IDENTIFICAREA SI RAPORTAREA ERORILOR DE ADMINISTRARE A MEDICAMENTELOR

EFECTE ADVERSE SI INTERACTIUNI ALE MEDICATIEI PSIHOTROPE VERSUS EFECTE NEUROPSIHICE INDUSE DE MEDICATIA NON-PSIHOTROPA

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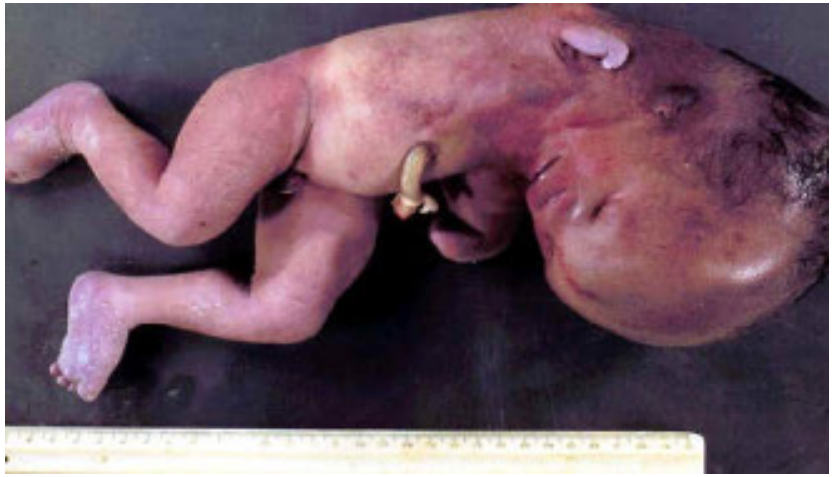
BUCURESTI, 12.12.2018

De la Farmacovigilenta la... competentele psihofarmacologice

sau trecerea de la perspectiva observationala la cea interventionala pentru obtinerea unui act medical de calitate

Drama talidomidei



Anii 1960 > 10000 copii cu malformaţii (amelie şi focomelie)

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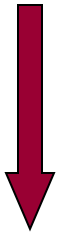
Definiţia Farmacovigilentei

↗ Totalitatea activităţilor de detectare, evaluare, validare şi prevenire a reacţiilor adverse determinate de medicamente



⇗ informaţii asupra siguranţei medicamentelor prin identificarea şi monitorizarea RA care apar după **autorizarea de punere pe piaţă**

RA vs EA

Reacţia adversă

- Reacţie nocivă care apare în urma administrării unui medicament în doze utilizate în mod obişnuit în scop profilactic, curativ sau de diagnostic

Eveniment advers

- Reacţie nocivă determinată de boala pentru care s-a administrat medicamentul, o boală intercurentă (inclusiv infecţie) sau o interacţiune medicamentoasă

(Volume 9 of the Rules Governing Medicinal Products in the European Union)

Obiectivele activităţii de Farmacovigilenta

- detectarea precoce a R.A. şi a I.M. neidentificate în studiile clinice
- stabilirea relaţiilor de cauzalitate între administrarea M şi apariţia R.A.
- monitorizarea frecvenţei R.A. cunoscute (din prospect)
- identificarea factorilor de risc (comorbidităţi)
- analiza datelor
- difuzarea informaţiilor între autorităţile competente şi specialişti

Istoricul Farmacovigilentei

~ Sec. XIX - primele studii metodice asupra RA

~ Anii 1960 - începuturile activitatii de Farmacovigilenta (teratogenitatea talidomidei)

~ Anii 1970- anticoncepţionalele orale şi tromboembolismul venos (controverse epidemiologice)

Ultimile decenii:

1982 → benoxaprofen (necroză hepatică, fotosensibilizare)

2001 → cerivastatina (rabdomioliza)

2003 → troglitazona (toxicitate hepatică)

2010 → sibutramina (efecte adverse cardiovasculare)

R.A. grave

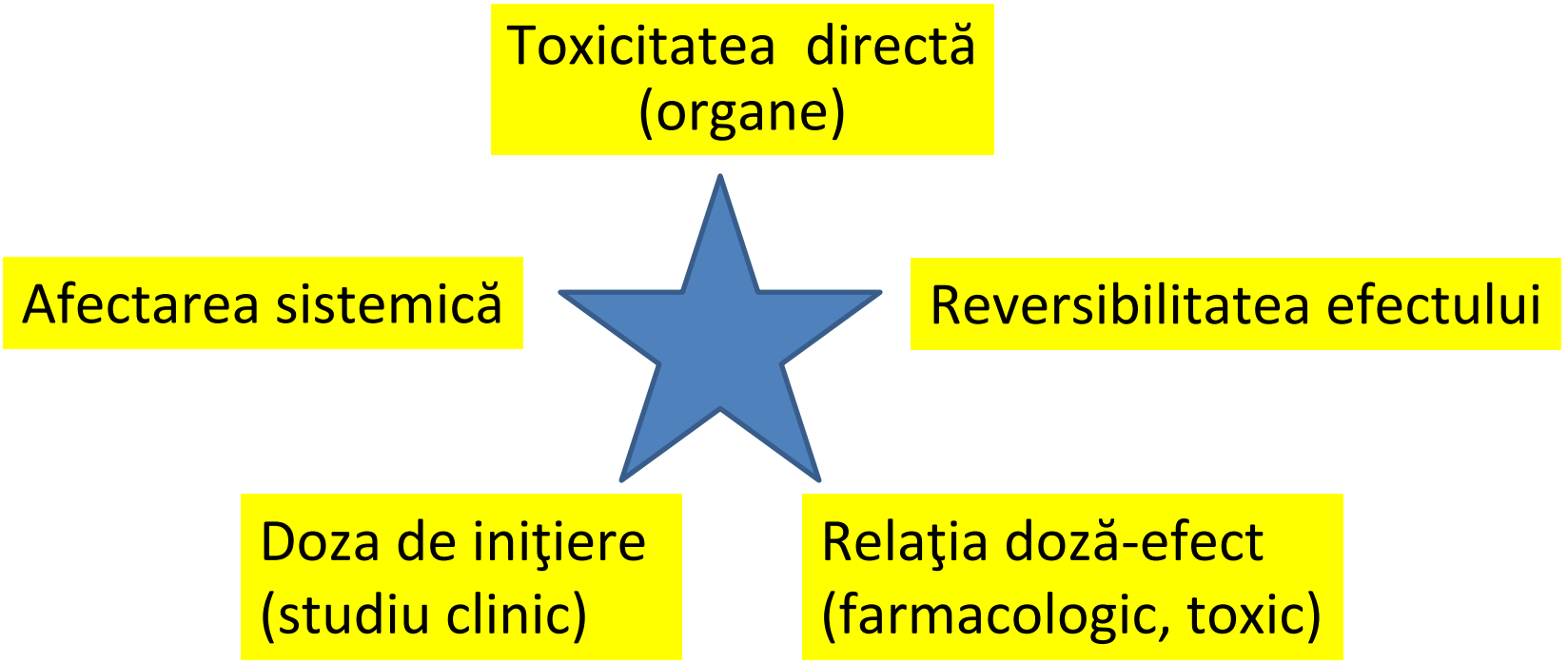
- Se finalizează cu deces sau pun în pericol viaţa
- Conduc la spitalizare prelungită
- Conduc la infirmitate sau malformaţii congenitale

6-7%- RA grave, 0,3%-fatale

Cauze ale morbidităţii ridicate în relaţie cu consumul de medicamente

- Numărul enorm de medicamente prescris
- Creşterea continuă a numărului de noi molecule autorizate
- Lipsa experienţei clinice pentru noile medicamente
- Promovarea ,,agresivă” a noilor produse medicamentoase
- Creşterea numărului de raportări

Studii preclinice pentru determinarea siguranţei



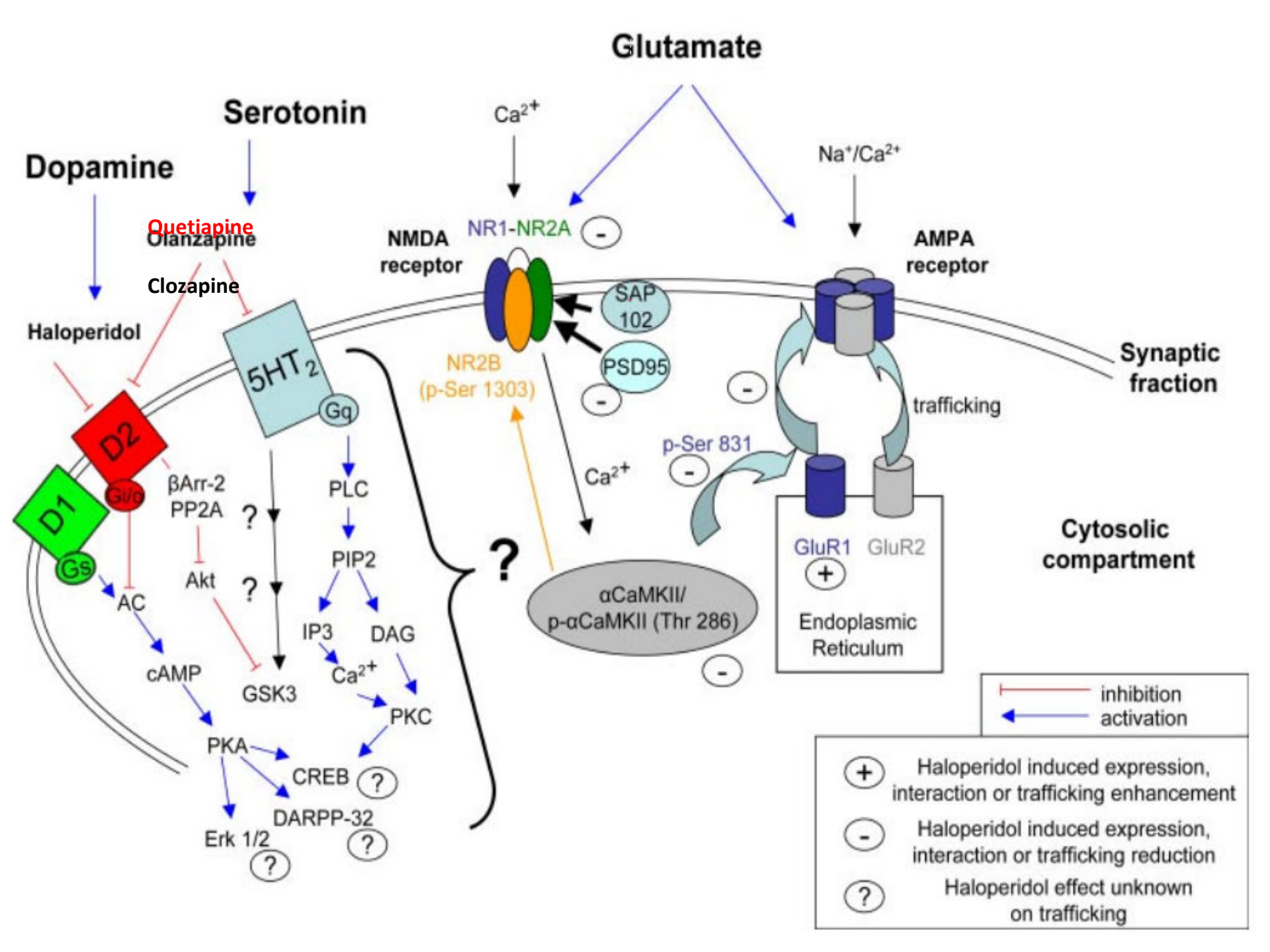
Particularitati ale sigurantei si eficacitatii terapiei in psihofarmacologie

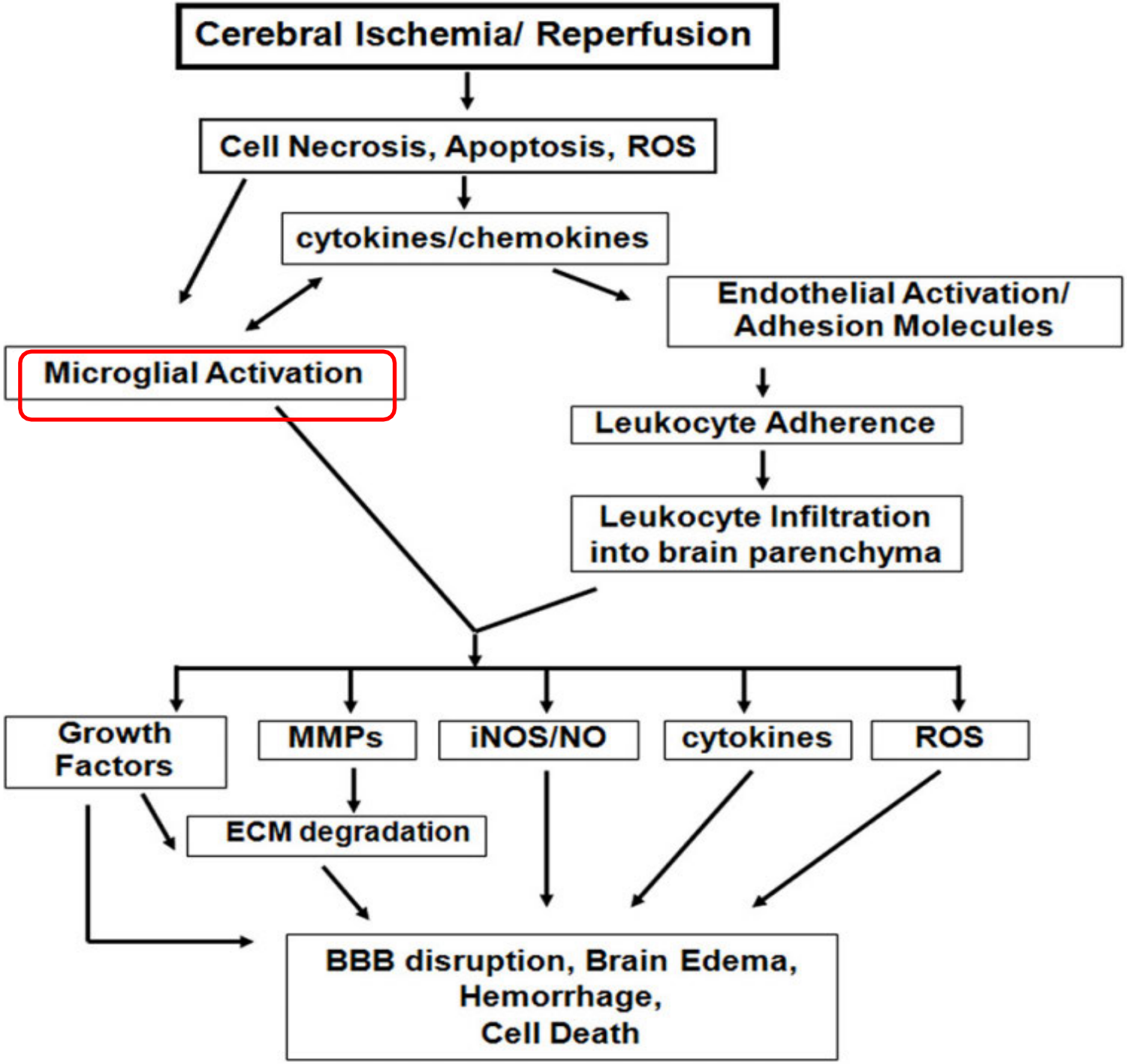
- Integritatea BHE
- Reactia inflamatorie, raportul neuron / activare microgliala
- Calitatea perfuziei sangvine cerebrale
- Integritatea functionala hepatica
- Suport metabolic cerebral

Neuropathology and Applied Neurobiology (2009), **35**, 132–146 doi: 10.1111/j.1365-2990.2008.01005.x

Review: Role of developmental inflammation and blood–brain barrier dysfunction in neurodevelopmental and neurodegenerative diseases

H. B. Stolp and K. M. Dziegielewska


Glutamate
Serotonin
Dopamine
Ca2+
Na+/Ca2+
Quetiapine
Olanzapine
Clozapine
Haloperidol
NMDA receptor
NR1-NR2A
AMPA receptor
SAP 102
PSD95
NR2B (p-Ser 1303)
Synaptic fraction
trafficking
p-Ser 831
5HT2
Gq
D2
Gi/o
D1
Gs
βArr-2 PP2A
PLC
PIP2
Akt
AC
IP3
DAG
cAMP
GSK3
Ca2+
PKC
PKA
CREB
DARPP-32
Erk 1/2
αCaMKII/ p-αCaMKII (Thr 286)
GluR1
GluR2
Endoplasmic Reticulum
Cytosolic compartment
inhibition
activation
Haloperidol induced expression, interaction or trafficking enhancement
Haloperidol induced expression, interaction or trafficking reduction
Haloperidol effect unknown on trafficking



Vexler et al., 2006

Factori de risc

- polipragmazie
- copii, vârstnici, sarcina
- sexul feminin
- comorbidităţi (boli neoplazice, imunosupresie, ciroză, diabet)
- disfuncţii de organ (cord, rinichi, ficat)
- malnutriţie
- exces de alcool, tutun
- enzimopatii (reacţii idiosincrazice)
- subiecţi atopici (alergii)
- medicamente expirate sau degradate

