

# THE SIDE EFFECTS OF PSYCHOPHARMACOTHERAPY: CONCEPTUAL, EXPLANATORY, ETHICAL AND MORAL ISSUES - CREATIVE PSYCHOPHARMACOLOGY INSTEAD OF TOXIC PSYCHIATRY

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## SUMMARY

*The side effects are a major issue in the contemporary psychopharmacotherapy. Treatment choices are largely determined by the side-effect profiles of mental health medications. The effects of psychopharmacotherapy result from highly complex interactions between mental health medications and the patient who takes them as well as from the context in which treatment occurs. A high level of care and caution is necessary during the whole course of psychopharmacotherapy to recognize any side effect and respond promptly and specifically. Creative psychopharmacotherapy demands a broad base of pharmacologic and neuroscience knowledge (evidence based practice), personal experience (practice based evidence) and favourable treatment context (well-being therapy, life coaching).*

**Key words:** *psychotropics - side-effects - creative psychopharmacotherapy - conceptual clarification*

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## INTRODUCTION

The risk of side-effects is a major issue in modern psychopharmacotherapy and psychiatry. The cardinal principle of medicine «primum non nocere» - «first of all do no harm» is also one of the basic principles in contemporary psychopharmacotherapy. But in a day-to-day practice the things are not so simple and the key point is how to do the least harm or to avoid harmful and unpleasant side effects. According to Jacques Derrida (1982) *pharmakon* means both «remedy» and «poison» (see Pakman 2003). It is interesting that the word «*pharmakon*» is closely related to «*pharmakeus*» - magician or sorcerer, and to «*pharmakos*» - scapegoat. The fact that remedy and poison are the same substance stresses the double-sided aspect of psychopharmacotherapy. But it is also the fact that no treatment of any kind, including psychotherapy and family therapy, is possible without unpleasant or harmful side-effects. Scientific, rational and successful psychopharmacotherapy is a matter of estimating risks (possible adverse effects) and benefits

(therapeutic effects) ratio. Evidence-based approach in contemporary psychopharmacotherapy raise a series of epistemological (conceptual), explanatory and moral / ethical questions regarding side and adverse effects. Various answers to these questions depend on the applied mechanistic, formistic, contextual or systemic thinking or information-processing meta-strategies (see Jakovljević 1995, 2008). Psychopharmacotherapy rooted in simplistic and reductionistic, mechanistic and formistic thinking or information processing is associated with more harmful side-effects, and frequently called «toxic psychiatry», (Breggin 1991) not only by antipsychiatrists.

## CONCEPTUAL QUESTIONS AND TERMINOLOGY CLARIFICATIONS

Conceptual questions are related to the various definitions and meanings of terms like side-effect, adverse drug effect, adverse event, adverse iatrogenic event, adverse drug reaction, unwanted effect, undesired and unfavourable reaction. These terms are closely related to the concepts of

tolerability, safety, acceptability, efficacy and effectiveness of psychopharmacotherapy, as well as to the concepts of treatment adherence and compliance.

Every mental health medication possess a spectrum of activity affecting multiple mental functions and organ systems. By convention we classify mental health medications (psychotropics, brain-mind altering substances) into different groups like antipsychotics, antidepressants, anxiolytics, hypnotics, mood stabilizers, cognitive enhancers (antidementives), etc. according to their the most important therapeutic effects. Besides the wanted therapeutic effects, every mental health medication may induce side-effects which may be undesired, unpleasant, and harmful (adverse effects).

The terms side-effects and adverse effects of psychopharmacotherapy are commonly used as synonyms. It is important to know the difference between these phenomena. According to some opinions adverse drug reaction is any undesired or unintended response to a medication that itself requires treatment or requires a change in the treatment strategy (Campbell 2004). The term adverse drug reactions refers to unfavourable and harmful consequences of medications, including administration of the wrong drug(s) in the wrong dosage (form, amount, route, or interval) at the wrong time and for the wrong disease (Melmon 1971, according to Keshavan 1992). The side-effect is any minor or major effect of a drug other than the desired or expected main therapeutic effect, while adverse effects are always unwanted side effects of medicine which are unpleasant, unfavourable, unhealthy, harmful, or interfere with actions of other medicines in negative way.

