

Chronic Infections Contributing to Autism Spectrum Disorders (ASD)

Infections and/or
other immune provocations
in genetically
susceptible individual

Aberrant immune reactions
causing inflammation,
oxidative stress, mitochondrial
dysfunction and excitotoxicity
resulting in impaired neural
development and dysfunction

Autism spectrum
disorders

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10th Psychoimmunology Expert Meeting – Ulm University,
Wissenschaftszentrum der Universität Ulm Schloss Reisensburg,
Günzburg, 14/11/09

Autism: A Syndrome of Many Different Etiologies & Comorbidities

- Comorbidity with any DSM Dx
- Epilepsy
- Mental retardation (30% mild to moderate, 40% serious to profound)
- Hearing & visual impairments
- Fragile X syndrome & multiple other genetic
- Tuberous sclerosis
- Cerebral palsy
- Phenylketonuria
- Neurofibromatosis
- Congenital rubella
- Rett's syndrome
- Rasmussen's encephalitis
- Lennox-Gastaut syndrome
- Post infectious
- Metabolic
- Pyruvate d hydrogenase deficiency
- Impaired purine metabolism (uric acid increased)
- Brain structural—cyst, etc.
- PKU phenylalanine
- Angelman's syndrome
- Landau-Kleffner syndrome
- Prader-Willi
- Williams
- Multiple other genetic impairments
- Associated with older paternal age

Infections & Autism Spectrum Disorder

- There is some evidence complex interactive infections, the immune reactions to them by the mother, fetus and infant appear to adversely effect developing neural tissue and contribute to the pathophysiology associated with causing autism spectrum disorders (ASD).

Chronic Infections, Lyme Disease Tick-Borne Disease (LYD/TBD) & Autism Spectrum Disorder (ASD)

- Nicolson GL, Gan R, Nicolson NL, Haier J. Evidence for *Mycoplasma*, *Chlamydia pneumoniae* and HHV-6 Co-infections in the blood of patients with Autism Spectrum Disorders. *J Neuroscience Res* 2007;85:1143-1148
- Bransfield RC, Wulfman JS, Harvey WT, Usman AI. The association between tick-borne infections, Lyme borreliosis and autism spectrum disorders *Medical Hypotheses*. 70(5), p.967-974 (2008)
- Nicholson G. Chronic Bacterial and Viral Infections in Neurodegenerative and Neurobehavioral Diseases *Laboratory Medicine* (2008)
- Bransfield RC. Preventable cases of autism: relationship between chronic infectious diseases and neurological outcome *Pediatric Health*. 70(3), No. 2, p.125-140 (2009)

A Model for Infections Contributing to Autism Spectrum Disorder

Infections and/or other immune provocations in genetically susceptible individual

Aberrant immune reactions causing inflammation, oxidative stress, mitochondrial dysfunction and excitotoxicity resulting in impaired neural development and dysfunction

Autism spectrum disorders

Clinical Observations

Autism & Chronic Infectious Diseases

- This association is seen as:
 - Infected mothers & children with autistic spectrum disorders (ASD)
 - Infected infants & children & ASD or autistic symptoms
- Chronic infections in adults often have symptoms suggestive of ASD (Sound sensitivity & sensory hyperacusis, emotional detachment, mood instability, decline of speech & language, intestinal, seizures)
- More severe symptoms are associated with infections at younger age and coinfections
- Antimicrobial treatment can reduce symptoms

LYD/TBD & ASD Respond to Similar Treatments

- Modafinil, armodafinil, memantine, stimulants, mood stabilizers, atypical agents SSRIs, diets, antimicrobials, mitochondrial enhancers, immune modulators, hyperbaric oxygen, glutathione, chelation and allergen elimination.

Testing ASD Patients for Lyme/TBD

Controlled Trials:

- Vojdani **22%** of (12/54) **LYD** tested positive for IgG and IgM by CDC criteria.
- LIAF **26%** positive for **LYD** of ASD children were compared to 0 controls.
- Nicolson **20–30%** positive for **LYD**.

58% were positive for **Mycoplasma species** while 5% of 45 age matched controls were positive for Mycoplasma (Odds ratio = 13.8) with **35% M. fermentans** vs. 0% control, **33% M. pneumoniae** vs. 5% control, **10% M. hominis** vs. 0% control, 2% M. penetrans vs. 0% control and 25% were M. fermentans and other species.

8% were positive for **C. pneumoniae** vs. 2% of controls (Odds ratio = 5.6)

29% were positive for **Human Herpes Virus-6 (HHV-6)** vs. 8% of controls.

6.5% of healthy family members were positive for Mycoplasma and 8% were positive for HHV-6 ($P < 0.001$) [18].

LYD WB positive patients had a **68% coinfection rate** with **Mycoplasma (M. Fermentans was 70%)**, Bartonella, Ehrlichia, and Babesia.

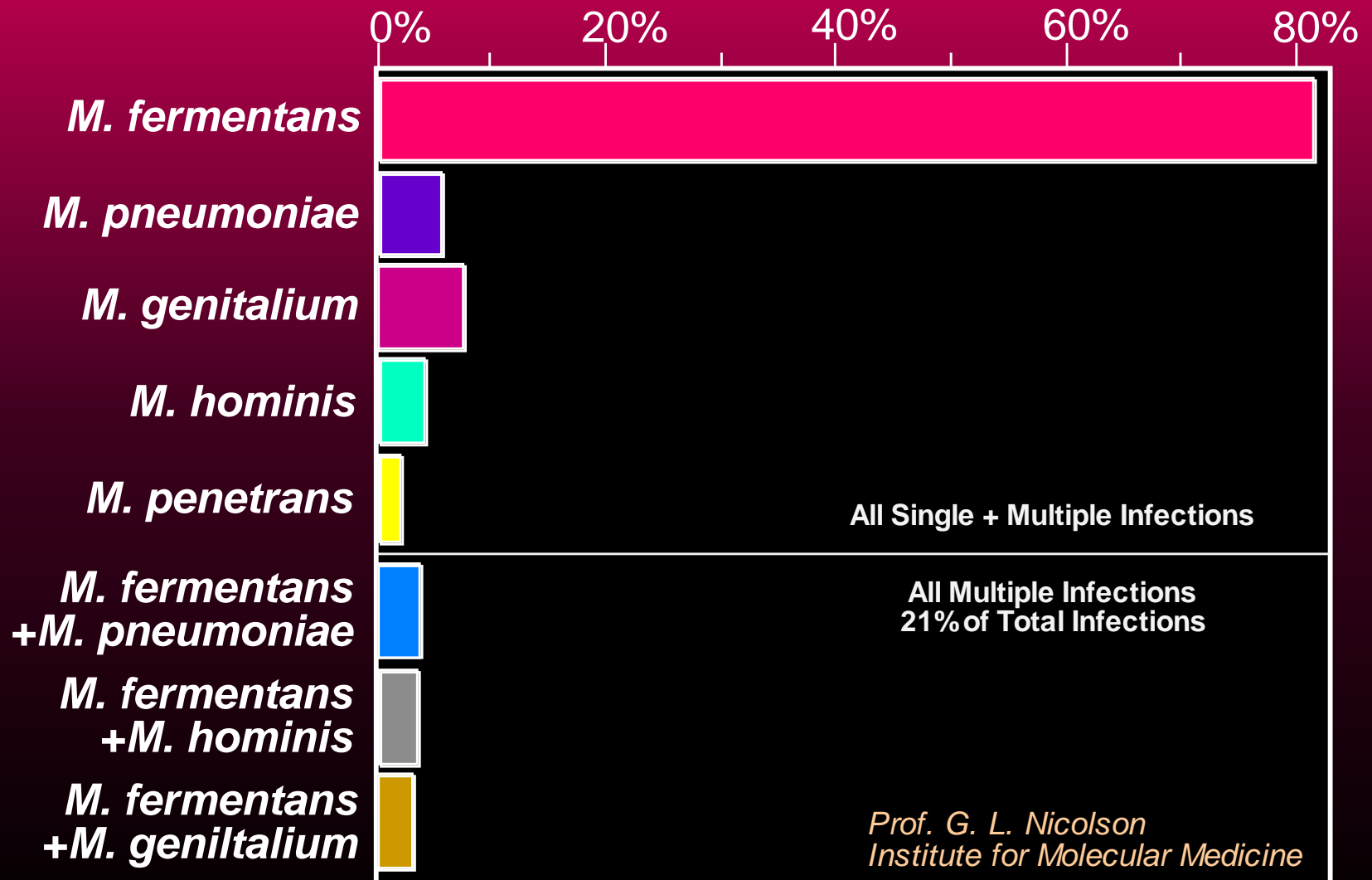
Case Series:

