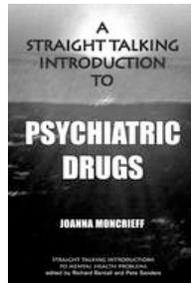


De-mystifying psychiatric drugs

Joanna Moncrieff,
UCL, NELFT, CPN,
September 2012

The Myth of the Chemical Cure
A Critique of Psychiatric Drug Treatment
Joanna Moncrieff



Models of drug action

Disease centred model	Drug centred model
Drugs correct an abnormal brain state	Drugs create an abnormal brain state
Drugs as disease treatments	Psychiatric drugs as <i>psychoactive drugs</i>
Therapeutic effects derived from effects on (presumed) disease pathology	Useful effects are a consequence of the drug induced state
Paradigm: insulin for diabetes	Paradigm: alcohol for social anxiety

Changes in Therapeutic Concepts

Pre 1950s:

- Sedatives
- Stimulants

Post 1950s:

- Antipsychotics
- Antidepressants
- Anxiolytics
- Mood stabilisers
- Hypnotics
- Treatment resistant psychosis

- No evidence that psychiatric drugs reverse underlying chemical imbalances or other biological abnormalities

Evidence for disease-centred model of drug action

- Placebo controlled trials do not distinguish disease-centred from drug-centred model

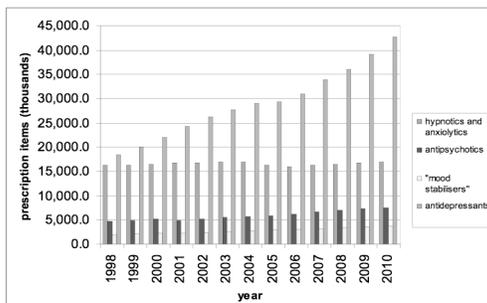
But disease-centred model might be supported if:

- Pathology of disease explains drug action
- Supposedly specific drugs better than non specific ones
- No therapeutic type effects in healthy volunteers
- Animal tests select specific drugs
- Outcome improved with use of specific drugs

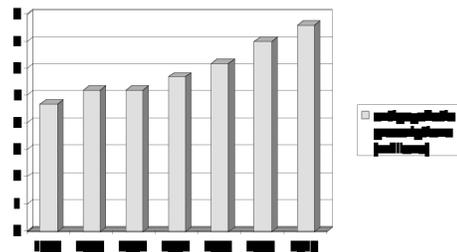
So how do psychiatric drugs work? The drug-centred model

- Direct effect of psychoactive effects
- Amplified placebo effects

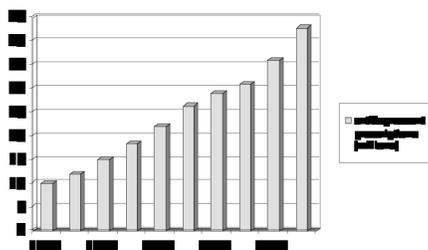
Trends in prescriptions in England 1998-2010



Community antipsychotic prescriptions 1998-2010 (PCA)



Trends in antidepressant prescribing 1992-2010



- What causes bipolar disorder?
Scientists don't know for sure what causes bipolar disorder, though they believe **it may be caused by chemical imbalances in the brain.** Current medicines are designed to help correct these imbalances and have been shown to be effective at improving symptoms for many people.



Pfizer, 2011

- ‘antipsychotic medicines are believed to work by balancing the chemicals found *naturally* in the brain’

Eli Lilly, zyprexa.com, 2011



- “People with depression may have an imbalance of the brain’s neurotransmitters” Eli Lilly, 2003
- “Paxil CR helps balance your brain’s chemistry” PaxilCR.com, 2009

Antidepressants are not very different from placebo

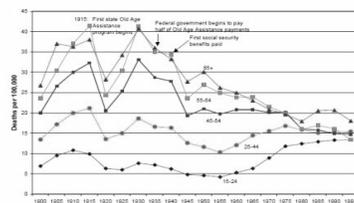
- Kirsch et al, 2002 meta-analysis: difference 1.7 points on HRSD
- Other recent meta-analyses similarly small differences (e.g. NICE, 2004).
- Even in people with severe depression, improvement is only around 4 points on HRSD (Kirsch, 2008)
- Differences easily accounted for by psychoactive effects of antidepressants
- Many other possible biases: publication bias, selective reporting, unblinding

Do antidepressants improve the outcome of depression

- Placebo controlled trials short-term
- Long-term outcomes for treated depression are poor – e.g. STAR*D study (also Goldberg, 1998; Tuma, 2000; Kennedy, 2003)
- People who take antidepressants do not do better than people who do not take them (Brugha et al, 1992; Ronalds, 1997)
- Increased antidepressant use associated with increased prevalence and duration of depression, increased sickness benefit claims and more time off work (Patten, 2004; Moncrieff & Pommerleau, 2000; Dewa et al, 2003)
- Suicide rates? ?

