

Què hi ha de nou... al tractament de l'agressió impulsiva

*I SI DIC QUE RES, QUÈ?
MARXEM?*

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AGRESIÓN

Cualquier forma de
comportamiento perjudicial
definido y observable
hacia cualquier objetivo

CONCEPTOS RELACIONADOS

IRRITABILIDAD

IRA

HOSTILIDAD

AGITACIÓN

Emociones que
preceden o
co-ocurren

con el comportamiento
agresivo

*y que no hay que confundir
con la agresión*

CONCEPTOS RELACIONADOS

IRRITABILIDAD

Propensión o vulnerabilidad a sentirse enojado

Núcleo del Trastorno de Disregulación Emocional

IRA

Estado: emoción que acompaña a la conducta agresiva.

La ira como rasgo (iracundo) se asocia con la frecuencia, duración e intensidad de las emociones de enojo

CONCEPTOS RELACIONADOS

HOSTILIDAD

Enojo y aversión hacia una persona o cosa

La "atribución hostil", es un sesgo cognitivo que implica interpretar los estímulos ambientales ambiguos como amenazantes

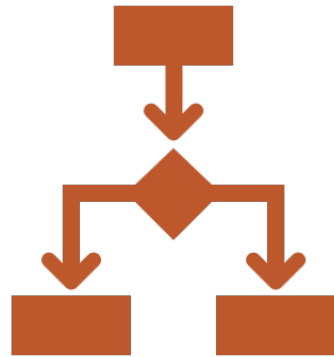
AGITACIÓN

Tensión interna, con irritabilidad y ansiedad

+

Síntomas exteriorizados (actividad motora excesiva)

AGRESIÓN

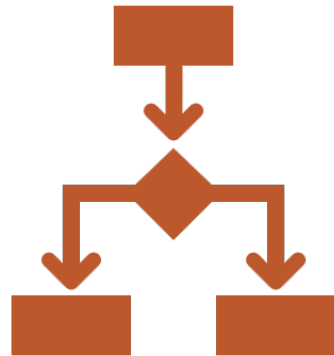


COMO DECISIÓN



COMO REACCIÓN

TRATAMIENTO DE LA AGRESIÓN



COMO DECISIÓN

Evidence-Based Psychosocial Treatments for Adolescents With Disruptive Behavior (2016)

Level 1: Well-Established Treatments

Combined Behavioral Therapy, CBT, and Family Therapy

Multisystemic Therapy^{c,d}

Treatment Foster Care Oregon (TFCO) (formerly Multidimensional Treatment Foster Care (MTFC))^e

Evidence-Based Psychosocial Treatments for Adolescents With Disruptive Behavior (2016)

Level 2: Probably Efficacious Treatments

CBT

Aggression Replacement Training + Positive Peer Culture
(Equipping Youth to Help One Another)^{d,f}

Solution-Focused Group Program^g

Combined Behavioral Therapy, CBT, and Family Therapy

Functional Family Therapy^{d,h}

Multisystemic Therapy^{d,i}

Evidence-Based Psychosocial Treatments for Adolescents With Disruptive Behavior (2016)

Level 3: Possibly Efficacious Treatments

Behavioral Therapy or Parenting Skills

Familias Unidas^f

Non-Violent Resistance^f

CBT

Cognitive Mediation^f

Combined Behavioral Therapy and CBT

Rational-Emotive Behavior Therapy^g

Support to Reunite, Involve, and Value Each Other^g

Evidence-Based Psychosocial Treatments for Adolescents With Disruptive Behavior (2016)

Level 4: Experimental Treatments

Behavioral Therapy or Parenting Skills

Behavior Management Training + Problem-Solving Communication Training

Parenting with Love and Limits

Triple P Teen (Self-Directed Enhanced with Phone Consultations)

CBT

Aggression Replacement Training (Learned Resourcefulness)

Anger Management + Think Good, Feel Good

Assertive Training

Cognitive-Behavioral Therapy

Cognitive Training + Phone Coaching (RealVictory Program)

Juvenile Cognitive Intervention

Juvenile Probation Services Intervention

Life Skills (Psychoeducation)

Mindfields

Multi-Family Group Counseling

Rational-Emotive Mental Health Program

*Family
Therapy*

Brief Strategic Family Therapy

Mentoring

Monitored Youth Mentoring Program

Combined Behavioral Therapy and CBT

Anger Control Training with Contingency Management

Anger Management for Female Juvenile Offenders

Dialectical Behavioral Therapy

Dialectical Behavior Therapy-Corrections Modified

Dialectical Behavior Therapy-Skills Training Only

Motivational Interviewing + Solution-Focused Counseling + Behavioral Shaping

Parent Management + Problem-Solving + Cognitive-Behavioral Therapy

Combined CBT and Mindfulness

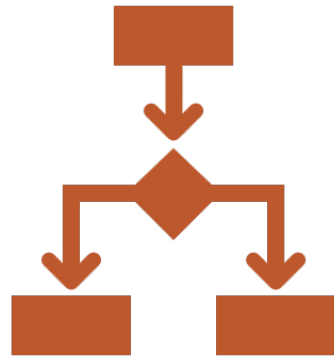
Meditation on the Soles of the Feet

Combined Behavioral Therapy and Attachment-Based

Connect Program

Multiple-Family Group Intervention

TRATAMIENTO FARMACOLÓGICO DE LA AGRESIÓN “C-U”



COMO DECISIÓN

The pharmacological treatment of aggression in children and adolescents with conduct disorder. Do callous–unemotional traits modulate the efficacy of medication? (2017)

Estimulantes (TDAH + TND/TD)

- OVER AGG: 0,84
- COVER AGG: 0,69
- Efecto dosis-dependiente

Antipsicóticos:

- Risperidona
- Quetiapina (1), Aripiprazol (0), Olanzapina (0), Paliperidona (0)

Estabilizadores:

- Litio, Valproato, Carbamacepina

Otros

- Atomoxetina
- Clonidina, Guanfacina
- Pindolol

Balia C, Carucci S, Coghill D, Zuddas A. The pharmacological treatment of aggression in children and adolescents with conduct disorder. Do callous—unemotional traits modulate the efficacy of medication? *Neuroscience & Biobehavioral Reviews* [Internet]. enero de 2017 [citado 3 de febrero de 2018]; Disponible en:

<http://linkinghub.elsevier.com/retrieve/pii/S014976341630149X>

The pharmacological treatment of aggression in children and adolescents with conduct disorder. Do callous–unemotional traits modulate the efficacy of medication? (2017)

Estim

- OV
 - CC
 - Efe
- The paucity of current evidences makes impossible to provide a comprehensive answer to the question of the present review.*

Anti

- Ris
 - Qu
 - Ol
- In fact, possible effects of medication on specific subtypes of aggression and the specific role of CU traits in modulating medication efficacy have rarely been investigated.*

Balia C, Carucci S, Coghill D, Zuddas A. The pharmacological treatment of aggression in children and adolescents with conduct disorder. Do callous—unemotional traits modulate the efficacy of medication? *Neuroscience & Biobehavioral Reviews* [Internet]. enero de 2017 [citado 3 de febrero de 2018]; Disponible en:

<http://linkinghub.elsevier.com/retrieve/pii/S014976341630149X>

AGRESIÓN COMO REACCIÓN



ADAPTATIVA

Es útil y psicológicamente entendible

Puede ser positiva o negativa

Si es negativa

- **Requiere** intervenciones psicosociales (justicia, familia, docencia, política, economía)

MALADAPTATIVA

No es útil ni psicológicamente entendible (patológica)