- Levin **100%** (9/9) **LYD** positive of ASD children in Connecticut with WB by IGeneX Laboratory criteria.

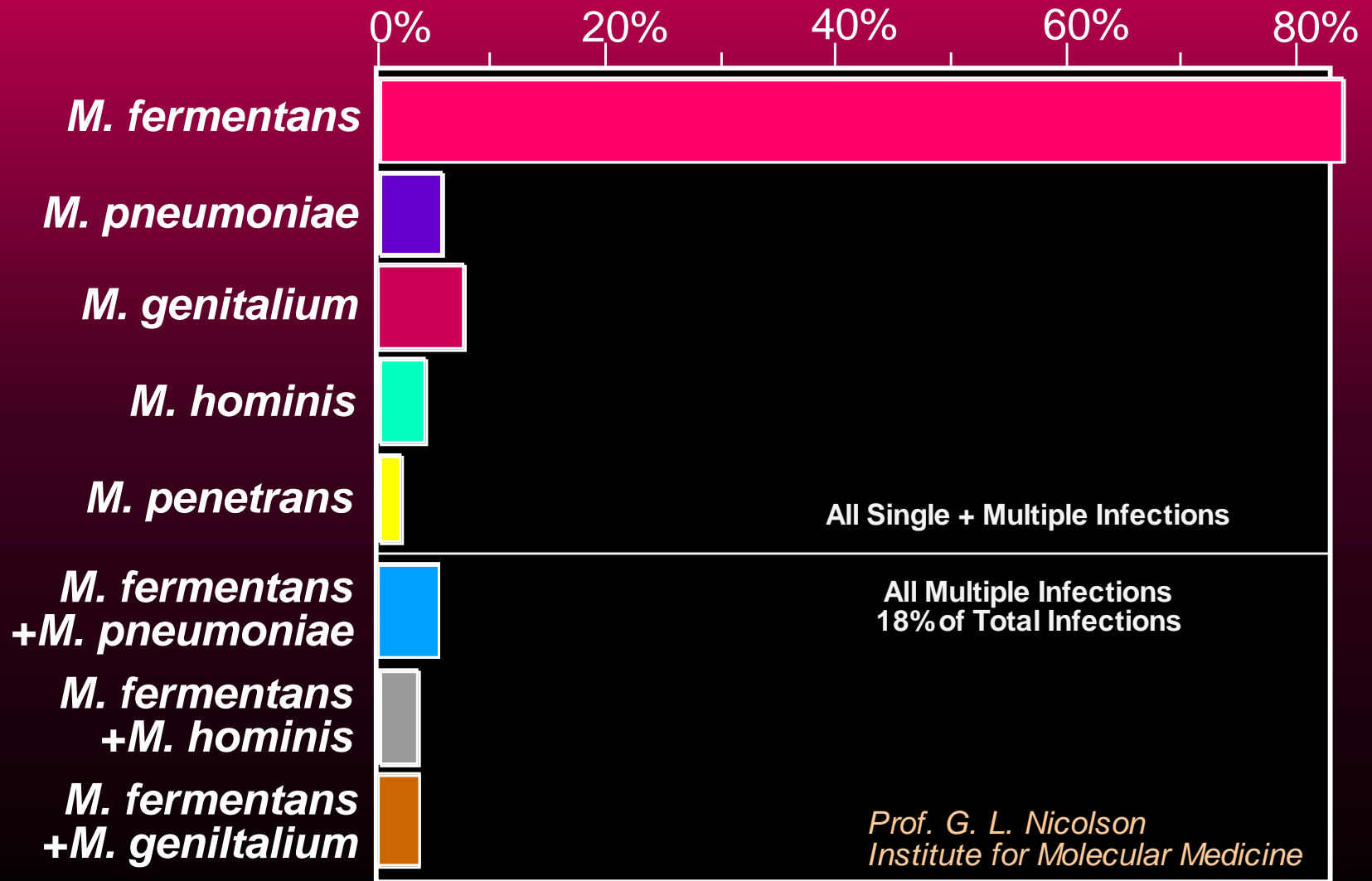
Gestational LYD/TBD & ASD

- Jones et al. performed a comprehensive case history review on the charts of 102 gestational LYD/TBD cases.
- **9% had been diagnosed with autism and 56% with attention deficit disorder.** Psychiatric symptoms included **irritability or mood swings (54%)**, anger or rage (23%), anxiety (21%), depression (13%), emotional (13%), OCD (11%) and suicidal thoughts (7%). Neurological symptoms included headache (50%), vertigo (30%), developmental delays (18%), tic disorders (14%), seizure disorders (11%), involuntary athetoid movements (9%) and hypotonia (7%). Sensory sensitivity symptoms included photophobia (43%), hyperacuity (36%), motion sickness (9%) and other (tactile, taste or smell) (23%). Cognitive symptoms included poor memory (39%), cognitive impairments (27%), speech delays (21%), reading/writing (19%), articulation (17%), auditory/visual processing (13%), word selectivity (12%), and dyslexia (18%). GI symptoms were common and included GERD (27%), abdominal pain (29%), diarrhea or constipation (32%), and nausea (23%).
- **As a control, 66 mothers with Lyme disease who were treated with antibiotics prior to conception and during the entire pregnancy; all gave birth to normal healthy infants.**