US suicide trends over 20th century.
Cutler & Meara, 2003 (In Perspectives on the Economics of Ageing, Ed D. Wise)

Fig. 14: Suicide deaths by age



Psychoactive effects of “antidepressants”

Tricyclic antidepressants:

- Profound sedation
- Cognitive and motor impairment
- EEG slowing
- Dysphoria
- Some have dopamine blocking activity at higher doses

Psychoactive effects of SSRIs and venlafaxine

- Sedative effects
- Cognitive impairment
- Emotional blunting
- Reduced libido

- Arousal/activation effects
- Emotional instability

- Not euphoriant (like stimulants or benzodiazepines)
- Not relaxant like benzodiazepines
- ?suicide-inducing

Psychoactive effects of antidepressants: (askapatient.com)

- "Increased anxiety initially, borderline panic, mild insomnia, listlessness and lethargy" (Fluoxetine).
- "Total loss of libido, sometimes suicidal, loss of appetite, inability to care about anything, mood swings" (Fluoxetine).

- "Fuzzy memory..loss of libido.. general numbness/mental blankness...memory loss" (venlafaxine).
- "Sleepy all the time, suicidal thoughts, irritability, don't care about anything" (venlafaxine).

A drug-centred approach to treating depression

- No evidence that any drug can specifically reverse or ameliorate depression or depressive feelings
- 80% of effect of antidepressants is a placebo effect
- Various psychoactive effects may suppress depressed feelings, or alter behaviour or emotions
- Sedatives may be useful to help insomnia, anxiety and agitation

- But...people may prefer alternative strategies!



Patient information

- The antidepressant will help normalise your serotonin levels

- The antidepressant will improve your depression

- The drug affects the way people think and feel (not just people with depression), but we are not sure how, because we haven't bothered to study it properly. It may dampen down your emotions, and make you feel mildly drugged or groggy.....

Delay and Deniker 1952

- "the apparent indifference, or delay in response to external stimuli, the emotional and affective neutrality, the decrease in both initiative and preoccupation without alteration of conscious awareness or in intellectual faculties, constitute the psychic syndrome due to treatment"

Experimental neurological syndromes and the new drug therapies in psychiatry

Pierre Deniker, *Comprehensive Psychiatry*, volume 1, 1960.

The subjective experience of taking antipsychotics medication
Moncrieff et al, 2009. From askapatient.com

- “extremely hard to move, think, talk” (haloperidol)
- “heavy mental and physical stagnance” (haloperidol)
- “emotionally empty, dead inside” (trifluoperazine)

From askapatient.com

- “no emotions, only a weird, spacey, empty feeling, no arousal, no excitement, no joy, nothing” (risperidone)
- “I’ve never been able to eat as much as I did when I was on Zyprexa. I gained 40lbs in no time and my mind was in a constant fog of lethargy and indifference. I didn’t care about anything. I just wanted to sit around and

From askapatient.com

- “decreased the intensity of inner voices” (risperidone)
- “stops my negative thoughts and feelings being amplified and overwhelming me” (risperidone)
- “hypersomnia (increased sleeping), calming of moods, general smoothing out of mania, calmness, less hallucinations” (olanzapine).

From askapatient.com

- “Although I felt very well, I felt as if I had absolutely nothing to talk about. I kept wondering about whatever [it] was that had been so interesting during most of my life that I had suddenly lost... But I was very much in contact with reality and for that I was thankful” (haloperidol)

Adverse effects

- Mental effects unpleasant
- Withdrawal effects
- Sexual impairment
- Weight gain
- Diabetes
- Heart conduction defects
- Tardive dyskinesia
- Reduced brain volume
- Death



- Drugs help some people to improve
- There is no evidence that they do this by reversing an underlying imbalance or disease
- They are prescribed to many people with little or no evidence that there will be any benefit
- Drugs produce altered physical and mental states
- The harmful consequences of treatment often outweigh any positive effects