



PWSA | USA 2023
NATIONAL CONVENTION

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The Role of Medications

For the Management of Behavioral Problems in Prader-Willi Syndrome

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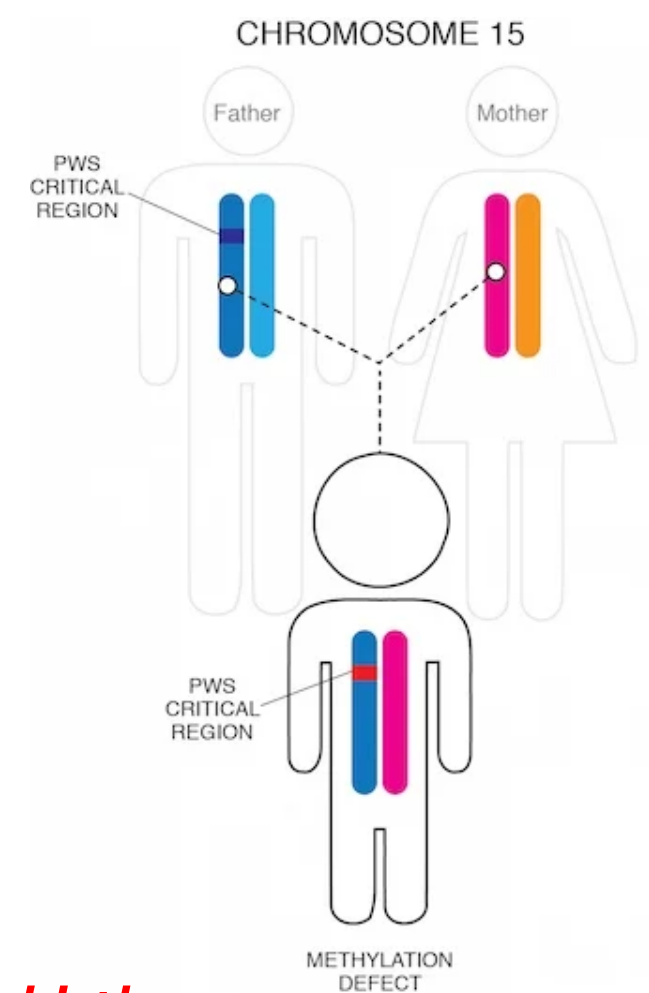
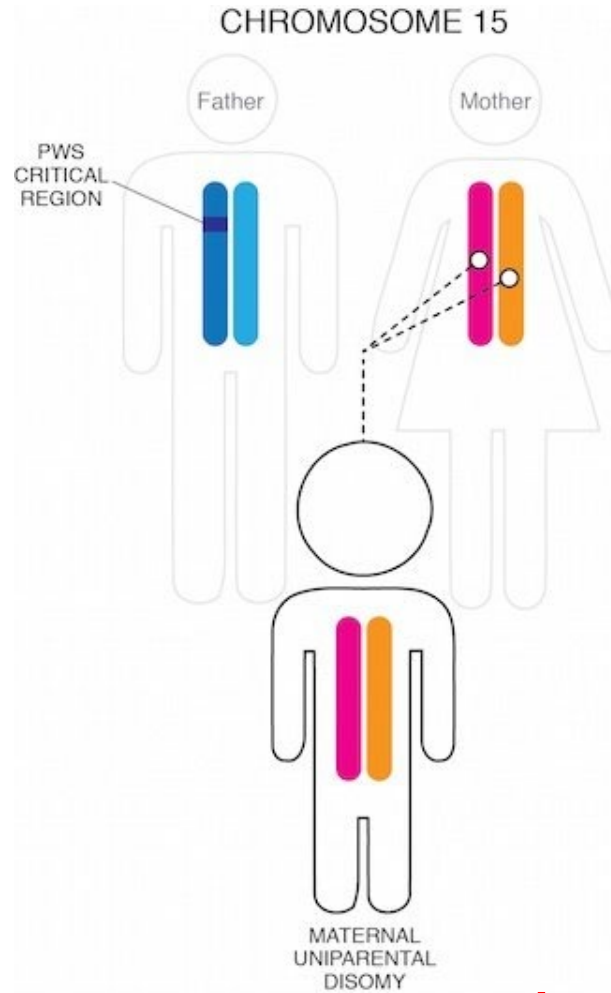
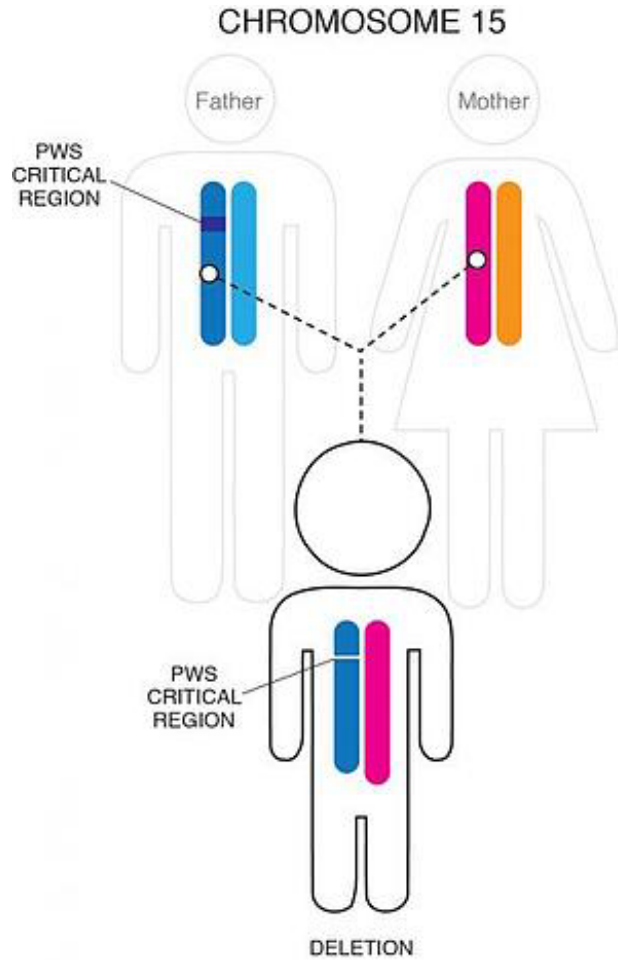
Disclosures