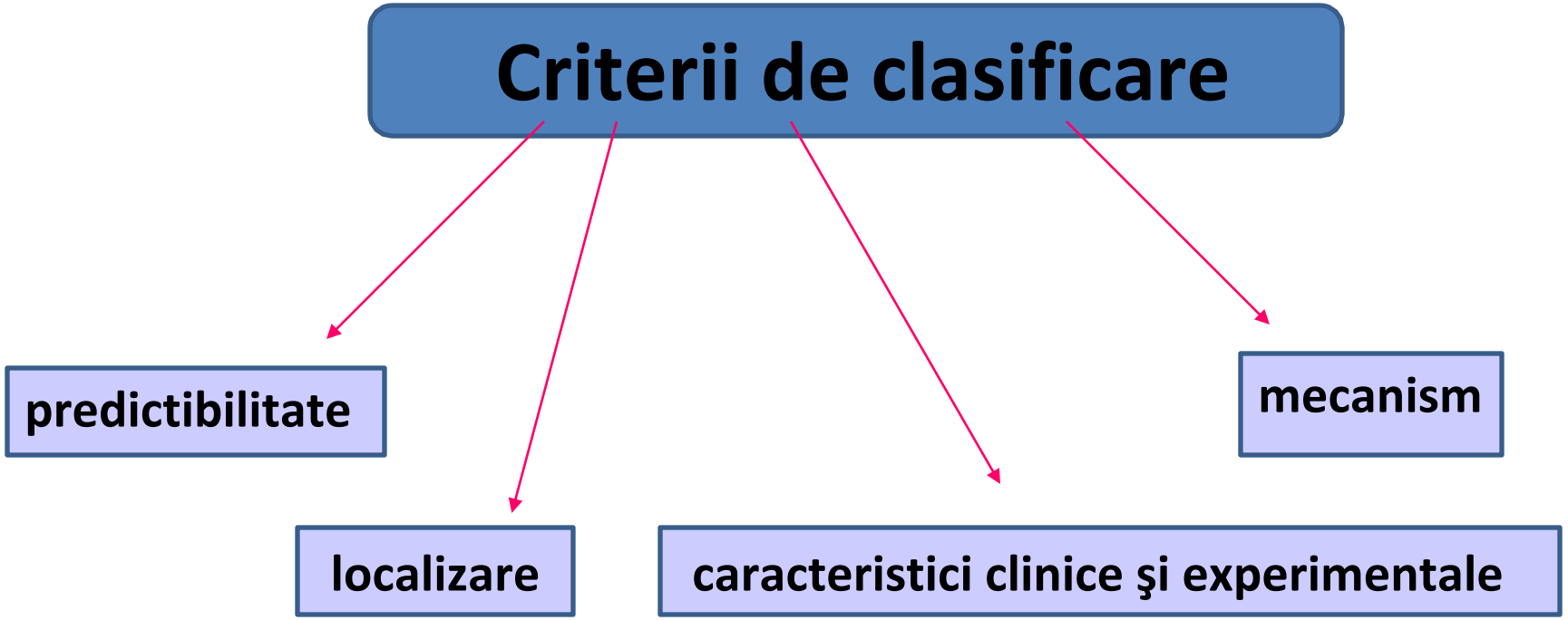
Clasele de medicamente cele mai implicate în RA

Clasa	Exemple de RA
Antimicrobiene	Diaree, rash, prurit
Antineoplazice	Supresie medulară, alopecie, greaţă, vomă
Anticoagulante	Hemoragie, vânătăi
Cardiovasculare	Aritmii, edeme, stop cardiac
Hipoglicemiante	Hipoglicemie, diaree, discomfort gastro-intestinal
AINS	Ulceraţii şi sângerare gastro-intestinală, IR
Analgezice opioide	Constipaţie, sedare, ameţeală
Diuretice	Hipokaliemie, hiperuricemie, hiperglicemie
Agenţi de diagnostic	Hipotensiune, nefrotoxicitate, reacţii alergice
Psihotrope	Ameţeli, tulburări de echilibru, halucinaţii, **sindrom neuroleptic malign**, **sindrom serotoninic**

Sistemele cele mai afectate de RA

Sistem	Exemple de RA
SNC	Anxietate, depresii, reacţii extrapiramidale, ataxie, hiperactivitate, insomnie, oboseală, vertij, distonie
Cardiovascular	Angină, aritmii, sincopă, hemoragie, tromboză, embolism
Endocrin	Ginecomastie, hipotiroidism, supresie suprarenală
Gastrointestinal şi hepatic	Gastrită, dispepsie, disfagie, colită, anorexie, hematemeză, pancreatite, ascite, icter, hepatite toxice
Renal şi genitourinar	Retenţie urinară, nefrită interstiţială, hematurie, dismenoree, vaginite
Hematologic	Discrazie sanguină, anemie, trombocitopenie
Dermatologic	Prurit, urticarie, alopecie, purpură, rash, peteşie
Metabolic	Osteoporoză, acidoză, alcaloză
Musculo-scheletal	Artralgii, mialgii, neuropatie, rabdomioliză
Respirator	Bronhospasm, rinite alergice, dispnee, depresie respiratorie, fibroză pulmonară, epistaxis, hemoptizie
Senzorial	Ototoxicitate, tinitus, tulburări de vedere

Consideraţii asupra reacţiilor adverse



Psihofarmacologie clinica

- Reactii adverse
- Interactiuni medicamentoase

Drug-Induced Serotonin Syndrome

Dana Bartlett, RN, BSN, MSN, MA, CSPI

Table 1 Agents that cause serotonin syndrome

Amphetamine
Buspirone
Cocaine
Dextromethorphan
Fentanyl
Linezolid
Lysergic acid diethylamide (LSD)
Monoamine oxidase inhibitors (MAOIs)
3,4-Methylene dioxymethamphetamine (MDMA; ecstasy)
Methylene blue
Ondansetron
Selective serotonin reuptake inhibitors (SSRIs)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)
St John's wort
Sumatriptan
Tramadol
Tricyclic antidepressants
Tryptophan

Table 2 Mechanisms of action of serotonin syndrome

Mechanism	Example
Direct serotonin receptor agonism	Buspirone, LSD
Decreased serotonin breakdown	MAOIs, methylene blue
Decreased reuptake of serotonin	Duloxetine, fluoxetine
Increased formation of serotonin	Tryptophan
Increased release of serotonin	Cocaine, fentanyl

Abbreviations: LSD, lysergic acid diethylamide; MAOIs, monoamine oxidase inhibitors.
Based on information from Hillman et al,[11] Ables and Nagubilli,[12] and Iqbal et al.[13]

Table 3 Clinical situations in serotonin syndrome

Abuse of illicit drugs
Drug-drug interactions
Intentional overdose of a serotonergic medication
Therapeutic use of a serotonergic medication or medications

Table 4 Signs and symptoms of serotonin syndrome

Agitation	Diarrhea	Muscular rigidity
Akathisia	Fever	Mydriasis
Clonus	Hyperreflexia	Tachycardia
Confusion	Hypertension	Tremor
Diaphoresis	Increased bowel sounds	

Table 5 Drug-induced syndromes and differential diagnosis for serotonin syndrome

Syndrome	Description
Anticholinergic poisoning	Dry, flushed skin, decreased bowel sounds, normal reflexes and muscular tone
Malignant hyperthermia	Caused by inhalational anesthetics or succinylcholine
Neuroleptic malignant syndrome	Bradyreflexia, pronounced "lead-pipe" rigidity, normal pupil size, develops slowly over several days and can occur even after uneventful long-term use of a neuroleptic agent
Sympathomimetic poisoning	Dry, flushed skin, no gastrointestinal signs, temperature can be normal or only mildly elevated
Substance withdrawal	

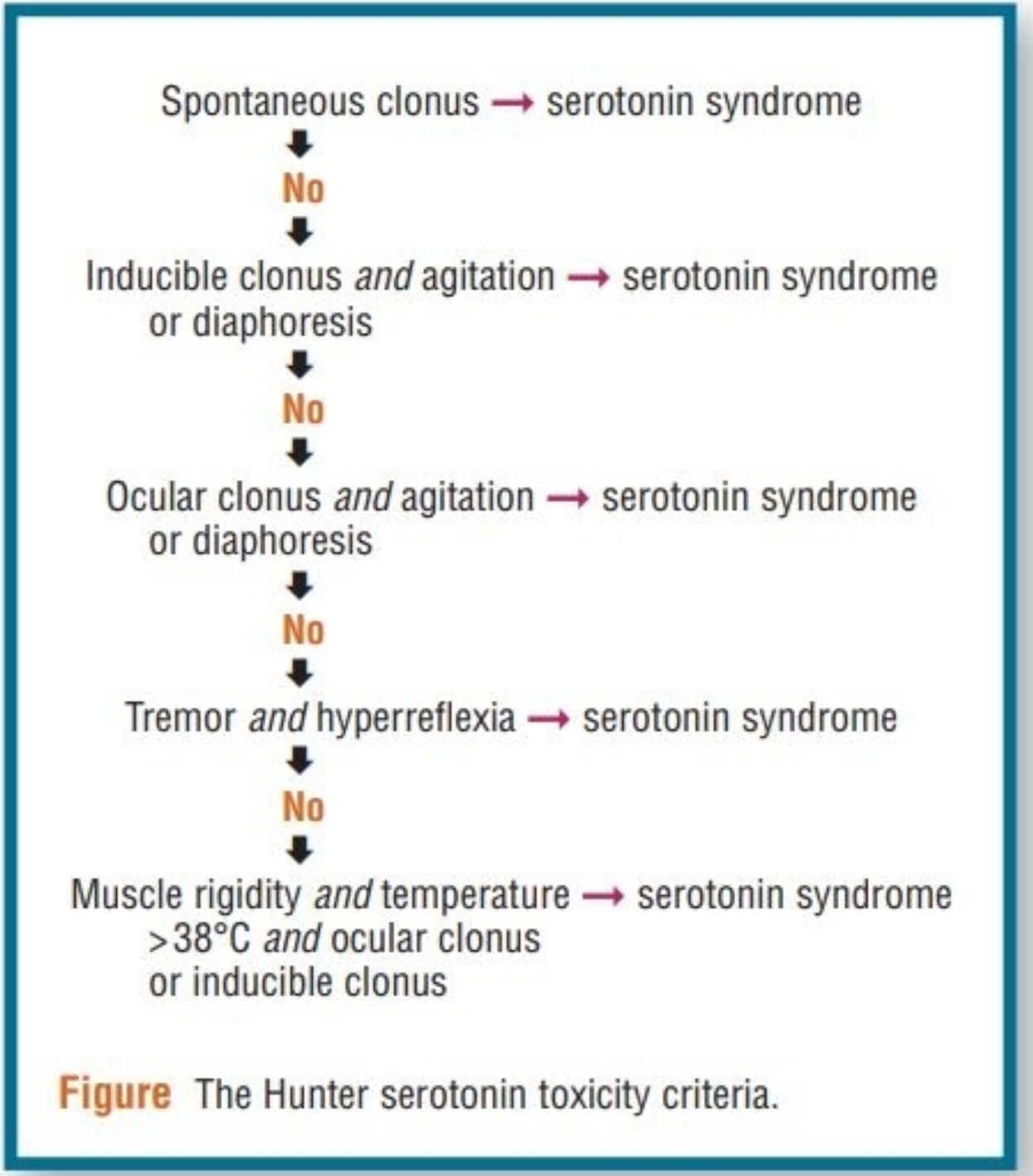
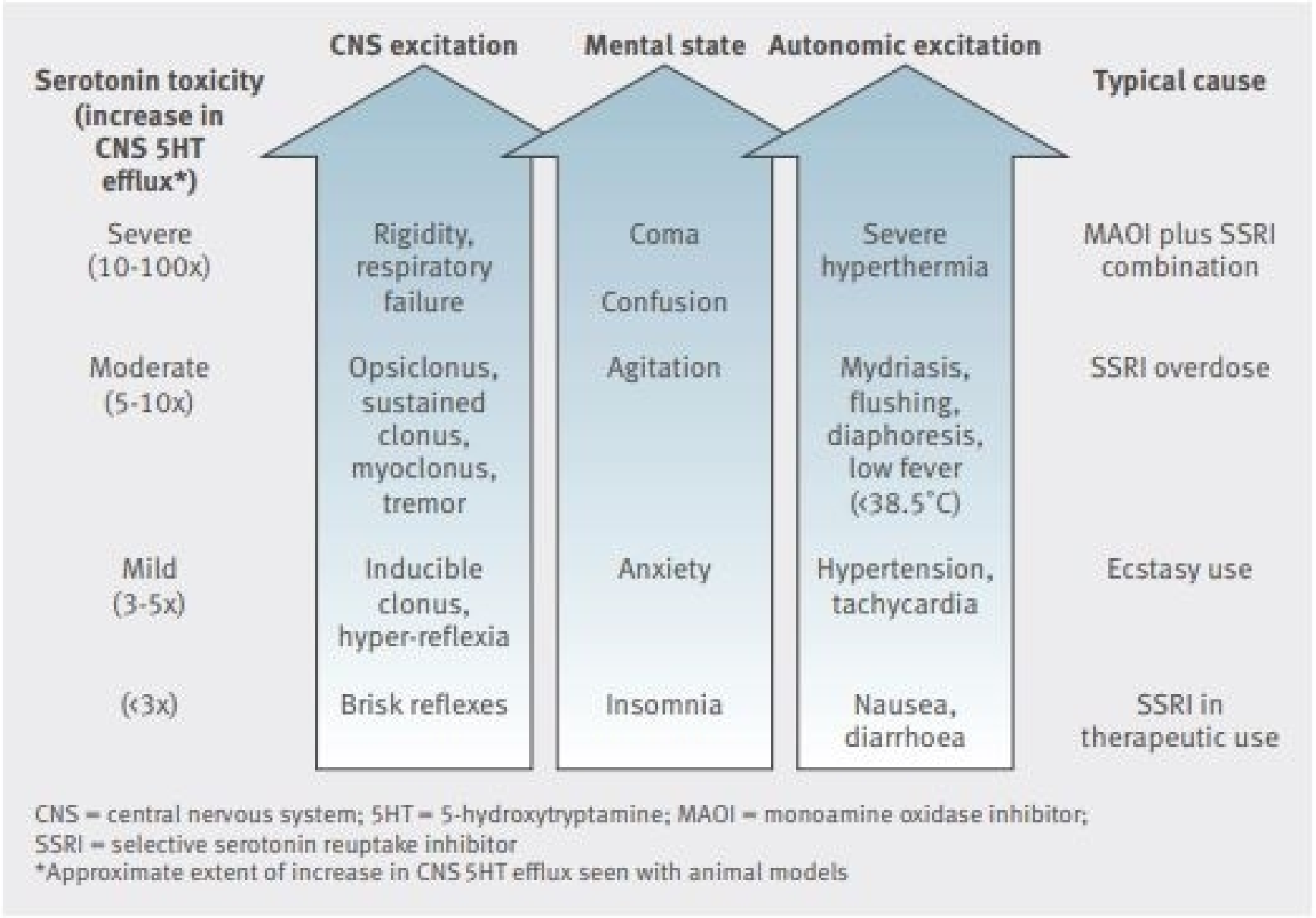
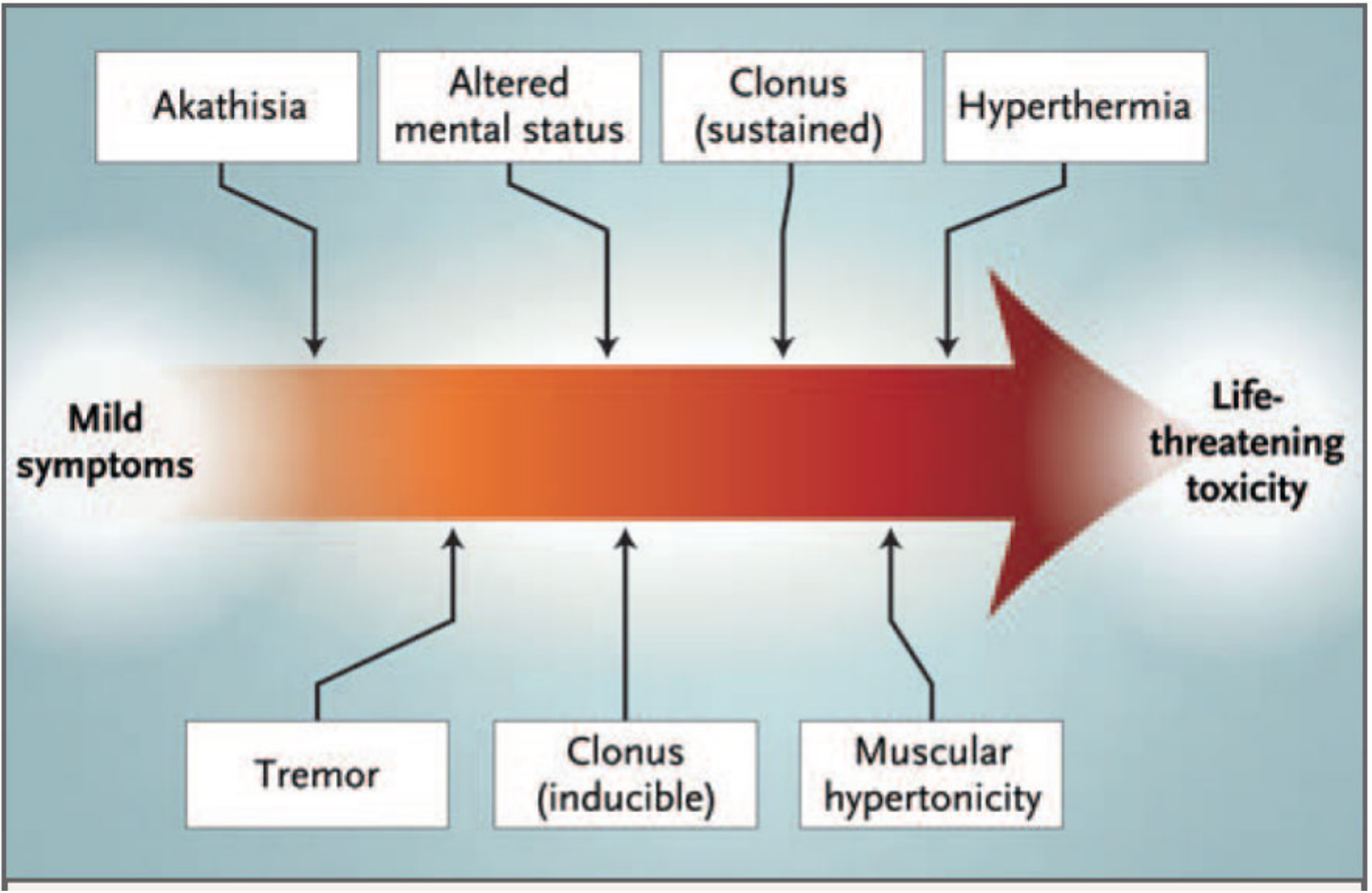


Figure The Hunter serotonin toxicity criteria.