It may be useful to make a difference between adverse effects and adverse reactions. The adverse effects are mainly related to the mechanisms of mental health medications. The adverse reactions are individual responses of the particular patients to the particular medications. Adverse event is any unpleasant, undesired or unfavourable change during the psychopharmacotherapy, not in every case caused by medications.

## EXPLANATORY QUESTIONS

Explanatory questions are relevant to mechanisms by which psycho-pharmacotherapy works and induce side and adverse effects. It is of the great importance to study side-effects for better understanding pharmacokinetics and pharmacodynamics of mental health medications as well as for applying the best tolerated and least toxic psychopharmacotherapy.

All mental health medications have multiple actions, consequently some of them result in wanted and therapeutic, the others in unwanted and harmful effects. What is useful and therapeutic effect in one patient may be useless or harmful and adverse effect in the another one. In general, therapeutic effects may be primary and secondary. Some side effects may be beneficial in some patients and so present secondary therapeutic effects. Side effects may be pleasant and unpleasant, useful or harmful, predictable and unpredictable, expected and non-expected, wanted and unwanted.

Psychopharmacotherapy adverse effects may be broadly categorized into those that are part of, or an extension of, the drug's known pharmacological profile (Type A – augmented reactions) and those that are not based on the known pharmacology of the drug (Type B – bizarre reactions) - (see Edwards 2004, Bernstein 1995). Type A adverse effects are predictable, dose-dependant and quantitatively abnormal drug effects (e.g. hypersedation, daily sleepiness, extrapyramidal symptoms, anticholinergic effects) and type B adverse-effects are unpredictable, idiosyncratic and qualitatively abnormal reactions (malignant neuroleptic syndrome, agranulocytosis, allergic skin rash).

As every mental illness has to do with meaning, psychiatric drugs works on account of meanings, expectations, and relationships, too. In addition to that fact, side-effects may be also related to the context in which psychiatrists prescribe and patients consume mental health medications. Side-effects of psychopharmacotherapy may reflect the way how it interferes with the patient's relationships, personal growing and creativity, with freedom and responsibility.

Side effects result from very complex interactions between medication and the patient who takes it. So adverse psychopharmacotherapy-related events may be associated with a variety of factors and causes like the toxic effects of a drug or impure additives, the patient's ability to metabolize and eliminate drugs, the patient's hypersensitivity, the allergic reactions to the drug or its additives, the interactions with food and other drugs, the presence of a concomitant physical illness or other psychiatric disorder, the context in which medication is administered, the negative expectation of patients and anxiety about treatment (patient's preoccupation with side-effects and negative reactions, nocebo-effect, pharmacophobia), and the patient-psychiatrist relationship.

## ETHICAL & MORAL QUESTIONS

Many psychiatric medications were called «dirty drugs» because they caused significant adverse effects and were poorly targeted to specific pharmacological actions (Pakman 2003). The moral philosophy of psychopharmacotherapy is significantly related to the safety, tolerability and acceptability of the administered medications by the particular patient. The fundamental question here is whether given psychopharmacotherapy can be justified regarding the patients' best interest, cost-effectiveness, risk-benefit ratio, and patient's preference. As other physicians, psychiatrists have adopted a moral point of view in the Hippocratic tradition to benefit patients according to the best achievements of current psychiatry. The perspective that medicine and science take toward the patient's welfare, not the patient's conception what is in her or his best interests, still prevails in modern psychopharmacotherapy. The trend toward greater respect for patient's personal autonomy, freedom of choice and decision-making with regard to the individual patients' perception of their best interests marks a departure from traditional paternalistic attitude dealing with patients as objects of care to a new ethical framework of the informed consent and shared responsibility for treatment outcome and prevention of serious side-effects of psychopharmacotherapy. Liability for psychopharmacotherapy-induced undesired side-

effects has been an issue of ever-increasing importance. The choice of psychopharmacotherapy that is in the best interests of a particular patient must always be considered during the all phases of treatment. The treatment choices are largely determined by side-effect profiles of the mental health medications.