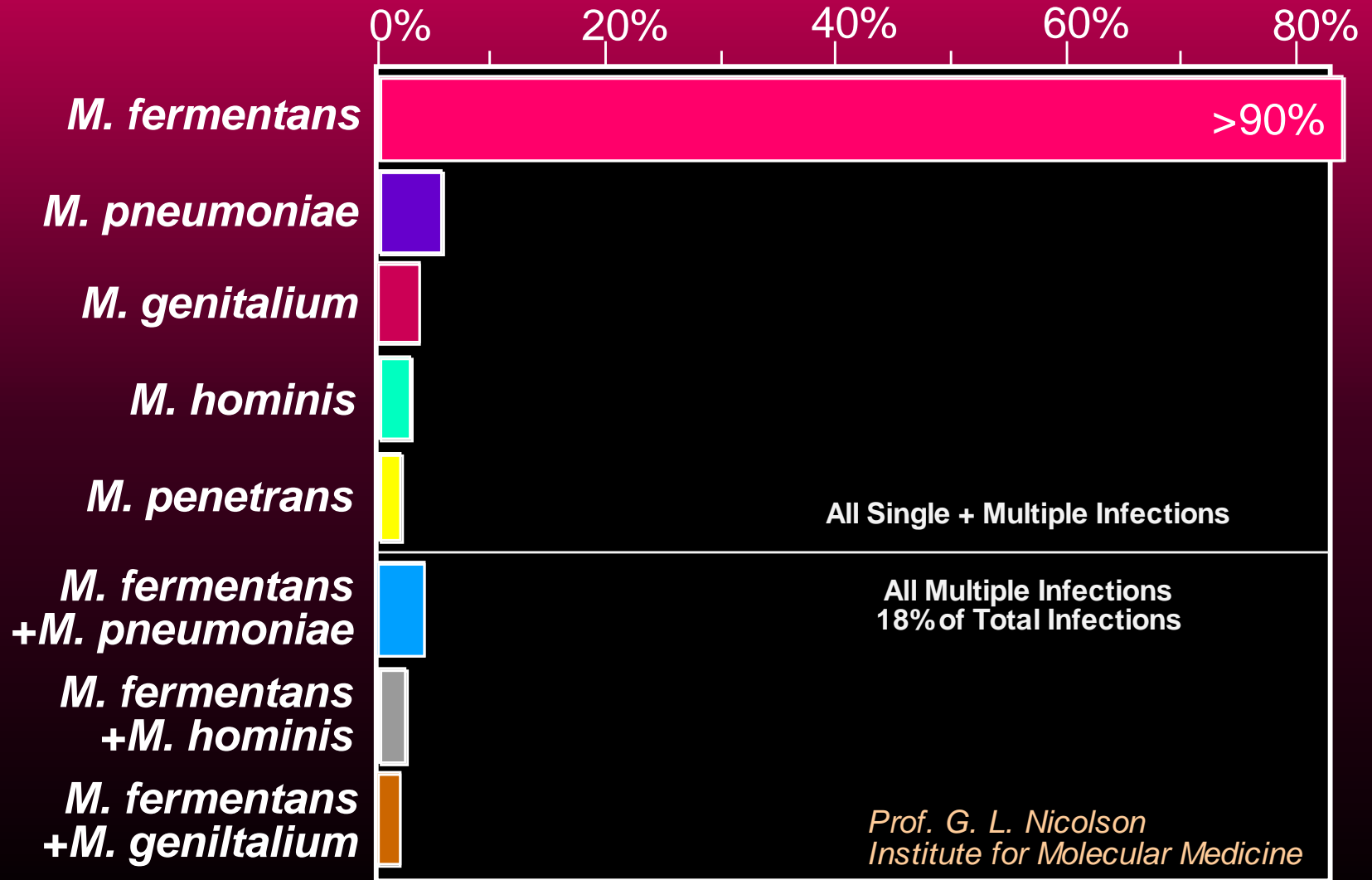
Percentage of GWI Patients with Mycoplasmal Infections



% of GWI CSF-Family with Mycoplasmal Infections



% of GWI Children/Autism with Mycoplasmal Infections



Biochemical Similarities LYD & ASD

- Disorders of an oxidoreductive system in cerebrospinal fluid and serum.
- Increases of superoxide dismutase, glutathione peroxidase activity, malondialdehyde levels, homocysteine/methionine metabolism.
- Impaired methylation & sulfation & decreased glutathione.

Brain Imaging Similarities LYD & ASD

- Both BI/TBI and ASD patients demonstrate significant temporal lobe dysfunction. Both BI/TBI and ASD demonstrate predominately white matter encephalopathy.
- Regional cerebral blood flow suggests that Lyme encephalopathy may primarily affect cerebral white matter.
- Sensory hyperacusis is supported by increased thalamus activity and increased activity in auditory and visual areas of cortex.

Top 15 States for Autism & Lyme Disease vs. Obesity (Control)

Autism

- 1, **Minnesota**
- 2, Oregon
- 3, Indiana
- 4, **Maine**
- 5, **Massachusetts**
- 6, Michigan
- 7, California
- 8, **Maryland**
- 9, **Connecticut**
- 10, **Wisconsin**
- 11, **Rhode Island**
- 12, **New Jersey**
- 13, **Pennsylvania**
- 14, Hawaii
- 15, **Virginia**

Lyme

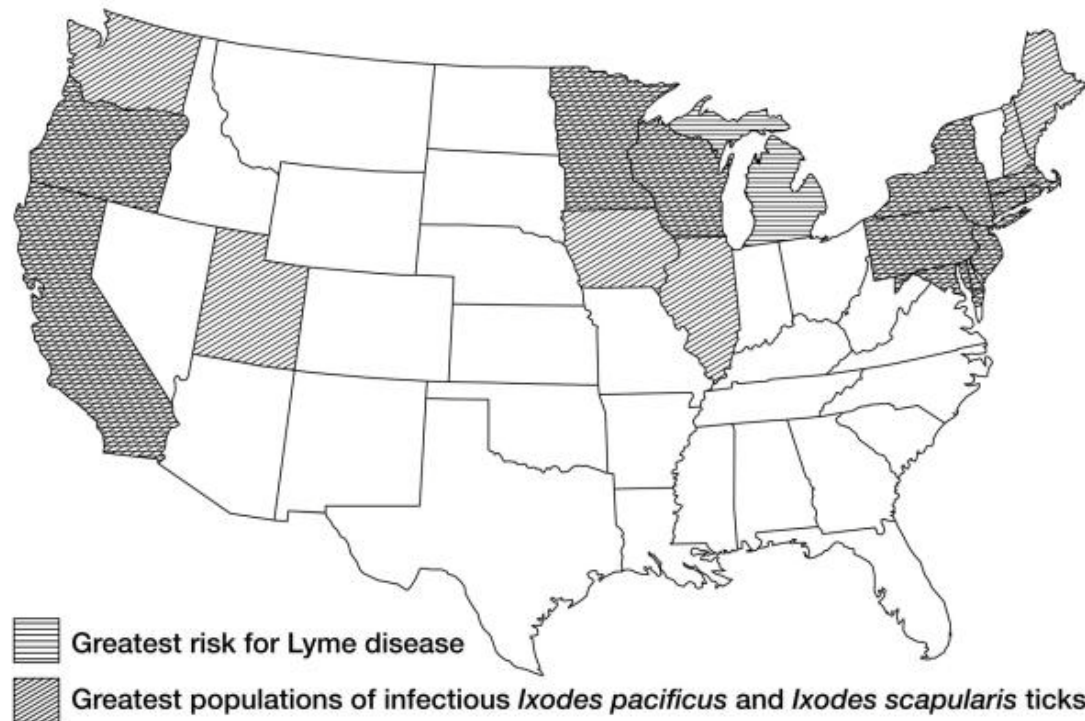
- 1, Delaware
- 2, **Connecticut**
- 3, **New Jersey**
- 4, **Massachusetts**
- 5, **Pennsylvania**
- 6, New York
- 7, **Wisconsin**
- 8, **Maryland**
- 9, New Hampshire
- 10, **Maine**
- 11, **Minnesota**
- 12, Vermont
- 13, **Rhode Island**
- 14, **Virginia**
- 15, **West Virginia**


