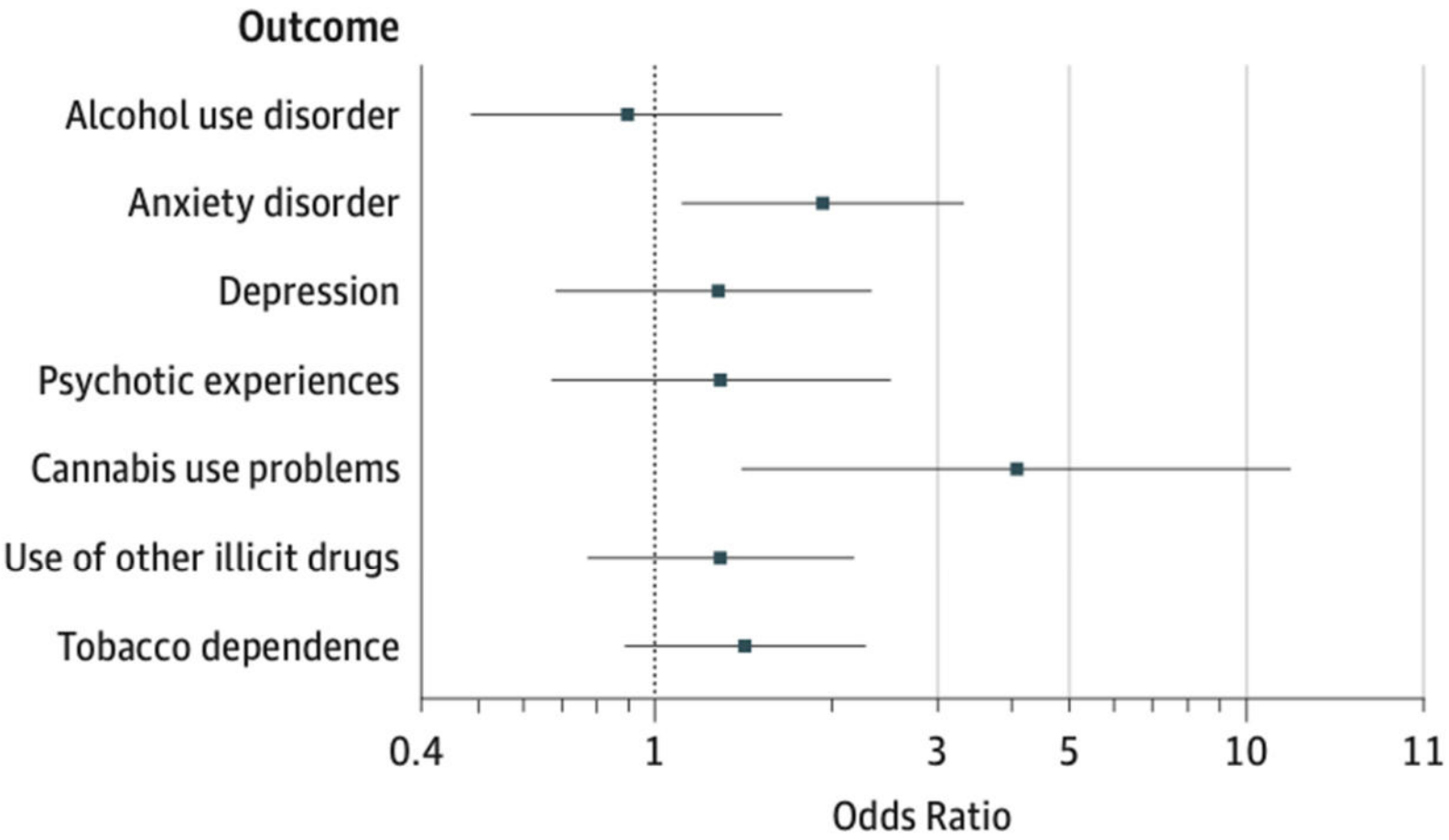
I TRATTAMENTI TERAPEUTICI: LE NUOVE SFIDE FARMACOLOGICHE, LA CONTINUITA DELLE CURE E IL MIGLIORAMENTO DEGLI OUTCOME

SERGIO DE FILIPPIS

Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence



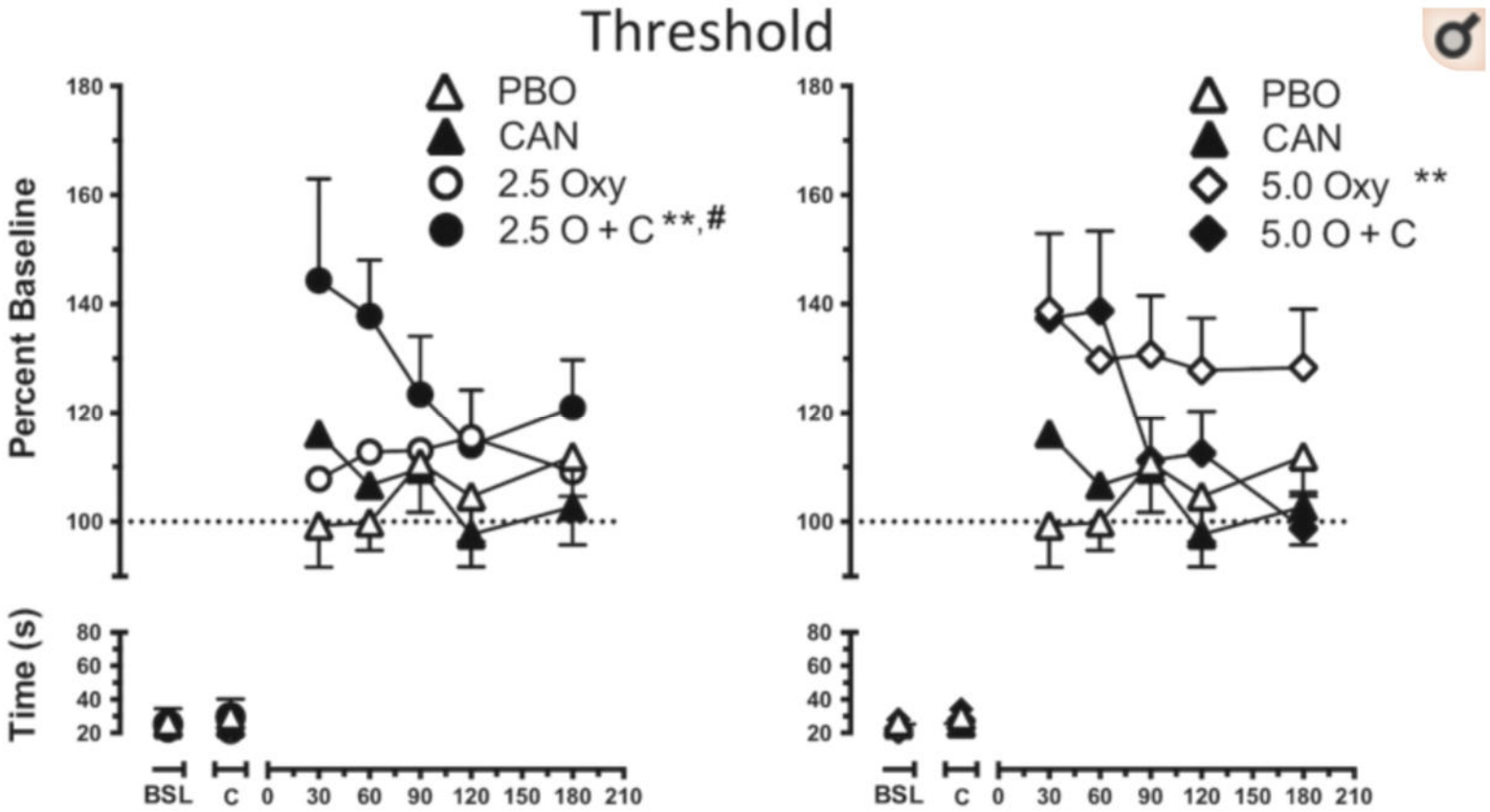
J Lindsey A. Hines et al, JAMA Psychiatry 2020

Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence

Characteristic	Cannabis use, %[a]		P value[b]
	High potency (n = 141) 12,8%	Lower potency (n = 946) 87,2%	
Regular cannabis use	56.8	17.6	≤.001
Cannabis use problems	10.1	0.8	≤.001
Use of other illicit drugs	82.9	66.5	≤.001
Tobacco dependence	37.0	15.1	≤.001
Alcohol use disorder	15.1	10.0	≤.001
Major depression (moderate or severe symptoms)	11.7	9.7	≤.001
Generalized anxiety disorder	19.1	11.6	≤.001
Psychotic-like experiences	12.4	7.1	≤.001
Male sex	71.6	43.4	≤.001
Low maternal educational level	19.2	13.1	≤.001
Lower parental occupational class	32.2	29.2	≤.001
Black or minority ethnic group	5.3	5.3	.94
Age at onset of cannabis use, mean (95% CI), y	14.7 (14.3-15.1)	16.9 (16.8-17.2)	NA
MFQ score at 13 y, mean (95% CI)	5.6 (4.65-6.49)	5.6 (5.26-5.95)	NA
No. PEs at 12 y, mean (95% CI)	0.33 (0.18-0.48)	0.20 (0.16-0.24)	NA

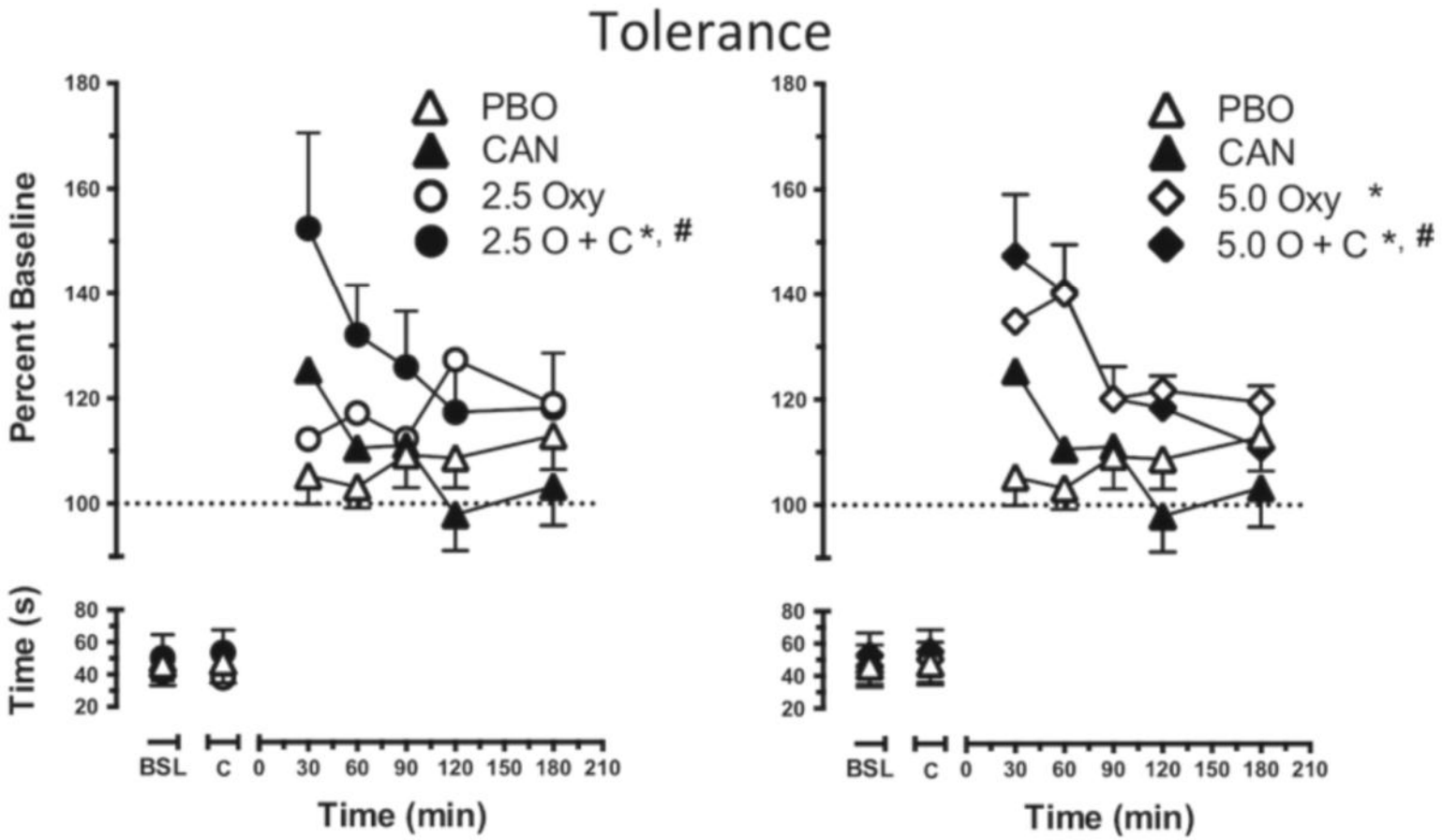
J Lindsey A. Hines et al, JAMA Psychiatry 2020

Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability

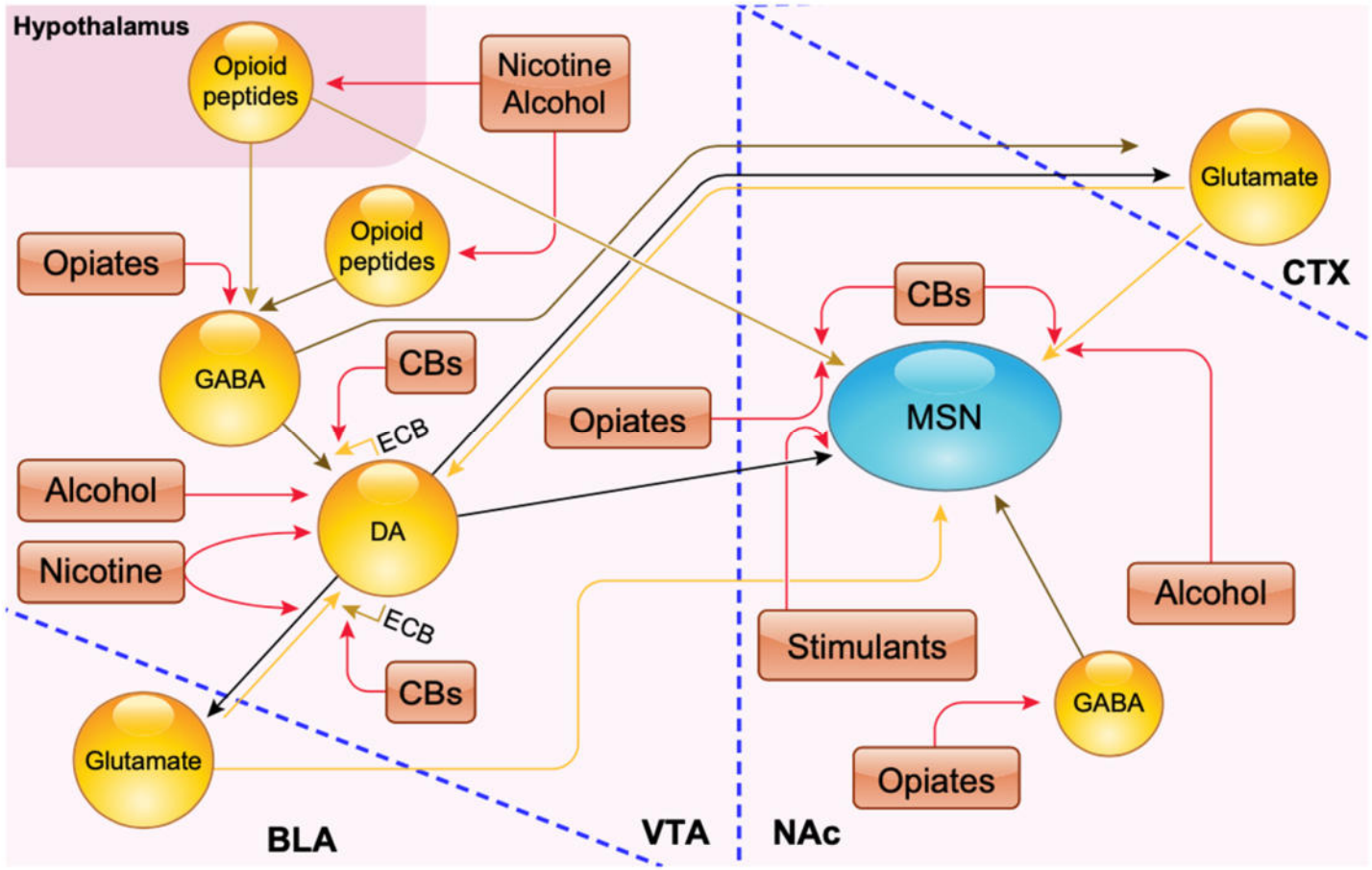


Z. D Cooper et al; Neuropsychopharmaology, 2018

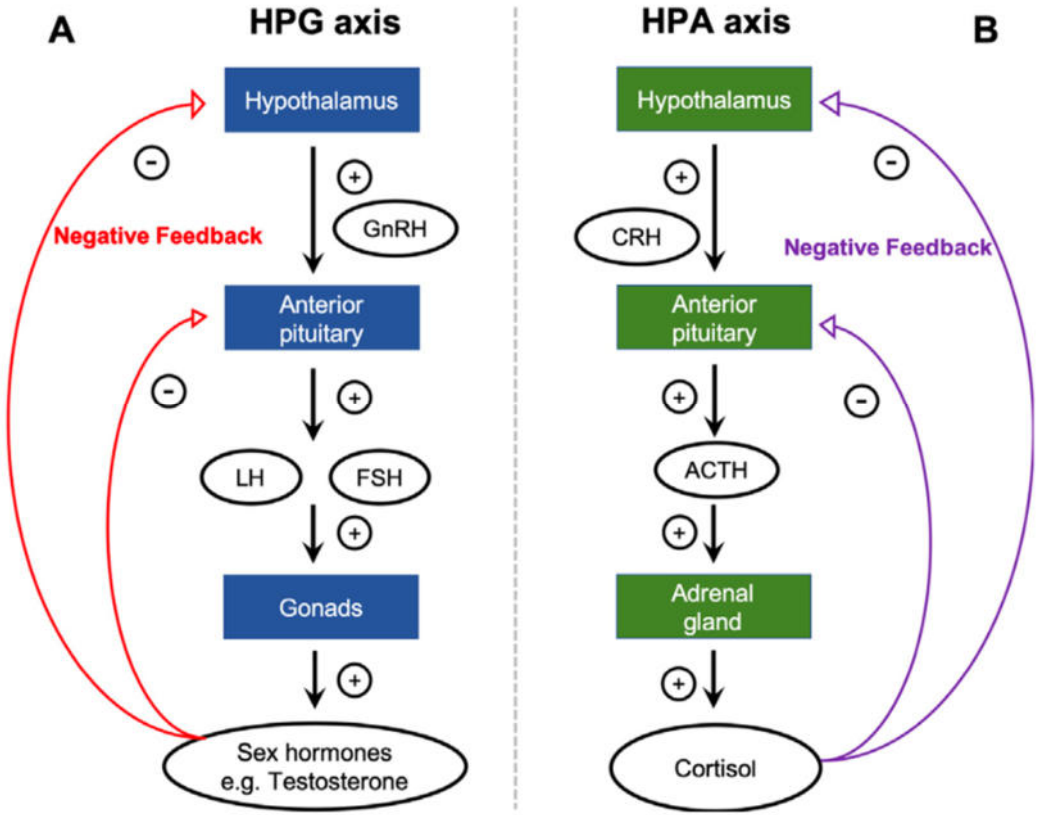
Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability



