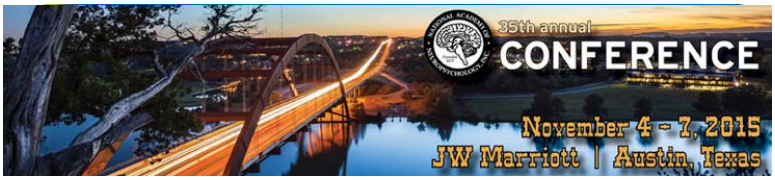
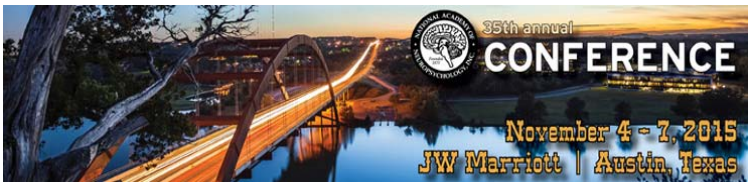


Adult Grand Rounds

Mike R. Schoenberg, PhD, ABPP – Chair

Gregory Lee, PhD, ABPP – Discussant
Clea Evans, PhD - Discussant
Robin Hilsabeck, PhD, ABPP - Discussant



FINANCIAL DISCLOSURE

M. Schoenberg

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C. Evans

- None to report

G. Lee

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R. Hilsabeck

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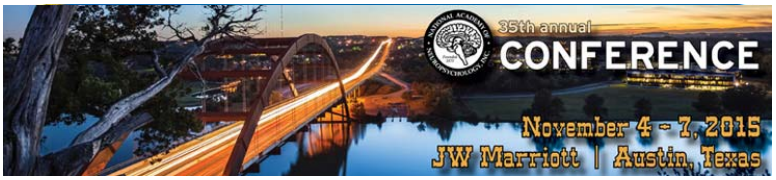

Lessons from a Neuropsychological Case Study of Adult Polyglucosan Body Disease (APBD) Initially Diagnosed as Multiple Sclerosis

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Stephanie Assuras, Ph.D.[3]

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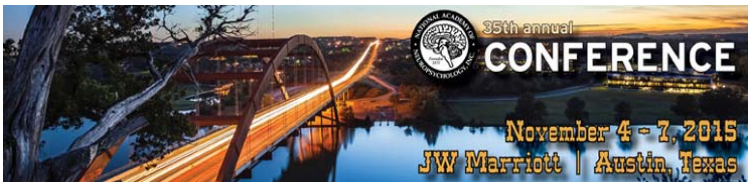
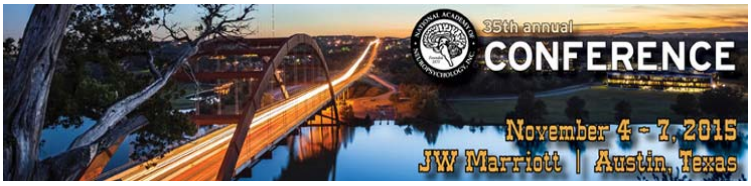


FINANCIAL DISCLOSURE

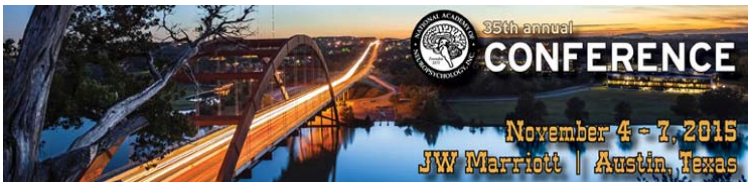
We have no financial relationships to disclose.



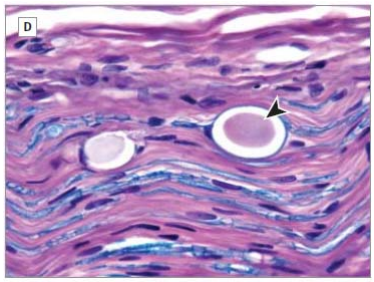
APBD: Transmission & Pathology

- APBD is an autosomal recessive disease → deficiency of glycogen branching enzyme gene (GBE1) encoded at chromosome 3p12.
- Affects central and peripheral nervous systems, as well as other tissue (e.g., liver).
- Neuroimaging markers include demyelination and gliosis:
  - Medullary and cervical spinal cord atrophy (100 %)
  - Subcortical and periventricular white matter lesions affecting posterior limb of internal capsule (93 %) and the brainstem (97 %)
  - Cerebellar atrophy (57 %)
  - Thinning of the corpus callosum (43%)

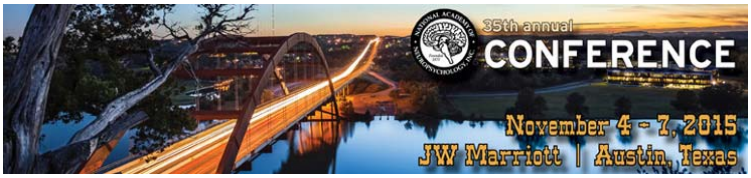
Klein, 2009; Mochel, et al. 2012; Hellman et al., 2015



Intracellular accumulation of polyglucosan bodies in neurons detected by Luxol fast blue staining for myelin.



Adapted from Paradas et al. 2014



APBD: Mechanism & Diagnosis

- Neuro-mechanism unknown
  - Astrocytic transport or energy deficit in glial cells?
- Diagnosis is based on:
  - Clinical exam
  - MRI of brain/spinal cord
  - Sural nerve biopsy
  - Assay of GBE activity
  - Genetic testing

Klein, 2009; Mochel et al., 2012

APBD: Typical Course

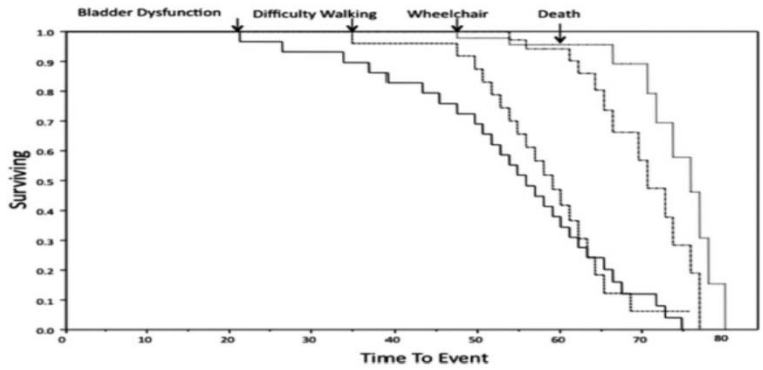
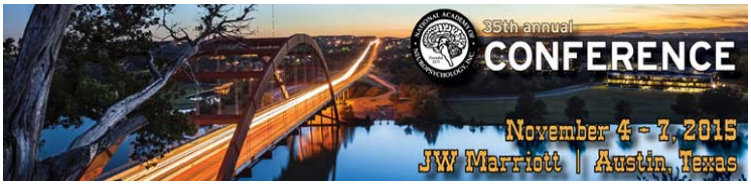


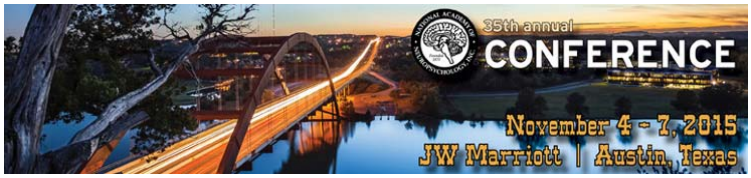
Figure 1.
Kaplan–Meier analyses indicate the natural history of 50 adult polyglucosan body disease patients for time to bladder dysfunction, difficulty walking, use of a wheelchair, and death.

