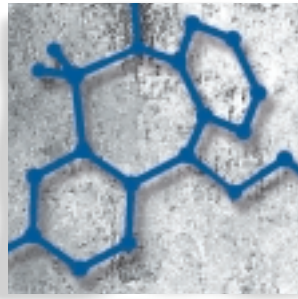# Pharmacological aspects

Psychiatric side effects of medications prescribed in internal medicine

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Several pharmacological treatments used in internal medicine can induce psychiatric side effects (PSEs) that mimic diagnoses seen in psychiatry. PSEs may occur upon withdrawal or intoxication, and also at usual therapeutic doses. Drugs that may lead to depressive, anxious, or psychotic syndromes include corticosteroids, isotretinoin, levodopa, mefloquine, interferon-α, and anabolic steroids, as well as some over-the-counter medications. PSEs are often difficult to diagnose and can be very harmful to patients. PSEs are discussed in this review, as well as diagnostic clues to facilitate their identification.

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Psychiatric side effects (PSEs) can be induced by the pharmacological treatment of physical illnesses. The clinical presentation of PSEs often resembles spontaneous psychiatric syndromes (ie, noniatrogenic, naturally occurring diseases). PSEs can occur at usual doses, in cases of intoxication, or during the days following withdrawal of a given treatment. PSEs range from short-lasting anxiety to severe confusion, and alleged cases of suicide have even been reported.

The *Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition (DSM-IV)*[1] defines some dozens of categories of PSE, according to the disorder and to the incriminated substance, eg, "persisting dementia induced by sedatives, hypnotics or anxiolytics." The *DSM-IV* categories include drugs for therapeutic purposes, medication taken abusively, and other substances. The *International Classification of Diseases*[2] is very similar to *DSM-IV* in its categorization, with minor differences in terms of category codes.

The challenge of PSEs in everyday practice is the difficulty in recognizing these frequent and potentially dangerous situations. The diagnosis of PSEs raises the same questions as the diagnosis of any psychiatric sign or symptom, which means that the clinician has to consider a rather long list of differential diagnoses. The following concepts refer to PSEs, as well as to other kinds of side effects:

- *Exposure*: The period of time the patient received the drug suspected of inducing a side effect.
- *Dechallenge*: The interruption of the suspected medication, regardless of the remission of adverse effects. *Positive dechallenge* means that remission was temporally associated with the interruption of medication.
- *Rechallenge*: The reintroduction of the suspected drug. *Positive rechallenge* means that symptom reappearance was temporally associated with suspected drug reintroduction.

Pharmacological aspects

A drug can be considered to have a high probability of causing side effects in cases of positive exposure, with a positive dechallenge and a positive rechallenge.

The importance of PSEs relates to the potential harm of these side effects and to their high incidence. Two examples are reserpine and corticosteroids. Reserpine, when it was prescribed, may have caused mood disorders in 10% of treated subjects. With corticosteroids, 6% of all patients develop some PSEs.[3]

The focus of this review is on depression, anxiety, and psychotic states, but a few other PSEs are also mentioned. A summary of the PSEs is presented and some examples are given in detail. In addition, diagnostic issues are discussed to facilitate identification of PSEs in internal medicine. PSEs secondary to psychotropic medication (such as antidepressants, anxiolytics, antipsychotics, or mood-stabilizing agents) are not described here. They probably induce more PSEs than the compounds quoted here, since they act directly on the nervous system.

Mechanisms of PSEs

As with any side effect, pharmacological mechanisms are divided according to their pharmacokinetic or pharmacodynamic nature. Patient-specific factors also lead to PSEs.

Pharmacodynamic mechanisms

Medications used in the treatment of physical disorders can modify neurotransmitter systems (as do psychotropic medications). These modes of action can imply a direct influence on neurotransmitters, as is the case for dopaminergic agents in the treatment of Parkinson's disease. Interleukin (IL) treatment is another example where there is a direct influence, since interleukins are involved in neurotransmission as well as in many other bodily functions. Other nonpsychotropic medications influence neurotransmitter systems in a more indirect manner, such as corticosteroids or sex steroids.

