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)
- *Chlamydophila pneumoniae* (chlamydia)
- *Chlamydophila psittaci* (chlamydia)
- *Coxiella burnetti* (Q-fever and post-Q fever fatigue syndrome)

**Yeast**
- *Candida albicans* (candidiasis)
- *Candida dubliensiis*

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

<table>
<thead>
<tr>
<th>Box 1. Some microbes associated with mental symptoms &amp; mental illness (cont.)</th>
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<tbody>
<tr>
<td><strong>Prion</strong></td>
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<td>• Variant Creutzfeldt–Jakob</td>
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<td><strong>Viruses</strong></td>
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<td>• Borna virus</td>
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<td>• Coxiavirus (Colorado tick fever)</td>
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<td>• Coxsackievirus</td>
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<td>• Cytomegalovirus</td>
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<td>• Enterovirus</td>
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<td>• Flaviviridae virus (Japanese B encephalitis)</td>
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<td>• Hepatitis C virus</td>
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<td>• Human endogenous retroviruses</td>
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<td>• Influenza virus</td>
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<td>• Pandemic influenza of 1918</td>
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<td>• Papovavirus</td>
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<td>• Parvo B19</td>
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<td>• Toga virus</td>
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<td>• Varicella zoster virus (chicken pox)</td>
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<td>• Viral meningitis</td>
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<td>• West Nile virus</td>
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<tr>
<td><strong>Protozoa</strong></td>
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<td>• Plasmodium (malaria)</td>
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<td>• Babesia microti (babesiosis)</td>
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<td>• Babesia duncanii (babesiosis)</td>
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<tr>
<td>• Other Babesia species (babesiosis)</td>
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<tr>
<td>• Toxoplasma gondii (toxoplasmosis)</td>
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<tr>
<td><strong>Parasites</strong></td>
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<td>• Blastocystis (blastocystosis)</td>
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<td>• Taenia solium (neurocysticercosis or cysticercosis)</td>
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<tr>
<td><strong>Fungal</strong></td>
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<td>• Cryptococcus</td>
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<td>• Coccidiomycosis</td>
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<td>• Histomycosis</td>
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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 Borrelia were recognised a quarter of a century ago…

"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

Even back in the 90s, statistics revealed neurological involvement in up to 40% of patients with Lyme disease. The article from Am J Psychiatry, 1994, reveals that up to 40% of patients with Lyme disease develop neurologic involvement of either the peripheral or central nervous system.
LB can underlie a vast number of neuropsychiatric disorders ...

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 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.

"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."

Source: Bransfield RC. Neuropsychiatric Lyme Borreliosis: An Overview with a Focus on a Specialty Psychiatrist’s Clinical Practice.
... in children as well as adults ...

Unraveling Diagnostic Uncertainty Surrounding Lyme Disease in Children with Neuropsychiatric Illness

Michael P. Koster, MD, MD, Aris Garro, MD, MPH

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. Although these case reports demonstrate that Lyme disease can present with atypical neuropsychiatric manifestations, it is important to note they are often difficult to distinguish from other conditions. Additionally, objective findings can help differentiate a positive Lyme serology with lumbar puncture and intrathecal production of Lyme antibodies from pseudoneuropsychiatric changes with increased signal on imaging.

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 symptoms are due to the infection or other comorbidities.

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

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- PANS/PANDAS
Many sources on Borreliosis-associated schizophrenia and schizoaffective-conditions


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


Undiagnosed Lyme disease in adults with schizophrenia

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

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

“Lyme Disease can present with symptoms similar to bipolar disorder”

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

"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."
“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.

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% significantly higher than the control group.
Association found between bipolar disorder and CMV/HSV2

“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.”

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

Dimitrios Avramopoulos, 1, 2, * Brad D. Pearce, 3 John McGrath, 2 Paula Wolyniec, 2 Rehwa Wang, 2 Nicole Eckart, 1 Alexandros Hatzimanolis, 2 Fernando S. Goes, 2 Gerald Nestadt, 2 Jennifer Mull, 3 Karen Conoley, 3, 4 Myfanwy Hopkins, 3 Ingo Ruczinski, 5 Robert Yolken, 6 and Ann E. Pulver 2

Abstract

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 gluten 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 CNTNAP3 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

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- PANS/PANDAS
Panic attacks/disorders can have an infectious driver ...