Adapted from Mochel et al. 2012

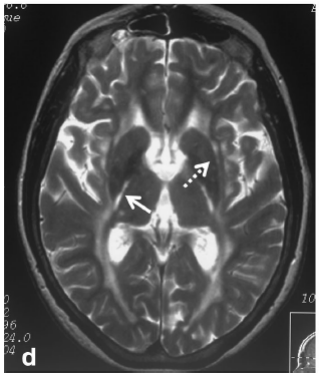


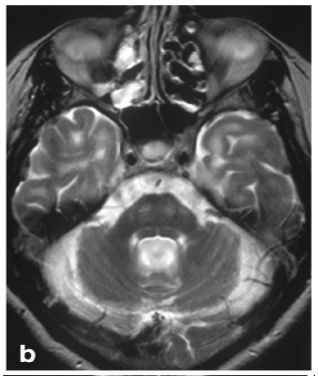
APBD: Epidemiology

- Frequency of GSDs is 1:10,000, GBE deficiencies account for ~3% (Mochel et al., 2012)
  - In Ashkenazi Jews, heterozygote frequency = 1:35 (Hussain et al., 2012)
  - Also Dx'd in Latinos, Pacific Islanders, Caucasians, Cambodians, Koreans, Italians (Lee et al., 2007; Dainese et al., 2012; Mochel et al., 2012; Colombo et al., 2015)
- Frequently misdiagnosed (Hellman et al. 2015):
  - Benign prostatic hypertrophy in males (53%)
    - → "inappropriate" prostatectomy (62%)
  - Cerebral Small Vessel Disease (27 %)
  - Peripheral Neuropathies (20 %)
  - Multiple Sclerosis (17 %)
  - Amyotrophic Lateral Sclerosis (17 %)
  - Cervical Spondylotic Myelopathy (10%)
  - Multiple System Atrophy (7%)

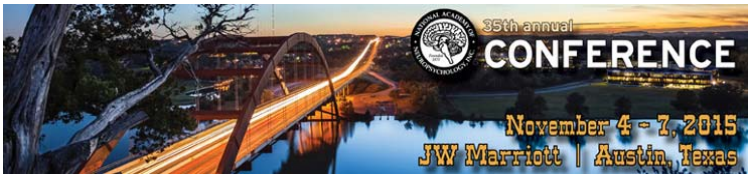


MRI of a 67-year-old female with APBD initially Dx'd as MSA



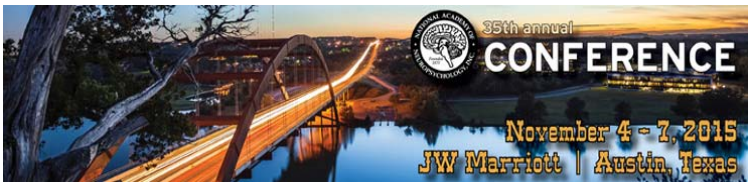


Adapted from Hellman et al. 2015



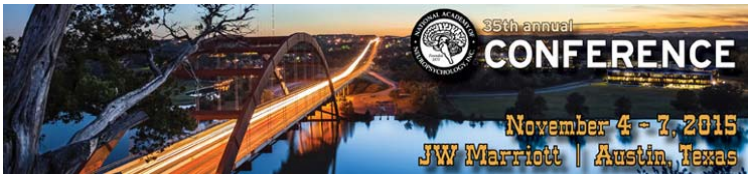
APBD: Treatment

- Experimental, open trial of triheptanoin diet therapy in 6 patients (Roe, Bottiglieri, Wallace, Arning & Martin, 2010):
  - Temporary perceived stabilization of symptoms
    - Increased strength
    - Decreased urinary frequency
    - Reduced ptosis and leg pain
  - Improved walking performance
- No FDA approved treatments
- Palliative and symptom-focused care
- Pre-conception genetic screening/family planning



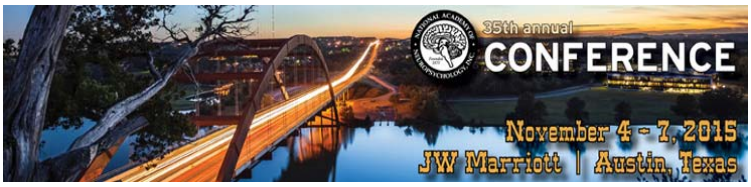
APBD: Cognitive Characteristics

- Riffai et al., (1994) described test performance in a 56 y/o male
  - Borderline FSIQ, deficient sustained attention, slow processing, impaired visuospatial skills, anomia, auditory comprehension problems, and recognition memory > free recall.
- Savage et al. (2006) described an 80 y/o female with moderate to severe impairments in memory, language, executive functioning, and visuoconstructional deficits that remained stable across 4-years.
- Billot et al., (2013) reported a case of transient severe attentional and dysexecutive deficits in a 35 y/o woman with APBD, undetected at F/U.
- Other reports have described APBD pathology co-morbidly with LBD (Trivedi et al., 2003) and FTLD (Farmer et al., 2013), and AD (Mochel et al., 2012).

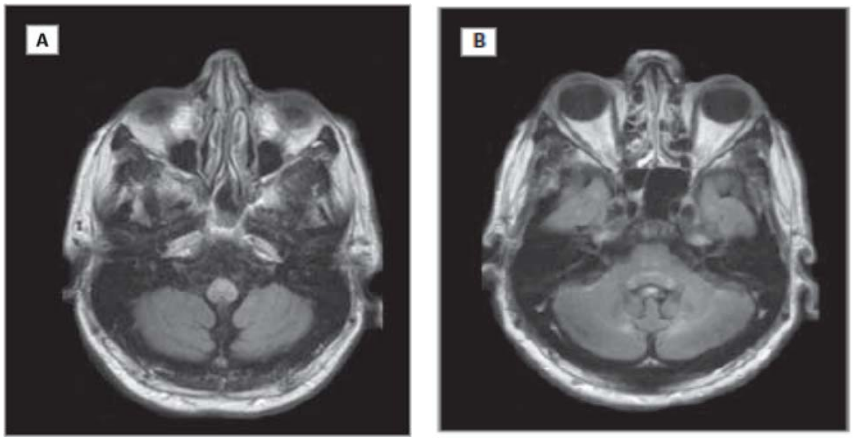


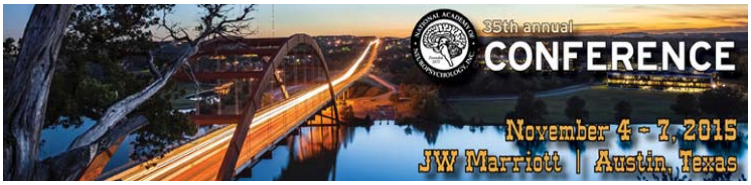
Present Case: Background

- 46 year-old, RH, married man with 18-years of education in the visual arts.
- Onset: At age 37, had hour-long episode of slurred speech, numbness/weakness in legs, difficulty walking, urinary urgency/incontinence and feeling "cloudy."
- Given MS diagnosis after MRI showed demyelination.
- Treated with *interferon beta-1a* for 5-years.
- These symptoms persisted along a relapsing-remitting course despite treatment.

