

**Mental illness and prescription medication:
Implications for offending behaviour**

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Limitations of expertise

As psychologists we claim expertise only in matters of human behaviour and cognition. We are required to be informed on the effects of psychoactive medication and implications for human behaviour and cognition from its use. We do not claim competence beyond this, particularly on: sentencing and other legal matters, prescribing or other medical or pharmaceutical matters.

ABSTRACT

Medications used "as directed" for mental and physical illnesses have side effects that in combination can have tragic outcomes. Everyday medications, such as antidepressants, analgesics, and sleeping tablets, in the quantities commonly prescribed by doctors can induce dependence and withdrawal syndromes, particularly if used over long periods. All of these medications may induce drowsiness, confusion, and can have psychotic side-effects in withdrawal, or when used "off and on", as many individuals do.

Side-effects of antidepressant medications can be experienced immediately while the intended effect can be delayed for two weeks. This means that when depressed individuals commence antidepressants they are particularly vulnerable to the side-effects of confusion, poor memory, impaired decision making from the medication as well as the confusion, poor memory, and impaired decision making ability that accompanies depression. In time, the depression is alleviated somewhat and the side-effects are less problematic for most but certainly not all patients.

Due to metabolic changes associated with aging, older patients may absorb these medications differently to younger people affecting the duration and severity of known side effects or the onset of the intended effect. Moreover, individuals with physical illnesses may also absorb medications differently to well patients. These issues are further complicated if the patient is taking other medications that interact with the psychoactive medication as is commonly the case with older or physically ill people.

So, there are two danger periods when individuals taking antidepressants may be at increased risk of offending: During initiating, withdrawing or changing dose; and if long-

term medications are not reviewed regularly when patients age or become physically ill. Although forensic psychologists, psychiatrists and medical practitioners are able to report on offenders' mental and physical illnesses and treatment options, they are not experts on side-effects of medications. Judges and magistrates may benefit from obtaining medication reviews from forensic pharmacists to assist sentencing decisions.

Introduction

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. Depression occurs in both men and women regardless of age and background. The condition can become chronic or recurrent and lead to substantial impairments in affected individuals' capacities to take care of their everyday responsibilities. At its worst, depression can lead to suicide, a tragic fatality associated with the loss of more than a million lives worldwide every year (World Health Organization, 2008).

Prevalence of Depression

Depression is the leading cause of disability worldwide as measured by Years Lived in Disability (YLDs) and the fourth leading contributor to the global burden of disease as measured by Disability Adjusted Life Years (DALYs). By the year 2020, depression is projected to reach second place of the ranking of DALYs, calculated for all ages and both sexes. Today, depression is already the second cause of DALYs in the age category 15-44 years for both sexes combined (Mathers & Loncar, 2006).

Using Comprehensive International Diagnostic Interview, Version 2.1 (World Health Organization, 1997), community surveys of the prevalence of depression amongst Australians show that approximately 20% of the population has experienced symptoms of clinical depression during their lifetime and approximately 6% meet criteria for a depressive illness in a twelve months period (Australian Bureau of Statistics, 2006). In 2003, the Australian suicide rates per 100,000 were 17.1 for men and 4.7 for women. (World Health Organization, 2008)

Butler & Allnutt (2003) also used Comprehensive International Diagnostic Interview, Version 2.1 (World Health Organization, 1997) in their survey of the mental health of NSW inmates. For the offender population, the lifetime risk for depressive illness is more than four times that of the community: 87.8% of offenders in NSW have met criteria for clinical depression at some stage in their lives. The odds are even greater for a depressive illness in the preceding 12 months for offenders in custody (five-fold risk) and unsentenced offenders (nine-fold risk) compared to community samples. Butler & Allnutt (2003) found that 32.8% of sentenced offenders and 55% of unsentenced offenders met criteria for a depressive illness during the year prior to interview.