THE NEUROSCIENCE OF DRUG REWARD AND ADDICTION

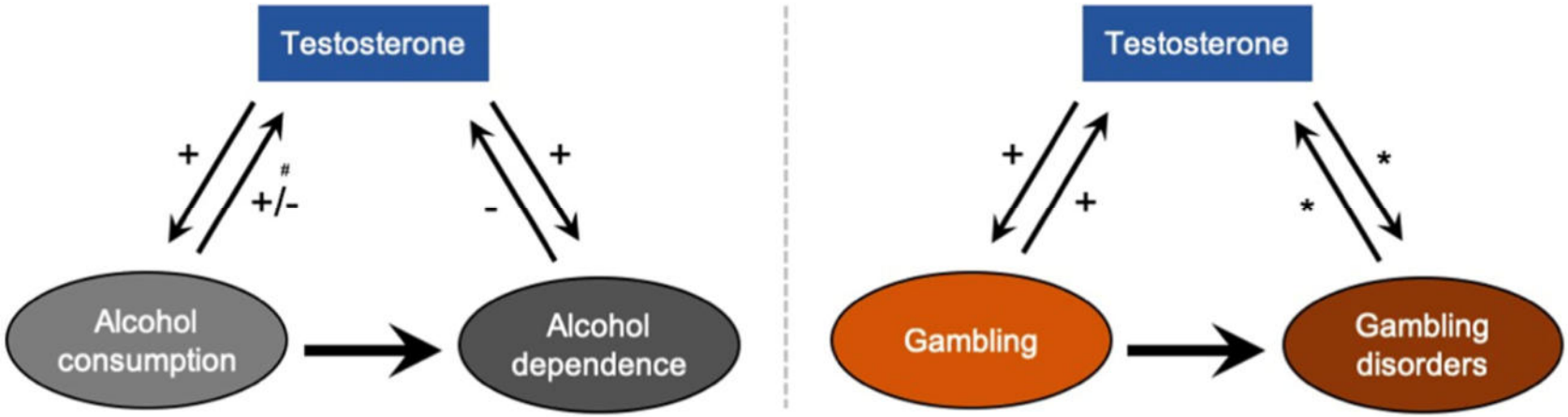


Hormonal responses in gambling versus alcohol abuse: A review of human T studies



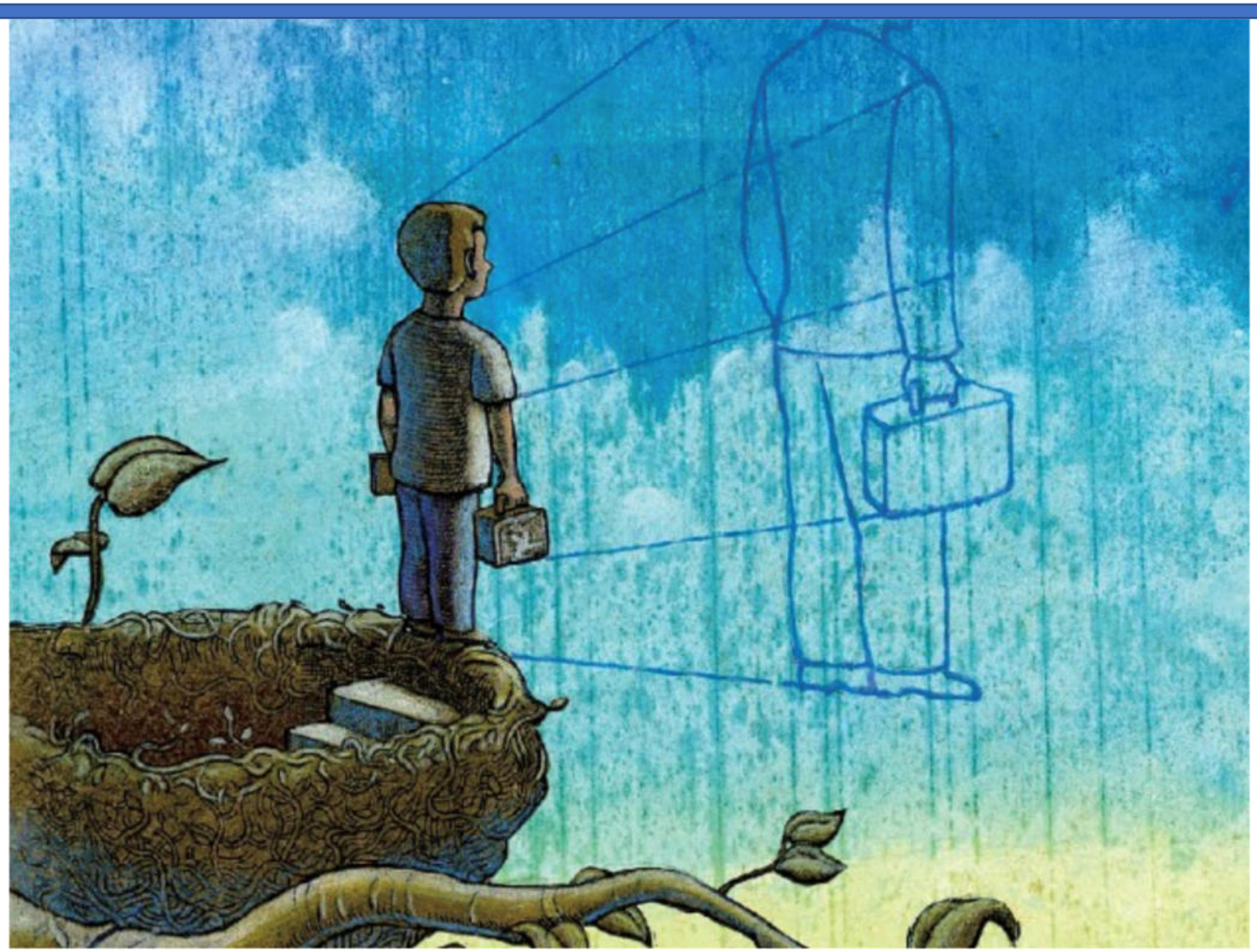
Y Lia,b, Nramozc, E Derringtond J-C Dreherd; Progress in Neuropsychopharmacology & Biological psychiatry 2020

Hormonal responses in gambling versus alcohol abuse: A review of human T studies

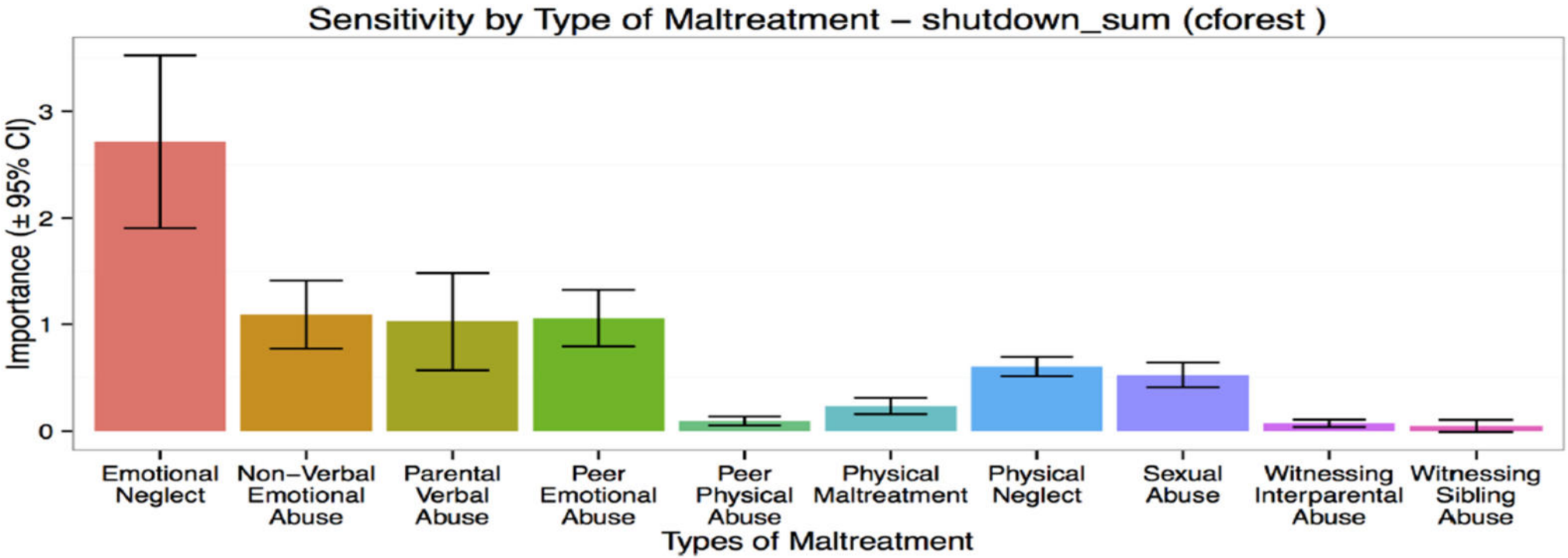


Y Lia,b, Nramozc, E Derringtond J-C Dreherd; Progress in Neuropsychopharmacology & Biological psychiatry 2020

INTERVENTO PRECOCE

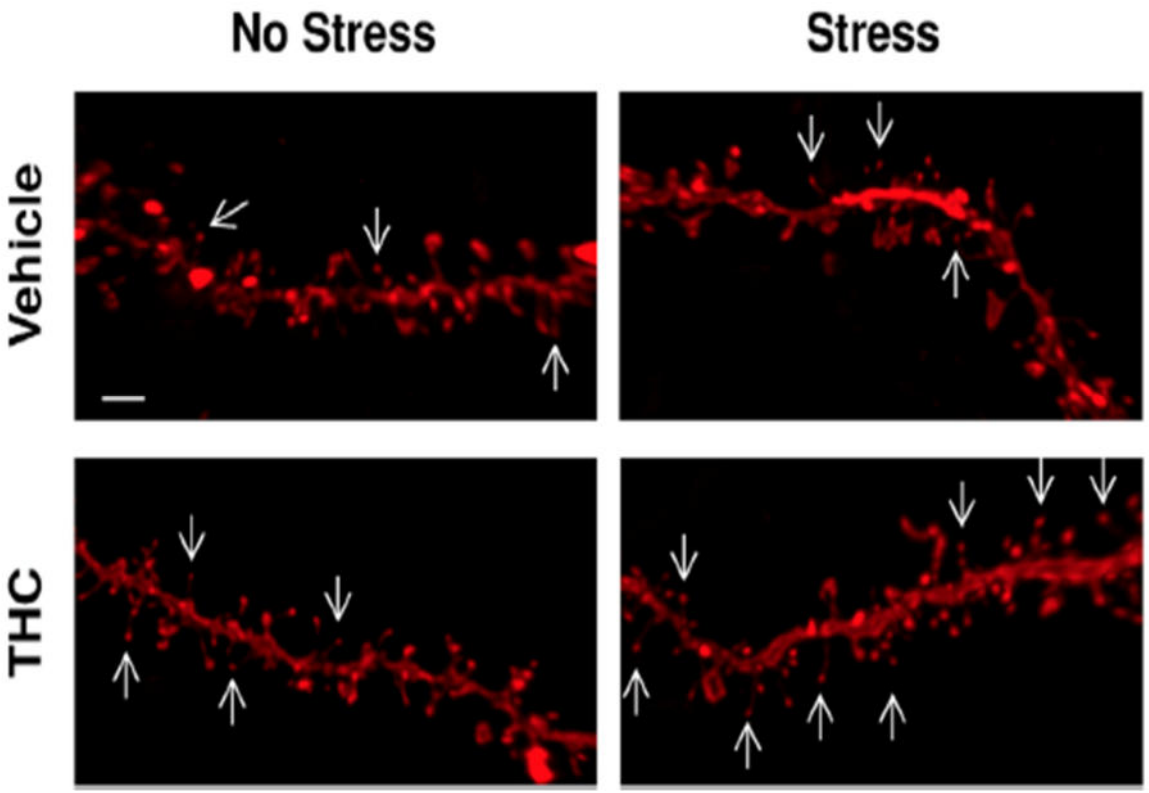


Type and timing of childhood maltreatment and severity of shutdown dissociation in patients with schizophrenia spectrum



I. Schalinski, M. H Telcher; Plos one; May 2015

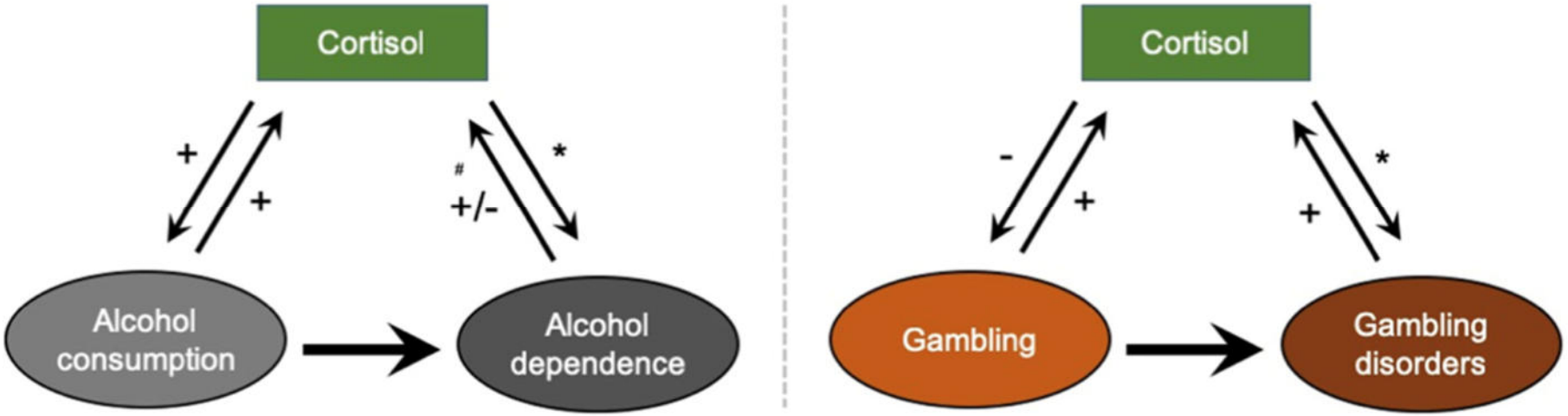
Concomitant THC and stress adolescent exposure induces impaired fear extinction and related neurobiological changes in adulthood



- Gli adolescenti che assumono THC e soggetti a stress presentano attacchi di panico e fobia sociale in età adulta
- Questo è associato ad uno squilibrio dei livelli plasmatici di corticosterone e ad una ridotta attività dell'amigdala
- L'aumento di corticosterone ha indotto una ipertrofia dendritica dei neuroni BLA e conseguente aumento attacchi di panico e fobia sociale in età adulta

