

Neuropsychiatric Aspects of Lyme Disease



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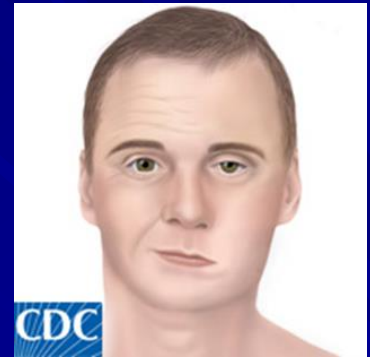
Disclosure: Brian A. Fallon, MD

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Signs of Lyme Disease

- Early: Erythema Migrans Rash
 - Only 20% of time is it a bull's eye
- Early or Late Disseminated:
 - **Dermatologic**: multiple EMs
 - **Neurologic**
 - Cranial nerves
 - Peripheral nerves
 - Central Nervous System
 - **Arthritis** (swelling or synovitis)
 - **Cardiac** (heart block, carditis)



“Bb in the Nervous System: The New Great Imitator” Case 1: Anorexia/OCD

Pachner A. Annals of NY Academy of Sciences, 1988

2. Behavioral Changes

Between 1982 and 1984, a 12-year-old boy had four attacks of swelling of the right knee; the diagnosis of Lyme arthritis was confirmed serologically. After the last attack, he was treated with doxycycline, 100 mg twice a day for 30 days. Two months later, the patient became withdrawn and depressed. He no longer interacted with his friends, spent most of this time alone, and would no longer do his school work. He ate very little and began to exercise compulsively. His weight dropped 14 kg. On admission to a psychiatric hospital, he was grossly depressed and uncommunicative. He was diagnosed as having anorexia nervosa.

Because of the history of Lyme disease, he was transferred to Yale-New Haven Hospital. Serum and CSF antibody titers to *B. burgdorferi* were elevated, but neurologic evaluation was normal. He was treated with intravenous penicillin, 20 million U a day for 14 days, and within several weeks he began to eat more, gain weight, and communicate. During the following several months, his behavior returned to normal, he went back to school, and has remained asymptomatic for the past 2 years.

Case 1: Dr. Mary

- 42 year old physician
 - During the 8 weeks after a tick bite, she developed fatigue, myalgias, cognitive problems. Lyme tests were positive. Treated with doxy...90% better.
 - Relapsed after 4 months – treated again – better again.
 - Relapsed a 3rd time, but then treated with azithromycin – this led to a sustained improvement.

Case 1 Comments

- 20% of patients with LD do not see a rash
- Cognitive problems occur – “brain fog”
- 10-20% develop recurrent symptoms after initial treatment
 - “Post-treatment Lyme Disease Syndrome”
 - “Chronic Lyme Disease”

PTLS vs Chronic Lyme Disease

- Terms make a difference
- PTLS requires well-documented prior Lyme disease, persistent Sx & impairment.
- Immune biomarkers of PTLS:
 - anti-neuronal Ab – comparable to SLE
 - Endothelial cell growth factor antibody
 - IL6 & expression of IF alpha
 - Chemokine CCL 19
 - CSF Complement cascade proteins

Functional Neuroimaging

■ Brain SPECT

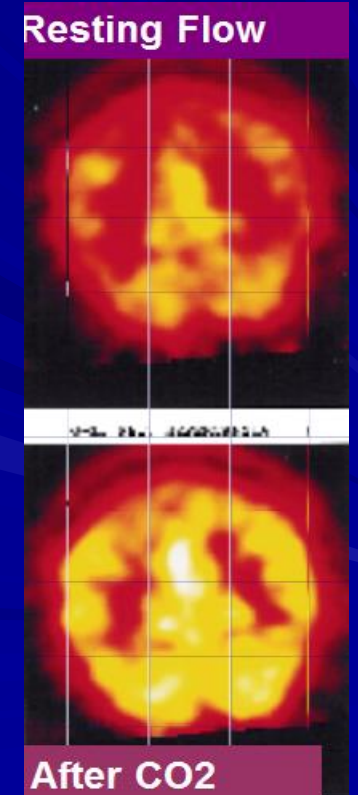
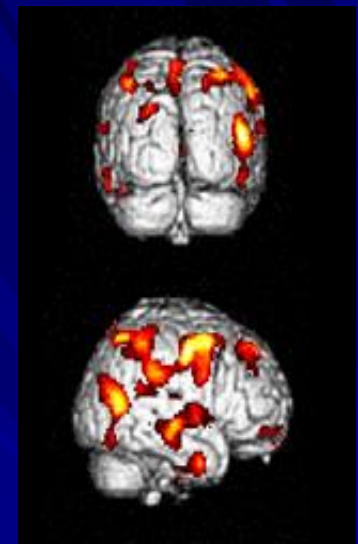
- May show moderate to severe heterogeneous hypoperfusion, but this is non-specific

