



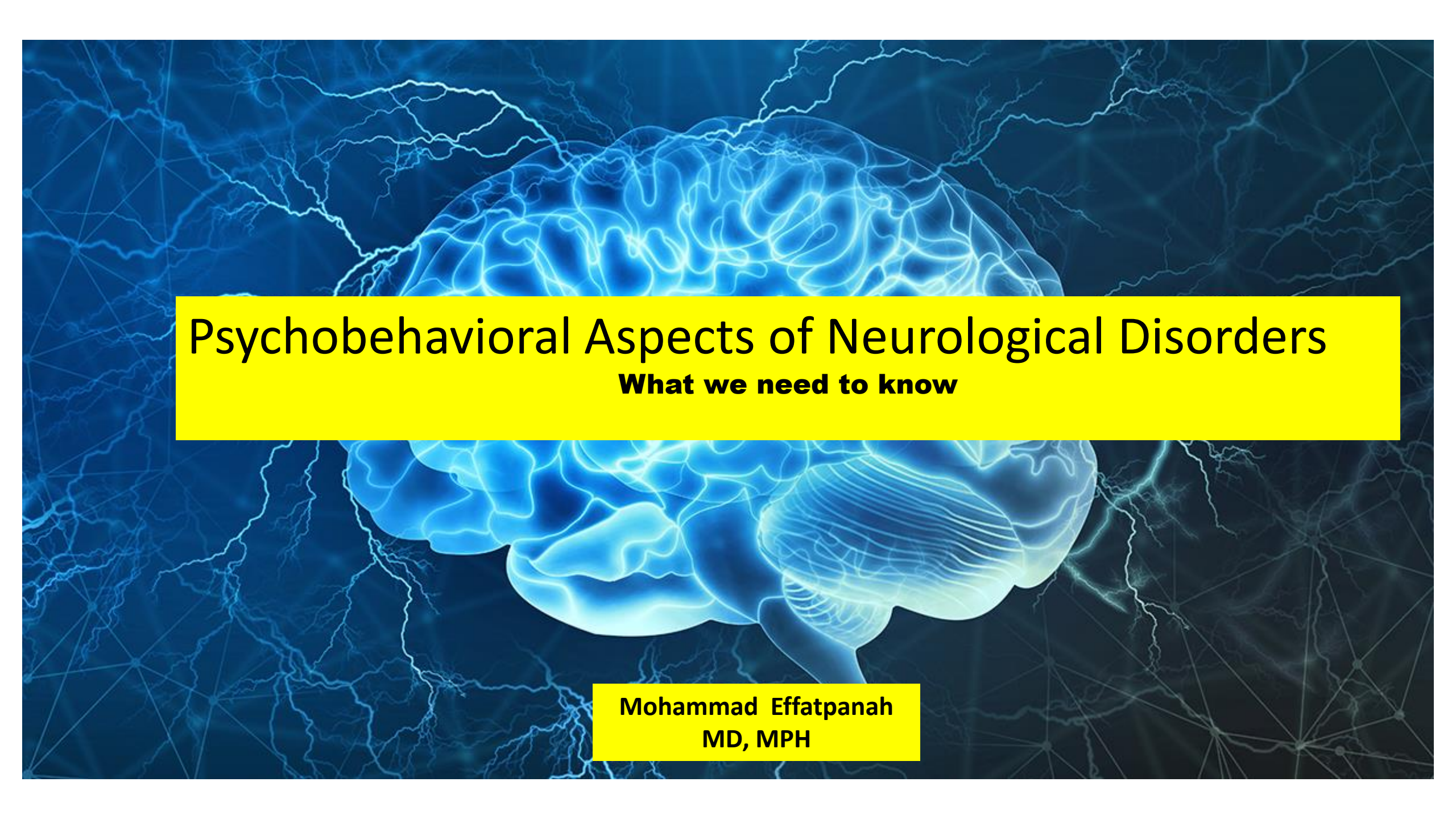
دانشگاه علوم پزشکی تهران



روز سوم
شنبه- ۱۴۰۴/۰۳/۲۴

سالن شهید یاسینی

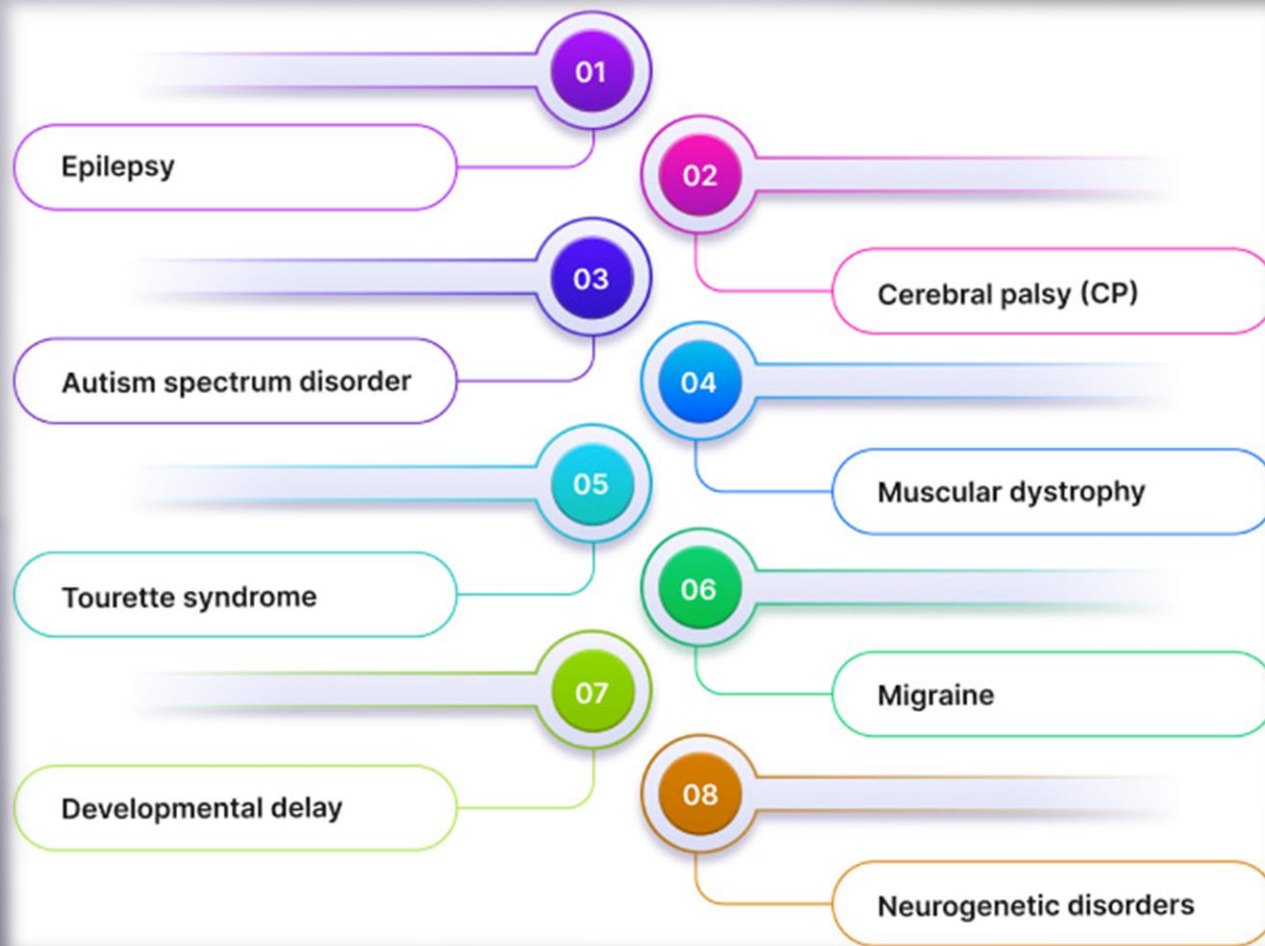
پانل رویکردهای چند رشته‌ای در نورولوژی کودکان		
ساعت	موضوع سخنرانی	سخنران
۸:۰۰-۸:۳۰	تازه‌های بیماری نورومتابولیک	دکتر محمودرضا اشرفی (ریاست پانل) فوق تخصص اعصاب کودکان
۸:۳۰-۹:۰۰	نقش مراکز جامع توانبخشی اعصاب در سلامت کودکان	دکتر محمدمهدی تقدیری فوق تخصص اعصاب کودکان
۹:۰۰-۹:۳۰	تازه‌های نوروفارماکولوژی در کودکان	دکتر شاهین آخوندزاده نورو فارماکولوژیست
۹:۳۰-۱۰:۰۰	Behavioral and psychological Aspects of Neurological Disorders	دکتر محمد عفت پناه فوق تخصص روان پزشکی کودک و نوجوان
		دکتر رضا شروین بدو فوق تخصص اعصاب کودکان
۱۰:۰۰-۱۰:۳۰	تومورهای مغزی کودکان، چالش‌ها و تازه‌ها	دکتر مرتضی اشرافی فلوشیپ جراحی مغز و اعصاب کودکان
۱۰:۳۰-۱۱:۰۰	استراحت	
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۱۲:۰۰-۱۳:۰۰	پرسش و پاسخ و بحث آزاد	
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Psychobehavioral Aspects of Neurological Disorders

What we need to know

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Psychobehavioral Aspects of Neurological Disorders

- Neurological diseases often lead to a wide range of neuropsychiatric symptoms, including **mood** disturbances, **cognitive** impairments, and **behavioral** changes.
- These diseases can significantly impact a patient's **quality of life** and **well-being**, **,emotional incontinence**, **anger**, **apathy** and **fatigue**. often alongside the physical symptoms of the neurological condition.

