Disruptive Mood Dysregulation Disorder (DMDD) Developing Treatment Strategies

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Medication Usage Disclaimer

- The following 2 medications that will be discussed in this presentation are being used off-label:

- 1) oxcarbazepine

- 2) amantadine HCl

OUTLINE

- 1) Disruptive Mood Dysregulation Disorder (DMDD): What is it?
- 2) How does DMDD compare to Bipolar Disorder or to Severe Mood Dysregulation?
- 3) What are the criteria; how common is it? What comorbid conditions are there?
- 4) What is known about the neuropathology?
- 5) What about treatment: Any research?
- 6) What about crisis management?

DMDD: What is it?
(McGough, 2014)

- A new diagnosis for DSM-5 (2013) for children with severe and chronic irritability with explosive temper outbursts.
- *AREN'T ALL CHILDREN IRRITABLE AT TIMES? Yes but DMDD refers to:*
  - Temper outbursts - at least three times a week
  - Irritable/angry moods almost daily for a year
  - Onset at least age 6 but before age 10; may continue as adult, if had childhood onset
  - With trouble functioning in multiple settings

DMDD: New DSM-5 Diagnosis
(Axelson et al., 2012)

- Designed to replace “broad spectrum” Bipolar Disorder in children and adolescence.
  - In DSM IV, mania describes discrete episodes of irritated moods (episodic irritability).
  - In DSM 5, DMDD describes non-episodic (chronic) irritability with frequent temper outbursts.
  - DMDD has very little research base, but it is very similar to the concept of Severe Mood Dysregulation (without hyper-arousal).

Epidemic of Bipolar Disorder (BD)?
(Leibenluft, 2011)

- Between 1994 and 2003 there was a 40 fold increase in the diagnosis of BD in children and adolescents. (Moreno,C. et al., 2007)
  - Psychiatrists had broadened the phenotype for pediatric bipolar, to include chronic irritability as a subtype of Bipolar Disorder.
- But, research does not support this change from narrow (episodic) to broad (chronic) phenotype.
  - Non-episodic irritability is unique; not a subtype of Bipolar Disorder (Geller et al. , 2008)

DSM-5 & Pediatric Neuropsychiatry
(Fisher et al., 2013; Schieveld et al., 2013)

- The vast majority of the children being diagnosed with Bipolar Disorder were not classic, or narrow phenotype, Bipolar Disorder.
  - They show non-episodic (chronic) irritability, rather than classic (episodic) irritability.
- Non-episodic (or chronic) irritability appears to be a distinct condition, separate from Bipolar.
  - This is the basis for Disruptive Mood Dysregulation Disorder (DMDD) in DSM-5.

DMDD versus Bipolar Disorder

- How does DMDD differ from Bipolar?

  – Non-episodic irritability (chronic)

  Bipolar Disorder has episodes of irritability with mania

  – No euphoria or grandiosity

  Bipolar Disorder may show this during mania

  – No psychosis

  Bipolar Disorder may show this

Abnormal Irritability
(Leibenluft, 2011)

- **Abnormal Irritability**:
- Is an impairing, and long-lasting mood disorder with temper outbursts:
- *"Temper outbursts that are developmentally inappropriate, frequent, and extreme with anger or sadness between outbursts."*
- may occur in association with mental illness*:*
- *Depression, Anxiety, Post-Traumatic Stress Disorder, Attention Deficit Hyperactivity Disorder, Bipolar Disorder, Autistic Spectrum*

DMDD Research

- Epidemiologic studies:
  - Copeland et al. (2013) showed: that
  - Non-episodic (chronic) irritability with rage outbursts (meeting DMDD criteria; age 6-10) are reported in only 3% of children.
  - This population shows many co-occurring conditions, particularly depressive disorders, with higher rates of social and behavioral difficulties, poverty, use of mental health services, and school problems.
  - Dougherty et al. (2014) found an 8.2% prevalence for DMDD in 6-year-old children.

Retrospective Study of DMDD
(Copeland et al., 2013)

- Used data from existing studies of school age children with mental illness to evaluate DMDD
  - About 50% had temper outbursts, but only 6-7% of these averaged 3 or more per week.
  - 8-13% showed negative moods (sad or irritable) but only 1.5%-2.8% had chronic irritability.
  - Cumulative prevalence after 4 separate assessments was 4.4% (Close to 1 child in 20 of this sample)
  - High rates of other co-existing psychiatric disorders.
  - High rates of impairment (family, school, social)
  - High rates of mental health service utilization

Disruptive Mood Dysregulation Disorder (DMDD) DSM-5 (Zepf & Holtmann, 2012)