Obesity

- 1. Mississippi
- 2. Alabama
- 3. **West Virginia**
- 4. Louisiana
- 5. Kentucky
- 6. Tennessee
- 7. Arkansas
- 8. Indiana (tie for 8th)
- 8. South Carolina
- 10. Texas
- 11. Michigan
- 12. Georgia
- 13. Oklahoma
- 14. Missouri
- 15. Alaska

Geographical correlation of schizophrenia to *Ixodes* ticks and Lyme disease in the USA

- The epidemiological correlation between *Ixodes* ticks and schizophrenia originally published by Brown has been adjusted according to the more recent epidemiological data on the risk of Lyme disease including zoonophylaxis.





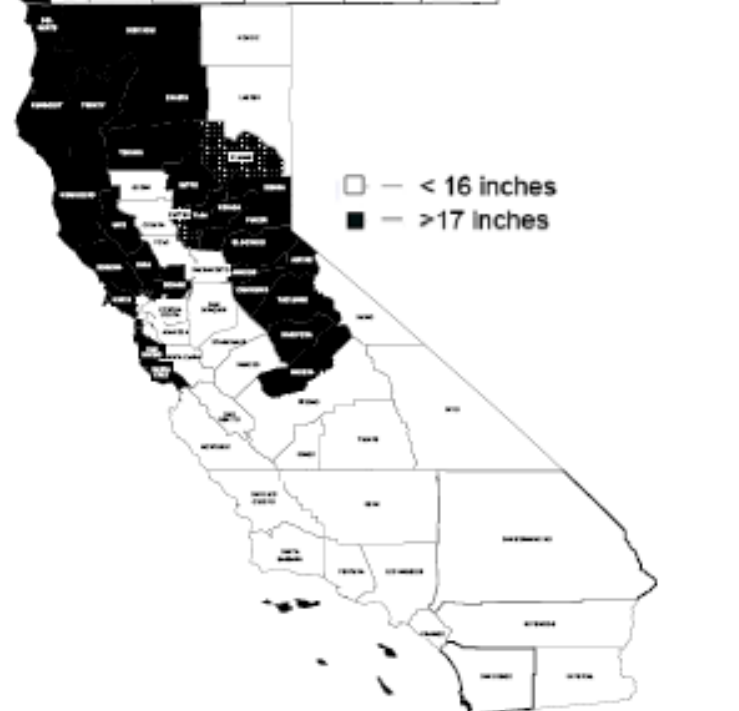
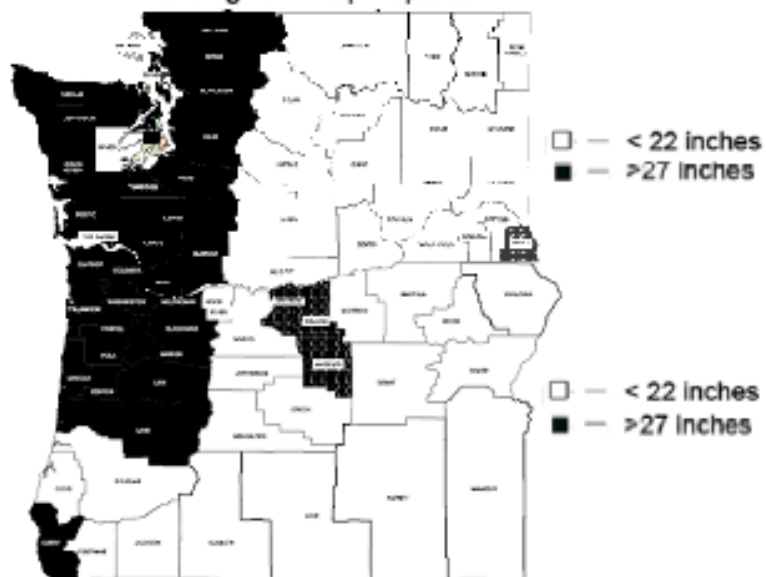
Autism prevalence and precipitation rates in California, Oregon, and Washington counties

- These results are consistent with an environmental trigger for autism among genetically vulnerable children that is positively associated with precipitation.