Psychobehavioral Aspects of Neurological Disorders



Pros

dual energy CT
consultation
medication
treatment
nonsteroidal
anti-inflammatory
drugs (NSAIDs)
pain reliever
corticosteroids
colchicine
non-medication
pain relief
cold packs
rest the joint
drink water
watch what you
eat and drink

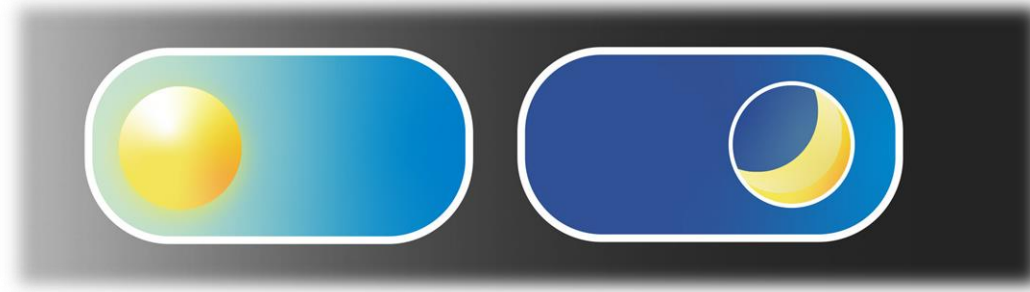
corticosteroids

Cons

healthy
body weight
limit intake
of meat,
fish and
poultry
choose low-fat
dairy products
limit or avoid
alcohol
keep your fluid
intake high
improves uric
acid removal
block uric acid production
control inflammation
and pain

Psychiatric Adverse Effects of **Corticosteroids**

The dark side



- Some studies have reported rates as high as **30%–50%** experiencing some **psychiatric disturbance**, other studies have found that nearly **28%** of patients experienced **mood-related symptoms**.

Key Mechanisms of Corticosteroid-Induced Psychiatric Disorders

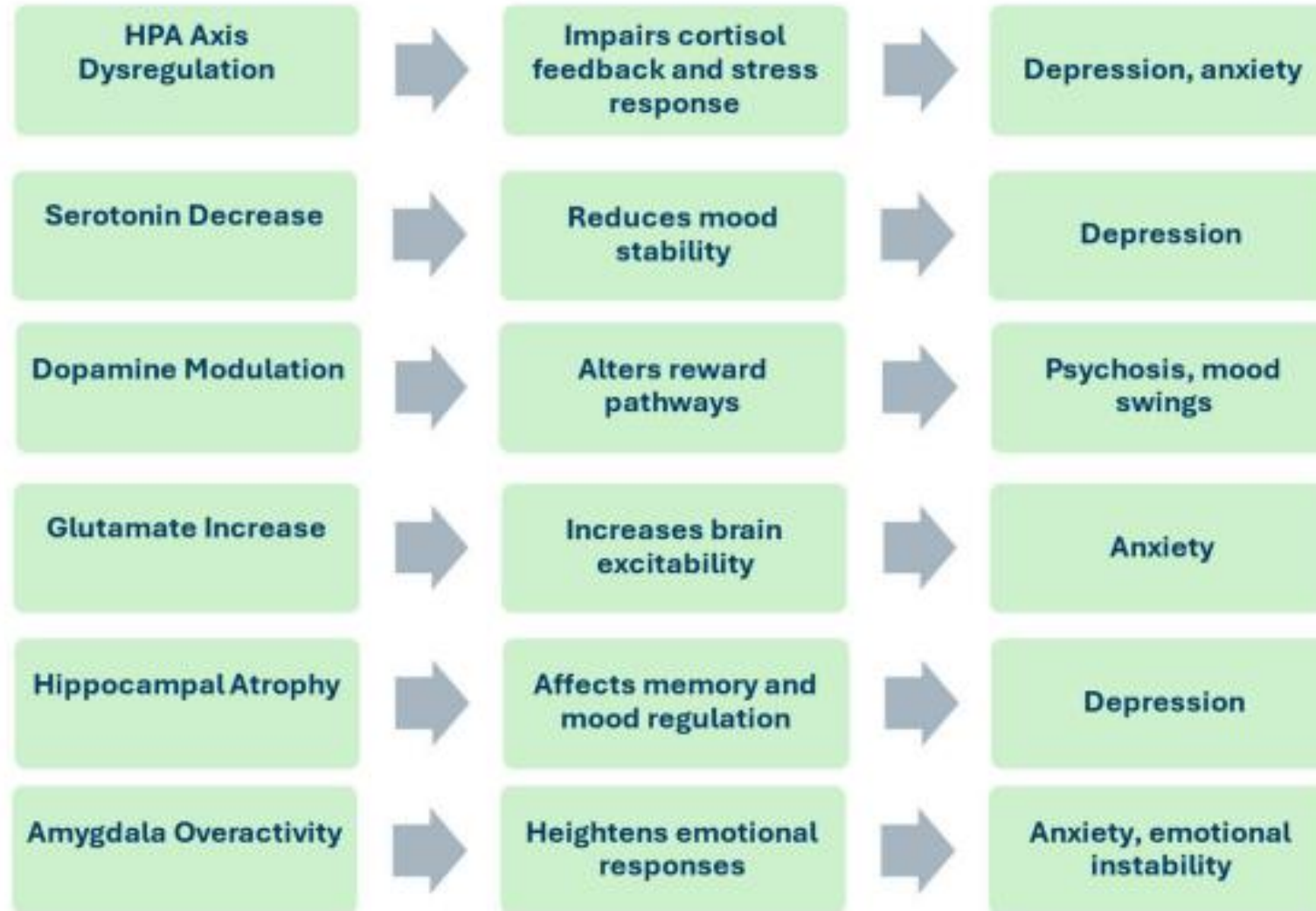


Figure 2. The key mechanism of corticosteroid-induced psychiatric disorders, through HPA axis dysregulation, neurotransmitter imbalances, and brain structure changes, contributing to depression, anxiety, and emotional instability.

Psychiatric Adverse Effects of Corticosteroids

The dark side

- Exogenous corticosteroids have been demonstrated to exert potent mood-altering effects in neuropsychiatric patients.
- In the **short term**, glucocorticoid use can increase energy and lead to varying degrees of euphoria, and if tolerated they are generally considered to be safe.
- **long-term** use or discontinuation of these agents can result in **depression** or exacerbate preexisting depression via various pathways, such as reduced serotonin and gamma-aminobutyric acid levels and overactivation of glucocorticoid receptors.

Psychiatric Adverse Effects of Corticosteroids

The dark side

- Corticosteroid-induced **psychosis** is a known, albeit not common, side effect of these medications, causing a range of psychiatric symptoms, including hallucinations and delusions.
- It's classified as a Substance/Medication-Induced Psychotic Disorder in the DSM-5.
- The reported incidence varies widely, from **2%** to **60%**, and the onset can be rapid, sometimes within a day of starting the medication.

Psychiatric Adverse Effects of Corticosteroids

The dark side

- **Management:**
- Treatment typically involves : Reducing or discontinuing the corticosteroid dose.
- Adding low-dose **atypical antipsychotics** if symptoms are severe.
- Considering other medications, such as **SSRIs**, for mood disturbances, with caution regarding drug interactions.

A close-up photograph of various pharmaceuticals, including white, orange, green, and pink tablets and capsules, scattered on a light blue surface. A yellow rectangular box is overlaid on the top left, and a white rectangular box with a black border is overlaid in the center.

drugs induced ...

drug induced by neurological drugs

Table 2. Psychosis With AEDs

Drug	Incidence (%)
Zonisamide	2.2-18.9
Topiramate	1.3-11.7
Ethotoin	8.7
Vigabatrin	0.7-6.7
Rufinamide	0.6-4.0
Levetiracetam	0.3-1.6
Primidone	1.4
Gabapentin, lacosamide, lamotrigine, perampanel	<1.0
Phenytoin	Toxic effect
Carbamazepine, clobazam, clonazepam, ethosuximide, ezogabine, oxcarbazepine, phenobarbital, pregabalin, tiagabine, valproate	NR

*AED: antiepileptic drug; NR: none reported.
Source: References 2, 21, 29, 35, 50-62.*



Table 1. Aggressive-Type Behavior With AEDs

Drug	Incidence (%)
Topiramate	1.9-81.8
Tiagabine	1.0-36.4
Clobazam	1.3-31.9
Levetiracetam	2.3-27.0
Vigabatrin	3.4-23.0
Perampanel	<1.0-20.0
Primidone	3.0-18.2
Gabapentin	9.4-13.0
Valproate	0.0-12.0
Rufinamide	3.0-11.6
Zonisamide	2.6-9.0
Ethotoin	8.7
Lacosamide	8.0
Lamotrigine	0.0-7.0
Carbamazepine	2.0-7.0
Oxcarbazepine	3.3
Ethosuximide	3.0
Ezogabine	1.0-2.0
Clonazepam, phenobarbital	CR
Phenytoin, pregabalin	NR

*AED: antiepileptic drug; CR: case reports; NR: none reported.
Source: References 2, 21-50.*

N 00300835031569

**TIAGABINE
HYDROCHLORIDE
Tablets
4 mg**

Medication Guide Required:
Each time tiagabine hydrochloride
tablets are dispensed, give the
patient a Medication Guide.

Rx only

30 TABLETS



U.S. Pharmacist
The Pharmacist's Resource for Clinical Excellence

Table 3. Hyperactivity/Restlessness With AEDs

Drug	Incidence (%)
Phenobarbital	10.0-42.0
Clobazam	4.0-27.0
Vigabatrin	6.1-25.7
Clonazepam	0.0-12.0
Carbamazepine	7.0-12.0
Lacosamide	11.8
Gabapentin	0.0-11.0
Ethosuximide	0.0-11.0
Valproate	0.0-10.0
Lamotrigine	0.0-10.0
Rufinamide	3.0-4.7
Primidone	4.5
Topiramate	2.7-4.4
Levetiracetam	2.5-3.8
Ethotoin, ezogabine, oxcarbazepine, perampanel, phenytoin, pregabalin, tiagabine, zonisamide	NR

AED: antiepileptic drug; NR: none reported.

Source: References 21, 22, 25, 29, 30, 32, 33, 35, 38, 40, 43, 53, 58, 61, 63-69, 70-72.

Table 4. Behavioral Disorder (NOS) With AEDs

Drug	Incidence (%)
Topiramate	0.0-43.8
Clobazam	1.4-41.1
Ethosuximide	0.0-32.0
Clonazepam	0.0-16.2
Levetiracetam	0.0-13.8
Lamotrigine	0.0-11.7
Rufinamide	8.3-10.0
Phenobarbital	9.0
Zonisamide	7.4
Lacosamide	6.3
Carbamazepine	CR
Ethotoin, ezogabine, gabapentin, oxcarbazepine, perampanel, phenytoin, pregabalin, primidone, tiagabine, valproate, vigabatrin	NR

AED: antiepileptic drug; CR: case reports; NOS: not otherwise specified; NR: none reported.

Source: References 22, 23, 25, 32, 34, 35, 53, 53, 63, 65, 68, 73-79.