CNS = central nervous system; 5HT = 5-hydroxytryptamine; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor

*Approximate extent of increase in CNS 5HT efflux seen with animal models


Akathisia
Altered mental status
Clonus (sustained)
Hyperthermia
Mild symptoms
Life-threatening toxicity
Tremor
Clonus (inducible)
Muscular hypertonicity

Neuroleptic Malignant Syndrome

Risk Factors	
Category	**Variable**
Pharmacological Treatment	Initial phases of treatment or, change of dosage High dose of AP Parenteral administration (i.v. or i.m.) Polypharmacy Antipsychotic treatment Other compounds: AD, MS, aP
Environmental factors	Physical restraint Dehydration High temperature
Demographics	Age Multimorbidities
Genetic liability	Previous NMS Family history of Catatonic Syndrome Muscle channelopathy

Levenson Criteria (1985)	**Pope Criteria (1986)**	**Addonizio Criteria (1987)**	**Lazarus Criteria (1989)**
All three major, or two major and four minor criteria suggest a high probability of NMS. **Major Criteria:** 1. Hyperthermia 2. Rigidity 3. Elevated CPK (usually > 1000 UI/L) **Minor Criteria:** 1. Altered consciousness level 2. Tachycardia 3. Labile arterial pressure 4. Tachypnea 5. Diaphoresis 6. Leukocytosis	Allows for prospective and retrospective diagnoses. **Prospective diagnoses** (all three required): 1. Hyperthermia (oral temperature >37.5°C) 2. EPS with at least two of the following: lead-pipe muscular rigidity, cogwheeling, sialorrhea, oculogyric crisis, retrocollis, opisthotonos, trismus, dysphagia, choreiform movements, dyskinetic movements, festinating gait, flexor-extensor posturing 3. Autonomic dysfunction with two or more of the following: hypertension (>20mmHg rise in diastolic above baseline), tachycardia (>30 beats/min above baseline), tachypnea (>25 respirations/min), prominent diaphoresis, incontinence	1. Hyperthermia 2. Rigidity 3. Dystonia 4. Blood pressure elevation (>140mmHg systolic, >90mmHg diastolic, or both) 5. Tachycardia 6. Diaphoresis 7. Elevated CPK 8. Leukocytosis	Requires all three major criteria, plus three minor criteria. **Major Criteria:** 1. Neuroleptic administration in past 7 days 2. Hyperthermia 3. Rigidity **Minor Criteria:** 1. Altered consciousness 2. Tachycardia 3. Labile arterial pressure 4. Tachypnea 5. Elevated CPK or myoglobinuria 6. Leukocytosis

Table 4. Differential diagnoses.

NMS Differential Diagnosis	
Diagnosis	**Key differential characteristics**
Central anticholinergic syndrome	No rigidity, CPK levels normal
Lithium toxic encephalopathy	No fever, CPK levels are normal
Malignant hyperthermia	There is history of anesthesia with fluoronade anesthesics
Heat shock related to neuroleptics	No diaphoresis, no rigidity
Heat shock	No diaphoresis, no rigidity; History of heat and sun exposition
CNS Infection	Abnormal CSF, usually there is neurological focality
Lethal Catatonia	Semiology can be very similar but there is no history of neuroleptic administration
Serotonin Syndrome	CPK levels are normal; no leukocytosis; no rigidity, but clonus and hyperreflexia are present

CPK, creatinine phosphokinase; *CNS*, central nervous system; *CSF*, cerebrospinal fluid.

Selected Agents Associated with Drug-Induced Movement Disorders

Acute and Tardive Akathisia

Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Antiepileptics
Carbamazepine
Psychotropics
Lithium
Neuroleptics
Haloperidol
Molindone
Phenothiazines (e.g., chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine)
Thioxanthenes (e.g., thiothexene)
Reserpine
Selective serotonin-reuptake inhibitors
Tricyclic antidepressants

Acute and Tardive Dyskinesia

Antiemetics
Metoclopramide
Prochlorperazine
Antiepileptics
Phenytoin
Psychotropics
Amoxapine
Haloperidol
Lithium
Molindone
Phenothiazines (e.g., chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine)
Olanzapine (high dosage)
Pimozide
Risperidone (high dosage)
Thioxanthenes (e.g., thiothexene)

Acute and Tardive Dystonia

Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Psychotropics
Amoxapine
Neuroleptics
Haloperidol
Molindone
Olanzapine (high dosage)
Phenothiazines (e.g., chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine)
Risperidone (high dose)
Thioxanthenes (e.g., thiothexene)

Parkinsonism

Antiemetics
Droperidol
Metoclopramide
Prochlorperazine
Promethazine
Antiepileptics
Valproate
Cardiovascular agents
Alpha-Methyldopa
Reserpine
Psychotropics
Amoxapine
Neuroleptics
Haloperidol
Molindone
Olanzapine (high dosages)
Phenothiazines (e.g., chlorpromazine, fluphenazine, mesoridazine, perphenazine, thioridazine, trifluoperazine)
Risperidone (high dosages)
Thioxanthenes (e.g., thiothexene)
Vestibular sedatives
Cinnarizine and Flunarizine*
Miscellaneous
Pimozide
Tetrabenazine*

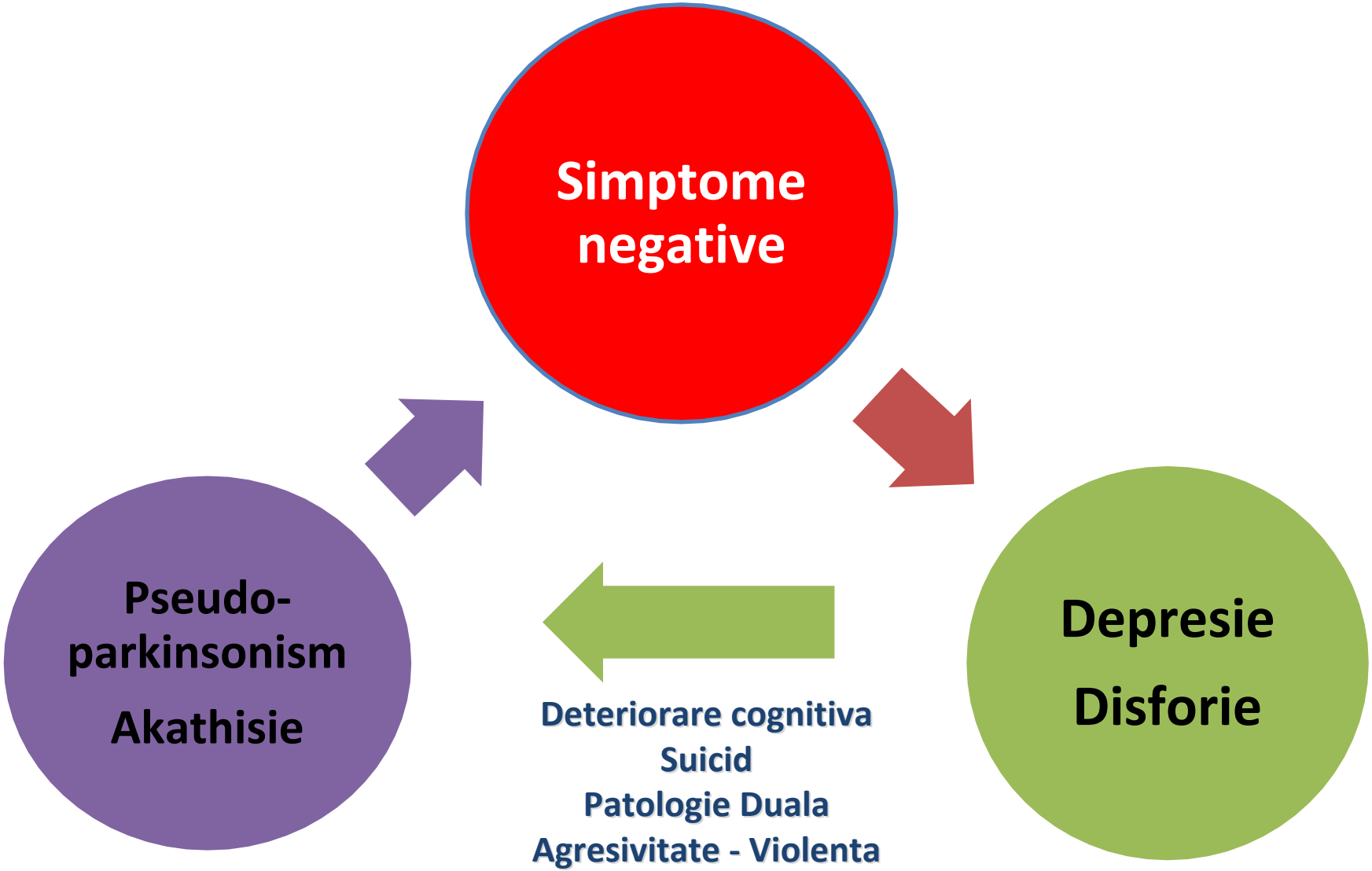
Risk Factors for Drug-Induced Movement Disorders

Akathisia	Tardive Dyskinesias	Dystonia	Parkinsonism
Advanced age	Advanced age	***Acute Dystonia***	Acquired immune deficiency syndrome
Affective disorder	Affective disorder	High-potency neuroleptics	Advanced age
Cognitive impairment	Alcoholism	History of electroconvulsive therapy	Dementia
Female sex	Diabetes mellitus	Male sex	Female sex
High-potency neuroleptics	Duration of treatment	Mental retardation	
High neuroleptic dosage	Electroconvulsive treatment	Young age	
History of akathisia	Female sex	***Tardive Dystonia***	
Iron deficiency	History of extrapyramidal reaction	Male sex	
Mental retardation	Intermittent neuroleptic treatment	Presence of tardive dyskinesia	
Negative symptoms of schizophrenia	Iron deficiency	Young age	
Rapid neuroleptic dosage escalation	Mental retardation		
	Organic brain disorder		
	Total daily drug dosage		

Reactii adverse consemnate in ghidurile terapeutice

Efecte adverse	AP convenţional	AP atipic
Simptome extrapiramidale	+ + +	+
Prolactinemie	+ +	+
Diskinezie tardivă	+ + +	+
Hipotensiune ortostatică	+ +	+
Prelungirea intervalului QT	+ + +	+
Sindrom metabolic	+	+ + +
Diabet zaharat	+	+ +
Moarte subită	+ +	+
Sindrom neuroleptic malign	+ + +	+
Sindrom serotoninergic*	+ -	+
Deteriorare cognitivă	+ + +	+ -

** risc amplificat de tratamente anterioare sau concomitente cu antidepresive serotoninergice.*



RISC SUICIDAR

Pacientii cu schizofrenie au un risc de mortalitate precoce de pana la 40% prin doua cauze:

Suicid Moarte ne-naturala

(Kahyee Hor, 2010)

Pacientii spitalizati dupa primul episod de schizofrenie si care nu au luat in mod regulat medicatia antipsihotica (**aderenta scazuta**) au avut un risc de deces:

- de 12 ori mai mare, prin orice cauza
- de 37 ori mai mare, prin suicid.

(Tiihonen 2006)

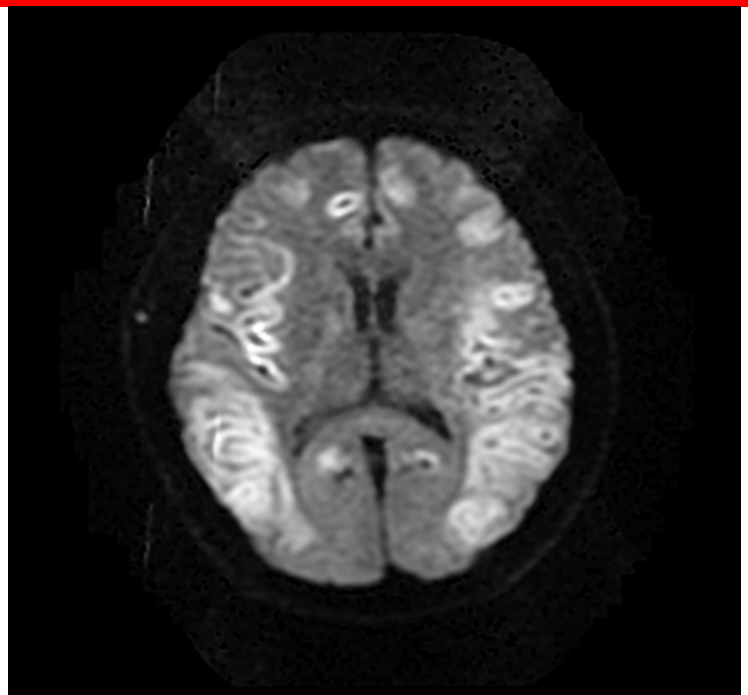
Suicidul este puternic corelat cu urmatorii factori de risc: varsta tanara, sexul masculin, nivelul educational inalt, depresia, tentativele anterioare de suicid, comorbiditatile somatice (Kahyee Hor, 2010).

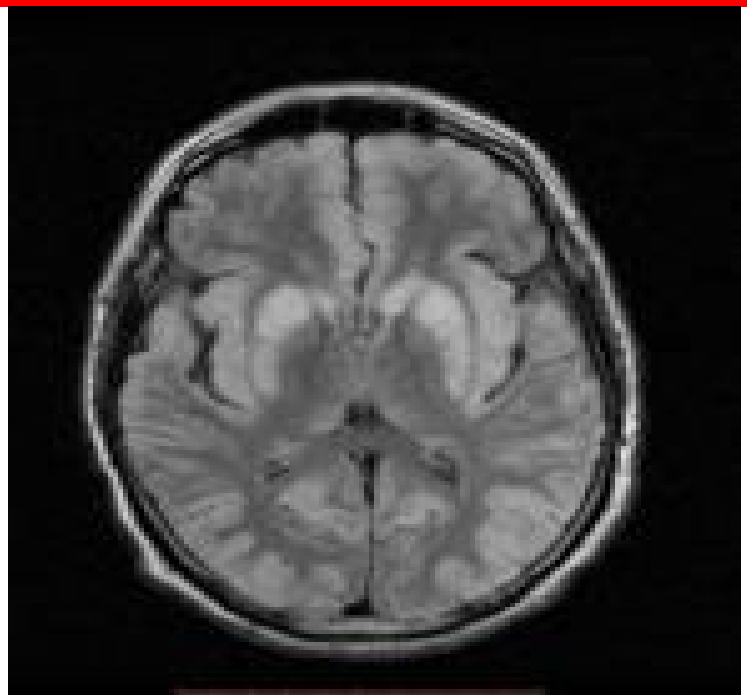
Principalele afectiuni comorbide somatice corelate cu afectiunile psihotice si terapia antipsihotica care influenteaza negativ prognosticul si cresc costurile de ingrijire:

- Diabet
- Afectiuni gastrointestinale
- Afectiuni pulmonare cronice
- Alcoolism
- Patologie cardio-cerebro-vasculara
- Afectiuni stomatologice cronice

There are characteristic changes affecting the posterior limb of the internal capsule, cerebral cortex (in particular parieto-occipital and insula), hippocampus and basal ganglia, typically bilateral. The cerebellum, brainstem and thalami are usually spared in adults but they are also involved in neonates. The splenium of the corpus callosum are also affected, producing the so-called boomerang sign.

Altered cellular physiology results in neuronal death. Hypoglycaemia leads to a cellular energy failure, as the brain is an obligate glucose metabolizer. The resulting energy shortage results in sodium/potassium pump failure and cellular swelling and tissue alkalosis. Some theories are based on cell damage due to increased extracellular aspartate and glutamate.





There were 34 (30.9%) studies based on inpatient samples and outcomes. When domain-based analyses were restricted to these studies, some differences emerged compared to the overall estimates. The substance misuse domain was less strongly associated with violence risk, although it remained significant. The psychopathology and positive symptoms domains were more strongly associated with violence risk. The negative symptoms, neuropsychological, demographic, premorbid, suicidality, and treatment-related domains were not significantly associated with violence risk

Risk Factors for Violence in Psychosis Katrina Witt, Richard van Dorn, Seena Fazel

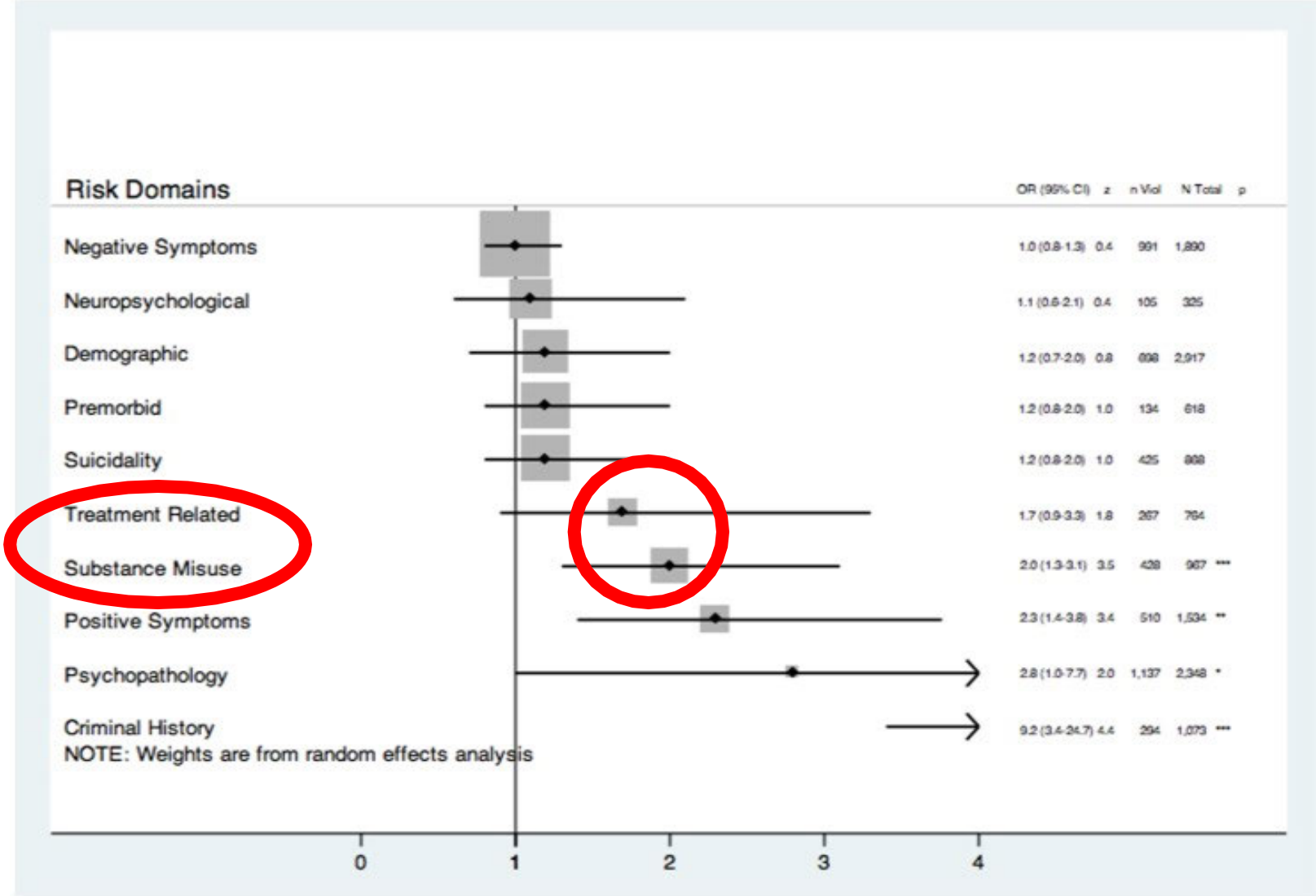


Table 2. Select Drug Categories and Drugs Associated With Hyperglycemia

- Antibiotics
  - Quinolone
    - Gatifloxacin (also associated with hypoglycemia)
    - Levofloxacin
- Atypical antipsychotics
  - Most Risky
    - Clozapine
    - Olanzapine
  - Intermediate
    - Paliperidone
    - Quietiapine
    - Risperidone
  - Least Risky
    - Aripiprazole
    - Ziprasidone
  - Unknown
    - Iloperidone
- β-blockers*
  - Atenolol
  - Metoprolol
  - Propanolol
- Corticosteroids
- Calcineurin inhibitors
  - Cyclosporine
  - Sirolimus
  - Tacrolimus
- Protease Inhibitors
  - Atazanavir
  - Darunavir
  - Fosamprenavir
  - Indinavir
  - Nelfinavir
  - Ritonivir
  - Saquinavir
  - Tipranivir
- Thiazide and thiazide-like diuretics
  - Chlorthiazide
  - Chlorthalidone
  - Diazoxide
  - Hydrochlorothiazide
  - Indapamide
  - Methyclothiazide
  - Metolazone

Note: Carvedilol and nebivolol are not associated with the development of hyperglycemia.