A. Temper Outburst

- Severe recurrent temper outbursts to common stressors
- Beyond provocation
- Not consistent with age (developmental age 6+)
- Onset before age 10
- Never elevated mood or grandiosity

B. Frequency

- Temper outbursts occur, on average, three or more times per week
- Between outbursts:
  - Mood chronically negative
  - Irritable, angry
  - Observed by others such as parents, teachers
  - For at least a year
  - In at least two settings
    - Home, school, peers

Underlying Neuropathology DMDD versus Bipolar Disorder

- Ryan, N.D. (2013) reported:
  - DMDD exhibited markedly **decreased** activation of **paralimbic** system (cingulate gyrus, striatal, thalamic, parietal, and parahippocampal regions) after negative feedback (frustrating) trials (not in Bipolar).
- Deveney et al. (2013) reported:
  - In DMDD, the **frontal lobe** tends to show **underactivity** in comparison to Bipolar Disorder which shows over activity.

Underlying Brain Disorders

Cause of DMDD is Unknown:

Possible genetic disorder?

Chen, T., Blum, K, Matthews, D., Fisher, L., et al. (2007).

Premature birth with hypoxia, drugs/alcohol in pregnancy, difficult birth, malnutrition, abuse?

- (Fisher, L., Matthews, D., & Matthews, G. (2013). Two Juvenile Cases of Disruptive Mood Dysregulation Disorder (DSM-5). Poster at *Texas Psychological Association*, November, Houston, TX)

Biological Markers for DMDD?

(Kowatch et al. , 2009)

- BD rates do not vary by gender, but chronic irritability kids are mostly male (66-77%) (suggesting a distinct gender-based disorder).

- Parents of Bipolar kids are more likely (33%) to have BD themselves than parents of DMDD kids (2.7%), (suggesting a distinct genetic pattern).

- Gene mapping may be a way to find biological markers for DMDD.

5) TREATMENT FOR DMDD?

- No treatment strategies have been established:
  - Deveney et al. (2013)
- But, Bipolar medications may NOT be needed.
  - Matthews, D., Fisher, L. & Matthews, G. (2012)
- The selection of medications for the management of maladaptive aggression in youth is a major clinical challenge in pediatric mental health
  - Kowatch et al., (2009); Fisher, Matthews & Matthews. (2013); Fisher, W., Johnson, A., Fisher, L., Sharma, S., & Ceballos, N., (2013)

TREATMENT OPTIONS?

Most experts suggest medication, parent training and psychotherapy.

- Alderman (2003)

Psychosocial interventions have low risk, but it may require a combination of medication and psychosocial interventions to manage the severity.

- Aman et al. (2014)

But, what medication protocol?

- Matthews, D., Fisher, L., & Matthews, G. (2013)

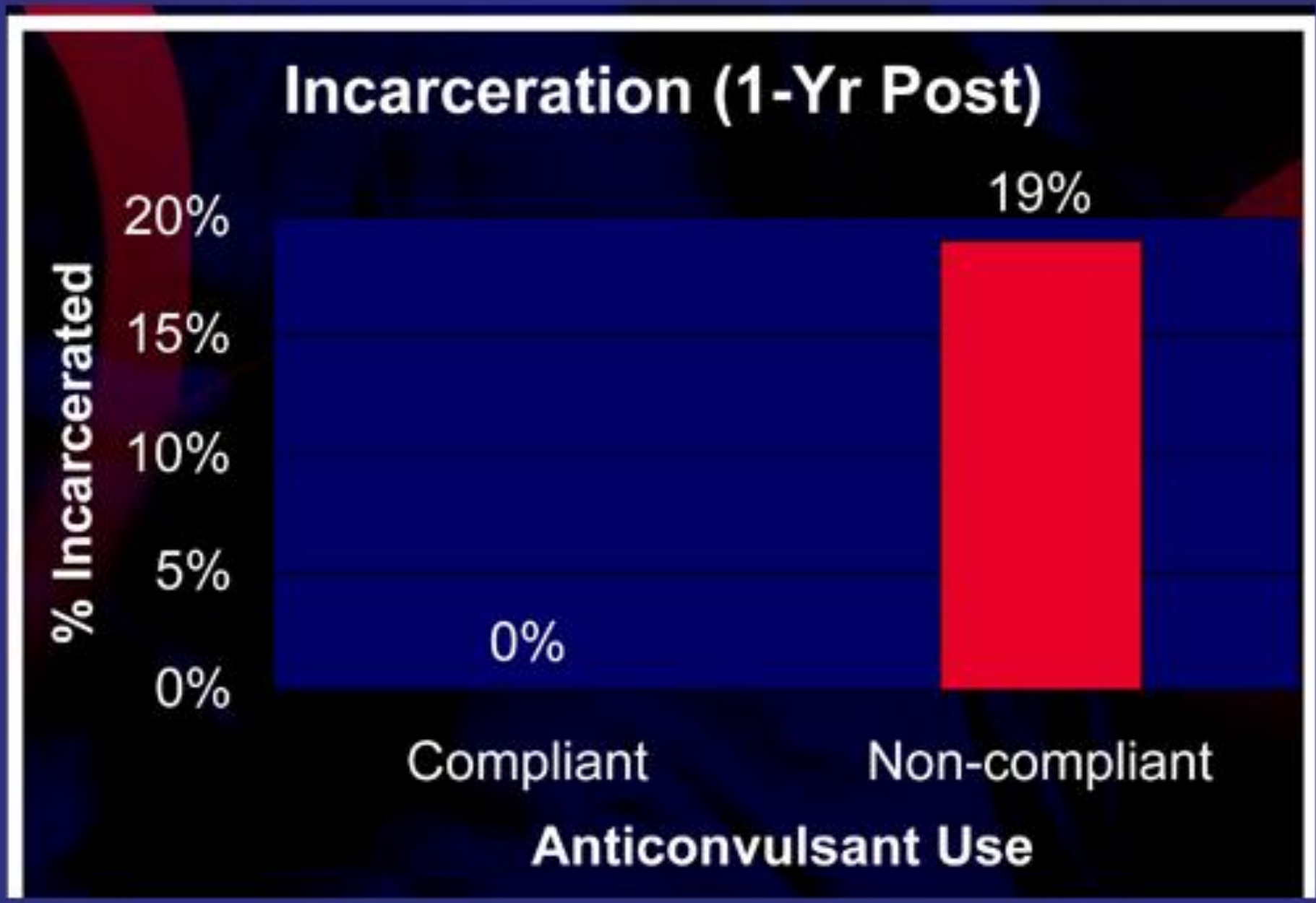
Medication Protocol: (Matthews et al., 2006; Matthews et al., 2009, Matthews et al., 2013)