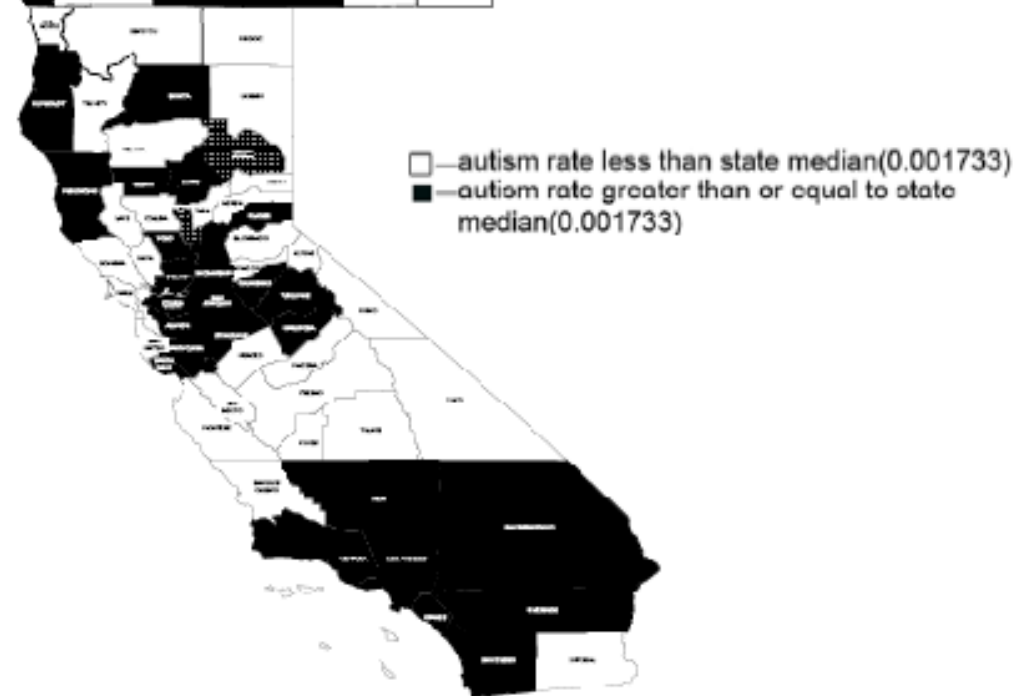
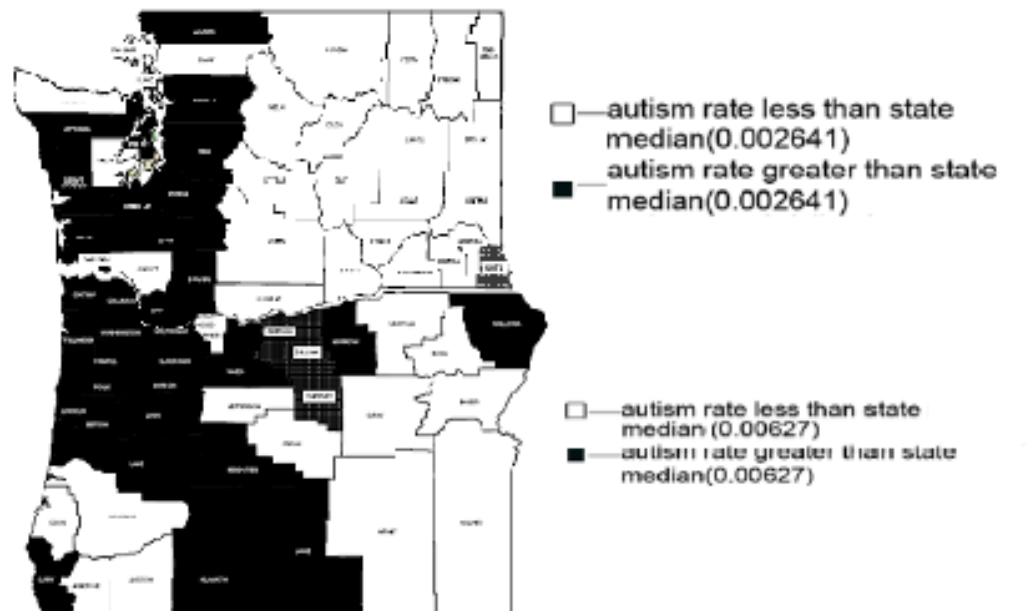


Precipitation

Average annual precipitation



Autism



⊞ — Autism or precipitation unknown

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* (rabbit 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* • *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 • *Papovavirus* • *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* • *Cryptocococcus* • *Coccidiomycosis* • *Histomycosis*

Infections associated with autism spectrum disorders

- *Babesia*
- *Bartonella*
- *Blastocystis*
- *Borna* (animal model)
- *Borrelia burgdorferi* and other tick-borne diseases
- *Chlamydia pneumoniae*
- *Cytomegalovirus*
- *Ehrlichia*
- *Herpes simplex*
- *Human Herpesvirus-6*
- *Herpes virus family*
- *Mycoplasma fermentans*
- *Mycoplasma genitalium*
- *Mycoplasma hominis*
- *Mycoplasma pneumoniae*
- *Plasmodium* (malaria)
- *Rubella*
- *Rubeola*
- *Shigella*
- *Taenia solium* (Neurocysticercosis)
- *Toxoplasma gondii* (Toxoplasmosis)
- *Treponema pallidum pallidum* (Syphilis)
- *Varicella*
- Unknown viral and other infectious
- *XMRV* (unpublished)

Chronic infections associated with autism spectrum disorder

- *Babesia*
- *Bartonella*
- *Blastocystis*
- *Borrelia burgdorferi*
- *Chlamydia pneumoniae*
- *Cytomegalovirus*
- *Ehrlichia*
- *Herpes simplex*
- *Herpes virus family*
- *Human heprevirus-6*
- *Mycoplasma fermentans*
- *Mycoplasma genitalium*
- *Mycoplasma hominis*
- *Mycoplasma pneumoniae*
- *Plasmodium*
- *Taenia solium*
- *Toxoplasma gondaii*
- *Treponema pallidum pallidum*
- *XMRV* (unpublished)

ASD & LYD/TBD Both Have

- A combination of inflammatory and autoimmune pathophysiology.
- Elevated TNF and IL-6 & reduced NKC
- Antibodies against neural tissue
- Microglial activation
- Oxidative stress
- Greater susceptibility to herpes and other viral infections
- HLA-DR4 genotypes frequently

Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models

- Brain developmental processes (i.e. cell proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis) occur at vulnerable periods during the development of the nervous system and are sensitive to environmental insults that can contribute to autism.

Maternal Immune Activation Alters Fetal Brain Development through Interleukin-6

- Here we show that the cytokine interleukin-6 (IL-6) is critical for mediating the behavioral and transcriptional changes in the offspring. A single maternal injection of IL-6 on day 12.5 of mouse pregnancy causes prepulse inhibition (PPI) and latent inhibition (LI) deficits in the adult offspring. Moreover, coadministration of an anti-IL-6 antibody in the poly(I:C) model of MIA prevents the PPI, LI, and exploratory and social deficits caused by poly(I:C) and normalizes the associated changes in gene expression in the brains of adult offspring. Finally, MIA in IL-6 knock-out mice does not result in several of the behavioral changes seen in the offspring of wild-type mice after MIA. The identification of IL-6 as a key intermediary should aid in the molecular dissection of the pathways whereby MIA alters fetal brain development, which can shed new light on the pathophysiological mechanisms that predispose to schizophrenia and autism.

Stereotypies and hyperactivity in rhesus monkeys exposed to IgG from mothers of children with autism

- Rhesus monkeys gestationally exposed to IgG class antibodies from mothers of children with ASD consistently demonstrated increased whole-body stereotypies across multiple testing paradigms. These monkeys were also hyperactive compared to controls.

Is ASD partially autoimmune?

- Based upon three different studies, antibodies that react to the 36, 37, 39, 61 and/or 73 kDa bands on Western Blot testing are associated with provoking an immune reaction and contribute to causing autism. Reactivity to these bands is also associated with *Borrelia burgdorferi* and to a lesser degree to *Bartonella henselae*, *Bartonella quintana*, *Mycoplasma*, *Chlamydia pneumonia* and *Streptococcus pneumoniae*.



Prenatal viral infection leads to pyramidal cell atrophy and macrocephaly in adulthood: implications for genesis of autism and schizophrenia

- Prenatal exposure of pregnant mice on Day 9 of pregnancy to influenza virus has both short-term and long-lasting deleterious effects on developing brain structure in the progeny as evident by altered pyramidal and nonpyramidal cell density values; atrophy of pyramidal cells.
- Moreover, abnormal corticogenesis is associated with development of abnormal behavior in the exposed adult mice.

Activation of the maternal immune system alters cerebellar development in the offspring

- The cerebellar pathology observed in the offspring of influenza- or poly(I:C)-exposed mice is strikingly similar to that observed in autism. The poly(I:C) findings indicate that deficits are likely caused by the activation of the maternal immune system. Finally, our data suggest that cerebellar abnormalities occur during embryonic development, and may be an early deficit in autism and schizophrenia.



