THE CREATIVE PSYCHOPHARMACOTHERAPY AND PERSONALIZED MEDICINE:
The art & practice of the learning organization

Miro Jakovljević
Department of Psychiatry, University Hospital Centre Zagreb, Croatia

SUMMARY
There is a huge gap between possibilities for achieving high treatment effectiveness and poor results in clinical practice. It is possible to achieve a more positive impact and better treatment outcome by individualizing and personalizing treatments in a more creative and rational manner. This review describes the short history and principles of creative psychopharmacotherapy.

Key words: creative psychopharmacotherapy - individualized treatment - personalized medicine

INTRODUCTION
The field of psychopharmacotherapy has expanded significantly during and after the decade of the brain with a lot of controversial concepts and treatment paradigms, creating both new opportunities and challenges. The advent of a significant number of effective and well tolerated mental health medicines has increased our possibilities to treat major mental disorders in more successful ways with much better treatment outcome including full recovery. Modern psychopharmacotherapy has claimed itself as scientific, rational, and technical, very much evidence-based. However, there is a huge gap between our possibilities for achieving high treatment effectiveness and poor results in clinical practice (Jakovljević 2007). There is much room for improvement in the practice of clinical psychopharmacology (Niculescu & Hulvershorn 2010). The concept of creative psychopharmacotherapy could advance everyday clinical practice and bridge the gap.

HISTORY OF THE CONCEPT OF CREATIVE PSYCHOPHARMACOLOGY
Dr. Jonatan Cole (1925-2009) coined the term Creative Psychopharmacology in 1992 referring to „the rational use of multiple medication simultaneously to treat difficult illnesses“ (Bernstein 1995). According to Bernstein (1995) „to properly use medicines in the Twentieth Century, one needs knowledge, reverence, caution, and enthusiasm; the latter being the origin of the creativity often necessary to achieve an optimal therapeutic result“. Bernstein's concept of creative psychopharmacology refers to 1. rational and safe combinations of multiple medications to achieve clinical improvement where simpler regimens have failed, 2. the use of novel drugs or those approved for non-psychiatric indications to treat mood and behavioral disorders, 3. when prescribing drugs thinking more in terms of differential effects of monoamine neurotransmitters and their imbalance on behaviour, than in terms of a strict diagnostic categorization.

Creative psychopharmacology is not an authorization to practice quackery or to treat patients with alternative remedies without scientific knowledge of rational mechanisms to support the novel therapy (Bernstein 1995). „Deficient dopaminergic function may be operative in generating inertia and behavioral retardation, since this transmitter appears to be important in governing goal directed behaviour. Noradrenergic deficiency may be seen as underlying anhedonia, therefore restoring adequate functional levels of this transmitter may result in reawakening the depressed patient's ability to experience pleasure. Serotonin on the other hand may partially function as a regulator of mood, aggression, and anxiety“ (Bernstein 1995). This approach is very similar to the concept of functional psychopharmacology and a goal-directed, dysfunction oriented psychopharmacotherapy (van Praag 1993).

THE CREATIVE PSYCHOPHARMACOTHERAPY FROM AUTHOR'S PERSPECTIVE:
The art & practice of the learning organization

What's in the name?
Creative psychopharmacotherapy represents the art and practice of the learning organization in the frame of transdisciplinary holistic, integrative and personalized psychiatry (Senge 2006, Jakovljević 2007, 2008). It is based on the creative thinking and systemic information processing strategy (Jakovljević 1995, 2005) integrating reason and intuition as well as on the creation of favourable treatment context and creative collaboration with patients and their families. Reason and intuition are
designed to work in harmony for us to achieve our potential intelligence, while systems thinking may hold a key to integrating them together (Senge 2006). Systems thinking leads to experiencing more and more of the interconnectedness of multifarious disease and its treatment aspects and to seeing wholes rather than parts. Each patient is built of different biological and psychological systems at different levels as well as each patient belongs to different systems, such as family, community, culture, society and universe. Treatment intervention in one system can influence other related systems too. Creative thinking refers to the original ideas and mental processes leading to a previously unrecognized opportunity for a solution of therapeutic problem in unique and more effective and rapid way. Creative thinking may use preexisting objects, information and ideas, but creates a new relationship between elements it uses, for example creating a more favourable treatment context and more effective and safer drug combinations.

