

Study to determine the risk of violent behaviour in people taking SSRIs.

Recent concerns about the adverse effects of selective serotonin reuptake inhibitor antidepressants (SSRIs) have focused on suicide risks. However, a new study published in the September 2006 journal, Public Library of Science (PLoS), reports that in addition to self-harm, the drugs can also cause some patients to become violent and homicidal.

Professors David Healy and David Menkes from Cardiff University in Britain, and Andrew Herxheimer from the Cochrane Centre, conducted the study to determine the risk of violent behavior in people taking SSRIs.

During their investigation, the researchers reviewed all available clinical data on SSRIs and summarized a series of what they refer to as "medico-legal" cases involving patients who became violent on SSRIs in which they have given evidence.

In addition, they analyzed 1,374 emails from patients on SSRIs sent in response to a British television program on Paxil featured on Panorama.

The authors focus mostly on Paxil because they had access to more medico-legal case material for Paxil patients than other drugs and because GlaxoSmithKline recently submitted data on the rates of "hostile" events for the review of SSRIs by the British regulatory Committee on Safety of Medicines Expert Working Group.

Dr Healy is one of the world's leading authorities on SSRIs. He is the author of over 120 articles and 12 books, including, *Let Them Eat Prozac*, *The Antidepressant Era*, and *The Creation of Psychopharmacology*.

His expert testimony at the trial of a Wyoming lawsuit involving violence associated with Paxil in 2001, was a deciding factor in the return of a favorable verdict for the plaintiffs. The trial involved the tragic case where 60-year-old, Donald Schell, shot and killed his wife, daughter and granddaughter and then himself after taking Paxil for only two days.

Mr Schell's surviving family members sued SmithKlineBeecham and won. Another decisive factor in the Wyoming case relevant to the results of the current study, is that the company's own internal clinical trial data revealed at trial showed that Glaxo knew prior to 1998, when the deaths occurred, that Paxil had caused some patients to become violent and suicidal.

The data included an unpublished study of incidents of serious aggression in 80 patients, 25 of which involved homicide. After weighing all the evidence, the jury said that Paxil "can cause some people to become homicidal and/or suicidal," and ordered Glaxo to pay the plaintiffs \$8 million.

In the PLoS study, Dr Healy and his colleagues warn that, "The new issues highlighted by these cases need urgent examination jointly by jurists and psychiatrists in all countries where antidepressants are widely used."

However, that might be easier said than done because according to Dr Healy, "even though PLoS is braver than most journals and less influenced by industry than most, it still took close to 18 months for this article to appear."

"I have several articles that have taken this long," he reports. "The hold up," he says, "is the journal - whether PLoS or BMJ being terrified of industry and a legal action against them."

"This stands in contrast" Dr Healy points out, "to the good news about drugs which industry manages to get out rapidly in the best quality, highest impact factor journals, apparently authored by the biggest name academics in the field."

"But these articles," he advises, "are based on selected data and no-one has access to the full dataset and no-one makes a judgment based on full access."

Investigative reporter, Kelly Patricia O'Meara, author of, "Psyched Out, How Psychiatry Sells Mental Illness and Pushes Pills That Kill (2006)," is also painfully aware of the difficulties involved in getting the information published about SSRIs and violence that most experts have known about for years.

"It seems to me that the "new" study is an old issue," she says. "I don't believe there is anyone remotely familiar with these drugs who wouldn't admit a strong correlation between them and violence."

"It is an issue that must be addressed," she warns, "given the numbers of violent acts that appear to be associated with their use."

"The issues the doctors raise about the medical/legal aspects," Ms O'Meara says, "are extremely pertinent."

Specifically, she notes, in recent weeks in the Washington DC area, there have been three cases reported in the Washington Post all dealing with violence/murder associated with "mental illness."

"While all three cases reportedly were receiving psychiatric care," she says, "only one of the cases mentions the use of psychotropic drugs."

"Naturally," she points out, "any progress on this will depend largely on whether the press is informed enough to even ask the question: were they on prescription mind-altering drugs?"

Dr Healy acknowledges that, "SSRIs can be very useful and there are unquestionably people who are hugely helped, but the benefits have been over-hyped," he says, "and the risks concealed and denied."

It would be helpful, he notes, to have access to all the data on the violence side effect associated with SSRIs. "Based on access to all the data in this area," he explains, "we might be able to work out if men or women are at greater risk or young or old or people being treated for anxiety rather than depression."