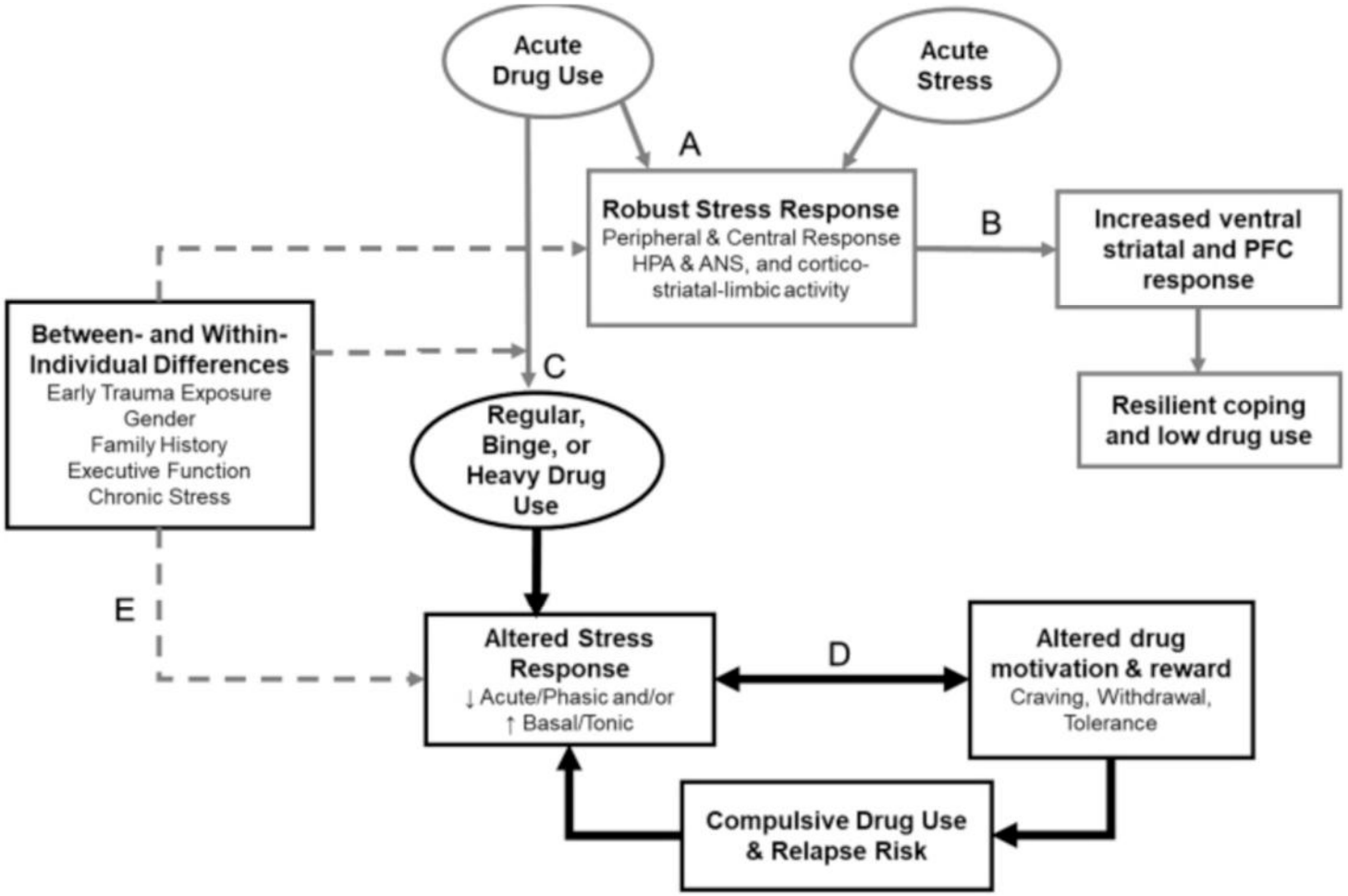
Rocio Saravia, et al; Neuropharmacology 2019

Hormonal responses in gambling versus alcohol abuse: A review of human T studies



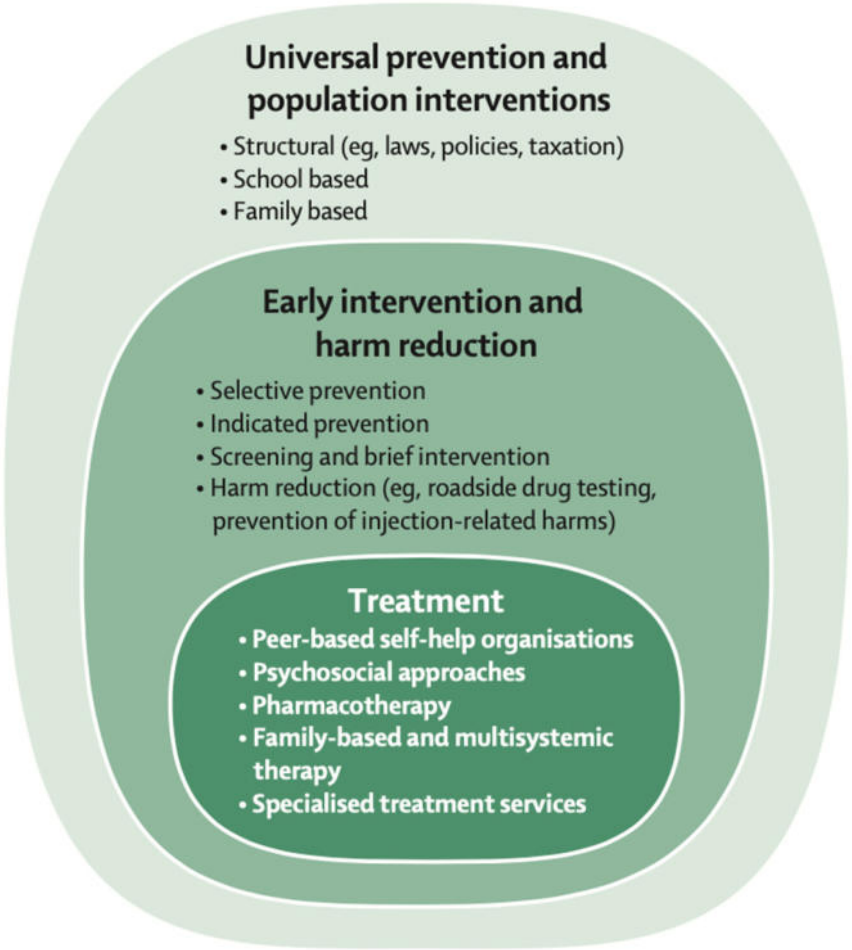
Y Lia,b, Nramozc, E Derringtond J-C Dreherd; Progress in Neuropsychopharmacology & Biological psychiatry 2020

Drug-induced stress responses and addiction risk and relapse



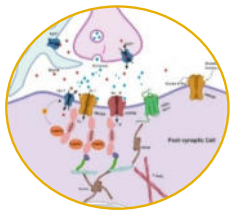
S E Wemm, R Sinha; Neurobiology of Stress 2019

Prevention, early intervention, harm reduction, and treatment of substance use in young people

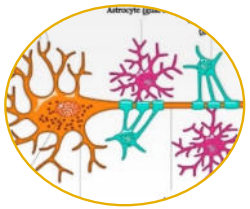


Emily Stockings et al; Lancet Psychiatry 2016

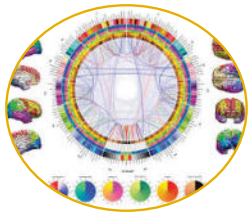
Schizofrenia Resistente Al Trattamento



Ipofunzione NMDA



Cellule gliali



Difetti di connettività

Genetica

SCHIZOFRENIA AD ESORDIO PRECOCE (EOS)

Esordio < 12 anni (COS/VeOS) prevalenza 0,04%

Esordio 13-18 anni (AdOS) prevalenza 0,5%

- Peggiore adattamento premorboso
- Maggiore durata di sintomi psicotici non trattati
- Abbandono prematuro degli studi
- Esiti a lungo termine peggiori
- Gravi deficit cognitivi
- Più alti tassi di suicidio e aggressività

84% sono resistenti al primo episodio

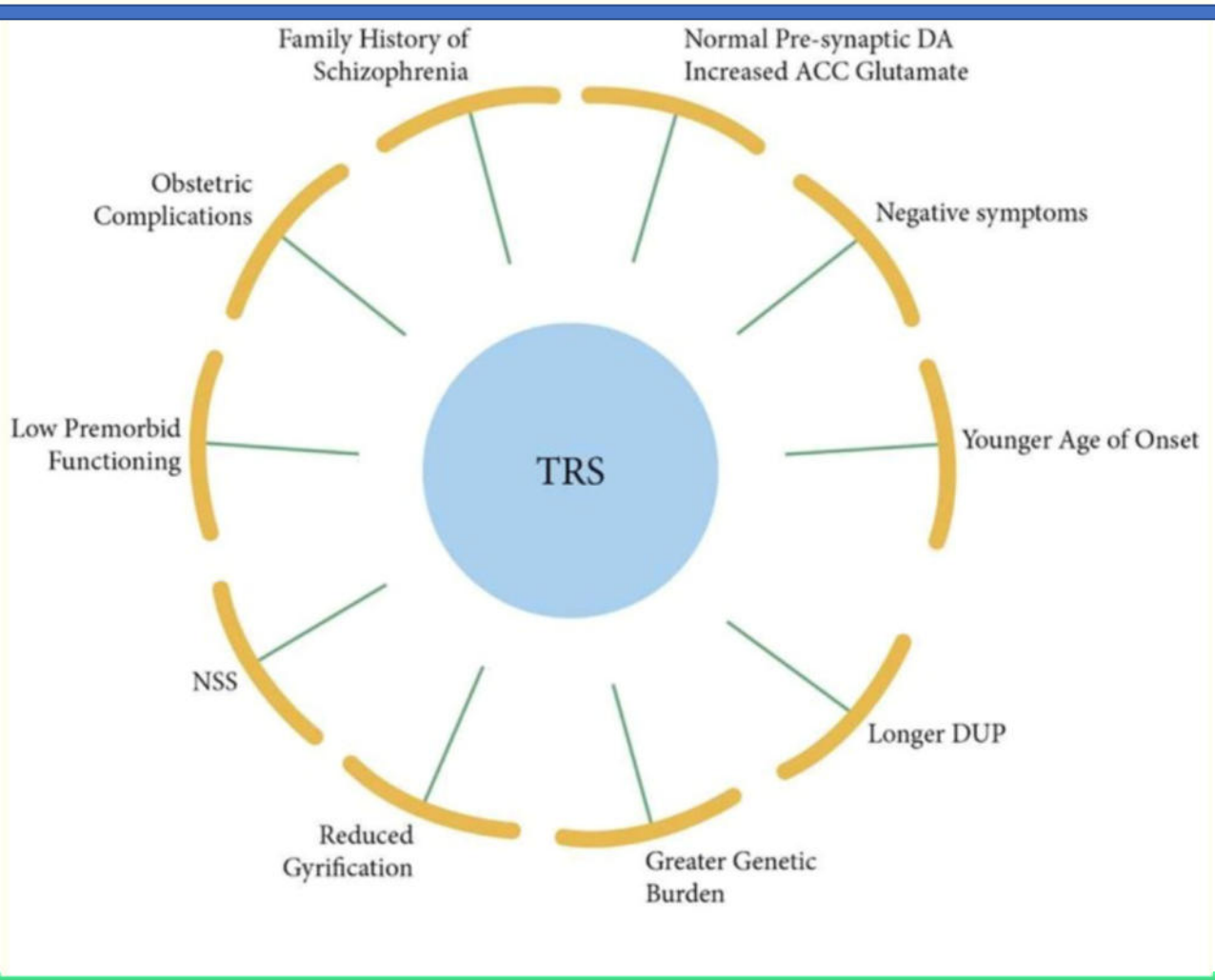
SCHIZOFRENIA RESISTENTE AL TRATTAMENTO (TRS)

25-30% dei soggetti affetti da schizofrenia

- Sintomi negativi più severi
- Maggiori deficit cognitivi
- Anomalie della morfologia cerebrale
- Alterazione dell'integrità della sostanza bianca
- Non risposta ai trattamenti convenzionali
- Segni Neurologici Sfumati più evidenti

