Submission No 11

REVIEW OF INQUIRY INTO COMPLAINTS HANDLING IN NSW HEALTH

Organisation: Forensic & Medico-Legal Psychiatry, Akathisia Clinic

Name: Dr Yolande Lucire

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Date Received: 11/07/2006

Subject:

Summary

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July 6, 2006

The Director
General Purpose Standing Committee No. 2
Legislative Council,
Parliament House,
Macquarie Street,

SYDNEY NSW 2000.

7 July 2006

Submission in three parts to the Honourable Patricia Forsythe MLC, Committee Chair, General Purpose Standing Committee No. 2, Legislative Council,

Should you be interested in investigating this matter, I have placed detailed submissions regarding the complaints in envelopes together with this letter.

This report concerns how the Greater Southern Area Health Service (at the time the Greater Murray Area Health Service) has dealt with nearly 40 reports of suicides, dangerous suicide attempts, a homicide, a serotonin syndrome death and many episodes of violence and psychosis due to how certain drugs were prescribed and co-prescribed by certain practitioners. These reports were made initially in 2002 but mostly from September 2004 to April 2005 and again from September 2005 to December 2006.

This is a pattern of cover-up of repeated acts, which caused serious adverse events including deaths.

THIS ISSUE:

After the Senate Inquiry into Mental Health (and others) had found a huge increase in mental health presentations as and in suicide of patients under mental health care, a spokesman for the Department of Human Services in Victoria that any ‘apparent increase in suicide among persons under mental health care has to be offset against the rising numbers using the service.’ I have has similar reasoning put to me in NSW as well.

However the increase in persons using services and the suicides have a common cause, which is the new drugs which have suicide induction, akathisia and psychosis among their listed and well reported side effects. Each completed suicide represents 10 to 20 unsuccessful attempts, all of which increase pressure on beds.

The factors that lead to suicide from antidepressant neurotoxicity are known, and were elucidated in 1990, by psychiatrist and akathisia expert, Martin Teicher and I have put them in the footnote.[1] They are much the same for new antipsychotics which are serotonin boosting as well. These side effects account for the increasing pressure on mental health beds by people needing care, the increase in suicides and attempts as reported in Tracking Tragedy, and elsewhere the report of the Sentinel Events Committee and the Department's own statistics as well the hugely increased death rate among those treated for schizophrenia.

New generation antidepressants and antipsychotics are toxic for some genetically polymorphic persons who do not have the metabolism to deal with them. Some individuals become suicidal, aggressive, homicidal, psychotic and delirious on these drugs. This problem I am bringing to you is the systematic refusal of an administration to accept my knowledge of these matters I report on a situation where the area health service staffed by very junior psychiatrists declined to listen to me and suicide attempts and deaths continued and still continue, which I m subjected to vilification and disregards.

The only way we have in Australia to identify the vulnerable and to protect them is by taking a good medication response history and watching and warning, titrating doses very carefully. Pharmacogenetic testing is available and used in the United States. The evidence for this is secure and this problem is well researched, and subject to United States Food and Drug Administration Public Health Advisories as well as Adverse Drug Reactions Committee (ADRAC) Bulletins.[2]

This information is contained in prescriber information and basic textbooks. The outcome of giving antidepressants to a large population of about a million Australians has resulted in their well-known side effects becoming epidemic.

I have put the worst ones into an appeal for the re-evaluation of my report by the HCCC in a letter to the Ombudsman and Mr Dix of the Medial Board. The Area dismissed all of them so I had to go beyond to the HCCC.

My complaints go unanswered or rejected in groups.

In summary:

1. I lodged thirty-five complaints about serious adverse events about two doctors and they have been dismissed and not properly investigated.
2. These complaints concern how certain drugs were used, without interviewing patients, without examining their mental state, without being mindful of listed side effects, without warning or monitoring or

and in a way entirely inconsistent with their prescriber information and relevant advisories.

