
TONY BUCKINGHAM/REX

Help luck along to find psychiatric medicines

To increase the chances of stumbling on existing drugs that can double as brain treatments, a systematic search is needed, says **David Nutt**.

Where will new psychiatric medicines come from? That there is a crisis in the drug-discovery pipeline for mental health is well known. Many pharmaceutical companies have given up on this realm, and a research director from one such firm has said that any business working in this field itself needs psychiatric help.

Scientists continue to search for the molecular and neurological clues that could allow informed development of new treatments, but it seems likely that, for now at least, we will have to rely on luck.

Serendipity is not be sniffed at. The antibiotic minocycline has emerged as a possible schizophrenia treatment after two Japanese people given it for infection saw remarkable improvement in their psychotic symptoms. The blood-clotting drug warfarin may also be useful in schizophrenia: in an audit of clinical work, a US haematology group found that the drug seems to relieve symptoms. There may be many explanations for these observations, and trials are required for confirmation. But if mechanisms can be determined, they could open useful avenues for schizophrenia research.

For depression, clinically relevant observations have been made by neuroscientists exploring brain function. Studies that used ketamine to model psychosis in normal volunteers found that the drug induced rapid improvement in mood. This led to clinical trials that proved its efficacy against depression. Psilocybin, the active psychedelic ingredient of magic mushrooms, has been used to study altered states of consciousness in healthy people, in whom it triggered long-lasting improvements in mood. This, coupled with effects on the subgenual cingulate cortex, an important brain region for depression, has led to a trial on treatment-resistant depression that will start in 2015, funded by the UK Medical Research Council.

Such accidental discoveries are not new: it can be argued that all the commonly used classes of psychiatric drugs have been arrived at through serendipity. The calming effects of the benzodiazepines and lithium were found accidentally in animal studies, and antidepressants and antipsychotics were discovered from unexpected beneficial psychological effects in humans. Early classes of antidepressants were originally developed as anti-tuberculosis and antipsychotic drugs. The mood of patients improved even though the underlying disorder did not. The first antipsychotic, chlorpromazine, showed anti-schizophrenia effects when used as a sedative.

On the basis of such insights, many other agents have been synthesized and tested. Often, these treatments are effective and carry fewer side effects than the original compounds. But they are all 'me too' drugs, based on the same mechanisms of action. So they do not advance knowledge of the neuroscience of antidepressants or antipsychotics, at least in terms of new molecular targets.

Every day, billions of people take medicines. Some of these drugs may have unexpected effects on symptoms of brain disorders, but at present there is no way to collect this information. If we are to rely on serendipity to bring us new drugs, how can we increase the chances of success?

Most Western nations already collect information on adverse effects. We should establish parallel schemes to report psychiatric benefits. Trials could be especially useful in countries such as Denmark and Sweden, which have existing databases for medicine use and for mental health. Commonly used medicines are considered safe, so trials for psychiatric benefits could be fast-tracked.

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Patient-led approaches are also possible. Online forums allow people to discuss their experiences of antipsychotic and antidepressant medications. Such sites may have millions of visitors per month and would be ideal hosts for large-scale public questionnaires, or web pages dedicated to reporting positive influences of prescription and over-the-counter medicines.

A rather different (and more radical) approach is to tap into the recreational use of non-prescription drugs. Millions of people take these compounds, and not all of the drugs are illegal. Indeed, certain 'legal highs' have chemical similarities with therapeutic drugs and could lift mood or reduce anxiety. Users are often keen to share their experiences, at least through online questionnaires.

Apart from the obvious political barrier to such research (tacit endorsement of illegal drug use), there is a big scientific stumbling block. Illegal recreational drugs are not subject to trading-standards regulations and may not contain what the name suggests. However, legal highs are usually a pure form of what they claim to be.

Insights from public use of drugs and medicines would not be from controlled trials, so formal publication in journals could be difficult. But dedicated databases to showcase findings would be cheap to establish. Perhaps companies that developed treatments on the basis of these discoveries could make a contribution to the costs. Maybe the registers could attract a small part of the intellectual property from any such discoveries. Companies with drugs currently in patent would certainly have a significant financial interest in the compounds being evaluated for new psychiatric indications.

The investment is worth it. The drugs that we need to ease the burden of mental illness could be out there — we just need to look. ■

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