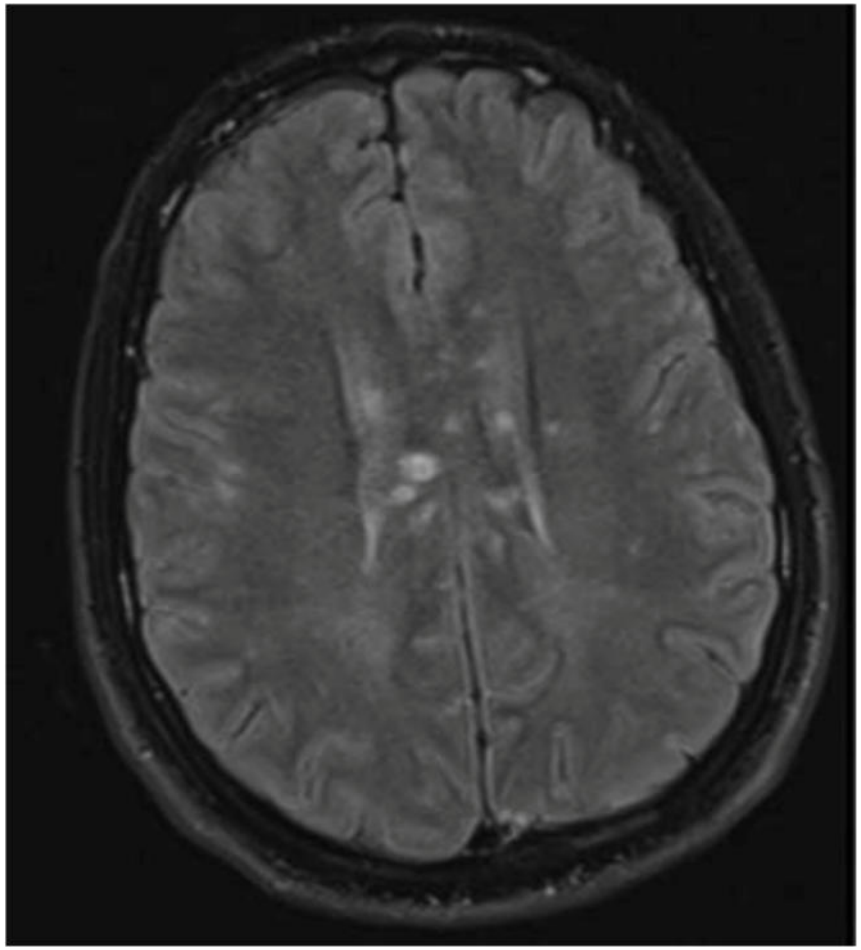
A Demjaha et al; Psychol Med 2017

Clinical Course, Neurobiology and Therapeutic Approaches to Treatment Resistant Schizophrenia. Toward an Integrated View



C Cheuk-Yan Leung, R Gadelrab, C U Ntephe, P K. McGuire, and A Demjaha Frontiers in Psychiatry 2019

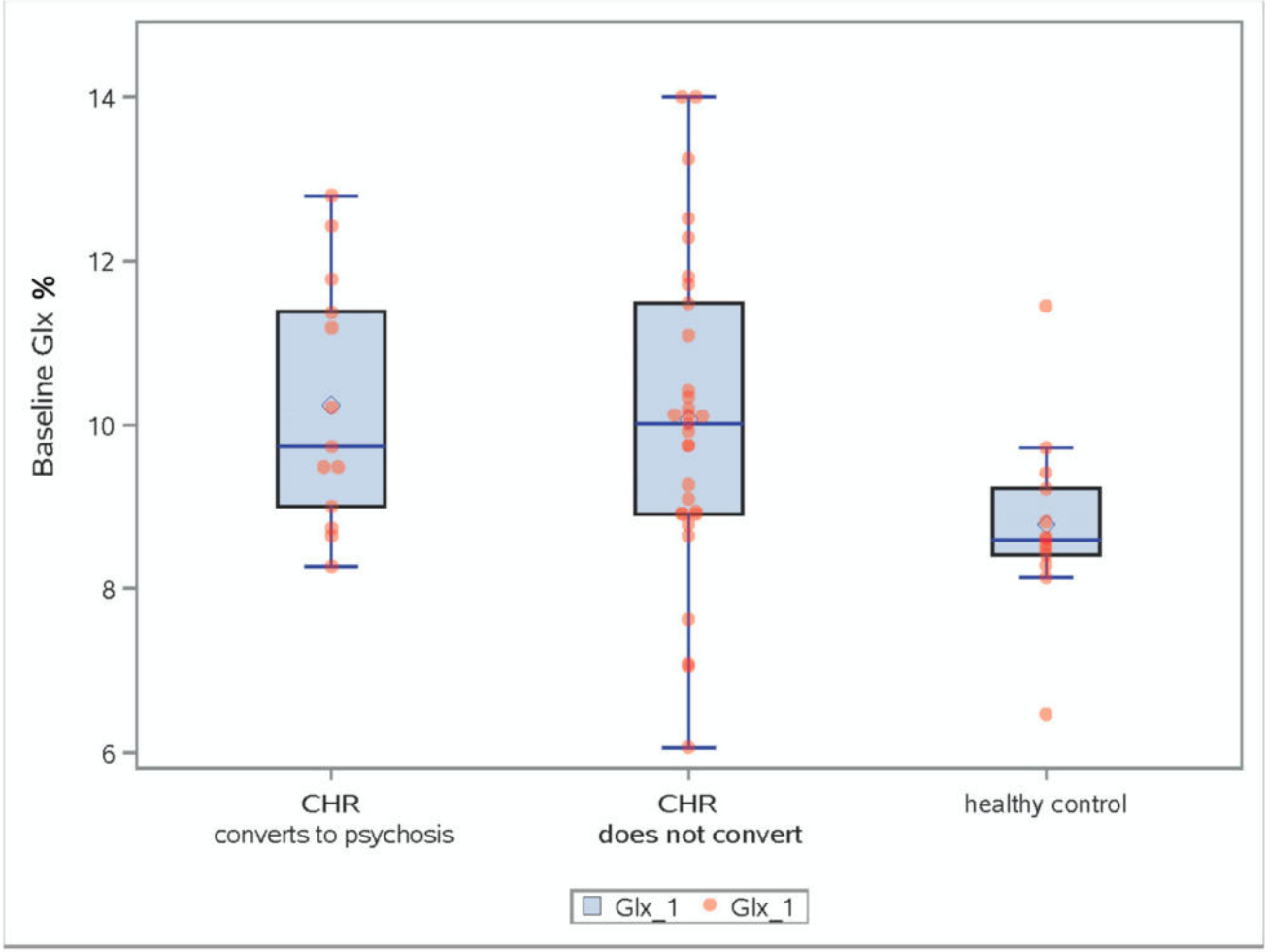
Autoimmune-Mediated Psychosis: A Case Of Susac Syndrome in a Drug user



- Paziente di 23 anni da 3 anni storia di dipendenza da cannabis e psicostimolanti. Familiarità negativa per malattie psichiatriche o autoimmuni. Presenza di Deliri paranoidei, allucinazioni uditive e agitazione psicomotoria

- Lesioni multiple iperintense con coinvolgimento della materia bianca e grigia. La maggior parte delle lesioni sono localizzate nel corpo calloso

Hippocampal Pathology in Clinical High-Risk Patients and the Onset of Schizophrenia

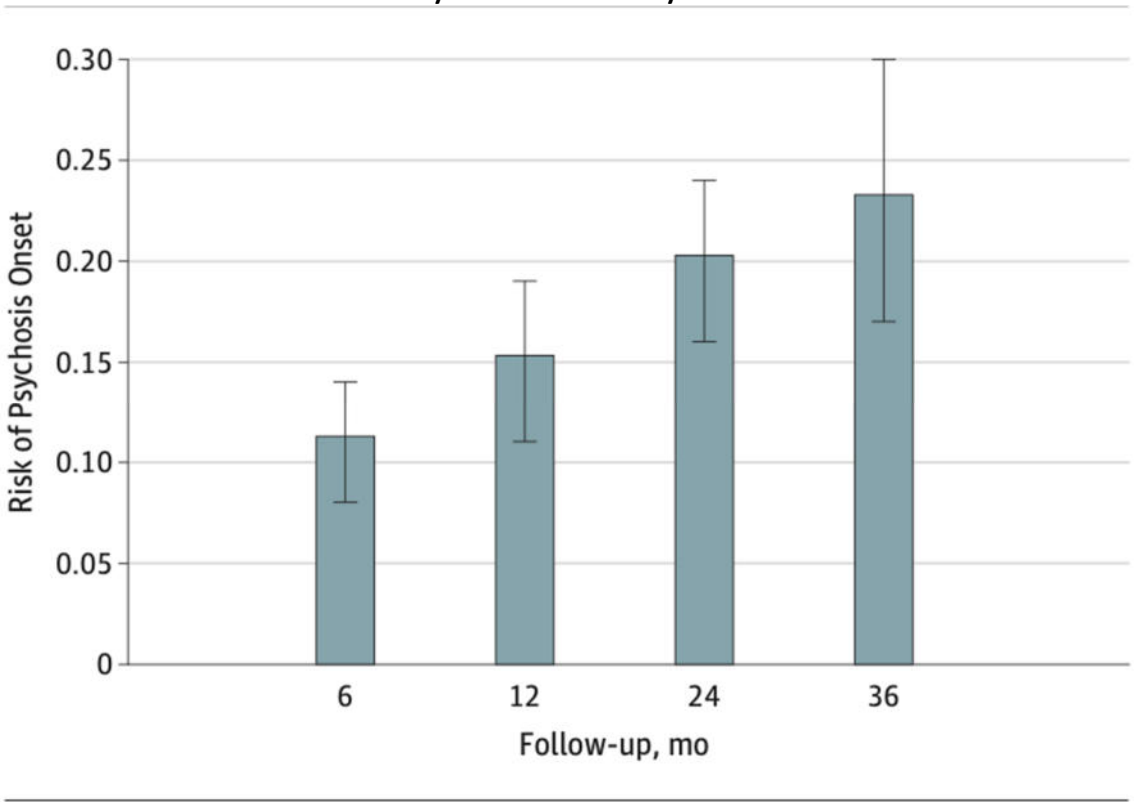


Frank A. Provenzano et al; Biological Psychiatry 2019

Clinical Validity of DSM-5 Attenuated Psychosis Syndrome

Advances in Diagnosis, Prognosis, and Treatment

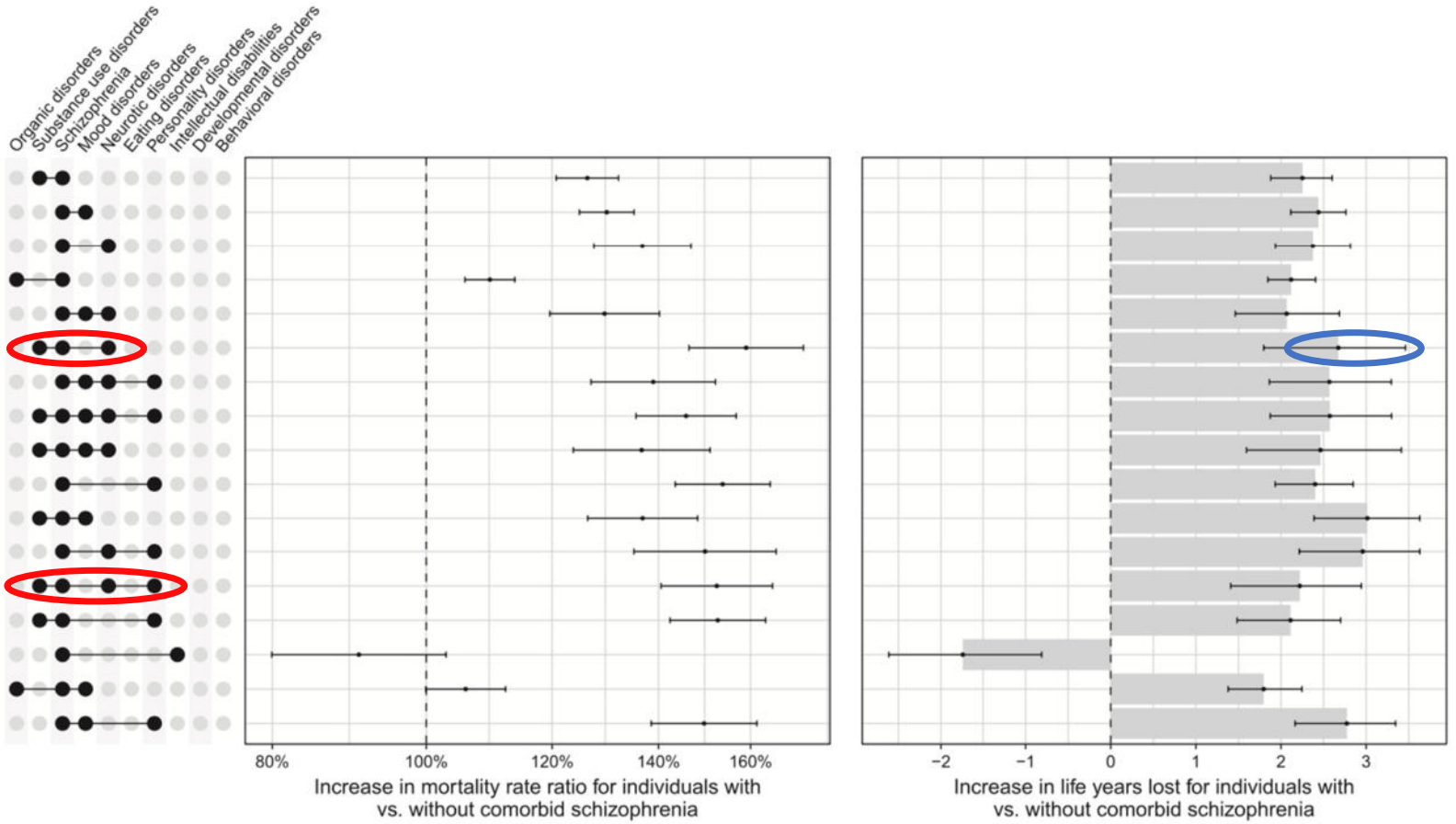
Cumulative Risk of Psychosis Onset Using *DSM-5* Attenuated Psychosis Syndrome or Attenuated Positive Symptom Syndrome Criteria Defined by the Structured Interview for Psychosis-Risk Syndromes