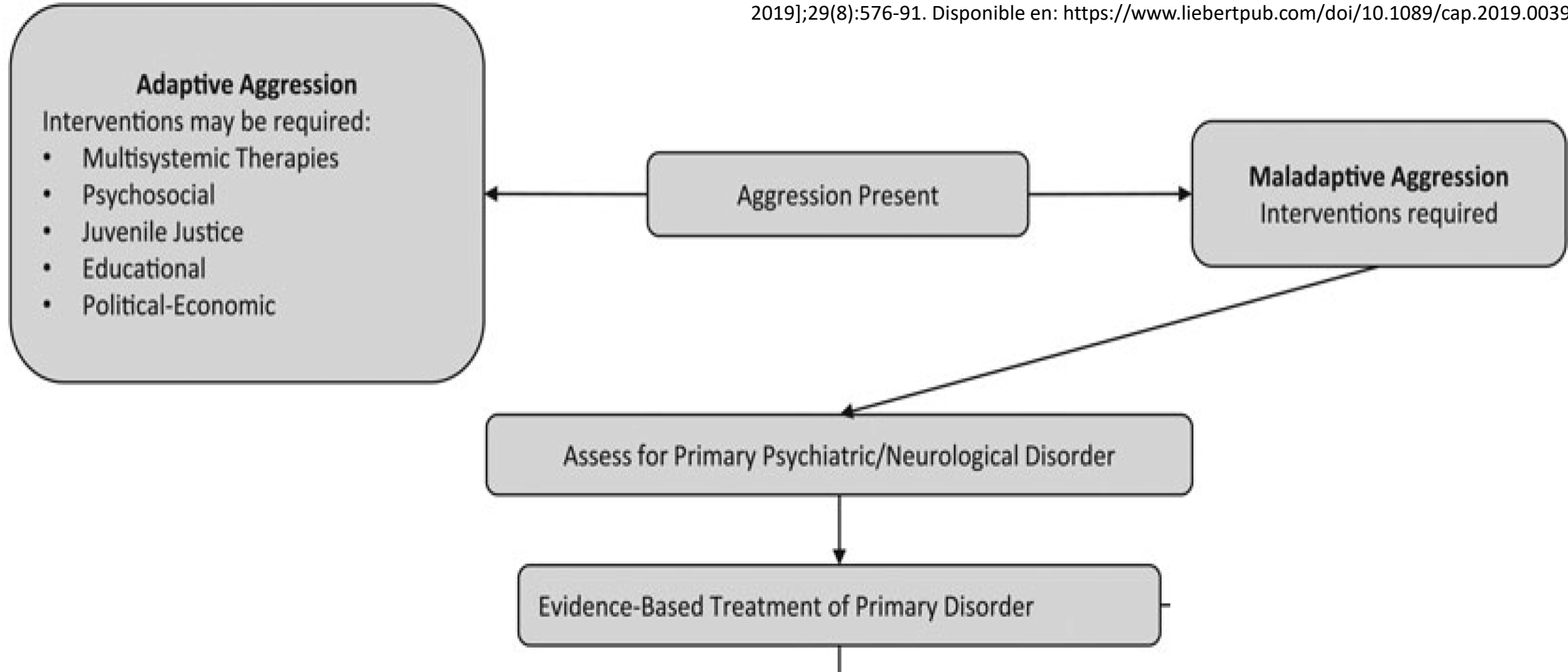
Habitualmente es negativa.

Si es negativa

- **Se beneficia** de intervenciones psicosociales y de la medicación

MALADAPTIVE AGGRESSION REVIEW

Connor DF, Newcorn JH, Saylor KE, Amann BH, Scahill L, Robb AS, et al. Maladaptive Aggression: With a Focus on Impulsive Aggression in Children and Adolescents. *Journal of Child and Adolescent Psychopharmacology* [Internet]. 1 de octubre de 2019 [citado 27 de octubre de 2019];29(8):576-91. Disponible en: <https://www.liebertpub.com/doi/10.1089/cap.2019.0039>



Psychopharmacologic Control of Aggression and Violence in Children and Adolescents (2011)