- **Grants:** FPWR
- **Consultation:** Soleno, Acadia, ConSynance
- Royalties: **Neurobehavioral manifestations of Prader-Willi Syndrome** (Cambridge)- images will be used in the presentation
- Non-FDA indicated use of FDA-approved medications is common in psychiatry and may be discussed in this presentation



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Genetics

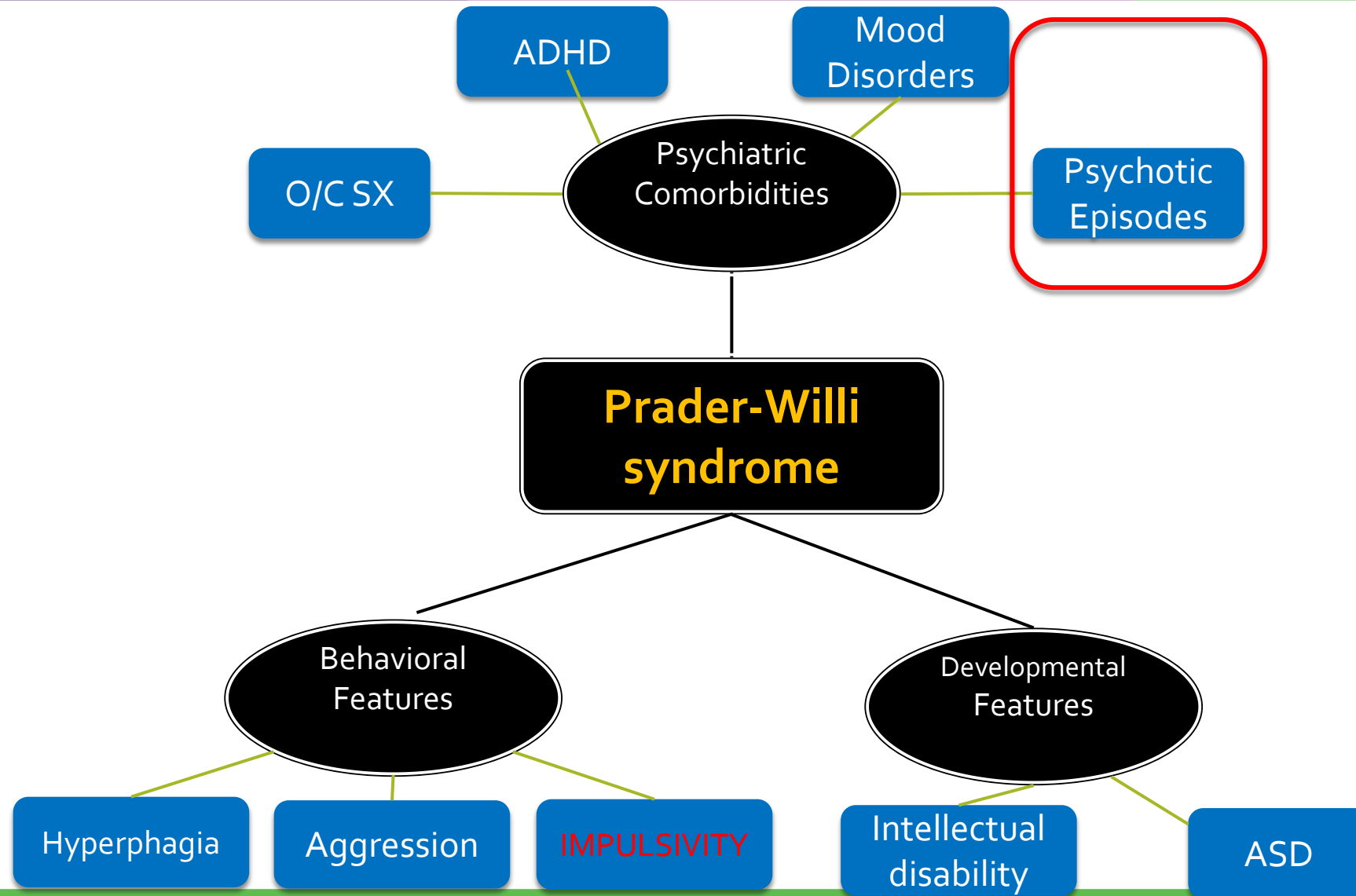


ON

Source: FPWR

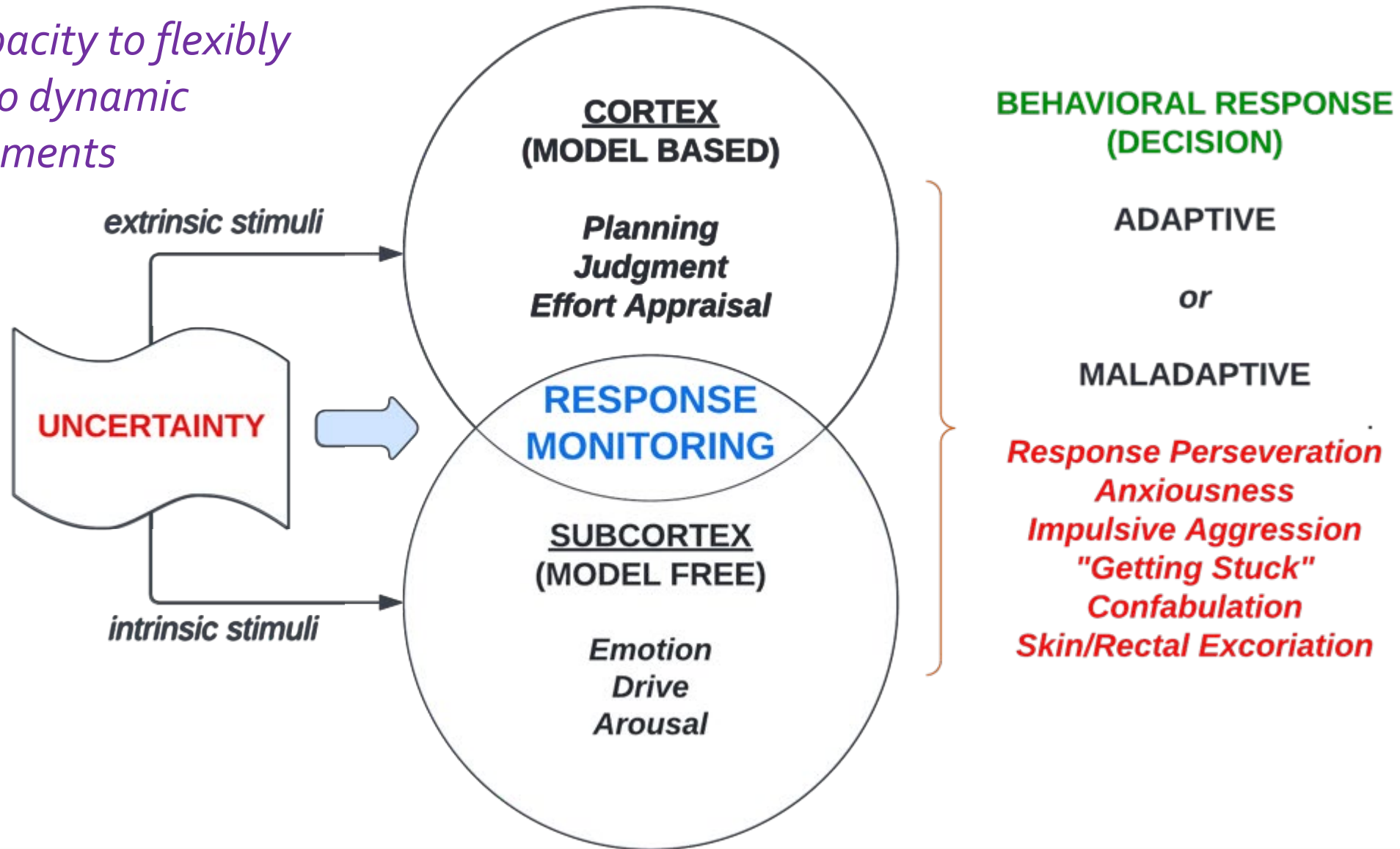
1:22000 to 25000 live births

RANGE OF SYMPTOMS



Response Monitoring:

The capacity to flexibly adapt to dynamic environments



Response Perseveration

- **RESPONSE PERSEVERATION:** the inappropriate repetition of a particular response despite the absence or cessation of reward.

- In PWS:
Related to **compulsivity**
Repetitive questioning and intrusive behavior **despite negative response by caregivers.**

Is it Anxiety?
Is it Impulsivity?
Or is it Response Perseveration?