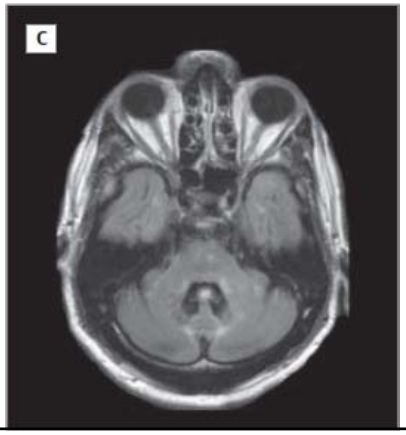


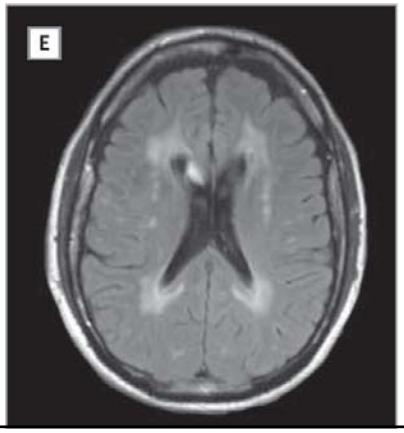
Present Case: Imaging

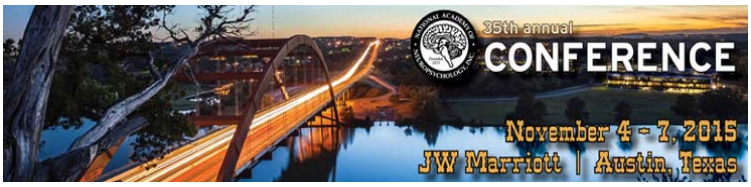




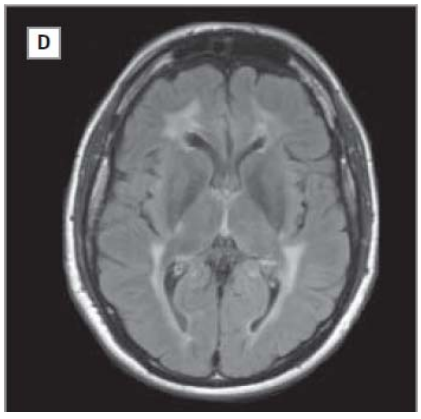
Present Case: Imaging Continued

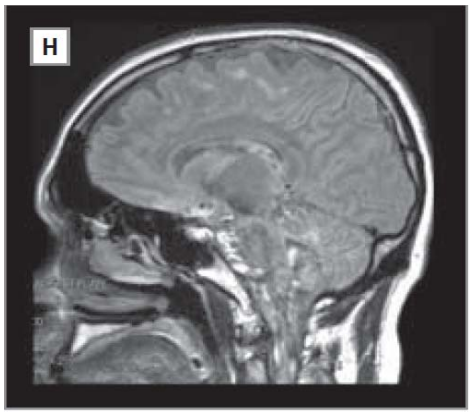


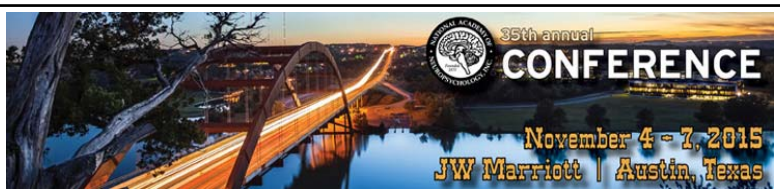




Present Case: Imaging Continued

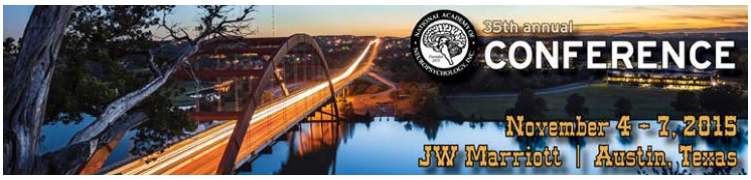






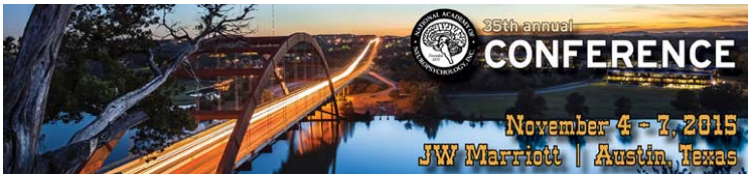
Present Case: Background Continued

- At age 43, medical providers learned that brother died at age 2 ½ of hepatopathy, following 2 failed liver transplants.
  - At autopsy, liver showed abnormal glycogen storage.
- *GBE1* mutations were detected in our patient and branching enzyme activity was <10% of normal.
- Diagnosis was changed to early adult–onset, relapsing-remitting, polyglucosan body disease.
- *interferon beta-1a* was discontinued.



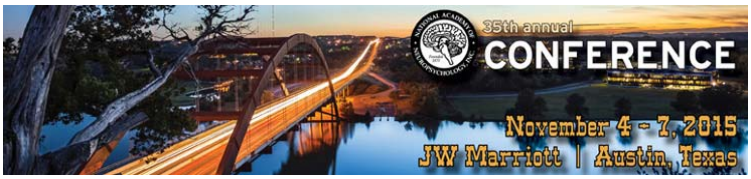
Present Case: Complaints

- Context of NP referral:
  - Referred following 2-years of new-onset cognitive complaints that appeared stable
- Cognitive
  - Trouble concentrating and initiating → errors on the job
  - Mild short-term memory problems, but "eventually remembers"
  - Increased effort to prioritize and complete tasks
- Functioning
  - Recent job loss (presumably due to cognitive problems)
- Mood
  - "Stressed": questions about how to live fully despite APBD
  - Recently started insight-oriented psychotherapy; no psychotropics
- Social
  - Marital Difficulties



Intellectual Functioning

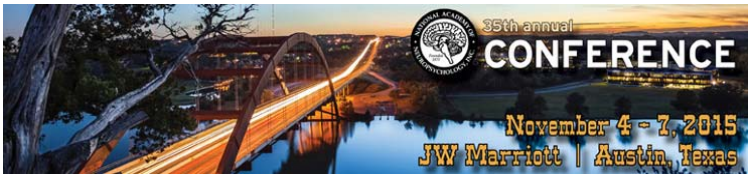
ACS TOPF	SS = 117	Above Average
WAIS-IV VCI	SS = 112	Above Average
WAIS-IV PRI	SS = 121	Superior
WAIS-IV WMI	SS = 86	Low Average
WAIS-IV PSI	SS = 94	Average
WAIS-IV FSIQ	SS = 107	Average
WAIS-IV GAI	SS = 120	Above Average



Attention

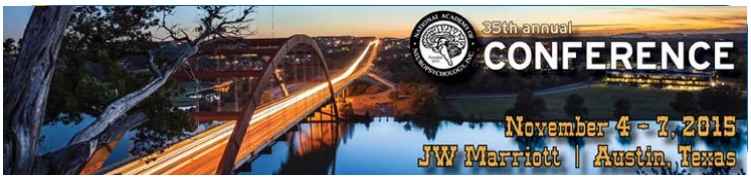
WAIS-IV LDF	Raw=6	21%	Low Average
WAIS-IV LDB	Raw=4	18%	Low Average
WAIS-IV LDS	Raw=5	18%	Low Average
WAIS-IV Arithmetic	ss=7	14%	Borderline

Conners' CPT-II	70%	Better Matches a Clinical Profile
Omissions	T=62	Moderately Atypical
Commissions	T=59	Mildly Atypical
Hit RT Block Change	T=61	Moderately Atypical
Hit SE Block Change	T=73	Markedly Atypical
Variability	T=65	Markedly Atypical