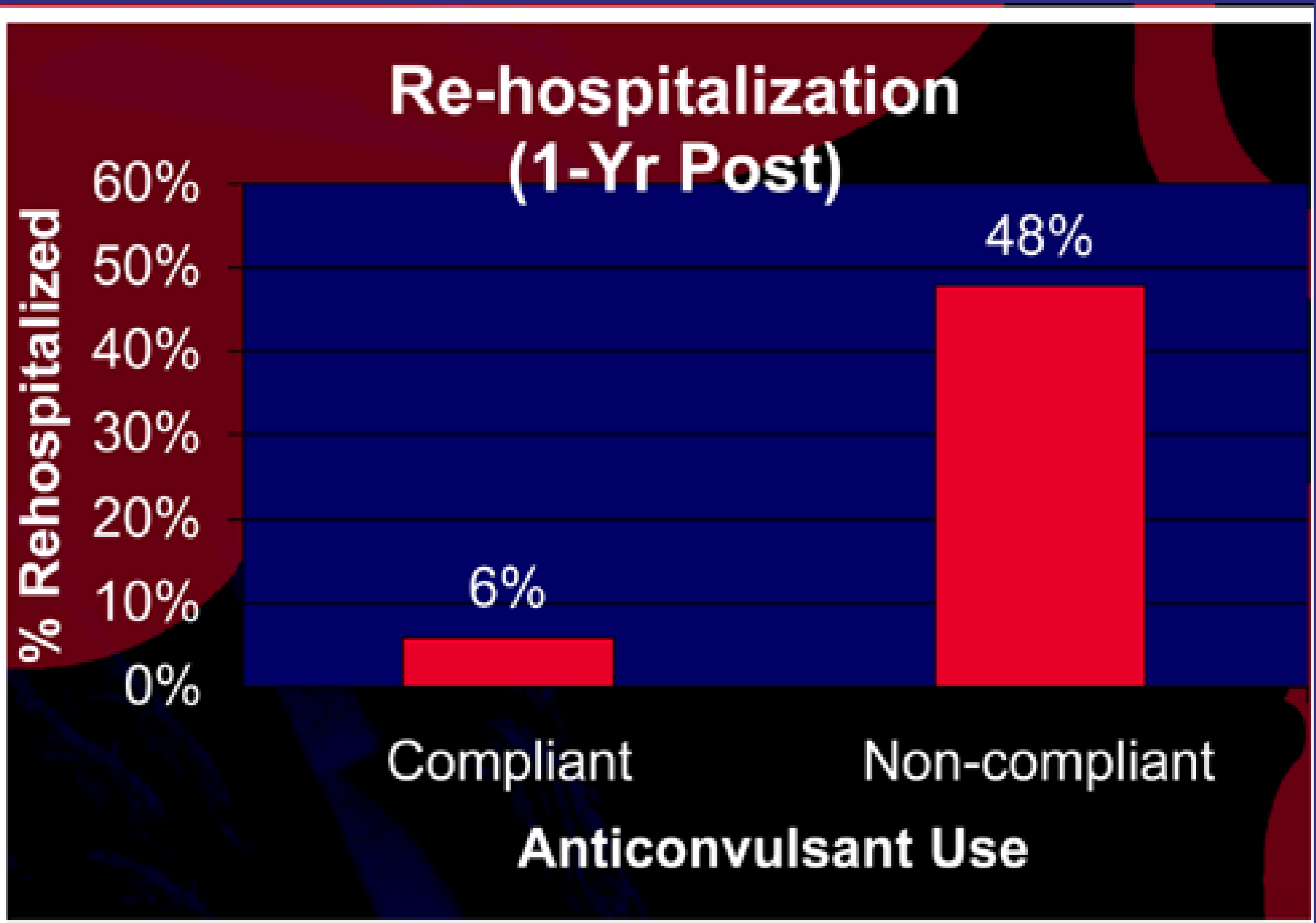
- A Neuropsychiatric approach to DMDD would suggest that medication strategies be based on brain issues.
- If it is true that DMDD represents a combination of top-down and bottom-up brain issues, then:
  - Medications should enhance frontal lobe function (top-down) to control irritability, and;
  - Medications should stabilize temporal-limbic (bottom-up) to stop explosive outbursts