It is interesting to compare the mode of action of nonpsychotropic medications with what is known concerning the postulated pathophysiology of psychiatric disorders. Indeed, the mechanisms of PSEs are sometimes compatible with a given hypothesis for the corresponding spontaneous syndromes. For example, the occurrence of hallucinations and delusions on dopamine agonists (eg, levodopa) is clearly within the domain of the dopaminergic hypothesis for schizophrenia. In this case, there is a clear relationship between the hypothesis for a disease and the postulated mechanisms of a side effect. In another example, that of depression as a side effect of interferons (IFNs), the relationship is not so easily identifiable. Stress and depression are associated with increased circulating concentrations of cytokines such as IL-1β, IL-6, γ-IFN, and positive acute-phase proteins, and hyperactivity of the hypothalamus-pituitary-adrenal axis. Immunological activation induces "stress-like" behavioral and neurochemical changes in animals.[4] An association of the cerebrospinal fluid (CSF) concentration of proinflammatory cytokines and major depressive disorders was reported in depressed patients with higher CSF concentrations of IL-1β, lower IL-6, and no change in tumor necrosis factor α (TNF-α).[5] A positive correlation was found between serum IL-1β and the severity of depression. Other studies suggest that antidepressants can act on neouroimmunomodulation, and have been shown to shift the cytokines toward a decreased production of proinflammatory cytokines.[6]

Pharmacokinetic mechanisms

Pharmacokinetic mechanisms are relevant when the PSE is known to follow a dose–response curve. A low clearance represents the main pharmacokinetic mechanism inducing PSEs, ie, other changes in the pharmacokinetics of drugs are of little relevance. Disease states, hepatic enzyme polymorphisms, and drug interactions leading to metabolic inhibition are the main reasons for a low clearance.

Interaction by metabolic inhibition is a general principle, applicable not only to PSEs, but also to other side effects. Many drugs inhibit one or more pathways of hepatic metabolism. Cytochrome P-450 (CYP450) enzymes metabolize endogenous as well as a variety of exogenous substrates, such as toxins and drugs. Some drugs are metabolized by one metabolic pathway, others by many. When all metabolic pathways of a medication are inhibited, then the concentration of this drug will rise, favoring the occurrence of side effects.

Antifungals can inhibit some metabolic pathways, including those of mefloquine, ie, the 3A4 isoenzyme of CYP450.[7] Mefloquine can rarely lead to serious PSEs at prophylactic doses,[8,9] but these risks are greater at high plasma concentrations.[10] The prescription of a macrolide antibiotic will probably raise concentrations of mefloquine, as most macrolides are 3A4 inhibitors. Hence, serious PSEs can occur even at usual doses of both drugs.

Risk factors

Patient-specific mechanisms of PSEs are more precisely defined as patient-related risk factors. The risk factors for developing PSEs can be medication-related or patient-related, as shown in *Table I*.

Polypharmacy is one of the most important iatrogenic risk factors for PSEs, because of the addition of pharmacological effects or due to metabolic inhibition. Addition of pharmacological effects is illustrated by the concomitant prescription of clozapine and biperiden. These drugs are both potent anticholinergics, so the risk of anticholinergic side effects is greater when they are taken together than with each medication taken alone. Polypharmacy mimics a slow metabolizer picture for many drugs, when hepatic metabolism is inhibited. There are many inhibitors of hepatic metabolism: omeprazole, cimetidine, antifungals, antivirals, HMG-CoA (3-hydroxy-3-methylglutaryl coenzyme A) reductase inhibitors (statins), antihypertensives, antiepileptics, antidepressants, grapefruit juice, and many other compounds. It is practically impossible to memorize all the CYP450 isoenzyme substrates, inhibitors, and inducers. Hence pocket tables[11] and software[12,13] are useful for obtaining rapid information about such drug–drug interactions, and potentially avoiding induction of PSEs. Many PSEs are dose-dependent, so their risk increases with factors that raise the concentration of drugs. The CYP450 2D6 isoenzyme has absent or impaired activity in 7% of Caucasians[14,15] and the 2C19 activity is absent or impaired in as many as 12% to 22% of Asians.[15]

