

Pharmacogenetics and Mental Health

The Negative Impact of Medication on Psychotherapy.

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Psychological Changes with General Medication.

A simple and practical example...

When Lansoprazole was prescribed for indigestion a particular patient suffered psychological side effects of restlessness and severe agitation.

After six months it was perceived that agitation, which is referred to in the Patient Information Leaflet, could be a side effect of Lansoprazole,

When Lansoprazole was discontinued, the patient's agitation and distress was reduced considerably.

The patient did not have the psychological awareness or knowledge to associate the agitation with the medication.

Furthermore the likely inability to metabolise Lansoprazole was not initially considered by the GP.

Psychotherapy and General Medication

By having an increased awareness of medications that have the potential to cause psychological adverse changes¹, psychotherapists would be providing a double safety net for their clients.

Perhaps due to ignorance or to a lack of psychological awareness resulting from adverse medication effects, not all patients will have the ability to assess logically whether a recently introduced medication has triggered mental changes.

However, should mental health changes occur, psychotherapists are in a position to enquire from patients about the status and any change of the potential interference of general medication. GP referrals could be made to ascertain whether a general medication could be the source of the altered mental health change.

Psychotherapy and Pharmacogenetics

“In current clinical practice, little account is taken of pharmacogenetics and failure of standard therapies is therefore quite common.”²

Psychotherapists need to take into account the relatively unknown psychological side effects of medication, especially of psychotropic medication. These are likely to be different for each patient depending on his/her different drug - gene interactions, namely - **pharmacogenetics**.

Pharmacogenetics relates to the ability or inability of the patient to metabolise a particular drug. An inability to metabolise increases the likelihood of side effects.

Psychological functioning can be influenced by pharmacogenetics and therefore can affect the therapeutic relationship and outcome.

Psychotherapy and Pharmacogenetics

Psychoactive Medications can Impair Judgement and Skills:

SSRI medication requires efficient **CYP 2D6** and **CYP 2C19** pathways for effective metabolism. Inefficient pathways for SSRIs may cause patients to experience the following psychological side effect symptoms:

Mania/impulsive behaviour	Suicidality
Psychosis	Drowsiness or somnolence
Schizophrenia	Apathy and extreme fatigue
Violence and aggression	Vivid or strange dreams
Mood disorders	Dizziness
Depression	Altered personality
Panic attacks	Confusion/memory impairment
Anxiety	Akathisia - inner restlessness

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Psychotherapy and Medication

The Negative Impact of Psychiatric Medication on Psychotherapy

“All effective biopsychiatric interventions work by causing generalised brain dysfunction affecting both emotional and cognitive functions”⁴

“ Bio psychiatric treatments produce their “therapeutic” effect by impairing higher human functions, including emotional responsiveness, social sensitivity, self-awareness or self insight, autonomy, and self – determination. More drastic effects include apathy, euphoria, and lobotomy-like indifference.”⁴

In other words: All biopsychiatric drugs have side effects by virtue of their working action. These side effects vary in severity dependent on the ability of the patient to metabolise the drugs.

Psychotherapy and Medication

“Spellbinding or Intoxication Anosognosia”

Anosognosia is defined as “the capacity of brain damage to cause denial of lost function.”⁵

Psychotropic medication may incur anosognosia or spellbinding, which results in some people failing “to perceive they are acting in an irrational, uncharacteristic, and dangerous manner and may become deeply mired in trouble before grasping what they are doing to themselves and to others.”⁴

“...the failure to recognise the harmful mental effects of psychoactive agents and the accompanying tendency to over estimate their positive mental effects”,⁴ is likely to have a negative impact on the therapeutic relationship.

Psychotherapy and Medication

Medications Designed to Treat Depression

"Recurrent depression is extremely common, with 50% of sufferers having more than one episode. After the second and third episode, the risk of relapse rises even higher to 70% and then 90%."⁶

Furthermore vulnerability to recurrent depression has been linked with antidepressant medication.⁷ Many studies over a 30-year research period using the Acute Tryptophan Depletion Test⁸ have “demonstrated that - **serotonin drugs create a lasting vulnerability to depressed mood via the serotonin system.**”⁹

After six months of antidepressant treatment, the drugs "generally fail to protect" against a return of depressive symptoms.¹⁰ In short, maintenance treatment is ineffective, compared to placebo.

SSRI medications inevitably will cause depletion of serotonin, thus depression returns. This relapse is **Iatrogenic**.

Psychotherapy and Medication

Medication Induced Emotional Blunting

“A barrier as the true self is not accessible.”

(Practicing Psychotherapist)

Any psychoactive medication can impair personal judgement or skills.

Antidepressants tend to blunt feelings in order to enable people to continue with day-to-day life and work. However emotionally blunted feelings may not be conducive to the success of those therapies where feelings are an important part of the therapeutic process for personality development and positive outcome.

This blunting could impede the progress of therapy and potentially leave clients with unresolved issues for many years.