Creation of the favourable treatment context is based on the shared decision model, managing patients’ mental models that improves their personal mastery as well as the shared learning with patients. Learning in this context does not mean getting more information, but expanding the ability to produce the results we truly want (Senge 2006) in psychiatric treatment. Mental models are deeply ingrained beliefs, assumptions, generalizations, or even pictures and images that influence how human beings understand the world and how they take action. Personal mastery goes beyond competence and skills, as well as beyond spiritual unfolding or opening, it means living life from a creative as opposed to reactive viewpoint (Senge 2006). Managing patients’ mental models involves surfacing, testing and improving their internal pictures of how world works as well as how they functionate in health and illness to increase their creative capacities. Creative collaboration with patients and their families includes building of the shared treatment goals as well as of the picture of the patients’ future that foster their genuine commitment and enrollment more than simple compliance. A shared vision is the first step in allowing people who mistrusted each other to begin to work together (Senge 2006).

**Some general principles of creative psychopharmacotherapy**

**Principle 1.** Creative psychopharmacotherapy is only a cornerstone of holistic and integrating treatment of mental disorders. According to many experts, psychopharmacotherapy alone is generally insufficient for complete recovery (e.g. Janicak et al. 2006). A creative approach to psychopharmacotherapy recognizes that the healing process is more than chemical equilibration related to mental health drugs bioavailability in the blood and brain. Framing a therapeutic context in which mental health medicines are prescribed and used by patients is of essential importance. Attention aimed at promoting healthy life styles, general well-being, social integration and spirituality are very important elements of holistic and integrating treatment that enhances favourable drug response, and vice versa psychopharmacotherapy supports better mental and social integration, self-directedness, cooperativity and spirituality (Jakovljević 2005, 2007 & 2008). An integrative and holistic approach involves simultaneous and synergistic application of mental health medications psychological, interpersonal and family interventions in the context of well-being oriented treatment and life coaching.

**Principle 2.** Creative psychopharmacotherapy is always highly personalized. A useful distinction between disease and illness is relevant for our understanding of the personalized psychopharmacotherapy. Disease is a disruption of biological structure or function, e.g. brain, its treatment mitigates or eradicates the symptoms and signs and does not demand attention to the whole person. Illness is a subjective experience, cultural and interpersonal manifestation of a disease. Illness is a problem of the whole person, not of a single organ or organ system. Simply treating a psychiatric diagnosis or a disease as only brain disorder without treating the whole patient, is no longer acceptable. The goals of treatment are not only to reduce, eliminate or prevent distressing and disabling symptoms, but also to help patients to learn new ways of thinking, feeling and behavior in order to achieve a fulfilling, meaningful, satisfying and valued life.

**Principle 3.** Creative psychopharmacotherapy is strictly individualized. The field of pharmacogenetics and epigenetics is a rapidly evolving science investigating the genotype as a possible reason for good, poor or no responding to drugs as well as for deleterious side-effects. Although this field heralds great promise for individualized patient healthcare, there are only a few reliable markers in clinical practice. While waiting Godot, it is important to choose medications that 1. can also treat comorbid conditions present, 2. avoid a particular side-effect, 3. avoid complicating a medical condition, 4. avoid an interaction with another medications, 5. have side-effect that may be to the patient’s benefit, 6. are proffered by the patient, 7. have been effective in a close relatives of he patient, 8. are affordable for the patient (Doran 2003). It is important to note that the overlap between comorbid disorders and their possible interdependence may afford parsimony in the number of medications used (Jakovljević 2009b, Niculescu III & Hulvershorn 2010).

**Principle 4.** Creative psychopharmacotherapy is psychopathological mechanisms or processes directed, not particular diagnosis oriented practice. The madness of King George is an extreme, but educative, example of how not-knowing of the underlying disease
(porphyria) mechanism can result in treatment failure and lead to considerably more health risk than benefit. In creative psychopharmacotherapy it is of great importance to target specific symptoms that may serve for the underlying psychopathology (Janicak et al. 2006). It is very important that treatment cover all important symptoms such as reality distortion, social withdrawal, mental disorganization, sleep disorders (insomnia, hypersomnia), anorexia, bulimia, sexual disturbances, depression, euphoria, mood bipolarity, impulsivity, obsessivity, compulsivity, agressivity, suicidality, fear, anxiety symptoms, etc. A continual monitoring of the presence or absence of all important symptoms and specific problems is needed over the entire course of treatment.