	Lower likelihood	Higher likelihood
Psychiatric/behavioral side effects	Carbamazepine Lacosamide Lamotrigine Eslicarbazepine Gabapentin Oxcarbazepine Pregabalin Valproic acid	Brivaracetam Clobazam Levetiracetam Perampanel Phenobarbital Topiramate Vigabatrin Zonisamide
Cognitive side effects	Brivaracetam Eslicarbazepine Gabapentin Lacosamide Lamotrigine Levetiracetam Perampanel Pregabalin Rufinamide Tiagabine Vigabatrin	Phenobarbital Primidone Topiramate Zonisamide Oxcarbazepine

Table 5: Psychotropics and seizures^[1,2]

High risk	Intermediate risk	Low risk
Antidepressants • Amoxapine • Bupropion • Clomipramine • Maprotiline • Mianserin • Imipramine in higher doses	Amitriptyline Imipramine	SSRIs Trazadone Venlafaxine MAOI Mirtazapine
Antipsychotics • Chlorpromazine (dose related) • Clozapine (titration and dose related)	Haloperidol	Fluphenazine Trifluoperazine Risperidone Olanzapine Quetiapine

SSRIs – Selective Serotonin Reuptake Inhibitors; MAOI – Monoamine Oxidase Inhibitors

Table

Proposed treatments for steroid-induced psychiatric symptoms^a

Symptom	Proposed treatments
Mania/hypomania	Mood stabilizers (valproate, lithium, lamotrigine) Antipsychotics (quetiapine, olanzapine, haloperidol), with or without a benzodiazepine
Depression	SSRIs (sertraline, paroxetine) Antipsychotics (especially risperidone) Lithium ECT
Agitation	Benzodiazepines Haloperidol Second-generation antipsychotics

^aThese proposed treatments are off-label and largely anecdotal

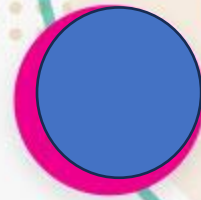
ECT: electroconvulsive therapy; SSRIs: selective serotonin reuptake inhibitors

Source: References 2-5,17,18



اینترفرون بتا 1

کنترل بیماری ام اس



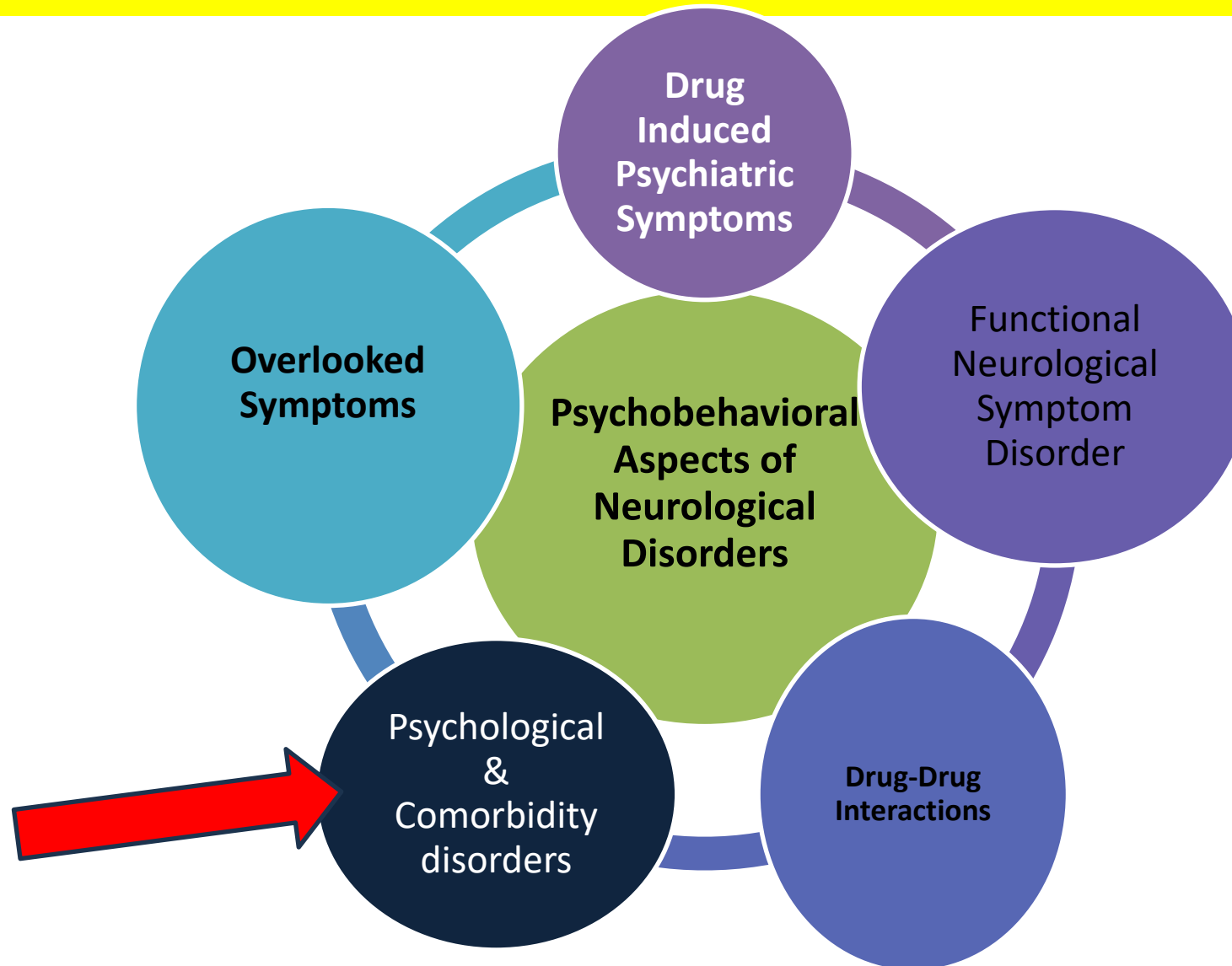
Psychosis may be induced by IFN- β medications in MS

- Psychosis can be induced by MS medications like IFN- β (interferon beta). This can manifest as auditory hallucinations, paranoid delusions, and increased aggressiveness.
- While the mechanisms aren't fully understood, some studies suggest a link between IFN- β and psychosis, particularly in individuals with pre-existing psychiatric conditions or vulnerability.

Psychosis may be induced by IFN- β medications in MS

- **Management:**
- In cases of IFN- β -induced psychosis, treatment often involves discontinuing the medication and prescribing antipsychotic medication.

Psychobehavioral Aspects of Neurological Disorders



- **Epilepsy** is frequently associated with a range of psychiatric consequences, with **up to 50%** of individuals experiencing mental health issues.

50%

50%



Anxiety and Epilepsy



51%
TIME

More than half of respondents said they did not have time during an office visit to address anxiety with their patients.

Respondents did not know which screening tools to use or where to refer people for treatment, or said they were uncomfortable addressing anxiety or had not received training on the topic.

43%
EDUCATION

30%
ACCESS

Respondents said they did not have access to psychological or psychiatric services for referral, or did not have access to screening tools.

Treatment of ANXIETY in patients with epilepsy

- Treating anxiety in people with epilepsy often involves a combination of approaches, including medication, behavioral therapies, and other supportive interventions.
- Medications like SSRIs, benzodiazepines (used cautiously), and specific AEDs (like pregabalin) can be used to manage anxiety symptoms.

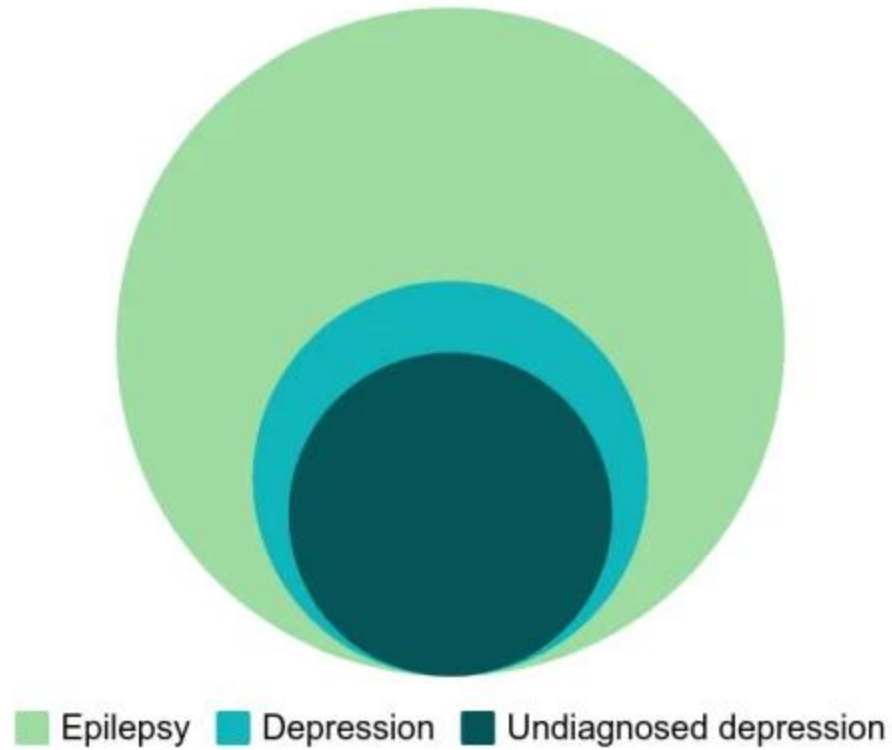
Medications for Anxiety:

- **Antidepressants (SSRIs):**
- Sertraline and citalopram are often considered **first-line options** for anxiety, especially in those with epilepsy.
- **Benzodiazepines:**
- While effective for anxiety, their long-term use can increase anxiety and potentially lead to misuse, so they are generally used as **second-line choices**.
- **Specific AEDs:**
- Some AEDs, like pregabalin, have demonstrated anxiolytic properties and may be used to manage anxiety in patients with epilepsy.
- **Other Antidepressants:**
- If necessary, high-dose antidepressants may be used, but careful monitoring is needed for potential side effects and interactions with AEDs.