A Dysfunction Waterfall Model of PWS

Genetics

Magel2, Necdin, IC, SNORD115, SNORD116

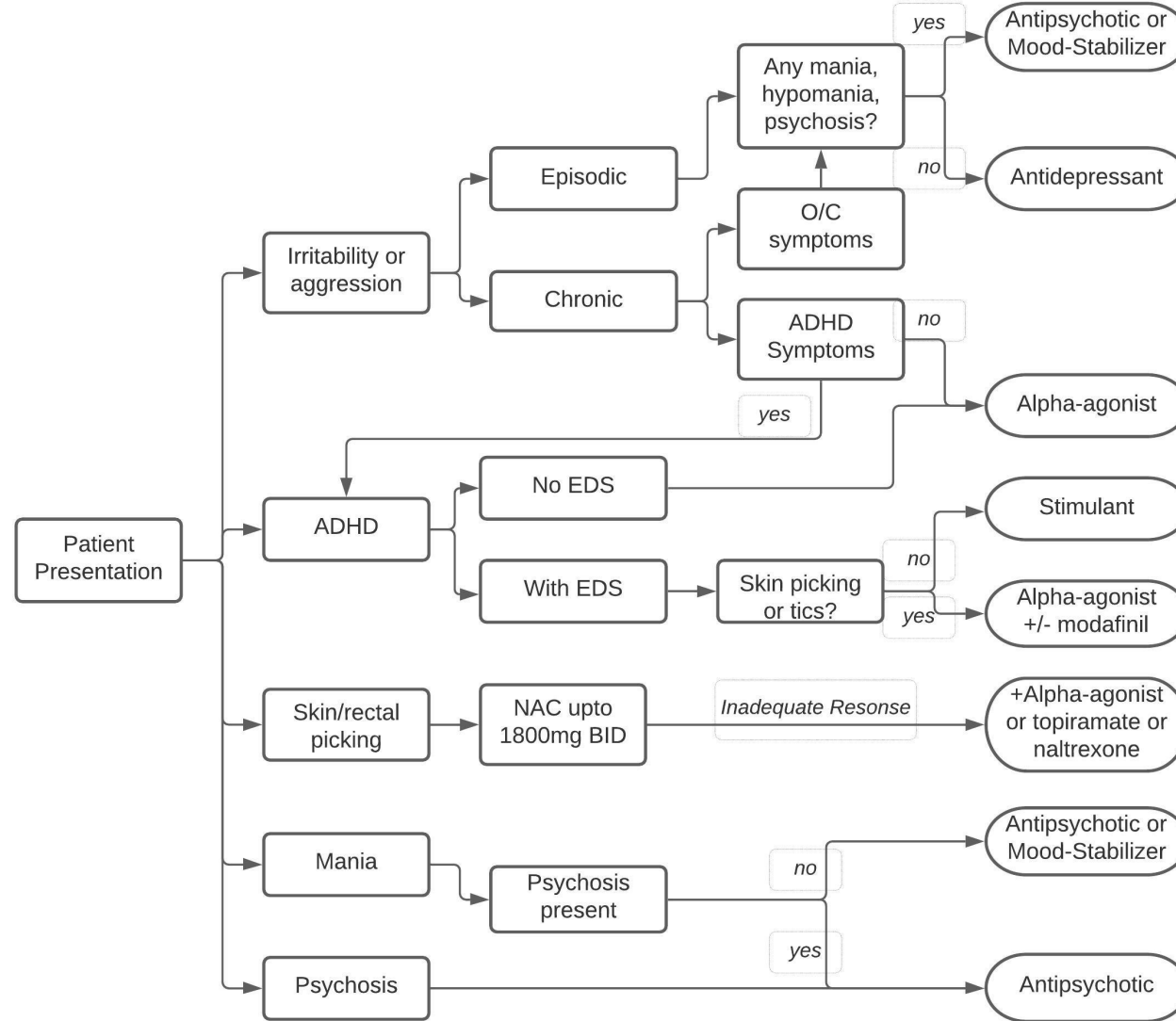
Neurobiology

*Hypothalamus, Grey & White Matter,
Neurotransmitters*

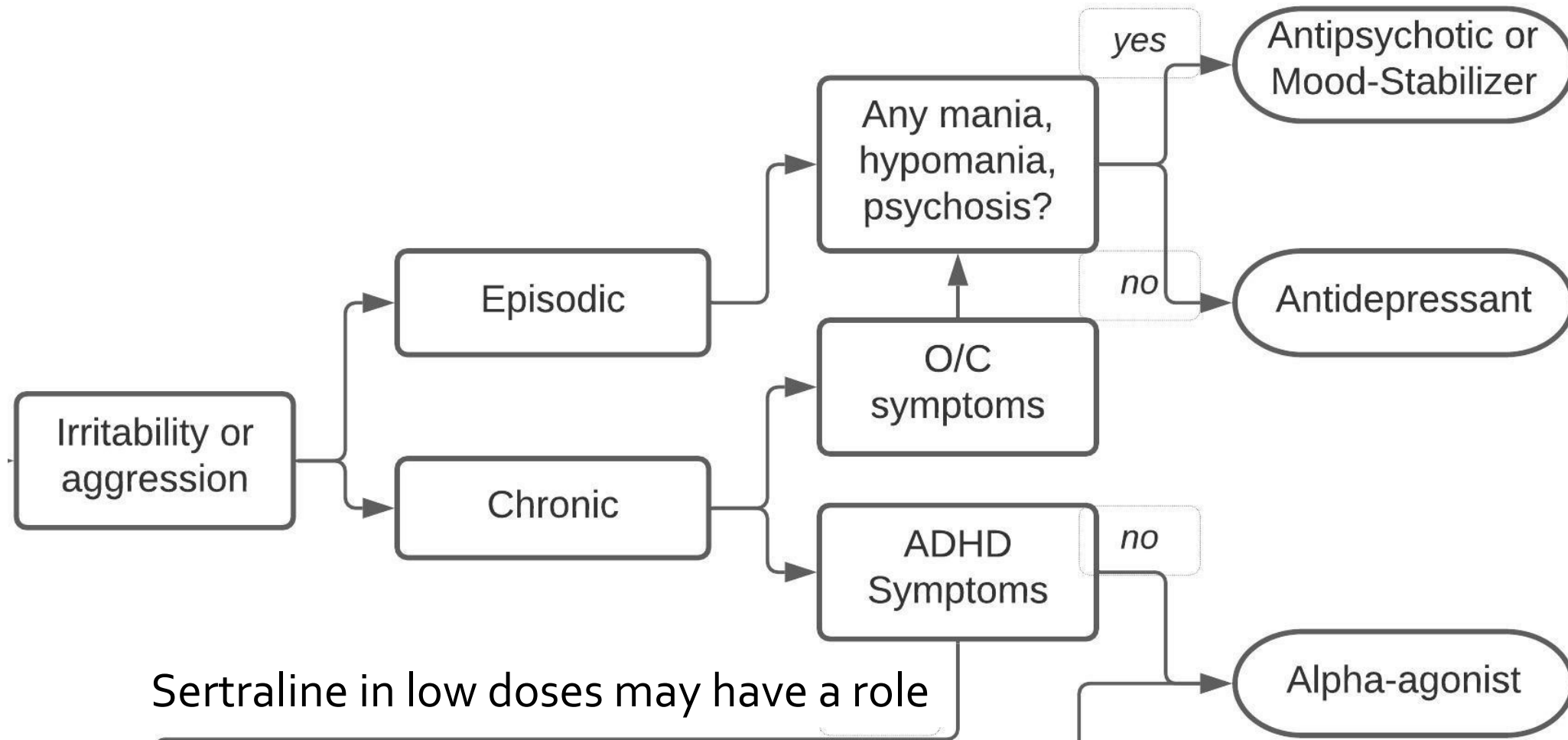
Behavioral Manifestations

Impulsivity, Response Perseveration, Cycloid Psychosis