Select Drug Categories and Drugs Associated With Hyperglycemia.

Antibioterapie

Antipsihotice atipice

Beta blocante

Corticosteroizi exogeni

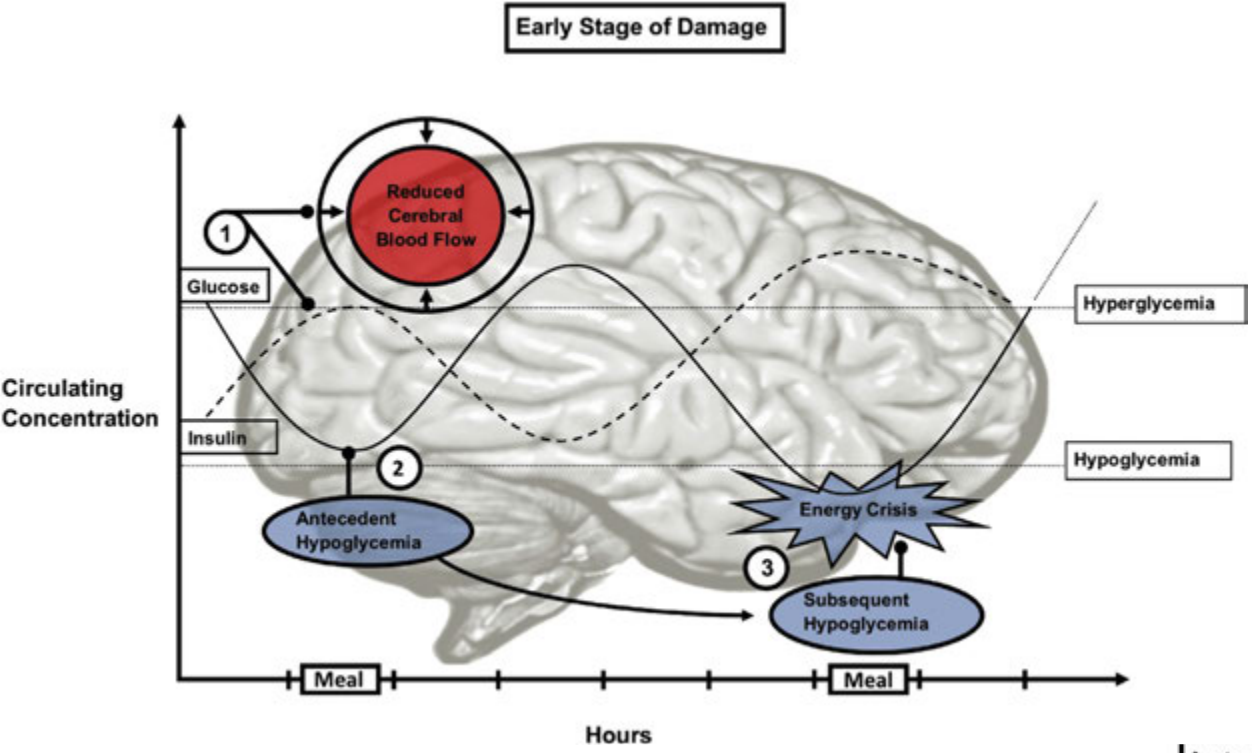
Ciclosporina

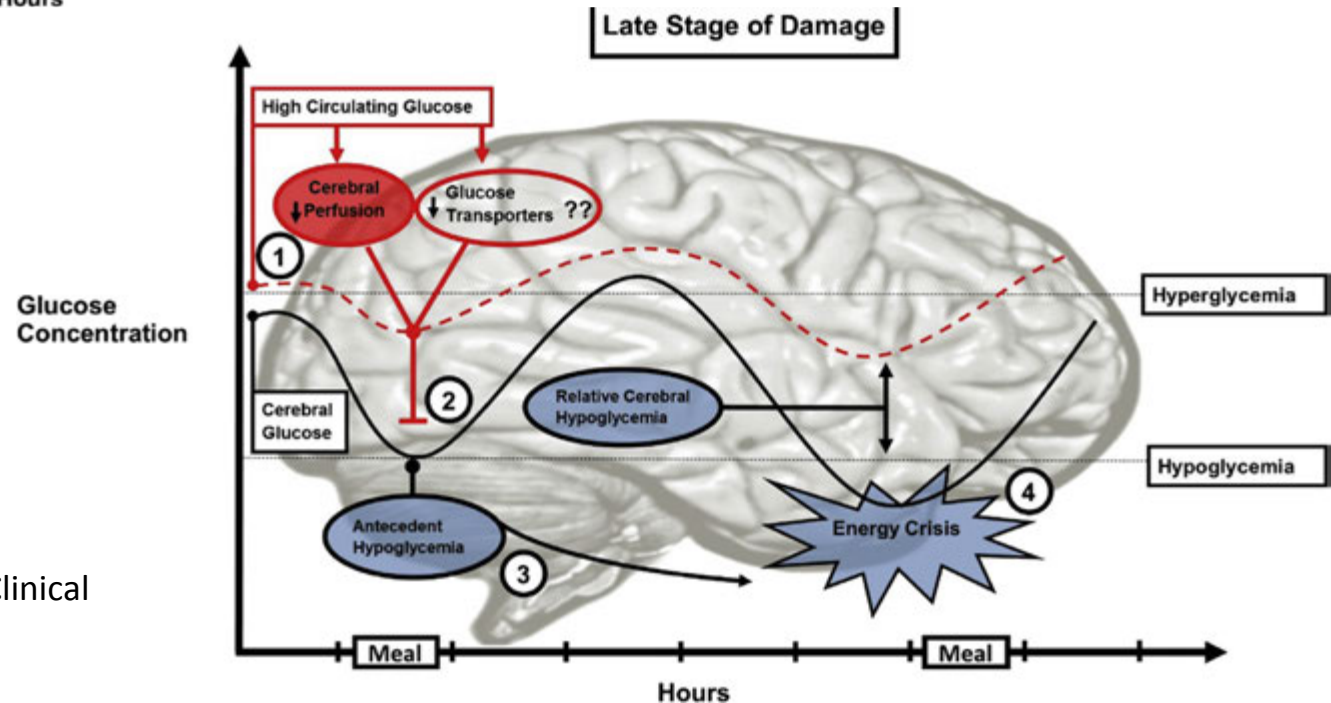
Antivirale – HIV

Diuretice tiazidice

Abdur Rehman et al. Diabetes Spectr 2011;24:234-238

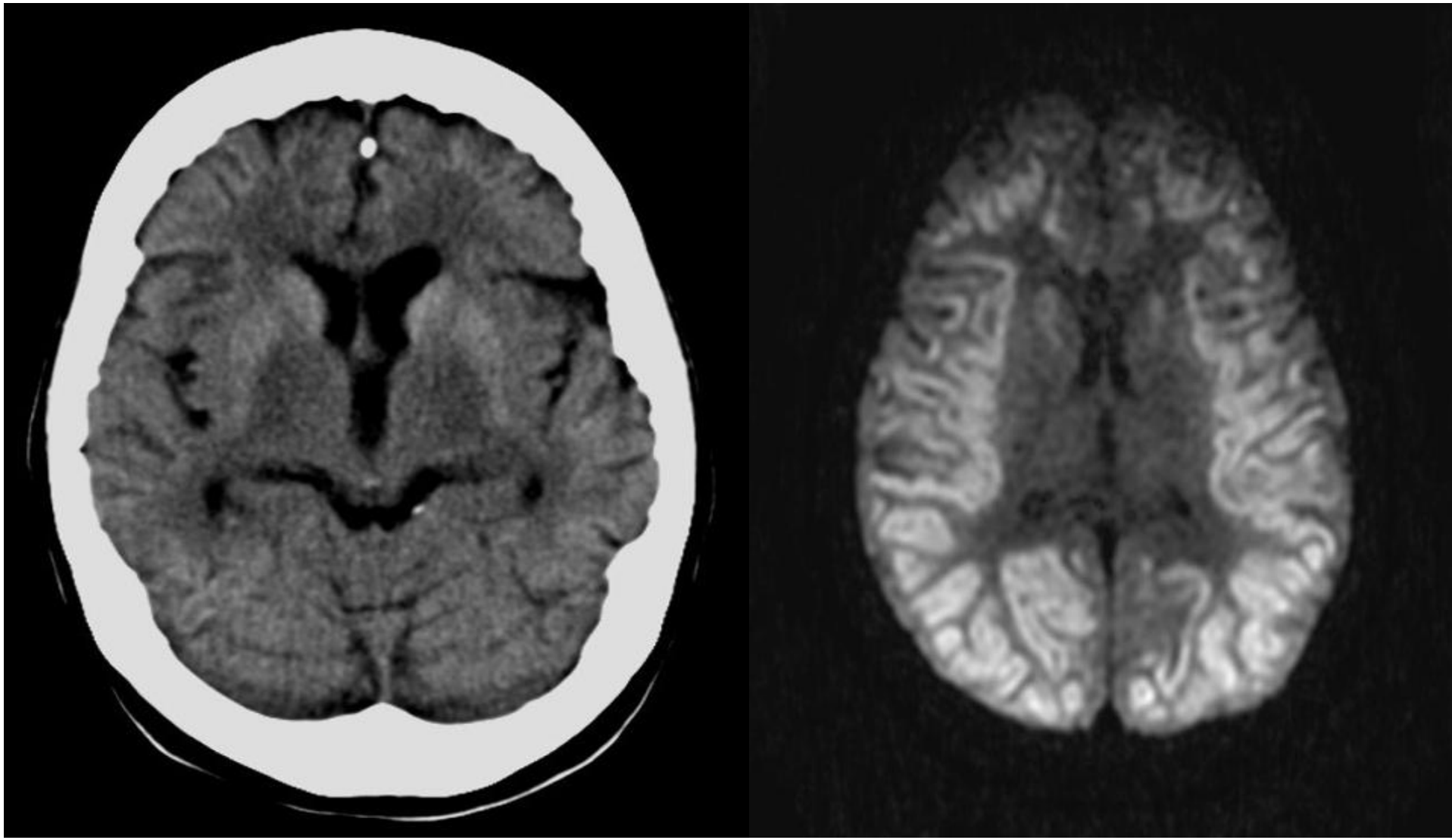
Afectarea cerebrala in hipoglicemie





M.J. Wheeler et al. / Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 291-300

Afectarea cerebrala in hipoxie



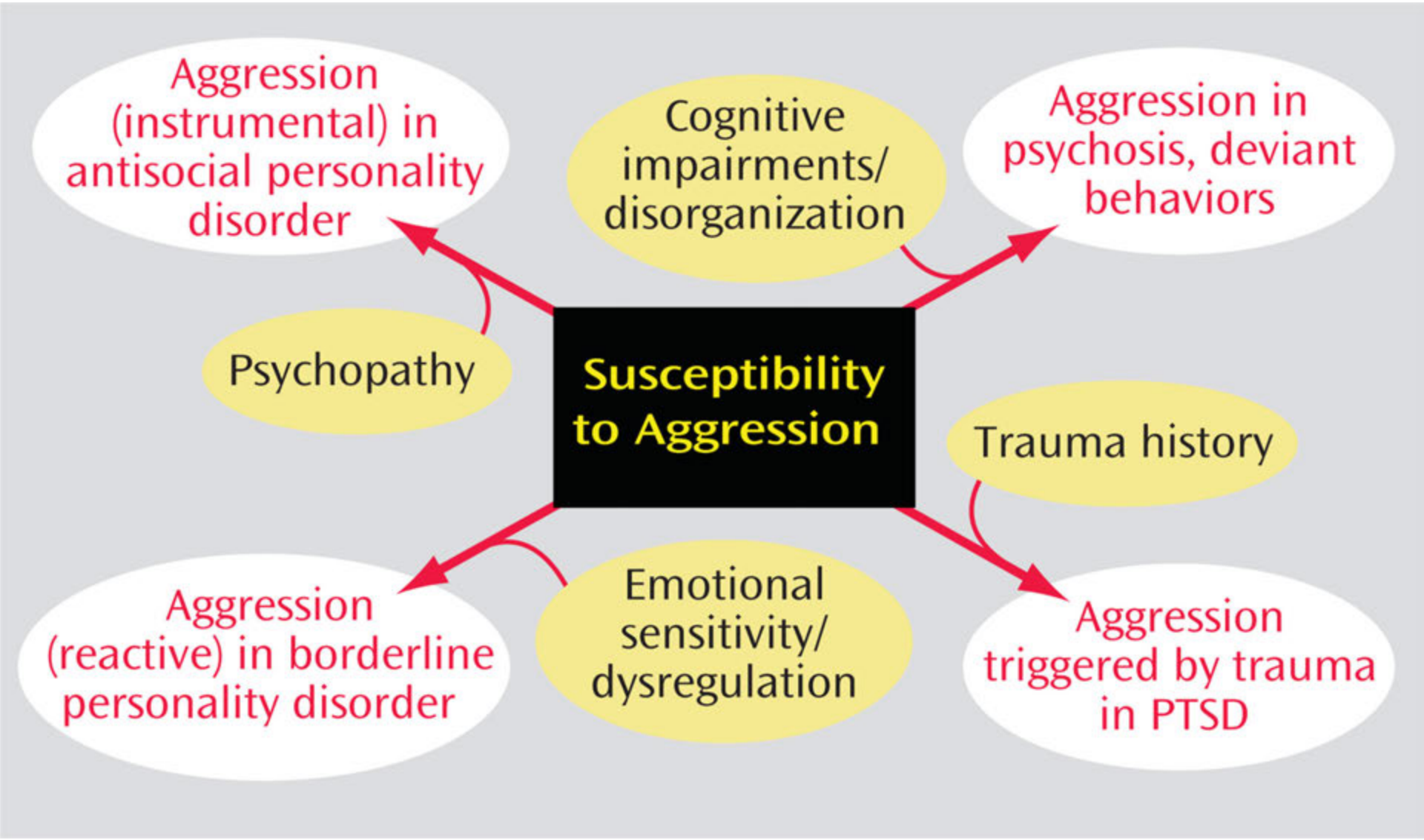
https://radiopaedia.org/articles/anoxic-brain-injury

Conditiile comorbide metabolice determina modificari structurale cerebrale

- Hipoglicemia (diabet zaharat)
- Hipoxia
- Hipoperfuzia vasculara

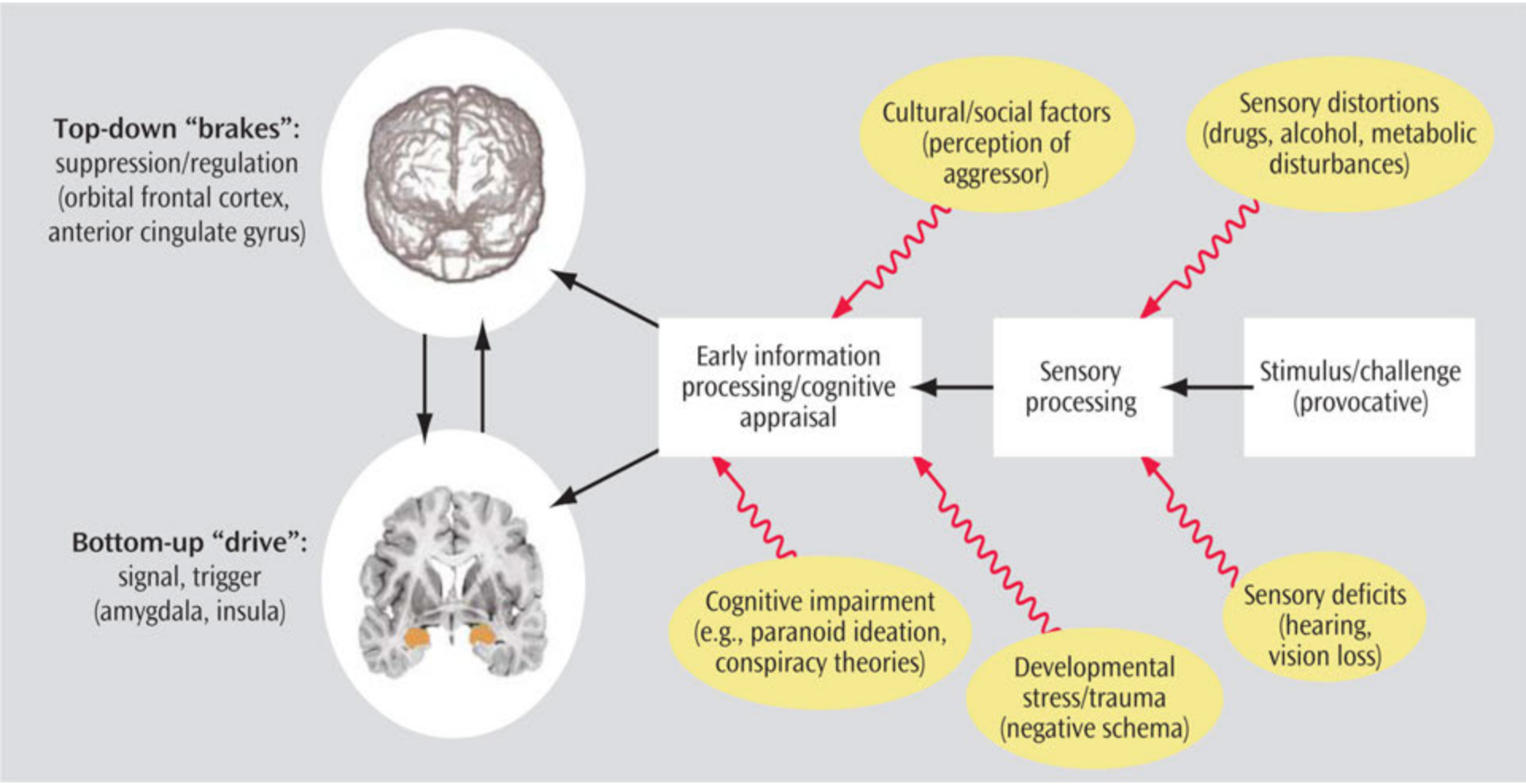
Cresterea nivelului de glutamat declanseaza reactii asociate cu modelul comportamentului exploziv de tip epileptiform

Neurobiological model of agression



Larry J. Siever, Neurobiology of Aggression and Violence, Am J Psychiatry. 2008 April ; 165(4): 429–442. doi:10.1176/appi.ajp.2008.07111774.

