory, and some degree of bizarre, shifting, and often excruciating neurological pain. Because these symptoms are atypical of primary panic disorder, they were very helpful in alerting the clinician to suspect an underlying physical illness. In each case, the results of testing revealed positive hallmarks of d
caused by the spirochete, Borrelia burgdorferi, babesiosis, and e
antimicrobial medications for their tick-borne infections, all three
specialist in Lyme disease allowed one of the women to disconti
medication to occasional use only. The third patient is no longer
of an antidepressant. Two of the patients have also needed ongo
disease.

"Each woman experienced symptoms that are not usual in panic disorder but are typical of neurological Lyme disease, including exquisite sensitivity to light, touch, and sounds, joint pain often in combination with cognitive changes including mental fogginess and loss of recent memory …"

PSYCHIATRIC NEWS — AMERICAN PSYCHIATRIC ASSOCIATION

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CLINICAL AND RESEARCH NEWS

Case Shows How Lyme Disease Can Mimic New-Onset Panic Disorder

LESLIE SINCLAIR

Published Online: 25 Jun 2013 | https://doi.org/10.1176/appi.pn.2013.6b19

Neuropsychiatric symptoms are commonly misdiagnosed, and delayed treatment for the real cause can lead to long-lasting impairment.

Syphilis, caused by the spirochete bacterium *Treponema pallidum*, has been called the "great imitator" because of its ability to affect numerous systems and confusion with other diseases. At a workshop at APA's 2013 annual meeting titled "Medical Conditions Mimicking Psychiatric Disorders Versus Psychiatric Disorders Mimicking Medical Conditions: Diagnostic and Treatment Challenges," presenter Yu Dong, M.D., Ph.D., a psychiatry resident at Baystate Medical Center in Springfield, Mass., detailed the case of another spirochetal imitator: *Borrelia burgdorferi*, the Lyme disease bacterium.

AONM ACADEMY of NUTRITIONAL MEDICINE

arminlabs DIAGNOSTICS TICK-BORNE DISEASES

… as can cognitive disorders/anxiety …

ORIGINAL ARTICLE

Annals of Agricultural and Environmental Medicine 2017, Vol 24, No 1, 33–38
www.aaem.pl

Estimation of cognitive and affective disorders occurrence in patients with Lyme borreliosis

Barbara Oczko-Grzesik[1], Lucjan Kępa[1], Monika Puszcz-Matlińska[2], Robert Pudlo[3], Anna Żurek[2], Teresa Badura-Głąbik[2]

[1] *Clinical Department of Infectious Diseases, Bytom, Medical University of Silesia, Katowice, Poland*
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Oczko-Grzesik B, Kępa L, Puszcz-Matlińska M, Pudlo R, Żurek A, Badura-Głąbik T. Estimation of cognitive and affective disorders occurrence in patients with Lyme borreliosis. Ann Agric Environ Med. 2017; 24(1): 33–38. doi: 10.5604/12321966.1229002

Abstract

Introduction and objective. Lyme borreliosis (LB) is a disease caused by the bacteria *Borrelia burgdorferi*. The most common symptoms are related to the skin, musculo-scelatal system, central and peripheral nervous system, rarely to the heart muscle and the eye, and may occur in the multistage course of the disease. LB may additionally be accompanied by psychopathological symptoms. The aim of the study is estimation of the cognitive and affective disorders occurence in patients with LB.

Material and methods. The study was carried out in the group of 121 patients (61 females, 60 males) aged 18–65; mean age 46 years. All patients were diagnosed with late-stage of LB: 46 patients (38%) with Lyme arthritis and 75 patients (62%) with neuroborreliosis. Evaluation of the cognitive and affective functioning of patients was performed on the basis of a standardized interview and test methods: the Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT) and the Beck Depression Inventory (BDI).

Results. Cognitive disorders occurred statistically significantly more often in patients with neuroborreliosis (14.7%) than in patients with Lyme arthritis (4.3%). A group of females with neuroborreliosis and a group of males with the same diagnosis demonstrated cognitive deficits significantly more often (23.3% and 8.9%, respectively), compared to groups of patients with Lyme arthritis (6.5% in females and no cognitive deficits in males). A significantly higher percentage of depressive disorders was also noted in the group of males and females with neuroborreliosis (50.7%), compared to the group of patients with Lyme arthritis (39.1%). The symptoms of depression were particularly frequent in the females with neuroborreliosis (60%). The severity of depression measured by BDI was mild or moderate in most cases. In the examined groups, more patients with neuroborreliosis (44%), both in females (36.7%) and males (48.9%), demonstrated anxiety disorders. The obtained results showed a higher frequency of affective disorders compared to cognitive deficits, both in patients with Lyme arthritis and neuroborreliosis.

Conclusions. An increased frequency of depressive and neurotic disorders was observed in patients with LB, particularly in patients with neuroborreliosis. Neurotic disorders, mainly adaptive, were most common in males with LB, while depressive disorders were more frequent in females. An increased frequency of cognitive deficits was observed in patients with neuroborreliosis, particularly in females.

"**Cognitive disorders occurred statistically significantly more often in patients with neuroborreliosis** (14.7%) than in patients with Lyme arthritis (4.3%)….. In the examined groups, more patients with neuroborreliosis (44%), both in females (36.7%) and males (48.9%), demonstrated anxiety disorders."

and-depression-due-lyme-disease-0

Mood disorders have been linked to HHV-6, which can in turn be reactivated by other infections

Front Microbiol. 2018; 9: 1955.
Published online 2018 Aug 21. doi: [10.3389/fmicb.2018.01955]
PMCID: PMC6110891
PMID: 30186267

Active HHV-6 Infection of Cerebellar Purkinje Cells in Mood Disorders

Bhupesh K. Prusty,[1,2,*] Nitish Gulve,[1] Sheila Govind,[3] Gerhard R. F. Krueger,[4] Julia Feichtinger,[5,6] Lee Larcombe,[7] Richard Aspinall,[8] Dharam V. Ablashi,[9] and Carla T. Toro[9,10,*]

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Abstract

Go to:

Early-life infections and associated neuroinflammation is incriminated in the pathogenesis of various mood disorders. Infection with human roseoloviruses, HHV-6A and HHV-6B, allows viral latency in the central nervous system and other tissues, which can later be activated causing cognitive and behavioral disturbances. Hence, this study was designed to evaluate possible association of HHV-6A and HHV-6B activation with three different groups of psychiatric patients. DNA qPCR, immunofluorescence and FISH studies were carried out in post-mortem posterior cerebellum from 50 cases each of bipolar disorder (BPD), schizophrenia, 15 major depressive disorder (MDD) and 50 appropriate control samples obtained from two well-known brain collections (Stanley Medical Research Institute). HHV-6A and HHV-6B late proteins (indicating active infection) and viral DNA were detected more frequently ($p < 0.001$ for each virus) in human cerebellum in MDD and BPD relative to controls. These roseolovirus proteins and DNA were found less frequently in schizophrenia cases. Active HHV-6A and HHV-6B infection in cerebellar Purkinje cells were detected frequently in BPD and MDD cases. Furthermore, we found a significant association of HHV-6A infection with reduced Purkinje cell size, suggesting virus-mediated abnormal Purkinje cell function in these disorders. Finally, gene expression analysis of cerebellar tissue revealed changes in pathways reflecting an inflammatory response possibly to HHV-6A infection. Our results provide molecular evidence to support a role for active HHV-6A and HHV-6B infection in BPD and MDD

"HHV-6A and HHV-6B late proteins (indicating active infection) and viral DNA were detected more frequently … in human cerebellum in MDD and BPD relative to controls."[1]

"…and infections with other pathogens have the potential to reactivate latent HHV-6A/"[1]
"Chlamydia trachomatis infection induces replication of latent HHV-6"[2]

Source: 1. Prusty BK et al. Active HHV-6 Infection of Cerebellar Purkinje Cells in Mood Disorders. Front Microbiol. 2018;9:1955. Published 2018 Aug 21.; 2. Prusty B et al. (2013b). Chlamydia trachomatis infection induces replication of latent HHV-6. PLoS One 8:e61400. 10.1371/journal.pone.0061400

Bartonella found in patients suffering from agitation, panic disorder and treatment-resistant depression

MedGenMed. 2007; 9(3): 54.
Published online 2007 Sep 13.