## CREATIVE PSYCHOPHARMACOLOGY: HOW TO USE SOME SIDE-EFFECTS, PREVENT AND TREAT ADVERSE EVENTS?

The categorization what is beneficial or therapeutic effect and what is an undesired side effect is made arbitrarily in the clinical context and it varies from case to case. An important tenet of the creative psychopharmacology is to use beneficially some-side effects and prevent adverse events in the best interest of patients.

The majority of adverse events during psychopharmacotherapy are avoidable or preventable. According to some estimations, less than 20% of all adverse reactions are caused by hypersensitivity or idiosyncrasy, which are difficult to predict (Keshavan 1992). Here are the «ten recommendations» of creative psychopharmacology that can help to avoid many adverse events: 1. Know the patient well before beginning psychopharmacotherapy, 2. Offer a treatment package (holistic integrative treatment), not just a prescription, 3. Inform and educate the patient, 4. Choose the right/best mental health medications, 5. Ensure alliance with the patient to take medications properly, 6. Be familiar with prescribed medications, 7. Use a few drugs as possible to obtain benefit maximum, 8. Tailor the psychopharmacotherapy to the patient's need on the principles of the patient-centred psychiatry, 9. Have a high level of care and caution to recognize any side-effect and respond promptly and specifically, 10. Consider the patient's viewpoint to create a shared vision of the treatment goals (see also Jakovljević 2007, 2008)

If any side effect does occur, the type and severity of the reaction as well as any triggering factors need to be elucidated. With dose-related adverse effects, adjustment of the dose may help,

while with the idiosyncratic adverse effects and intoxication, the medication should be stopped.

For mild unwanted effects education and discussing the symptom as a side effect, along with support the patient, is usually sufficient. In the case of the moderately undesired side-effects, the problem usually can be solved without changing ongoing medications. Problem-solving intervention may include splitting the dosage, taking the medication at a different time of day, changing to a long-acting drug formulation, or recommending changes in diet and/or exercise (Doran 2003). Significant adverse effects, either because of the patient's discomfort or the psychiatrist's assessment of risk should be addressed promptly and specifically. In contrary, the patient may lose confidence and stop taking the medication without informing the psychiatrist. For serious adverse events, a quickly and decisively response is an imperative. The areas of serious risk to health and safety include serotonin syndrome, neuroleptic malignant syndrome, anticholinergic intoxication, QTc interval prolongation, extrapyramidal symptoms and other movement disorders, tardive dyskinesia, seizures, hepatotoxicity, agranulocytosis and other blood dyskrasias, lithium toxicity, P450 interactions, monoamine inhibitor interactions. When serious adverse effects occur, the psychiatrist's written records are crucial and provide documentation of the clinical assessment, thinking and interventions (Doran 2003).

Creative psychopharmacology (the term coined by dr. Jonatan Cole) demands a broad base of pharmacologic knowledge, which may allow safe combinations of multiple medications to achieve clinical improvement (Bernstein 1995) as well as to decrease the risk of adverse effects. With rational combinations, lower than usual doses of medications may decrease risk of adverse effects and increase treatment adherence and effectiveness. A classical view of biological psychiatry and psychopharmacotherapy has tended to focus more on the disease demotion and illness decrease than on health promotion and wellness (well being) increase. Transdisciplinary holistic integrative treatment includes both disease & illness demotion and health & wellness promotion in the same time as well as combined parallel and sequential

treatments with additive and synergistic effects, including creative psychopharmacotherapy (Jakovljevic 2008). Good clinical practice in psychopharmacotherapy requires a sensitive understanding of the patient which may evoke a placebo response in addition to favourable pharmacological actions, instead a nocebo response.

## CONCLUSIONS

Modern mental health medications are relatively safe, well-tolerated, non-addicting if used properly. In day-to-day clinical practice, most psychiatric medication side-effects are uncomfortable and bothersome. However, serious adverse events with high risk of morbidity, or rarely mortality are also occur. A key point is that for any particular patient the best and most effective psychopharmacotherapy should be determined at any particular point in time or phase of the treatment. It is necessary to watch carefully for the appearance of adverse effects through the entire course of psychopharmacotherapy as well as to respond promptly and suitably.

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