3. As far as I am aware, four suicide deaths that should have been investigated by root cause analysis have not been investigated properly by any of the Area Health Service, the Department of Health, the HCCC or drawn to the attention of the Minister.
4. Twenty or more suicide attempts of varying dangerousness (three by inpatients) have not been subjected to root cause analysis.
5. A dozen patients became psychotic and violent on serotonin boosting antidepressants having never been like that before.
6. Other patients had their lives destroyed by being given antidepressants, for trivial purposes and these drugs caused chronic akathisia for up to ten years. These patients have been ignored and have received no frank and full apology. One recently committed suicide after he had been denied care in February of 2005.
7. I now know that certain persons were threatened with reprisal if they dealt with my correspondence and undertook the procedures that the Department of Health advised in the case of medical error and repeated serious adverse outcomes. I have been threatened with being reported to ICAC if I continued my alleged 'harassment' of a Director of Clinical Services who had ignored my reports, which, by that time, included four deaths. This threat should be investigated by ICAC.
8. My complaints have been ridiculed because there were so many. However one third of the admissions in 2003 and 2004 were for suicidal and homicidal thinking and acts. In the vast majority, it was General Practitioners who had prescribed these medicines as advised by drug companies to the effect that they were safe as sweets.
9. I was asked by the Director of Clinical Services, 'to desist from sending' any more academic information because, in his words, it was 'a terrible waste of paper'. He hoped I was not using hospital facilities to copy it. (I sent information packs to general practitioners whose patients had suffered from adverse drug events.)
10. I have been deemed to be 'not in the mainstream' by doctors whose education comes from drug companies alone, and who have no idea of either the nature or magnitude of the problem, which has more than doubled mental health presentations since 1992. These doctors seem to be not familiar with basic textbooks or prescriber information, as you see from my response to in the matter of XXX.
11. When I started to defend myself against complaints made about me and to make these reports, I had no idea that younger psychiatrists knew nothing of this problem. I now realise that lack of knowledge is

widespread (but not universal) and that some psychiatrists do not want to see it.

12. The HCCC was repeatedly provided with false and misleading information about events that simply had not happened and was used as a tool to harass me. One of the psychiatrists involved also has a well-documented involvement with advising the HCCC. The HCCC refused to act on my reports that the complaints were simply not true but subjected them to peer reviewers who judged me as if the events described had really taken place.
13. The HCCC has not examined the suicide deaths. As a consequence of their refusal to see this set of reports as a series, as evidence of a public health problem, the pattern, one that is obvious to an intelligent layman, cannot fully emerge.
14. I have been asked by the HCCC to get consent from aboriginal relatives of a patient who died from akathisia and Serotonin Syndrome but, of course, I have no access to this information. The HCCC threatens not to investigate this death unless I can provide this information. Yet it pursues patently false allegations about me.
15. The Administration repeatedly accused me of being the problem, 'a nuisance' because I complained, but ignored the prescribers who are still causing the suicide events and suicides continue.
16. One patient under my care died from causes which both police and coroners told em were unrelated to my treatment of him. Yet, having ignored all the suicide deaths the Director of Clinical Services called a 'root cause analysis on this death after I had left. This seemed to be yet another form of harassments of me, and an outrageous misuse of resources in the circumstances.

The cost of providing mental health services to misdiagnosed persons had been enormous.

I initially took this problem to be a product of local psychiatrists because that was where I was exposed to it. By mid 2004, I realised, on reading Tracking Tragedy, that the problem of pharmacological iatrogenesis of mental illness was more general in NSW, and of concern in the United States and UK as well as in Australia and this region. When I informed the Director of Clinical Services that this problem was wide spread, I was advised to leave work immediately and not to return until I provided a certificate from a psychiatrist to the effect that I was fit for work. Nurses and colleagues rallied and advised that there was nothing wrong with me, and I ignored the advice.