PMCID: PMC2100128
PMID: 18092060

Do *Bartonella* Infections Cause Agitation, Panic Disorder, and Treatment-Resistant Depression?

James L. Schaller, MD, MAR, Director, Professional Medical Services of Naples, Glenn A. Burkland, DMD, Associate Clinical Professor, and P.J. Langhoff, science research assistant and medical writer

Abstract

Go to:

Introduction

Go to:

Bartonella is an emerging infection found in cities, suburbs, and rural locations. Routine national labs offer testing for only 2 species, but at least 9 have been discovered as human infections within the last 15 years. Some authors discuss *Bartonella* cases having *atypical* presentations, with serious morbidity considered uncharacteristic of more routine *Bartonella* infections. Some atypical findings include distortion of vision, abdominal pain, severe liver and spleen tissue abnormalities, thrombocytopenic purpura, bone infection, arthritis, abscesses, heart tissue and heart valve problems. While some articles discuss *Bartonella* as a cause of neurologic illnesses, psychiatric illnesses have received limited attention. Case reports usually do not focus on psychiatric symptoms and typically only as incidental comorbid findings. In this article, we discuss patients exhibiting new-onset agitation, panic attacks, and treatment-resistant depression, all of which may be attributed to *Bartonella*.

Methods

Go to:

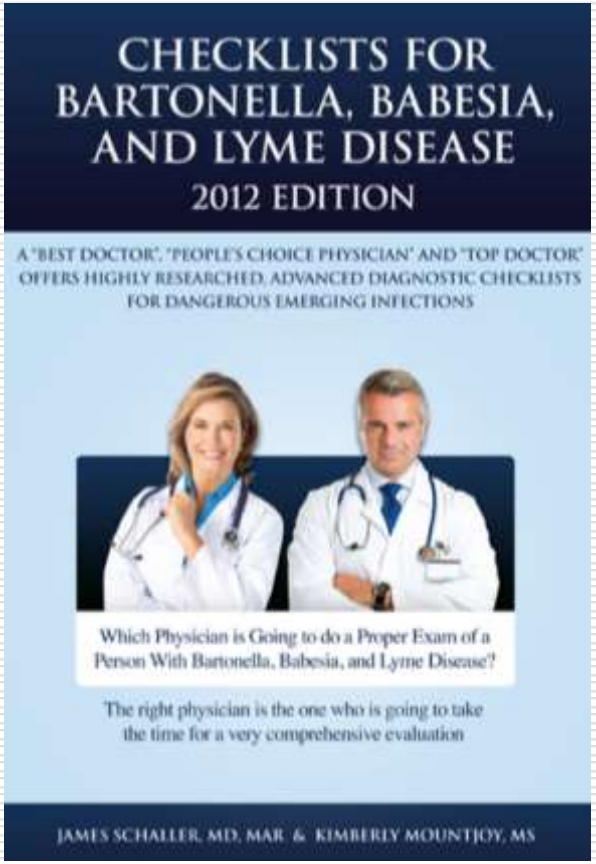
Three patients receiving care in an outpatient clinical setting developed acute onset personality changes and agitation, depression, and panic attacks. They were retrospectively examined for evidence of *Bartonella* infections. The medical and psychiatric treatment progress of each patient was tracked until both were significantly resolved and the *Bartonella* was cured.

"... we discuss patients exhibiting new-onset agitation, panic attacks, and treatment-resistant depression, all of which may be attributed to *Bartonella*...

***Bartonella* can clearly cause neurologic disorders...."**

Source: Schaller JL, Burkland GA, Langhoff PJ. Do Bartonella Infections Cause Agitation, Panic Disorder, and Treatment-Resistant Depression? Medscape General Medicine. 2007;9(3):54.

In Schaller and Mountjoy's seminal book, psychiatric symptoms are the first (and longest) Bartonella checklist



"It's going to be missed 99.9% of the time".

THE BARTONELLA CHECKLIST

James Schaller, M.D., M.A.R.

(Please Check Any Symptoms That Apply)

PSYCHIATRIC AND NEUROLOGICAL

- ☐ Current anxiety that was not present at age ten
- ☐ Current depression not present at age sixteen
- ☐ Knee-jerk emotional responses worse than past decades and worsening
- ☐ Brain fog
- ☐ Depression
- ☐ Depression that is not **fully** controlled on **routine anti-depressant doses,** or high dose antidepressants are required to control mood [**Improvement of mood** or being "less depressed" is not successful depression treatment.]
- ☐ Anxiety is poorly controlled with average dosing
- ☐ Depression is poorly controlled by reasonable treatment trials.
- ☐ Suicidal feelings or routine thoughts of death
- ☐ Crying
- ☐ Obsessive thoughts or fear in excess of event
- ☐ Obsessive thoughts that intrude into the mind which are in excess of normal
- ☐ A decrease in pleasure
- ☐ Rage worse with time
- ☐ Irritability worse with time

Impatience is greater when compared to ten years ago [in a child--any irritability in excess of what is common for most children with an identical age]

Cursing or hostile speech that is worse over time

Increased addictions that are very resistant to typical recovery ranges

Increased impulsivity in contrast to past years or past decades

Severe neurological disorders without a clear cause

Severe psychiatric troubles that do not seem to fit with the diagnostic criteria or there is trouble controlling symptoms with treatment

New physical, emotional or verbal abuse in the home which was not present in the past

Panic attacks that were not present at ten years of age

Anxiety medication has to be increased to **very high levels** to continue past benefit

Diagnosed as having bipolar disorder, but do not fit the criteria well

Any psychiatric disorder that also shows **medical pathology in laboratory tests**

Restlessness

Combative behavior

A parent, grandparent, child or sibling with suicide attempts

A parent, grandparent, child or sibling who has started physical or extreme verbal fights

Intermittent confusion

Panic/Anxiety/Cognitive/Mood disorders

1. Borrelia SeraSpot + Borrelia-EliSpot + Tickplex Basic + CD57-cells
2. Bartonella IgG/IgM antibodies + Bartonella EliSpot
3. Toxoplasma IgG/IgM antibodies
4. HHV-6 IgG/IgM antibodies

Tailored testing protocols

- Borreliosis and neuropsychiatric disorders: an overview
- Schizophrenia
- Panic/Anxiety/Cognitive/Mood disorders
- **Autism spectrum disorder (ASD)**
- Obsessive Compulsive Disorder (OCD)/Tourette's Syndrome
- PANS/PANDAS

Borreliosis may be a contributor in 20 - 30% of ASD

Medical Hypotheses
Volume 70, Issue 5, 2008, Pages 967-974

The association between tick-borne infections, Lyme borreliosis and autism spectrum disorders

Robert C. Bransfield [a], Jeffrey S. Wulfman [b], William T. Harvey [c], Anju I. Usman [d]

Show more

https://doi.org/10.1016/j.mehy.2007.09.006

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Summary

Chronic infectious diseases, including tick-borne infections such as *Borrelia burgdorferi* may have direct effects, promote other infections and create a weakened, sensitized and immunologically vulnerable state during fetal development and infancy leading to increased vulnerability for developing autism spectrum disorders. A dysfunctional synergism with other predisposing and contributing factors may contribute to autism spectrum disorders by provoking innate and adaptive immune reactions to cause and perpetuate effects in susceptible individuals that result in inflammation, molecular mimicry, kynurenine pathway changes, increased quinolinic acid and decreased serotonin, oxidative stress, mitochondrial dysfunction and excitotoxicity that impair the development of the amygdala and other neural structures and neural networks resulting in a partial Klüver–Bucy Syndrome and other deficits resulting in autism spectrum disorders and/or exacerbating autism spectrum disorders from other causes throughout life.

Support for this hypothesis includes multiple cases of mothers with Lyme disease and children with autism spectrum disorders; fetal neurological abnormalities associated with

"Vojdani tested Autism samples from different clinics in Northern CA, NY, NJ and CT. 22% of (12/54) tested IgG and IgM positive for Bbsl *[Borrelia burgdorferi sensu lato]* by Immunosciences Lab"

"A LIAF study tested the blood of 19 children with an ASD diagnoses plus an indication of immune dysfunction and five normal controls…

26% of the ASD children were positive compared to 0 controls."

