

## "Do Antidepressants Cure or Create Abnormal Brain States?"

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A provocative article by Dr. Joanna Moncrieff and Dr. David Cohen, PLOS Medicine, June 5.

In their provocative essay, Dr. Joanna Moncrieff of University College London and Professor David Cohen\* of Florida International University in Miami, challenge the "disease-based" paradigm in psychiatry, arguing that the class of drugs known as antidepressants, and indeed all psychotropic drugs, produce their desired effects by creating abnormal brain states.

Psychotropic drugs induce sedation, or stimulation, or indifference, or a "plethora of psychobiological states," and may thus coincidentally relieve symptoms of psychiatric disorders. But Drs. Moncrieff and Cohen write that this in no way suggests that patients have "chemical imbalances" and they warn that these drug-induced states, though usually short-lived and may create more problems than they solve.

Drs. Moncrieff and Cohen argue that psychiatry's dominant "disease-centered model"-which holds that drugs correct "biochemical imbalances"-is far from established, and this for several reasons.

In the case of antidepressants, Moncrieff and Cohen show that all studies have failed to support the existence of pre-existing brain abnormalities among psychiatric patients. Animal models that try to mimic mental disorders fail to select drugs that are supposed to be effective for these disorders. In clinical trials testing antidepressants, rating scales include many items that would respond to any drug with sedative effects, thus outperforming placebos, but not because the drugs have specific "antidepressant" properties. Also, several other types of drugs, including benzodiazepines, antipsychotics, opiates, and others have been found to relieve depressive symptoms in controlled clinical trials.

Moncrieff and Cohen also show that so-called antidepressants affect healthy volunteers just like they do psychiatric patients-which weakens the idea that patients have abnormal brains. Finally, the authors remind us that the widespread use of so-called antidepressants, which are supposedly disorder-specific-"selective serotonin reuptake inhibitors"-have not led to demonstrable improvements in short or long-term outcomes of depression.

Drs. Moncrieff and Cohen propose instead that a "drug-centered model" best explains observed effects of antidepressants, in clinical trials and in ordinary patients' lives. They suggest that most tricyclic antidepressants are very sedating and produce EEG disturbances, causing cognitive dysfunctions.

SSRIs appear to be mildly stimulating and sedative simultaneously, but can also have effects that progress to "frank agitation." In addition, these various drugs may share antipsychotics' and opiates' particularly blunting effects. Together, these sedative and stimulating effects explain antidepressants' popularity and perceived "effectiveness" among their users.

Moncrieff and Cohen warn that some drugs cause euphoria among some users, but this comes at a cost: "Drugs known to produce short-term euphoria require an increasing dose to maintain this effect (tolerance) and are associated with a compensatory dysphoria on discontinuation. ."

Tolerance requiring increased dose confirms the drugs pose a risk of drug-dependency (or addiction).

"So far, however, there is no compelling evidence that there exists any drug induced effect consisting of a sustained elevation of mood."

Moncrieff and Cohen conclude as follows: "Many patients are led to believe by their physicians and by advertising that antidepressant drugs will act on the biological cause of their depressed state by rectifying a 'chemical imbalance'.

On the contrary, our analysis indicates that there are no specific antidepressant drugs, that most short term effects of antidepressants are shared by numerous other drugs and that long term drug treatment with antidepressants or anything else has not been shown to lead to elevation of mood. We suggest the term "antidepressant" should be abandoned."

Read this original article in its entirety at: <http://dx.doi.org/10.1371/journal.pmed.0030240>

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