Depression and Epilepsy



Depression in people with epilepsy

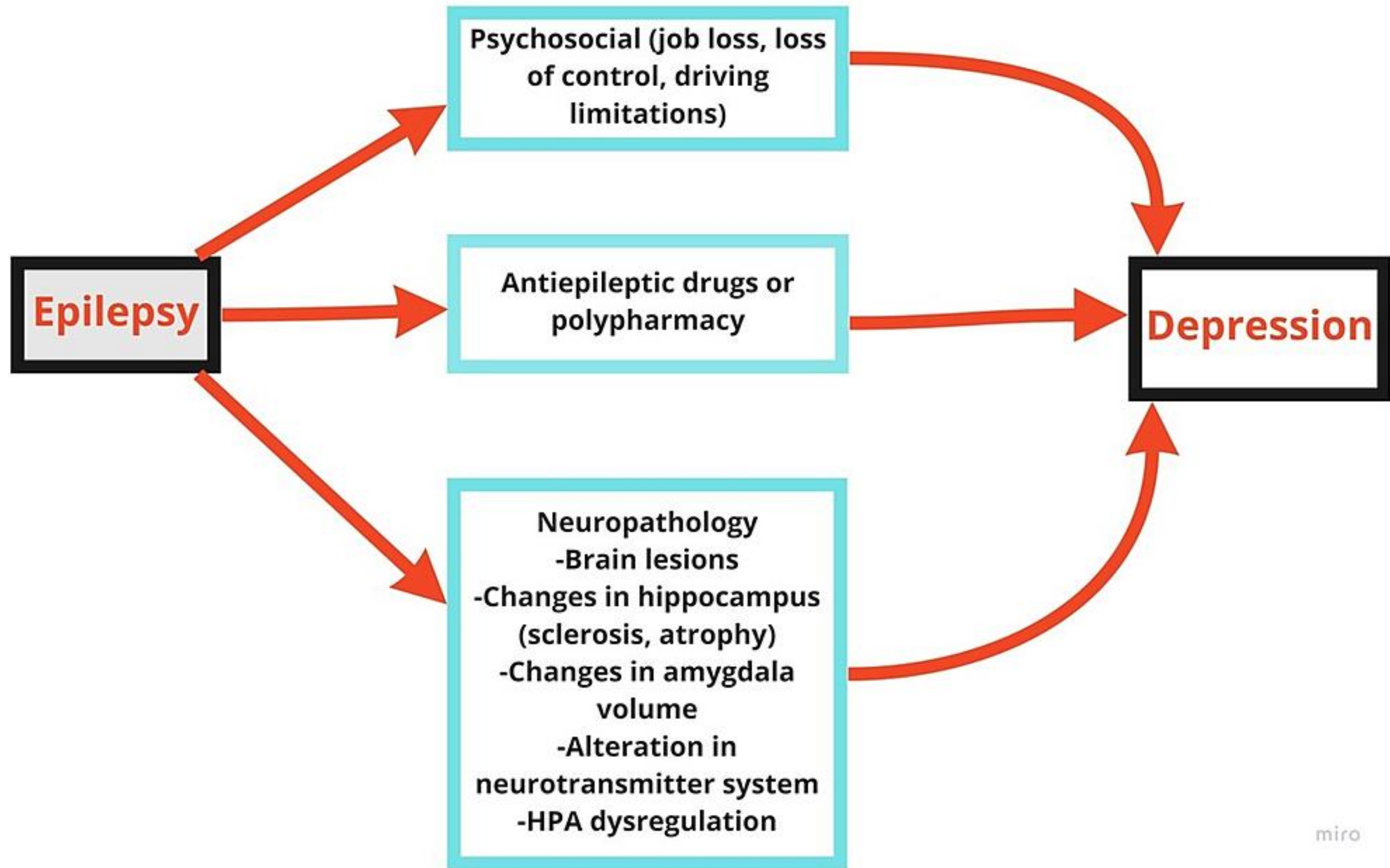


50%

Between 20% and 55% of people with epilepsy have depression, but only a fraction of them are being diagnosed and treated.

Depression and Epilepsy

- Untreated, depression is associated with lower quality of life, poor treatment adherence, higher health care utilization and a risk for suicide **up to 30** times higher than average.



Treatment of depression in patients with epilepsy

- Treating depression in people with epilepsy requires a multifaceted approach that addresses both the epilepsy and the depression. This includes optimizing seizure control, managing antiepileptic drug side effects, and utilizing psychotherapy and/or antidepressant medications.
- **Prioritize seizure management:**
- Effective seizure control is crucial as uncontrolled seizures can negatively impact mood and increase the risk of depression.
- **Review and adjust AEDs:**
- If possible, consider switching to or adding an AED with mood-stabilizing properties.
- **Minimize side effects:**
- Antiepileptic drugs can have side effects that contribute to depression, so careful monitoring and adjustment of dosage or medication may be necessary.

Antidepressant Medication:

- **SSRI and SNRI medications:**
- Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are often considered **first-line options** for treating depression in people with epilepsy.
- **Citalopram and sertraline:**
- **Citalopram** and **sertraline** are frequently recommended as suitable options for individuals with epilepsy and chronic health problems, according to NICE CKS guidance.
- **Avoid Tricyclic Antidepressants:**
- Tricyclic antidepressants (TCAs) should be used with caution in people with epilepsy due to the potential for seizures at toxic doses.

Table 1 – Antidepressants in PWE. Based on [18,19,50].

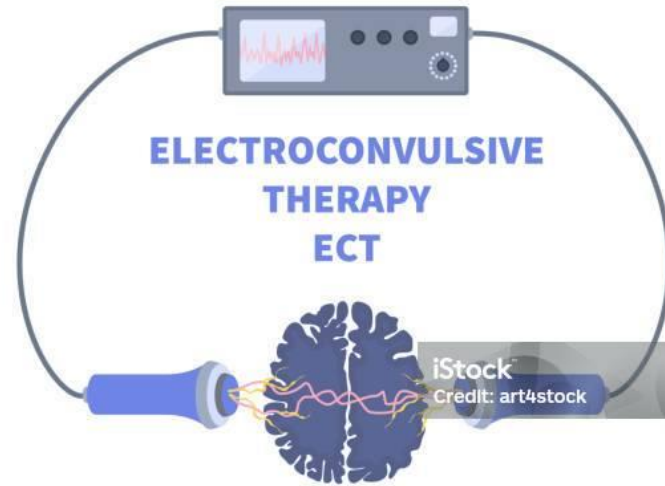
Drug	Dosing	Metabolism	Interaction with ASDs	Seizure risk	Level of evidence
SSRIs	Approved therapeutic doses	Liver (CYP450)	Carbamazepine, phenytoin (decrease level of some SSRIs)	Low/no influence	II
SNRIs	Approved therapeutic doses	Liver (CYP450)	Carbamazepine (decreases level of duloxetine)	Low/no influence	II
Mirtazapine	15–45 mg	Liver (demethylation, oxidation, conjugation with proteins)	Topiramate (increase sedation) Carbamazepine, phenytoin (increase metabolism)	Low/no influence	IA
Reboxetine	4–12 mg	Liver (CYP3A4)	Phenytoin, carbamazepine, phenobarbital (decrease level)	Low/no influence	III
Imipramine	30–300 mg	Liver (CYP1A2, CYP3A4, CYP2C19, CYP2D6)	Phenytoin, carbamazepine, phenobarbital, topiramate, (decrease level)	Medium (0.1–0.9%)	III
Bupropion	150–300 mg	Liver (mainly CYP2B6)	Carbamazepine (increases metabolism) Valproate (decreases metabolism)	Medium/high	IA
Amoxapine	200–600 mg	Liver (CYP450)	Carbamazepine (increased metabolism) Topiramate (increased sedation)	High	II
Clomipramine	10–225 mg	Liver (CYP3A4, CYP2C19, CYP1A2)	Phenytoin, carbamazepine, topiramate (decrease level)	High	II
Maprotiline	25–150 mg	Liver (CYP2D6, CYP1A2)	Phenobarbital, topiramate (increase sedation) Carbamazepine (decrease level)	High	III

Nonpharmacologic Treatment

- Depressive reactions can be treated with supportive therapy, counseling, and rehabilitation.
- Supportive therapy should be offered to patients newly diagnosed with epilepsy, as well as to their family members.
- Supportive therapy will help educate patients and their family members about epilepsy and determine a patient's state of mind regarding, and emotional reaction to, the disorder.

Non Pharmacologic Treatment

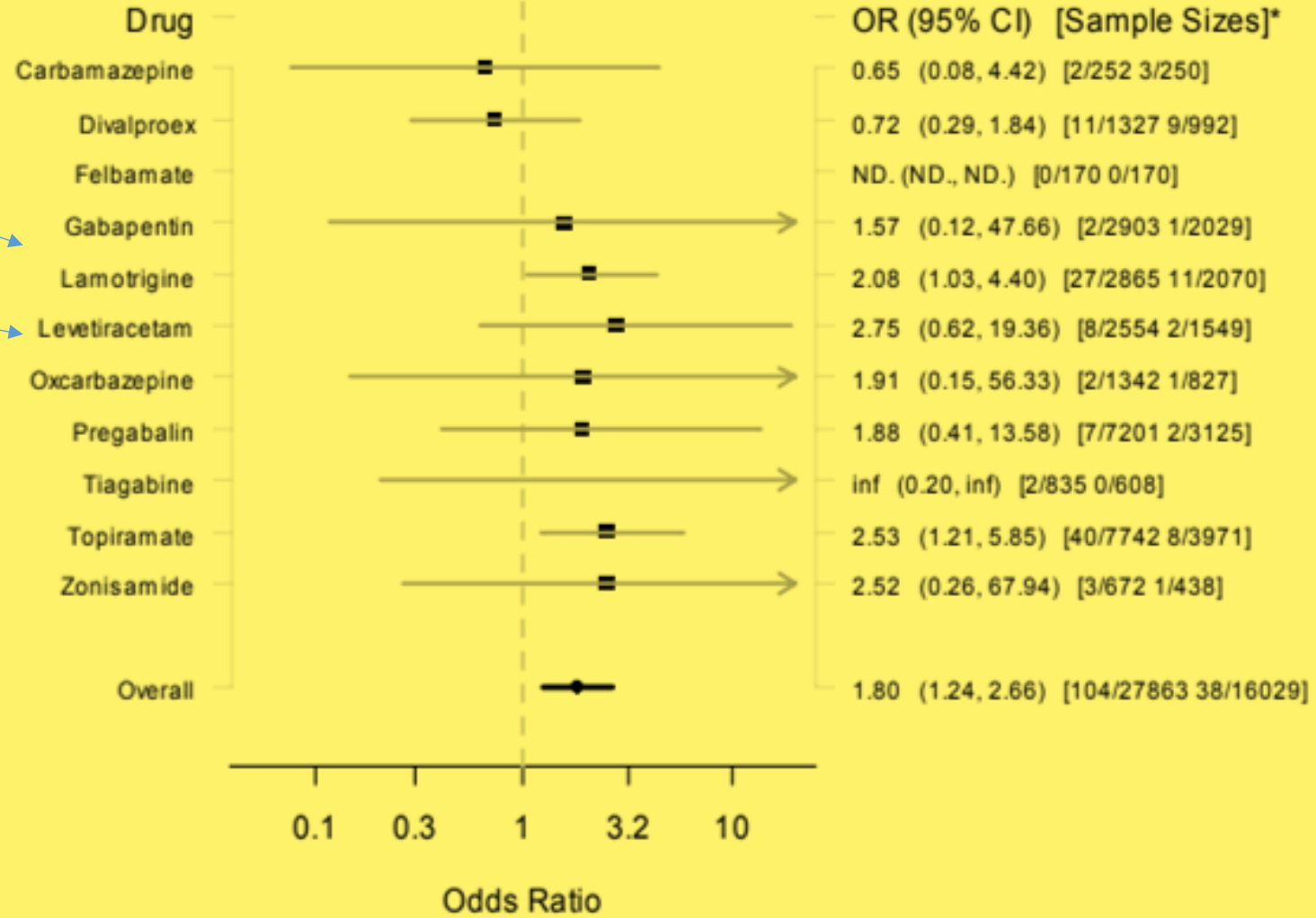
- More severe reactions may require psychotherapy (e.g., cognitive-behavioral therapy), which can improve a patient's coping skills.
- In some cases in which a patient does not respond to antidepressants, or in a situation in which antidepressant use increases the patient's risk of seizures, **electroconvulsive therapy (ECT)** may be used as an alternative treatment.
- ECT has been shown to be well tolerated among epilepsy patients.