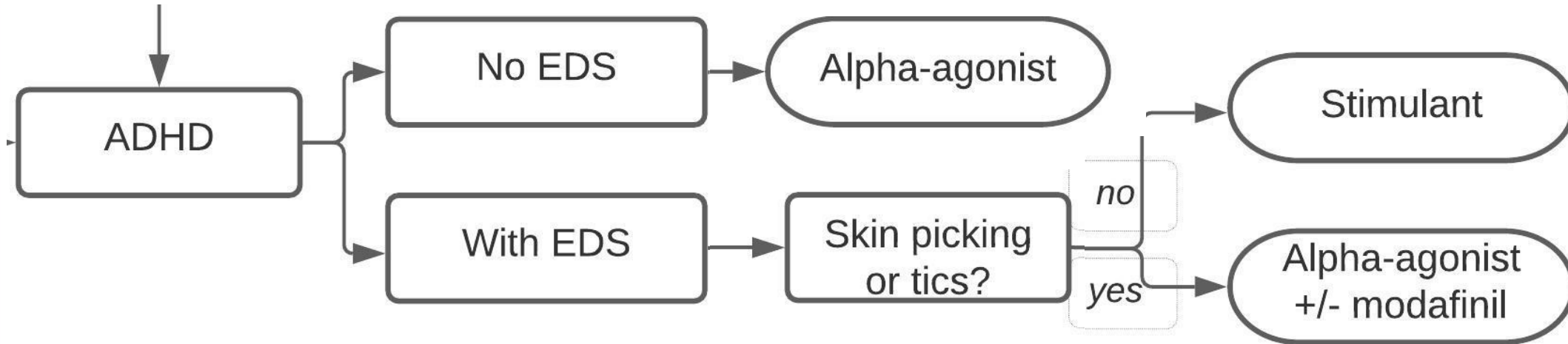
Overview



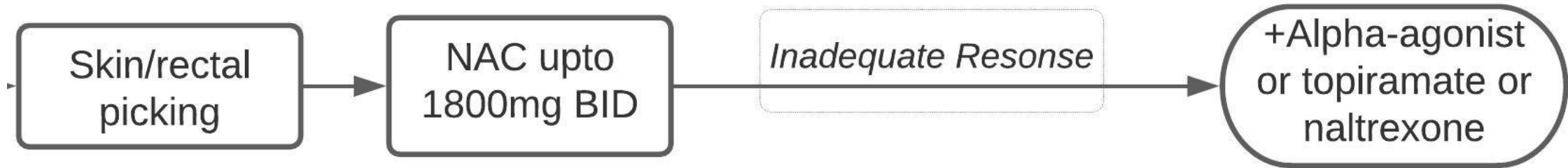
Irritability/Aggression



ADHD



Picking

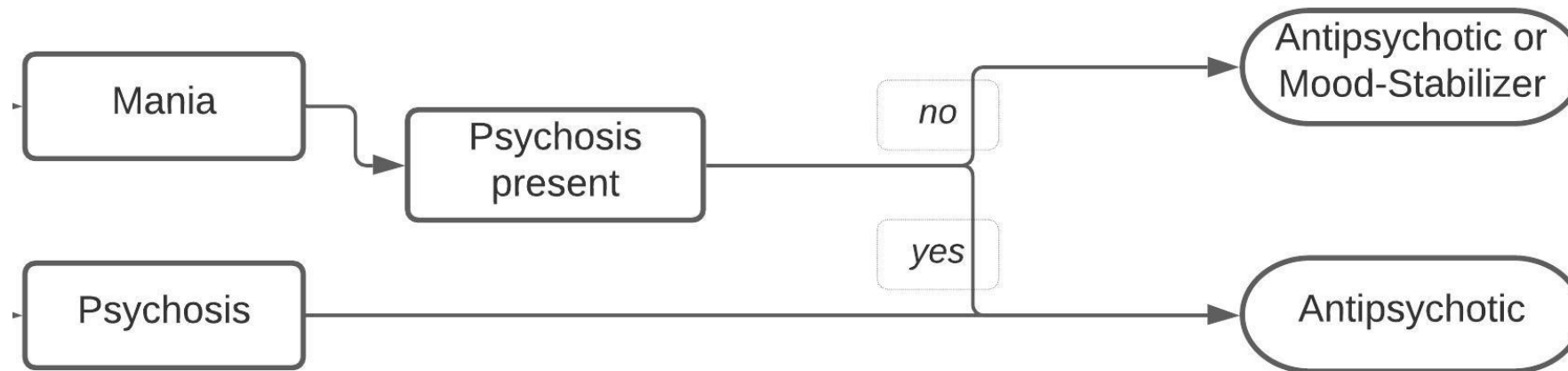


- Both Topiramate and Naltrexone have added benefit of weighloss
- Topiramate may reduce hyperphagia