Medication-related PSEs
Polypharmacy
High doses
Route of administration (eg, intravenous or intrathecal)
Faster administration (by any route)
Narrow therapeutic index
Patient-related PSEs
Present or past mental illnesses
Hepatic insufficiency, slow metabolizer, and other metabolic conditions
Augmented permeability of the blood-brain barrier (eg, meningitis or porphyria)
Very young or elderly patients
Postpartum
Other situations of stress (eg, intensive care unit)

Table I. Risk factors for psychiatric side effects (PSEs).

Diagnosis and differential diagnosis

The diagnosis of PSEs can be challenging. The clinical presentations of depressive, anxious, or psychotic PSEs meet most criteria of the *DSM-IV* for the corresponding spontaneous (noniatrogenic) syndromes. Therefore, almost any psychiatric symptom or syndrome could be considered as a potential PSE, until one has proven the contrary.

A simple case would be that of a peculiar or unusual psychiatric symptom, observed in a person who has started (or interrupted) a medical treatment recently and has no history of a previous psychiatric decompensation and no evident susceptibility to develop such a decompensation. A difficult case would be that of a person who has already suffered from many decompensations of psychiatric disorders and who develops a recurrence that presents itself clinically in a similar manner as that known for the subject. In this case, a PSE can easily be overlooked, ie, the role of a medical treatment as a relevant factor is difficult to identify. Another case is that of a physical disorder that can also induce psychiatric signs. For example, the clinician might not be able to determine whether a case of depression relates to the patient's multiple sclerosis or to the corticosteroid treatment. Another example would be a malaria patient treated with mefloquine and presenting delirium: is the delirium due to the malaria rather than to the mefloquine?

The fact of being hospitalized for a severe physical illness constitutes a strain: in an intensive care unit, the patient is exposed to pain, sleep deprivation, unusual environment, and threat of disability or even death. In this context, it is difficult to distinguish reactive or drug-induced psychological signs. Complex medical cases receive polypharmacy: some patients can receive antiarrhythmics, bronchodilatators, analgesics, antibiotics, benzodiazepines, and other medications. Among these complex situations, it can become practically impossible to determine a single cause for a PSE. Yet, making such a diagnosis is necessary. For example, in systemic lupus erythematosus, the occurrence of PSEs can be due to corticosteroid treatment, but also to the lupus cerebritis; the latter is associated with high levels of antibodies to P ribosomal proteins, in both CSF and serum.[16] This differential diagnosis is relevant, since the corticosteroid dose may need to be increased.

The differential diagnoses of PSEs are summarized in *Table II*. History and chronology of drug administration are first-line tools to diagnose a PSE. As already mentioned, an anamnesis with a positive exposure, positive

dechallenge, and positive rechallenge, indicates a high probability of a causal link between a psychiatric sign and a prescribed medication.

A PSE can differ from a spontaneous psychiatric syndrome in duration, since the duration of the PSE is more linked to the presence or withdrawal of the offending agent. Once the incriminated treatment is interrupted, behavioral symptoms usually remit within days to weeks, depending on the half-life of the substance or the presence of a withdrawal syndrome. In complex cases of polypharmacy, if the chronology of medication cannot help determine which medication caused the side effect, a trial could be done by replacing one of the suspected drugs by another with a lesser risk of PSEs.

Another issue about chronology concerns what can occur after interruption of treatment. This can be illustrated by the case of an elderly male patient, who took St John's wort for 4 months, with partial improvement of his depression. The dose was gradually increased, but without a complete remission of the depression. Travel to an endemic zone of malaria was planned and mefloquine prophylaxis was introduced. No side effect occurred during the first 10 days, until the clinician decided to replace St John's wort by citalopram, without changes in the mefloquine prophylaxis. The patient rapidly developed hallucinations after the introduction of citalopram. He had no mental status changes when he received St John's wort and mefloquine, so the clinician stopped citalopram. The hallucinations persisted. When mefloquine was discontinued, the hallucinations remitted. The message is that even the interruption of a drug can lead to an increase in the plasma concentra-

tions of another drug, causing side effects. St John's wort induces mefloquine metabolism, which means that, in this case, mefloquine concentrations were lower while St John's wort was given. Hallucinations are known side effects of mefloquine.