The Area received correct advice and prescribing guidelines from Dr. Andrew Campbell, who was sent by the Mental Health Unit of the Department of Health. His advice was entirely consistent with the advice I had been providing, as the United States Food and Drug Administration had been forced to disclose what had been revealed in legal actions. Dr Campbell's advice was that the US FDA

Public Health Advisories posted on March 22, 2004 on suicidal behaviours and other side effects of this group of drugs should be 'used as a template". These have been followed by Bulletins on the same topic from ADRAC.[3] These advisories have been updated to reflect true causation of suicide by antidepressants. For example, GlaxoSmithKline was forced to post on its website on May 5, 2006 that they always knew but did not reveal to prescribers the relative risk of suicide on Aropax (paroxetine) is six over sugar pills.) This means that persons periled Aropax are six time more likely to kill themselves than if left untreated and they suffer all the antecedents of suicide as well leading to admissions and chronic m iatrogenic mental illness.

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The worst of these side effects is akathisia,[4] which is associated with suicide attempts, violence and medication-induced psychotic states.

Every textbook I have read has a chapter on the side effects of antipsychotic medicines on some users, including akathisia.[5] For example, the commonly accessed *Wikipedia* encyclopaedia, which is a resource familiar to health care professionals, lawyers, suicidologists, laymen and patients.[6]:

> ***.... Akathisia may range in intensity from a mild sense of disquiet or anxiety (which may be easily overlooked) to a total inability to sit still with overwhelming anxiety and severe dysphoria (manifesting as an almost indescribable sense of terror and doom). In the most severe cases, dysphoria can be so severe that the patient is literally compelled to take action, leading, possibly, to suicide attempts. It is not unknown to have patients literally run out of a hospital or emergency room.***
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> ***... Akathisia is often misdiagnosed and can lead the patient to commit suicide in or outside the hospital.***
>
> ***... Treatment includes the discontinuation or reduction of dose of the causative agent and the use of typical or atypical antipsychotics (also called major tranquilizers) to reduce the agitation and anxiety. Unfortunately, these neuroleptics are often the cause of the condition and are known to cause irreversible akathisia in some cases. While the administration of these drugs may temporarily ameliorate the symptoms, there is a serious risk of worsening the condition over the longterm.***
>
> ***… Most of the clinical cases of akathisia can be prevented by not administering the drugs that cause the condition.***

Dr Campbell's recommendations were in every way the same as my practice and quite contrary to the practices of the complained about doctors.

The accused doctors ignored this advice and continued with dangerous prescribing, with failing to monitor or elicit side effects more people committed suicide, became suicidal and attempted suicide from these causes, the last a month ago.

It will be challenging for a certain psychiatrist to explain why the 'peer' reviewers who are supposed to be anonymous have made the same errors of fact, as did the psychiatrist behind the complaints.

If this kind of activity is allowed to go on without external input or intellectual integrity, there is little chance that emerging issues in psychiatry or medicine will be picked up and attended before a large number of people die or have their lives adversely affected by medicines what are unsuitable for them. Genetic testing to see if patients are able metabolise these drugs is available in the United States and the United Kingdom.

Yours sincerely,

Yolande Lucire
Consultant Psychiatrist.

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[1] Teicher, M.H., C.A. Glod and J.O. Cole, The emergence of fluoxetine-induced suicidality. Drug Safety, 1993. 8(3): p. 186-212. Although antidepressant medications represent the cornerstone of treatment for patients with moderate to severe clinical depression, they also carry serious risks.

There is evidence which suggests that antidepressants can, in some instances, induce or exacerbate suicidal tendencies. Nine clinical mechanisms have been proposed through which this may occur.

These are:

(a) energizing depressed patients to act on pre-existing suicidal ideation;

(b) paradoxically worsening depression;

(c) inducing akathisia with associated self-destructive or aggressive impulses;

(d) inducing panic attacks;

(e) switching patients into manic or mixed states;

(f) producing severe insomnia or interfering with sleep architecture;

(g) inducing an organic obsessional state;

(h) producing an organic personality disorder with borderline features; and

(i) exacerbating or inducing electroencephalogram (EEG) or other neurological disturbances.