Psychosis in PWS

- Not schizophrenia although in some cases might persist
- Sudden, alarming change in behavior
- Sleep disturbance, catatonic symptoms
- Confusion, voice-hearing, voice hearing, paranoia
- Rapid response to treatment

Psychosis/Mania



Seeking an Alternate Path- Guanfacine XR

- Selective $\alpha 2$ adrenoceptor agonist
- Moderates left DLPFC activation
- ADHD- FDA approval
- Reduces ADHD/impulsiveness in autism
- Most common S/E- sedation/fatigue

Guanfacine Extended Release for the Reduction of Aggression, Attention-Deficit/Hyperactivity Disorder Symptoms, and Self-Injurious Behavior in Prader-Willi Syndrome—A Retrospective Cohort Study

Deepan Singh, MD,¹ Yuji Wakimoto, BS,² Carole Filangieri, PhD,¹ Aaron Pinkhasov, MD,¹ and Moris Angulo, MD³

Abstract

Objective: To examine the role of Guanfacine Extended Release (GXR) in the management of behavioral disturbances in patients with Prader-Willi Syndrome (PWS).

Methods: Twenty from a total of 27 individuals with genetically confirmed PWS, 6–26 years of age, with the following symptoms were identified: significant aggression/agitation, skin picking, and/or symptoms of attention-deficit/hyperactivity disorder (ADHD). Response to GXR for the above noted symptoms was categorized as improved, worsened, or unchanged, while assessing for side effects and tolerability.

Results: Eleven of the 20 individuals reported skin-picking, 17 reported aggression/agitation, and 16 reported symptoms of ADHD. Nine (81.8%), 14 (82.3%), and 15 (93.7%) individuals showed an improvement in skin-picking, aggression/agitation, and ADHD, respectively, while on GXR treatment. Two patients with prior complaints of psychotic symptoms did not respond to GXR. Of note, no abnormal weight gain or significant adverse reaction was observed in this group, while on GXR.

Conclusions: In this study, GXR demonstrated improvement in symptoms of skin picking, aggression/agitation, and ADHD in patients with PWS. GXR was not effective in reducing psychosis or agitation related to psychotic symptoms. Future studies are warranted to further establish the utility of GXR in PWS patients.



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Interim Analysis Guanfacine XR

Subject ID	Group	Visit 5 CGI-S Score	Response Y/N	Visit 9 CGI-S Score	Response Y/N
001	Placebo	3	N	2	N
002	Placebo	5	N	5	N
003	GXR	1	Y	1	Y
004	Placebo	5	N	1	Y
008	GXR	1	Y	1	Y
009	GXR	2	Y	1	Y
010	Placebo	2	Y	1	Y
011	GXR	1	Y	1	Y
012	Placebo	6	N		
013	GXR	3	N		
014*	Placebo	3	N		

Response Rate at Visit 5 (Unblinding)