Pediatr Clin N Am
58 (2011) 73–84

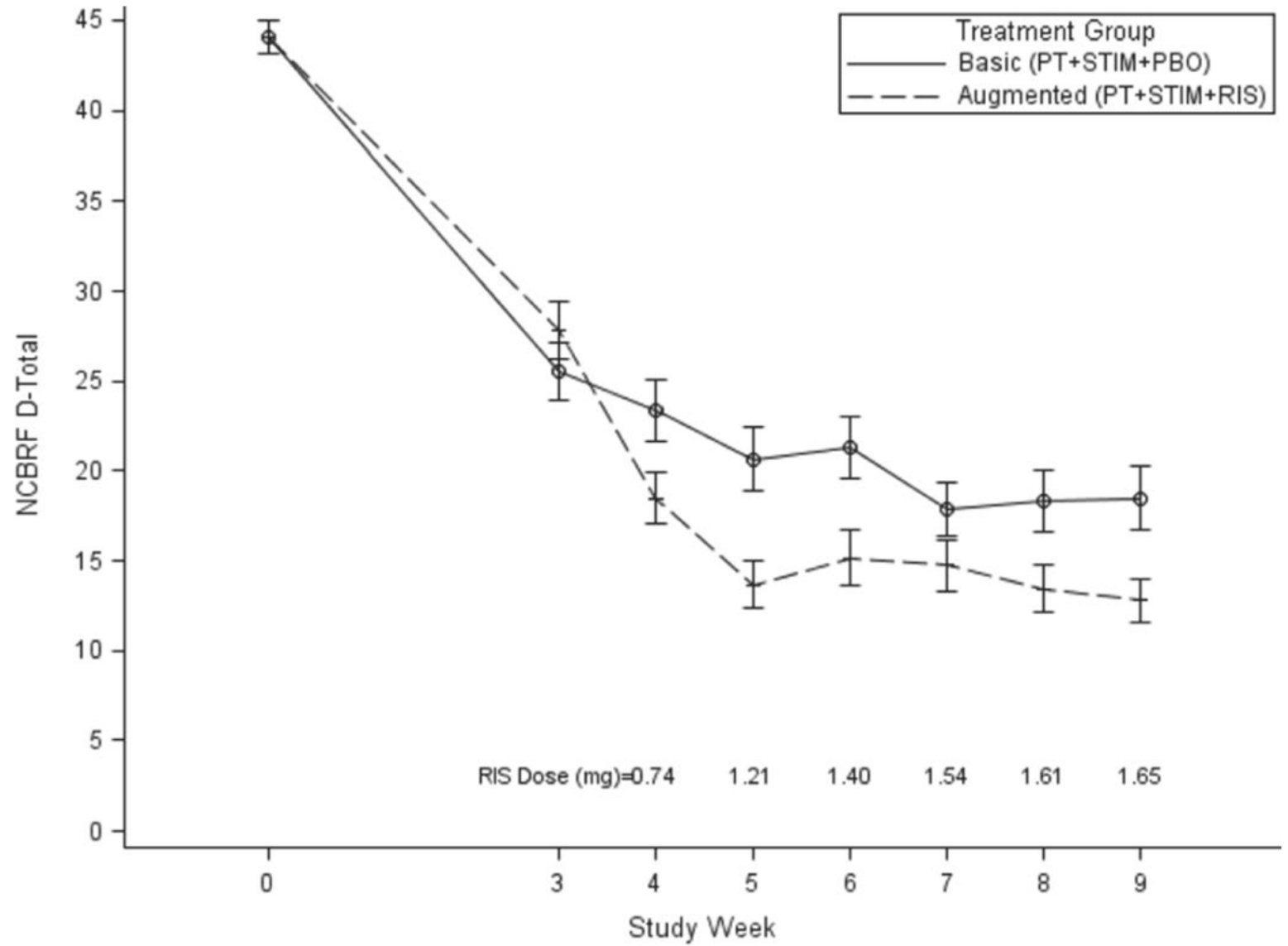
doi:10.1016/j.pcl.
2010.11.002

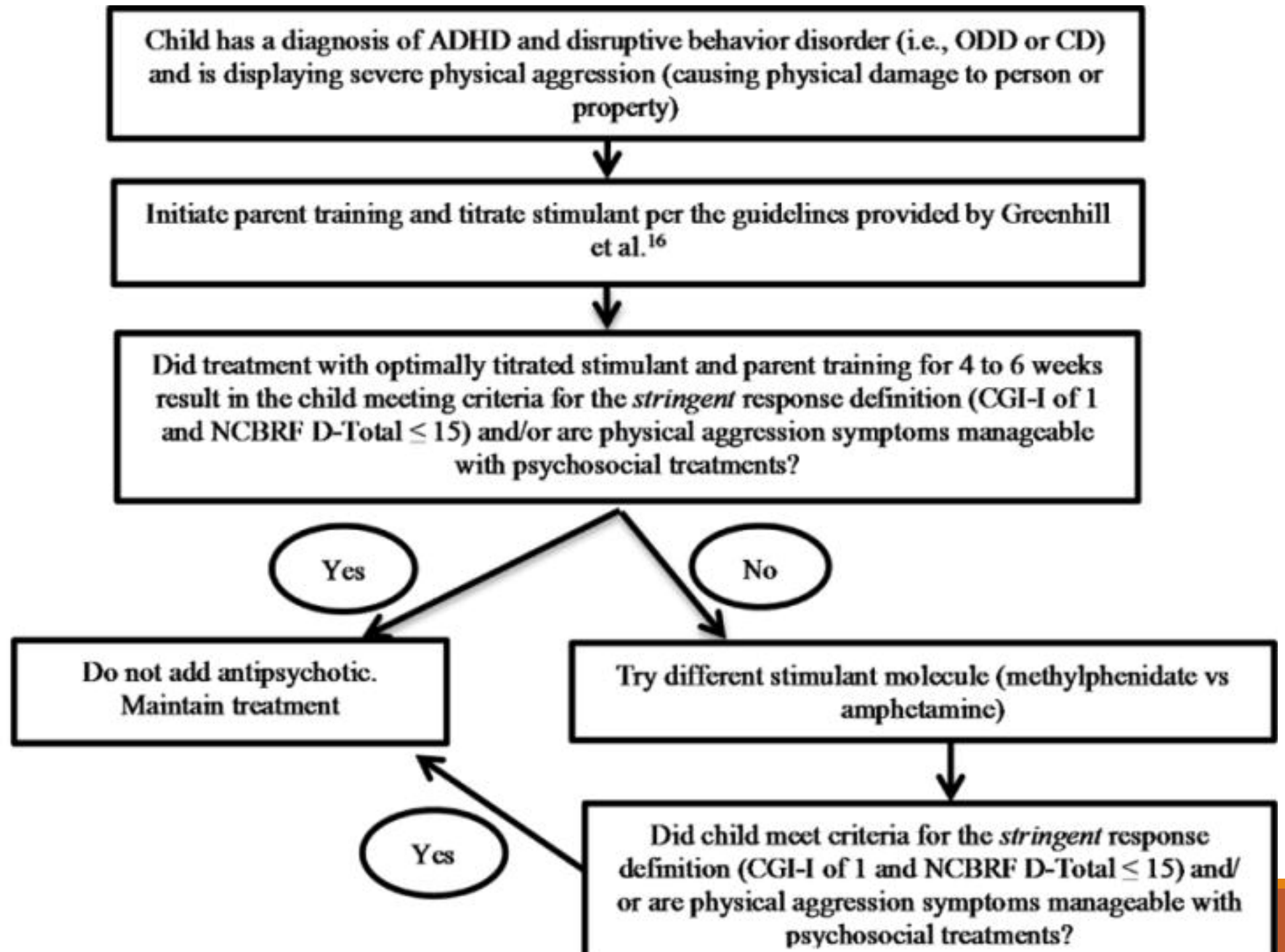
Table 1
Disorders associated with aggressive behaviors and recommended pharmacotherapeutic strategies

Disorder	Medications ^a		
	First-line	Second-line	Third-line
ADHD	MPH or MAS	Stimulant not tried as first-line treatment	Atomoxetine
ODD	MPH or MAS	Atomoxetine	VPA, RIS, or clonidine
CD	Li ± AA	ARI, OLZ, or RIS	VPA
MDD	Fluoxetine	Escitalopram	A third SSRI or an SNRI
Bipolar disorder	Li, VPA, CBZ, OLZ, QUE or RIS	Drug class not tried as first-line treatment	Drug class not tried as first-line or second-line treatment
SMD	First-line treatment depends on the presence of comorbid conditions, eg, ADHD		
<u>PTSD</u>	Sertraline	Paroxetine or another SSRI	AA, AED, or clonidine
<u>Panic disorder</u>	SSRI	A second SSRI	A third SSRI or an SNRI
<u>Schizophrenia</u>	RIS or OLZ	AA not tried as first-line treatment	Clozapine
Tourette disorder	RIS	A second AA	A third AA
IED	Lithium or AED	Drug class not tried as first-line treatment	A second AED or an AA

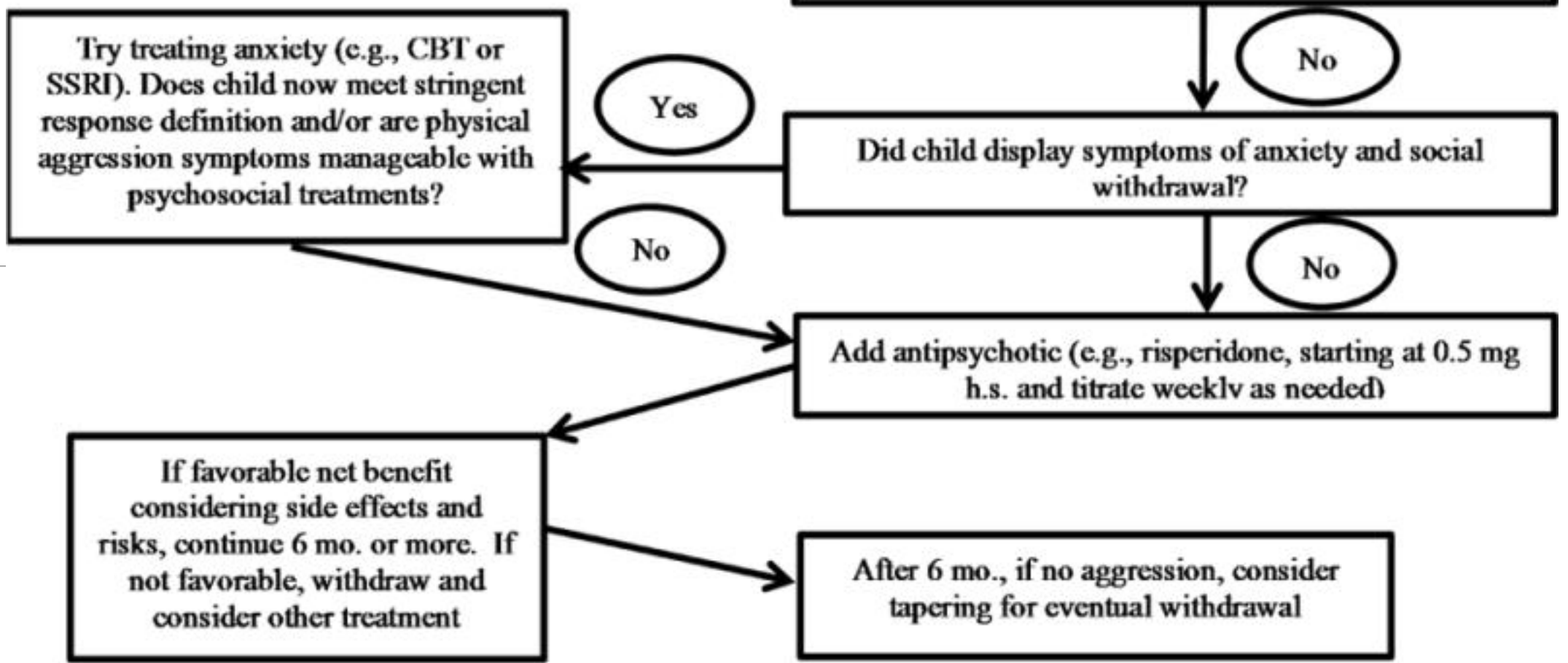
TOSCA (2017)