G S de Pablo; A Catalan; P Fusar-Poli; JAMA Psychiatry 2019

Nature and prevalence of combinations of mental disorders and their association with excess mortality in a population-based cohort study

We designed a population-based cohort study including all 7,505,576 persons living in Denmark at some point between January 1995 and December 2016.



Oleguer Plana-Ripoll; World Psychiatry 2020

Suggested physical and laboratory assessments for patients with schizophrenia

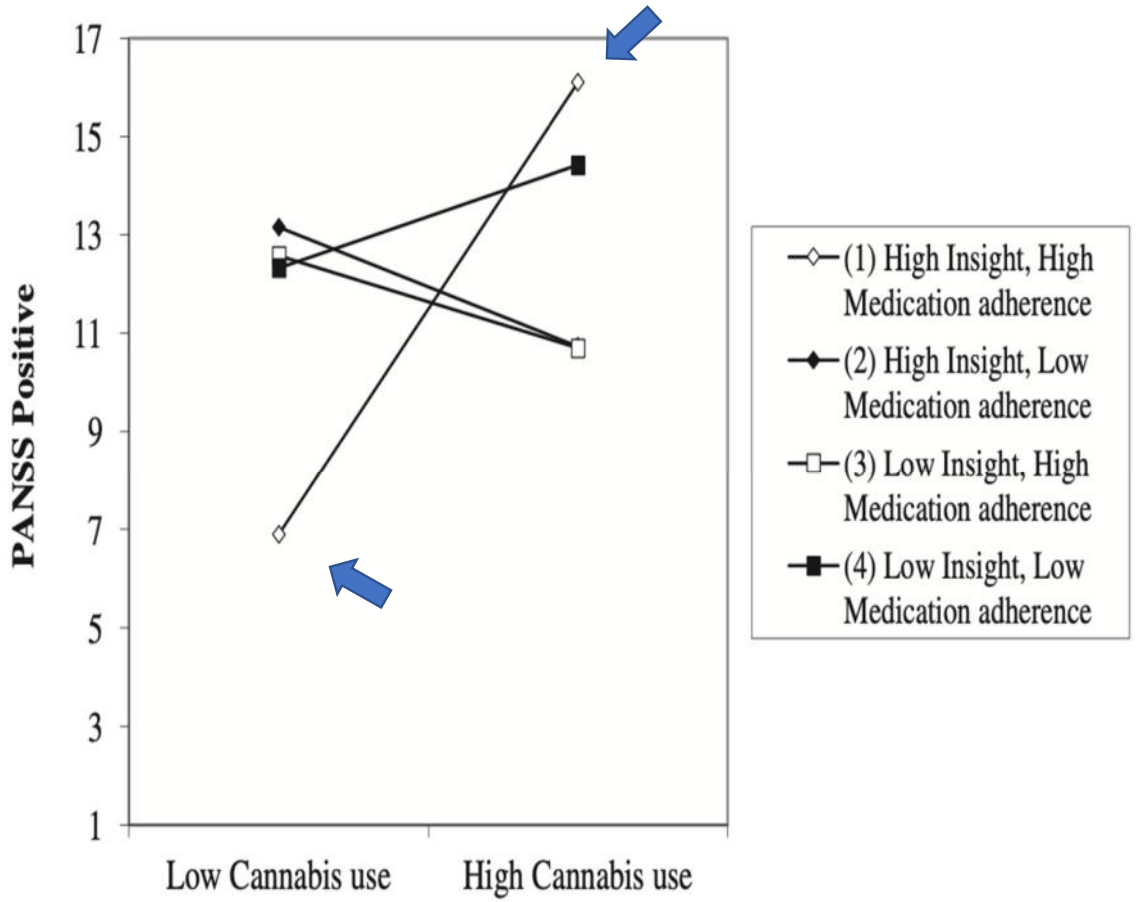
Assessments related to other specific side effects of treatment		
Diabetes[f]	Screening for diabetes risk factors,[g] fasting blood glucose[h]	Fasting blood glucose or hemoglobin A1C at 4 months after initiating a new treatment and at least annually thereafter[h]
Hyperlipidemia	Lipid panel[i]	Lipid panel[i] at 4 months after initiating a new antipsychotic medication and at least annually thereafter
Metabolic syndrome	Determine whether metabolic syndrome criteria are met[j]	Determine whether metabolic syndrome criteria are met[j] at 4 months after initiating a new antipsychotic medication and at least annually thereafter
QTc prolongation	ECG before treatment with chlorpromazine, droperidol, iloperidone, pimozide, thioridazine, or ziprasidone[k] or in the presence of cardiac risk factors[l]	ECG with significant change in dose of chlorpromazine, droperidol, iloperidone, pimozide, thioridazine, or ziprasidone[k] or with the addition of other medications that can affect QTc interval in patients with cardiac risk factors[l] or elevated baseline QTc intervals
Hyperprolactinemia	Screening for symptoms of hyperprolactinemia[m] Prolactin level, if indicated on the basis of clinical history	Screening for symptoms of hyperprolactinemia at each visit until stable, then yearly if treated with an antipsychotic known to increase prolactin[m] Prolactin level, if indicated on the basis of clinical history

PERSONALIZZAZIONE DELLE CURE

PSICOSI SINTETICA

- E’ un paziente diverso dallo psicotico classico
- Va stabilizzata l’astinenza
- Rientrato il delirium
- Ridotta la sintomatologia psicotica
- Utilizzare, solo se fortemente necessario, la contenzione fisica
- Stabilire una relazione contrattuale con il paziente
- Contattare il SerD

Moderating role of cannabis use between insight and depression in early psychosis

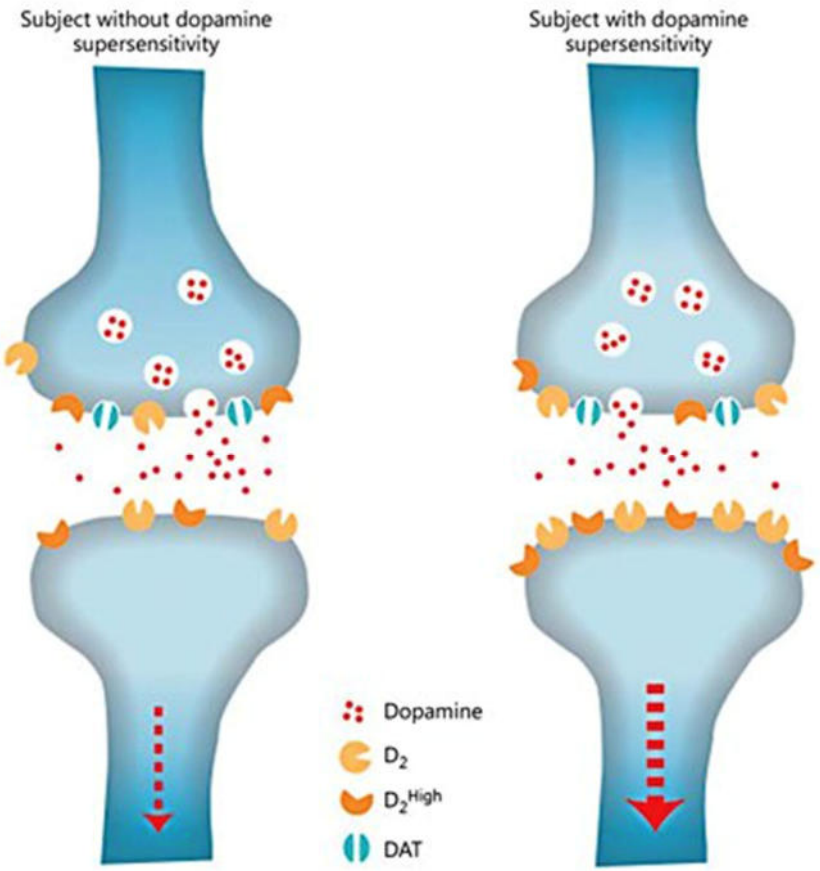


Pazienti con alto livello di insight ed elevata aderenza ai farmaci, ma con un alto consumo di cannabis tendono ad avere un punteggio della PANSS più alto

La PANSS diminuisce significativamente nei pazienti con un alto livello di insight, un alta aderenza ai farmaci ma con un basso consumo di cannabis

Julien Elowe et al; Schizophrenia Research 2019

Antipsychotic-Induced Dopamine Supersensitivity Psychosis: Pharmacology, Criteria, and Therapy



- L'esposizione cronica a farmaci antipsicotici con un forte blocco D2 aumenta il numero di recettori D2 più prominentemente nel caudato-putamen e nel nucleo accumbens causando una supersensitività.

- I pazienti identificati come affetti da SP presentano psicosi da rimbalzo, tolleranza agli effetti terapeutici degli AP e TD.