■ Brain FDG PET & O-15 PET

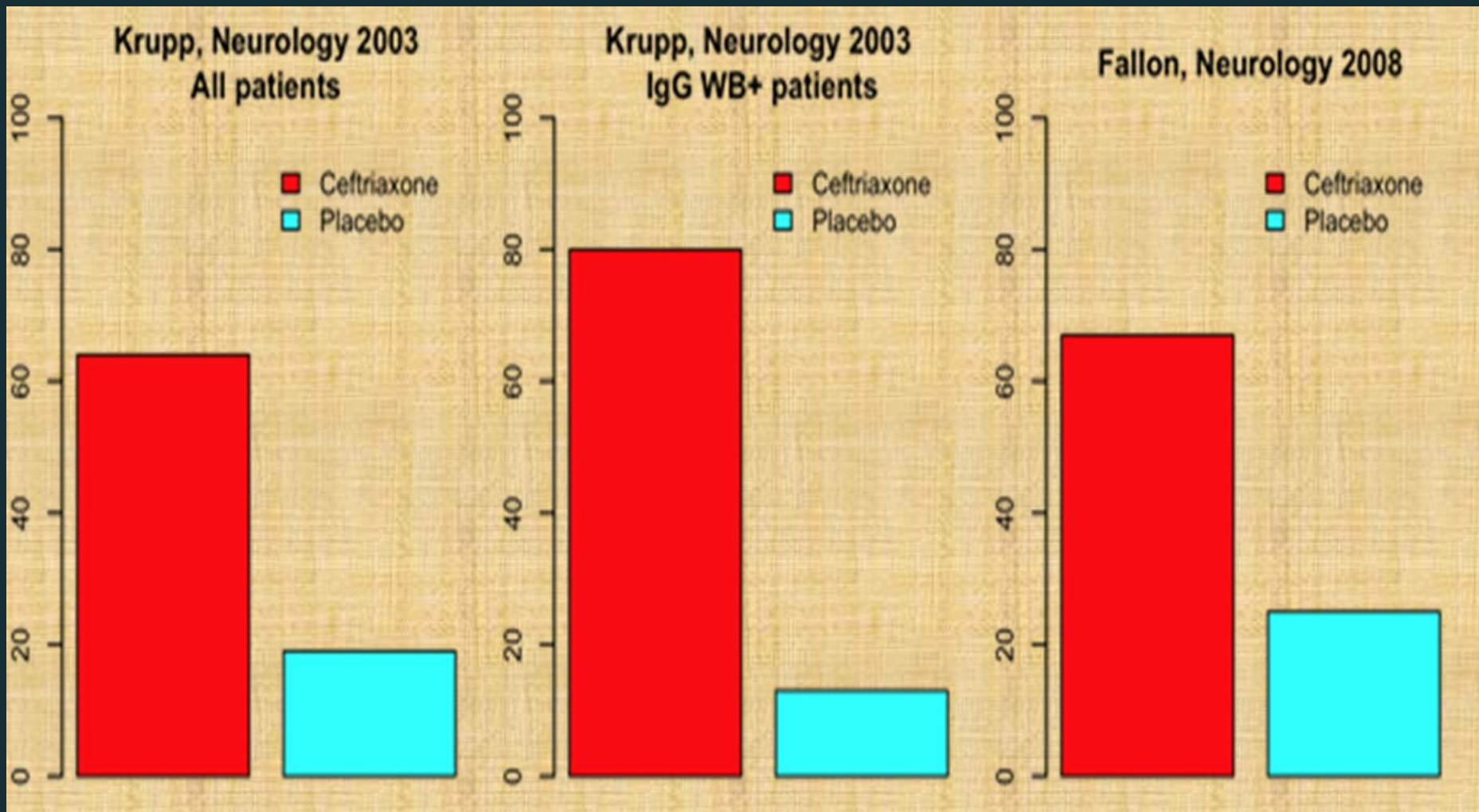
- Temporal & parietal hypometabolism

The patient group showed a diminished ability to enhance blood flow compared to controls (8.2% for patients vs 28.1% for controls, $p < .02$)