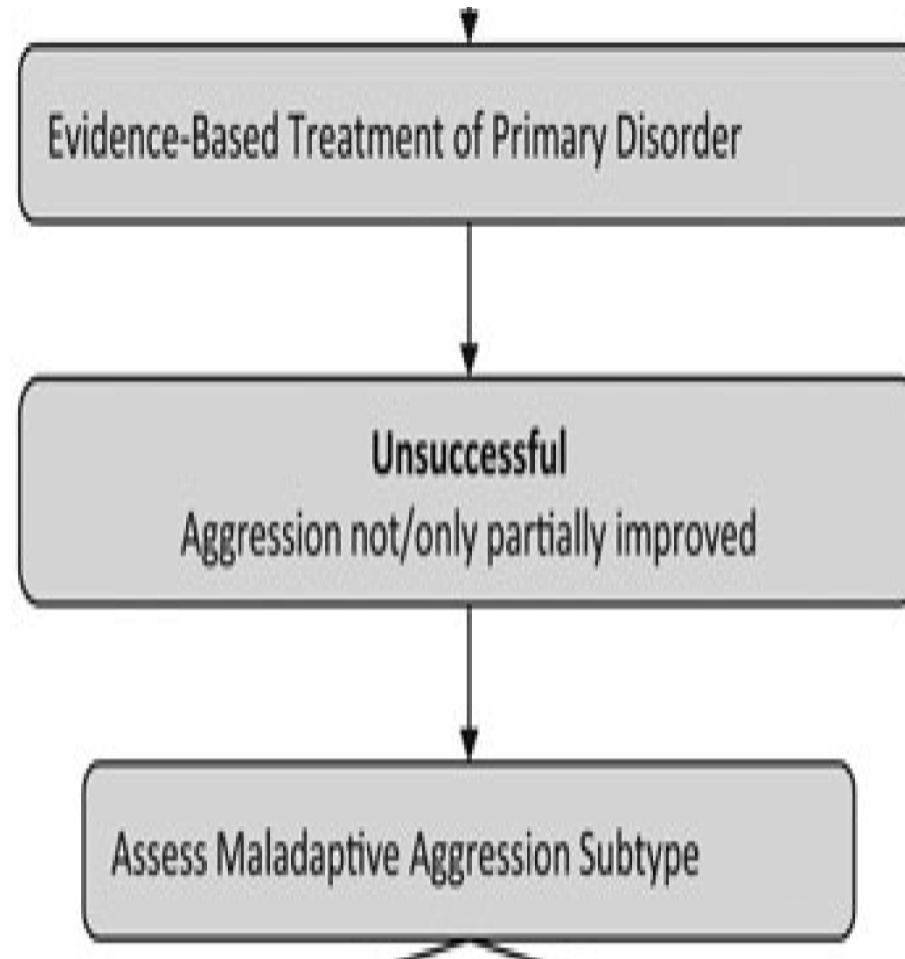
Nisonger Child
Behavior Rating
Form Disruptive
Behavior Total
score as a
function of
treatment
condition and
study visit