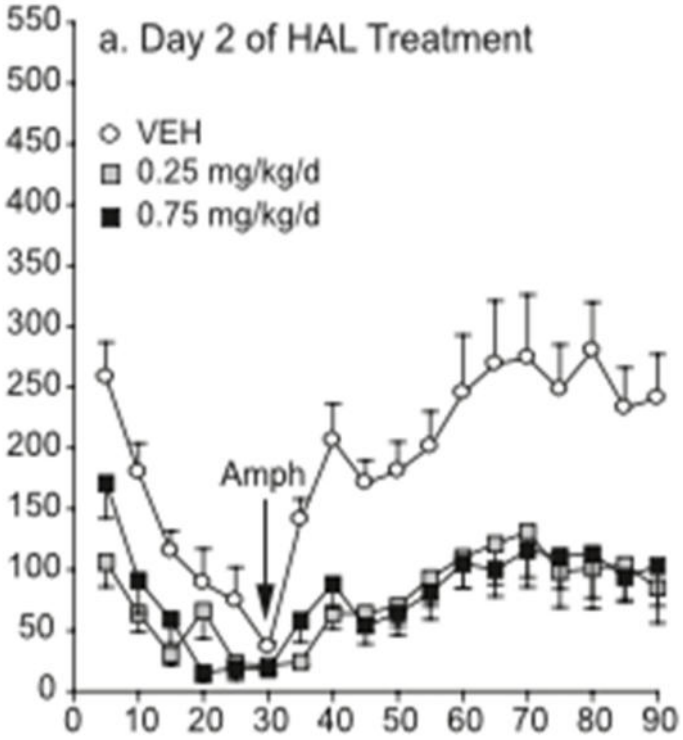
G S de Pablo; A Catalan; P Fusar-Poli; JAMA Psychiatry 2019

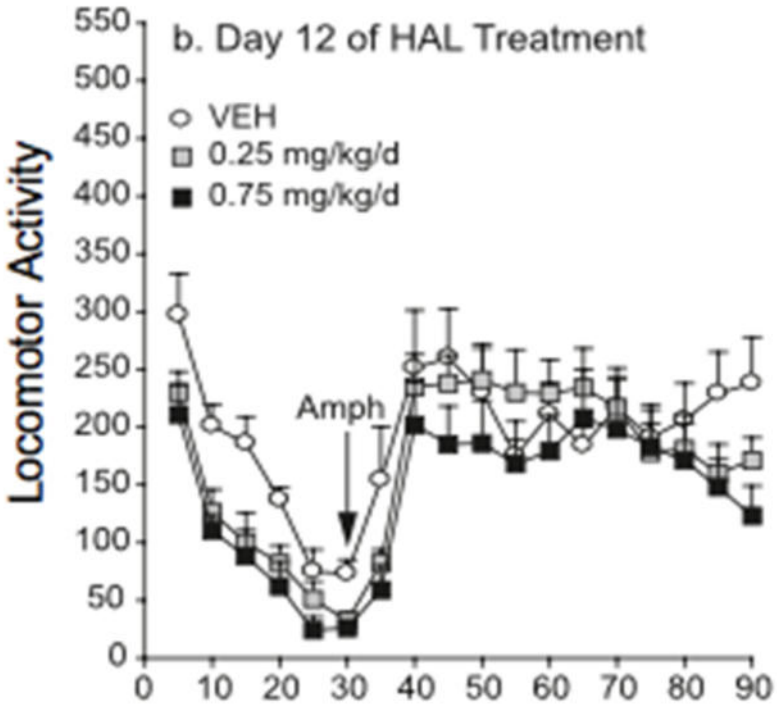
Response, tolerability and futility thresholds for select antipsychotics

	Response Threshold (ng/ml)	Tolerability Threshold (ng/ml)	Point of Futility (ng/ml)
Haloperidol	3–5	18–20	30
Fluphenazine	0.8–1.0	2.7–2.8	4.0
Clozapine	350	800–1000	>1000
Risperidone + 9-OH Risperidone	??	??	112
Olanzapine	23.2	176	200

Jonathan M. Meyer; CNS Spectrums 2019

Dopamine Supersensitivity reakthrough during Ongoing Antipsychotic Treatment Leads to Treatment Failure over Time





A-N Samaha, P Seeman, J Stewart, H Rajabi, and S Kapur; The Journal of Neuroscience, 2007

Canadian Network for Mood and Anxiety Treatments (CANMAT) And International Society for Bipolar Disorders (ISBD) 2018 Guidelines for the management of patients with bipolar disorder

TABLE 11 Level of evidence and recommendations for short-term pharmacological management of agitation[a]

Level of recommendation	Agent	Formulation	Level of evidence	Dose range of studies[b]	
				Single dose	Max/24 h
First-line	Aripiprazole	IM	2	9.75 mg	15 mg
	Lorazepam	IM	2	2 mg IM	
	Loxapine	Inhaled	1	5 mg	10 mg
	Olanzapine	IM	2	2.5 mg	10 mg[c]
Second-line	Asenapine	Sublingual	3	10 mg	
	Haloperidol	IM	3	5 mg	15 mg
	Haloperidol + midazolam	IM	3	2.5 mg (haloperidol) + 7.5 mg (midazolam)	5 mg (haloperidol) + 15mg (midazolam)
	Haloperidol + promethazine	IM[e]	3	2.5 mg (haloperidol) + 25 mg (promethazine)	5 mg (haloperidol) + 50 mg (promethazine)
	Risperidone	ODT[e]	3	2 mg	4 mg
	Ziprasidone	IM[e]	3	2 mg	20 mg
Third-line	Haloperidol	PO[d]	4	5 mg	15 mg
	Loxapine	IM	4	N/A	
	Quetiapine	PO[d]	4	Mean (SD) = 486.7 (317.2) mg/day	
	Risperidone	PO[e]	4	2 mg	

INTERVENTO IN ACUTO NEL PAZIENTE CON USO DI SOSTANZE

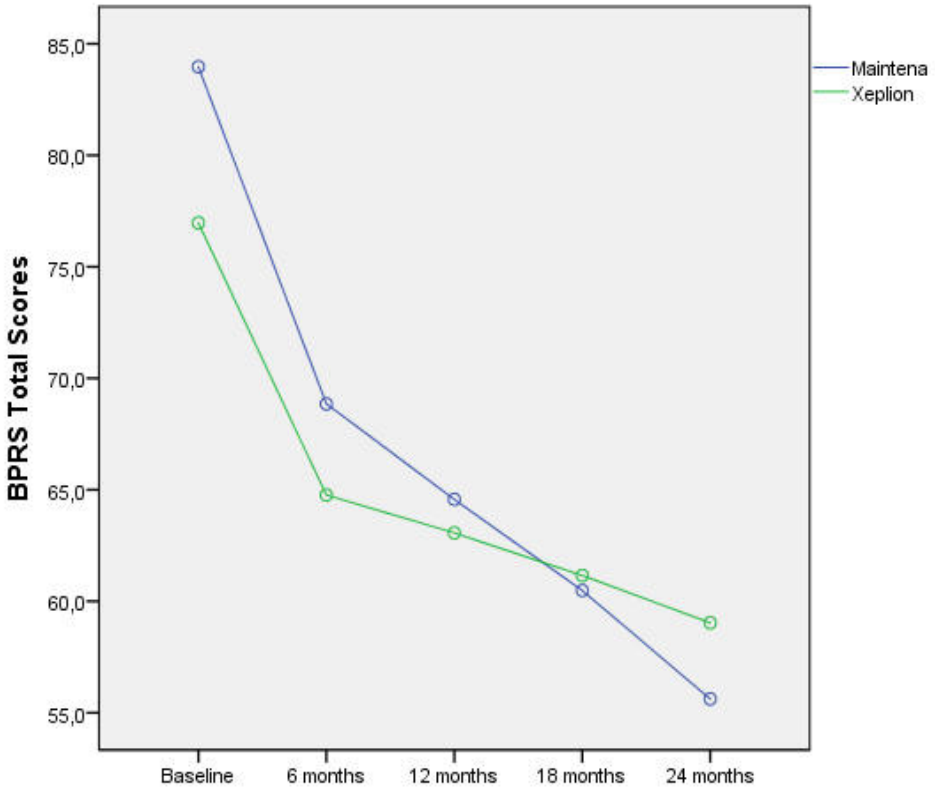
- Somministrare Lorazepam 4 mg fl im, in alternativa Delorazepam 5 mg im
- Somministrare Aripiprazolo fl i.m, in alternativa Clorpromazina 25 mg fl im
- Accesso venoso : esami ematici;
- Soluzione fisiologica con sodio valproato fl in 100 di fisiologica anche 4 volte al dì
- Clonidina 5 mg cerotto ogni 5 giorni
- Soluzione fisiologica con Tiapride fl 2 volte al dì
- Soluzione fisiologica Trazodone fl 2 volte al dì
- N-Acetilcisteina 2400 mg per 10 giorni poi 1800 mg
- Parametri vitali;
- Esame obiettivo fisico;
- ECG;
- Idratazione

Aripiprazole i.m. and p.o. in acute patients with agitation and nonadherence

Day	Aripiprazole vial 9.75 mg (=1.3 mL) i.m.	Aripiprazole tablet 10 mg p.o.	Aripiprazole monohydrate 400 mg i.m. (LAI)	Morning	Afternoon	Evening
1-6	×			×	×	×
7-10	×	●		×	●	×
11-13	×	●		×	●	●
14		●	●		●	●
15-28		●			●	●
29-43						
44			●			

G Giordano, L Tomassini, I Cuomo, E Amici, F Perrini, G Callovini, A Carannante, G D. Kotzalidis, S De Filippis; Frontiers in Psychiatry 2020

EFFICACIA DI ARIPIPRAZOLO E PALIPERIDONE SULLA PSICOPATOLOGIA GENERALE



La psicopatologia generale misurata con la BPRS decresce significativamente ($p>0,001$) e in maniera progressiva a 6, 12, 18 e 24 mesi dall'inizio della terapia con Aripiprazolo o Paliperidone

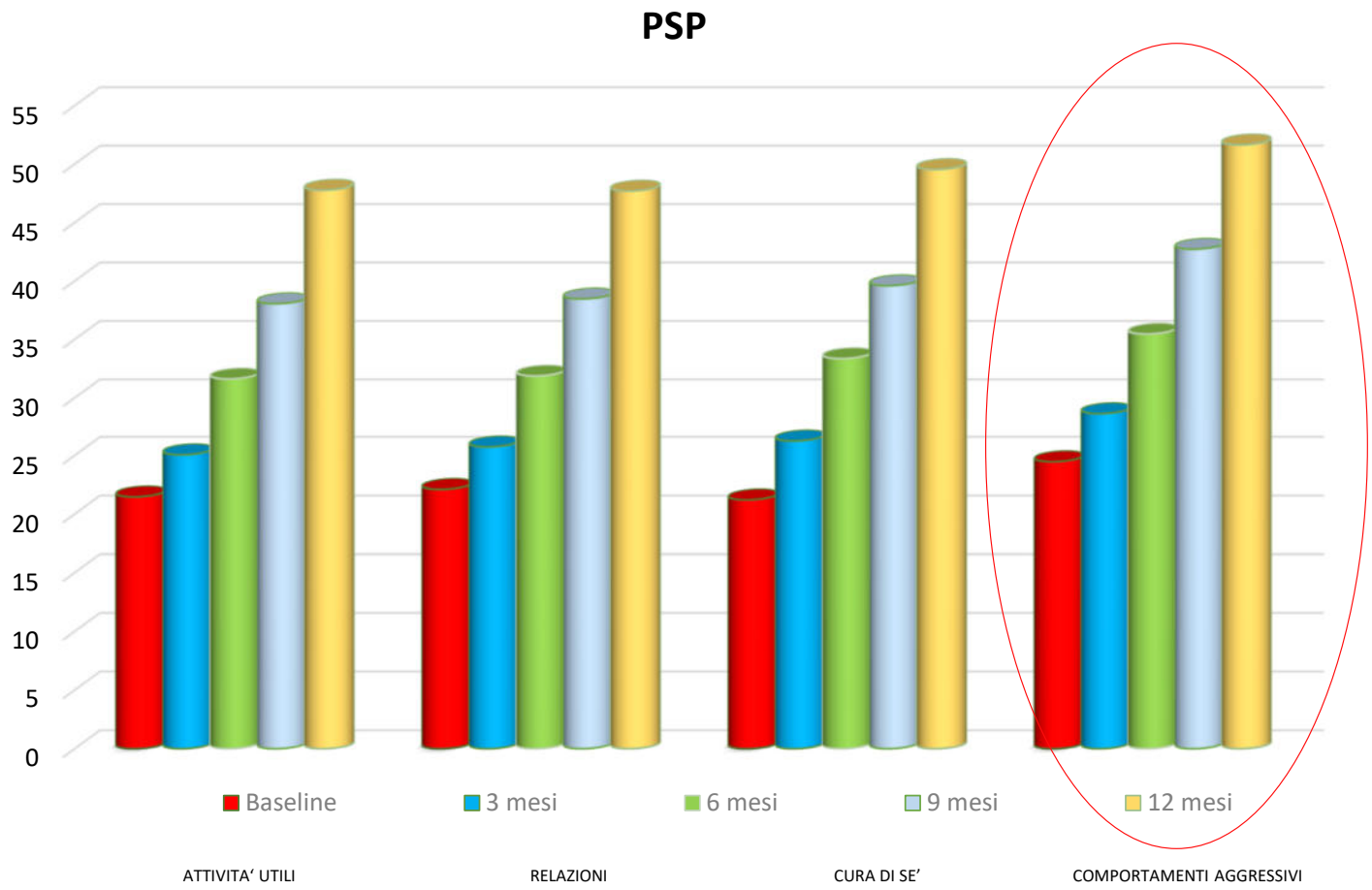
I pazienti trattati con Aripiprazolo riportano una riduzione maggiore della psicopatologia generale ($p<0,005$)