To improve the detection of PSEs, the physician should look for the anamnestic key factors listed below:

- Dates of occurrence of psychiatric symptoms suspected of being side effects.
- Dates of medication exposure, dechallenge, and rechallenge.
- Previous psychiatric history.
- If polypharmacy is given, dates of introduction or discontinuation of other drugs.
- Dates of factors worsening existing comorbidities.
- Plasma concentration measurements.

The most useful complementary examination for PSE investigation is generally the monitoring of plasma concentrations of suspected medications. Monitoring of drug concentration is frequently performed for some drugs with high risk of toxicity, eg, digoxin, theophylline, or lidocaine. Many other compounds can also be dosed in specialized laboratories.

If past analyses were performed for a given patient, they may also provide valuable clues. This may apply even if different medications were measured. This occurs because an abnormally high concentration of a medication may suggest a weak or absent metabolic pathway, as discussed in the mechanisms section above. Knowledge of the patient's deficiencies in metabolism allows avoidance of some PSEs by future prescriptions. Genotyping is a complementary examination to detect polymorphisms of hepatic enzymes.

Description of psychiatric side effects

Table III [3,8,9,17-197] gives a list of medications that might induce depression, mania, anxiety, or psychotic syndromes (defined by delusions and/or hallucinations). This information is qualitative, in the sense that the severity or the frequency of these side effects under each medication or class is not indicated. Specific information can be found in the bibliography. Some psychotropics, such as benzodiazepines, are listed in *Table III* because they are frequently prescribed in internal medicine. Obviously, more than one of these PSEs can occur in a given patient. For example, many depressive states are accompanied by anxiety. Some clinically relevant examples of medications presented in *Table III* are discussed below in more detail.

Diagnoses other than medication side effects
Underlying physical illnesses with psychiatric symptoms (eg, multiple sclerosis, systemic neoplasias, electrolytic disturbances, lupus erythematosus)
Aggravation of an existing psychiatric illness
Inaugural psychiatric decompensation in individuals with no evident susceptibility
Differential diagnoses among PSEs
PSEs at usual doses
Withdrawal-related PSEs. Side effects can occur after the discontinuation of antiparkinsonian agents, benzodiazepines, antipsychotics, antidepressants, anabolic androgen steroids, etc
Intoxication-related PSEs

Table II. Differential diagnoses of psychiatric side effects (PSEs) of medications.

Mefloquine and chloroquine

Mefloquine, which is prescribed for the prophylaxis or treatment of malaria, frequently causes PSEs. These PSEs can be severe: psychosis, delusion, and even suicidal ideation. Disabling PSEs occur in less than 1% of patients under mefloquine at therapeutic doses, and in less than

	Depression	Mania	Anxiety	Psychotic symptoms
Amantadine[17-22]	X	X	X	X
Aminoglycosides[23,24]				X
Amphetamines[25-30]	X	X	X	X
Anabolic steroids[31-33]	X	X	X	X
Anesthetics[21,22,34,35]		X		X
Anticholinergics[21,36-39]	X		X	X
Antihistamines[21,22,40]	X	X		
Antitubercular agents[22,41-45]	X		X	X
Antivirals[46-53]	X		X	X
Baclofen[22,54-58]	X	X	X	X
Barbiturates[22,59]	X	X	X	X
Benzodiazepines[21,22,60-62]		X	X	X
β-Blockers[21,22,63-72]	X	X	X	X
Bromocriptine[21,73-77]		X	X	X
Cephalosporins[22,78-80]		X		X
Chloroquine[81-88]	X	X	X	X
Clonidine[21,22,89-93]	X	X	X	X
Corticosteroids[3,21,22,94-112]	X	X	X	X
Digoxin[21,22,113-115]	X	X		X
Disulfiram[21,22,116-118]	X	X	X	X
Interferon-α[22,119-131]	X	X	X	X
Isotretinoin[22,132-137]	X			X
Levodopa[21,22,138-152]	X	X	X	X
Lidocaine[153-157]	X	X	X	X
Mefloquine[8,9,22,158-160]	X	X	X	X
Methyldopa[21,22]	X		X	X
Methylphenidate[22,161-163]		X	X	X
Metoclopramide[21,22,164-169]	X	X	X	
Metronidazole[22,170-175]				X
Opioids[21,22,176-181]	X	X	X	X
Oral contraceptives[21,22,182,183]	X		X	
Procainamide[21,184-188]	X	X	X	X
Pseudoephedrine[22,189-192]			X	X
Quinidine[21,22,193,194]			X	X
Quinolones[22,195]	X		X	X
Thiazide diuretics[22,196]	X			