Principle 5. Creative psychopharmacotherapy is a context dependent practice. Mental health medicines work also on account of meanings, expectations, and relationships. So, treatment effectiveness also depends on 1. what psychiatrists and patients believe how medications work, 2. quality of a physician-patient relationship including the patient's confidence in the physician and in psychiatry as a whole, 3. communication and emotional expressiveness within the patient's family, 4. the patients' human right respect. Many of the concepts of mental health, wellness and illness as well as the use of psychiatric medications are often mysterious for patients and their families and filled with myths, prejudice and fears. The creation of favourable treatment context as well as a creative collaboration with patient and her or his family may significantly improve treatment outcome.

Principle 6. Appropriate medications should be applied in every phase of treatment. Different mental health medications fit different phases of psychopharmacotherapy. Some medications are quite appropriate for application in an acute phase of treatment, but not in maintenance or prophylactic treatment phase. Vice versa is also true: certain medications are not so effective in acute phase, but are exceptionally beneficial applied in maintenance or prophylactic treatment phase (see Janicak et al. 2006). At each phase of treatment it is very important to select the primary treatment perspective that best fit the patient (see Jakovljević 2008).

Principle 7. Psychopharmacotherapy must follow the principles of a human rights-based (FREDA) approach to health care. FREDA approach to health care is based on premise that ignoring and violating patients’ human rights has a detrimental effect on their health, and vice versa, using this approach can improve health outcomes and deliver better quality, person-centered health-care (Curtice & Exworthy 2010). Patient's human rights should be protected in clinical practice during psychopharmacotherapy by adherence to the core values of fairness, respect, equality, dignity and autonomy (FREDA).

Principle 8. Building shared vision of treatment goals with patients and their families is an important component of learning organization and favourable treatment context. The patient's beliefs concerning the origin of symptoms and mental health medicines action may contribute positively (placebo) and negatively (nocebo) to drug treatment response. Shared decision making is one of the key components of creative psychopharmacotherapy.

Principle 9. The risk-benefit evaluation is one of the basic tenets when planning a treatment strategy. Assessment of psychic, neurologic and somatic status as well as recognition of contraindications for individual medications is of huge importance. Cardinal principle is: „primum non nocere” – „first of all do not harm", and treatment benefit must significantly overcome treatment risks. It is obligatory to watch carefully for the appearance of adverse events through entire course of psychopharmacotherapy as well as to respond promptly and suitably (Jakovljević 2009a).

Principle 10. Achieving as soon as possible a complete remission. As mental disorders contribute enormously to psychological, social and economic suffering of patients and their families. Rapid remission and complete recovery can be achieved in the majority of cases only with rational drug combinations and creative polypharmacy. Antipsychotics are not effective in treating the entire range of symptoms in schizophrenia as well as antidepressants in monotherapy do not cover all aspects of psychopathology in depression (Jakovljević 2005). Creative and rational polypharmacy means multiple drug treatment with „only as many drugs as necessary, each for a specific target symptom, each evaluated individually for efficacy and side effects and adjusted optimally, with the elimination of each one that is no longer necessary” (Joseph 1997). Combined medications should provide synergistic benefits and mitigate or eliminate adverse effects by using lower doses of each medication and targeting complementary physiological (compensatory) mechanisms (Niculescu III & Hulvershorn 2010).

Principle 11. Careful monitoring over the entire course of treatment. It is necessary to continually look for the further possible improvement of the patient's well-being. It is very important to monitor treatment adherence, patient's commitment to treatment goals and possible development of medication tolerance. Good adherence with drug treatments is associated with better-tailored treatments that lead to more satisfied and insightful patients and to fewer undesirable side-effects and better treatment acceptability by patients.

CONCLUSION

With available mental health medications, it is possible to achieve a more positive impact and better treatment outcome by individualizing and personalizing treatments in a more creative and rational manner.
REFERENCES


Correspondence:
Prof. dr. Miro Jakovljević, MD, PhD
Department of Psychiatry, University Clinical Hospital Centre Zagreb
Kišpatičeva 12, 10000 Zagreb, Croatia
E-mail: predstojnik_psi@kbc-zagreb.hr