Angry kid

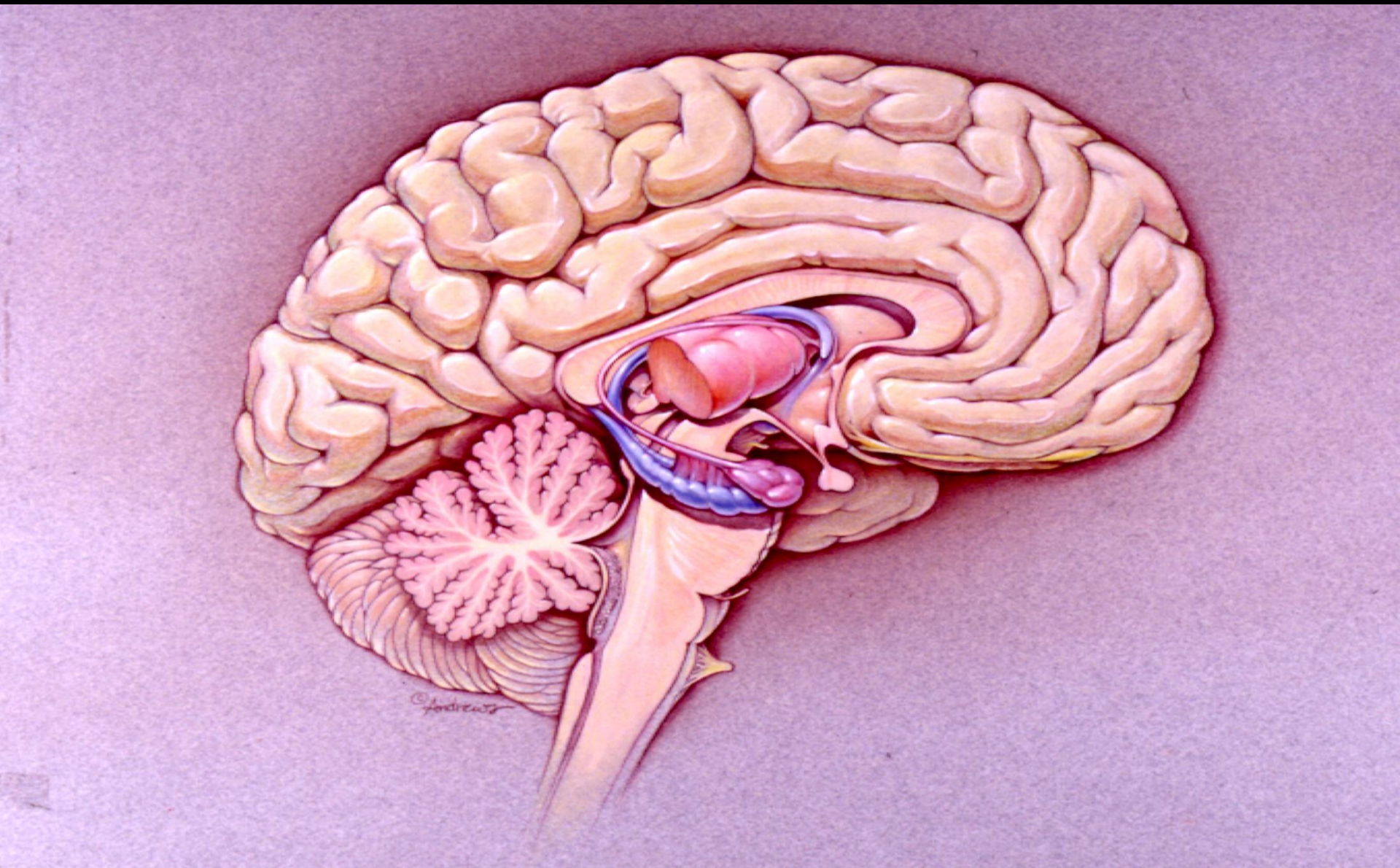
Explosive Kid

- Glassy-eyed, jaw clenched, tight muscles= RAGE