ECT is generally considered safe for patients with epilepsy. Studies have shown that ECT does not cause or worsen epilepsy. In fact, ECT can even have a beneficial anticonvulsant effect.

Suicidality and epilepsy

- This systematic review and meta-analysis found that PWE have a significantly greater risk of suicidality (2.60 times), including suicidal ideation (2.70 times), suicide attempts (2.74 times) and completed suicide (2.36 times). The rates of suicidal ideation, suicide attempts and completed suicide in PWE were 19.73, 5.96, and 0.24%, respectively.



*[Treat. Events/Treat. n Plac. Events/Placebo n]

Figure 2: Suicidal Behavior or Ideation Odds Ratio Estimates, Placebo-Controlled Trials.

Suicidality and epilepsy

- Effective management of behavioural alterations in epilepsy patients requires a multidisciplinary approach, integrating pharmacological, neurological, and psychological factors.
- Close collaboration between psychiatry and neurology is essential for optimizing outcomes. Gradual medication adjustments and careful monitoring can lead to long-term stability and improved quality of life.

ADHD like symptoms due to antiepileptic drugs



ADHD like symptoms

- Some antiepileptic drugs (AEDs) can, in certain individuals, induce or exacerbate ADHD-like symptoms, particularly inattention, hyperactivity, and impulsivity.
- While not all AEDs have this effect, certain medications, like **phenobarbital**, **topiramate**, and **valproic acid**, have been associated with such adverse effects, according to the Cleveland Clinic and an article published in PubMed Central.
- However, other AEDs, like **levetiracetam** and **gabapentin**, may have limited effects on behavior, and some, like **lacosamide** and **carbamazepine**, may even be associated with beneficial effects on attention and behavior.

ADHD like symptoms

- **Phenytoin and Zonisamide**: May worsen **attention** and cause **behavioral** disturbances.
- **Phenobarbital, Valproic acid, and Topiramate**: May have a **negative** impact on attention.
- **Levetiracetam and Gabapentin**: May have limited effects on behavior and attention.
- **Lacosamide and Carbamazepine**: May have beneficial effects on behavior.
- **Other AEDs**: Some AEDs may worsen attention, while others have neutral or even beneficial effects on behavior and attention, according to an article in PubMed Central.

The co-occurrence of autism spectrum disorder (ASD) and epilepsy



Pharmacological Treatment for ASD

- Children with autism are at an increased risk for various neurological disorders, including epilepsy, macrocephaly, hydrocephalus, cerebral palsy, and migraines.
- Up to 60% of children with autism may show abnormal electroencephalogram (EEG) results, and 10% to 30% may develop epilepsy.
- Conversely, autism occurs in approximately 8% of children with epilepsy.

Pharmacological Treatment for ASD

- Currently, only two medications are approved in the US and many European countries specifically for treating these symptoms in individuals with ASD: aripiprazole and risperidone, which are both indicated for children and adolescents.
- Reports indicate that adverse effects occur in up to 61% of patients treated with aripiprazole and 77% of patients treated with risperidone.

Pharmacological Treatment for ASD

- Other atypical antipsychotics, including **quetiapine**, ziprasidone, and paliperidone, may be used for patients who do not respond to initial treatments.
- **Olanzapine** is less commonly prescribed due to its high risk of causing weight gain.
- **Clozapine** can be considered for **treatment-resistant patients** displaying significant disruptive behaviors, but its use is limited by potential risks such as agranulocytosis and myocarditis.

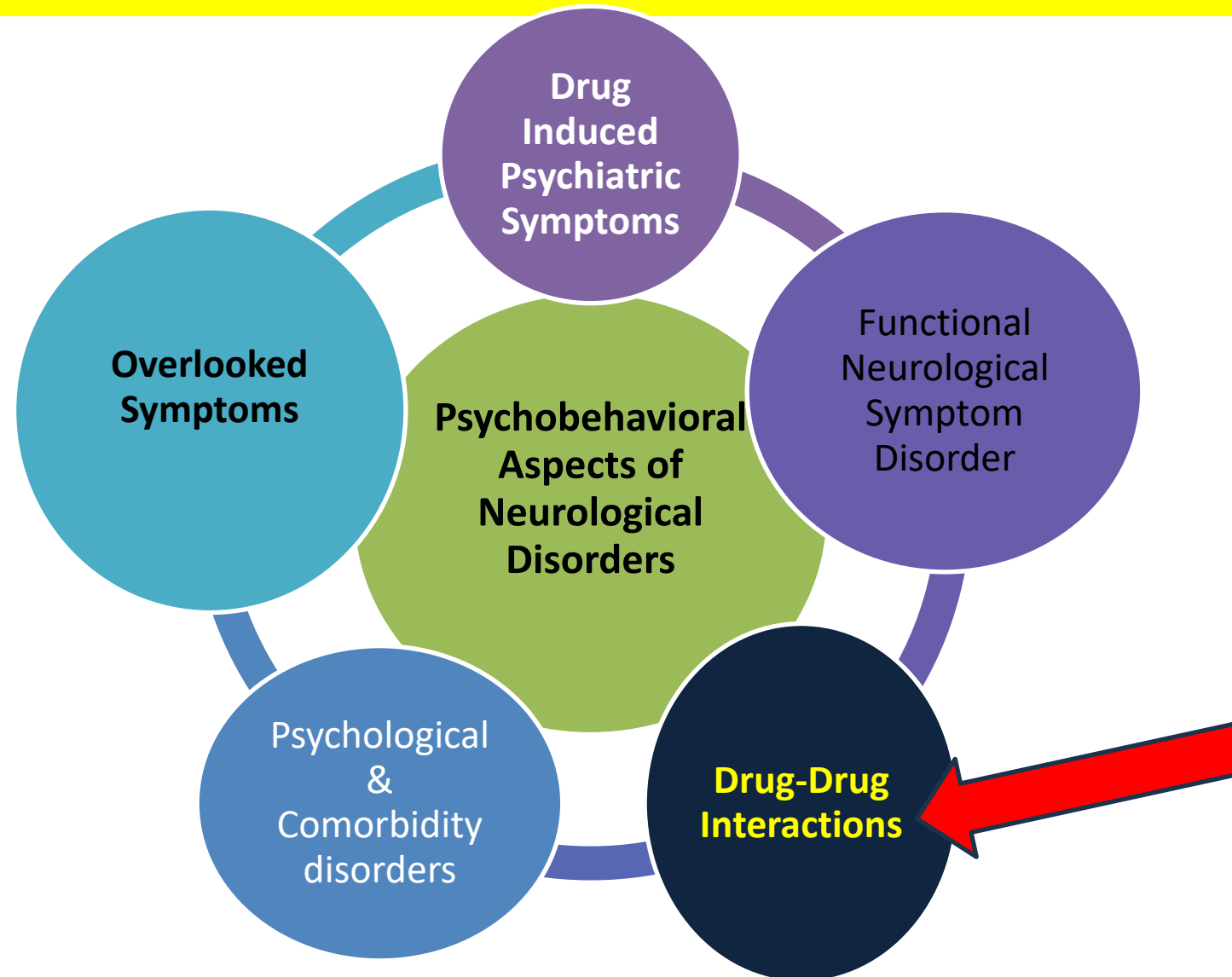
Pharmacological Treatment for ASD

- First-generation antipsychotics, like **haloperidol** and **chlorpromazine**, are also options for **treatment-resistant irritability or aggression**.
- **Valproate** serves as an alternative therapy, particularly in patients with concurrent epilepsy, for addressing irritability.
- **N-acetylcysteine (NAC)** has been associated with a notable decrease in hyperactivity and irritability.
- For patients with co-occurring ADHD, **methylphenidate** and **alpha-2 adrenergic agonists** are recommended to manage hyperactivity and attention difficulties.

Neuropsychiatric profile of commonly prescribed anti-seizure medications based upon clinical opinion

Drugs to be used with caution if there are cognitive concerns	Phenobarbital Phenytoin Topiramate Zonisamide
Drugs to be used with caution if there are psychiatric/behavioral concerns	Phenobarbital Phenytoin Topiramate Zonisamide Levetiracetam Perampanel Gabapentin
Drugs with the potential for positive mood-stabilizing properties	Valproate Lamotrigine Carbamazepine

Psychobehavioral Aspects of Neurological Disorders



Drug-Drug Interactions

- Most antidepressants **inhibit one or more CYP450** isoenzymes and are metabolized in the liver.
- SSRIs' inhibition of P450 can result in **toxic levels of antiepileptics** such as **phenytoin**, **phenobarbital**, and **carbamazepine**.
- Elevated levels **carbamazepine** levels were observed when the drug was given with fluoxetine, fluvoxamine, or nefazodone.