"Nicolson tested 48 ASD patients with forensic PCR and Southern Blot confirmation … **58% were positive for Mycoplasma species**"2

Proc. Intern. Mind of a Child Conference, Sydney, Australia 2002

Chronic Mycoplasmal Infections in Autism Patients

Garth L. Nicolson,[1] PhD, Marwan Y. Nasralla,[2] PhD, Paul Berns,[1] MD and Jeorg Haier,[3] MD, PhD

[1]The Institute for Molecular Medicine, Huntington Beach, California, USA,' [2]International Molecular Diagnostics, Inc., Huntington Beach, California, USA, [3]Department of Internal Medicine, and [3]Department of Surgery, Wilhelm-University, Munste

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gnicolson@immed.org; Website: www.immed.org

Abstract

A majority of Autism patients have systemic bacterial, viral and fu
an important part in their illnesses. We found that immediate
diagnosed with Gulf War Illnesses (GWI) often complain of f
analysis they report similar signs and symptoms as their veteran
their children are often diagnosed with Autism. Since a relativ
patients is a bacterial infection due to *Mycoplasma fermentans*, w
(149 patients: 42 veterans, 40 spouses, 32 other relatives and 35 chi
complaint of illness) selected from a group of 110 veterans wi
(~42%) for mycoplasmal infections. Consistent with previous resul
who were positive for blood mycoplasmal infections had only
fermentans. In healthy control subjects the incidence of mycoplas
none were found to have multiple mycoplasmal species ($P<0.001$)
mycoplasma-positive GWI patients there were 57 patients (53%)
signs and symptoms as the veterans and were diagnosed with
(CFS/ME) and/or Fibromyalgia Syndrome. The majority of childr

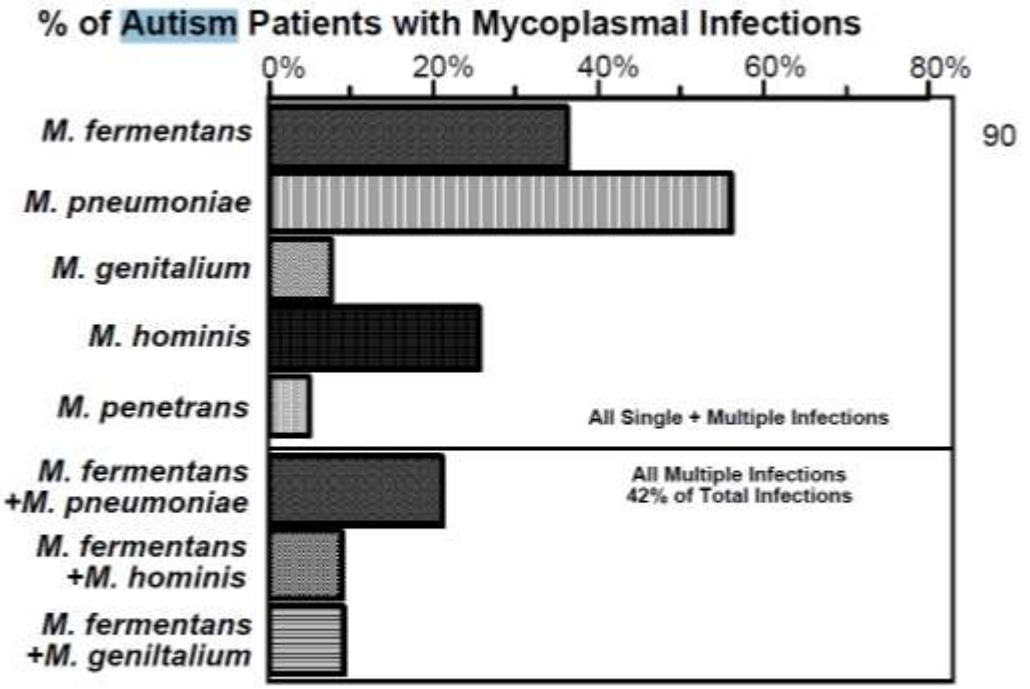
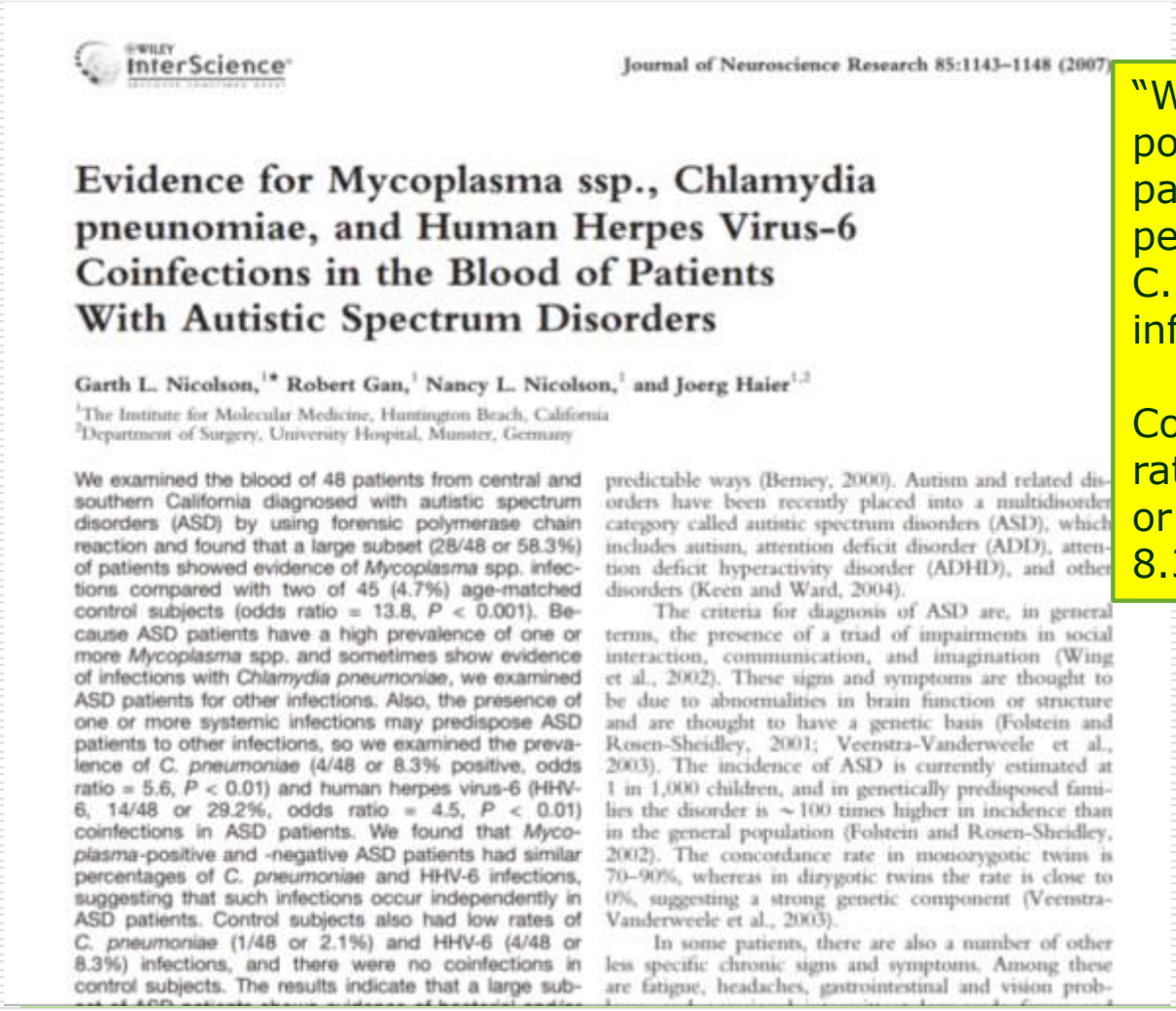


Figure 4. The incidence of various mycoplasma species in patients with Autism from Central California. All cases of multiple mycoplasmal infections were combinations of *M. fermentans*.