Table III. Psychiatric side effects potentially induced by pharmacological treatment.

1:10 000 under mefloquine prophylaxis. This indicates that the PSEs are dose-related. However, suicide attempts have even been reported at prophylactic doses.[158,159] Mefloquine PSEs may begin some hours after the first dose.[8,160] Their mechanism is not clearly understood; actions as a *N*-methyl-D-aspartate (NMDA) receptor antagonist or on sigma receptors have been proposed. Chloroquine, another antimalarial, also produces psychiatric and neurological side effects: agitation, aggressiveness, amnesia, confusion, depression, hallucinations, and mania. Psychiatric changes under chloroquine may develop insidiously. Memory or perception changes can be the only clues to side effects in this developing phase. The half-life of chloroquine is long at around 1 month. Therefore, remission of a chloroquine-related PSE may take days. Children appear to be at greatest risk to psychosis under chloroquine treatment.[81]

Metronidazole

The common side effects of metronidazole are confusion, paresthesia, dizziness, vertigo, and syncope. Seizures and encephalopathy are rare. Psychotic symptoms have also been described.[170,171] Brain toxicity can occur at usual doses of metronidazole. However, at larger or chronic doses, an increased prevalence (as high as 25%) has been observed. An interaction between metronidazole and alcohol, similar to the disulfiram effect, was first described in the 1960s,[172] and many publications on this topic followed. One death has been attributed to this interaction.[173] This PSE was believed to result from a metronidazole blockade of hepatic aldehyde dehydrogenase, an enzyme in the metabolism of ethanol, followed by the accumulation of acetaldehyde in the blood. However, these early publications have been called into question.[174] A placebo-controlled study[197] found no effect on blood acetaldehyde concentrations when 12 subjects ingested metronidazole with ethanol; it induced no objective or subjective disulfiram-like effects.

Isotretinoin

The Food and Drug Administration (FDA) has received reports of depression and suicide attempts in patients treated with isotretinoin. The authors who commented these cases[132] affirm that "factors suggesting a possible association between isotretinoin and depression include a temporal association between use of the drug and depression, positive dechallenges (often with psychiatric treatment), positive rechallenges, and possible biologic plausibility.

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Compared with all drugs in the FDA's Adverse Event Reporting System database to June 2000, isotretinoin ranked within the top 10 for number of reports of depression and suicide attempt." An American drug database[198] also warns that isotretinoin "may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts, suicide, and aggressive and/or violent behaviors." Despite some publications contrary to this association,[199,200] the possibility of depression and suicidal ideation should be taken into account when prescribing isotretinoin. Establishing a causality link between isotretinoin and these PSEs can be complex. Most isotretinoin-treated patients are young, and young people are also at greater risk for depression. Another aspect is that disfiguring dermatological conditions could be associated with a greater prevalence of depression and suicidal ideation,[201] while isotretinoin improves the aspect of patients suffering from severe forms of acne. The improvement in these severe forms of acne after isotretinoin treatment may reduce anxiety and depression.[202]