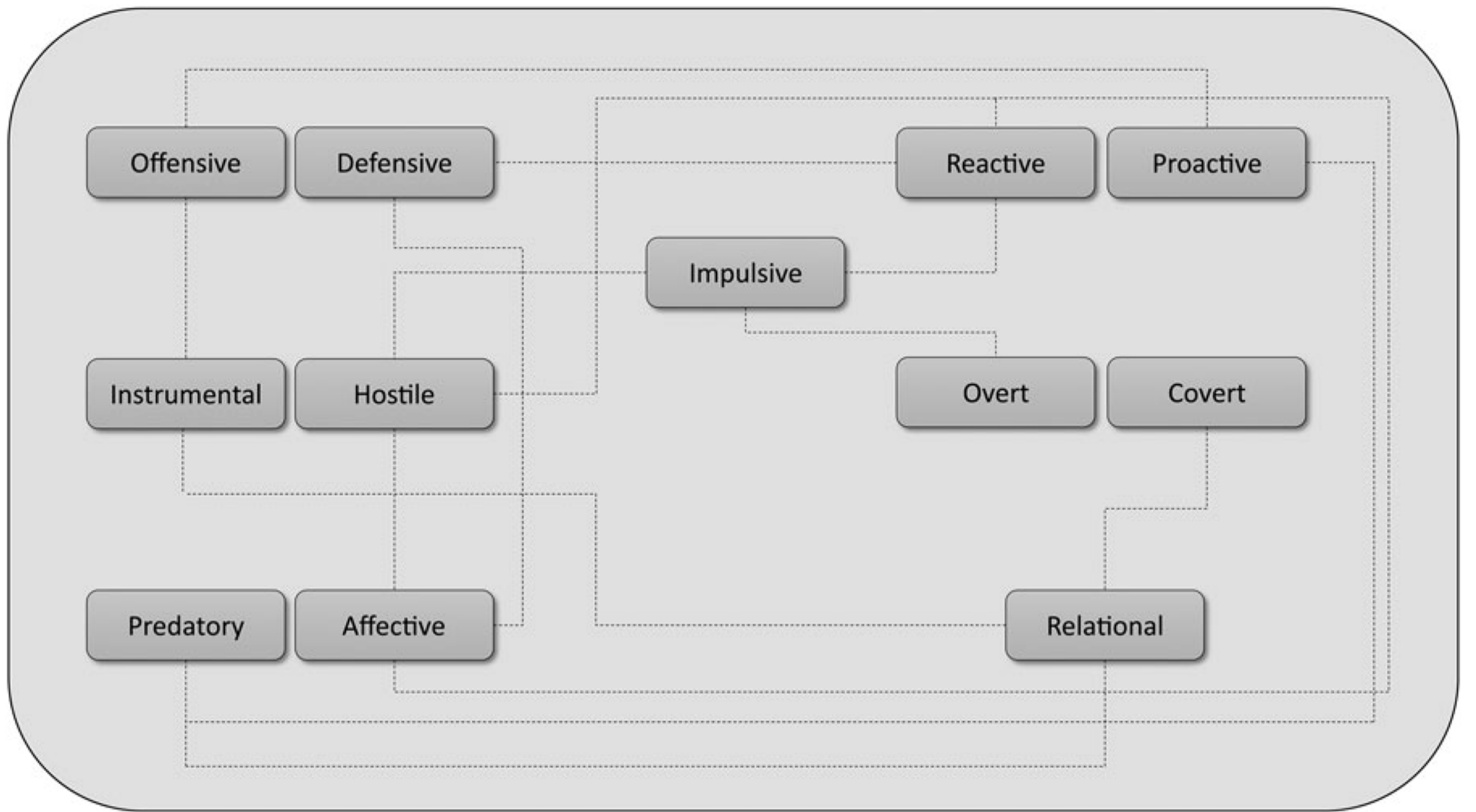


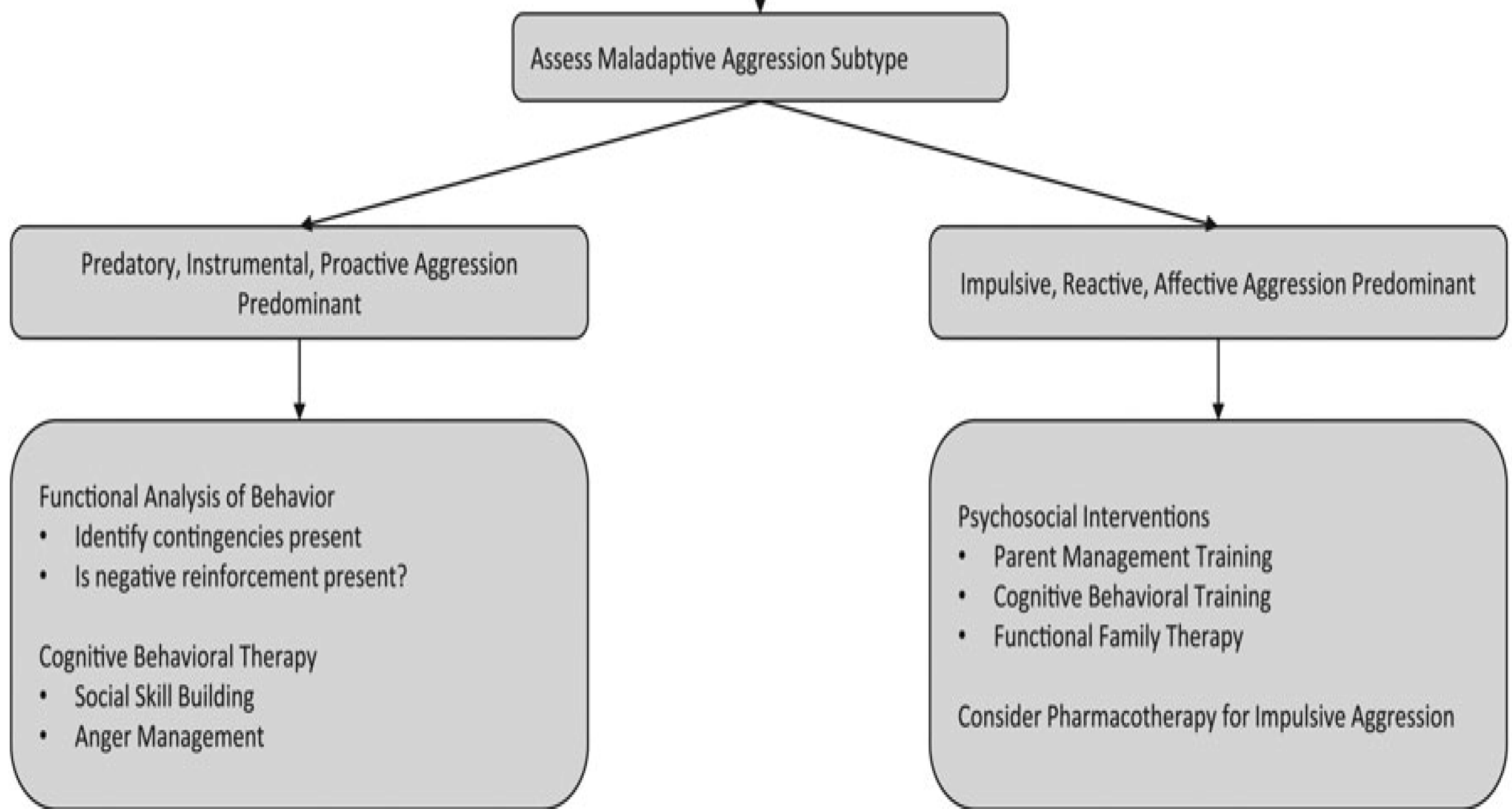


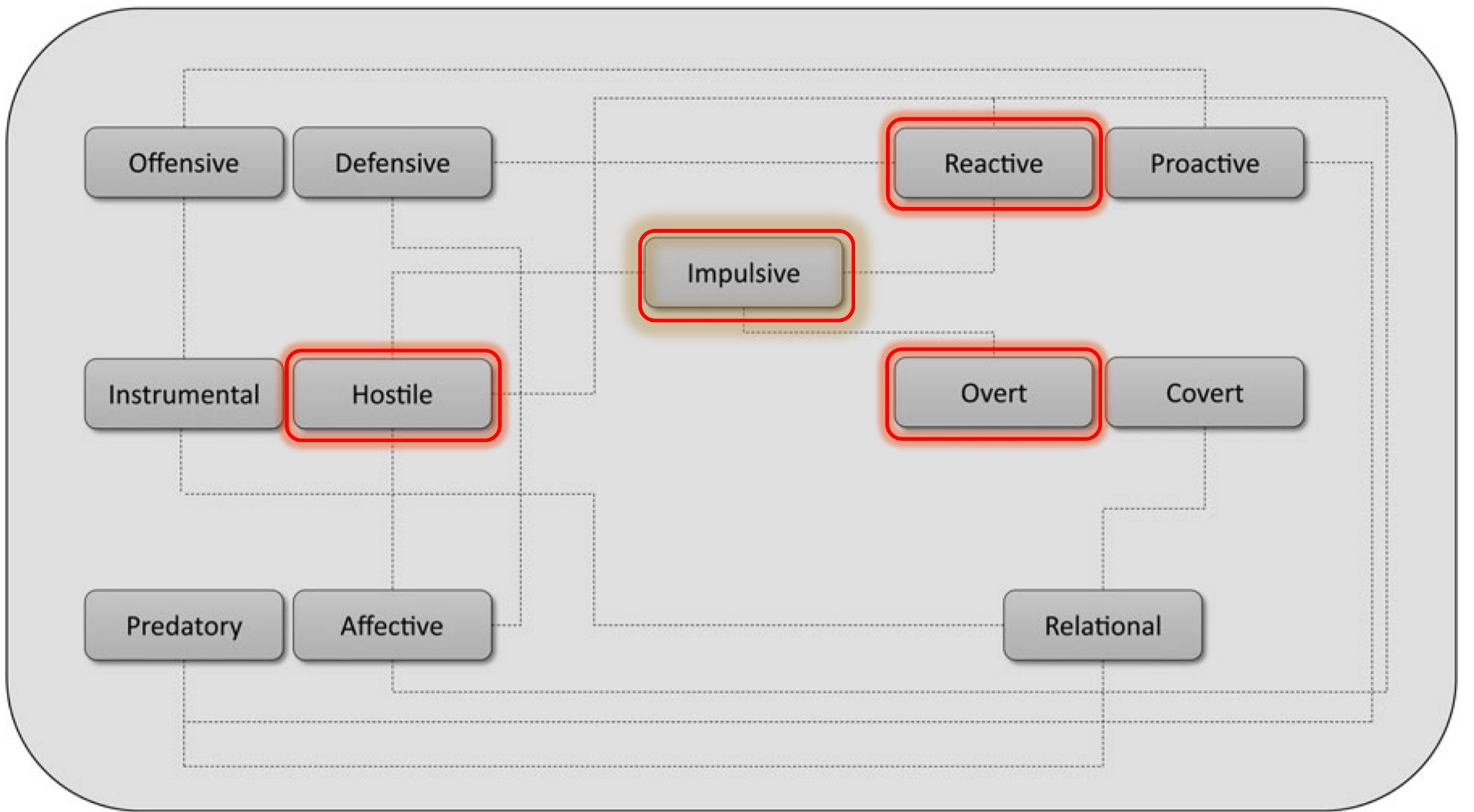
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¿TRATAMIENTO FARMACOLÓGICO DE LA AGRESIÓN IMPULSIVA URGENTE?