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

Barbara Oczko-Grzesik¹, Lucjan Kępa¹, Monika Puszczy-Matlińska², Robert Pudło³, Anna Żurek², Teresa Badura- Głąbiκ³

¹ Clinical Department of Infectious Diseases, Bytom, Medical University of Silesia, Katowice, Poland
² Department of Infectious Diseases, Specialistic Hospital No 1, Bytom, Poland
³ Clinical Department of Psychiatry, Tarnowskie Góry, Medical University of Silesia, Katowice, Poland


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-skeletal 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 occurrence 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 (39.3%). 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.
Mood disorders have been linked to HHV-6, which can in turn be reactivated by other infections

“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.”

“...and infections with other pathogens have the potential to reactivate latent HHV-6A/”

“Chlamydia trachomatis infection induces replication of latent HHV-6”

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

“... 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....”

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.”
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
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- 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

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

Robert C. Bransfield, Jeffrey S. Wulffman, William T. Harvey, Anju I. Usman

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, kynurenino 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.”
Chronic Mycoplasmal Infections in Autism Patients

Garth L. Nicolson, PhD, Marwan Y. Nasralla, PhD, Paul Berns, MD and Jeorg Haier, MD, PhD

The Institute for Molecular Medicine, Huntington Beach, California, USA. 2International Molecular Diagnostics, Inc., Huntington Beach, California, USA. 3Department of Internal Medicine, and 4Department of Surgery, Wilhelm-University, Munster

Abstract

A majority of Autism patients have systemic bacterial, viral and fungal infections in their illnesses. We found that immediate diagnosis with Gulf War Illnesses (GWI) often complain of fatigue and muscle pain. They report similar signs and symptoms as their veteran medical history. Their children are often diagnosed with Autism. Since a relative has a bacterial infection due to Mycoplasma fermentans, which is found in 149 patients: 42 veterans, 40 spouses, 32 other relatives and 35 children (each with a complaint of illness) selected from a group of 110 veterans with GWI (~42%) for mycoplasmal infections. Consistent with previous results, 84% of the patients were positive for blood mycoplasmal infections had only M. fermentans. In healthy control subjects the incidence of mycoplasmal infection was found to have multiple mycoplasmal species (P<0.001). In a mycoplasma-positive GWI patients there were 57 patients (53%) of this group. In children, signs and symptoms as the veterans and were diagnosed with fibromyalgia and/or Fibromyalgia Syndrome. The majority of children had fever, muscle pain and fatigue. Nicolson tested 48 ASD patients with forensic PCR and Southern Blot confirmation.

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.
Evidence also for Chlamydia pneumoniae and HHV-6 in ASD

“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.


Gentile I¹, Zappulo E², Riccio MP², Binda S³, Bubba L⁴, Pellegrinelli L⁴, Scognamiglio D⁵, Operto F⁶, Margari L⁷, Borgia G², Bravaccio G⁷.

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
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- PANS/PANDAS
“Greater frequency of Lyme disease symptoms and disease-related impairment was related to greater OCS”


“... greater OCS occurred in the group who experienced the symptoms, in comparison to the group that did not experience that symptom.”
Presence of Toxoplasma gondii more frequent in OCD patients than in controls (2017 study, 7471 subjects)

**Toxoplasma-infected subjects report an Obsessive-Compulsive Disorder diagnosis more often and score higher in Obsessive-Compulsive Inventory.**

**Flegr J, Horáček J.**

**Abstract**

**BACKGROUND:** Latent toxoplasmosis, the life-long presence of dormant stages of Toxoplasma in individuals with anamnestic IgG antibodies in blood, affects about 30% of humans. Infected subjects have an increased risk of developing neuropsychiatric disorders including schizophrenia. Several studies, as well as the character of toxoplasmosis-associated disturbed personality, suggest that 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 volunteered subjects, was to assess the association between toxoplasmosis and OCD, and toxoplasmosis and psychological symptoms of OCD estimated via Obsessive-Compulsive 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 underestimating 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]."
Mycoplasma also associated with OCD and Tourette’s

"Mycoplasma has also been associated with OCD, Tourette’s syndrome, parkinsonism, and dystonia.137–139"
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
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- **PANS/PANDAS**
Many infectious triggers are associated with PANS/PANDAS

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

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

Source: Courtesy of Dr. Craig Shimasaki, CEO Moleculera Labs, Oklahoma
Mycoplasma involvement in PANS/PANDAS conditions

“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 ...”
“... 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; Chambert-Loir et al. 2009; Rhee and Cameron, 2012).”
Autoimmune encephalitis can be triggered after herpes simplex encephalitis

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!