Interferons

IFN-α is prescribed in viral hepatitis and in some neoplasias; IFN-β is prescribed in multiple sclerosis and hepatitis. Frequent side effects limit their use. IFN-α induces more PSEs than IFN-β. Psychiatric manifestations of IFNs are depression, personality disorders, panic attacks, other anxiety states, manic and psychotic symptoms,[119] impulsiveness, and aggressive behavior.[203] More than 10% of patients receiving IFN-α manifest PSEs.[120-122] Depressive states related to IFNs usually occur in the first weeks of treatment. They are more prevalent and severe in people who also suffered from depression before IFN treatment. Suicidal behavior is an alleged side effect of IFN-α.[123-127] IFN-α–related depression or suicidal behavior may continue after interruption of treatment.[123,126] This feature has rarely been attributed to IFN-β.[50,204] Since suicide attempts were described after withdrawal of IFN-α, even without a depressive episode during the treatment, some authors[123] advise psychiatric supervision "even more frequently after interferon withdrawal."

A randomized controlled trial[121] found a favorable effect upon the prescription of a selective serotonin reuptake inhibitor (SSRI) as prophylaxis of depression in patients who are programmed to receive IFN-α. SSRIs are also useful for treatment of depression,[128] once IFN-α is started. Paroxetine is the most studied,[121,128] but other SSRIs, such as sertraline,[129] citalopram,[130] fluoxetine,[131] and fluvoxamine may also be effective. There is no consensus on whether SSRIs should be given as prophylaxis for all patients programmed to receive IFN-α or only to those who develop depression.

Corticosteroids

Corticosteroid treatment may lead to many PSEs. The most frequent PSEs are depression, mania, anxiety, insomnia, delusions (paranoia or other themes), hallucinations, agitation, and confusional states. Rarer ones include serious heteroaggressivity, disturbances of consciousness, and depersonalization.[3,95,205] These PSEs can start after just 1 day of treatment. In more than half of patients, side effects usually remit after interruption of corticosteroids.[206] However, side effects can also occur during the withdrawal period, eg, anhedonia and fatigue may last several weeks.[207,208] The risk of PSEs is high: about 6% of patients manifest some PSEs. Prednisone is the most implicated corticosteroid, but PSEs were also described with methylprednisolone, dexamethasone, and beclomethasone. A dose–response effect is clearly seen with prednisone: doses greater than 40 mg/day are related to greater psychiatric morbidity. Moreover, hypoalbuminemia leads to an increase in plasma prednisone free fraction, potentially increasing the amount of prednisone that reaches brain. Hence, hypoalbuminemia might be associated with an increase in PSE incidence, but this has not been confirmed. Small neuroleptic doses can lead to a favorable response of corticosteroid PSEs in some days.[94,206] Treatment with lithium may be helpful.[94] Prophylaxis of corticosteroid PSEs with lithium[96-98] or valproate[99] has been described, but these approaches can be harmful to patients on corticosteroids who might not develop PSEs. Patients on corticosteroids should be monitored for psychiatric and cognitive side effects.[31]

Anabolic androgen steroids

Anabolic androgen steroids (testosterone and its synthetic derivatives) are associated with a number of PSEs: impulsiveness, irritability, and belligerence ("steroid rage"), delusions, hypersexuality, auditory and visual hallucinations, and dependence.[31] Mania, hypomania, and major depression have been significantly associated with exposure to steroids.[32] PSEs due to anabolic androgen steroids are mostly seen in abusive users. These PSEs relate to drug

concentrations in a definite pattern. Hypomania is correlated with anabolic androgen intake and major depression follows its withdrawal.[31] In chronic users of slow-liberation forms, lassitude or depression may be seen just before administration of the next dose. The abuse of anabolic androgen steroids seems prevalent among teenagers wishing to increase muscular mass. It was found in subjects as young as 9 years old,[209] with a possible peak at ages 15 and 16.[210] In another study, with a sample of 12 000 American high-school students, a prevalence of 4% was found in young males.[211] Steroid users often seek medical care for the acne these medications induce or exacerbate. If family members complain of aggressiveness and mood changes (which are less noticed by the users themselves), the clinician might suspect of anabolic androgen abuse, especially in teenagers of male sex.