Neurobiological model of agression (2)



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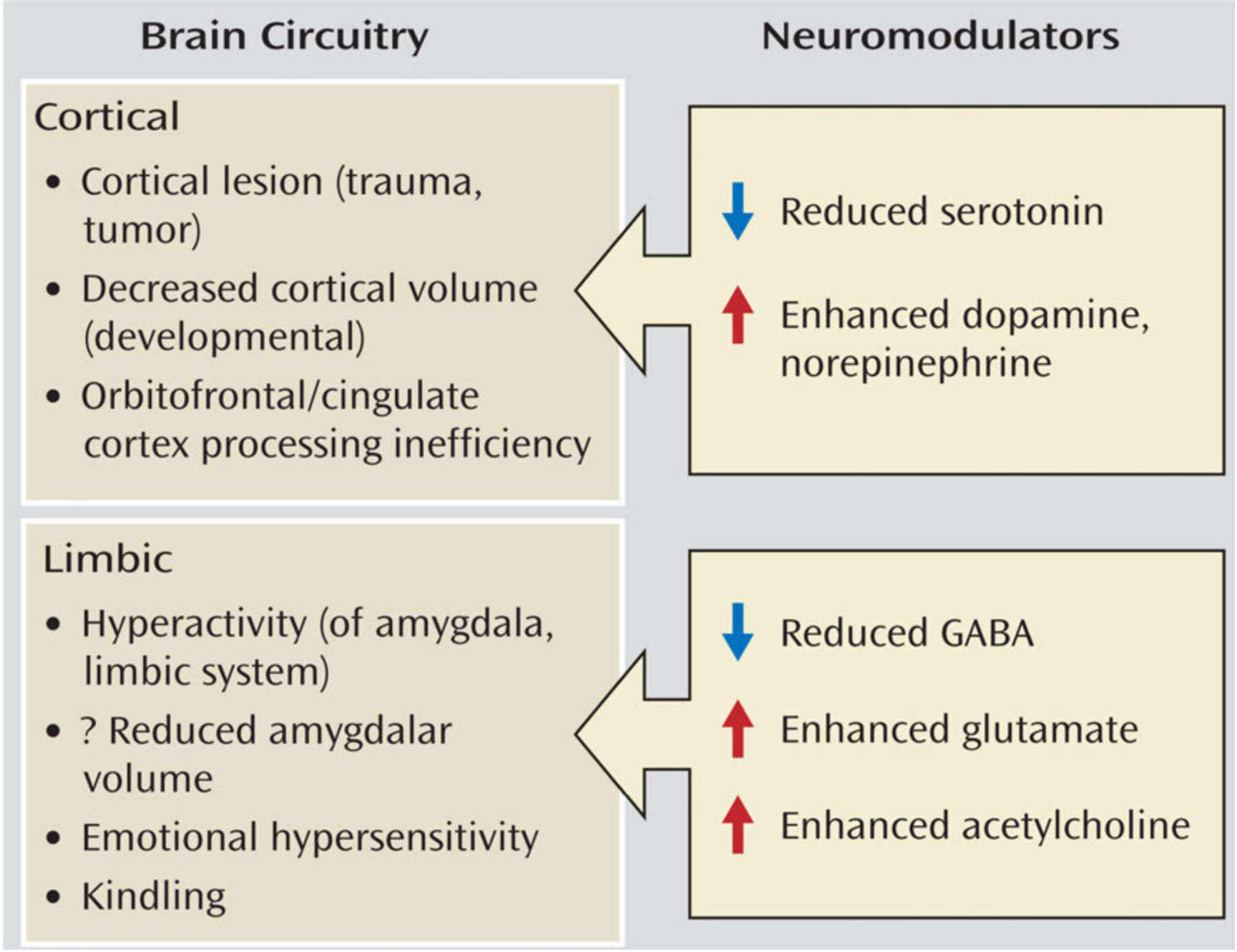


Larry J. Siever, Neurobiology of Aggression and Violence, Am J Psychiatry. 2008 April ; 165(4): 429–442. doi:10.1176/appi.ajp.2008.07111774.

Larry J. Siever, Neurobiology of Aggression and Violence, Am J Psychiatry. 2008 April ; 165(4): 429–442. doi:10.1176/appi.ajp.2008.07111774.

Comportamentul agresiv – crima

Pacientii cu psihoza au comis crime de 4 ori mai mult decat populatia generala

Factorii neurobiologici si psihofarmacologici care favorizeaza comportamentul criminal:

- Utilizarea medicatiei pentru afectiuni asociate
- Afectiuni comorbide de personalitate (personalitate antisociala)
- Lipsa aderentei la tratament
- Lipsa compliantei la tratament

1. Tuninger 2001
2. Jan Volavka Treatament approeaches to agressive behavior in schizophenia, cap 16 (2006) Crime and schizoprenia causes and cures

Exista suficiente argumente neurobiologice si psihofarmacologice care sa permita preventia secundara a comportamentelor agresive sau suicidare !

Crima de la metrou.

http://www.gds.ro

Pacient ucis intr-un sanatoriu de neuropsihiatrie din Botosani. Agresorul nu poate fi pedepsit, deoarece e bolnav psihic

https://stirileprotv.ro

Medicamente care induc hipoglicemia cresc riscul comportamentelor violente si suicidare

	Clinical Setting
Ciabenzoline	Chronic and acute: few had diabetes and renal insufficiency
Clinafloxacin	Acute: pneumonia and sepsis
Gatifloxacin	Acute: various infections
Glucagon	Chronic: endoscopy patients
Indomethacin	Chronic: infants with patent ductus arteriosus
Pentamidine	Acute: infections in immunocompromised host
Quinine	Acute: malaria and cerebral malaria
Artesunate/artemisin/artemether	Acute: malaria and cerebral malaria
Chloroquineoxaline sulfonamide	Chronic: malignancy (mainly lung and colon)
IGF-I	Chronic: diabetes or isolated GH deficiency
Lithium	Chronic: postglucose hypoglycemia
Propoxyphene and	Chronic: renal insufficiency, few had

Drug-induced hypoglycemia

can be severe and cause significant morbidity. Prescribers should strive to avoid these adverse events particularly in elderly patients, patients with sepsis, renal or hepatic disease

M. Hassan Murad et al, Drug-Induced Hypoglycemia: A Systematic Review, The Journal of Clinical Endocrinology & Metabolism, Volume 94, Issue 3, 1 March 2009,

Drug-induced hypoglycemia

Example	Mechanism of action
Insulin	Exogenous hyperinsulinaemia
Sulfonylureas	Increased insulin output
Meglitinides	
Salicylates	Impairment of gluconeogenesis
Pentamidine	β cell toxin
Quinine	Increased insulin output
Alcohol	Stimulates an exaggerated release of insulin by diverting blood flow to the endocrine part of the pancreas. Also impaired gluconeogenesis

Elora Mukherjee et al, Endocrine and Metabolic Emergencies: Hypoglycaemia, Ther Adv Endocrinol Metab. 2011 Apr; 2(2): 81–93.

Drug-induced weight gain: Rethinking our choices

How these antidiabetic drugs affect weight[3]

Weight gain	Weight neutral	Weight loss
Insulin	Alpha-glucosidase inhibitors	GLP-1 agonists
Meglitinides	Bromocriptine	Metformin
Sulfonylureas	Colesevelam	Pramlintide
Thiazolidinediones	DPP-4 inhibitors	SGLT2 inhibitors

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose co-transporter 2.

Antihypertensives and weight[3]

Weight gain	Weight neutral
Alpha-adrenergic blockers	ACE inhibitors
Beta-adrenergic blockers (atenolol, metoprolol, nadolol, propranolol)	Angiotensin receptor blockers
	Beta-adrenergic blockers (carvedilol, nebivolol)
	CCBs
	Thiazides

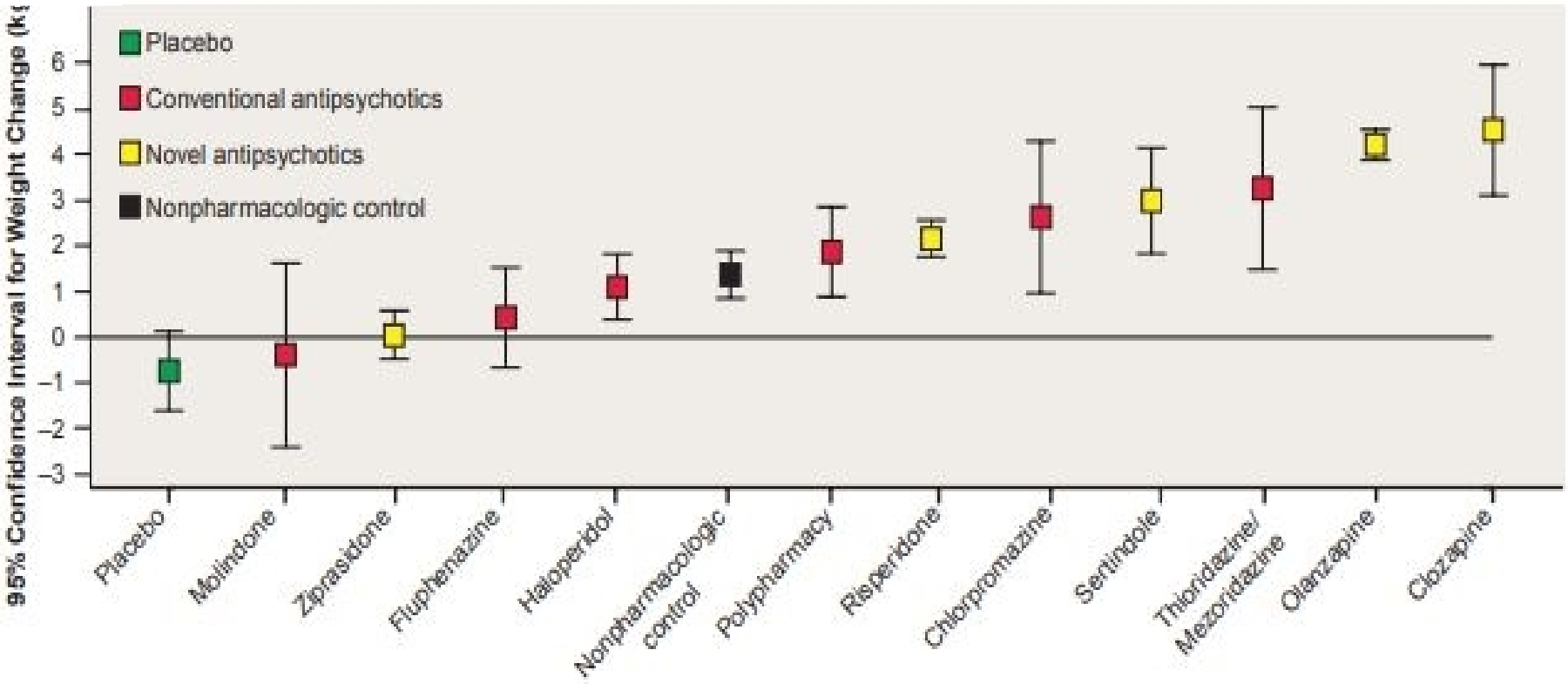
ACE, angiotensin-converting enzyme; CCBs, calcium channel blockers.

Weighing in on antidepressants[3]

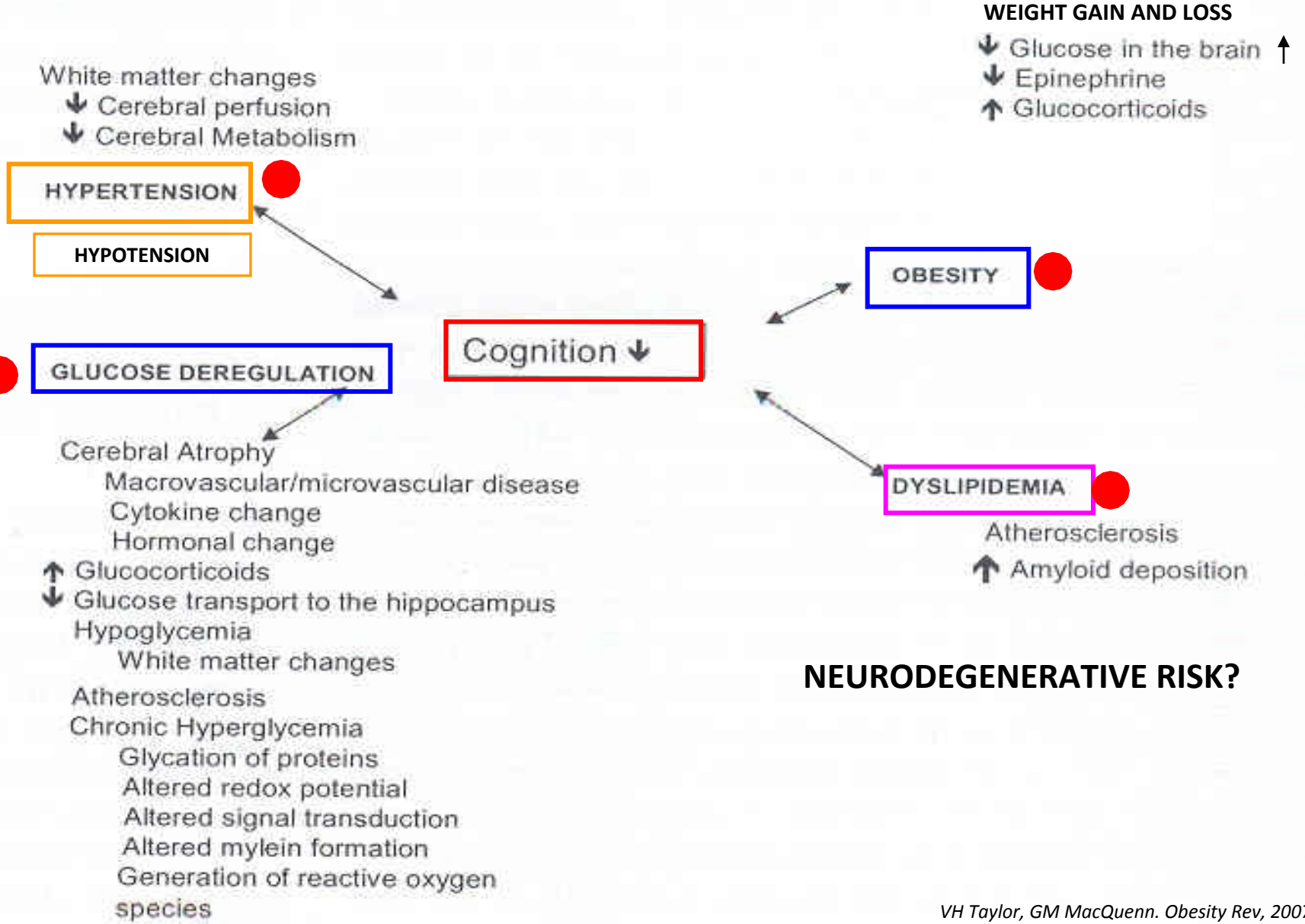
Weight gain	Weight neutral	Weight loss
TCAs (amitriptyline, doxepin, imipramine, nortriptyline)	SSRIs (fluoxetine, sertraline)	Bupropion
MAOIs		
Mirtazapine		
SSRI (paroxetine)		

MAOIs, monoamine oxidase inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

FIGURE 1. 95% Confidence Intervals for Weight Change After 10 Weeks on Standard Drug Doses, Estimated From a Random Effects Model



MECHANISMS MEDIATING THE EFFECTS OF METABOLIC SYNDROME ON COGNITION



VH Taylor, GM MacQuenn. Obesity Rev, 2007, 8:409-418

An approach to drug induced delirium in the elderly

Box 1: Deliriants (drugs causing delirium)

Prescription drugs

- Central acting agents:
  - Sedative hypnotics (for example, benzodiazepines).
  - Anticonvulsants (for example, barbiturates).
  - Antiparkinsonian agents (for example, benztropine, trihexyphenidyl).
- Analgesics:
  - Narcotics (NB. meperidine*).
  - Non-steroidal anti-inflammatory drugs*.
- Antihistamines (first generation—for example, hydroxyzine).
- Gastrointestinal agents:
  - Antispasmodics.
  - H_2-blockers*.
- Antinauseants:
  - Scopolamine.
  - Dimenhydrinate.
- Antibiotics:
  - Fluoroquinolones*.
- Psychotropic medications:
  - Tricyclic antidepressants.
  - Lithium*.
- Cardiac medications:
  - Antiarrhythmics.
  - Digitalis*.
  - Antihypertensives (β-blockers, methyldopa)
- Miscellaneous:
  - Skeletal muscle relaxants.
  - Steroids.

Over the counter medications and complementary/alternative medications

- Antihistamines (NB. first generation— for example, diphenhydramine, chlorpheniramine).
- Antinauseants (for example, dimenhydrinate, scopolamine).
- Liquid medications containing alcohol.
- Mandrake.
- Henbane.
- Jimson weed.
- Atropa belladonna extract.