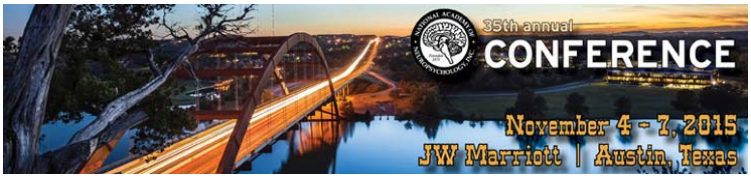
Processing Speed

DKEFS Motor Speed	11	Average
DKEFS Combined Number & Letter Sequencing	12	Above Average
DKEFS Color Naming	11	Average
DKEFS Word Reading	12	Above Average
WAIS-IV Coding	9	Average
WAIS-IV Symbol Search	9	Average



Executive Functioning

DKEFS Number Letter Switching	9	Average
DKEFS Category Switching	11	Average
DKEFS Color Word Inhibition	10	Average
DKEFS Inhibition/Switching (I/S)	10	Average
I/S Uncorrected Errors	14%	Borderline
DKEFS Tower: Move Accuracy	7	Borderline
WAIS-IV Similarities	11	Average
WAIS-IV Matrix Reasoning	12	High Average
WCST-64 Categories	Raw=3	Non-Impaired
WCST-64 Total Errors	T=41	Low Average
WCST-64 Perseverative Errors	T=33	Mildly-Moderately Impaired

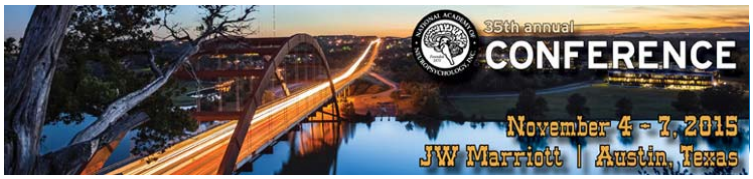


Language

WAIS-IV Vocabulary	46	12	Above Average
BNT-2 Total Score	59	T=54	Average
DKEFS Category Fluency (CF)	35	9	Average
DKEFS Letter Fluency (LF)	25	6	Mildly Impaired

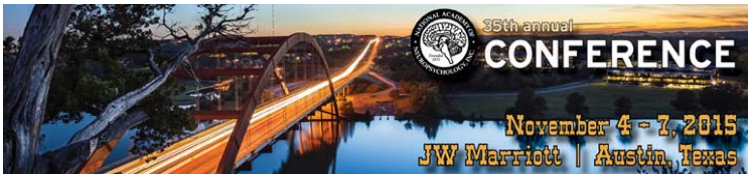
Visuospatial

RCFT Copy	Raw=36/36	Non-Impaired
WAIS-IV Block Design	14	Above Average
WAIS-IV Matrix Reasoning	12	Above Average
WAIS-IV Visual Puzzles	15	Superior



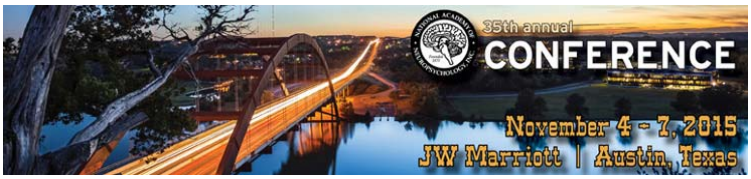
Visual Learning & Memory

BVMT-R: Total Recall	T=56	Average
BVMT-R: Delayed Recall	T=59	Above Average
BVMT-R: Discriminability	>16	Non-Impaired
RCFT: Immediate Recall	T=59	Above Average
RCFT: Delayed Recall	T=57	Above Average
RCFT: Discriminability	T=57	Above Average



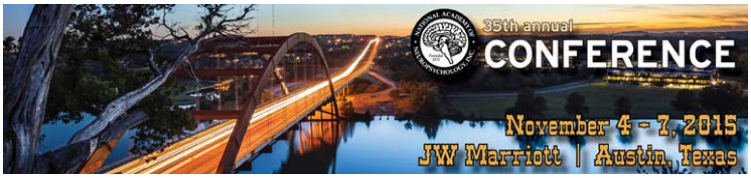
Verbal Learning & Memory

CVLT-2: Total Recall	T=68	Superior
CVLT-2: Trial B	T=40	Low Average
CVLT-2: Proactive Interference	T=40	Low Average
CVLT-2: Short Delay Free	T=65	Above Average
CVLT-2: Long Delay Free	T=65	Above Average
CVLT-2: Discriminability	T=60	Above Average
WMS-IV LM I	ss=7	Borderline
WMS-IV LM II	ss=7	Borderline
WMS-IV LM Discriminability	26-50%	Average



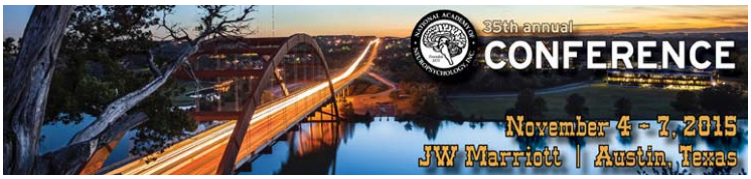
Emotional Functioning

BDI-2	21	Moderately Elevated
BAI	19	Moderately Elevated



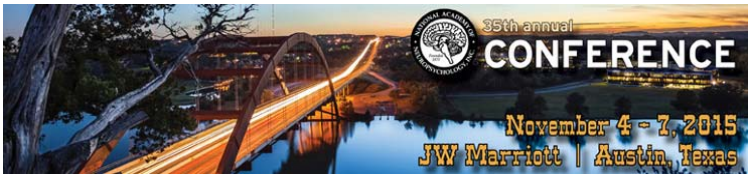
Summary

- Reduced attention/working memory, sustained attention, and initiation/fluency were prominent features of the NP profile.
- As cognitive complexity increased, mild but consistent reductions in planning and problem-solving emerged.
- Strengths included visuospatial analysis, reasoning, language, and learning/memory.
- Illness-related maladjustment was observed.



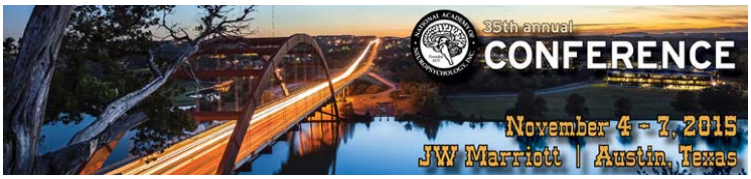
Integration/Interpretation

- Test findings mirror perceived difficulties.
- Attentional and executive deficits may be consistent with white matter degeneration in frontal lobes and/or cerebellar lesions.
- Emotional distress may have contributed to cognitive weaknesses.



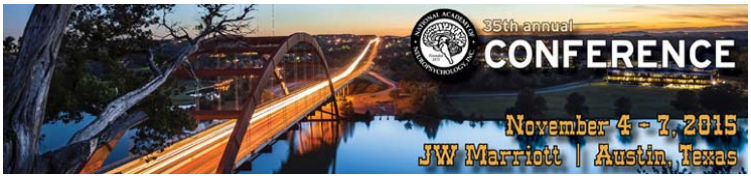
Recommendations

- Psychiatry referral.
  - CBT for depression, anxiety, maladjustment.
  - Psychotropics for mood and attention.
- Cognitive remediation referral.
  - Emphasized learning compensatory strategies.
- Encouraged marital counseling.
- Encouraged to take advantage of support resources at http://apbdrf.org/.