β-Adrenergic antagonists (β-blockers)

Depression, nightmares, and sexual dysfunction are commonly reported PSEs of β-blockers. Hallucinations have been attributed to propranolol.[63-68] With oral administration, depression and agitation related to propranolol might be dose-dependent.[69] Ophthalmic preparations of β-blockers may also induce these PSEs, eg, timolol.[70] Withdrawal reactions to β-blockers can occur even with ophthalmic presentations; cases of rebound tachycardia were reported after ophthalmic timolol interruption. It has long been recognized that β-blockers cause psychiatric and sexual side effects. However, this has become controversial, according to recent studies. In a placebo-controlled trial, the authors found no difference between propranolol and placebo groups for the occurrence of depressive symptoms or sexual dysfunction.[212] A later review stated that "β-blockers have no significant increased risk of depressive symptoms and only small increased risks of fatigue and sexual dys-

function."[213] Nevertheless, it could be that the risk of suicide increases in users of β-blockers.[71] The conflicting results on β-blocker depression suggest that some may improve depression (eg, pindolol), others may worsen it, and others may have little effect.[214]

Conclusion

This review shows that drug-induced PSEs may occur with several medications prescribed in internal medicine and that these side effects might be overlooked. A PSE can be a stressful and traumatic life event for patients and their families. For example, a person without known psychiatric antecedents who develops a drug-induced psychosis might suffer sequelae from the fear of having lost their mind or from hospitalization in a psychiatric ward. In given cases, a PSE might even lead to a post-traumatic stress disorder, either because of the severity of the PSE itself, or because of a deficient explanation of the side effect to the patient.

Another issue is the importance of making a correct diagnosis of a PSE. This is relevant for several reasons. The main one is probably to help patients to make adequate attributions and conclusions concerning their psychological changes. Indeed, for someone who experiences a PSE, knowing that it is a side effect has a different signification than wondering if oneself is mentally insane. Detecting a PSE avoids its confusion with a sign of a psychiatric disease; since spontaneous psychiatric diseases frequently require long-term treatment, the correct diagnosis of a PSE can spare the patient the stigma, distress, and other costs of an unjustified long-term psychiatric treatment. Finally, the correct diagnosis of a PSE also enables the prescriber to communicate suspected side effects to the organization responsible for pharmacovigilance. ❏

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Efectos secundarios psiquiátricos de los medicamentos prescritos en medicina interna

Varios tratamientos farmacológicos utilizados en medicina interna pueden inducir efectos secundarios psiquiátricos (ESP) que simulan diagnósticos observados en psiquiatría. Los ESP se pueden producir durante la retirada de un medicamento, por una intoxicación y también cuando se utiliza en dosis terapéuticas habituales. Entre los fármacos que pueden inducir síndromes depresivos, ansiosos o psicóticos están los corticoides, la isotretinoína, la levodopa, la mefloquina, el interferon alfa y los esteroides anabólicos, al igual que algunos medicamentos de venta libre. Los ESP a menudo son difíciles de diagnosticar y pueden ser muy peligrosos para los pacientes. En esta revisión se discuten los ESP y también los elementos diagnósticos que facilitan su identificación.

Effets secondaires psychiatriques des médicaments prescrits en médecine interne

Plusieurs traitements pharmacologiques en médecine interne peuvent entraîner des effets secondaires psychiatriques (ESP) simulant des pathologies vues en psychiatrie. Ces ESP peuvent survenir lors du sevrage d'un médicament, lors d'intoxication ou aux doses thérapeutiques usuelles. Parmi les médicaments qui peuvent induire des syndromes dépressifs, anxieux ou psychotiques, on note les corticoïdes, l'isotrétinoïne, la lévodopa, la méfloquine, l'interféron alpha et les stéroïdes anabolisants, tout comme quelques médicaments en vente libre. Les ESP sont souvent difficiles à diagnostiquer et peuvent être très délétères pour les patients. Cet article passe en revue les ESP, ainsi que les éléments de diagnostic qui facilitent leur identification.

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