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REGULAR ARTICLE

How psychotropic drugs are used; an explanatory paradigm

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Abstract Traditionally, two divergent approaches are used to explain the mechanism of action of psychotropic drugs. The dominant "Disease-centred" view emphasises the biochemical imbalance caused by 'illnesses'. In contrast the "Drug-centred" view emphasises the psychoactive properties of these drugs and their ability to induce an 'altered-state' of mind. In this article we propose a new paradigm for classifying the therapeutic uses of psychotropic drugs based on the relation between their psychoactive effects and symptoms of indicated mental illness; as well as their clinical responses e.g. emerging tolerance, paradoxical initial worsening and being recommended for long/short term use. Based on this premise, therapeutic uses of psychotropic drugs can be placed on a continuum between two distinguishable modes. We define these modes as "Psycho-antagonistic" and "Psycho-agonistic". 105 therapeutic uses of 85 psychotropic drugs are placed on this continuum; 74% on the Psycho-agnostic spectrum and 25% on the Psycho-antagonistic side. Hypnotic agents used for insomnia are clear examples of Psycho-antagonistic mode of use. Citalopram for treatment of Panic disorder is a clear example of using a drug in Psycho-agonistic mode. Only the therapeutic use of Lithium for bipolar affective disorder could not be allocated to any mode and considered as borderline. The paradigm highlights the possibility of initial worsening in majority of therapeutic uses of psychotropic drugs and importance of using lower doses. Further studies and clinical trials are needed to explore the full extent of the clinical implications of this paradigm in psychiatry and perhaps in other branches of medicine.

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Introduction

Psychotropic drugs are used successfully to treat mentally unwell patients. Alteration in brain neuro-chemistry has been the best evidenced and most accepted explanation of the effects of such drugs since the 1950–60 s [1]. Indeed most of the recent advances in our pharmacological toolkit are due to scientific advances and clinical trials based on this 'Disease-centred' model. This model has replaced an older, more clinically oriented model of how psychotropic drugs may work. This latter approach is based on the concept of the psychoactive properties of psychotropic medication and the possibility of inducing an altered mental state to explain the mechanism of action of same [2]. For example, Deniker in 1960 suggested that neuroleptic drugs work by inducing a neurological syndrome consisting of physical restriction and mental symptoms such as cognitive slowing, apathy, and emotional flattening, which resembled Parkinson's disease [3].

This point of view has recently led to the development of a 'Drug-centred' model by Dr. Joanna Moncrieff [4] to explain the mechanism of action of psychotropic drugs. In this approach the effect of psychotropic drugs are considered to be similar to the effects of psychoactive substances that: ''induce complex, varied, often unpredictable physical and mental states that patients typically experience as global, rather than distinct therapeutic effects and side effects'' and that their ''therapeutic effects are the consequence of being in an altered mental state'' [4]. Whilst the model is clearly at odds with current scientific thinking, there may be some benefit in exploring how psychological alterations produced by psychotropic drugs interact with the symptoms experienced by patients with clearly defined mental illness.

In addition, Moncrieff's model suggests that any such approach needs to consider the psychological changes due to psychotropic drugs on healthy subjects – otherwise the effect of the drug may be altered or masked by the symptoms of the illness. For example the sedative properties of a drug might be completely different when prescribed to an aroused in contrast to a drowsy patient. In reality however, it is rare to find such studies on healthy subjects in the published medical literature [4].

Within the spirit of an exploratory approach to the interaction between the psychoactive properties of a psychotropic drug and the symptoms of mental illness that it is licensed to treat we propose an alternative option. This is to use the published summaries of the toxicity and side effect profiles of each psychotropic drug as a proxy measure of their psychoactive effect in a healthy subject. This information also presents the unintended but still psychoactive properties of psychotropic drugs. In clinical practice the interface between the therapeutic properties and side effects of a drug becomes blurred on some situations. Using the reported side effect of Mirtazapine of 'increasing appetite' as a desirable property in treating an anorexic patient with depression is a good example of how reported side effects can have therapeutic uses [5]. Therefore, in this article we shall use the terms 'Side-effect' and 'Psychoactive properties/effects' synonymously and interchangeably.

Hypothesis

Based on this premise, we propose that therapeutic uses of psychotropic drugs can be placed on a continuum between two distinguishable modes. Their locus along the continuum is based on the relationship between their psychoactive effects and the symptoms of the illness for which they are prescribed in addition to their therapeutic responses. We define these modes as ''Psycho-antagonistic'' and ''Psycho-agonistic'' and their defining characteristics are outlined below (Table 1).

We propose that all psychotropic drugs could be placed along this continuum as illustrated (Fig. 1) by using the number of the criteria they meet. It is important to highlight here that the terms Psycho-antagonistic and Psycho-agonistic are descriptive only and do not imply any disease-targeted mechanism or receptor oriented theory.

Evaluation of hypothesis

The first and second authors (FS & MG) conducted a review of the medical literature on the reported side effect profile and clinical responses of psychotropic medication in relation to the symptoms of those mental illnesses they are prescribed to treat (clinical indication). They independently reviewed each drug in the British National Formulary's (BNF) classes 4.1–4.4 and 4.11 [6] along with their specific clinical indications, from August 2009 to Nov 2015. Any discrepancy was discussed in order to arrive at a consensus. In the BNF the clinical indications are listed as an illness/mental disorder (e.g. Schizophrenia) or a symptom (e.g. insomnia). In the case of mental illness/disorder, the symptom profile was taken from the definition of the illness/disorder as specified in the International Classification of Diseases, 10th edition (ICD-10) [7]. In the

Figure 1 The continuum of therapeutic uses.

Table 1 Modes of therapeutic uses.

Mode	Definition of therapeutic use
Psycho-antagonistic	1. The drug's psychoactive effect is opposite to the symptoms of its indicated mental illness/disorder 2. It is recommended for short term use 3. Tolerance is likely to develop with use over a few weeks
Psycho-agonistic	1. The drug's psychoactive effect mimics the symptoms of its indicated mental illness/disorder 2. It is recommended for longer term use. 'Symptom reduction' occurs gradually over time without the development of tolerance 3. There is a possibility of an initial worsening of some symptoms