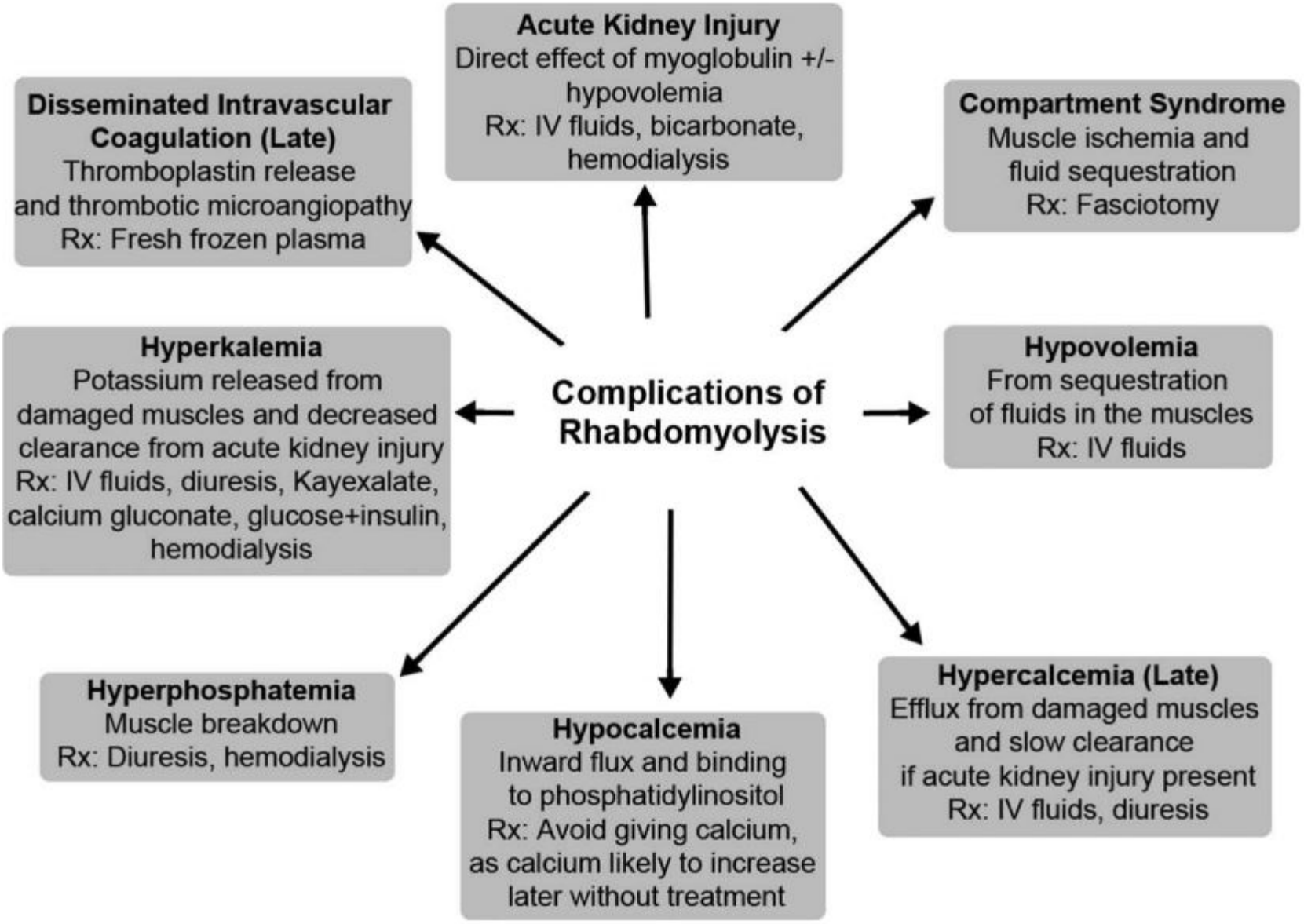
* Requires adjustment in renal impairment.

DRUG-INDUCED RHABDOMYOLYSIS

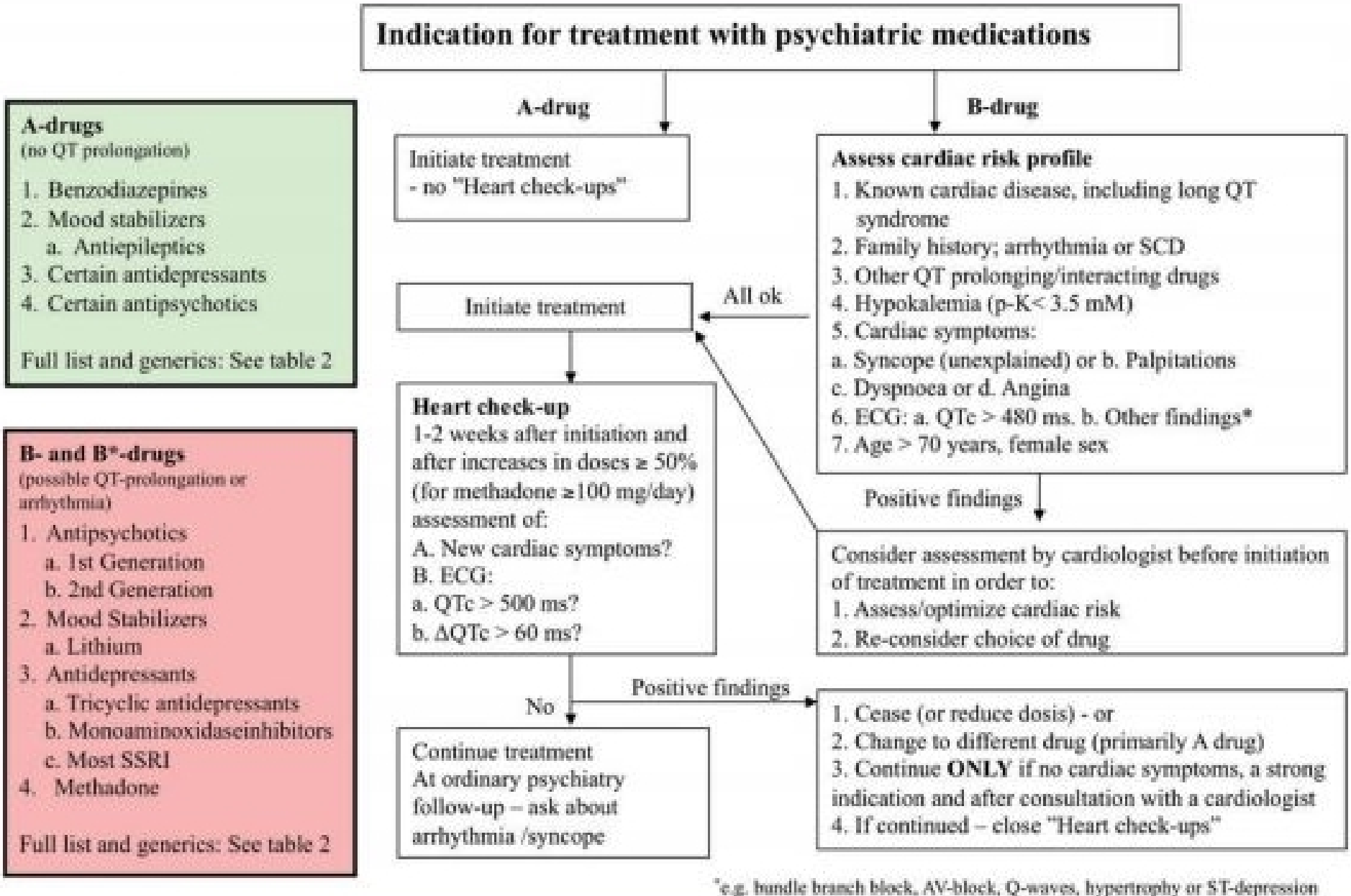
Statins	Other Antilipid Agents	Psychiatric Agents	Abused Substances	Antihistamines	Other
Lovastatin	Ezetimibe	Amitriptyline	Alcohol	Diphenhydramine	Amphotericin B
Pravastatin	Bezafibrate	Amoxapine	Cocaine	Doxylamine	Arsenic
Simvastatin	Clozafibrate	Doxepin	Heroin/Opiates		Azathioprine
Fluvastatin	Ciprofibrate	Fluoxetine	Amphetamines		Carbon monoxide
Atorvastatin	Clofibrate	Fluphenazine	Methamphetamines		Halothane
Rosuvastatin	Gemfibrozil	Haloperidol	Lysergic acid diethylamide		Naltrexone
		Lithium	Phencyclidine		Quinidine
		Protriptyline			Penicillamine
		Perphenazine			Pentamidine
		Promethazine			Propofol
		Chlorpromazine			Salicylates
		Trifluoperazine			Succinylcholine
		Venlafaxine			Theophylline
		Benzodiazepines			Terbutaline
		Barbiturates			Thiazides
					Vasopressin

Table 4. Proposed Risk Factors for Statin-Induced Rhabdomyolysis

Endogenous Risks	Exogenous Risks
Advanced age (>80 years)	Alcohol consumption
Small body frame and frailty	Heavy exercise
Multisystem disease	Surgery with severe metabolic demands
•Renal dysfunction	Agents affecting the cytochrome P450 system, especially
•Hepatic dysfunction	•Fibrates
Thyroid disorders, especially hypothyroidism	•Nicotinic acid
Hypertriglyceridemia	•Cyclosporine
Metabolic muscle disease	•Azole antifungals
•Carnitine palmitoyltransferase II deficiency	•Macrolide antibiotics
•McArdle disease	•Human immunodeficiency virus protease inhibitors
•Myoadenylate deaminase deficiency	•Nefazodone (antidepressant)
	•Verapamil
	•Amiodarone
	•Warfarin
	•Consumption of >1 quart daily of grapefruit juice


Complications of Rhabdomyolysis
Acute Kidney Injury
Direct effect of myoglobulin +/- hypovolemia
Rx: IV fluids, bicarbonate, hemodialysis
Disseminated Intravascular Coagulation (Late)
Thromboplastin release and thrombotic microangiopathy
Rx: Fresh frozen plasma
Compartment Syndrome
Muscle ischemia and fluid sequestration
Rx: Fasciotomy
Hyperkalemia
Potassium released from damaged muscles and decreased clearance from acute kidney injury
Rx: IV fluids, diuresis, Kayexalate, calcium gluconate, glucose+insulin, hemodialysis
Hypovolemia
From sequestration of fluids in the muscles
Rx: IV fluids
Hyperphosphatemia
Muscle breakdown
Rx: Diuresis, hemodialysis
Hypocalcemia
Inward flux and binding to phosphatidylinositol
Rx: Avoid giving calcium, as calcium likely to increase later without treatment
Hypercalcemia (Late)
Efflux from damaged muscles and slow clearance if acute kidney injury present
Rx: IV fluids, diuresis

Risk of arrhythmia induced by psychotropic medications:



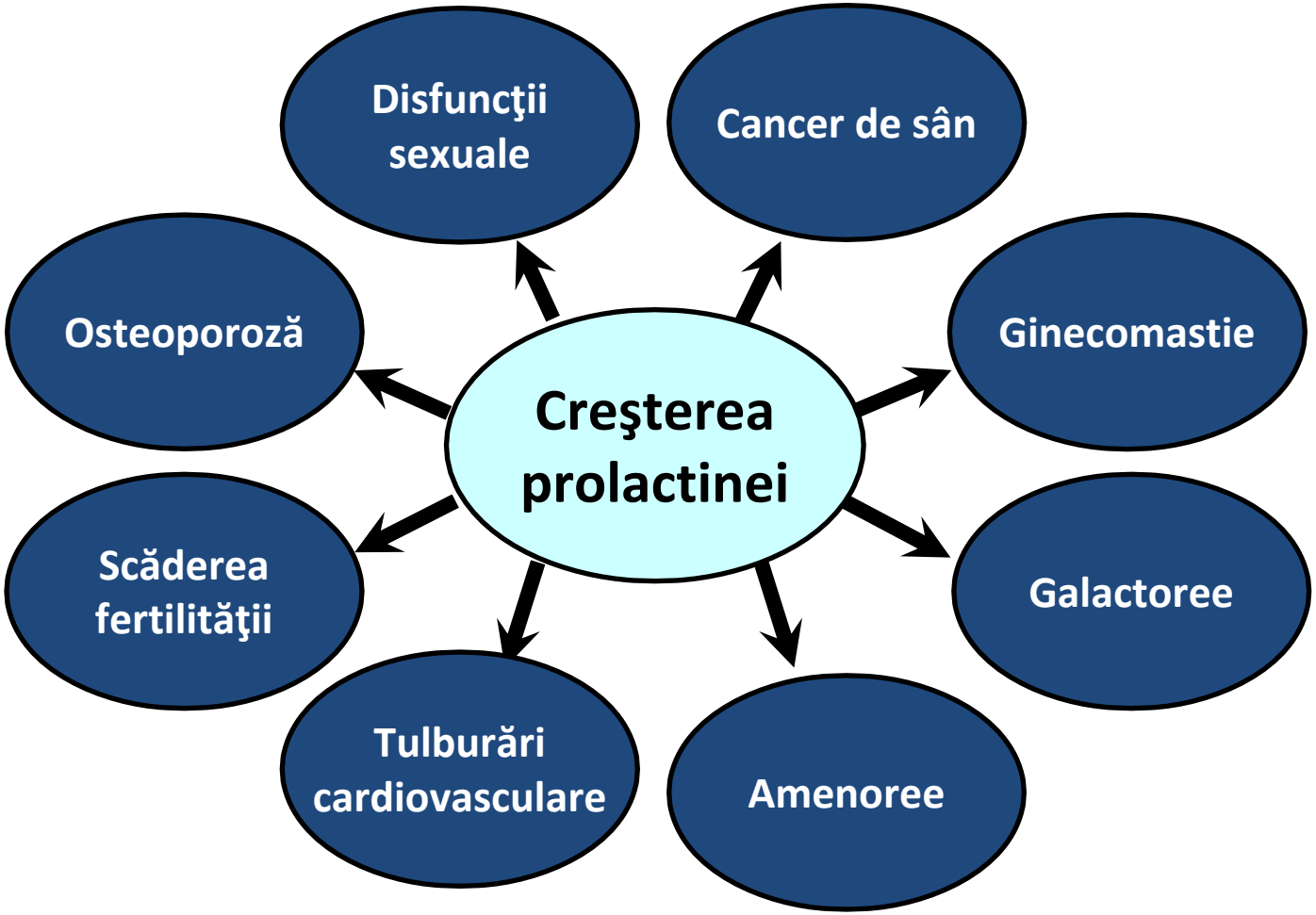
DRUGS INDUCING SUSTAINED HYPERPROLACTINEMIA

Antipsychotics	***Typical***	Haloperidol Chlorpromazine, Thioridazine, Thiothixene
	Atypical	Risperidone, Amisulpride Molindone, Zotepine
Antidepressants	***Tricyclics***	Amitriptyline, Desipramine Clomipramine Amoxapine
	SSRI	Sertraline, Fluoxetine, Paroxetine
	MAO-I	Pargyline, Clorgyline
Other Psychotropics		Buspirone Alprazolam
Prokinetics		Metoclopramide, Domperidone
Antihypertensive		Alpha-methyldopa, Reserpine, Verapamil
Opiates		Morphine
H_2 Antagonists		Cimetidine, Ranitidine
Others		Fenfluramine, Physostigmine Chemotherapics

Note: Only drugs with demonstrated ability to induce hyperprolactinemia above the normal range have been included in this table.

La Torre, 2007

Efectele adverse ale hiperprolactinemiei



Halbreich et al 2003

Some possible mechanisms of drug-induced depression

DRUG OR DRUG CLASS	POSSIBLE MECHANISM FOR DID
Nifedipine, other calcium channel blockers	Block slow influx of calcium into the cell, inhibiting calcium-dependent neurotransmitter release and reducing neurotransmitter amplification through the second-messenger system[20]
Benzodiazepines	Based on rodent studies: decreased release of serotonin in hippocampus (except with alprazolam)[23]
Exogenous corticosteroids	Based on rodent development studies: dexamethasone administration leads to deficits in the number and size of neural cells; reduced function of G-protein-coupled catecholaminergic or cholinergic receptors[24]
Varenicline	Displaces nicotine from acetylcholine receptors, produces low-to-moderate levels of dopamine release, and stimulates mesolimbic dopamine system. May upset the balance in cholinergic-adrenergic tone potentially leading to depression or mania[25]

Rogers & Pies, 2008

Citocromul p450 controleaza interactiunile medicamentoase

CYP450*

INHIBIȚIE / COMPETIȚIE / INDUCȚIE

INTERACȚIUNI MEDICAMENTOASE

Circuitul de metabolizare al altor medicamente uzuale

CYP1A2	CYP2C	CYP2D6	CYP3A4.5.7
Amitriptilină	Amitriptilină	Amitriptilină	Fluvoxamină
Clomipramină	Clomipramină	Clomipramină	Propranolol
Imipramină	Imipramină	Desipramină	Amlodipină
Fluvoxamină	**Escitalopram**	Nortriptilină	Diltiazem
Propranolol	Fluoxetină	Fluoxetină	Felodipină
Verapamil	Fluvoxamină	Fluvoxamină	Lercanidipină
Warfarină	Paroxetină	Paroxetină	Nifedipină
	Sertralină	**Sertralină**	Nitrendipină
	Irbesartan	**Venlafaxină**	Verapamil
	Losartan	*Carvedilol*	Amiodaronă
	Warfarină	*Propranolol*	Quinidină
	Citalopram	*Metoprolol*	*Atorvastatină*
	Moclobemid	*Timolol*	*Rosuvastatină*
	Propranolol	Flecainidină	*Simvastatină*
	Warfarină	Lidocaină	*Cerivastatină*
		Quinidină	

Mechanisms of Drug Induced QT Interval Prolongation

. Possible Drug-Drug Interactions of Drug that prolong QTc and are metabbolized by Cytochromes

Cytochrome	Substrates that prolong QTc		Cytochrome Inhibitors	
CYP1A2	Amitriptyline Clozapine Desipramine Imipramine Nortriptyline		Cimetidine Ciprofloxacin Diltiazem Erythromycin Fluvoxamine	Grapefruit juice Mexiletine Norfloxacin Ritonavir Tacrine
CYP2C	Amitriptyline Imipramine		Amiodarone Cimetidine Fluconazole Fluoxetine	Fluvastatin Fluvoxamine Omeprazole Ritonavir
CYP2D6	Amitriptyline Clozapine Desipramine Flecainide Fluoxetine Haloperidol Imipramine	Mexiletine Nortriptyline Paroxetine Risperidone Sertindole Tamoxifen Thioridazine	Amiodarone Cimetidine Fluoxetine Haloperidol Paroxetine	Propafenone Quinidine Ritonavir Thioridazine
CYP3A4	Amiodarone Cisapride Disopyramide Erythromycin Imipramine Quinidine	Sertraline Tacrolimus Tamoxifen Terfenadine Pimozide	Amiodarone Cimetidine Clarithromycin Diltiazem Erythromycin Fluconazole Fluoxetine Fluvoxamine Indinavir	Itraconazole Ketoconazole Metronidazole Nefazodone Nelfinavir Omeprazole Quinidine Ritonavir Saquinavir

Table 7. Causes that can induce QTc- Prolongation

- Bradycardia
- Central nervous System disease (intracranial trauma, subarachnoid hemorrhage, stroke)
- Congenital long QT syndrome
- Dysautonomy (Diabetes mellitus, amyloidosis, others)
- Elderly
- Electrolyte disturbance (hypomagnesemia, hypokalemia)
- Heart failure
- Hypoglycaemia
- Hypothermia
- Hypothyroidism
- Ion channel polymorphism
- Ischemic myocardiopathy
- Obesity
- Reduced repolarization reserve (see the text)

Pro-Arrhythmic Potential of Oral Antihistamines (H1): Combining Adverse Event Reports with Drug Utilization Data across Europe

Elisabetta Poluzzi[1], Emanuel Raschi[1], Brian Godman[2,3], Ariola Koci[1], Ugo Moretti[4], Marija Kalaba[5], Bjorn Wettermark[2,6,7], Miriam Sturkenboom[8], Fabrizio De Ponti[1]*

Conclusions

Combined analysis of pharmacovigilance and drug utilisation data can provide useful elements for clinicians and regulators in terms of population perspectives of safety concerns of drugs.