Conclusions

- Case sheds light on neuropsychological characteristics of APBD.
- Pattern of executive dysfunction provides further evidence that cerebellar white matter degeneration may produce cognitive profiles reflecting frontal-systems involvement.
- Although profile could be consistent with more common demyelinating conditions, clinicians should note how critical family history was in reaching accurate diagnosis.



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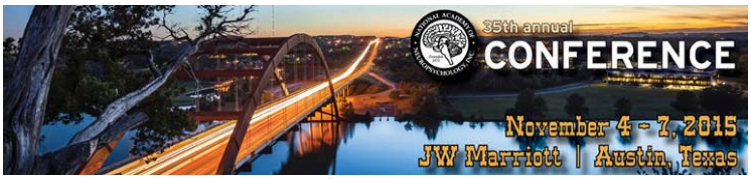

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Comprehensive Neuropsychological Assessment in Late-Onset Wilson's Disease

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Financial Disclosure

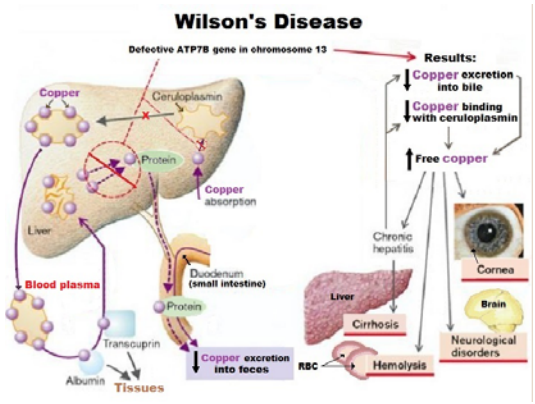
I have no financial relationships to disclose

What is Wilson's Disease

- Autosomal recessive genetic disorder
- Copper accumulation in liver, brain, organs
- 1/30,000
- Ages 12-23, up to age 40
- Hepatic/renal failure

Keller et al., 1999; Lindsay et al., 2004

Pathophysiology



Initial Symptoms & Diagnostic Features

Symptoms	Diagnostic Features:
Fatigue	*Kayser-Fleischer rings
Jaundice	Abnormal liver tests
Bruise easily	Presence of various symptoms
Fluid in legs/abdomen	
Problems w/ speech or swallowing	
Motor symptoms	
Psychiatric symptoms	
Cognitive dysfunction	

Keller et al., 1999; Lindsay et al., 2004; Seniow et al., 2003

Symptom Presentation

40%- Parkinsonian Features:

Micrographia, tremors, dystonia, ataxia, rigidity, dysarthria, excessive salivation, and choreaform movements

40%- Hepatic Features:

Acute hepatitis, cirrhosis, jaundice

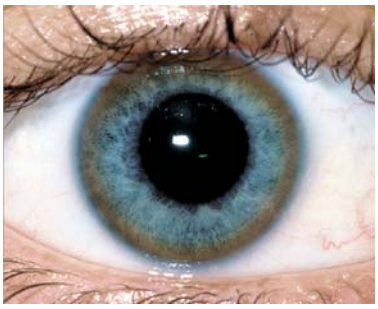
20%- Psychiatric Features:

Depression, suicidal ideation, anxiety, psychosis, personality changes, and aggression

Blumenfeld, 2002; Lindsay & Bone, 2004

Kayser-Fleischer Rings

- The most characteristic sign
- Not always visible to the naked eye
- ~50% of cases



Keller et al., 1999; Lindsay et al., 2004

Treatment

- Penicillamine may be effective
- Most improve w/ some residual symptoms
- Proportion remain symptomatic or deteriorate
- Difference in outcomes not well studied

Keller et al., 1999; Lindsay et al., 2004

Neurocognitive Deficits

- Limited studies
- Cognitive deficits due to disease *and* medication effects
- Motor/mental speed and higher order cognitive functions most compromised
- Patients with neurological symptoms perform worse than controls and asymptomatic patients on motor, memory, executive functioning, and visuospatial tasks
- Recent study: evidence for decreased ACC activity, suggesting problems with inhibition; associated with symptom severity

Goldstein et al., 1968; Isaacs-Glaberman et al., 1989; Knehr et al., 1956; Lang et al., 1990; Medalia et al., 1988; Portala et al., 2001; Rathbun et al., 1996; Scheinberg et al., 1968; Seniow et al., 2002; Stock et al., 2015

Epilepsy in Wilson's Disease

- Prevalence of epilepsy is 6-8%
- Related disease and medication effects
- 20% precede WD diagnosis, 45% begin at the time of diagnosis, and 30% occur after treatment
- 70% GTCs; 68% had no recurrence after ~9 years

Dening et al., 1988; Prashanth et al., 2010

Case- Mr. X

- 63 year old, R-handed, Caucasian, married male with 18 years of education working as a Professor at a major university
- Various cognitive and motor complaints
- Possible hallucinations and one episode of disorientation/unconsciousness
- Depressed mood, personality changes
- Suspected ataxia vs. PD vs. ET
- Testing confirmed **Wilson's Disease**

Behavioral Observations

- On time, with wife
- Appropriately dressed, slightly disheveled
- Very slow (gait, motor movements, speech, thought patterns)
- Shuffling gait
- Tremor and dyskinesias
- Verbose and very reflective
- Pleasant
- At times, anxious and concerned with performance
- Needed assistance/modifications

Domain	Test(s)
Premorbid	Wechsler Test of Premorbid Functioning
General Intellectual Fx	Wechsler Adult Intelligence Scale
Memory	Wechsler Memory Scale-IV – Logical Memory subtest, Brief Visuospatial Memory Test, California Verbal Learning Test- Second Edition
Language	Verbal Fluency tasks, WAIS Subtests
Attention/Processing/Executive	Trail Making Test, Stroop Color and Word Test, Wisconsin Card Sorting Test-64 item, Iowa Gambling Task, WAIS subtests, Symbol Digit Modality Test
Visuospatial	Benton Facial Recognition Test, Judgment of Line Orientation, WAIS subtests
Motor	Grooved Pegboard Test, Go/No Go (frontal-motor)
Effort	CVLT Forced Choice, Reliable Digit Span, Recognition
Mood/Behavioral Fx	Beck Depression Inventory- Second Edition; Beck Anxiety Inventory, Minnesota Multiphasic Personality Inventory-II Restructured Form, The Frontal Systems Behavior Scale (self and informant), and Behavior Rating Inventory of Executive Function

Premorbid Functioning & General Intellect

	Raw	SS	Dem SS	E-FSIQ
TOPF	55	112	115	113

WAIS-IV Factor	VCI	PRI	WMI	PSI	FSIQ
Standard Score	122	75	92	65	88
Demographic T-Score	55	22	33	17	28

Attention/Working memory

WAIS-IV WMI	Raw	Norm
Digit Span		ss = 9/DemT = 38
Forward	8	ss =8
Backward	10	ss = 12
Sequencing	7	ss= 9
Longest Span FW	5	C% = 94.5
Longest Span BW	5	C% = 45
Longest Span Seq.	5	C% = 81.5
Arithmetic	8	DemT=31

Processing Speed

WAIS-IV PSI	Raw	Norm
Symbol Search	17	ss = 5/DemT = 27
Coding	16	ss =2/DemT = 10
Trail-Making	**Raw**	**Norm**
TMT-A	89.4"	-8.3
Symbol-Digit Modality Test	**Raw**	**Norm**
Oral	24	Z = -2.8