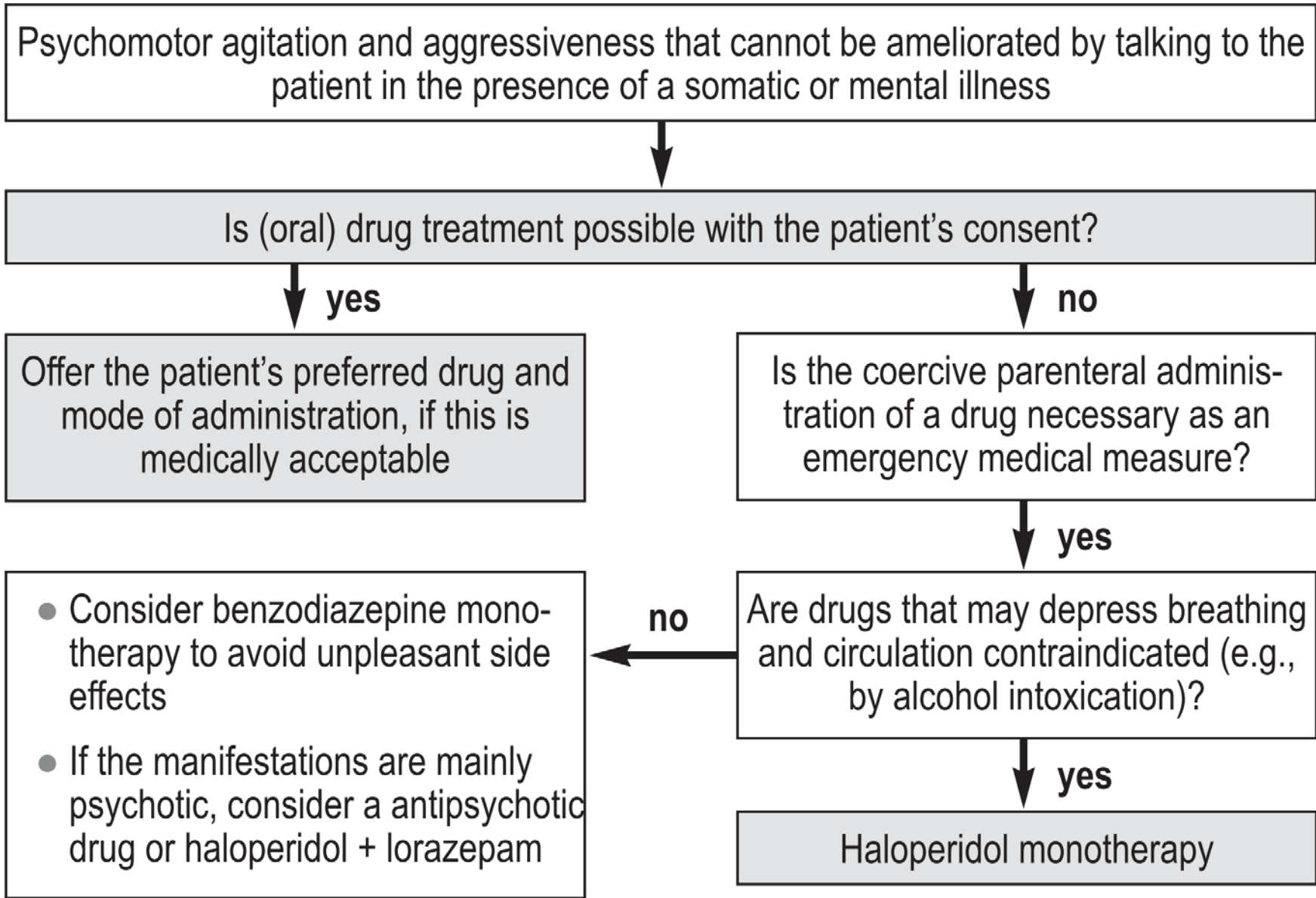
COMO REACCIÓN

Review Article

The Use of Rapid Tranquilization in Aggressive Behavior

Sophie Hirsch and Tilman Steinert

Hirsch S, Steinert T. The Use of Rapid Tranquilization in Aggressive Behavior. Dtsch Arztebl Int [Internet]. junio de 2019 [citado 30 de octubre de 2019];116(26):445-52. Disponible en: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6712906/>



ANTIPSIKÓTICOS ORALES

RISPERIDONA
(2 mg)
+
LORACEPÁN
(2 mg)

- Efecto comparable a Haloperidol (5 mg) + Loracepán (2 mg) intramuscular

OLANZAPINA ◦
RISPERIDONA ◦
HALOPERIDOL

- Efecto semejante

ANTIPSIKÓTICOS ORALES

ASENAPINA sublingual

- NNT 3
- Similar IM – AP

OLANZAPINA bucodispersable

- Igual que im
- Mejor que HAL im

MOLINDONA

Fase 2A: Molindona **inmediata**: mejorías en TDAH con conductas agresivas graves y persistentes

Fase 2B: Molindona de **liberación prolongada** (SPN-810) mejorías frente a placebo en TDAH con agresión impulsiva refractaria

Fase 3: “en marcha”

BENZODIACEPINAS

ORALES

Uso puntual,
pueden incrementar la agresión

Loracepán >> Diacepán

INTRAMUSCULARES

HALOPERIDOL + LORACEPÁN im

→ NNT 3, en 60 minutos

En MONOTERAPIA

- No son mejores que el placebo
- No son peores que los AP
- Son peores que en combinación con AP (Haloperidol más Loracepán)

El **MIDAZOLAM** no está aprobado / recomendado
(riesgo de depresión respiratoria).

HALOPERIDOL INTRAMUSCULAR

Monoterapia con HALOPERIDOL

- Es mejor que placebo y que Aripiprazol
- No es mejor que Loracepán

HALOPERIDOL + LORACEPÁN

→ NNT 3, en 60 minutos

Riesgo de depresión respiratoria

HALOPERIDOL + PROMETACINA

- Mejor que monoterapia con midazolam, loracepán, olanzapina, ziprasidona y haloperidol
- A los 30 minutos la proporción de pacientes que siguen agitados es marcadamente menor
- No induce depresión respiratoria
- Puede combatir la distonía
- Pero puede prolongar el QT

OTROS ANTIPSIKÓTICOS INTRAMUSCULARES

ZIPRASIDONA – NNT 3

- Mejor que Haloperidol + Prometacina / Midazolam
- 

OLANZAPINA – NNT 4

- Mortalidad aumentada con BZD, OH u otros
- 

ARIPIPRAZOL – NNT5

- Realmente NO es rápida

¿NOVEDADES?



KETAMINA INTRAMUSCULAR

- Efecto en 3-5 minutos (Midazolam: 15-20 min)
- No deprime la respiración ni afecta el reflejo respiratorio
- 40% vómitos o sialorrea profusa en el 40%
- Necesidad de intubación en el 11% (dosis menor de 4 mg/kg) hasta el 57% (dosis superiores)
- Requiere nuevas contenciones químicas (efecto poco duradero)

Scaggs TR, Glass DM, Hutchcraft MG, Weir WB. Prehospital Ketamine is a Safe and Effective Treatment for Excited Delirium in a Community Hospital Based EMS System. Prehospital and Disaster Medicine. octubre de 2016;31(5):563-9.

INHALACIÓN – LOXAPINA

NNT 3 en reducción de la agitación en
Esquizofrenia y T. Bipolar en los estudios de
aprobación

Contraindicada en patología respiratoria por
riesgo de broncoespasmo

INHALACIÓN – LOXAPINA

Tabla 2. Características de los pacientes con agitación psicomotriz y tratamiento con loxapina

Paciente	Edad	Sexo	Grado agitación	Colabora inhalación	CGI antes	CGI después	PANSS-EC antes	PANSS-EC después	Tto. adicional	CGI después tto. adicional	PANSS-EC después tto. adicional
1	52	M	Leve	Sí	3	1	17	5	No	–	–
2	60	M	Moderada	Sí	4	1	21	6	No	–	–
3	46	M	Grave	Sí	6	1	30	8	No	–	–
4	49	M	Extrema	No	7	–	33	–	–	–	–
5	20	M	Extrema	No	7	–	33	–	–	–	–
6	21	V	Leve	Sí	3	1	14	5	No	–	–
7	47	V	Moderada	Sí	4	1	21	7	No	–	–
8	65	V	Grave	Sí	6	1	31	10	No	–	–
9	63	V	Grave	Sí	6	3	28	16	Sí	1	9
10	46	V	Grave-Moderada	Sí	5	1	26	6	No	–	–
11	33	V	Grave-Moderada	Sí	5	1	24	8	No	–	–
12	37	V	Extrema	Sí	7	4	33	21	Sí	1	6
13	28	M	Grave	Sí	6	3	35	15	No	–	–
14	28	M	Moderada	Sí	4	1	22	5	No	–	–

CGI: Impresión Clínica Global; PANSS–EC: Escala de Síntomas Positivos y Negativos–Componente de Excitación; Tto.: tratamiento.