For tests, please go to
www.aonm.org
https://aonm.org/arminlabs

or call the AONM helpline
on 0333 121 0305
END
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 neuropsychiatric 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

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<tr>
<th>Study</th>
<th>N</th>
<th>Diagnosis</th>
<th>Measures</th>
<th>Comparison Group</th>
<th>Results</th>
<th>comments</th>
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<tbody>
<tr>
<td>Logigian et al.</td>
<td>27</td>
<td>Late neurologic Lyme disease</td>
<td>MMPI (score &gt;70 signified depression)</td>
<td>None</td>
<td>26% had extreme irritability; 33% were depressed</td>
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</tr>
<tr>
<td>Barr et al.</td>
<td>88</td>
<td>Lyme disease</td>
<td>Beck Depression Inventory, Spielberger anxiety scale</td>
<td>Seronegative patients</td>
<td>Significantly more depression among seropositive patients</td>
<td></td>
</tr>
<tr>
<td>Belman et al.</td>
<td>96</td>
<td>Neurologic Lyme disease</td>
<td>Neurologic examination</td>
<td>None</td>
<td>38% had behavioral changes (irritability, lability, poor attention)</td>
<td></td>
</tr>
<tr>
<td>Krupp et al.</td>
<td>15</td>
<td>Late Lyme disease and cognitive symptoms</td>
<td>Center for Epidemiologic Studies Depression Scale neuropsychological battery</td>
<td>None</td>
<td>Most common symptom was headaches</td>
<td></td>
</tr>
<tr>
<td>Fallon et al.</td>
<td>51</td>
<td>Chronic, seropositive Lyme disease</td>
<td>Survey using DSM-III-R criteria</td>
<td>10 healthy age- and sex-matched subjects</td>
<td>Lyme disease patients were significantly more depressed</td>
<td>The most depressed patients did not have abnormal neuropsychological findings.</td>
</tr>
<tr>
<td>Halperin et al.</td>
<td>17</td>
<td>Neurologic Lyme disease</td>
<td>Beck Depression Inventory</td>
<td></td>
<td>32% of Lyme disease patients reported panic attacks (versus 19% of comparison patients; n.s.)</td>
<td></td>
</tr>
<tr>
<td>Kaplan et al.</td>
<td>20</td>
<td>Lyme encephalopathy</td>
<td>Beck Depression Inventory, MMPI</td>
<td></td>
<td>Mean Beck scores did not show depression</td>
<td>Only 13 of the 20 patients completed the Beck inventory</td>
</tr>
<tr>
<td>Reik et al.</td>
<td>18</td>
<td>Neurologic Lyme disease</td>
<td>Clinical interview</td>
<td></td>
<td>Mean Beck scores were not significantly different between groups</td>
<td></td>
</tr>
<tr>
<td>Ackerman et al.</td>
<td>44</td>
<td>Borrelia encephalomyelitis</td>
<td>Clinical interview</td>
<td></td>
<td>Lyme disease diagnosed by history of erythema migrans or Lyme disease arthritis</td>
<td></td>
</tr>
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</table>

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


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

Brown JS Jr.

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
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."