Epidemiological and controlled studies also provide data on the association between antidepressant drugs and suicidal ideation, attempts and fatalities.

[2] **Suicidality with SSRIs: adults and children**

In 2004, ADRAC published a statement on the use of SSRI antidepressants* in children and adolescents, in view of evidence that use of these agents in these age

groups was associated with an increased risk of suicidality, including suicidal ideation, suicide attempts and self-harm events.1 SSRIs are not registered for the treatment of depression in those less than 18 years of age, and neither are any other antidepressants.

Recently, ADRAC conducted a review of the evidence of suicidal thoughts and behaviour associated with the use of SSRIs in adults. The Committee concluded that, in most adult patients, SSRIs in the treatment of depression are beneficial or cause no harm. However, it was noted that individual case reports, including some describing dechallenge and rechallenge, support an association between SSRI use and new onset suicidality.2,3 When this syndrome occurred it tended to develop soon after introduction of an SSRI, or an increase in the dose and to be associated with akathisia, agitation, nervousness and anxiety. The effect often persisted with continuing treatment. Similar symptoms can follow withdrawal of the SSRI.

Despite evidence of the infrequent occurrence of suicidal thoughts and behaviour with SSRIs, a recent large case control study by Jick et al found that prescription of fluoxetine or paroxetine, both SSRIs, was not associated with suicidal behaviour more frequently than prescription of the tricyclic antidepressant (TCA), dothiepin.4 Participants were all first-time users of antidepressants and individuals at high risk of suicidality were excluded.

The Jick study included 17 suicides, and these occurred much more frequently in the first 9 days after starting antidepressants than later in the treatment period. This increased risk of suicide early in therapy may occur because the antidepressant has not yet taken effect, because the medication was begun when the depression was at its worst, or because of an activation effect of the medication.

A meta-analysis of 702 randomised controlled trials found an association between treatment with an SSRI and suicide attempt when compared with placebo, but in common with the Jick study, when TCAs were the comparator no difference in frequency was found.5 There was no difference between SSRIs and placebo for fatal suicide attempts.

Increased prescribing of antidepressants in Australia during 1991-2000 was associated with decreasing suicide rates, with the trend being most apparent in older age groups.6 These results do not demonstrate a causal relationship, but the authors suggest the trend may be indicative of improved overall management of depression, including treatment at the primary care level, use of psychosocial intervention and prescribing of SSRIs (first available in the early 1990s). The SSRIs have brought many advantages, including once daily administration, lower rates of key adverse reactions, and safety in overdose.

Because of the risk of suicidal ideation and behaviour in both adults and children being treated for major depression and other psychiatric disorders, the TGA has recently required the sponsors of antidepressants, including the SSRIs, to update their Australian product information with appropriate warnings. The warnings provide the following advice:

- Worsening of depressive symptoms and emergence of suicidality may occur with treated or untreated depressive illness;
- Patients should be closely monitored for suicidality in the first weeks of treatment, and if there is a change in dose (up or down);
- Consideration should be given to changing or discontinuing therapy if worsening of symptoms persists or emergence of suicidality occurs with treatment;
- Patients and caregivers should be advised to monitor for worsening illness, suicidal or selfharm-related thoughts and behaviour and advised to seek medical assistance immediately should these occur.

* The SSRI antidepressants included are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline, and the related medicine, venlafaxine.

References

1 ADRAC. Use of SSRI antidepressants in children and adolescents. *Aust Adv Drug Reactions Bull* 2004;23:22.

2 Healy D, Whitaker C. Antidepressants and suicide: risk-benefit conundrums. *J Psychiatry Neurosci* 2003;28:331-7.

3 Breggin PR. Suicidality, violence and mania caused by selective serotonin reuptake inhibitors (SSRIs): a review and analysis. *Intern J Risk & Safety in Medicine* 2003/2004;16:31-49.