Brain SPECT: Mother with Lyme Disease & 3 ASD Children

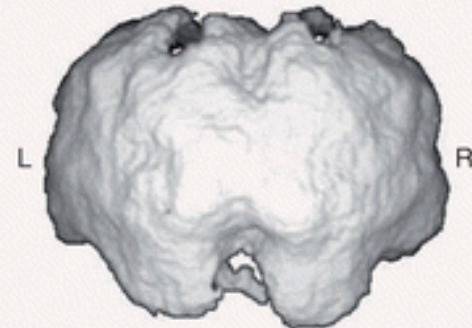
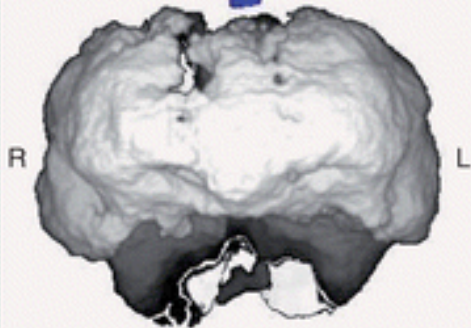
- SPECT scans of a mother with LYD/TBD and her three children with ASD.
- 4 generations of Lyme disease and multiple coinfections.

Multi-threshold volume report
Study ID: corrected baseline volume masked
Patient sex: female; age: 48 years

SPECT with Chang AC
ID: brain
Acq. date: 20/6/2007

Threshold = 60%

Threshold = 60%

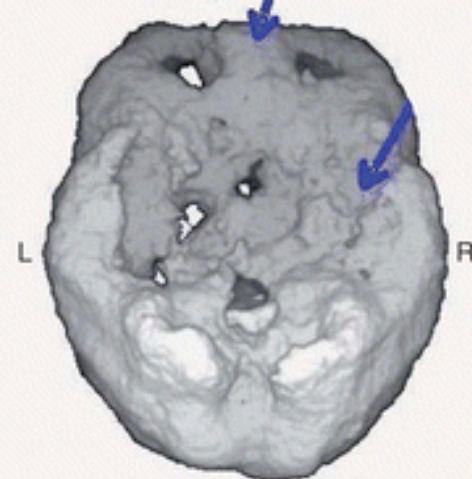
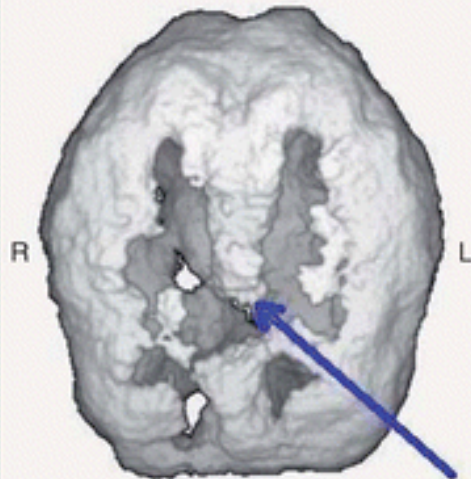


Anterior

Posterior

Threshold = 60%

Threshold = 60%



Vertex

Underside

Underside tilt = -10 degrees Vertex tilt = 10 degrees

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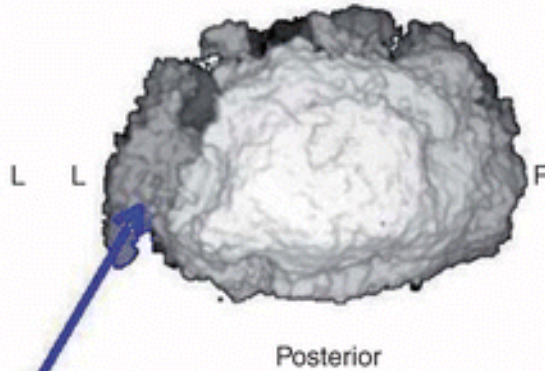
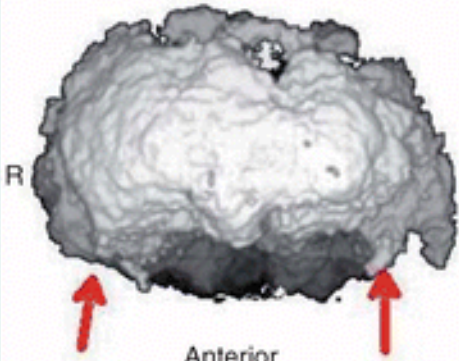
- Mother, 48: There is an extensive hypoperfusion pattern, prominently in the cerebral cortices and much of the frontal lobes, with a lesser degree in the temporal lobes and a small degree hypoperfusion in the cerebellum. The hypoperfusion is moderately extensive and is likely associated with toxic, inflammatory and infectious processes. There is hyperperfusion of the Basal Ganglia, which is associated with anxiety and mood dysregulation. The diagnosis is chronic fatigue syndrome, multiple sclerosis, depression and possible congenital Lyme disease. Lab testing was positive for *Borrelia burgdorferi*, *Babesia duncani*, *Bartonella henselae*, *Mycoplasma fermentans*, HHV-6, EBV, high anti-streptolysin o titre and gamma Strep in stool.

Multi-threshold report
Study ID: corrected baseline volume 6.18 masked
Patient sex: male; age: 26 years

SPECT with Chang AC
ID: brain
Acq. date: 20/6/2007

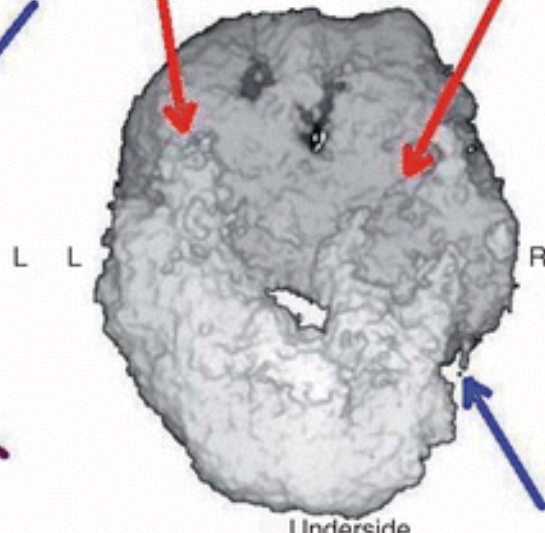
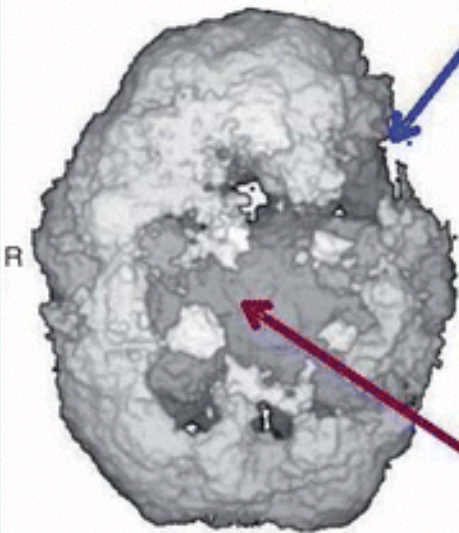
Threshold = 60%