Source: Nicolson, Garth & Nasralla, Marwan & Berns, Paul & Haier, Jeorg. (2002). Chronic Mycoplasmal Infections in Autism Patients. Mind of a Child; 2.
Medical Hypotheses Volume 70, Issue 5, 2008, Pages 967–974 The association between tick-borne infections, Lyme borreliosis and autism spectrum disorders
Robert C. Bransfield, Jeffrey S. Wulfman, William T. Harvey, Anju I. Usman[d]

Evidence also for Chlamydia pneumoniae and HHV-6 in ASD



InterScience

Journal of Neuroscience Research 85:1143–1148 (2007)

Evidence for Mycoplasma ssp., Chlamydia pneunomiae, and Human Herpes Virus-6 Coinfections in the Blood of Patients With Autistic Spectrum Disorders

Garth L. Nicolson,[1]* Robert Gan,[1] Nancy L. Nicolson,[1] and Joerg Haier[1,2]

[1]The Institute for Molecular Medicine, Huntington Beach, California
[2]Department of Surgery, University Hospital, Munster, Germany

We examined the blood of 48 patients from central and southern California diagnosed with autistic spectrum disorders (ASD) by using forensic polymerase chain reaction and found that a large subset (28/48 or 58.3%) of patients showed evidence of *Mycoplasma* spp. infections compared with two of 45 (4.7%) age-matched control subjects (odds ratio = 13.8, $P < 0.001$). Because ASD patients have a high prevalence of one or more *Mycoplasma* spp. and sometimes show evidence of infections with *Chlamydia pneumoniae*, we examined ASD patients for other infections. Also, the presence of one or more systemic infections may predispose ASD patients to other infections, so we examined the prevalence of *C. pneumoniae* (4/48 or 8.3% positive, odds ratio = 5.6, $P < 0.01$) and human herpes virus-6 (HHV-6, 14/48 or 29.2%, odds ratio = 4.5, $P < 0.01$) coinfections in ASD patients. We found that *Mycoplasma*-positive and -negative ASD patients had similar percentages of *C. pneumoniae* and HHV-6 infections, suggesting that such infections occur independently in ASD patients. Control subjects also had low rates of *C. pneumoniae* (1/48 or 2.1%) and HHV-6 (4/48 or 8.3%) infections, and there were no coinfections in control subjects. The results indicate that a large sub-

predictable ways (Berney, 2000). Autism and related disorders have been recently placed into a multidisorder category called autistic spectrum disorders (ASD), which includes autism, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), and other disorders (Keen and Ward, 2004).

The criteria for diagnosis of ASD are, in general terms, the presence of a triad of impairments in social interaction, communication, and imagination (Wing et al., 2002). These signs and symptoms are thought to be due to abnormalities in brain function or structure and are thought to have a genetic basis (Folstein and Rosen-Sheidley, 2001; Veenstra-Vanderweele et al., 2003). The incidence of ASD is currently estimated at 1 in 1,000 children, and in genetically predisposed families the disorder is ~100 times higher in incidence than in the general population (Folstein and Rosen-Sheidley, 2002). The concordance rate in monozygotic twins is 70–90%, whereas in dizygotic twins the rate is close to 0%, suggesting a strong genetic component (Veenstra-Vanderweele et al., 2003).

In some patients, there are also a number of other less specific chronic signs and symptoms. Among these are fatigue, headaches, gastrointestinal and vision prob-

"We found that Mycoplasma-positive and -negative ASD patients had similar percentages of C. pneumoniae and HHV-6 infections …

Control subjects had low rates of C. pneumoniae (1/48 or 2.1%) and HHV-6 (4/48 or 8.3%) infections."

The prevalence of congenital CMV was 10-fold higher in children with ASD than in controls in this 2017 study

In Vivo. 2017 May-Jun;31(3):467-473.

Prevalence of Congenital Cytomegalovirus Infection Assessed Through Viral Genome Detection in Dried Blood Spots in Children with Autism Spectrum Disorders.

Gentile I[1], Zappulo E[2], Riccio MP[3], Binda S[4], Bubba L[4], Pellegrinelli L[4], Scognamiglio D[5], Operto F[6], Margari L[6], Borgia G[2], Bravaccio C[7].

Author information

Abstract

BACKGROUND/AIM: Autism spectrum disorders (ASD) are neurodevelopmental disorders without a definitive etiology in most cases. Environmental factors, such as viral infections, have been linked with anomalies in brain growth, neuronal development, and functional connectivity. Congenital cytomegalovirus (CMV) infection has been associated with the onset of ASD in several case reports. The aim of this study was to evaluate the prevalence of congenital CMV infection in children with ASD and in healthy controls.

PATIENTS AND METHODS: The CMV genome was tested by polymerase chain reaction (PCR) on dried blood spots collected at birth from 82 children (38 with ASD and 44 controls).

RESULTS: The prevalence of congenital CMV infection was 5.3% (2/38) in cases and 0% (0/44) in controls (p=0.212).

CONCLUSION: The infection rate was about 10-fold higher in patients with ASD than in the general Italian population at birth. For this reason, detection of CMV-DNA on dried blood spots could be considered in the work-up that is usually performed at ASD diagnosis to rule-out a secondary form. Given the potential prevention and treatment of CMV infection, this study could have intriguing consequences, at least for a group of patients with ASD.

"The infection rate was about 10-fold higher in patients with ASD than in the general Italian population at birth."

Autism

1. Borrelia SeraSpot + Borrelia-EliSpot + Tickplex Basic + CD57-cells
2. Mycoplasma pneumoniae IgG/IgA antibodies + Mycoplasma pneumoniae EliSpot
3. Chlamydia pneumoniae IgG/IgA antibodies + Chlamydia pneumoniae EliSpot
4. CMV EliSpot; CMV IgG/IgM antibodies
5. HHV-6 IgG/IgM antibodies
6. Anti-streptolysin titer

Tailored testing protocols

- Borreliosis and neuropsychiatric disorders: an overview
- Schizophrenia
- Panic/Anxiety/Cognitive/Mood disorders
- Autism spectrum disorder (ASD)
- **Obsessive Compulsive Disorder (OCD)/Tourette's Syndrome**
- PANS/PANDAS

"Greater frequency of Lyme disease symptoms and disease-related impairment was related to greater OCS"

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General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

Obsessive-compulsive symptoms in adults with Lyme disease

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[f] Baylor College of Medicine, Houston, TX, USA

ARTICLE INFO

Keywords:
Lyme disease
Obsessive compulsive disorder
OCD
Lyme

ABSTRACT

Objective: This study examined the phenomenology and clinical characteristics of obsessive compulsive symptoms (OCS) in adults diagnosed with Lyme disease.

Method: Participants were 147 adults aged 18–82 years (M = 43.81, SD = 12.98) who reported having been diagnosed with Lyme disease. Participants were recruited from online support groups for individuals with Lyme disease, and completed an online questionnaire about their experience of OCS, Lyme disease characteristics, and the temporal relationship between these symptoms.

Results: OCS were common, with 84% endorsing clini
symptoms onset during the six months following their L
symptoms were temporally related. Despite the common
identified these symptoms as problematic. Greater freq
impairment was related to greater OCS. In the majority of
to psychological and pharmacological treatment. Around
improvement in OCS following antibiotic treatment.

"… greater OCS occurred in the group who experienced the symptoms, in comparison to the group that did not experience that symptom."

Source: Johnco C, Kugler BB, Murphy TK, Storch EA. Obsessive-compulsive symptoms in adults with Lyme disease. Gen Hosp Psychiatry. 2018;51:85-89.

Presence of Toxoplasma gondii more frequent in OCD patients than in controls *(2017 study, 7471 subjects)*

Eur Psychiatry. 2017 Feb;40:82-87. doi: 10.1016/j.eurpsy.2016.09.001. Epub 2016 Dec 16.

Toxoplasma-infected subjects report an Obsessive-Compulsive Diso and score higher in Obsessive-Compulsive Inventory.

Flegr J[1], Horáček J[2].

Author information

Abstract

BACKGROUND: Latent toxoplasmosis, the life-long presence of dormant stages of Toxoplasma in in anamnestic IgG antibodies in blood, affects about 30% of humans. Infected subjects have an increas including schizophrenia. Several studies, as well as the character of toxoplasmosis-associated distu toxoplasmosis could also play an etiological role in Obsessive-Compulsive Disorder (OCD).

METHODS: The aim of the present cross-sectional study performed on a population of 7471 volunte between toxoplasmosis and OCD, and toxoplasmosis and psychological symptoms of OCD estimate Inventory-Revised (OCI-R).

RESULTS: Incidence of OCD was 2.18% (n=39) in men and 2.28% (n=83) in women. Subjects with toxoplasmosis had about a 2.5 times higher odds of OCD and about a 2.7 times higher odds of learning disabilities. The incidence of 18 other neuropsychiatric disorders did not differ between Toxoplasma-infected and Toxoplasma-free subjects. The infected subjects, even the OCD-free subjects, scored higher on the OCI-R.