4 Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. *J Amer Med Assoc* 2004;292:338-43.

5 Fergusson D, Doucette S, Cranley Glass K, Shapiro S, Healy D et al. Association between suicide attempts and selective serotonin reuptake inhibitors: systematic review of randomised controlled trials. *BMJ* 2005;330:396-99.

6 Hall WD, Mant A, Mitchell PB, Rendle VA, Hickie IB, McManus P. Association between antidepressant prescribing and suicide in Australia, 1991-2000: trend analysis. *BMJ* 2003;326:1008-11.

[3] FDA Public Health Advisory March 22, 2004

Subject: WORSENING DEPRESSION AND SUICIDALITY IN PATIENTS BEING TREATED WITH ANTIDEPRESSANT MEDICATIONS

Today the Food and Drug Administration (FDA) asked manufacturers of the following antidepressant drugs to include in their labeling a Warning statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality. The drugs that are the focus of this new Warning are: Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvox

(fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and Remeron (mirtazapine).

Warning Information

* Health care providers should carefully monitor patients receiving antidepressants for possible worsening of depression or suicidality, especially at the beginning of therapy or when the dose either increases or decreases. Although FDA has not concluded that these drugs cause worsening depression or suicidality, health care providers should be aware that worsening of symptoms could be due to the underlying disease or might be a result of drug therapy.

* Heath care providers should carefully evaluate patients in whom depression persistently worsens, or emergent suicidality is severe, abrupt in onset, or was not part of the presenting symptoms, to determine what intervention, including discontinuing or modifying the current drug therapy, is indicated.

* Anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia (severe restlessness), hypomania, and mania have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although FDA has not concluded that these symptoms are a precursor to either worsening of depression or the emergence of suicidal impulses, there is concern that patients who experience one or more of these symptoms may be at increased risk for worsening depression or suicidality. Therefore, therapy should be evaluated, and medications may need to be discontinued, when symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

* If a decision is made to discontinue treatment, certain of these medications should be tapered rather than stopped abruptly (see labeling for individual drug products for details).

* Because antidepressants are believed to have the potential for inducing manic episodes in patients with bipolar disorder, there is a concern about using antidepressants alone in this population. Therefore, patients should be adequately screened to determine if they are at risk for bipolar disorder before initiating antidepressant treatment so that they can be appropriately monitored during treatment. Such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder and depression.

Health care providers should instruct patients, their families and their caregivers to be alert for the emergence of agitation, irritability, and the other symptoms described above, as well as the emergence of suicidality and worsening depression, and to report such symptoms immediately to their health care provider.

[4] Akathisia[4] (or "acathisia") is an often extremely unpleasant subjective sensation of "inner" restlessness that manifests itself with an inability to sit still or remain motionless, hence its the origin of its name: Greek a (without) + akathisia (to sit). It is a common side effect of certain drugs, notably typical or atypical antipsychotics (also called major tranquillisers), such as haloperidol (Haldol®) and droperidol, olanzapine (Zyprexa®); SSRIs, such as paroxetine (Paxil®); tricyclic antidepressants, certain antihistamines,

such as promethazine and diphenhydramine (Benadryl®); and certain anti-emetic drugs, particularly the dopamine blockers (e.g. metoclopramide (Reglan®) and prochlorperazine (Compazine®)).

Akathisia may range in intensity from a mild sense of disquiet or anxiety (which may be easily overlooked) to a total inability to sit still with overwhelming anxiety and severe dysphoria (manifesting as an almost indescribable sense of terror and doom). In the most severe cases, dysphoria can be so severe that the patient is literally compelled to take action, leading, possibly, to suicide attempts. It is not unknown to have patients literally run out of a hospital or emergency room.

Akathisia is often misdiagnosed and can lead the patient to commit suicide in or outside the hospital.