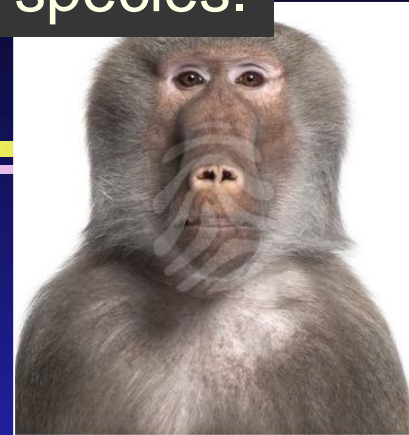
Fallon et al, JAMA Psychiatry 2009



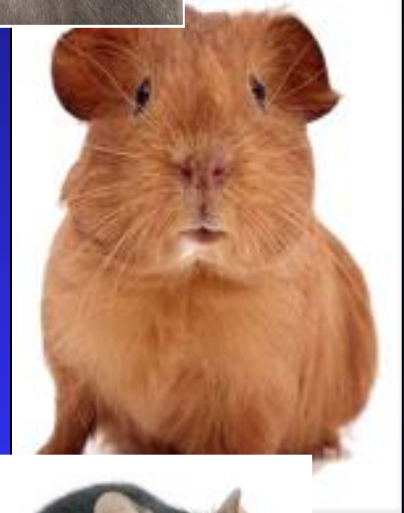
Repeated Treatment significantly reduced fatigue in two RCTs



Borrelia persist despite antibiotics.
This has been shown in many species.



Often with minimal or
No Disease



Slide courtesy of Stephen Barthold, UC Davis

Xenodiagnosis – an old technique to detect spirochetes in mice & humans

- When blood and tissue sampling fail to detect Bb spirochetes, ticks come to the rescue – attracting spirochetal DNA.



(Marques, Hu, et al, CID, 2014)



1 of 9 PTLs tested positive by xenodiagnosis

Case 2. Bill. 27 year old man with intermittent paranoia

- Paranoia...months later encephalopathic
- ICU:
 - CSF & serum + for Bb antibodies & WBC
 - IV Ceftriaxone Tx – 80% better, discharged
- 3 weeks later – joint/cognition deteriorates
- Hosp: retreated with IV Ceftriaxone – no benefit
 - Conclusion – “This must be a psych problem.”
- Minocycline eventually leads to marked improvement

Case 2. Comments

- Psychiatric sx may be presenting feature
- Cognitive problems are usually mild-moderate – but rarely can be severe
- Relapse after good response can occur
- While IV ceftriaxone is excellent for neurologic Lyme disease, in some cases other antibiotics may also be useful.

Diagnostic Evaluation

- Blood Tests
 - C6 Peptide ELISA
 - Two-tier assay: ELISA & Western blot
- Spinal Fluid: remember to send serum collected on same day
- Cognitive Testing: especially verbal fluency
- Other: Neuroimaging, Nerve Conduction Studies, Small Nerve fiber Skin Biopsy

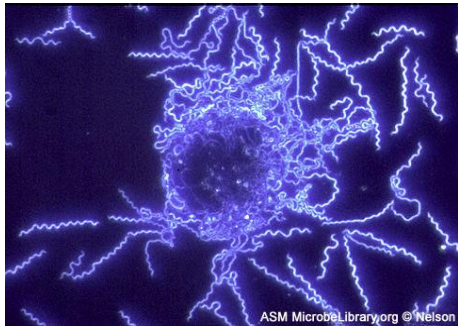
Serologic Tests

- **ELISA:** Whole Cell Sonicate, **C6 Peptide**, VlsE
 - Sensitivity: 30-50% early LD, 70-90% neurologic LD
- **Western blot**
 - IgM (meaningful in first 4-6 weeks after infection)
 - This can stay positive for many months, long after treatment resolved symptoms
 - Some patients do not seroswitch from IgM to IgG
 - IgG (5 bands meet CDC criteria, but 4 are highly suspicious)
- If seronegative but clinical profile is strong, look for early antibiotics as these may have abrogated Ab response

Standard Blood tests are helpful but not definitive

- Ab response – can stay positive for years
 - Do not clarify whether infection resolves
- False positives & false negatives occur
 - False positives may occur with ELISA and IgM WB, esp after mono infection.
- IgG WB has non-specific antigens (e.g.41, 66)

A good test would be positive when the infection is present & negative when the infection has resolved



Borrelia sensu lato
-B. garinii (EU)
-B. afzelii (EU)
-B. burgdorferi (EU/USA)



Ixodes species
-Ricinus (EU)
-Scapularis & Pacificus (USA)



Arthritis (Rheumatologic)
Neuroborreliosis
ACA (Skin inflammation)

**Lyme
Borreliosis**

Recovery

Post-treatment Lyme
Syndrome

Cerebrospinal Fluid Testing for Neuroborreliosis

■ CSF Findings

- Intrathecal Antibody production (paired serum & CSF)
- May see elevated protein & WBC
- Oligoclonal bands are uncommon
- PCR & Culture are insensitive
- CXCLXIII – sensitive marker of active NB

■ Spinal fluid may test positive for Bb antibodies even if serum is negative

■ Experimental assays suggest CSF may be falsely negative in 20% of cases.