Threshold = 60%



Threshold = 60%

Threshold = 60%



Underside tilt = -10 degrees Vertex tilt = 10 degrees

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• Son, 26: Some motion artifacts, however significant hypoperfusion pattern is both focal as well as generalized. The focal pattern is throughout the cerebral cortex bilaterally and the cerebellar hemispheres (which demonstrate atrophy on MRI) There is mild hyperperfusion of the basal ganglia and a focally intense hyperperfusion area in the deep white matter of the temporal lobe. There is a hyperperfusion pattern involving the temporal lobes and cerebellar hemispheres. The focal decrease is more suggestive of etiologies that would include hypoxic, neuroimmune, traumatic factors, infectious and inflammatory. There is a hyperperfusion pattern of the basal ganglia which may be associated with element of anxiety, whereas the focal intense areas can be associated with present interictal seizure focus and is clinically significant as the present dose of anticonvulsant is not controlling this area. The patient is low functioning with autism spectrum disorder since two years, grand mal seizures, movement disorder, ataxia, hypotonia, megacolon, possible mitochondrial disorder, mild hypergammaglobulinemia and syncope.

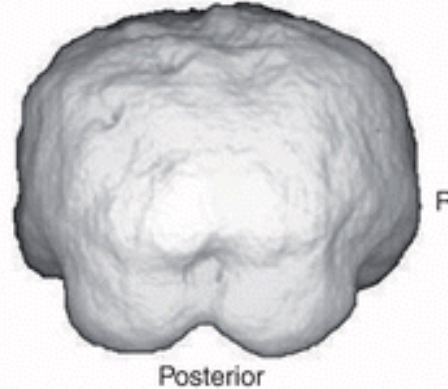
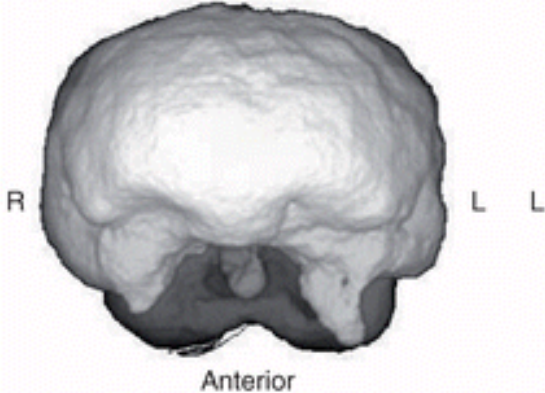
Lab testing was positive for *Borrelia burgdorferi*, *Babesia duncani*, *Bartonella henselae*, *Mycoplasma fermentans*, *HHV-6*, *EBV* and high strep titers; stool positive for *Citrobacter fundii*, *Klebsiella p.* and *gamma Strep* in stool.

Multi-threshold report
Study ID: corrected baseline volume masked
Patient sex: female; age: 23 years

SPECT with Chang AC
ID: brain
Acq. date: 20/6/2007

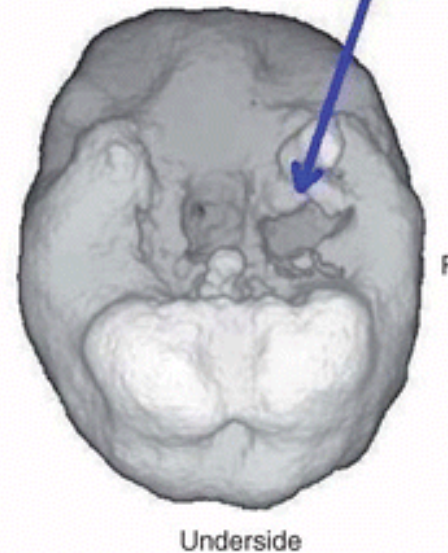
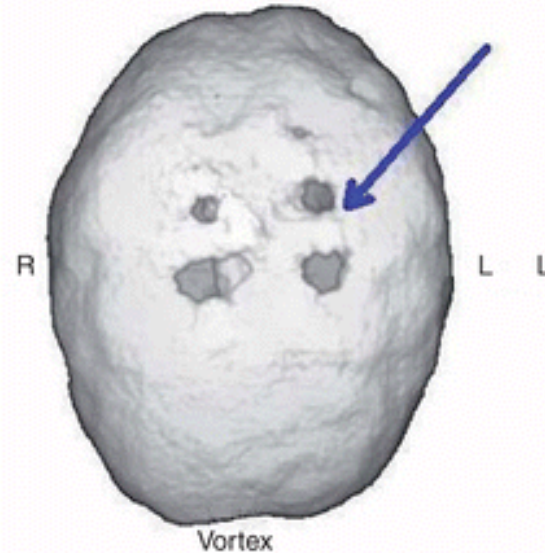
Threshold = 60%

Threshold = 60%



Threshold = 60%

Threshold = 60%



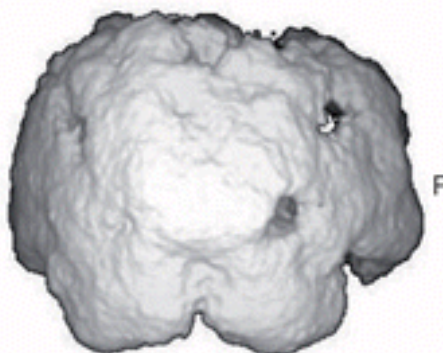
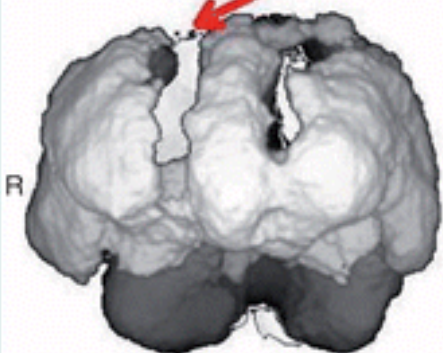
- Daughter, 23: There is an extensive hyperperfusion pattern in the cerebral cortices, temporal lobes and cerebellum and hypoperfusion of the frontal lobes and is likely associated with toxic, inflammatory and infectious processes. The diagnosis is Asperger's, obsessive compulsive disorder, generalized anxiety, social anxiety disorder, depression, posttraumatic stress disorder from an auto accident, possible narcolepsy, tremors, cardiac disease, myocardial infarction, osteopenia, arthritis and pseudo rheumatoid nodules since 5 years of age. Lab testing was positive for *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, *Mycoplasma fermentans*, *Homophilis*, *HHV-6*, *EBV*, elevated Strep titres; stool was positive for *Toxoplasmosis*, *Cornybacteria* and *gamma Strep*.