Placebo	GXR
Non-Responders: 5	Non-Responders: 1
Responders: 1	Responders: 4

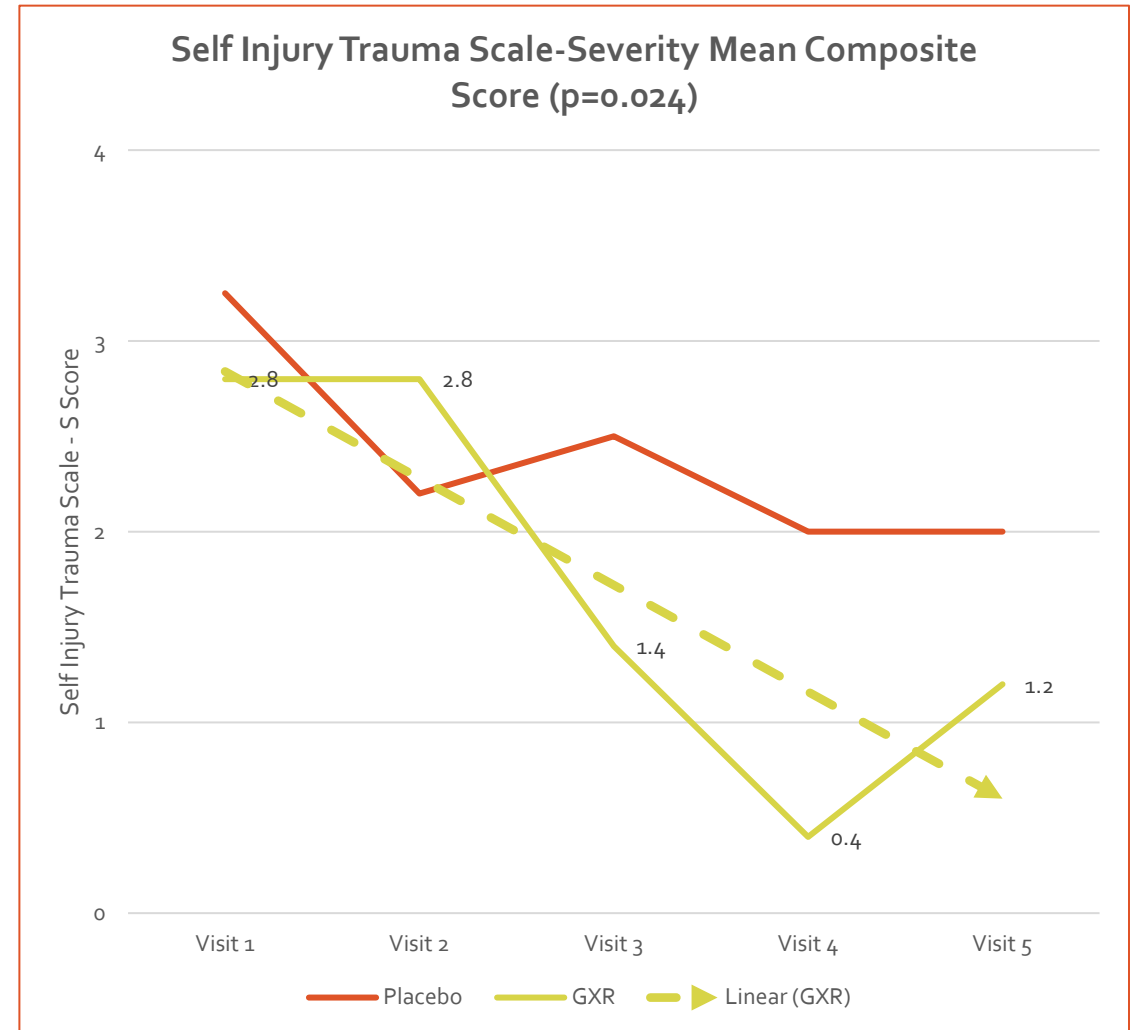
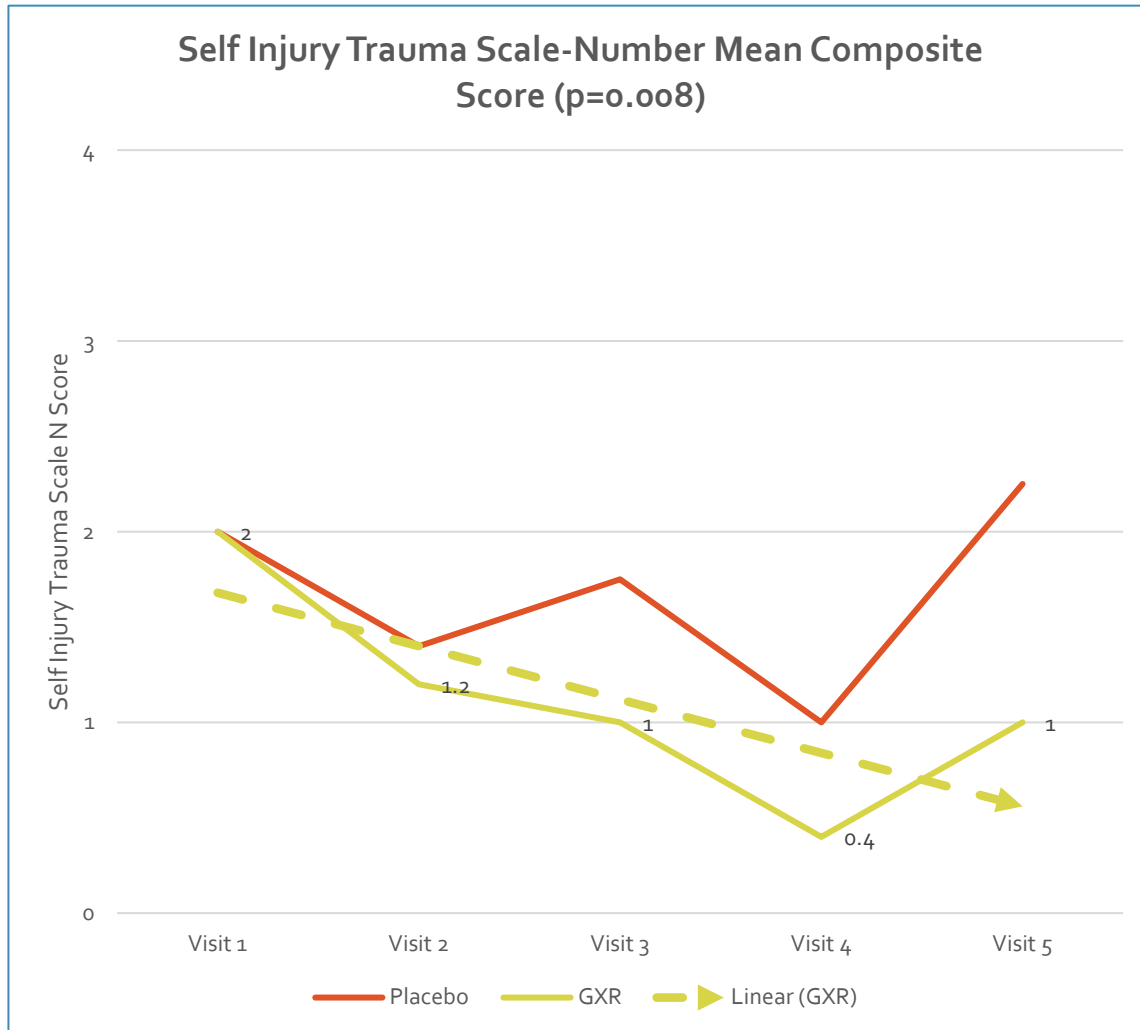
Response Rate at Visit 9 (End of Treatment)