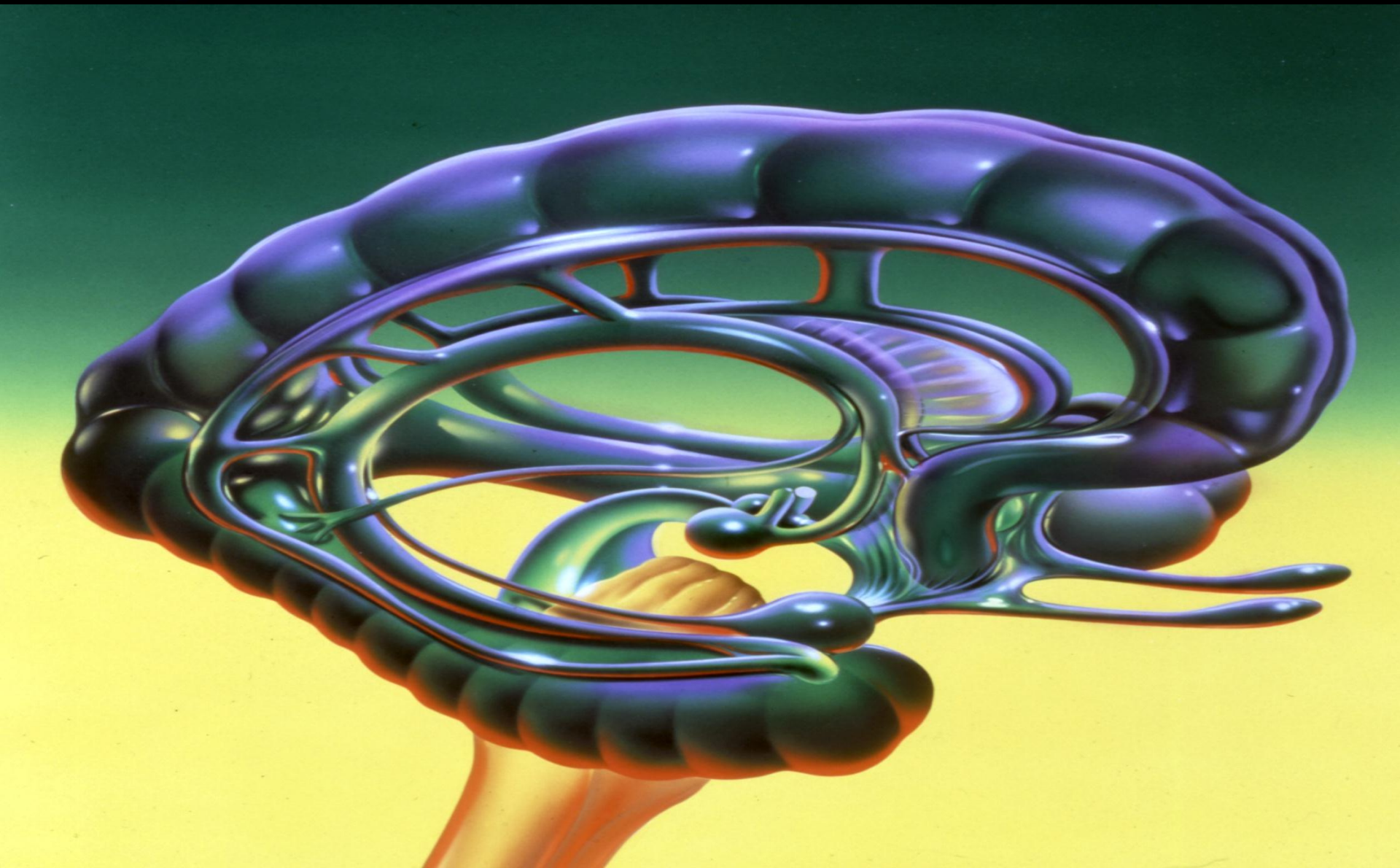

Incarceration (1-Yr Post)
% Incarcerated
20%
15%
10%
5%
0%
19%
0%
Compliant
Non-compliant
Anticonvulsant Use