LIMITATIONS: Examined subjects provided the information about their toxoplasmosis and OCD statuses themselves, which could result in underrating the strength of observed associations.

CONCLUSIONS: The results confirmed earlier reports of the association between toxoplasmosis and OCD. They also support recent claims that latent toxoplasmosis is in fact a serious disease with many impacts on quality of life of patients.

"…. the presence of anti-Toxoplasma gondii IgG in serum was more frequent in OCD patients than in controls …

In a 1991 study, Strittmatter and colleagues showed that the CNS areas most affected by T. gondii were the cerebral hemispheres (91%) and the basal ganglia (78%) which are implicated in OCD neurobiology [146]."

Source: Flegr, J.; Horacek, J. Toxoplasma-infected subjects report an obsessive-compulsive disorder diagnosis more often and score higher in obsessive-compulsive inventory. Eur. Psychiatry 2017, 40, 82–87.

Mycoplasma also associated with OCD and Tourette's

Open Neurol J. 2012; 6: 124–128.
Published online 2012 Nov 16. doi: [10.2174/1874205X01206010124]
Suppl 1

PMCID: PMC3514747
PMID: 23230453

The Relationship between Tourette's Syndrome and Infections

Daniela L Krause* and Norbert Müller

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This article has been cited by other articles in PMC.

Abstract

Increasing evidence shows that infections and an activated immune status might be involved in the pathogene-sis of tic disorders. Studies discuss the influence of neurotrophic bacteria and viruses on different psychiatric disorders. In addition, signs of inflammation and immunological abnormalities have been described especially in schizophrenia and Tourette's syndrome (tic disorder). Neuroimaging studies revealed increased microglial activation in psychiatric diseases; indicating an inflammatory state of the CNS.

However, it still remains unclear what the underlying mechanism is of how infectious agents could contribute to tic symp-toms. One hypothesis is that not only one particular infectious agent causes directly to the disease; instead different (chronic) infections influence the immune balance and are therefore involved in the pathology. In tic disorders, infections with group A streptococci, *Borrelia burgdorferi* or *Mycoplasma pneumoniae* seem to be associated with symptoms of the disease. Studies have shown that immunologic treatment improves and prevents the re-occurrence of clinical symptoms in Tourette's syndrome. Also post-infectious events by cross-reactive antibodies(against M-protein) and an altered dopamine rgic(noradrenergic) neurotransmission as well as inflammatory/immunological dysregulations were considered as possible mechanisms to cause symptoms. Another contributing factor to the pathogenesis of these diseases could be an activation of the tryptophan catabolism through infectious

"*Mycoplasma* has also been associated with OCD, Tourette's syndrome, parkinsonism, and dystonia.137–139"[1]

Source: 1. Rhee H, Cameron DJ. Lyme disease and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS): an overview. International Journal of General Medicine. 2012;5:163-174; 2. Muller N, Riedel M, Forderreuther S, Blendinger C, Abele-Horn M. Tourette's syndrome and Mycoplasma pneumoniae infection. Am J Psychiatry. 2000;157(3):481–482

OCD/Tourette's Syndrome

1. Borrelia SeraSpot + Borrelia-EliSpot + Tickplex Basic + CD57-cells
2. Toxoplasma IgG/IgM
3. Mycoplasma pneumoniae IgG/IgA antibodies + Mycoplasma EliSpot
4. Toxoplasma IgG/IgM antibodies
5. Anti-streptolysin titer

Tailored testing protocols

- Borreliosis and neuropsychiatric disorders: an overview
- Schizophrenia
- Panic/Anxiety/Cognitive/Mood disorders
- Autism spectrum disorder (ASD)
- Obsessive Compulsive Disorder/Tourette's Syndrome
- **PANS/PANDAS**

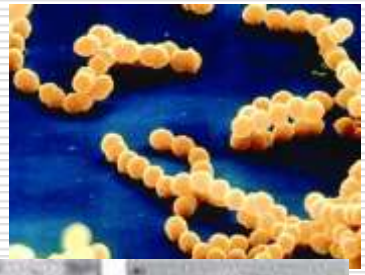
Many infectious triggers are associated with PANS/PANDAS

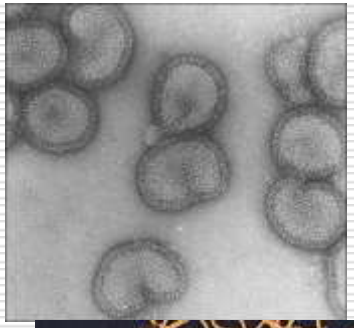
- Group A streptococci
- Influenza A
- Varicella (chickenpox)
- Mycoplasma
- Lyme disease
- Babesia
- Bartonella
- Coxsackie virus

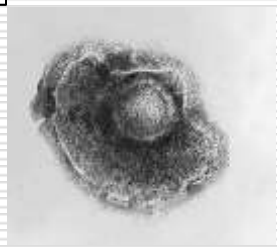

Yes, You Can Catch Insanity

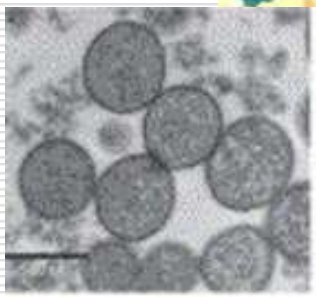
A controversial disease revives the debate about the immune system and mental illness.

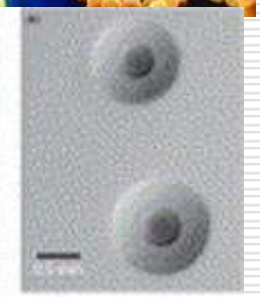
BY ANDREW CURRY
ILLUSTRATION BY HADLEY HOOPER
APRIL 18, 2015

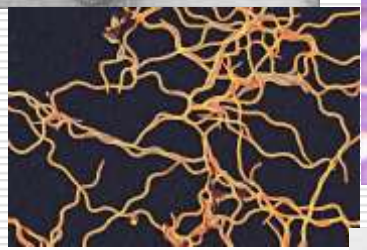


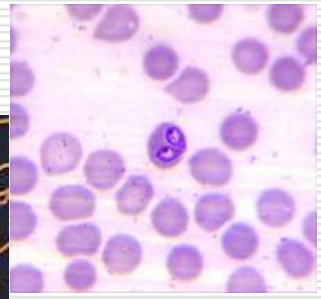


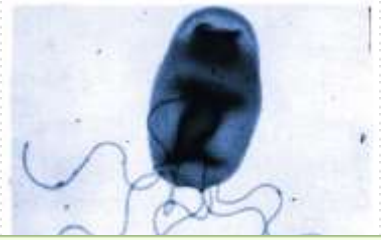


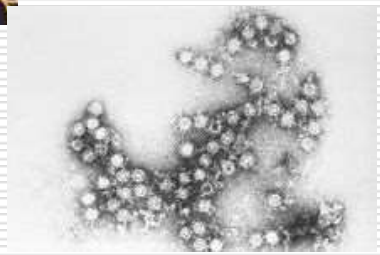












Patients often have more than one infection, and can be subclinical

Source: Courtesy of Dr. Craig Shimasaki, CEO Moleculera Labs, Oklahoa

Mycoplasma involvement in PANS/PANDAS conditions

International Journal of Neuropsychopharmacology (2001), 4, 191–198. Copyright © 2001 CINP

Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS)

Henrietta L. Leonard[1] and Susan E. Swedo[2]

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[2] *Pediatric and Developmental Neuropsychiatry Branch, NIMH, Bethesda, MD USA*

Abstract

The evidence to date, both published and unpublished, which addresses the validity of the proposed unique subgroup of children with early and abrupt onset of obsessive–compulsive disorder (OCD) and/or tic

concluded that the rapid efficacy of antibiotic treatment followed by a decrease in *Borrelia*-specific antibody titres were evidence that the multiple motor and vocal tics were caused, at least in part, by the tertiary stage of borreliosis.