Executive Functions

Trail-Making Test	Raw	Norm
TMT-B	285" (2 errors)	z = -11.9
Stroop	**Raw**	**Norm**
Word	73	T = 33
Color	32	T = 18
Color-Word	14	T = 19
Color-Word Interference	-8	T = 42
COWAT	**Raw**	**Norm**
FAS	30	z = -1

Executive Functions Continued

Wisconsin Card Sorting Test	Raw	Norm
Categories Completed	3	>16th %ile
Total Errors	21	T = 41
Total Perseverative Responses	7	T = 53
Trials to 1st Category/FMS	12/0	>16th %ile/NA
Iowa Gambling Test	**Raw**	**Norm**
Total Score	-32	T = 36
WAIS VCI/PRI	**Raw**	**Norm**
Similarities	29	ss= 12/DemT =49
Matrix Reasoning	7	ss=5/DemT = 21

Motor/Frontal Motor

Grooved Pegboard	Raw	Norm
Dominant Right Hand	2 rows in 94" 92 drops)	impaired
Nondominsnat Left Hand	2 rows in 83"	impaired
Luria Front-Motor	**Raw**	**Norm**
Contrasting	9/10	wnl
Go/No-Go	9/10	wnl

Language

WAIS VCI	Raw	Norm
Vocabulary	51	ss = 14/DemT=55
Information	24	ss = 16/DemT=60
Animal Fluency	**Raw**	**Norm**
Total Score	14	z = -1

Visuospatial Functions

WAIS PRI	Raw	Norm
Visual Puzzles	7	ss= 6/DemT = 25
Block Design	20	ss = 5/DemT = 21
Benton Tests	**Raw**	**Norm**
Line Orientation	24 (25 corrected)	56th%ile
Facial Recognition	43 (44 corrected)	41st%ile

Learning & Memory

CVLT-II	Raw	Norm
Total Learning	31	T = 39
Trial 5	7	z = -1.5
Short Delay Free/Cued Recall	5/5	z = -1/z = -2
Long Delay Free/ Cued Recall	7/8	z = -.5/z = -.5
Recognition	15	z = .5
WMS Logical Memory	**Raw**	**Norm**
Immediate Recall	19	ss =7/DemT= 35
Delayed Recall	14	ss = 7/DemT=37
Recognition	24	26-50%ile

Learning & Memory

BVMT	Raw	Norm
Total	30	z = .2
Trial 3	10	z = .6
Delay	9	z = .3
Recognition Hits	6	z = -.3
False Positives	0	z = 0

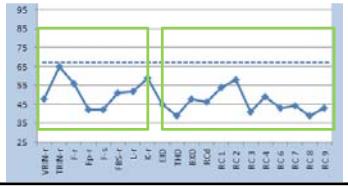
Effort

CVLT	Raw	Norm
Forced Choice	16/16	wnl
Digit Span	**Raw**	**Norm**
Reliable Digits	10	wnl

Self Report of Mood &Psychological Functioning

BDI	Raw	Norm
Total Score	8	normal
BAI	**Raw**	**Norm**
Total Score	10	mild

MMPI



Report of Executive Control & Frontal Systems

BRIEF- Self Report	Raw	Norm
All Scales	--	wnl
FRSBE- Self Report	**Raw**	**Norm**
All Scales	--	wnl

FRSBE- Self Report	Raw	Norm
Post Injury Executive Dysfunction	Before- 31/After- 51	T = 85
Post-Injury Total	Before- 76/After- 103	T = 73

Summary

- Cognitive decline
- Marked deceases in processing speed and perceptual skills; relative preservation of verbal skills
- Additional weaknesses in attention, cognitive flexibility, judgment, abstract reasoning, motor speed, and visuospatial construction
- Some problems with encoding of verbal information; nonverbal memory was intact

Summary Continued

- Reported symptoms of depression, anxiety, and frustration during the clinical interview
- Denied affective distress on objective measures
- Denied problems with executive control and frontal systems changes
- Wife reported executive dysfunction and overall changes in frontal systems
- May suggest problems with insight

Summary Continued

- Well-educated, high professional achievement
- Obvious decline from baseline, across domains; generally slowing; motor disturbance
- Consistent with other severe cases *(Wilson, 1912; Rosseli et al., 1987; & Riley et al., 2001)*
- "Subcortical" dysfunction *(Wenisch et al., 2013)*
- Personality changes *(Akil et al., 1990)*
- Dx: Major Neurocognitive Disorder due to Wilson's Disease

Summary Continued

- Motor disturbance
- Event when he "passed out" and episodes of "disorientation"

Formulation

- Cognitive, psychological, and motor effects that are unfortunately interfering with his daily life and typical level of functioning
- Meets criteria for Major Neurocognitive Disorder due to Wilson's disease

Recommendations

1) Continue treatment plan (medication management, physical therapy, etc.)
2) Monitor mood; individual, group, and/or family therapy
3) EEG study may be warranted, given increased incidence of epilepsy Medical leave of absence, but stay active
4) Repeat NP testing

Discharging Neuropsychological Responsibilities: Consideration of Epileptiform Abnormalities on Neuropsychological Findings

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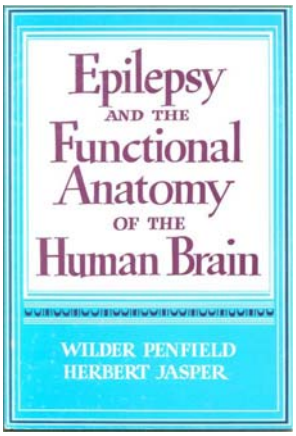
Emory University School of Medicine

National Academy of Neuropsychology
November 6, 2015

Preoperative Neuropsychological Evaluation

- Identify area of focal dysfunction associated with seizure focus
- Minimize/predict post-operative cognitive morbidity
- Characterize cognitive morbidity of different interventions or tissue resected



Epilepsy Surgery Candidate

- Right-handed male in late 20s; no history of familial sinistrality
- Epilepsy duration of approximately 2 years
- No established epilepsy risk factors; no family history of seizures
- Complex partial seizures – brief lapses of responsiveness, difficulty speaking, difficulty comprehending
- Seizure frequency ranged up to 20+ month, rare secondary generalization

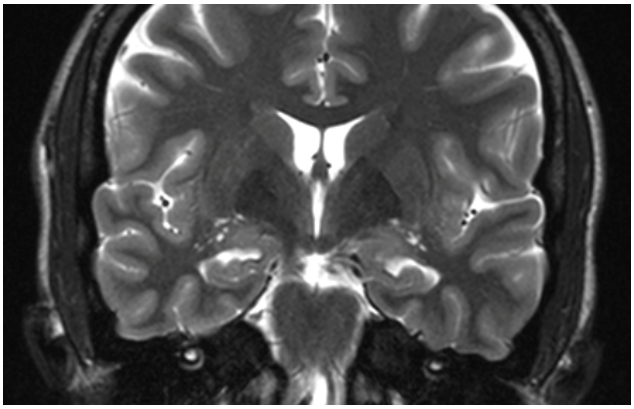
Epilepsy Surgery Candidate

- College education and employed
- History of depression
- History of alcohol and substance abuse predating seizure onset
- Anger management
- Anti-epilepsy drugs (AEDs): levetiracetam (4000 mg) and oxcarbazepine (600 mg)

Epilepsy Surgery Workup

- Interictal EEGs
  - occasional left temporal sharp waves (F_7, T_3)
- EMU admission
  - 3 seizures recorded; 2 with expressive speech difficulty, 1 with receptive speech difficulty
  - rhythmic theta from left anterior temporal lobe evolving into electrographic seizure