Causes:

*	*typical or atypical antipsychotics (also called major tranquillisers), such as haloperidol (Haldol®) and droperidol, olanzapine (Zyprexa®);*
*	*SSRIs, such as paroxetine (Paxil®);*[4]
* as	*tricyclic antidepressants, certain antihistamines, such promethazine and diphenhydramine (Benadryl®);*
* dopamine	*and certain anti-emetic drugs, particularly the blockers (e.g. metoclopramide (Reglan®) and prochlorperazine (Compazine®)).*

Treatment includes the discontinuation or reduction of dose of the causative agent and the use of typical or atypical antipsychotics (also called major tranquilizers) to reduce the agitation and anxiety. Unfortunately, these neuroleptics are often the cause of the condition and are known to cause irreversible akathisia in some cases. While the administration of these drugs may temporarily ameliorate the symptoms, there is a serious risk of worsening the condition over the longterm.

… Most of the clinical cases of akathisia can be prevented by not administering the drugs that cause the condition.

[5] APPENDIX 1 SSRIs & MECHANISMS OF SUICIDE: David Healy

Agitation/Akathisia

The evidence that SSRIs cause agitation comes directly from the clinical trial programs run by the market authorization holders, where approximately 5% of patients have dropped out because of drug induced agitation. Rates of drop-out for agitation are significantly greater than for placebo.

These clinical trial findings in depressed patients are corroborated by the results from healthy volunteer studies. In these phase 1 studies, the companies generally code akathisia to agitation or to hyperkinesis. The critical point that emerges from these studies is how the market authorization holders can argue that their drugs do not lead to s suicide against a background of their drugs causing agitation severe enough to

lead to drop-outs from clinical trials at an up to 5% rate - in addition to all the less severe forms of agitation caused and to agitation at an approximately 25% rate, occurring in a dose dependent fashion, in healthy volunteers. These data were all in place from the 1980s. In their early clinical trial program with Prozac, Lilly and their investigators specifically noted the emergence of akathisia/agitation and arranged for the concomitant administration of benzodiazepines to minimize this problem.

Company reviewers have conceded the fact that SSRIs cause akathisia and by regulators and DSM-IV AND COMPANY reviewers have recognized a link between akathisia and suicide.

It has been long recognized in the medical community that akathisia can cause suicidality and this fact has been extensively documented in the medical literature.

The first emergence of this link came with reserpine, a psychotropic agent with comparable efficacy to SSRIs in trials for anxious depressives done in the 1950s (Davies and Shepherd 1955). This drug however led to suicide and did so in the hypertensive patients to whom it was being given rather than in the psychiatric patients to whom it was also prescribed in higher doses (Healy and Savage 1998). It can be noted that despite causing suicide, reserpine is still prescribed to and can be effective for depressed patients (Price et al 1987).

Reserpine led to a state that could appear within hours or days of treatment commencing. This was characterised as follows:

"Increased tenseness, restlessness, insomnia and a feeling of being very uncomfortable" (Achor et al 1955),

"the first few doses frequently made them anxious and apprehensive... they reported increased feelings of strangeness, verbalized by statements such as ‘ I don’ t feel like myself’ .. or ‘ I’ m afraid of some of the unusual impulses that I have’ " (Faucett et al 1957).

Sarwer-Foner and Ogle (1955) describe the case of CJ who on the first day of treatment reacted with marked anxiety and weeping and on the second day "felt so terrible with such marked panic at night that the medication was cancelled".

Such reactions were interpreted by some as evidence in favour of the then current theory that patients with essential hypertension had a suppressed rage close to the surface (Faucett et al 1957). A description by Ayd (1958), however, seems to point to something else - "they had motor restlessness which made their muscles taut, compelled them to pace the floor and did not permit them to sit without moving their legs".

Akathisia was later confused with tardive dyskinesia. It was retrieved from the realm of the dyskinesias by Theodore Van Putten in 1975 who wrote that akathisia was a drug-induced psychosis, which had extremely bizarre characteristics with suicidal overtones. His descriptions make it clear that there are similarities between akathisia and symptoms such as anxiety, restlessness and agitation.