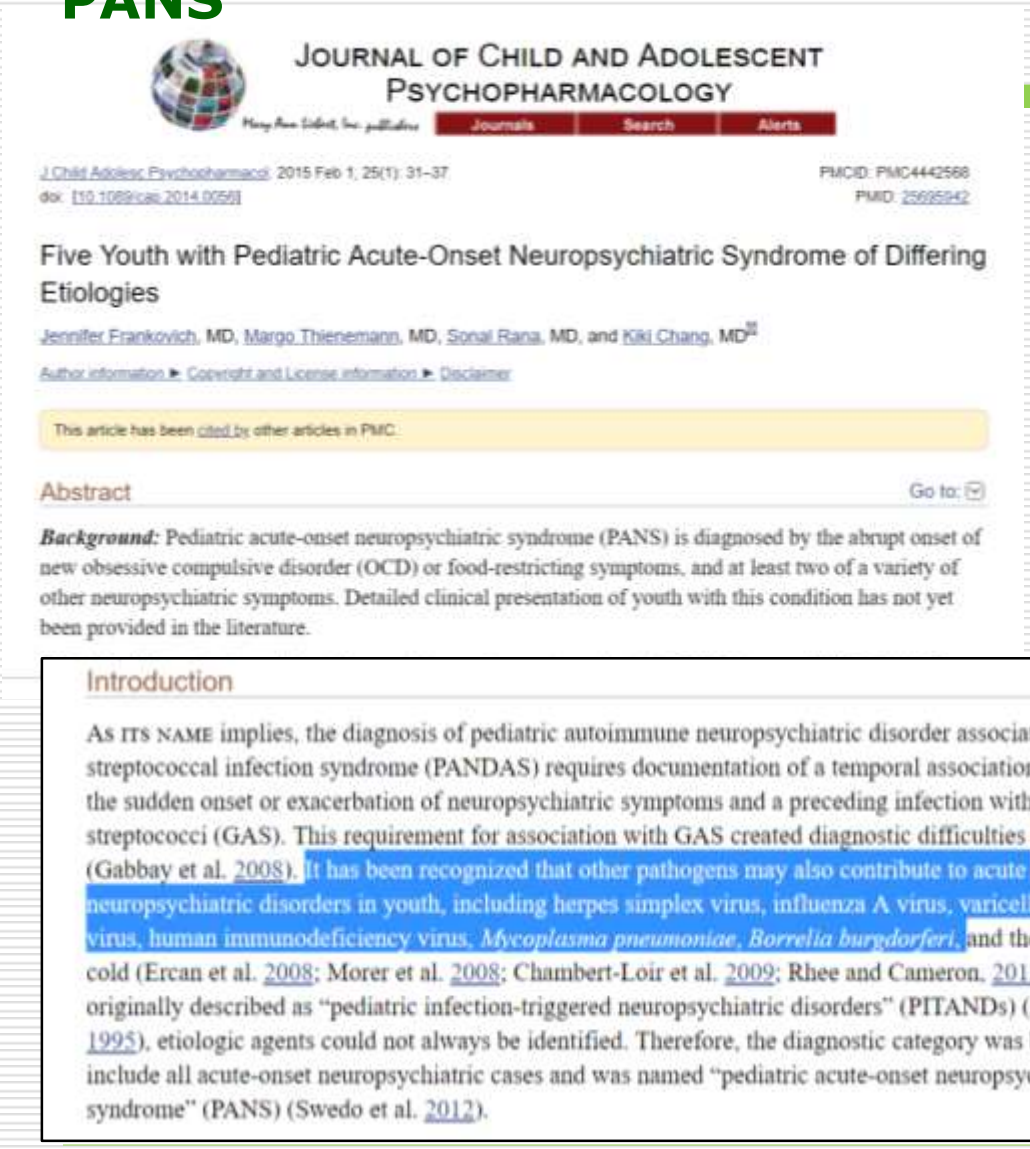
Mycoplasma pneumoniae encephalitis has also been reported to cause a Tourette-like syndrome. Two children with mild tics were reported to have a dramatic exacerbation in symptoms concomitant with their *M. pneumoniae* infection. In both cases, the tics resolved rapidly in response to successful antibiotic treatment of the infection (Muller et al., 2000). *Mycoplasma pneumoniae* encephalitis has been reported to cause basal ganglia lesions and movement disorders, but this was the first report of severe motor and vocal tics. The authors suggested that tics might be a final common pathway of various disorders that have different aetiologies. A variety of infectious and non-infectious illnesses that impact on the basal ganglia could cause similar symptoms, if regional localization was similar.

Although there is an increased rate of OCD in S
does not mean that PANDAS is in the spectru
rheumatic fever. Although one might speculate
PANDAS represents a dual genetic vulnerability (C
tics and rheumatic fever) this will require syste
family studies to determine whether it is valid. Prelin
family studies of first-degree relatives of PAN
probands reported that the rates of tic disorders and
were higher than those reported in the general popu
and similar to those reported previously for tic dis
and OCD (Lougee et al., 2000). Identification of r
genetic vulnerability for rheumatic fever, will ha
come from future genetic studies (e.g. identificati
HLA profiles).

Current theories of post-streptococcal autoimmunity include theories of humoral (presence of anti-neuronal antibodies), cell-mediated (cytokine shifts and/or V-beta abnormalities), and super-antigen aetiologies. All of these mechanism are possible explanations for post-streptococcal OCD/tic disorders, but none have been proven

"Mycoplasma pneumoniae encephalitis has also been reported to cause a Tourette-like syndrome … Mycoplasma pneumoniae encephalitis has been reported to cause basal ganglia lesions and movement disorder …"

HSV, VZV, Mycoplasma, Borrelia can contribute to PANS



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J Child Adolesc Psychopharmacol. 2015 Feb 1; 25(1): 31–37.
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PMID: 25695942

Five Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome of Differing Etiologies

Jennifer Frankovich, MD, Margo Thienemann, MD, Sonal Rana, MD, and Kiki Chang, MD

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Abstract

Background: Pediatric acute-onset neuropsychiatric syndrome (PANS) is diagnosed by the abrupt onset of new obsessive compulsive disorder (OCD) or food-restricting symptoms, and at least two of a variety of other neuropsychiatric symptoms. Detailed clinical presentation of youth with this condition has not yet been provided in the literature.

Introduction

As its name implies, the diagnosis of pediatric autoimmune neuropsychiatric disorder associate streptococcal infection syndrome (PANDAS) requires documentation of a temporal association the sudden onset or exacerbation of neuropsychiatric symptoms and a preceding infection with streptococci (GAS). This requirement for association with GAS created diagnostic difficulties f (Gabbay et al. 2008). It has been recognized that other pathogens may also contribute to acute neuropsychiatric disorders in youth, including herpes simplex virus, influenza A virus, varicella virus, human immunodeficiency virus, *Mycoplasma pneumoniae*, *Borrelia burgdorferi*, and the common cold (Ercan et al. 2008; Morer et al. 2008; Chambert-Loir et al. 2009; Rhee and Cameron, 2012). Although originally described as "pediatric infection-triggered neuropsychiatric disorders" (PITANDs) (Allen et al. 1995), etiologic agents could not always be identified. Therefore, the diagnostic category was broadened to include all acute-onset neuropsychiatric cases and was named "pediatric acute-onset neuropsychiatric syndrome" (PANS) (Swedo et al. 2012).

"… **other pathogens may also contribute to acute neuropsychiatric disorders** in youth, including **herpes simplex virus, influenza A virus, varicella zoster virus, human immunodeficiency virus, Mycoplasma pneumoniae, Borrelia burgdorferi**, and the common cold (Ercan et al. 2008; Morer et al. 2008; ChambertLoir et al. 2009; Rhee and Cameron, 2012)."