GXR (Open Label Phase)	
Non-Responders: 1	
Responders: 7	



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Interim Analysis Guanfacine XR



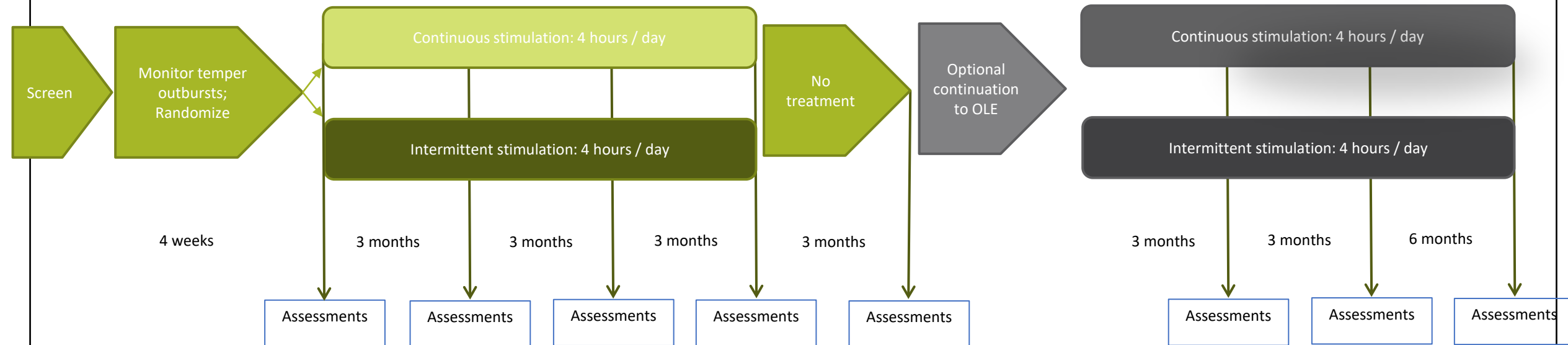
Interim Analysis Guanfacine XR- FPWR

	Treatment: Guanfacine	
Outcome measure	B (95% CI)	p-value
ABC	-11.615 (16.27, -6.97)	<0.001
ABC - Subscale 1	-3.94 (-6.9, -0.99)	<0.001
ABC - Subscale 2	-0.640 (-2.73, 1.45)	0.549
ABC - Subscale 3	-1.28 (-1.72, -0.839)	<0.001
ABC - Subscale 4	-5.25 (-6.89, -3.81)	<0.001
ABC - Subscale 5	-0.976 (-1.64, -0.32)	<0.001
ESS	4.52 (1.89, 7.15)	<0.001

STUDY DESIGN



- A phase 3 device study to reduce temper outbursts in people with PWS
- IRB-approved and deemed non-significant risk



Intermittent is 28 sec on / 32 sec off; 4 hrs can be split up over the day

PW Research Center @ Maimonides Medical Center



Thank You!

Current PWS Research at Maimonides:

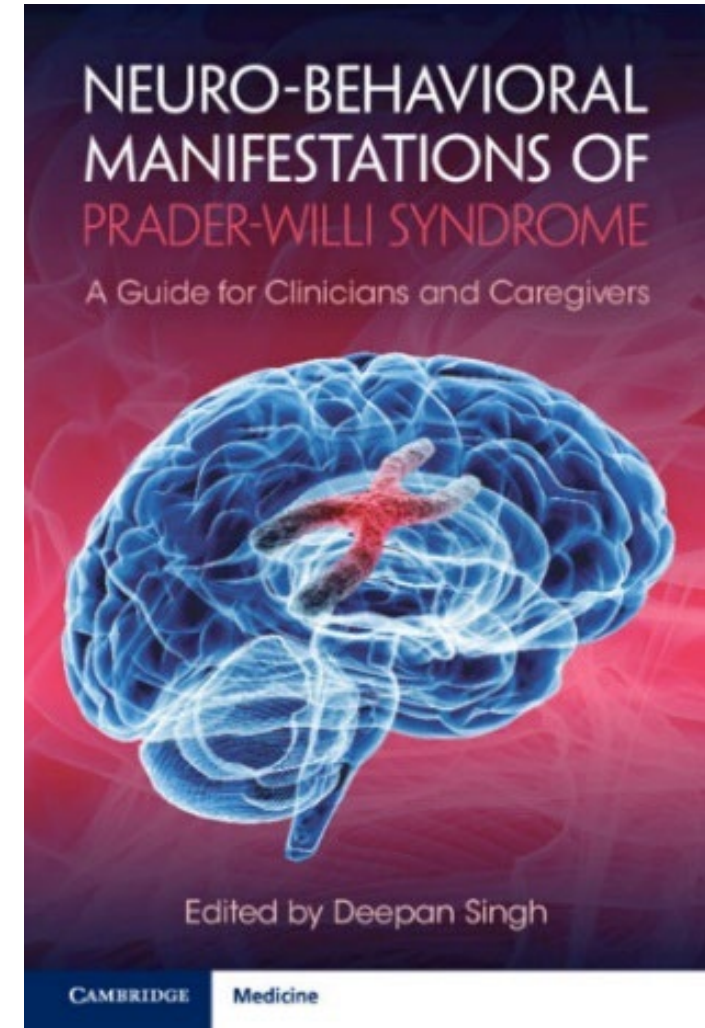
Guanfacine XR

Bright Light Therapy

Hyperphagia (Gedeon-Richter)

tVNS coming soon!

Phone: (718) 283-8170





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THANK YOU



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