In 1983, Shear et al. reported suicide associated with akathisia with treatment of depot fluphenazine.

In a 1985 paper, Schulte linked akathisia with psychotic acts of murder and suicide. He wrote, "The following five cases are reported to bring attention to the potential for severe violence, as a result of akathisia, following such administration of a neuroleptic (major tranquilizer) for acute psychiatric symptoms."

In another 1985 paper, Drake and Ehrlich reported further on the link between akathisia and suicide attempts.

With the advent of the SSRIs, evidence emerged regarding SSRI-induced akathisia and suicidality. A rechallenge study conducted by Rothschild and Locke in McLean Hospital brought this out clearly. The authors described Prozac-induced emergent suicidality associated with akathisia in several patients. In order to test whether the emergent suicidality was coincidental or was associated in a cause and effect way with Prozac, they withdrew Prozac, then re-administered it and all three cases after having made a previous serious suicide attempt on Prozac experienced the exact same effect on rechallenge. "All three patients developed severe akathisia during treatment with fluoxetine and stated that the development of the akathisia made them feel suicidal and that it had precipitated their prior suicide attempts."

Wirshing and Van Putten described a further set of patients who became suicidal during treatment with Prozac as follows: "[n]one (of the patients discussed) had a history of significant suicidal behavior; all described their distress as an intense and novel somatic-emotional state; all reported an urge to pace that paralleled the intensity of the distress; all experienced suicidal thoughts at the peak of their restless agitation; and all experienced a remission of their agitation, restlessness, pacing urge, and suicidality after the fluoxetine was discontinued."

This article was followed up by the peer-reviewed article, "Akathisia, Suicidality and Fluoxetine," by Hamilton and Opler which ties SSRI-induced akathisia to suicidality, "[t]he proposed link between fluoxetine and suicidal ideation is explained by fluoxetine-induced akathisia and other dysphoric extrapyramidal reactions," and provides an extensive history of drug-induced akathisia causing suicidality:

"Several reports already exist in the literature documenting the development of EPS [extrapyramidal symptoms] in association with fluoxetine, but without necessarily linking this to an increased incidence in suicidal ideation. Specifically, Lipinski et al. first reported the occurrence of akathisia in five patients treated with fluoxetine. Bouchard et al. reported that EPS developed in several of their patients while they were being treated with fluoxetine and in other patients the baseline levels of EPS worsened during fluoxetine treatment. Symptoms noted included bradykinesia, cogwheel rigidity, and akathisia. Tate reported that a patient who had previously tolerated haloperidol alone had an increase of EPS (including parkinsonism and akathisia) when fluoxetine was added. Stein reported a case of tardive dyskinesia that developed when a low dose of haloperidol was added to fluoxetine. In the case reported by Teicher et al., four of the six patients described complained of an inner restlessness which Opler has previously argued could reflect that they were experiencing akathisia. Wirshing et al. recently reported that five patients treated with fluoxetine experienced ‘ agitation, restless motor movement, dysphoria, pacing, an internal sense of desperation, and suicidal ideation,’ and they too suggest ‘ that fluoxetine-induced akathisia can lead to suicidal ruminations.’