Use of antidepressants in the Australian population

The use of antidepressant medication has increased substantially since the introduction of the newer forms such as selective serotonin reuptake inhibitors (SSRI). These have a lower toxicity in overdose compared to the earlier tricyclic antidepressant (TCA)

medications. The rapid uptake of the SSRIs was accompanied by a decrease of only 35% in prescribing TCAs, suggesting that individuals with milder forms of depression were now being offered a pharmacological intervention for their depression rather than SSRIs completely replacing TCAs (Mant et al, 2004). Since 1991, there has been both a reduction in suicide rates and an increase in antidepressant use by older adults in Australia. This suggests that the greater readiness of doctors to prescribe SSRIs may have contributed to a reduction in depression and suicide for this segment of the population (Hall et al, 2003).

Depression as a defence or mitigating circumstance

Under section 23A of the Crimes Act (1900), a plea of manslaughter rather than murder may be accepted for persons committing a crime while suffering substantial impairment of their capacity due to an abnormality of mind arising from an underlying condition, including a major depressive illness.

In the case of *R v Daniella Dawes* (2004), an appeal by the Crown against a five year bond imposed for the manslaughter of her 10 year old autistic son was dismissed. Three psychiatrists attested that she was severely depressed at the time of the offence and not capable of thinking clearly and her GP confirmed that her depression had worsened despite taking antidepressant medication.

Homicide & Suicide by NSW Mental Health Patients

In the “Tracking Tragedy” reports, the systemic review of homicides and suicides by mental health patients, the NSW Mental Health Sentinel Events Review Committee (2007) found that all cases had been receiving antidepressant medication but follow up for symptoms and side-effects was inadequate. In addition, fewer than half had been offered psychological interventions. The committee was critical of the inadequacy of assessment, diagnosis and care for some court referrals for a psychiatric report, including cases discharged from inpatient wards for “malingering”. The committee also commented on the inadequate liaison between health staff, police, and community offender services staff, where, in hindsight, confidentiality issues had restricted the sharing of important information.

One of the cases quoted in the third “Tracking Tragedy” report describes a woman who killed her six-month-old baby and attempted suicide. She had been identified as being at risk of post-natal depression and discharged to the care of her general practitioner. She had contacted the Child & Family team by phone three days before the tragedy stating that she was okay. At the time of the offence, she was found in an agitated psychotic depression with her dead baby.

The committee noted the recent publication of information linking an increased risk of suicide and homicide for some individuals commencing antidepressant medication. However, their sample size is too small, as yet, for meaningful comment on this issue.

FDA label change for antidepressant medication

In 2007, the United States Food and Drug Administration (FDA) strengthened black box warnings for antidepressants. Warnings concerning the pediatric use of antidepressant medications had already been issued in 2004. In 2007 the FDA noted the increased risk,

compared to placebo, of suicidal behaviour for young adults and adolescents as well as children taking antidepressant medication, including SSRIs. This warning recommends that all patients treated with antidepressants be monitored for unusual changes in behaviour, particularly during the initial few months and when decreasing or increasing dose.

Furthermore, family and care-givers are advised to be alert for the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behaviour, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down.. Families and caregivers of patients are advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt.

How Do Antidepressants Work?

Clinical studies consistently identify changes in prefrontal cortex, hippocampus and amygdala that may be related to the course of a depressive illness and may be prevented with successful treatment. However, it is no longer generally accepted that antidepressants “rebalance” brain biochemistry, nor that they work in the same way in all individuals. As the neurobiology of mood disorders and the mechanisms of action of antidepressant drugs continue to be clarified, there has been a shift in emphasis from changes in neurotransmitter release and metabolism to regulation of gene expression (Lesch & Schmitt, 2002).

The effect of antidepressant treatments on the function of transcription factors that regulate expression of several genes involved in neuroplasticity, cell survival, and cognition, has been extensively studied. Although there is general agreement that antidepressants stimulate a number of major pathways, conflicting results suggest that different effects may depend on drug type, drug dosage, as well as the genetic make-up of the individual (Tardito et al, 2006).