Backed by clear statistical evidence

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

<table>
<thead>
<tr>
<th></th>
<th>OCI-R total</th>
<th>Checking</th>
<th>Hoarding</th>
<th>Neutralizing</th>
<th>Obsessing</th>
<th>Ordering</th>
<th>Washing</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>778.0**</td>
<td>1066.5</td>
<td>686.5**</td>
<td>910.00**</td>
<td>775.00**</td>
<td>880.50**</td>
<td>1131.00</td>
<td>128</td>
<td>86.5</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1098.50*</td>
<td>1125.50*</td>
<td>1355.00</td>
<td>1221.50</td>
<td>1070.00*</td>
<td>1291.50</td>
<td>1264.50</td>
<td>123</td>
<td>83.1</td>
</tr>
<tr>
<td>Panic attacks</td>
<td>1494.50***</td>
<td>1741.50**</td>
<td>1935.00*</td>
<td>1930.00**</td>
<td>1354.00***</td>
<td>1730.50**</td>
<td>2052.50*</td>
<td>96</td>
<td>64.9</td>
</tr>
<tr>
<td>Mood swings</td>
<td>1182.00**</td>
<td>1464.50</td>
<td>1494.00</td>
<td>1516.00</td>
<td>1027.50**</td>
<td>1222.00*</td>
<td>1496.00</td>
<td>118</td>
<td>79.7</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>1520.00***</td>
<td>2025.50*</td>
<td>2067.00*</td>
<td>2054.00</td>
<td>1493.50**</td>
<td>1743.50**</td>
<td>1936.00**</td>
<td>56</td>
<td>37.8</td>
</tr>
<tr>
<td>Delusions</td>
<td>1368.50***</td>
<td>1821.50*</td>
<td>1946.00**</td>
<td>2015.50**</td>
<td>1362.00**</td>
<td>1743.50**</td>
<td>1765.00***</td>
<td>57</td>
<td>38.5</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory problems</td>
<td>862.00*</td>
<td>845.00*</td>
<td>707.50**</td>
<td>1049.00</td>
<td>1078.00</td>
<td>1111.00</td>
<td>1060.50</td>
<td>128</td>
<td>86.5</td>
</tr>
<tr>
<td>Confusion</td>
<td>1159.50**</td>
<td>1233.50**</td>
<td>1282.50**</td>
<td>1604.00</td>
<td>1284.50**</td>
<td>1569.50</td>
<td>1561.00**</td>
<td>115</td>
<td>77.7</td>
</tr>
<tr>
<td>Concentration</td>
<td>727.50*</td>
<td>834.00*</td>
<td>783.50</td>
<td>1052.00</td>
<td>876.50*</td>
<td>953.50</td>
<td>884.00*</td>
<td>129</td>
<td>87.2</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>617.50*</td>
<td>571.50*</td>
<td>502.00**</td>
<td>800.50</td>
<td>823.50</td>
<td>816.50</td>
<td>740.50</td>
<td>134</td>
<td>90.5</td>
</tr>
<tr>
<td>Word finding problems</td>
<td>843.00</td>
<td>775.50**</td>
<td>980.50</td>
<td>999.00</td>
<td>1152.50</td>
<td>991.00</td>
<td>805.00*</td>
<td>128</td>
<td>86.5</td>
</tr>
<tr>
<td>Disorientation</td>
<td>1975.00**</td>
<td>1971.00*</td>
<td>2168.50</td>
<td>2336.00</td>
<td>2138.00*</td>
<td>2349.50</td>
<td>2032.50*</td>
<td>99</td>
<td>66.9</td>
</tr>
<tr>
<td>Speech problems</td>
<td>1376.50**</td>
<td>1307.50**</td>
<td>1740.00</td>
<td>1850.50</td>
<td>1515.50**</td>
<td>1611.50</td>
<td>1449.50**</td>
<td>112</td>
<td>75.7</td>
</tr>
<tr>
<td>Seizures</td>
<td>1756.00**</td>
<td>2074.00</td>
<td>2138.00</td>
<td>2133.00</td>
<td>1720.50</td>
<td>1868.00*</td>
<td>2032.50</td>
<td>49</td>
<td>33.1</td>
</tr>
</tbody>
</table>

Correlation

<table>
<thead>
<tr>
<th></th>
<th>OCI-R total</th>
<th>Checking</th>
<th>Hoarding</th>
<th>Neutralizing</th>
<th>Obsessing</th>
<th>Ordering</th>
<th>Washing</th>
<th>Range</th>
<th>M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Lyme disease symptoms</td>
<td>0.37***</td>
<td>0.27**</td>
<td>0.27**</td>
<td>0.20</td>
<td>0.36***</td>
<td>0.23**</td>
<td>0.27**</td>
<td>0–14</td>
<td>8.87 (3.63)</td>
</tr>
<tr>
<td>Total psychological symptoms</td>
<td>0.37***</td>
<td>0.20</td>
<td>0.24**</td>
<td>0.21</td>
<td>0.44***</td>
<td>0.28**</td>
<td>0.25**</td>
<td>0–6</td>
<td>3.91 (1.87)</td>
</tr>
<tr>
<td>Total neurological symptoms</td>
<td>0.29***</td>
<td>0.29***</td>
<td>0.24**</td>
<td>0.15</td>
<td>0.23**</td>
<td>0.15</td>
<td>0.23**</td>
<td>0–8</td>
<td>5.97 (2.16)</td>
</tr>
</tbody>
</table>

Note. 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.

OCI-R = Obsessive–Compulsive Inventory – Revised.

* < 0.05.
** < 0.01.
*** < 0.001.

Viruses, including influenza, can trigger acute-onset symptoms

In particular, Mycoplasma pneumonia (MP) has also been implicated in neurological sequelae, and has been considered in the etiology of TS. Müller and colleagues 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. 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 retiral of prednisone.

Lyme disease has been investigated as a potential infectious trigger in PANS, as OCD is often present in patients with Lyme disease. 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. Children with Lyme disease have also been reported to have oppositional behavior, anxiety disorders, and ADHD. In addition,