Autoimmune encephalitis can be triggered after herpes simplex encephalitis

	Patients ≤4 years (n=27)	Patients >4 years (n=31)	Comparison
Median age, range	11 months (7–17), range 2–48	42 years (18–60), range 6–80	--
Median interval between herpes simplex encephalitis and autoimmune encephalitis, range	26 days (24–32), range 7–61	43 days (25–54), range 11–306	p=0·0073
Main symptoms of autoimmune encephalitis			
Change of behaviour*	26 (96%)	28 (90%)	p=0·615
Seizures	15 (56%)†	7 (23%)‡	p=0·015
Choreoathetosis	27 (100%)	0	p<0·001
Decreased level of consciousness§	26 (96%)	7 (23%)	p<0·001
Dysautonomia	9 (33%)	6 (19%)	p=0·247
Antibodies			
NMDA receptor	24 (89%)¶	19 (61%)	p=0·033
Unknown antigens	3 (11%)	12 (39%)	p=0·030
Immunotherapy			
No immunotherapy	2 (7%)	4 (13%)	p=0·675
First line	25 (93%)‖	27 (87%)**	p=0·675
Second line	15 (56%)††	8 (26%)‡‡	p=0·030
Seizures at 12 months' follow-up	12/19 (63%)	3/23 (13%)	p=0·001
Taking anti-epileptic drugs at 12 months' follow-up	19/19 (100%)	13/23 (57%)	p=0·001
Median mRS at follow-up			
6 months	4 (4–5)	3 (2–3)	p<0·001
12 months	4 (4–4)	2 (2–3)	p<0·001

Data are median (IQR), n (%), or n/N (%), unless otherwise stated. mRS=modified Rankin Scale. *Manifested as irritability and poor response to stimuli and environment in very young children (≤4 years); among children older than 4 years, and adults, 18 patients developed full-blown psychosis. †Ten patients with status epilepticus (six with infantile spasms). ‡Four patients with status epilepticus. §Including loss of contact with environment in children. ¶One patient with co-existing $GABA_A$ receptor antibodies. ‖Combined intravenous methylprednisolone and intravenous immunoglobulins (n=13), combined intravenous methylprednisolone, intravenous immunoglobulins, and plasma exchange (n=7), intravenous methylprednisolone alone (n=3), intravenous immunoglobulins alone (n=1), and plasma exchange alone (n=1). **Combined intravenous methylprednisolone and intravenous immunoglobulins (n=11), combined intravenous methylprednisolone, intravenous immunoglobulins, and plasma exchange (n=3), intravenous methylprednisolone alone (n=12), and intravenous immunoglobulins and oral corticosteroids (n=1). ††All 15 patients were treated with rituximab and six patients also received cyclophosphamide. ‡‡All eight patients were treated with rituximab and four patients also received cyclophosphamide.

***Table 3:* Symptoms of antibody-confirmed autoimmune encephalitis after herpes simplex encephalitis, in Cohorts A and B, stratified by age**

Huge study just completed August 2018, reported in Lancet Neurology

Source: Armangue T et al. Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after herpes simplex encephalitis: A prospective observational study and retrospective analysis. Lancet Neurol 2018 Sep; 17:760

Possible testing protocol for PANS (Paediatric Acute-onset Neuropsychiatric Syndrome/PANDAS (Paediatric Autoimmune Disorders Associated with Strep)

1. Borrelia SeraSpot + Borrelia EliSpot + Tickplex Basic
2. Mycoplasma pneumoniae Elispot and IgG/IgA antibodies
3. Coxsackie Virus IgG/IgA antibodies
4. Babesia Elispot
5. Bartonella Elispot
6. HSV1
7. VZV Elispot and IgG/IgA/IgM antibodies
8. Streptococcal titres
9. (Etc.)

Source: Conversation with Professor Craig Shimasaki, Moleculera Laboratories, 20th February 2018

Thank you very much for your attention!

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END

Different types of Bb infection in neuropsychiatric conditions

healthcare

MDPI

Review

Neuropsychiatric Lyme Borreliosis: An Overview with a Focus on a Specialty Psychiatrist's Clinical Practice

Robert C. Bransfield

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Received: 10 July 2018; Accepted: 23 August 2018; Published: 25 August 2018

Abstract: There is increasing evidence and recognition that Lyme borreliosis (LB) causes m symptoms. This article draws from databases, search engines and clinical experience to review cu information on LB. LB causes immune and metabolic effects that result in a gradually develo spectrum of neuropsychiatric symptoms, usually presenting with significant comorbidity w may include developmental disorders, autism spectrum disorders, schizoaffective disorders, bi disorder, depression, anxiety disorders (panic disorder, social anxiety disorder, generalized an disorder, posttraumatic stress disorder, intrusive symptoms), eating disorders, decreased libido, disorders, addiction, opioid addiction, cognitive impairments, dementia, seizure disorders, su violence, anhedonia, depersonalization, dissociative episodes, derealization and other impairments. Screening assessment followed by a thorough history, comprehensive psychiatric clinical exam, review of systems, mental status exam, neurological exam and physical exam relevant to the patient's complaints and findings with clinical judgment, pattern recognition and knowledgeable interpretation of laboratory findings facilitates diagnosis. Psychotropics and antibiotics may help improve functioning and prevent further disease progression. Awareness of the association between LB and neuropsychiatric impairments and studies of their prevalence in neuropsychiatric conditions can improve understanding of the causes of mental illness and violence and result in more effective prevention, diagnosis and treatment.

"There are three basic types of *B. burgdorferi* infections causing neuropsychiatric symptoms—
1. the meningovascular form associated with cerebrovascular infarcts;
2. the second is infection within the central nervous system (CNS), which is the atrophic form of Lyme meningoencephalitis and is associated with cortical atrophy, gliosis and dementia
3. the third is infection outside the CNS causing immune and other effects within the CNS that contribute to neuropsychiatric symptoms."

"A LB patient with neuro-psychiatric symptoms may have one or more than one of these three types of infections."

A 1990 New England Journal of Medicine study found 89% of PX with late neurologic LD had encephalopathy

Table 2.
Psychiatric Disorders in Larger Series of Patients With Lyme Disease

Study	N	Diagnosis	Measures	Comparison Group	Results	Comments
Logigian et al. (23)	27	Late neurologic Lyme disease	MMPI (score >70 signified depression)	None	26% had extreme irritability; 33% were depressed	89% had encephalopathy
Barr et al. (71)	88	Lyme disease	Beck Depression Inventory, Spielberger anxiety scale	Seronegative patients	Significantly more depression among seropositive patients	
Belman et al. (72)	96 children	Neurologic Lyme disease	Neurologic examination	None	38% had behavioral changes (irritability, lability, poor attention)	Most common system was headaches
Krupp et al. (57)	15	Late Lyme disease and cognitive symptoms	Center for Epidemiologic Studies Depression Scale neuropsychological battery	10 healthy age- and sex-matched subjects	Lyme disease patients were significantly more depressed	The most depressed patients did not have abnormal neuropsychological findings.
Fallon et al. (73)	51	Chronic, seropositive Lyme disease	Survey using DSM-III-R criteria	30 non-Lyme disease patients with arthritis	Lyme disease patients were significantly more likely to have DSM-III-R depression (66% versus 23%)	32% of Lyme disease patients reported panic attacks (versus 19% of comparison patients; n.s.)
Halperin et al. (27)	17	Neurologic Lyme disease	Beck Depression Inventory	None	Mean Beck scores did not show depression	Depressed patients may have beenn excluded from study
Kaplan et al. (56)	20 a	Lyme encephalopathy	Beck Depression Inventory, MMPI	11 fibromyalgia and 11 nonpsychotic depressed patients	Mean Beck scores were not significantly different between groups	Only 13 of the 20 patients completed the Beck inventory
Reik et al. (74)	18	Neurologic Lyme disease	Clinical interview	None	39% had mood lability and irritability; 22% had marked depression	Lyme disease diagnosed by history of erythema migrans or Lyme disease arthritis
Ackerman et al. (32)	44	Borrelia encephalomyelitis	Clinical interview	None	12 patients had mild memory and mood problems; 2 patients had dementia-like deficits	Diagnosis based on intrathecal production of Bb antibodies and clinical features.

a A subgroup of patients from the study by Logigian et al. (23).

Source: Fallon, B. A., & Nields, J. A. (1994). Lyme disease: A neuropsychiatric illness. The American Journal of Psychiatry, 151(11), 1571-1583; Logigian EL, Kaplan RF, Steere AC.: Chronic neurologic manifestations of Lyme disease. N Engl J Med 1990; 323:1438-1444.

Geographic correlation identified between schizophrenia and ticks/TBE in the USA

Schizophr Bull. 1994;20(4):755-75.

Geographic correlation of schizophrenia to ticks and tick-borne encephalitis.

Brown JS Jr[1].