Re-hospitalization
(1-Yr Post)
% Rehospitalized
60%
50%
40%
30%
20%
10%
0%
6%
48%
Compliant
Non-compliant
Anticonvulsant Use

Impulse Control & Concentration



Emotion Generation System [Limbic Brain]

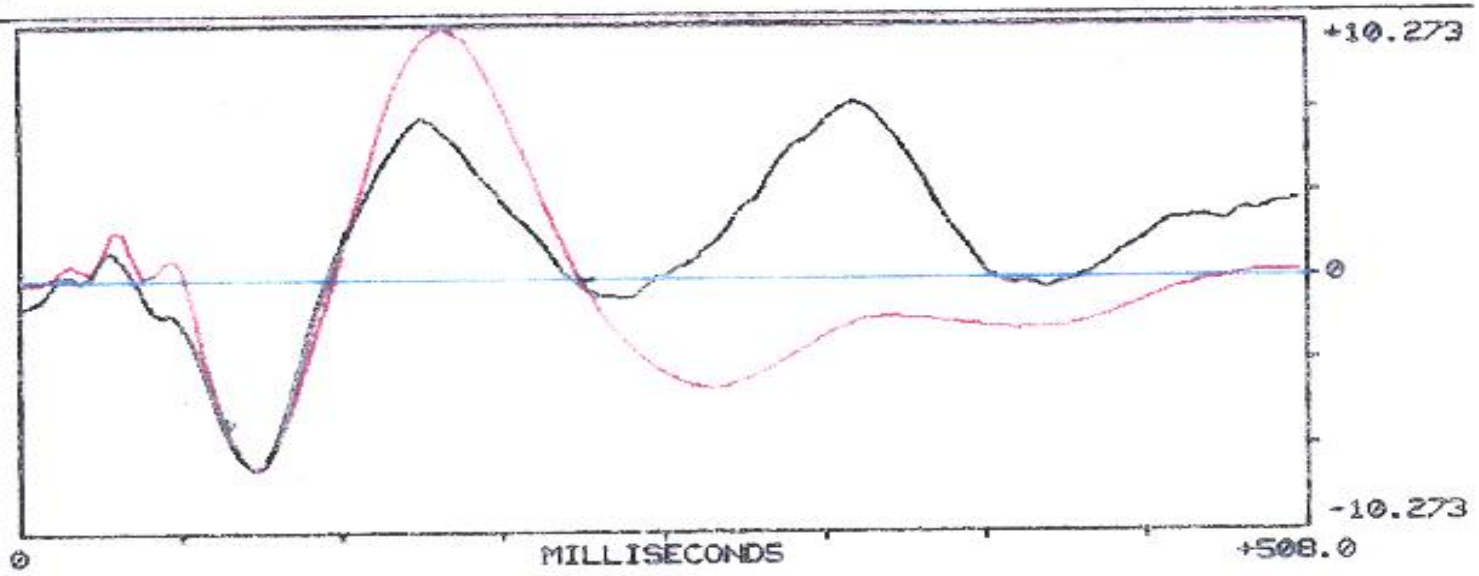


Auditory Evoked Response

Age: 15.114
Visit: 1
Tue Apr 6 1993

Reason: cerebral dysrhythmia
Sensory Deficit: reading glasses

Protocol: xbasic

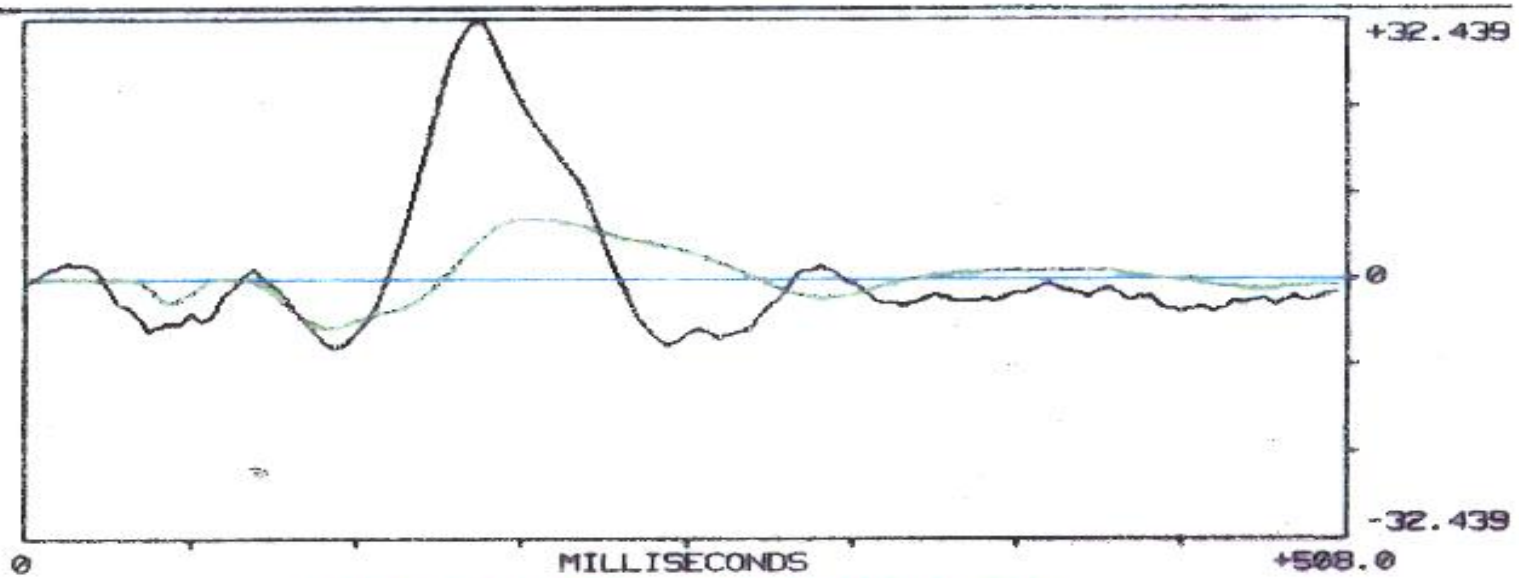


Visual Evoked Response

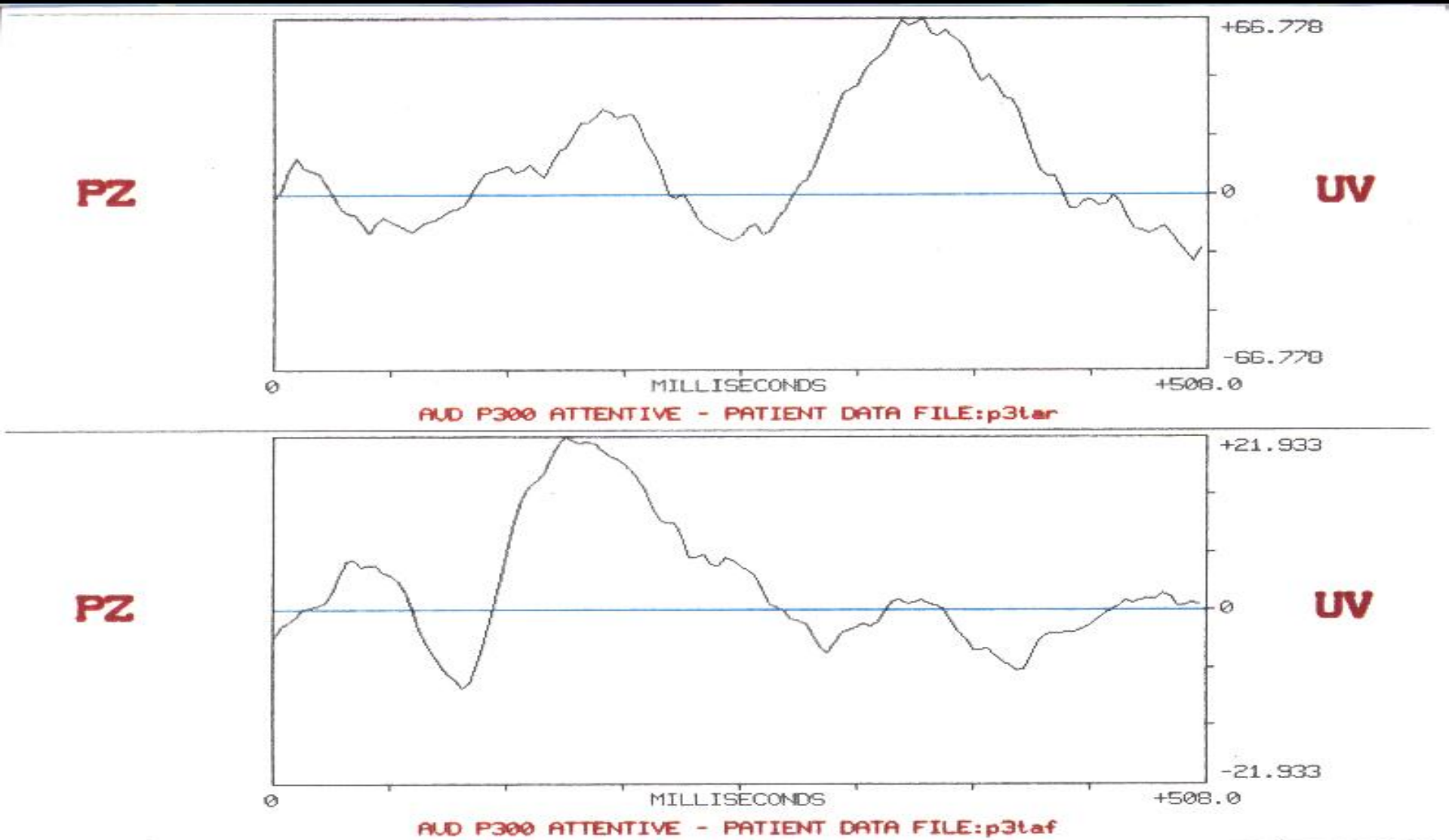
Age: 15.350
Visit: 1
Tue Apr 6 1993

Reason: cerebral dysrhythmia

Protocol: xbasic



P-300's


PZ
+66.778
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UV
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MILLISECONDS
+508.0
AUD P300 ATTENTIVE - PATIENT DATA FILE:p3tar
PZ
+21.933
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UV
-21.933
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MILLISECONDS
+508.0
AUD P300 ATTENTIVE - PATIENT DATA FILE:p3taf

Treatment Interventions

- Medications
  1) Anticonvulsants – Limbic instability
  2) Amantadine HCl or alpha-adrenergic agonists – Frontal lobe dysfunction
  3) Stimulants – attentional deficits
- Psychosocial and Psycho-educational
  1) Psychotherapy (family and individual)
  2) Specialized academic interventions
  3) Skill-based therapies