Neurons, neurotransmitters and receptor types

Neurons have specialized projections called dendrites and axons. Dendrites bring information to the cell body and axons take information away from the cell body. Neurotransmitters are made in the cell body of the neuron and then transported to the axon terminal to be stored in vesicles until required. For communication between neurons to occur, an electrical impulse must travel down an axon to the synaptic terminal. At the synaptic terminal, an electrical impulse will trigger the migration of vesicles containing molecules of neurotransmitters toward the pre-synaptic membrane. The vesicle membrane will fuse with the pre-synaptic membrane releasing the neurotransmitters into the synaptic cleft. When neurotransmitter molecules diffuse across the synaptic cleft they can bind with receptor sites on the postsynaptic ending to influence the electrical response in the postsynaptic neuron. Neurotransmitters will bind only to specific receptors on the postsynaptic membrane that recognize them (Kandel et al, 2000).

When a neurotransmitter binds to a receptor on the postsynaptic side of the synapse, it changes the postsynaptic cell's excitability: it makes the postsynaptic cell either more or less likely to fire an action potential. If the number of excitatory postsynaptic events is large enough, they will add together to cause an action potential in the postsynaptic cell and a continuation of the "message." Many psychoactive drugs, including antidepressants, change the properties of neurotransmitter release, neurotransmitter reuptake and the availability of receptor binding sites (Sulzer, et al, 2005).

Upon landing at the receptor site of a neuron, the chemical message of the neurotransmitter may either be changed into an electrical impulse and continue on its way through the next neuron, or it may stop where it is. In either case the neurotransmitter releases from the receptor site and floats back into the synapse. It is then removed from the synapse in one of two ways. The neurotransmitter may be broken down by a chemical called monoamine oxidase, or it may be taken back in by the neuron that originally released it, that is, reuptake by the neuron (Kandel et al, 2000).

Based on their structural and functional characteristics, neurotransmitter receptors can be classified into two broad categories: metabotropic and ionotropic receptors. In contrast to the latter, metabotropic receptors do not form an ion channel pore; rather, they are indirectly linked with ion-channels on the plasma membrane of the cell through signal transduction mechanisms. Metabotropic receptors have neurotransmitters as ligands that, when bound to the receptors, initiate cascades that can lead to channel-opening or other cellular effects. Since opening channels by metabotropic receptors involves activating a number of molecules in turn, channels associated with these receptors take longer to open than ionotropic receptors do, and they are thus not involved in mechanisms that require quick responses (Kandel et al., 2000, p. 240). Moreover, metabotropic receptors remain open from seconds to minutes (Kandel et al., 2000, p. 250-251). Thus they have a much longer-lasting effect than ionotropic receptors, which open quickly but only remain open for a few milliseconds (Austin, 2004).

While ionotropic channels have an effect only in the immediate region of the receptor, the effects of metabotropic receptors can be more widespread through the cell. The metabotropic class of receptors includes most serotonin receptors, as well as receptors for norepinephrine, epinephrine, histamine, dopamine, the metabotropic glutamate receptors, muscarinic acetylcholine receptors, GABA_B receptors, and neuropeptides (Austin, 2004).

Functions of neurotransmitters implicated in depression

Of the 30 or so neurotransmitters that have been identified, researchers have discovered associations between clinical depression and the function of three primary ones: serotonin, norepinephrine, and dopamine. These three neurotransmitters function within structures of the brain that regulate emotions, reactions to stress, and the physical drives of sleep, appetite, and sexuality. Structures that have received a great deal of attention from depression researchers include the limbic system and hypothalamus (Nestler, et al, 2002).

Dopamine (DA) Functions

Projections from the substantia nigra, midbrain, and hypothalamus to the basal ganglia, nucleus accumbens, limbic cortex, and pituitary gland can produce many behavioural and psychological effects when the dopamine system is activated. In addition to elevated mood, these projections can produce a number of effects including: visual and sexual problems; movement disorders, eg, tardive dyskinesia; delusions, hallucinations and symptoms of schizophrenia. The effect of dopamine on the reward system underlies the recreational use and potential for abuse of alcohol and other drugs (Koob, et al, 2004).