A separate clinical literature suggests that akathisia can at times lead to emergence of suicidal ideation. Akathisia is defined as an ‘ inner sense of restlessness’ and an ‘ inability to sit still.’ Patients who experience this often give reports such as ‘ I feel like I’ m jumping out of my skin.’ As akathisia is a common side effect of neuroleptic medications, information regarding subjective response to akathisia exists primarily, although not exclusively, in the literature on schizophrenia. In 1974 Van Putten et al. noted that nine schizophrenics treated with high-potency neuroleptics showed ‘ behavioral toxicity’ associated with akathisia. Three of these patients developed de novo suicidal ideation. Schulte reported five cases of violent behavior, including completed suicides, as a result of akathisia in patients treated with neuroleptics. Shear et al. reported two cases of completed suicide by jumping in patients who the authors argue were suffering from akathisia. Drake and Ehrich also reported two cases of suicidal ideation secondary to akathisia. In one case the patient stated that he did not intend to die but that he would do anything to escape the intolerable feeling of restlessness. Drake and Ehrlich noted that these patients were unable to distinguish the akathisia from the ongoing symptoms of their psychiatric illness. Weiden reported that the use of prochlorperazine for nausea in a patient receiving chemotherapy led to akathisia which was very distressing to the patient. In 1986 Weddington and Banner successfully used chlorpromazine and metoclopramide to treat intractable hiccups but found that after 3 days of treatment the patient became restless, felt like he was ‘ going crazy,’ and began obsessing about suicide. During a crossover study involving haloperidol and BW2344-U (which is characterized by the absence of dopamine receptor affinity), Shaw et al noted that during haloperidol treatment the patients experienced a clinical decline characterized by severe akathisia and an increase in violent behaviors as well as suicidal ideation and homicidal thinking. None of the symptoms were present with BW2344-U. In a 1987 review article, Van Putten et al. cite several studies in which it was noted that akathisia leads to suicidal ideation or homicidal thinking. They called this the ‘ behavioral toxicity’ of antipsychotic medication. By 1988 Hermesh et al. began studying the use of propranolol to treat akathisia because of the authors’ familiarity with the above literature and their concern that akathisia might lead to suicide attempts."

The Lipinski article was also referenced by Bonnet-Brilhault and colleagues in a 1998 article on paroxetine induced akathisia as follows:

"Since the publication in 1989 of the article by Lipinski et al., reporting the occurrence of akathisia in five patients treated with fluoxetine, there have been several reports of akathisia associated with other selective serotonin reuptake inhibitors (SSRIs) such as sertraline, and, lately, paroxetine. In addition to the discomfort felt by patients, the most notable secondary complications are non compliance and suicidal ideation or behavior."

The association between akathisia and suicidality and its implications is, perhaps, best expressed by Roger Lane in 1998 when he was working for Pfizer:

"It may be less of a question of patients experiencing fluoxetine-induced suicidal ideation, than patients feeling that ‘ death is a welcome result’ when the acutely discomforting symptoms of akathisia are experienced on top of already distressing disorders. Hamilton and Opler (1992) stated that the term ‘ suicidal ideation’ to describe the apparent suicidality associated with akathisia was misleading as the ‘ suicidal ideation’ reported in patients receiving fluoxetine was a reaction to the side-

effect of akathisia (i.e. unbearable discomfort and restlessness) and not true suicidal ideation as is typically described by depressed patients experiencing suicidal ideation."

The recognition of a link between akathisia and suicide is not confined to the US/UK. In 1998, Marsalek noted:

"Suicidal ideation and behavior can sometimes emerge in persons with obsessive or panic features who take antidepressants or neuroleptics. Typical for such state is rapid development, impulsive and/or obsessive characteristic of suicidal ideation, an independence of the course of depression, severe tension and anxiety, an intense violence of suicidal fantasies and attempts, and their prompt disappearance after the discontinuation of the antidepressant. . . . There is clinical evidence of the link between akathisia and suicidal tendencies. . . . The reduction or the discontinuation of antidepressants or neuroleptics, and the treatment with benzodiazepines or beta blockers should be recommended when the drug-induced suicidal tendencies are recognized."

Finally, as with SSRI-induced akathisia, DSM-IV TR also acknowledges the association of akathisia and suicidality:

"The subjective distress resulting from akathisia is significant and can lead to noncompliance with neuroleptic treatment. Akathisia may be associated with dysphoria, irritability, aggression, or suicide attempts."

There is no textbook, reference work or peer reviewed trial anywhere saying that akathisia or agitation do not predispose to suicidality.

[6] AkathisiaICD-10 code: ICD-9 code781.0, DSM 333.99 Wikipedia® is a registered trademark of the Wikimedia Foundation, Inc.