Author information

Abstract

Schizophrenia prevalence in the United States is highest in urbanized Northeastern, Northwestern, and Great Lakes States. The viral theory of schizophrenia attributes this distribution to enhanced susceptibility to viral infections in crowded, urban areas. Such infections during fetal or perinatal development are hypothesized to result in the eventual onset of schizophrenia. This study attempts to identify which viral infections have a similar geographical distribution to schizophrenia. Examination of the geographical distribution of infectious diseases in the United States reveals that the spreading foci of Lyme disease and its primary vectors, Ixodid ticks, correlate significantly with high schizophrenia rate areas. Ixodid ticks are vectors in North America and throughout the world of tick-borne encephalitis (TBE). The international distribution of TBE is shown to be concentrated in countries where the highest rates of schizophrenia are found: Croatia, Norway, Finland, Germany, Ireland, and others. The geographical specificity of this correlation and the plausibility of a tick-associated or TBE theory of schizophrenia are discussed.

PMID: 7701281

… even eating disorders

In Europe, two recent review articles have stated that psychiatric symptoms can be a prominent feature of Lyme borreliosis, including agitated depression and psychosis (36,37). Kohler described a staging of psychiatric symptoms which parallel the neurologic ones. In stage I, fibromyalgia, painful muscular fasciculations, and mild depression may dominate the clinical picture. In stage II, a lymphocytic meningopolyneuritis may occur along with an organic psychiatric disorder, such as an organic affective syndrome or an organic personality syndrome. In stage III, chronic encephalitides and myelitides may be accompanied by severe psychiatric syndromes, such as organic psychoses, dementia, and anorexia nervosa. This staging was based on clinical observation not systematic studies.

In the United States, Pachner (38) presented two patients whose symptoms were largely psychiatric. A 12 year old boy with confirmed Lyme arthritis treated with oral antibiotics subsequently became depressed and anorectic. After being admitted to a psychiatric hospital with the diagnosis of anorexia nervosa, he was noted to have positive serologic tests for Borrelia burgdorferi. Treatment with a 14 day course of intravenous antibiotics led to a resolution of his depression and anorexia; this improvement was sustained on 3 year follow-up. A 21 year old man seropositive for Borrelia burgdorferi developed progressive confusion, agitation, disorientation, inappropriate laughter, and violent outbursts, a temporal lobe biopsy revealed spirochetes. Treatment with IV penicillin resulted in a return to normality within 3 months.

In one U.S. study of 27 patients with late neuroborreliosis, 33% were depressed based on their scores on the Minnesota Multiphasic Personality Inventory (2). 89% of these 27 patients also had evidence of a mild encephalopathy, characterized by memory loss (81%), excessive daytime sleepiness (30%), extreme irritability (26%), and word finding difficulties (19%). Controlled studies indicate significantly more depression among patients with late Lyme borreliosis than among normal controls (20) and other chronically ill patients (39).

"After being admitted to a psychiatric hospital with the diagnosis of **anorexia nervosa**, he was noted to have **positive serologic tests for Borrelia burgdorferi**. Treatment with a 14 day course of intravenous antibiotics led to a **resolution of his depression and anorexia; this improvement was sustained on 3 year follow-up**."

Source: Fallon, B. A., Nields, J. A., Burrascano, J. J., Liegner, K., DelBene, D., & Liebowitz, M. R. (1992). The neuropsychiatric manifestations of Lyme borreliosis. Psychiatric Quarterly, 63(1), 95-117.

Backed by clear statistical evidence

Table 3
Comparison between obsessive compulsive symptoms and Lyme-associated neuropsychological symptoms (N = 147).

Mann-Whitney *U*	OCI-R total	Checking	Hoarding	Neutralizing	Obsessing	Ordering	Washing	N	%
Psychological symptoms									
Depression	778.0**	1066.5	688.50**	910.00*	775.00**	880.50*	1131.00	128	86.5
Anxiety	1098.50*	1125.50*	1355.00	1221.50	1070.00*	1291.50	1264.50	123	83.1
Panic attacks	1494.50***	1741.50**	1953.00*	1930.00**	1354.00***	1730.50**	2052.50*	96	64.9
Mood swings	1182.00**	1464.50	1494.00	1516.00	1027.50***	1222.00**	1496.00	118	79.7
Hallucinations	1520.00***	2025.50*	2087.00*	2054.00*	1493.50***	1743.50**	1936.00**	56	37.8
Delusions	1368.50***	1821.50**	1946.00**	2015.50*	1362.00***	1743.50**	1765.00***	57	38.5
Neurological symptoms									
Memory problems	862.00*	845.00*	707.50**	1049.00	1078.00	1111.00	1060.50	128	86.5
Confusion	1159.50**	1233.50**	1282.50**	1604.00	1284.00**	1569.50	1361.00**	115	77.7
Concentration	727.50**	834.00*	783.50*	1052.00	870.50*	953.50	884.00*	129	87.2
Forgetfulness	617.50*	571.50*	502.00**	800.50	823.50	816.50	740.50	134	90.5
Word finding problems	843.00*	775.50**	980.50	999.00	1152.50	991.00	895.00*	128	86.5
Disorientation	1975.00**	1971.00**	2168.50	2336.00	2138.00*	2349.50	2023.50**	99	66.9
Speech problems	1376.50**	1307.00**	1740.00	1850.50	1515.50*	1611.50	1449.50**	112	75.7
Seizures	1756.00**	2074.00	2138.00	2133.00	1720**	1868.00*	2032.50	49	33.1

Correlation	OCI-R total	Checking	Hoarding	Neutralizing	Obsessing	Ordering	Washing	Range	M (SD)
Total Lyme disease symptoms	0.37***	0.27**	0.27**	0.20*	0.36***	0.23**	0.27**	0–14	9.87 (3.63)
Total psychological symptoms	0.37***	0.20*	0.24**	0.21*	0.44***	0.28**	0.25**	0–6	3.91 (1.87)
Total neurological symptoms	0.29***	0.29***	0.24**	0.15	0.23**	0.15	0.23**	0–8	5.97 (2.16)

Note. For all significant results, greater obsessive compulsive symptoms occurred in the group who experienced th
symptom.
OCI-R = Obsessive–Compulsive Inventory – Revised.
* < 0.05.
** < 0.01.
*** < 0.001.

"For all significant results, greater obsessive compulsive symptoms occurred in the group who experienced the symptoms, in comparison to the group that did not experience that symptom."

Source: Johnco C, Kugler BB, Murphy TK, Storch EA. Obsessive-compulsive symptoms in adults with Lyme disease. Gen Hosp Psychiatry. 2018;51:85-89.

Viruses, including influenza, can trigger acute-onset symptoms

Pediatric Acute-Onset Neuropsychiatric Syndrome

Tanya K. Murphy MD, MS, Diana M. Gerardi MA and James F. Leckman MD, PhD

Psychiatric Clinics of North America, 2014-09-01, Volume 37, Issue 3, Pages 353-374, Copyright © 2014 Elsevier Inc.

Whether some instances of obsessive-compulsive disorder are secondary to infectious and/or autoimmune processes is still under scientific debate. The nosology has undergone an iterative process of criteria and acronyms from PITANDS to PANDAS to PANS (or CANS for neurology). This review focuses on the clinical presentation, assessment, proposed pathophysiology, and treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcus (PANDAS), and the newest iteration, pediatric acute-on

known a

In particular, *Mycoplasma* pneumonia (MP) has also been implicated in neurological sequelae,[76] and has been considered in the etiology of TS.[77] Müller and colleagues[78] noted a case in which 2 patients, who both experienced tic exacerbation after MP infection, were treated successfully with erythromycin for 4 weeks. In a study of 29 patients with TS, 59% of TS patients (compared with 3% of healthy controls) had positive or suspected positive antibody titers against MP.

Viruses, including influenza, have also been reported as a potential infectious trigger for acute-onset OCD and tics.[79] One subject, a 10-year-old boy, experienced acute-onset OCD, including contamination fears, and was successfully treated with plasmapheresis. Another subject, a 13-year-old boy, was treated with prednisone for acute-onset tics, and experienced symptom remittance for 2 weeks. Of note, this subject experienced a tic flare, potentially triggered by a viral respiratory infection and allergic reaction to an influenza immunization, weeks after prednisone treatment, and continued to suffer from tics despite a retrial of prednisone.

Lyme disease has been investigated as a potential infectious trigger in PANS, as OCD is often present in patients with Lyme disease.[80–82] Of note, the neuropsychiatric and cognitive symptoms of Lyme disease share some similarity with those of PANS, including distractibility, schoolwork deterioration, irritability/depression, insomnia, and sensitivity to light and/or sound.[83] Children with Lyme disease have also been reported to have oppositional behavior, anxiety disorders, and ADHD.[82] In addition,