Drug-Drug Interactions

- Coadministration of **fluoxetine** and **carbamazepine** can lead to **toxic serotonin syndrome**, which is characterized by uncontrollable shivering, agitation, incoordination, restlessness in the feet when sitting, involuntary contractions progressing to myoclonic-like leg movements, and hyperreflexia.
- The SSRI **citalopram** has **no pharmacokinetic interactions with antiepileptic drugs** and thus may be used as an alternative.

Drug-Drug Interactions

- Antiepileptic agents such as phenytoin, carbamazepine, phenobarbital, and primidone are potent CYP450 enzyme inducers.
- A result of this inducing effect is the accelerated metabolism of antidepressants. (esp. paroxetine).
- However, the inducing effect is significantly reduced with the newer antiepileptics (e.g., gabapentin, lamotrigine, levetiracetam).

osteopenia and osteoporosis



Osteopenia and Osteoporosis

- Several population-based studies have suggested that exposure to **SSRIs** is associated with decreased bone mineral density (BMD) and bone fractures (level IIb).
- Clearly, these data raise the question of whether the use of SSRIs increases the risk of osteopenia and osteoporosis, which has been recognized for a long time with **enzyme-inducing AEDs**.

SNRIs and Serum Sodium



SNRIs and Serum Sodium: Understanding the Risk of Hyponatremia

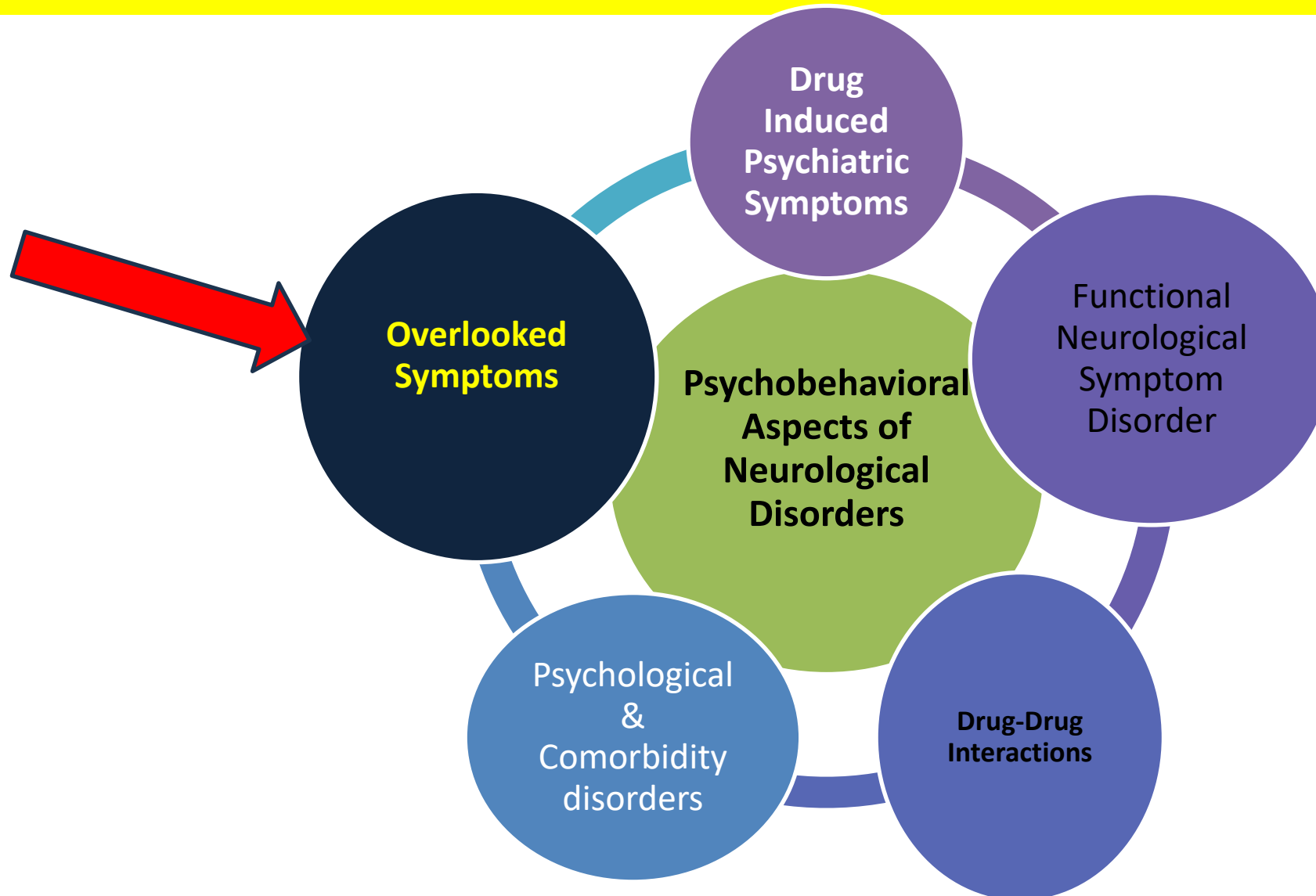
- Selective serotonin-norepinephrine reuptake inhibitors (SNRIs), like other serotonergic antidepressants, have been associated with **hyponatremia** (low serum sodium levels, typically defined as $\text{Na}^+ < 135 \text{ mEq/L}$).
- This side effect is thought to be related to the syndrome of inappropriate antidiuretic hormone secretion (**SIADH**).
- **Serum sodium** must be monitored when SNRIs are used together with carbamazepine, oxcarbazepine, and eslicarbazepine.

SNRI antidepressants	Duloxetine, levomilnacipran, milnacipran, desvenlafaxine, venlafaxine
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SNRIs and Serum Sodium: Understanding the Risk of Hyponatremia

- **SNRIs with Reported Hyponatremia Risk:**
- **Venlafaxine (Effexor)** – Higher risk, especially at higher doses (noradrenergic effects may also play a role).
- **Duloxetine (Cymbalta)** – Moderate risk, but cases have been reported.
- **Desvenlafaxine (Pristiq)** – Lower risk than venlafaxine, but still possible.
- **Milnacipran (Savella)** – Less data, but theoretically possible.

Psychobehavioral Aspects of Neurological Disorders



Managing Sleep Disorders:

- SSRIs, SNRIs, vortioxetine, and sustained-release bupropion have a relatively low risk of insomnia.
- Fluoxetine and sertraline have the highest risk of insomnia, and vortioxetine and levomilnacipran have the lowest.
- If sedative effects are required, mirtazapine and trazodone may be more beneficial.
- Due to their high anticholinergic effects, tricyclic antidepressants (TCAs) are also beneficial for insomnia; however, the risk of cognitive impairment is high.

Pharmacological Treatment for Sleep Disorders in Children and Adolescents with Autism Spectrum Disorder

- Melatonin appearing to be safe and effective may be an evidence-based and efficacious first-line treatment for treating insomnia symptoms in children and adolescents with ASD.
- Antipsychotics (e.g. low dose quetiapine), antidepressants with strong sedative effects such as trazodone and mirtazapine, antihistamines (e.g. diphenhydramine, niaprazine), alpha-adrenergic drugs (e.g. clonidine), benzodiazepines (e.g. clonazepam) and other hypnotic drugs, anticonvulsants (e.g. gabapentin), Alzheimer's drugs (e.g. donepezil), superoxide and iron treatment are other drugs used in pharmacological treatment.

Managing Fatigue:

- Based on NE's positive effect on energy level, SNRIs can be recommended when fatigue is a major symptom.
- Desvenlafaxine, **duloxetine**, and levomilnacipran have the lowest risk of drowsiness, with duloxetine preferred when fatigue and pain are involved.
- Because SSRIs similarly have a low risk of drowsiness, they are also a therapeutic option, particularly fluoxetine.
- **Bupropion**, a norepinephrine-dopamine reuptake inhibitor, also may be recommended for fatigue.

Managing Appetite Changes:

- Of the SSRIs, **fluoxetine** has the least propensity for weight gain, whereas **paroxetine** has the highest.
- Levomilnacipran, **bupropion**, vilazodone, and vortioxetine have minimal to no risk of weight gain.
- If weight gain is necessary, **mirtazepine** and some TCAs may be beneficial. However, the cognitive impairment associated with TCAs may limit their use.