Psychotherapy and Medication

Psychotherapy and Exposure to Antidepressants

The psychological side effects of SSRIs can include acts of disinhibition, obsessive thoughts, acts of violence and mania.¹¹

The potential for induced suicidality is very real. Without knowledge of psychological side effects, psychotherapy practitioners may have difficulty in differentiating between suicidality as a result of psychological trauma and **SSRI** medication induced suicidality.

Overall the impact of SSRIs on the brain can cause:

- Interruption of psychotherapy continuity due to mania and suicidality resulting in hospital admission.
- Extended psychotherapy due to impairment of higher human functions.
- Therapy can be nullified due to the ‘real’ person being masked by medication.
- No amount of therapy will alter the negative mental changes incurred with antidepressants.

Psychotherapy and Medication

Medication Withdrawal/Discontinuation

A patient may be going through *antidepressant* withdrawal symptoms at time of therapy, even after one missed dose if the antidepressant has a short half-life. e.g. Venlafaxine/Effexor.¹²

Psychiatric Symptoms of SSRI discontinuation:

Anxiety	Irritability
Crying spells	Mood lability
Insomnia	Vivid dreams ^{13&14}

These are the **psychological symptoms** of SSRI withdrawal.

“Withdrawal from medications and substances, including alcohol and tranquilizers, may trigger nightmares.¹⁵

Psychotherapy and Medication

Medication and Withdrawal/Discontinuation

Possible Signs of Withdrawal Syndrome include:

- * INSOMNIA
- * FEELING LOW
- * HEADACHES
- * NIGHT MARES
- * DEPRESSION
- * EUPHORIA
- * AMNESIA
- * MOOD CHANGES
- * CONFUSION
- * DISTURBED SLEEP
- * HALLUCINATIONS
- * THOUGHTS OF SUICIDE
- * MALAISE
- * LOSS OF LIBIDO

A decline and more serious states of:

- * MANIA
- * AGGRESSIVE BEHAVIOUR
- * PSYCHOSIS
- * SUICIDAL THOUGHTS¹⁶

N.B. All these signs are replicated in drug intolerance.

Psychotherapy and Medication

Medication and Withdrawal/Discontinuation

Withdrawal/discontinuation¹⁴ can cause severe psychological changes that can affect the ability of clients to communicate and impede the psychotherapist's therapeutic progress.

Whilst every **IAPT** session includes measuring scales to assess progress, symptoms of withdrawal/discontinuation could be attributed to worsening of the underlying depression condition.

IAPT does not alert psychotherapists to antidepressant withdrawal effects and are unaware of the many difficult psychological and physical experiences¹⁷ that some people encounter.

Psychotherapy and Medication

Medication and Withdrawal/Discontinuation Symptoms

During withdrawal, either one of two things could happen:

- If the therapist is **unaware** of withdrawal effects the therapist will potentially refer back to the GP for medication assessment or referral to secondary services.
- Even when the therapist **IS** aware of the withdrawal difficulties, the therapeutic process is likely to be compromised.

Psychotherapy and Medication

Many people who take SSRIs are likely to:

- Continue with life long prescribing due to dependency
- Experience **iatrogenic** recurrent depression
- Require on going secondary care needed to address the psychological harm incurred by SSRI induced mania and psychosis.
- Two-thirds will suffer "residual symptoms," with "anxiety, insomnia, fatigue, cognitive impairment, and irritability being the most commonly reported."^{10&18}
- Develop permanent structural brain changes¹⁹ due to long term prescribing of SSRI medication.

Psychotherapy and Medication

Early Warning Signs of Medication Intolerance

“A number of medications also are known to contribute to nightmare frequency. Drugs that act on chemicals in the brain, such as antidepressants and narcotics, are often associated with nightmares. Non-psychological medications, including some blood pressure medications, can also cause nightmares in adults.”¹⁵

Nightmares and disturbed sleep, which coincide with the introduction of a new medication, are potentially **warning signs** of intolerance/inability to metabolise the medication. If this situation is not addressed, it could lead to a severe deterioration in mental health.

A discussion with the doctor with the aim of careful and gradual tapering of the medication with full awareness by both doctor and the patient of likely withdrawal effects is suggested to avoid further distress to the patient.

Information Available to Professionals and Patients about Medication Information Provided by NICE

NICE provides only limited information about adverse reactions of medication, in particular psychological side effects because research is sourced from drug companies. There is a conflict of interests.

NICE excludes relevant up-to-date medication knowledge sourced from epidemiology studies, which provide details of adverse long-term consequences of **SSRI** medication.

NICE excludes details of mania and psychosis adverse reactions resulting from antidepressant medication.

NICE omits completely the issue of individual drug responses, i.e. whether a person can metabolise **SSRIs** or not in relation with side effects.²⁰

Information Available to Professionals and Patients about Medication

IAPT is obliged to be in line with **NICE** and sources medication knowledge from **NICE**. However, it appears that any proposed **IAPT** Medication Guide may not give appropriate information in respect of the full potential range of psychological adverse effects arising from **SSRI** and other antidepressant adverse effects.¹⁷

Again **NICE** offers minimal advice for **IAPT** therapists working with patients who may be taking medications.