MRI



Verbal Memory

- Rey AVLT
  - Total=40/75, 1st percentile
  - Immediate=6/75, 1st percentile
  - Delay=0/15, <1st percentile
  - Recognition=9/15, 4 FPs, < 1st percentile
- Verbal Paired Associates
  - Immediate=20, 30th percentile
  - Delay=8, 70th percentile

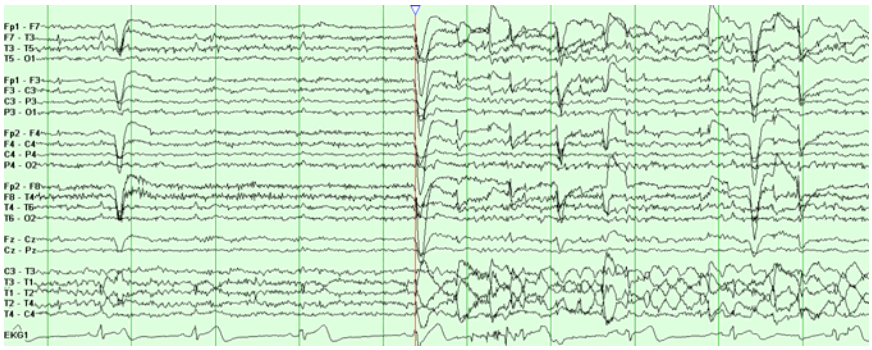
Visual Memory

- Visual Reproduction
  - Immediate=13, 95th percentile
  - Delay=2, 1st percentile
  - Recognition=3/4, low average
- Complex Figure (Copy =36/36)
  - Immediate=20.5, 21st percentile
  - Delay=16.5, 4th percentile

Neuropsychological Test Results

- FSIQ=110 (VCI=114; PRI=105, WMI=122)
- Boston Naming=56/60, wnl
- Oral WMT=87.5, 82.5, 87.5
  - Average of 3 genuine memory trials 50%
  - GMIP Profile
  - Delayed Recall only 20%

1/5



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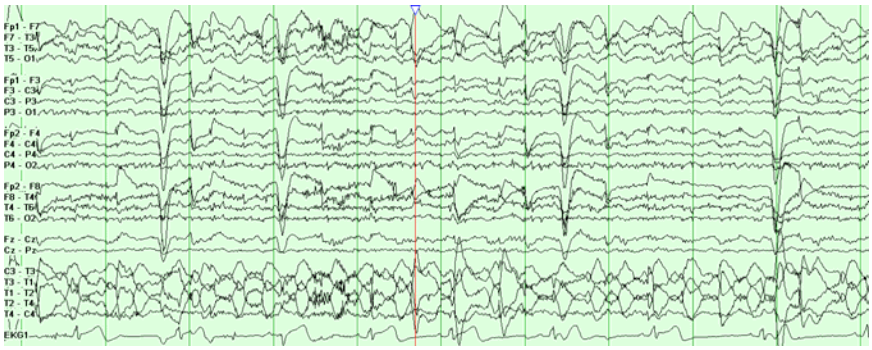
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T5 - O1
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
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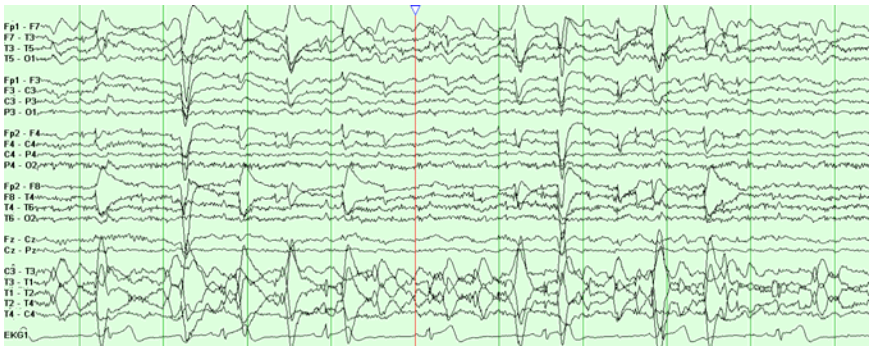
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
Fz - Cz
Cz - Pz
C3 - T3
T3 - T1
T1 - T2
T2 - T4
T4 - C4
EKG1

3/5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C4 - P4
P4 - O2
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
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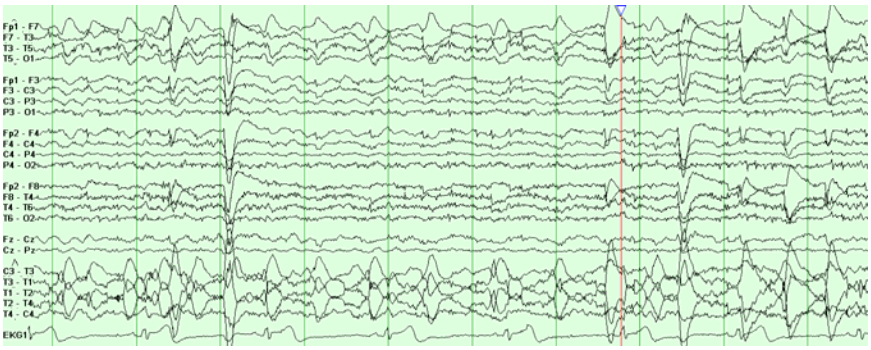
T4 - C4
EKG1

4/5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Fp2 - F8
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T4 - T6
T6 - O2
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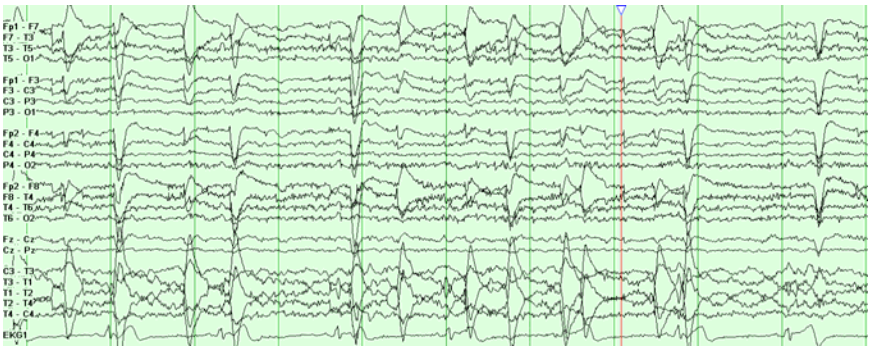
T4 - C4
EKG1

5/5


Fp1 - F7
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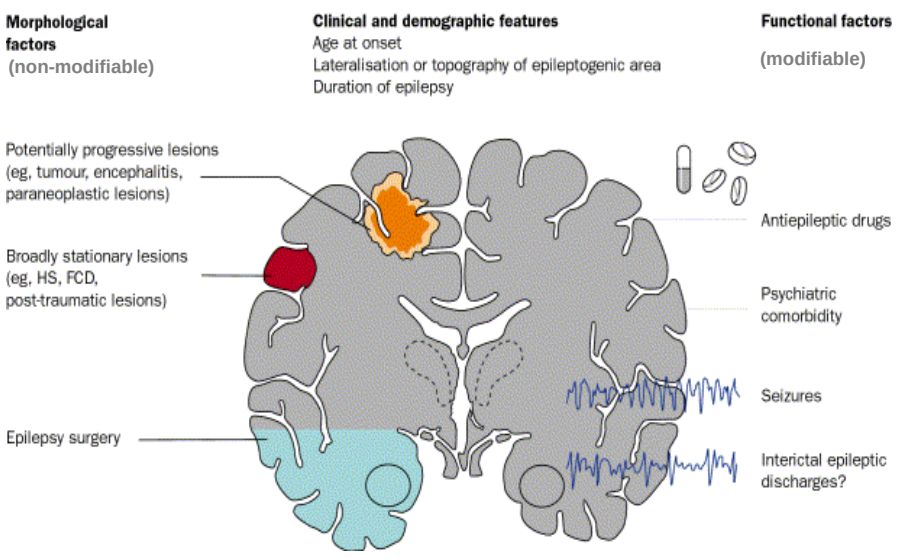
F4 - C4
C4 - P4
P4 - O2
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
Fz - Cz
Cz - Pz
C3 - T3
T3 - T1
T1 - T2
T2 - T4
T4 - C4
EKG1