Anticonvulsants

Name
Carbamazepine (Tegretol)
Oxcarbazepine (Trileptal)
Levetiracetam (Keppra)
Valproate sodium (Depakote)
Lamotrigine (Lamictal)

Abnormal Hippocampal Attention

- Abnormal P-300 (cognitive evoked) responses indicate inadequate Hippocampal attentional function.
- P-300 responses and attentional function are normalized at appropriate dosages of neuro-stimulant medications.
- Dextroamphetamine 0.2-0.3 mg/kg/dose 3x/day.
- Methylphenidate 0.4-0.6 mg/kg/dose 3x/day.
- Stimulants can be transitioned to a long-acting formulation after the most efficacious dosage has been determined.

Abnormal Frontal Lobe Function

Symptoms are:

Chronic irritability, impulsivity, memory problems and concentration problems.

Best addressed with amantadine HCl.

Angry kid

Explosive Kid

- Glassy-eyed, jaw clenched, tight muscles= RAGE

What is Crisis Mgt. for Defensive RAGE?

- SEE RAGE? Stop VERBAL de-escalation, don't touch him/her
  - No more talk, remove others, allow rage (if safe)
- SEE RAGE FACE: Slowly, very slowly, back away
  - Even if he/she follows, threatens, curses, throws stuff
- Don't look threatening – it is a defensive "seizure"
  - Make your face, body posture - non-threatening
- Don't approach or touch – unless hold must occur,
  - but only for absolutely imminent danger