An up to date compilation of antidepressant psychological side effects can be found in:

**Professional Mental Health Information Series:
ANTIDEPRESSANT ADVERSE REACTIONS.²¹**

Information Available to Professionals and Patients about Medication

In the New Ways Working in Mental Health, the DH states that “Medication Management is everybody’s business”²² and includes health and social care practitioners.

It does not suggest that medication issues are only in the domain of GPs. All psychotherapists and psychologists need to take responsibility in ensuring medication is their business.

Pharmacogenetics and Patient Information

Patient Information Leaflet (PIL) and ‘side effects’

Pharmaceutical companies prepare the Patient Information Leaflet which is included in the packaging of all prescribed medication. These leaflets along with other information, itemise the potential side effects of the medication.

However the PIL fails to include pharmacogenetic information (the genetic breakdown of the medication), which would allow patients who are Poor / Intermediate Metabolisers to have a greater understanding of why such patients are likely to experience side effects more than others: the reason being that this group of patients are unable to metabolise medication efficiently.

Pharmacogenetics and Patient Information

Psychological Changes Described as Mood Changes.

Mood changes and confusion are listed as side effects with some general and psychiatric medications in Patient UK website.²³

For example:

Anti-malarial - Mefloquine

Proton Pump Inhibitor for stomach ulcers - Lansoprazole

Antidepressant - Fluoxetine/Prozac

Mood changes are invariably placed towards the end of Patient Information Leaflets, thus the importance of psychological side effects in comparison with physical side effects is minimised.

Additionally 'Mood changes' does not describe the intensity of the severe mental health changes experienced by people who are Poor and Intermediate Metabolisers being *unable to breakdown and metabolise these medications efficiently*.

Pharmacogenetics and Professional Information

How Medication Side Effects are Sourced

NICE sources common medication side effects from the British National Formulary (BNF), which directly obtains its information from the **Summaries of Product Characteristics** (SmPCs) written by pharmaceutical companies.

The SmPCs do provide information on drug dosages, contraindications, side effects, the body's internal pathways that break down each medication and the occasional reference to Poor / Intermediate Metabolisers. However, there is no reference to PM/IM Metabolisers in connection with side effects.

Therefore the BNF does not provide pharmacogenetic information linking Adverse Reactions, known as 'side effects', with the inability to breakdown and metabolise medications efficiently.

Pharmacogenetics and Informed Consent

Pharmacogenetics has not been part of the British Medical School (BMS) curriculum. Therefore the vast majority of doctors practising in the NHS are unable to share pharmacogenetic awareness in Multi-disciplinary Team meetings for delivering best treatment options for patients.

Following the General Medical Council decision to include **pharmacogenetics** in the BMS Foundation Course, genetic susceptibility to adverse drug reactions may become better known within Foundation Trusts and Primary Care Teams. This genetic knowledge is essential to move towards ensuring patients' safety throughout all cultures.

Pharmacogenetics and Informed Consent

However the pharmacogenetic module within the postgraduate Foundation Course is optional and as such many doctors will continue to graduate and treat patients without knowledge of the connection genetic susceptibility and adverse drug reactions.

The situation is further compounded because pharmacogenetics is **not** included in current **DH**, **NICE** and **IAPT** documentations, PIL or Choice & Medication.

Meanwhile many pharmacogenetic naive GP's will inadvertently and unknowingly collude with antidepressants ADR/iatrogenic conditions; – potentially, the patient is likely to be blamed and be referred higher up **IAPT**/ **NICE** steps and given another DSM diagnostic label.

Pharmacogenetics and Informed Consent

Fully Informed Consent

There is apparently a lack of transparency from the DH about medication adverse effects, leading to patients not being able to give meaningful and informed consent prior to embarking upon medication treatment.

Along with the potential side effects of taking medication, therapists, clients and carers need to think seriously about alternatives to medication and options such as such as non medicated psychotherapy and counselling.

In addition prior to coming to an informed consent there is a need for all to be aware, there is a possibility antidepressant medications may cause iatrogenic psychological changes or hallucinations and suicidal ideas.²⁴

Pharmacogenetics and Additional Information

There are other metabolising systems that have an infinite number of genetic variations that all effect the individual's metabolising process and reaction to various medications:

P-glycoproteins²⁵ (P-gp's)

U-glucuronisil transferases²⁵ (UGTs)

Serotonin Transporter Gene²⁶ (SERT)

Dopamine Transporter Gene²⁷ (DAT)

These are some of the many other factors that impede a person from efficiently metabolising drugs.

Pharmacogenetics and Additional Information

A simple Genotyping Test to help avoid Adverse Drug Reactions according to genotype/metaboliser status and resultant recommended drug doses is available privately from:

- **Genelex (USA)**

www.genelex.com

<http://www.healthanddna.com/drug-safety-dna-testing/dna-drug-reaction-testing.html>

A doctor's permission is not required and the results are sent directly to the patient.

For information on Medications:



electronic Medicines Compendium (eMC)

<http://www.medicines.org.uk/emc>



Patient UK

*Comprehensive health information
as provided by GPs and nurses to
patients during consultations*

www.patient.co.uk

<http://www.patient.co.uk/display/16777227/>

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A guide for service users, carers and health and social care practitioners

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