"Until then," he advises, "the key thing is that people being put on these pills need to be warned that they may not suit them and if they feel odd or more anxious they should either stop treatment or return to their doctor."

"The worry," Dr Healy has, "is that doctors indoctrinated by company input on this will still only see the risks from the condition being treated and faced with a patient saying they feel worse will double the dose of the treatment rather than reducing the dose or halting the treatment or switching to a different kind of treatment."

"This would be exactly the wrong thing to do if the drug is the source of the problem," he warns.

Other recognized experts on SSRIs share the same concerns. According to Dr John Abramson MD, author of *Overdosed America*, and clinical instructor at Harvard Medical School, a double standard exists in the way that information is received by physicians.

"Commercially advantageous "knowledge" travels fast and is delivered by many paths," he says, "while commercially disadvantageous information, though available sometimes in a legalistic sense, is not communicated in the way that doctors have been formally and informally trained to receive new information."

In the Paxil trials reviewed for the PLoS study, aggression and violence were coded under the term "hostility" which included homicide, homicidal acts, and homicidal ideation as well as aggressive events and conduct disorders, but no homicides were reported in the trials.

When combined, hostile events in both the adult and pediatric trials, during therapy and the 30-day tapering off phase, 60 out of 9,219 patients experienced hostile events.

The study found hostile events in excess in both adults and children, and across all indications. The hostility rates were highest among children with obsessive-compulsive disorder, where the rate of a events was 17 times greater.

In their submissions to the Committee on Safety of Medicines, Glaxo also reported clinical trials comparing 11,491 patients on Paxil and on other SSRIs, and there were 44 hostile events in patients on Paxil or other drugs.

In the trials comparing Paxil with another SSRI, there were 16 hostile events in a group of 2,418 patients. These SSRI comparator trials may be confounded by indication, the researchers note. They might, for instance, have included a higher proportion of OCD patients.

However, most noteworthy in this review, the researchers found that in healthy volunteer clinical trials that took place in the late 1980s or early 1990s, hostile events occurred in three of the 271 healthy volunteers taking Paxil, while none occurred in the 138 volunteers taking a placebo.

"Although not statistically significant," the authors point out, "this finding is striking because hostile events are unusual in healthy volunteer trials, and this figure was higher than the rate reported in clinical populations above."

Glaxo attributed these events to the fact that the volunteers were confined, although the study authors note that both the Paxil and placebo volunteers were confined.

But here again, Dr Healy acknowledged the significance of the findings in the healthy volunteer trials 6 years ago. "We can make healthy volunteers belligerent, fearful, suicidal and even pose a risk to others," he wrote in the June 2000, Primary Care Psychiatry.

"People don't care about the normal consequences as you might expect," he stated. "They're not bothered about contemplating something they would usually be scared of."

Four years later, on September 21, 2004, Dr Healy is sounding the alarm again and quoted by The Guardian, as saying, "I think there is very clear evidence for all of the SSRI group of drugs that in addition to making people suicidal, they can make people homicidal or seriously aggressive and the data have been sitting in the MHRA's files on this issue."

"It is there for children across a range of different problems," he said, "it is there for healthy volunteers and a range of adults and the MHRA has paid no heed to this."

Another recognized expert on SSRIs, Ann Blake Tracy, PhD, Executive Director, International Coalition For Drug Awareness, and author of, "Prozac: Panacea or Pandor?" has been investigating the adverse events associated with SSRIs for the better part of two decades and says that, "This study confirms all of the previous data we have on increased levels of serotonin and violence."

Ms Tracy has been working to make her findings public for the past 16 years. "This understanding that increased levels of serotonin - the exact so called "therapeutic" effect that antidepressants are designed to have," she states, "has long been associated with psychosis, mania, suicide, violent crime (including rape, arson, murder), and could have saved many, many lives in the past two decades that these drugs have been in such widespread use worldwide."

According to Ms Tracy, research has shown that impairing serotonin metabolism will produce tension and anxiety which appear from out of nowhere, depression, suicide - especially very violent suicide, hostility, violent crime, impulsive behavior with no concern for punishment, and argumentative behavior.

"How anyone ever thought it would be "therapeutic" to chemically induce these reactions is beyond me," she states. "Yet, these reactions are exactly what we have witnessed in our society over the past decade and a half as a result of the widespread use of these drugs."

She makes a very good point when she poses a thought provoking question. "Can you remember two decades ago," she asks, "when depressed people used to slip

away quietly to kill themselves rather than killing everyone around them and then themselves as they do while taking SSRI antidepressants?"