Some antihistamines resulted in signals of torsadogenic risk and most of them are largely used especially in some European Countries.

National Agencies should focus their attention on own peculiar uses of antihistamines and define strategies to minimise proarrhythmic potential, also in the light of their multiple place in therapy and the difficulty in monitoring their use by physicians because of the high frequency of self-medication. Educational initiatives focussed on recognition of patient susceptibility and possible differences in the potential risk among single agents should be addressed.

Antimicrobials and QT prolongation

Jay W. Mason*

Table 1. Antibiotic classes associated with QT prolongation

Class	Example (and citation)
Macrolides	erythromycin[24]
Fluoroquinolones	moxifloxacin[25]
Antimalarials	chloroquine[26]
Pentamidine	pentamidine[27]
Azoles	ketoconazole[28]
Antivirals	
NNRTI	rilpivirine[29]
PI	saquinavir[30]

Eficienta medicatiei si lipsa RA se coreleaza cu:

- Factorii genetici, farmacogenomica
- Integritatea functionala hepatica – hepatosteatoza alcoolica si non alcoolica
- Calitatea circulanta a proteinelor de legare a medicamentelor – hipoalbuminemia
- Integritatea functiei renale - clearance creatinina
- Integritatea BHE

OBLIGATORIU: transaminaze, albumina serica, creatinina

Costuri

3.5 million persons with schizophrenia in the US in 2013

Economic burden of $155.7 billion:

$37.7 billion for direct health care

$9.3 billion for direct non–health care

$117.3 billion for indirect costs.

The average annual cost

$44,773 / person

Indirect costs

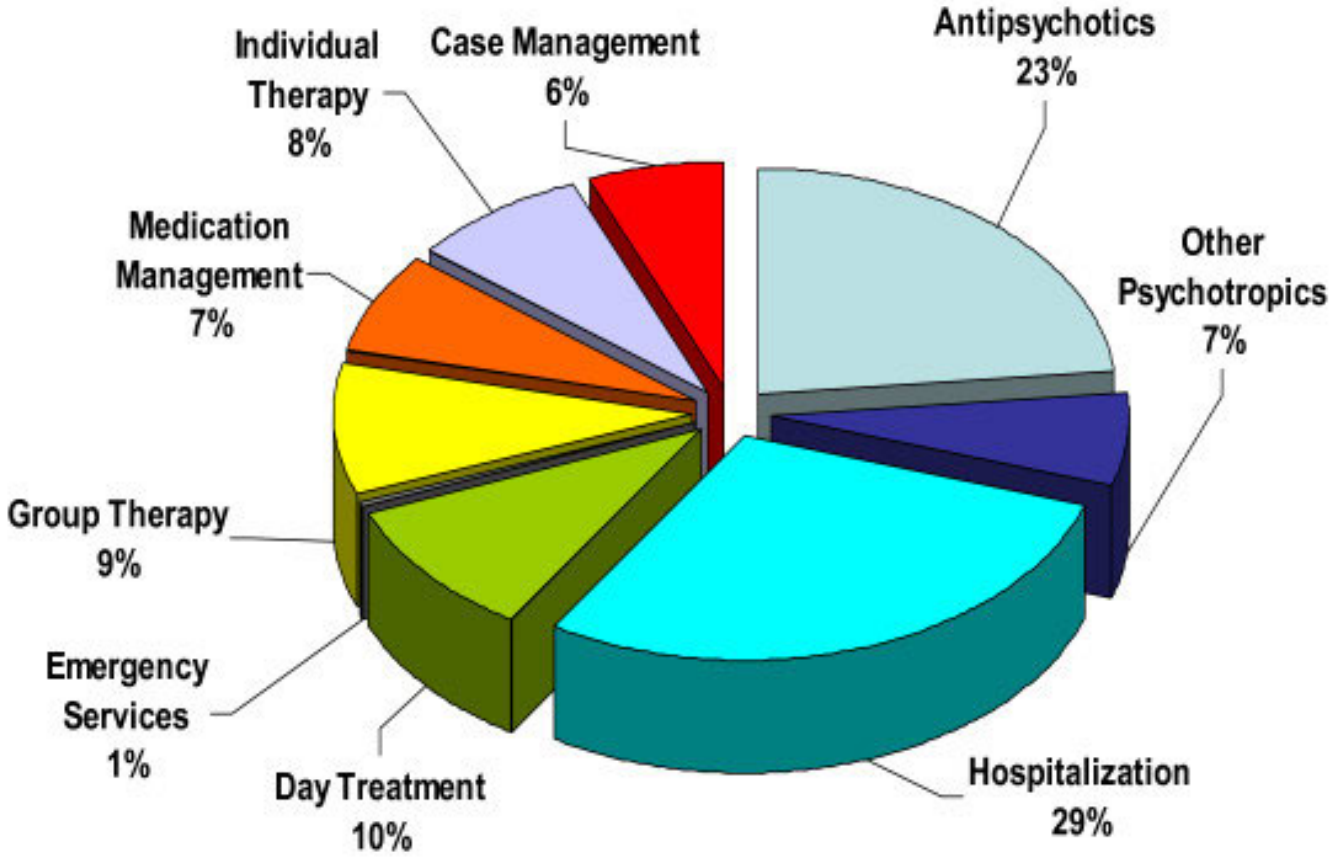
(1) % of uninsured patients with schizophrenia,
(2) % of patients who are victims of a crime,
(3) the annual number of caregiving hours,
(4) % of patients with schizophrenia in regular contact with family caregivers

Brian Miller, The Heavy Economic Burden of Schizophrenia, 2016

Schizophrenia is a chronic disorder associated with a high economic burden.

- Direct health care costs (hospital inpatient treatment, outpatient and emergency department visits, and medications)
- Direct non–health care costs (law enforcement, incarceration, and homeless shelters)
- Indirect costs (unemployment, lost productivity, premature mortality, reduced work productivity, caregiving).

Mental health cost components as a proportion of total annual mental health costs. Of the 1-year per patient total mental health treatment cost of $16,098, the largest single contributor was the cost of hospitalization (29%), followed by antipsychotic medication (23%).



Costs of treating patients with schizophrenia who have illness-related crisis events, Baojin Zhu, BMC Psychiatry. 2008; 8: 72

Proportion of participants in each crisis event category and degree of overlap between categories

(n = 1557)	Hospitalized in prior 6 months	Arrested in previous 6 months	Violent behavior in previous 4 weeks	Concurrent substance abuse diagnosis	Attempted suicide in past 4 weeks
Hospitalized in prior 6 months (N = 240)	__	22 (9.2%)	17 (7.1%)	87 (36.3%)	11 (4.6%)
Arrested in previous 6 months (N = 56)	22 (39.3%)	__	5 (8.9%)	26 (46.4%)	1 (1.8%)
Violent behavior in previous 4 weeks (N = 62)	17 (27.4%)	5 (8.1%)	__	26 (41.9%)	2 (3.2%)
Concurrent substance abuse diagnosis (N = 413)	87 (21.1%)	26 (6.6%)	26 (6.6%)	__	8 (2.0%)
Attempted suicide in past 4 weeks (N = 18)	11 (61.1%)	1 (5.6%)	2 (11.1%)	8 (44.4%)	__

Costs of treating patients with schizophrenia who have illness-related crisis events, Baojin Zhu, BMC Psychiatry. 2008; 8: 72

Mean 1-year costs for patients with and without specific number of crisis event categories

	Number of types of crisis events			
	None	**One only**	**Two or more**	**Three or more**
Patients with event, N (%)	938 (60.2%)	481 (30.9%)	138 (8.9%)	29 (1.9%)
Mean 1-year cost of hospitalization per patient	$830	$6,912 *	$23,149 *	$33,199 *
Mean 1-year total mental health cost per patient	$11,739	$19,066 *	$35,385 *	$44,599 *
Mean number of days hospitalized	3.7	21.8	72.7	101.1
Mean number of hospital admissions	0.2	0.8	1.7	2.7

Costs of treating patients with schizophrenia who have illness-related crisis events, Baojin Zhu, BMC Psychiatry. 2008; 8: 72

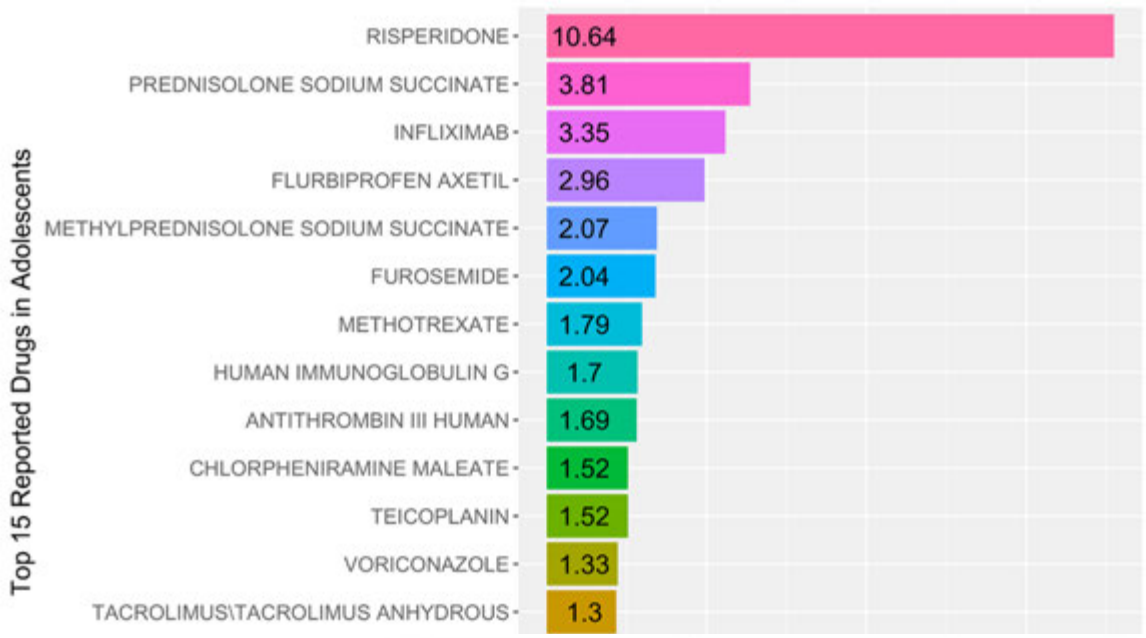
Algorithm of the patient-reported causality assessment

Item	Description	Answer Scores
1	Nu am experimentat acest simptom înainte de a începe să iau medicamentul	Yes 1
2	Simptomul a început imediat după ce am început să iau medicamentele	Yes 1
3	Am experimentat acest simptom rar înainte de a începe să iau medicamentele	Yes 1
4	Simptomul a fost mai puțin grav înainte de a începe să iau medicamentele	Yes 1
5	Simptomul a dispărut când am încetat medicatia dar a reaparut când am început să o iau din nou	Yes 2
6	Simptomul a dispărut când am încetat să mai iau medicamentele	Yes 1
7	Simptomul a început sau a devenit mai grav atunci când doza de medicament a crescut	Yes 1
8	Simptomul a scăzut sau a dispărut când doza de medicament a scăzut	Yes 1
	Alte motive: Credeți că există alte motive pentru a vă confrunta cu acest efect secundar (altul decât medicamentul)?	Yes -1

Sieta T de Vries, Flora M Haaijer-Ruskamp, Dick de Zeeuw, and Petra Denig, Construct and concurrent validity of a patient-reported adverse drug event questionnaire: a cross-sectional study, Health Qual Life Outcomes. 2014; 12: 103. Published online 2014 Aug 13. doi: [10.1186/s12955-014-0103-6]

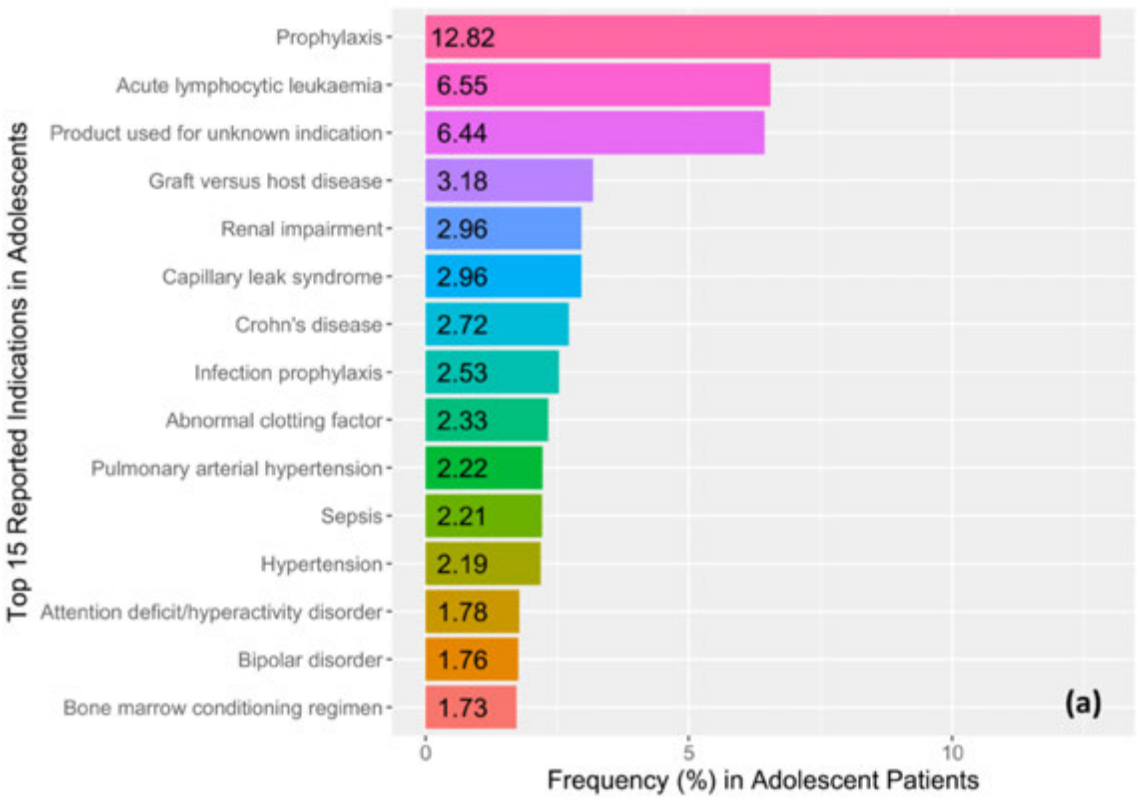
Method	Feasibility	Yield	Usefulness
General Practitioners registering events	+/-	+/-	- Different kind of events - Setting areas for improvement per practice in patient safety
Pharmacist registering events	+	-	- Only medication errors - Guidance in improving patient safety in prescribing medication
Patients' questionnaire about patient safety	++	+	- Different kind of events - Revealing GPs' blind spots - Setting areas for improvement per practice in patient safety
Random audit of medical records	+/-	+	- ***Mostly therapeutic*** and communication events - Time consuming
Audit of medical records of deceased patients	+	+/-	- Different kind of events - Low number of patients
Clinical Pharmacologist	**++**	**+**	**- Different kind of events - Adverse Events - Drug interaction - Improve patient care through the safe, economic and effective use of medicines.**

1. BMC Family Practice Research article Open Access Mix of methods is needed to identify adverse events in general practice: A prospective observational study Raymond Wetzels1, René Wolters, Chris van Weel, Michel Wensing. 2. The role of the clinical pharmacologist in the management of adverse drug reactions, Moore N, Drug Saf. 2001 Jan;24(1):1-7.