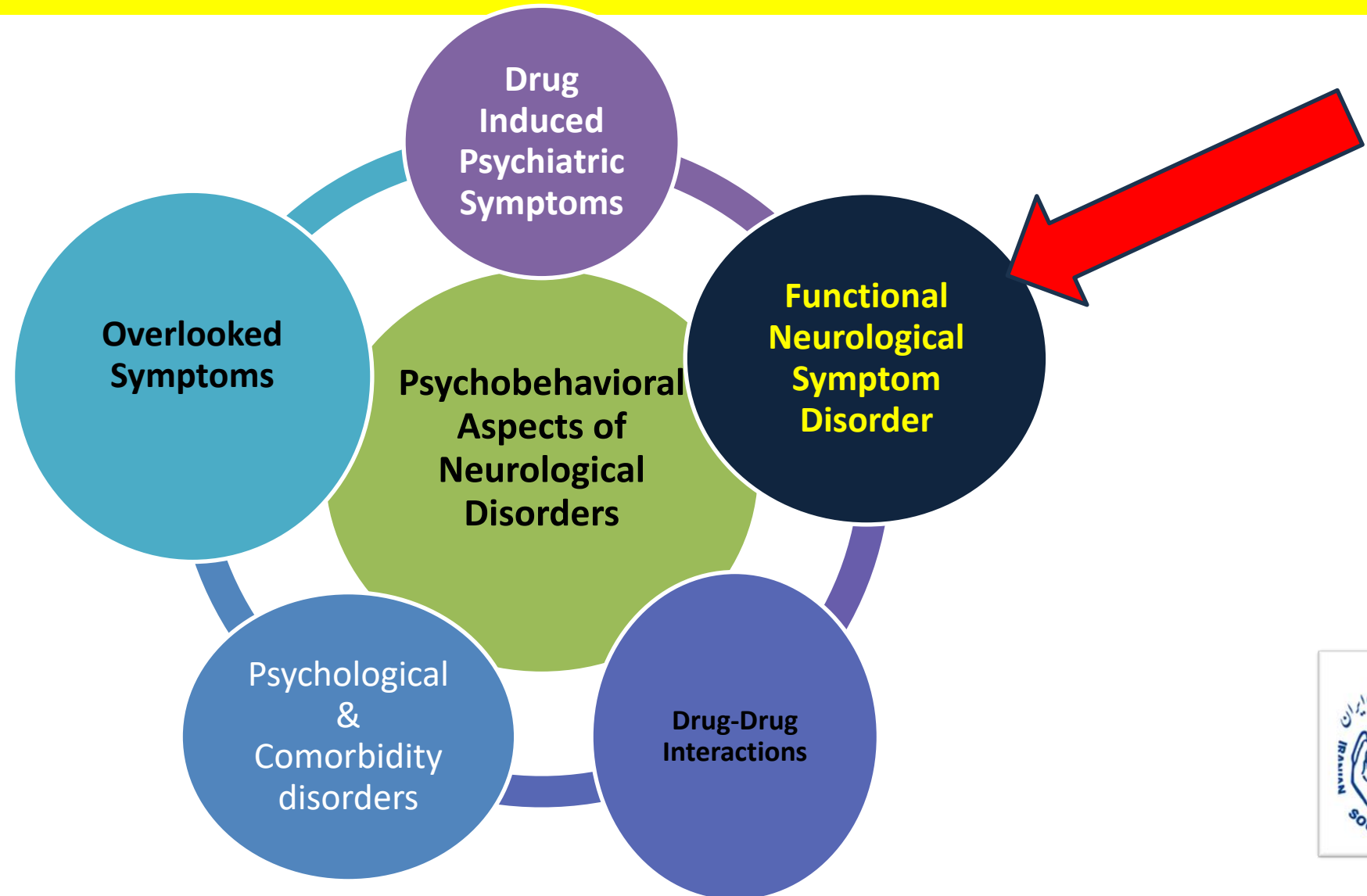
Managing Impaired Cognition:

- Most antidepressants have a low risk of cognitive impairment, **except** for those with anticholinergic effects, such as TCAs and paroxetine.
- Because of NE's positive effect on attention, cognition, and concentration, **SNRIs** and **bupropion** may be advisable.

Managing Sexual Dysfunction:

- In general, SSRIs and TCAs are the most likely to cause sexual dysfunction.
- **Paroxetine** has the highest risk of sexual dysfunction in the SSRI class; however, based on its anticholinergic effects, this agent may be beneficial if the dysfunction involves premature ejaculation.
- Therefore, bupropion and duloxetine may be preferred. Extended-release bupropion or duloxetine may be added on to an SSRI if time is needed to taper down or off the SSRI.

Psychobehavioral Aspects of Neurological Disorders





**SEIZURE
VS
PSEUDOSEIZURE**

Conversion Disorder (Functional Neurological Symptom Disorder)

Functional disorders (FD), previously referred to as “psychogenic” disorders

- **Movement disorders:** Psychogenic tremors, dystonia, Parkinsonism, or gait abnormalities.
- **Pain:** Psychogenic pain, which may be chronic and not related to any organic injury or disease.
- **Seizures:** Psychogenic seizures, where seizures occur without a neurological cause.
- **Paralysis or Weakness:** Functional limb weakness or paralysis, where physical weakness is experienced in the absence of neurological disease.

Conversion Disorder

(Functional Neurological Symptom Disorder)

Diagnostic Criteria

- A. One or more symptoms of altered voluntary motor or sensory function.
- B. Clinical findings provide evidence of incompatibility between the symptom and recognized neurological or medical conditions.
- C. The symptom or deficit is not better explained by another medical or mental disorder.
- D. The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.

Coding note: The ICD-9-CM code for conversion disorder is **300.11**, which is assigned regardless of the symptom type. The ICD-10-CM code depends on the symptom type (see below).

Specify symptom type:

(F44.4) With weakness or paralysis

(F44.4) With abnormal movement (e.g., tremor, dystonic movement, myoclonus, gait disorder)

(F44.4) With swallowing symptoms

(F44.4) With speech symptom (e.g., dysphonia, slurred speech)

(F44.5) With attacks or seizures

(F44.6) With anesthesia or sensory loss

(F44.6) With special sensory symptom (e.g., visual, olfactory, or hearing disturbance)

(F44.7) With mixed symptoms

Functional movement disorders (FMD)

- Types of Functional Movement Disorders
- Functional Tremor
- Functional Dystonia
- Functional Myoclonus
- Functional Parkinsonism
- Functional Tics
- Functional Paroxysmal Dyskinesia
- Functional Gait Disorders

COMPARISON OF SOMATIC DISORDERS, FACTITIOUS DISORDER, AND MALINGERING

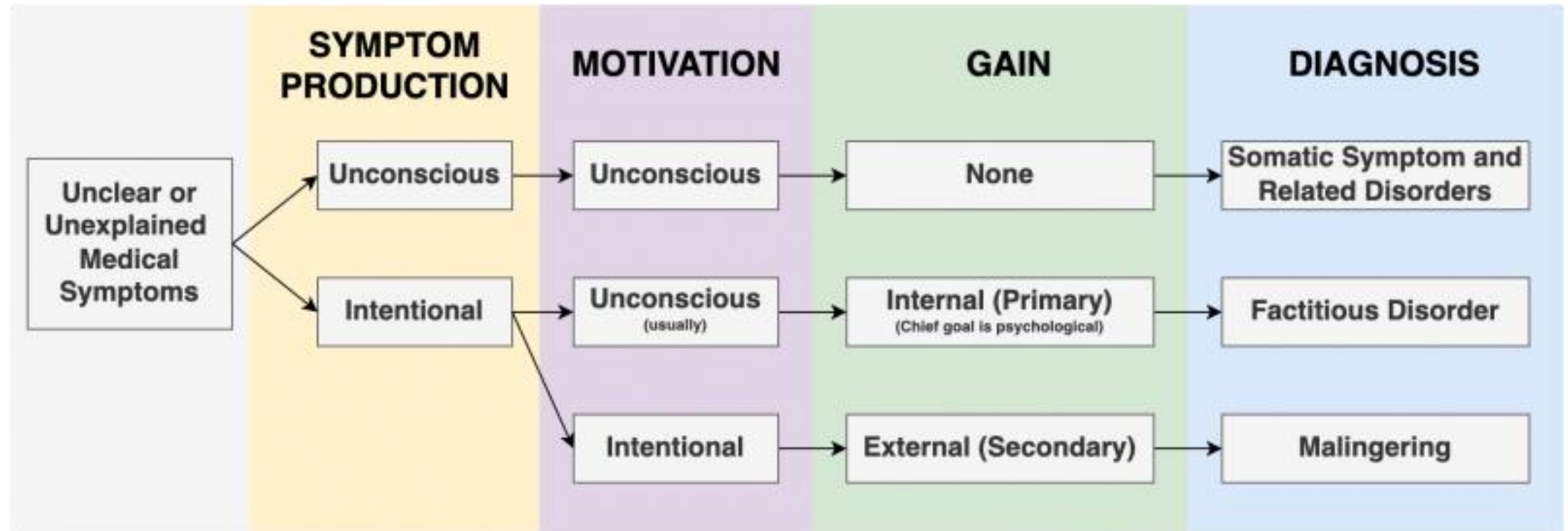


TABLE 4

Differential diagnosis of FND⁶

Neurological and physiological conditions
Autoimmune limbic encephalitis
Cortical blindness (secondary to stroke)
Epilepsy
Laryngeal dystonia
Multiple sclerosis
Movement disorders
Spinal or brain injuries or disorders
Stiff person syndrome
Stroke
Psychiatric conditions
Anxiety disorders
Body dysmorphic disorder
Depersonalization and de-realization disorder
Depressive disorders
Hypochondriasis
Panic attacks
Psychosis
Other
Factitious disorder
Iatrogenic
Malingering
Substance use

FND, functional neurological disorder.

Psychogenic Nonepileptic Seizure (PNES)

- **Comorbidities:**
- Individuals with PNES often have comorbid psychiatric conditions such as mood disorders, anxiety disorders, PTSD, and dissociative disorders.
- **Diagnosis:**
- Diagnosis involves video EEG monitoring, psychological evaluation, and differentiation from epileptic seizures.
- **Treatment:**
- Treatment may involve psychotherapy, cognitive behavior therapy, and addressing underlying psychological distress.

Diagnosis and Tests

- Diagnosing PNES can be difficult because symptoms look very similar to epilepsy.
- An EEG measures and records your brain's electrical signals. During an EEG, a technician places small metal disks (electrodes) on your scalp. The electrodes attach to a machine that gives your provider information about your brain's activity.
- If your episodes are functional, an EEG will show normal electrical brain activity during an episode. However, in those who have epilepsy, EEG will show abnormal electrical activity during a seizure.
- Many people with these seizures first receive a misdiagnosis of epilepsy. It's also possible to have both epileptic and functional seizures in rare cases.

Functional Neurologic Disorder

- Symptoms that are associated with functional seizures may include:
- Eye closure during the episode
- Side-to-side head movement
- Pelvic thrusting
- Prolonged attacks
- Hyperventilation
- Shaking all over the body (with awareness)

Semiology of Epileptic v. Non-Epileptic Seizures

	Epileptic Seizures	Psychogenic Non-Epileptic Seizures (PNES)
Duration	Short (<5 minutes)	Longer (up to 20 minutes), fluctuating and inconsistent
Ocular Activity	Partially open, "rolled back"	Variable: eye closure, eyes open and able to track motion
Head Movement	Minimal	Side-to-side motion, mouth closure
Body Movement	* Tonic-clonic motor activity, focal limb movements, automatisms	Asymmetric, asynchronous, pelvic thrusting, back arching, bilateral limb movements
Consciousness	Unconscious, prolonged post-ictal period	Preserved awareness, respond to painful stimuli, minimal post-ictal confusion
Other	Loss of continence, tongue biting	Teddy-bear sign

* Depending on seizure type and location

TABLE 1**Signs, symptoms, and other findings of FND^{15a}**

Alexithymia or inability to describe feelings verbally (associated with increased risk of somatization)
Close association with psychological stressors
Denial of possible psychiatric cause of symptoms
History of coexisting functional disorder
History of multiple surgeries and extensive multispecialty work-up
History of psychiatric symptoms or disorders
Histrionic personality traits
Marked inconsistency on repeat physical examination
No serious injuries associated with falls or assumed seizures
Nonanatomic distribution of abnormalities
Normal neurological examination
Notable worsening of signs of the disorder in the presence of other people
Persistent symptoms despite tailored medical treatment
Vague or inconsistent description of symptoms by the patient

FND, functional neurological disorder.