LORACEPÁN INTRANASAL

CASE REPORT

A 7-year-old boy with a long-standing history of anxiety and oppositional defiant disorder presented to the ED with aggression and violent behavior at home. The patient had a history of one ED visit to an outside hospital, which necessitated intramuscular chlorpromazine for sedation, and had begun receiving sertraline 3 weeks before presentation. On arrival by emergency medical services, the patient was kicking the door of the room, throwing chairs at the walls, spitting at hospital personnel, punching his parents, and refusing to follow directions, including donning a hospital gown. His anger erupted without provocation, and he threatened the medical staff with death if they continued to hold him imprisoned in the room. Attempts by ED personnel to verbally de-escalate the situation were unsuccessful; the patient refused to cooperate with oral sedatives, and physical and chemical restraints were required. The

patient's parents expressed concern in regard to intramuscular sedative administration because they thought the patient had been "traumatized" by the intramuscular sedative he had received at his previous ED visit. We administered intranasal lorazepam (2 mg/mL) at a dose of 1.5 mg (0.05 mg/kg), using a mucosal atomization device, with the total volume divided in half and administered into both nares. Health care providers and hospital personnel donned masks with eye shields to protect themselves from exposure to bodily fluids, and security guards provided physical restraint and stabilization of the head during administration of the intranasal medication.

At 5 minutes after intranasal lorazepam administration, the patient was calm and sitting on the stretcher without physical restraints. He was cooperative and interactive with

POTENCIALES - GABOXADOL



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

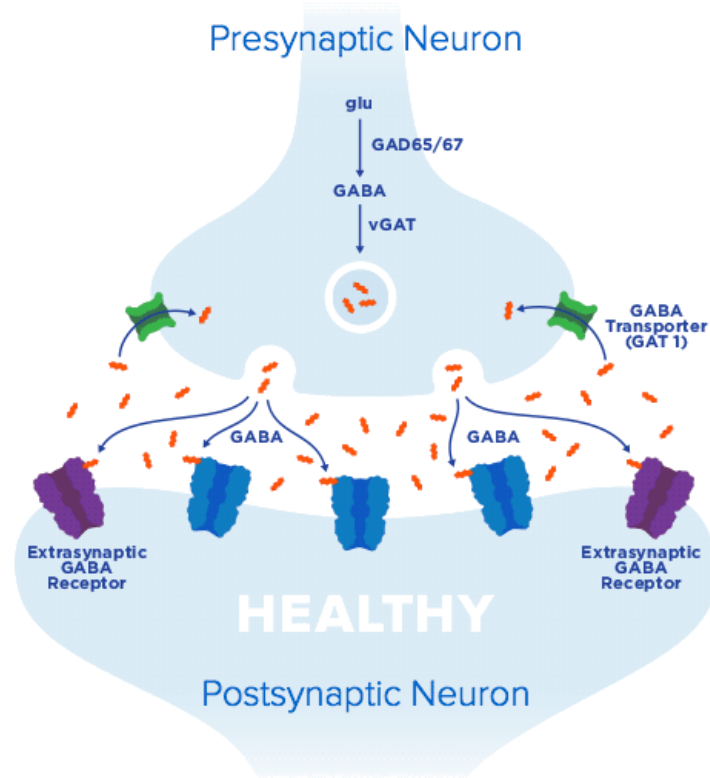
16 September 2029
EMADOC-628903358-1033

Public summary of opinion on orphan designation

Gaboxadol monohydrate for the treatment of Angelman syndrome

On 28 June 2019, orphan designation EU/3/19/2172 was granted by the European Commission to FGK Representative Service GmbH, Germany, for gaboxadol monohydrate for the treatment of Angelman syndrome.

POTENCIALES - GABOXADOL



Agonista subunidad DELTA de los receptores GABA-A extrasinápticos (dSEGA)

El Síndrome X –Frágil (SXF) muestra baja disponibilidad de receptores GABA-A

> 90% humanos con SFX muestran agresividad en un año

- 33% varones y 20% mujeres grave como para dañar a cuidadores

El Gaboxadol normaliza las conductas aberrantes del ratón Fmr1 KO2 (Modelo animal del SXF)

Cogram P, Deacon RMJ, Warner-Schmidt JL, von Schimmelmann MJ, Abrahams BS, During MJ. Gaboxadol Normalizes Behavioral Abnormalities in a Mouse Model of Fragile X Syndrome. Front Behav Neurosci [Internet]. 25 de junio de 2019 [citado 30 de octubre de 2019];13. Disponible en: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6603241/>

POTENCIALES - GABOXADOL

		WT	KO	KO	KO	KO	KO	KO	KO	KO
		GABOXADOL								
<u>BEHAVIORAL TEST</u>		vehicle	vehicle	0.5 mg/kg	1.0 mg/kg	1.5 mg/kg	2.0 mg/kg	3.0 mg/kg	4.0 mg/kg	5.0 mg/kg
<i>Anxiety-like</i>	Center distance	Green	Red	Green	Red	Red	Red	Red	Red	Red
	Light/dark transitions	Green	Red	Green	Red	Red	Red	Red	Red	Red
	Successive alleys	Green	Red	Green	Red	Red	Red	Red	Red	Red
<i>Irritability and Aggression</i>	Tail rattling	Green	Red	Green	Red	Yellow	Red	Red	Red	Green
	Number of bites	Green	Red	Green	Red	Green	Red	Red	Red	Green
	Number of mounts	Green	Red	Green	Red	Yellow	Red	Red	Yellow	Green
	Attack latency	Green	Red	Green	Red	Green	Red	Red	Red	Red
<i>Repetitive behaviors</i>	CCW revolutions	Green	Red	Green	Green	Red	Red	Red	Red	Red
	Grooming	Green	Red	Green	Red	Red	Red	Red	Red	Red
	Sterotypy	Green	Red	Green	Red	Red	Red	Red	Red	Red
<i>Activity</i>	Distance traveled	Green	Red	Green	Red	Red	Red	Red	Red	Red



Aggression and Violent Behavior

Reducing aggression with martial arts: A meta-analysis of child and youth studies

Anna Harwood ^a, Michal Lavidor ^{a,b}, Yuri Rassovsky ^{a,b,c,*}

Harwood A, Lavidor M, Rassovsky Y. Reducing aggression with martial arts: A meta-analysis of child and youth studies. *Aggression and Violent Behavior*. mayo de 2017;34:96-101. <http://dx.doi.org/10.1016/j.avb.2017.03.001>