Serotonin (5HT) Functions

The serotonin system has projections from the raphe nuclei to the frontal cortex, basal ganglia, limbic cortex, hypothalamus, brainstem and spinal cord. In addition to mood regulation, there can be problems with akathisia, agitation, anxiety, panic, eating disorders, insomnia, nausea, sexual response, constipation and diarrhea. However, serotonin tends not to activate the reward centres, making this system a safer target for antidepressants in terms of the risk of abuse or recreational use (Nemeroff & Schatzberg, 2002).

Norepinephrine (NE) Functions

Projections from the locus coeruleus to frontal cortex (β_1 & α_2 sites), limbic cortex, and cerebellum, brain stem & peripheral nervous system produces a number of behavioural and psychological effects when the norepinephrine system is activated. Problems include depressed mood, emotional lability, fatigue, psychomotor agitation or retardation, tremor, and difficulties in attention, concentration, and working memory. There can also be adverse effects on blood pressure, heart rate, bladder control. Some of the newer antidepressants attempt to selectively target the norepinephrine system in addition to serotonin system (Nemeroff & Schatzberg, 2002).

Side effects from undesired neurotransmitter activation

Although the newer antidepressants attempt to reduce their side-effect profile by selectively targeting only the serotonin and/or norepinephrine systems, the selection is only relative to the older tricyclic and monoamine oxidase inhibitor medications. Moreover, with the action of antidepressant medications being mediated by gene expression, there is the likelihood of idiopathic side-effects from other neurotransmitters. Commonly, non-target neurotransmitters can produce problems in judgement, memory, and muscular control, among others (Albert, P, 2004; Nemeroff & Schatzberg, 2002).

Akathisia

Akathisia is a combined state of stimulation and depression with a high risk of suicide and violent behaviour. There is a stimulant continuum from milder forms presenting with insomnia, nervousness, anxiety, hyperactivity and irritability, through to severe agitation, restlessness and aggression. Extreme forms of akathisia can include disinhibition, grandiosity, and out-of-control aggressive behaviour.

According to Diagnostic and Statistical Manual of Mental Disorders 4th Edition – Text Revision (DSM IV-TR), serotonin-specific reuptake inhibitor antidepressant medications may produce an akathisia that appears to be identical in phenomenology and treatment response to the better-known neuroleptic-induced acute akathisia. The suggested

diagnosis in this case is medication-induced movement disorder not otherwise specified (American Psychiatric Association, 2000, p801).

Medication Akathisia

Numerous psychiatric medications have been reported to induce akathisia and it is increasingly being identified in patients treated with antidepressants. Estimates suggest that antidepressants may produce akathisia in 1-3% of cases (Moyazani & Ramon, 2004, p634), as well as the self-destructive and aggressive impulses often seen with akathisia (Muller-Oerlinghausen & Berghofer, 1999). Of the antidepressants, the selective serotonin reuptake inhibitors (SSRIs) are more commonly associated with akathisia than are the traditional tricyclic antidepressants (TCAs) and all of the SSRIs have been reported to induce akathisia (Gill et al, 1997).

Many medications, including all antidepressants, are metabolized by the P450 cytochrome system, which requires more than 1000 enzymes produced by approximately 50 genes. Individual differences in genetic structure, age and metabolism can compromise this system and result in undesirable side-effects including akathisia (Tanaka & Hisawa, 1999).

There are multiple factors that have been postulated to increase an individual's risk of developing akathisia: infection with HIV; the concomitant use of antidepressants and neuroleptics; a past history of treatment with a high-potency conventional antipsychotic agent; or a history of organic brain disease (Jauss et al, 1998). It has also been reported that akathisia occurs more commonly in middle-aged female patients (Janicek et al, 2001; Kaplan & Saddock, 2003).