^a A normal neurological examination or the presence of any of the signs and symptoms listed in this **TABLE** does not definitively exclude an organic cause. A thorough evaluation and treatment plan still need to be implemented before making a diagnosis of FND.

TABLE 2

The physical examination in suspected FND¹⁵⁻²⁴

Functional area of impact	Diagnosis	Alternative terminology ^a	Characteristics	Diagnostic observations and examinations
Motor	Functional gait abnormality	Hysterical gait Astasia–abasia	Ambulatory dysfunction Variable gait pattern, with rapid fluctuation over minutes Other patterns that do not commonly duplicate those of neurological disability Involves uneconomic postures, slowness, fatigue, and trembling Able to catch self before falling ¹⁶	Normal reflexes, muscle tone, and strength Absence of fall-related injury Motor inconsistency ^{18,19b} Dragging monoplegic gait ^{16,19b} Uneconomic posture (eg, camptocormia [bent-spine syndrome]) ¹⁶ “Walking-on-ice” pattern ¹⁶ Pseudoataxia ¹⁶ Sudden knee-buckling ¹⁶ Normal neurological function on magnetic resonance imaging ¹⁷ Chair test ^{18,19b}
	Functional paralysis or weakness	Pseudo-paralysis	Sudden onset of symptoms with involvement of a single limb or half of the body Weakness does not follow anatomic patterns ¹⁶ Inconsistency on repeat examination ¹⁶	Hoover test ^{18,19b} Abductor sign ^{18,19b} Abductor finger sign ^{18,19b} Spinal injury test ^{18,19b} Motor inconsistency ^{18,19b} Normal reflexes, muscle tone, and sphincter function Collapsing weakness (intermittent weakness) ^{16,19} Co-contraction of antagonist muscle ^{16,19} Negative Babinski signs ¹⁶ Functional magnetic resonance imaging (left hemisphere or anterior and medial prefrontal activation) ¹⁷
	Functional movement disorder	Psychogenic movement disorder	Can mimic tremor, parkinsonism, myoclonus, dystonia, tics, and dyskinesia, but has atypical onset, course, or manifestations ¹⁶ Rapid onset (unusual in organic disease) ¹⁶	Motor inconsistency ^{18,19b} Abnormal movement stops when distracted Variability of unwanted movements in distribution, frequency, and amplitude ¹⁶ Increased weighted amplitude (organic tremor decreases) ¹⁶ Dystonia waxes and wanes ¹⁶ Electromyography ²⁰

CONTINUED

TABLE 2

The physical examination in suspected FND¹⁵⁻²⁴ (*cont'd*)

Functional area of impact	Diagnosis	Alternative terminology ^a	Characteristics	Diagnostic observations and examinations
Neurological	Nonorganic coma	Pseudo-coma	Alteration of consciousness precipitated by stress and presence of an observer Slumps to floor without hitting head²¹ Offers resistance on physical exam Uncooperative upon “wake up”	Normal pupils, corneal reflexes, plantar reflexes, and sphincters Bell phenomenon, in which the eyes roll up when the lids are raised—unlike in true coma, in which the eyes remain in a neutral position²¹ Avoids unpleasant stimuli Caloric testing with cold water, nystagmus with nonorganic coma, due to intact cerebral cortex and brainstem (might have nausea and vomiting²²)
	Nonepileptic seizures	Hysterical seizures Psychogenic seizures	Paroxysmal and involuntary events with changes in the level of consciousness, behavior, motor activity, and autonomic function²³ Seizures are frequent and occur in front of an observer²⁴ Characteristic pelvic thrusting, side-to-side head shaking, asymmetric limb-shaking²⁴ Can act out or recall what occurred during the seizure Long duration, eyes closed, asynchronous movements, frequent recurrence in the same context²⁴ Occurrence of seizures waxes and wanes No post-ictal confusion	Normal electroencephalographic activity (including when sleep deprived and during 24-hour monitoring)²⁴ Tip-of-tongue biting (instead of lateral biting)²⁴ Clenched teeth, as opposed to open mouth, during “tonic” phase Consider measuring the serum prolactin level within 20 min of a seizure (the level is increased 300% in epilepsy); however, false-positive results are seen with syncope and false-negatives are seen with partial seizures; also, the test is often performed incorrectly¹⁶
Sensory	Functional ophthalmologic syndromes	Pseudo-blindness Pseudo-ophthalmologic syndrome	—	Normal pupillary response and optokinetic nystagmus (fixation reflex)¹⁵ Unable to sign name or bring fingers together in front of eyes, which the patient should be able to do¹⁶
	Functional anesthesia	Numbness or anesthesia	All sensory modalities (touch, pain, vibration, proprioception) disappear at a discrete border (joint, skin crease, midline)—unlike true sensory loss, in which borders overlap ¹⁶	Increased pulse (20-30 beats/min) or withdrawal from painful stimuli applied to the “numb” part¹⁵ Hemisensory syndrome or midline splitting^{16,19b} Vibratory loss on half of the skull, sternum, or pelvis with the tuning fork test is physiologically impossible due to bone conduction¹⁹ Nonanatomic sensory loss^{19b} Migrating sensory loss^{19b} Erroneous identification with a proprioception test of the big toe

CONTINUED

TABLE 2

The physical examination in suspected FND¹⁵⁻²⁴ (*cont'd*)

Functional area of impact	Diagnosis	Alternative terminology ^a	Characteristics	Diagnostic observations and examinations
Speech and swallowing	Functional aphonia Functional dysarthria Functional dysphagia	Globus hystericus Hysterical aphonia	—	Muteness Normal cough Normal laryngoscopy ¹⁵ Pressured whispering ¹⁶ Sensation of something in throat ¹⁶ Stutter or extremely slow speech with long pauses ¹⁶

FND, functional neurological disorder.

^a The authors caution against using "pseudo"/"hysterical" in conversation with patients, although these terms may still be encountered in the literature.

^b See **TABLE 3**.

TABLE 3

Specialized tests for FND^{15,18,19}

Functional area of impact	Validated test (sensitivity, specificity)	Instructions
Motor	Hoover test (94%, 99% ^{15,18,19})	Relies on the principle of synergistic muscle contraction. ^{18,19} 1. Place a hand under the heel of the patient's impaired leg, while pressing down on the good leg with the other hand. Ask the patient to lift the good leg against resistance. If you feel counter-pressure under the impaired leg, this normally means that the leg is not paralyzed from an organic cause. 2. Switch hand positions. Ask the patient to lift the impaired leg. If you do not feel counter-pressure under the heel of the good leg, the patient is not being compliant. ^{15,19}
	Abductor sign (100%, 100% ^{15,18,19})	Instruct the patient to abduct each leg. Oppose this movement with your hands placed on the lateral surfaces of the patient's legs. When the paretic leg is abducted, the good leg stays in organic paresis but moves in the hyperadducting direction in nonorganic paresis. ^{15,18,19}
	Abductor finger sign (100%, 100% ^{18,19})	Relies on the same principle as the Hoover sign. Test the abduction of fingers in the healthy hand. The fifth finger of the presumed affected hand will display synkinetic abduction. ^{18,19}
	Spinal injury test (100%, 97.9% ^{18,19})	Passively position the legs in a flexed posture when the patient is lying in bed. When the paretic leg falls, the test is considered negative; when it stays in a flexed posture, the test is considered positive. ^{18,19}
	Collapsing give-way weakness (63%, 97% ^{18,19})	The limb collapses from a normal position with a light touch, or normal strength is developed and suddenly "gives way" (collapses). ^{18,19}
	Co-contraction of antagonist muscles (17%, 100% ^{18,19})	During strength testing, an antagonist muscle contracts simultaneously when an agonist muscle contracts voluntarily. The sign is positive if simultaneous contraction of agonist and antagonist muscles results in little or no movement. The sign can be measured with surface electromyography. ^{18,19}
	Motor inconsistency (13%, 98% ^{18,19})	The patient's assertion of the impossibility of a given movement of a muscle even though a different movement using the same muscle is possible. Example: A patient with complete plegia of a limb when tested supine stands on the previously plegic limb and walks out of examination room. ^{18,19}

CONTINUED

TABLE 3

Specialized tests for FND^{15,18,19} (*cont'd*)

Functional area of impact	Validated test (sensitivity, specificity)	Instructions
Sensory	Midline splitting (20%, 93% ¹⁹)	Sensory loss of half the body (with face, trunk, arm, and leg involvement) with a clear edge on the midline. The sign is positive if the patient reports precise splitting of sensation in the midline during sensory exam. ¹⁹
	Splitting of vibration (95%, 14% ¹⁹)	Placing a tuning fork on the right or left side of the forehead or the sternum is thus expected to be felt identically because the same bone is involved. The sign is positive if there is a reported difference in the sensation of the tuning fork placed over the left side, compared to the right side, of the sternum or frontal bone. ¹⁹
	Nonanatomic sensory loss (74%, 100% ¹⁹)	Diminished sensation fitting a nondermatomal pattern. Classically, the following findings are considered nonanatomic ¹⁹ : • truncal deficits that have only an anterior level but not a posterior level • sharply demarcated boundaries at the shoulder or at the groin • sensory loss follows the strict outline of a stocking–glove distribution unilaterally • involvement of only half of a limb.
	Inconsistency or changing pattern of sensory loss (79%, 70% ¹⁹)	Inconsistency and nonreproducibility of sensory signs in repeated sensory testing. No precise description exists of how to perform the repeated tests. ¹⁹
Gait	Dragging monoplegic gait (8.4%, 100% ¹⁹)	The leg is dragged at the hip behind the body instead of performing circumduction. ¹⁹
	Chair test (89%, 100% ¹⁹)	The inability to stand or walk despite normal function in bed, in a patient who was observed performing well in propelling a chair. The sign is positive when the patient is observed propelling a swivel chair better than walking. ¹⁹

FND, functional neurological disorder.

The End

- Comments
- Question and answer
- Thank you!



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