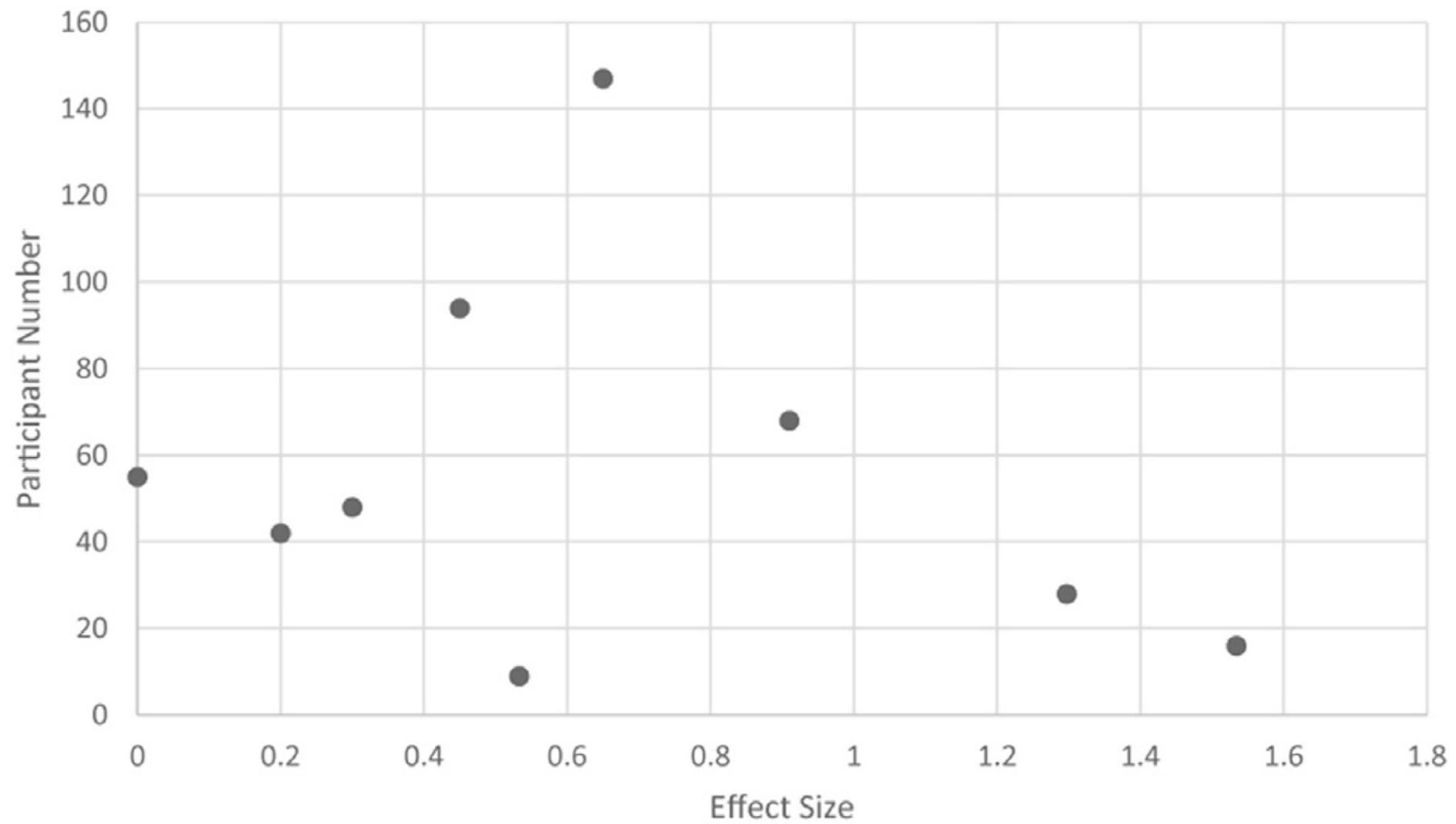
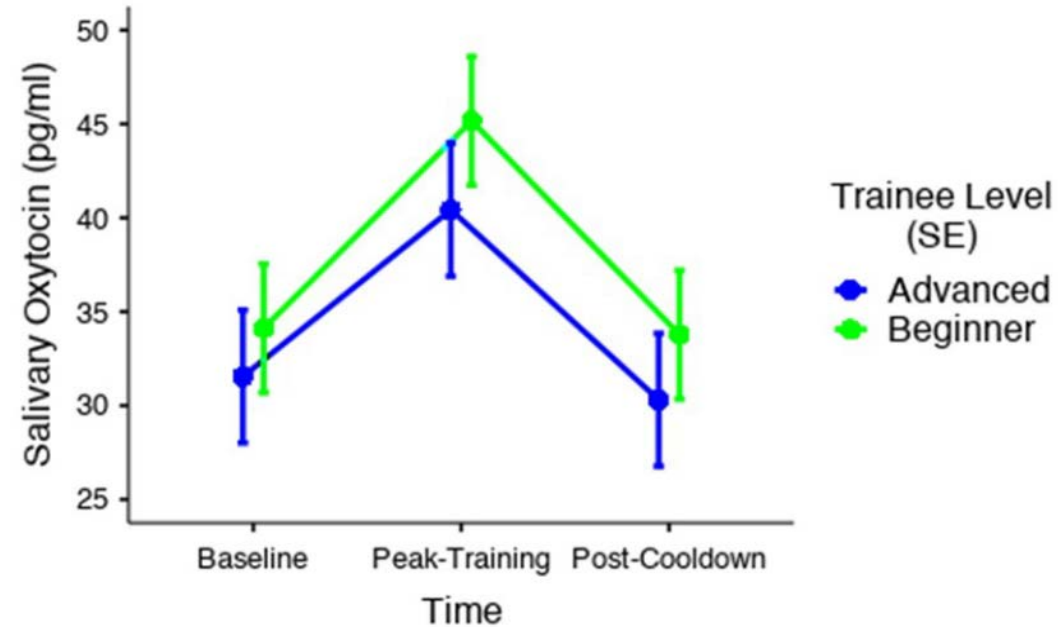


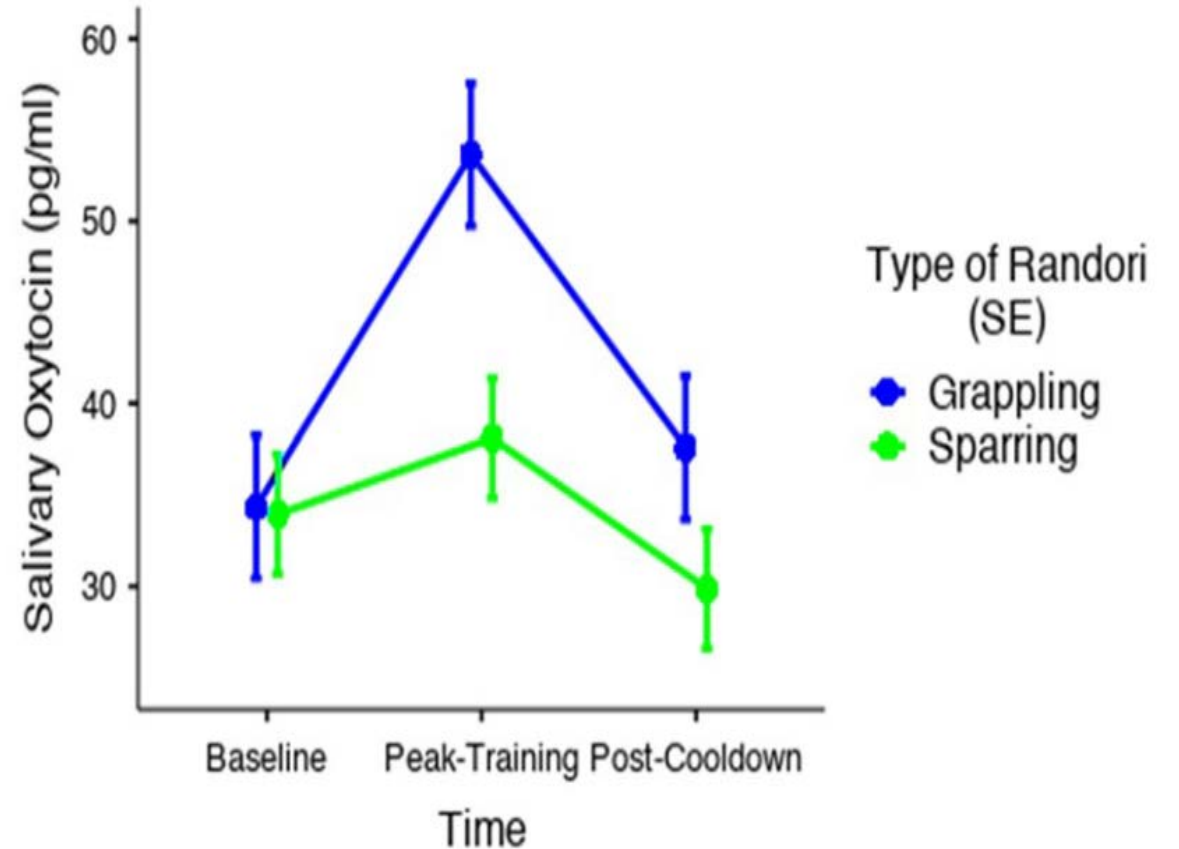
Fig. 1. Funnel plot showing effect sizes for martial arts meta-analysis delineated by sample size.

Martial arts increase oxytocin production

Yuri Rassovsky^{1,2}, Anna Harwood¹, Orna Zagoory-Sharon³ & Ruth Feldman^{1,3}



Oxitocina - Jujitsu



ALGUNAS NOVEDADES EN EL TRATAMIENTO DE LA AGRESIÓN

TOMÁS J. CANTÓ 2019



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