Serotonin Syndrome and Motiveless Crime

In the extreme, serotonin-induced akathisia produces very disoriented and disorganized behaviour. Crimes committed by affected persons reflect this high degree of disorganization and disorientation: The victim is non-threatening, closely located and engaged without premeditated plotting. The crime appears to be without obvious motive and the perpetrator continues confused until the medication is completely metabolized, returning to normal functioning if no further medication is consumed. Serotonin syndrome may be distinguished from mania by this return to normal function when the medication is used up by the system (Moyazani & Ramon, 2004, p634).

Involuntary Intoxication by Antidepressant Medication as a Defence

USA: Pharmaceutical Company Held Liable In a Murder-Suicide

In 2001, a US federal jury ordered SmithKline Beecham (now GlaxoSmithKline) to pay \$US6.4 million to relatives of Donald Schell. Aged 60 years, he had been taking Paxil for just 48 hours when he shot and killed his wife, his daughter, his granddaughter and himself. Before taking Paxil, he had been on other antidepressants including Prozac. There seemed to be no other motivation for the murder-suicide: He had no obvious marital problems and clearly adored his daughter and granddaughter (Thompson, 2001).

UK: Charges dropped for armed robber withdrawing from paroxetine

In November 2002, two days after coming paroxetine, Douglas-Hamilton, 30, used a pair of wire cutters to hold up a garage, walking away with only a packet of cigarettes. A CCTV recording of the event shows his bizarre behaviour, where he joked with customers. Two weeks later, he stole some CDs from a record shop. Douglas-Hamilton admits the offences, but claims his personality and behaviour were completely altered by the withdrawal effects of the drug. "It seemed to destroy my conscience and my fear. I found myself walking out of the house with knives; I had every intention of killing people" (Revelli, 2003).

USA: Non-custodial sentence for embezzler using antidepressant

Studies show that Paxil can cause people with bipolar disorder to behave in bizarre, arrogant and uncontrollable ways. Stewart, who had been recently diagnosed with bipolar disorder, had been taking Paxil during the two-year period that he methodically stole \$US1.8-million from ex-employer Jabil Circuit. U.S. District Court Judge James Moody Jr said that that he believed Stewart's claim that he was not wholly responsible for his crime and that it served no one's interest to send the father of two young girls and an older stepdaughter to prison. Stewart was sentenced to 12 months of home confinement and five years' probation (Barancik, 2006).

Australian Examples

After commencing Zoloft, David Hawkins, 76, "snapped and strangled" his 70 year old wife. Justice O'Keefe found him not guilty of murder but rather manslaughter (Bowden, 2001).

Prescribed antidepressants, Merrilee Bentley was charged with attempted murder (with attempted suicide) of her young daughters. Police were not notified by the hospital until two weeks after she admitted herself for psychiatric treatment. She received a two-year suspended sentence (ABC News, 2003).

A 53 year old depressed mother, Therese Henry-Erlandson, set fire to her Brisbane house in 2006. At the time of the offence she was taking high dosage antidepressants and was agitated and suicidal. Judge Noud sentenced her to a three year term and released her immediately to parole based on psychiatric reports (Kellet, 2007).

After taking a double dose of her antidepressant medication, a Gosford woman drowned her son in her arms in the bath. Justice Elizabeth Fullerton found that by reason of mental illness the woman's capacity to think rationally on that day was temporarily suspended. She was acquitted without criminal conviction (Cooke, 2007).

Conclusion

Newer forms of antidepressant medication have significantly improved the quality of life and reduced suicides for millions of people world-wide. A small proportion of individuals are genetically predisposed to react catastrophically to even low doses of some medications, including the newer antidepressants. Side-effects are most severe when initiating, withdrawing, or changing dose level either up or down. Age, health and interaction with other medications and substances can be a factor in the severity of side-effects. Courts considering the possibility of a defendant's behaviour having been influenced by an antidepressant or other prescription medication may find a forensic

pharmacist report helpful.

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