Multi-threshold volume report
Study ID: corrected baseline volume masked
Patient sex: female; age: 20 years

SPECT with Chang AC
ID: brain
Acq. date: 20/6/2007

Threshold = 60%

Threshold = 60%

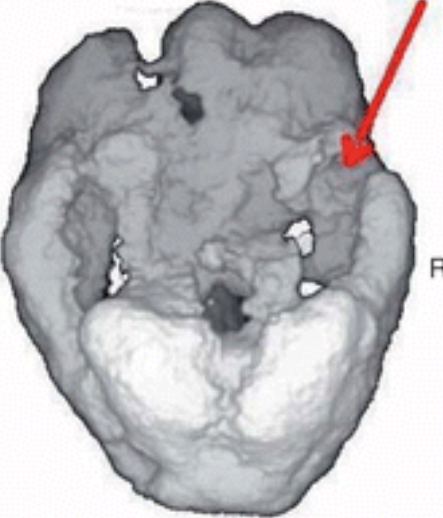
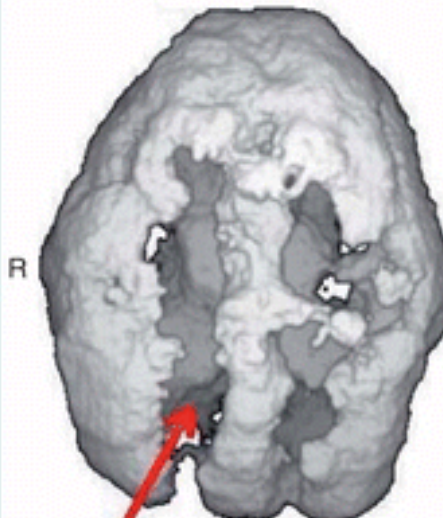


Anterior

Posterior

Threshold = 60%

Threshold = 60%



Vortex

Underside

Underside tilt = -10 degrees Vertex tilt = 10 degrees

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- Daughter, 20: there is extensive hypoperfusion in the frontal lobes, temporal lobes and to a lesser degree to the occipital lobes and slightly to the cerebellum. There is hyperperfusion in the right cerebellar hemisphere. The hypoperfusion is likely associated with neuroinflammatory, neuroimmunological, infectious and toxic substance exposure. There is a seizure focus with hyperperfusion in the right cerebellar hemisphere. The diagnosis is autism spectrum disorder since 14 months, petit mal seizure disorder, hypotonia, perceptual impairments, and anxiety. Lab testing was positive for *Borrelia burgdorferi*, *Bartonella henselae*, *Mycoplasma fermentans*, *HHV-6*; stool positive for *Parvo/B-19*, *Klebsiella, p.*, *Citrobacter f.* and *gamma Strep.*



Prevalence of Parent-Reported Diagnosis of Autism Spectrum Disorder Among Children in the US, 2007

- The weighted current ASD point-prevalence was 11 per 1000. We estimate that 673,000 US children have ASD.[1]
- According to background information in the study, the **life-time healthcare costs for a person with autism are estimated to be more than \$16 million.**[1]
- Chronic infections may be a contributor in well over 50% which would be trillions of dollars.

A Possible Treatment for XMRV: Artesunate could inhibit XMRV via NF Kappa B inhibition*

- **Anti-malarial agent artesunate inhibits TNF-alpha-induced production of proinflammatory cytokines via inhibition of NF-kappaB and PI3 kinase/Akt signal pathway in human rheumatoid arthritis fibroblast-like synoviocytes.**
- **RESULTS:** Artesunate decreased the secretion of IL-1beta, IL-6 and IL-8 from TNF-alpha-stimulated rheumatoid arthritis (RA) fibroblast-like synoviocytes RA FLS in a dose-dependent manner. Artesunate also prevented TNF-alpha-induced nuclear NF-kappaB translocation, DNA-binding activity and gene transcriptional activity, as well as phosphorylation and degradation of I kappa B alpha, but phosphorylation of p38 mitogen-activated protein kinase, extracellular signal-regulated kinase and c-Jun N-terminal kinase were unaffected. The production of IL-1beta, IL-6 and IL-8 induced by TNF-alpha was decreased by pyrrolidine dithiocarbamate (PDTC), a chemical inhibitor of NF-kappaB. These observations suggest that artesunate inhibits production of IL-1beta, IL-6 and IL-8 through inhibition of NF-kappaB signalling pathway. We also showed that artesunate prevented Akt phosphorylation. TNF-alpha-induced production of IL-1beta, IL-6 and IL-8 was hampered by treatment with the phosphatidylinositol 3 (PI3) kinase inhibitor LY294002, suggesting that inhibition of Akt activation might inhibit IL-1beta, IL-6 and IL-8 production induced by TNF-alpha. **CONCLUSIONS:** Our results indicate that artesunate exerts an anti-inflammatory effect in RA FLS and provide the evidence that artesunate may have therapeutic potential for RA.

Opinion expressed by Judy Mikovitz

Xu H, He Y, Yang X, et al. Rheumatology (Oxford). 2007 Jun;46(6):920-6.

Vaccines a risk for pregnant women?

- “Vaccinating a pregnant woman may be risky if her immune response interferes with neuronal growth in her unborn baby’s brain.”

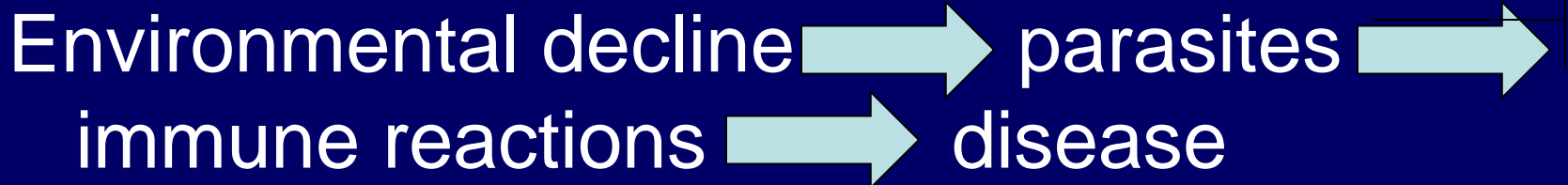
Chronic Infections Contributing to Autism Spectrum Disorders

- Immune reactivity in the mother, fetus and child appear to adversely effect developing neural tissue and contribute to the pathophysiology associated with autism spectrum disorders. This reactivity can be evoked by a number of causes including both acute and persistent infections such as *Anaplasma*, *Babesia*, *Bartonella*, *Borrelia burgdorferi*, *Chlamydia pneumoniae*, *Ehrlichia*, *Human heprevirus-6*, *Mycoplasma* (in particular *Mycoplasma fermentans*) and *XMRV*. Possible pathophysiological mechanisms include both inflammatory processes as well as autoantibodies to developing neural tissue.
- In response to these findings, it is advisable to effectively prevent, diagnose and treat chronic infections in women who are planning on becoming pregnant or who are pregnant, especially if they demonstrate symptoms of an infection or a systemic illness with persistent inflammatory symptoms.

Are microbes or environment the cause?

- “Claude Bernard was right, I was wrong. The germ is nothing, the environment is everything.”

Louis Pasteur on his deathbed



Thanks for Your Attention