Crisis Management for Explosive Kid

- RAGE-like a seizure (time limited, OUT-OF-CONTROL)- just keep it safe, it will go away in a few minutes.
- Do not try to de-escalate rage (NO MORE TALK)
  - Do not touch or it will take an hour to stop it.
- You let it wind down on its own (like an emotional seizure). No restraint, or you will hold for an hour.
- Remove others from the room (don't move enraged kid). Defensive rage will subside on its own.

Explosive Kid: Crisis Management

- No show of force by staff (THIS WILL TRIGGER AN ATTACK)
- Back off and watch for safety (HOLDING IS A LAST RESORT)
- Rage will run out of steam on its own (IF NO THREAT)
- Afterwards, expect fatigue, poor recall (remorse?)
- No point to punishment of out-of-control RAGE
- Use this strategy, not verbal de-escalation.

SUMMARY

- DMDD is a new diagnosis in DSM-5 for 2013.
- This severe mood disorder is relatively common (DMDD at least 3%, versus 1% for BD)
- DMDD is a distinct condition, with chronic (non-episodic) irritability, that does not evolve into BD.
- No established treatment strategies for DMDD.
- DMDD might be managable with combination of :
- 1) Medication Protocol, 2) Parent Training, 3) Cognitive Behavioral Therapy, 4) Modified crisis management strategies.

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