Neuropsych Results

Test	Results	EEG Comment
IQ	FSIQ=110 (VCI=114 PRI=105, WMI=122)	Variable EEG discharges throughout
PVT	Failed 1/3 oral WMT; GMIP	Epileptiform activity present prior to test administration
Boston Naming	56/60; WNL	Assessed in PM; 2 hours after EEG abnormalities ceased
AVLT	40/75, 1st percentile Delay=0/15, Recognition=9/15	EEG present prior to and during testing
Verbal Pairs	Imm=30th percentile Delay=70th percentile	Completed in PM; no discharges
Visual Reproduction	Imm=95th percentile Delay=1st percentile	Completed in AM; shortly after EEG discharges
Complex Figure	Imm=95th percentile Delay=4th percentile	Completed in PM; no discharges



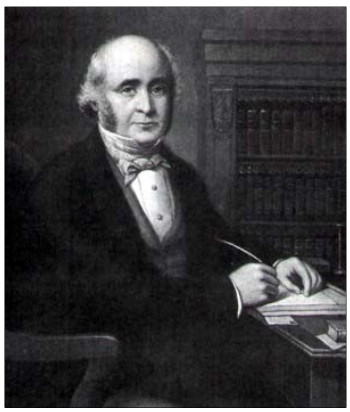
Elger et al. Lancet Neurology 2004;3:663-672.

Seizures / EEG Abnormalities

- Long-term
- Postictal
- Interictal dc's
  - transient cognitive impairment

Dali (1916)

Robert Bentley Todd (1809-1860)



- Professor of Anatomy and Physiology at King's College
- Introduced "afferent" and "efferent"
- Localized major lesion of tabes dorsalis
- Wine and brandy copiously prescribed for fevers

Todd's Paralysis

- Post-ictal focal neurologic deficit/weakness
- Neuronal "exhaustion" from seizure
- Resolves within minutes or hours

Postictal Language Assessment

- Inability to accurately read aloud "They heard him speak on the radio last night" within 60 sec after sz end
- Not associated with Frontal onset unless spread to TL
- Paraphasic errors

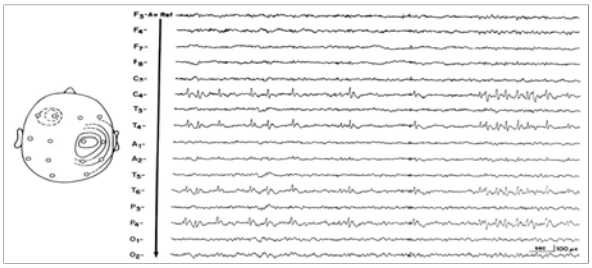
Postictal vs Non-ictal Memory

(z scores)

Pt	TLE	Verbal	VS	Laterality
1	R	+0.4	-2.1	+2.5
2	R	-0.9	-1.1	+0.2
3	R	-0.9	-1.8	+0.9
4	R	-2.9	-2.9	+0.0
5	L	-2.6	-1.5	-1.1
6	L	-2.4	-2.1	-0.3
7	L	-0.7	-0.4	-0.3
8	L	-2.6	+0.2	-2.7

Andrewes et al., *Neuropsychologia* 1990;28:957-967

Transient Cognitive Impairment (TCI)



Frederic A. Gibbs (1903-1992)

- Relationship of interictal EEG discharges to cognition (*masked* or *larval* epilepsy)

Subclinical Discharges and Driving

- 6 pts, frequent DCs; 4 sz free 4+ years
- Lateral position effects in 3 and trend in 1
- Mean speed, speed SD impaired in 3 (p=.10)

- Discharge frequency decreased while driving compared to sitting in parking lot
- Temporary increase while waiting at red light

Kasteleijn-Nolst Trenite (1987, 2005).

Material Specificity

- Material Specific Videogame Memory Tasks
  - Corsi Block Tapping Type Task
  - Word Sequencing
- Adaptive level of difficulty
- 11/22 with focal/asymmetric generalized discharges with TCI
- 13/24 with symmetric generalized discharges with TCI

Aarts et al. *Brain* 1984, **107**(1):293-308.

Focal Nature of Impairment

Activity	Corsi Task	Verbal Task
Right sided	4/5	1/5
Symmetrical	12/16	4/16
Left sided	3/12	9/12

Error rates higher when DCs occurred during stimulus compared to DCs during response (no DC effect)

Aarts et a. *Brain* 1984, **107**(1):293-308.

Interictal EEG and short non-convulsive seizures

- Short non-convulsive seizures effects ranged from 0.5 to 1.0 SD (8/12 tests)
  - IQ, information processing, memory
- Interictal EEG abnormalities more subtle (3/12 tests)
  - Reading, Arithmetic, memory
- EEG abnormalities >1% worse on 6/12 tests; no effect for >1% but < 10%

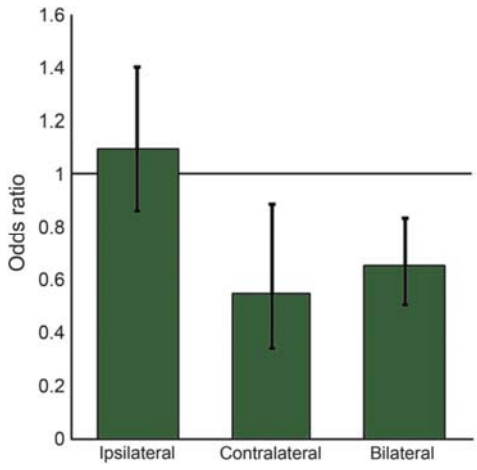
Nicolai et al. *Epilepsia* 2012, **53**(6):1051-1059.

Hippocampal EEG abnormalities

- 10 patients with depth electrodes
- Sternberg memory task – not "memory" in usual sense
- Hippocampal discharges disrupted maintenance and retrieval, not encoding

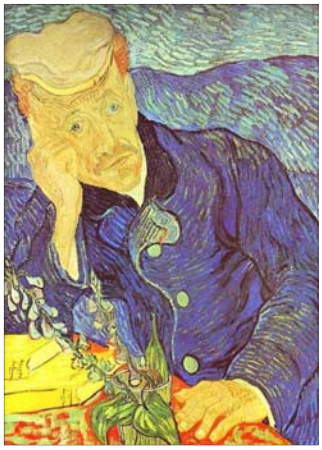
Kleen et al *Neurology* 2013, **81**(1):18-24.

Interictal Epileptiform Discharges During Sternberg Task Retrieval



Kleen et al *Neurology* 2013, **81**(1):18-24.

Problems for Epilepsy Surgery Neuropsychological Evaluations



Van Gogh (1890)

- Discharging focus resection may mitigate assessed surgical cognitive morbidity
- "False" baseline → may mask genuine decline or suggest improvement