Common Tick-borne Coinfections

- *Borrelia miyamotoi*

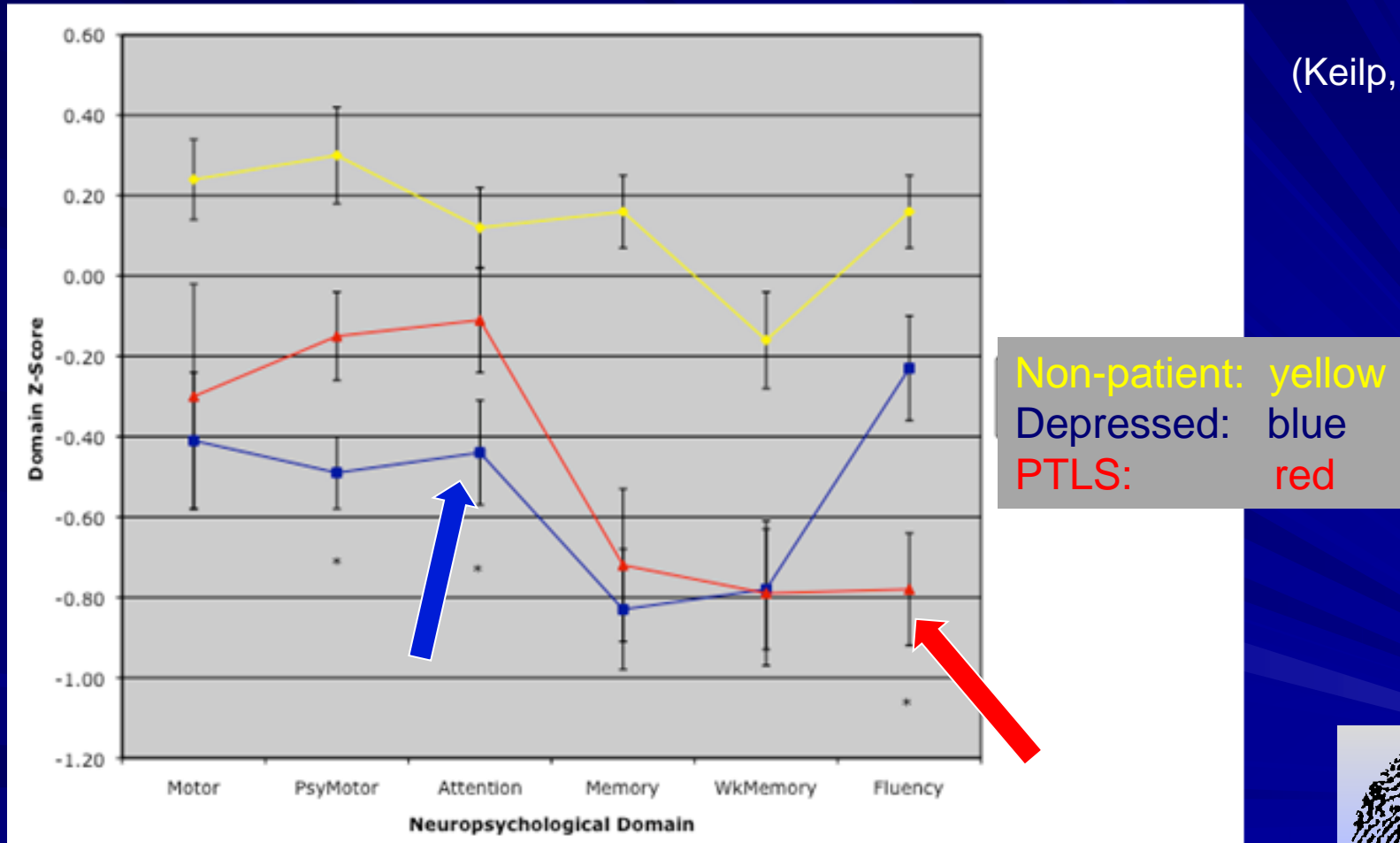
- *Babesia microti*

- *Ehrlichia*

- *Anaplasma*

Which cognitive domains differentiate memory impaired patients? PTLs vs Depression

Demographically-adjusted aggregate domain Z-scores for neuropsychological measures in memory impaired patient groups and healthy comparison subjects.



Verbal Fluency is worse in PTLs (red)
while **Attention is worse in Depression (blue)**



Other Treatment approaches to consider if symptoms persist

- Immune modulatory therapy (e.g, IVIg)
- Pharmacotherapy for pain, sleep, mood
- Brain Stimulation (eg, TMS)
- Psychotherapy

For More Information about Lyme & Tick-borne Diseases

Website: www.columbia-lyme.org

Conquering Lyme Disease

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All Proceeds support research