RISPERIDONE

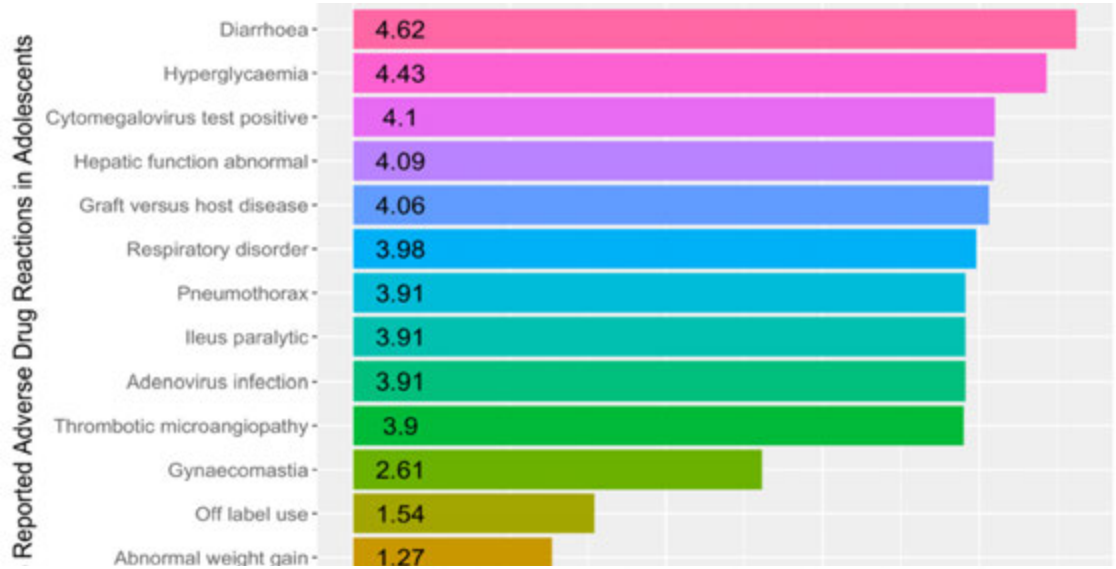
Frequencies for the top 15 reported drugs in adolescent patient records identified in the FDA Adverse Events Reporting System (2014-2017)

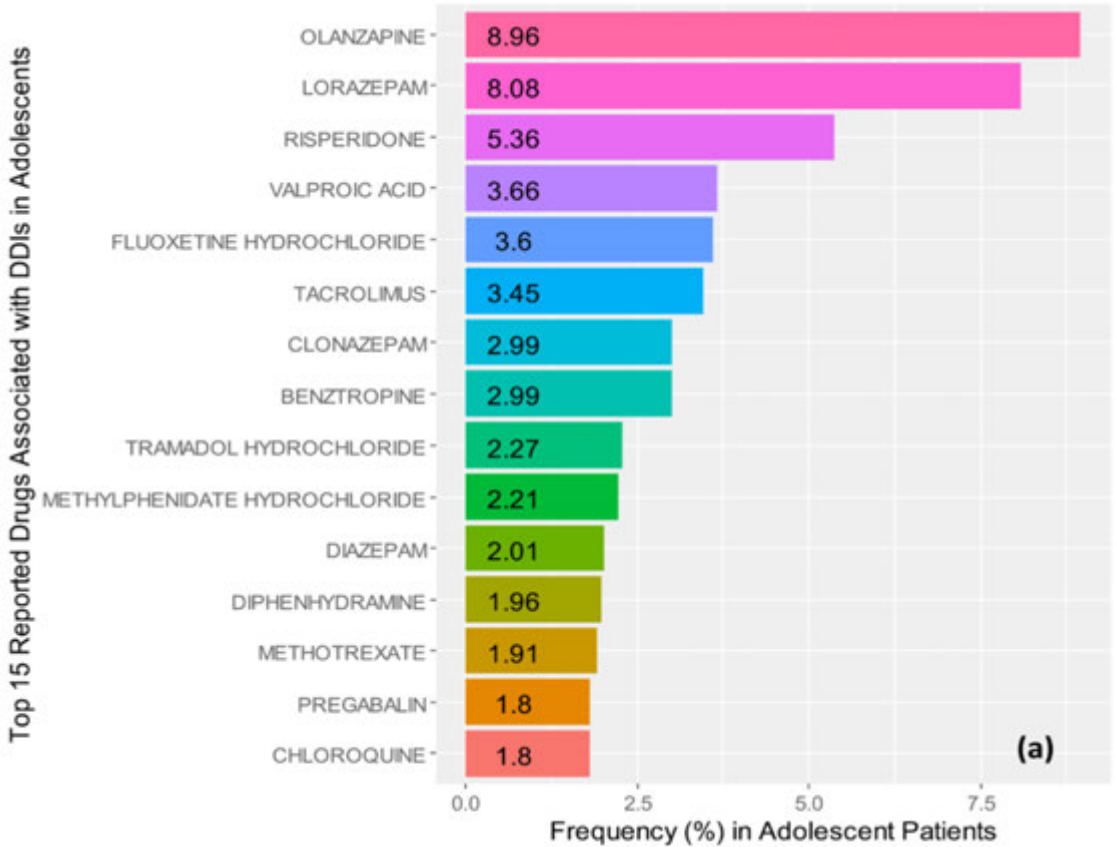


PROPHYLAXIS

Frequencies for the top 15 reported clinical indications

Andy R. Eugene, Beata Eugene, An opportunity for clinical pharmacology trained physicians to improve patient drug safety: A retrospective analysis of adverse drug reactions in teenagers, F1000Research 2018, 7:677





HYPERGLYCEMIA #2

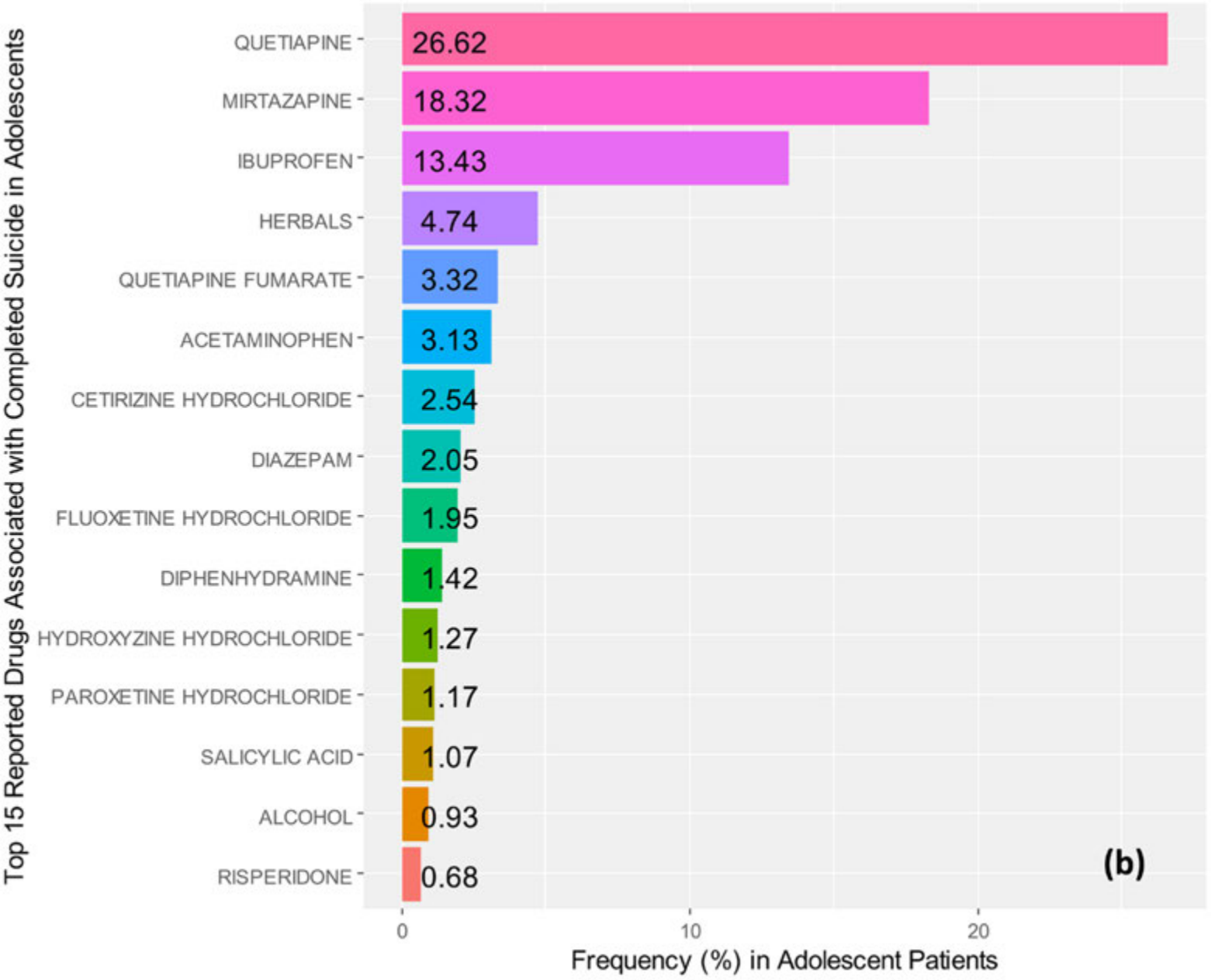
Frequencies for the top 15 reported adverse drug reactions (ADRs) in adolescent patient records identified in the FDA Adverse Events Reporting system

OLANZAPINE

Frequencies for the top 15 reported medications associated with drug-drug interactions (DDIs)

Andy R. Eugene, Beata Eugene, An opportunity for clinical pharmacology trained physicians to improve patient drug safety: A retrospective analysis of adverse drug reactions in teenagers, F1000Research 2018, 7:677

Frequencies for the top 15 reported completed suicide in adolescent patient records identified in the FDA Adverse Events Reporting system ranging



Andy R. Eugene, Beata Eugene, An opportunity for clinical pharmacology trained physicians to improve patient drug safety: A retrospective analysis of adverse drug reactions in teenagers, F1000Research 2018, 7:677

Registries for Evaluating Patient Outcomes: A User's Guide. 3rd edition. (USA)

- **Changes in medical status**
- **Changes in patient characteristics**
- Changes in provider characteristics
- Changes in financial status
- Residence
- **Changes to, additions to, or discontinuation of exposures (medications, environment, behaviors, procedures)**
- Changes in health insurance coverage
- **Sources of care (e.g., where hospitalized)**
- **Changes in individual attitudes, behaviors**

ADVERSE EVENTS IN HOSPITALS: METHODS FOR IDENTIFYING EVENTS, Department of Health and Human Services OFFICE OF INSPECTOR GENERAL, USA, March 2010, OEI-06-08-00221

Methods for Identifying Events in the Case Study

The first stage

Five screening methods for possible events:

1. Nurse ***standardized*** reviews of medical records

2. Interviews of Medicare beneficiaries

3. Analysis of POA (present on admission) indicators

4. Analysis of Patient Safety Indicators

5. Reviews of internal hospital incident reports.

If any screening method identified a possible event, it was labeled a **"flag"** and the medical record proceeded to the second stage of review.

The second stage

consisted of physician reviews of those medical records for which at least one of the screening methods indicated that an event had possibly occurred.

CLINICAL AUDIT

- **Flags:** if a nurse review indicated that a patient contracted an infection during the hospitalization.
- If the nurse review also indicated that a patient fell during the hospital stay.

ADVERSE EVENTS IN HOSPITALS: METHODS FOR IDENTIFYING EVENTS, Department of Health and Human Services OFFICE OF INSPECTOR GENERAL, USA, March 2010, OEI-06-08-00221

The National Action Plan for Adverse Drug Event Prevention (ADE Action Plan) was established to address two key objectives:
(1) *identify common, preventable, and measurable adverse drug events* (ADEs) that may result in significant patient harm;
(2) align the efforts of Federal health agencies to reduce patient harms from these specific ADEs nationally.

- **On the basis of national ADE data from inpatient and outpatient settings, three types of ADEs were considered to be *common, clinically significant, preventable, and measureable*, and were therefore selected as the high-priority targets of the ADE AP.**
- **Anticoagulants (primary ADE of concern: bleeding)**
- **Diabetes agents (primary ADE of concern: hypoglycemia)**
- **Opioids (primary ADE of concern: accidental overdoses/oversedation /respiratory depression)**

- **The ADE Action Plan suggests a four-pronged approach to reduce patient harms from these three ADEs: Surveillance, Prevention, Incentives and Oversight (Explore opportunities, including financial incentives and oversight) and Research.**
- **Surveillance—Coordinate existing Federal surveillance resources and data to assess the health burden and rates of ADEs.**
- **Prevention—Share existing evidence-based prevention tools across Federal Agencies and with non-Federal health care providers and patients.**
- **Incentives and Oversight—Explore opportunities, including financial incentives and oversight authorities, to promote ADE prevention.**
- **Research - Identify current knowledge gaps and future research needs (unanswered questions) for ADE prevention.**

U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. (2014). National Action Plan for Adverse Drug Event Prevention. Washington, DC

PENTRU EVALUATORUL DE SPITAL

PENTRU AUDITUL CLINIC

- **Registrul de reactii adverse raportate pe sectie: cate, de catre cine, managementul reactiilor adverse**
- **Standardizare formular reactii adverse medic (anexa FOCG)**
- **Standardizare formular reactii adverse asistent medical – foaia de ingrijire**
- **Analiza prelungirii spitalizarii – media pe boala – cauze**
- **Revenire neprogramata (solicitare ambulatoriu, reinternare, urgenta)**
- **Reinternare – prin lipsa de eficienta a tratamentului, prin RA/interactiuni medicamentoase in alte sectii (cardiologie, dermatologie, neurologie, psihiatrie)**
- **Consulturi intersectie, altele decat cele prevazute la internare**
- **Diagnostice la externare vs diagnostic la internare / 72 ore**
- **Medicatie asociata**
- **Deces**

CONCLUZII

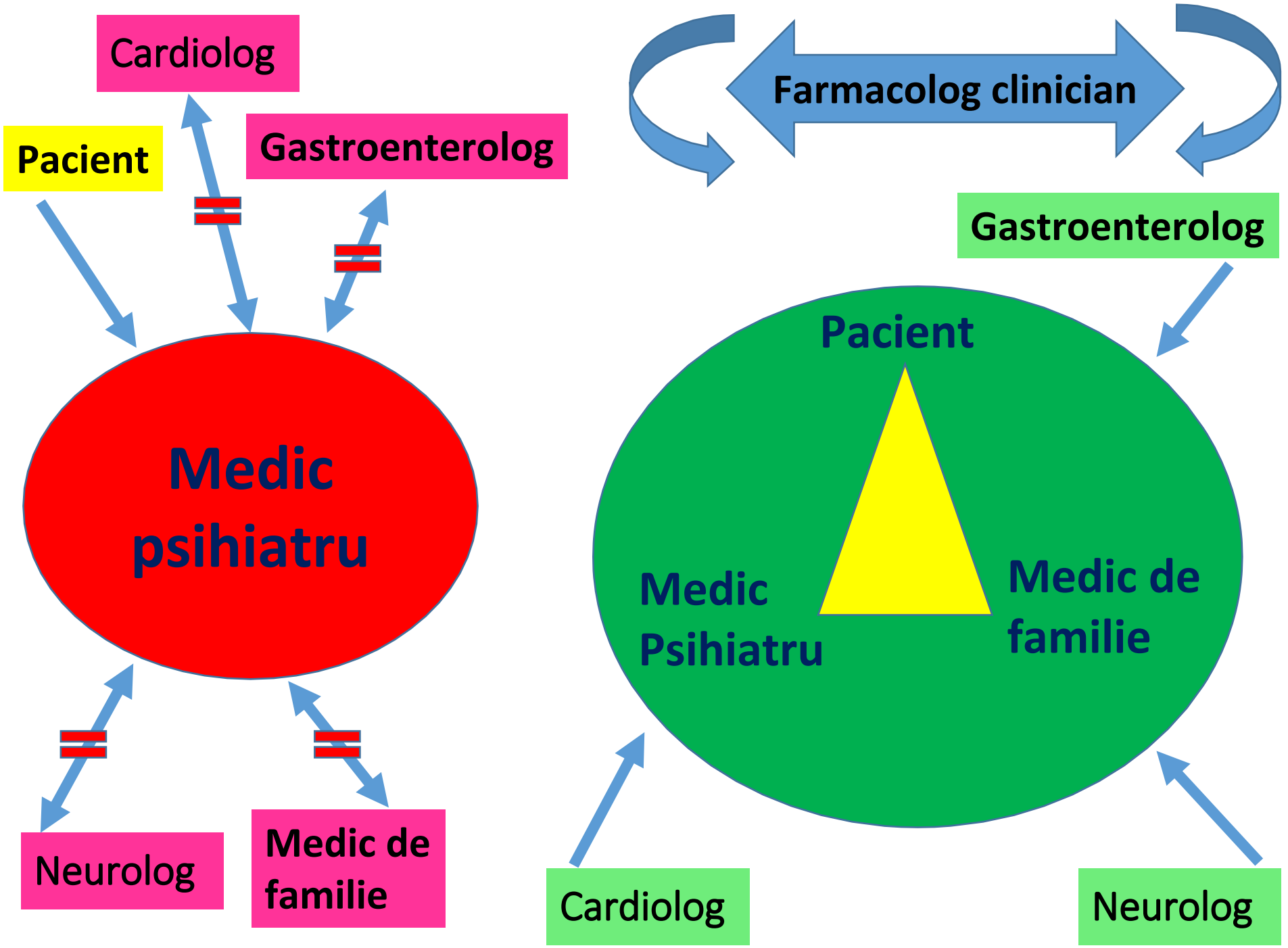
- **Eficacitatea medicatiei depinde de tratamentul precoce si aderenta la tratament**
- **Aderenta la tratament scade cu aparitia RA**
- **Conditiile din spitale in general scad aderenta la tratament**
- **Trebuie monitorizate si efectele pe termen lung ale medicatiei psihotrope inadecvate**
- **Lipsa comunicarii inter-specialitati**
- **Lipsa rezultate terapeutice – rezistenta la tratament**
- **Cresterea nr. ingrijirilor cronice conduce la o calitate scazuta a ingrijirii.**
- **Educarea cadrelor medicale cu privire la importanta reactiilor adverse – ce este o RA, de ce trebuie identificata o RA, cum se identifica o RA.**
- **Brosura privind siguranta pacientului – posibile reactii adverse frecvente, interactiuni medicamentoase**

TINTE 2019-2020

- **O echipa 3-5 experti va monitoriza unitatile psihiatrice si medicii de familie din 3 judete (Oltenia) – program pilot**
- **Program de training pentru medicii psihiatri cu privire la recunoasterea si raportarea reactiilor adverse si a interactiunilor medicamentoase**
- **Program de training pentru nursingul pihiatric cu privire la recunoasterea si raportarea reactiilor adverse si a interactiunilor medicamentoase**
- **Abordarea interdisciplinara la nivelul medicilor specialisti**
- **Elaborarea unor materiale educationale medic/asistent/pacient**

ARGUMENTE

- **Costuri financiare - farmacoeconomie**
- **Costuri morale – victimizarea psihiatriei ca specialitate**
- **Discrepanta intre ghiduri si decontarea de catre casa (9 zile pentru depresie cand 14-21 zile isi fac efectul medicamentelor si se poate aprecia evolutia - armonizarea legislatiei**
- **Particularitatile pacientului cu suferinta psihotica**
- **Spitale de acuti care nu au laboratoare de analize / alte dotari**


Cardiolog
Pacient
Gastroenterolog
Medic psihiatru
Neurolog
Medic de familie
Farmacolog clinician
Gastroenterolog
Pacient
Medic Psihiatru
Medic de familie
Cardiolog
Neurolog

FISA MONITORIZARE FARMACOLOGICA UNITATI PSIHIATRIE

- 1. Pacientul a avut tratament cu Romparkin? (identificarea sindromului extrapiramidal)
- DA / NU Daca DA, detaliati …….
- 2. Comportament violent al pacientului consemnat in registru. DA / NU
- 3. Suplimentarea medicatiei pentru reducerea agitatiei psihomotorii. DA / NU
- Daca DA, detaliati ……..
- 4. Regim alimentar pentru diabet sau consult diabet. DA / NU
- Daca DA, detaliati ……..
- 5. Consult cardiologic DA / NU
- Daca DA, detaliati ……..
- 6. Alte consulturi intersectie DA / NU
- Daca DA, detaliati ……..
- 7. Pacientul a fost izolat DA / NU
- 8. Pacientul a prezentat simptomatologie de tip gastrointestinal DA / NU
- Daca DA, detaliati …….
- 9. Pacientul a avut episoade de confuzie mentala sau dezorientare DA / NU
- 10. Pacientul a avut comportament agresiv sau suicidar DA / NU