S. De Filippis, E. Amici, G. Callovini, G. Giordano, I. Cuomo, F. Perrini, A. Carannante, L. Tomassini, G. Kotzalidis; Ecnp 2019

Long-acting injectable antipsychotic medications: pharmacological characteristics

	Trade name	Time to peak plasma level	Time to steady state	Elimination half-life	Comments[a]
First-generation antipsychotics					
Fluphenazine	Prolixin Decanoate	8–10 hours	2 months	6–9 days for single injection and 14–26 days for multiple doses	Major CYP2D6 substrate
Haloperidol	Haldol Decanoate	6 days	3–4 months	21 days	Major CYP2D6 and CYP3A4 substrate
Second-generation antipsychotics					
Aripiprazole monohydrate	Abilify Maintena	4 days (deltoid); 5–7 days (gluteal)	By fourth dose	300 mg: 29.9 days 400 mg: 46.5 days (400 mg) with gluteal injection	Give no sooner than 26 days between injections. Major CYP2D6 and CYP3A4 substrate
Aripiprazole lauroxil	Aristada Initio	16–35 days (median 27 days)	Not applicable	15–18 days	Not interchangeable with Aristada because of differing pharmacokinetic profiles CYP2D6 and CYP3A4 substrate
Aripiprazole lauroxil	Aristada	Not available	4 months	53.9–57.2 days	Not interchangeable with Aristada Initio because of differing pharmacokinetic profiles CYP2D6 and CYP3A4 substrate
Olanzapine	Zyprexa Relprevv	7 days	~3 months	30 days	Major CYP1A2 substrate
Paliperidone palmitate	Invega Sustenna	13 days	2–3 months	25–49 days; increased in renal disease	CrCl 50–79 mL/minute: initiate at 156 mg on day 1, followed by 117 mg 1 week later, both administered in the deltoid muscle. Maintenance dose of 78 mg. Use not recommended in patients with CrCl <50 mL/minute. Substrate of P-glycoprotein/ABCB1
Paliperidone palmitate	Invega Trinza	30–33 days	Not applicable	84–95 days with deltoid injection; 118–139 days with gluteal injection; increased in renal disease	Do not use in patients with CrCl <50 mL/minute. Substrate of P-glycoprotein/ABCB1

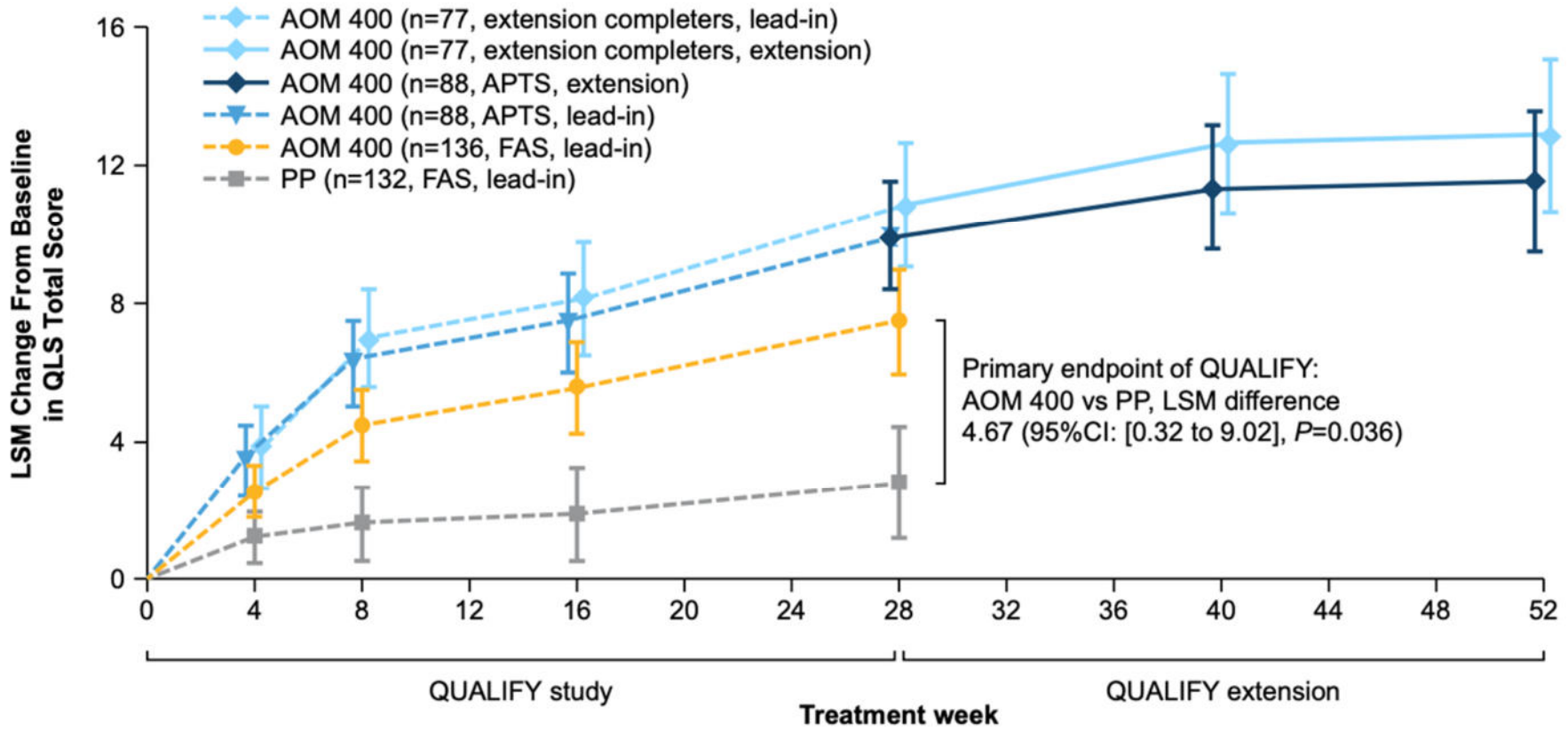
ARIPIPRAZOLO LAI SUL FUNZIONAMENTO SOCIALE E PERSONALE NEI PAZIENTI CON ESORDIO PSICOTICO



Il funzionamento sociale e personale migliora progressivamente a 3, 6, 9 e 12 mesi dall'inizio della terapia con Aripiprazolo nei pazienti con esordio psicotico

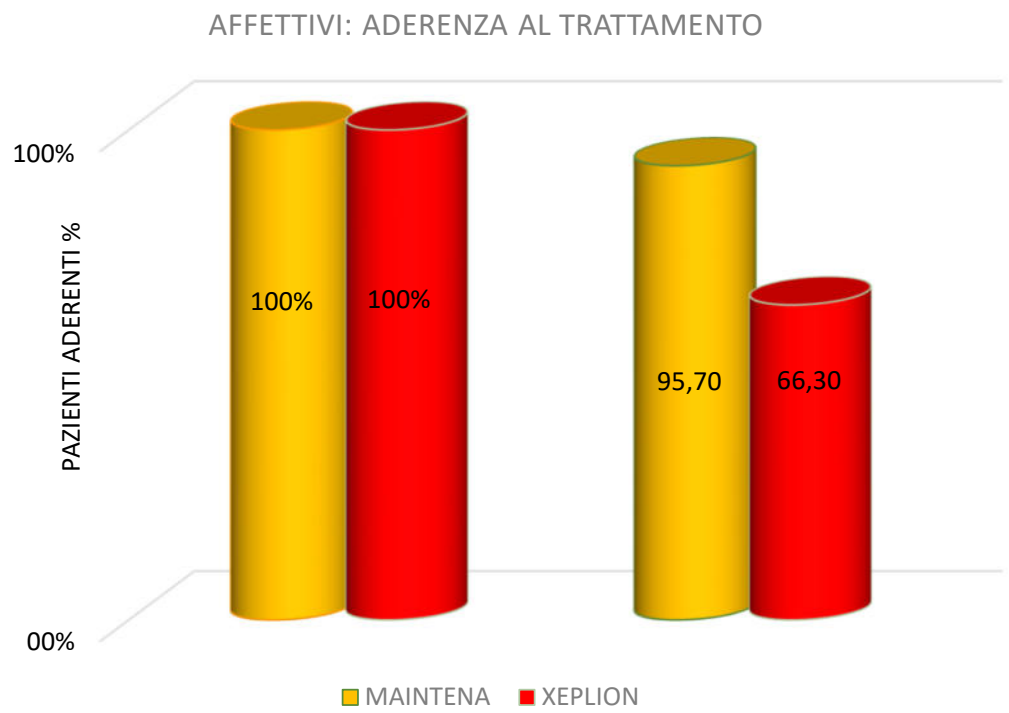
G Giordano, L Tomassini, I Cuomo, E Amici, F Perrini, G Callovini, A Carannante, G D. Kotzalidis, S De Filippis; Frontiers in Psychiatry 2020

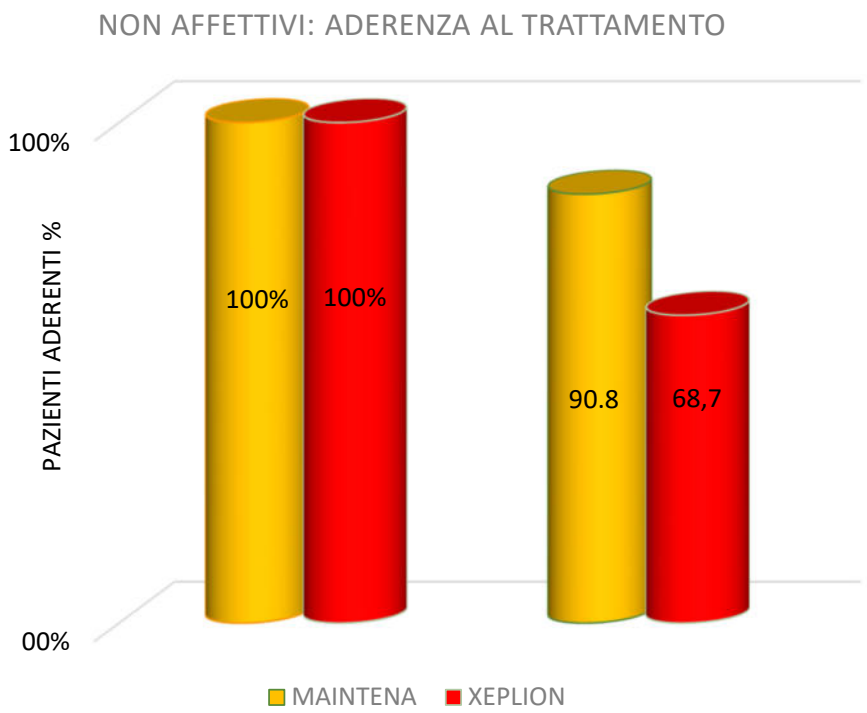
Long-term effectiveness of aripiprazole once-monthly for schizophrenia is maintained in the QUALIFY extension study



D. Naber et al; Schizophrenia Research 2017

Aripiprazolo e paliperidone: aderenza al trattamento in pazienti affettivi e non affettivi





I Cuomo, G. D. Kotzalidis, S. de Persis, D. Piacentino, F. Perrini, E. Amici, S. De Filippis; Neuropsychiatric Disease and Treatment 2018

APA *recommends* that patients with schizophrenia receive psychoeducation

Obiettivi Primari

- Promuovere un'adeguata coscienza di malattia
- Riconoscere precocemente i sintomi
- Migliorare l'aderenza al trattamento farmacologico

Obiettivi Secondari

- Accettazione della malattia
- Responsabilizzazione del paziente
- Gestione dello stress
- Regolarizzazione dello stile di vita
- Riduzione dello stigma
- Riduzione del senso di isolamento
- Aumento del benessere generale