In the PLoS violence study, the authors provide an excellent example of the bizarre violent murders and suicides that Ms Tracy refers to, when they discuss the 1989 case of Joseph Wesbecker who shot and killed eight people, and injured 12 others, before killing himself at his place of employment in Kentucky after taking Prozac for about four weeks.

This incident also led to a lawsuit against Prozac maker Eli Lilly. The case was tried and settled in 1994, and a number of documents about drug-induced activation were made public back then.

The cases of out of character acts of violence by persons taking SSRIs are not isolated incidents or limited to certain age groups. Delnora Duprey has observed first hand the horror that can result from prescribing SSRIs to children. She is the maternal grandmother of Christopher Pittman, who at 12-years-old was placed on Paxil and Zoloft simultaneously, and subsequently murdered his paternal grandparents by shooting them as they lay sleeping and then burning the house down.

The following morning, two hunters found young Christopher hysterical in the woods yelling and waving a loaded shotgun over his head.

Ms Duprey says that she would like to stress as a family member who has gone through a terrible tragedy due to these drugs, that she knows how they can change people. "Our Christopher went from a sweet shy good kid," she recalls, "to an angry hyper aggressive person in a very short time period."

"This was not a normal change in a personality," she states, "it was the medication."

Ms Duprey, along with every other relative, blames the SSRIs, and says that Christopher would never have murdered his grandparents because he adored them both.

"While off the medication our Chris is back," she says, "he has gotten his GED and has done very well under some rough conditions."

Christopher has remained in jail ever since the night he killed his grandparents in 2001.

He was tried as an adult, found guilty and sentenced to 30 years in prison.

At a sentencing hearing his aunt, Melinda, the daughter of the slain grandparents, begged the court to show mercy toward her nephew, stating that her parents would want the court to show mercy toward Christopher.

The South Carolina Supreme Court has opted to hear an appeal and the case is set for a hearing in October 2006.

Through their review of adverse event records in the UK, Dr Healy and his colleagues found that by 2003, there were already 121 cases of aggression in patients on Paxil reported to the Medicines and Healthcare Products Regulatory Agency, and furthermore, by January 2006 that number had risen to 211.

The authors specifically point out that such reporting systems estimate that doctors only report between one and ten percent of adverse effects.

The data reviewed for the study that was submitted by Pfizer on Zoloft's pediatric trials showed aggression to be the most common cause for discontinuation in the two Zoloft placebo-controlled trials in depressed children.

In the Pfizer trials, eight of 189 patients in the Zoloft group discontinued for aggression, agitation, or hyperkinesia (a coding term for akathisia), compared to no dropouts for these reasons in the group of 184 patients on a placebo.

When discontinuations were considered for any treatment-induced activation including suicidal ideation or attempts, aggression, agitation, hyperkinesia, or aggravated depression, there were 15 drop outs by patients on Zoloft and only two in the placebo group.

In the only other placebo-controlled Zoloft pediatric trial, of children with OCD, out of 92 patients on Zoloft, there were ten dropouts. Five for behavioral activation, two for agitation, one for aggression, one for nervousness, and one for emotional lability.

In comparison, in the group of 95 children taking placebos, there was one discontinuation for hyperkinesia out of two dropouts overall.

In addition, in one healthy volunteer trial on Zoloft run by Dr Healy, one of twenty volunteers reported aggressive behavior. This is not the only Zoloft healthy volunteer trial to show hostility after Zoloft intake, Dr Healy says, but the other data remain unpublished.

Finally, in pediatric trials of Wyeth's Effexor, 2% of the children dropped out because of hostility, more than double the rate of children on a placebo.

The researchers also analyzed the 1,374 emails that were received by the BBC television following a program on Paxil and found that many people described emotional storms and thoughts and acts of violence or self-harm.

The analysis, they said, indicated a clear link between severe mood changes when Paxil treatment began, or later when the dosage was increased, decreased, or withdrawn.

Remarkably, the analysis found reports of violence in patients with no prior history of violent behavior. The results, the authors note, were also consistent with an analysis of reports by people on Paxil submitted to the MHRA by doctors between 1991 and 2002.

The authors say the strength of the current study showing an association between violence and SSRIs is that the data are unselected, but consistent even though it comes from a variety of sources.

"A weakness of the study," they note, "is that we have been able to include only a subset of existing data in the analysis."

"Data on aggression on other antidepressants will necessarily have been collected as part of the development programmes for these drugs," they state, "but these data are not in the public domain."

"Earlier reports have linked antidepressants to violence," they note, "but this is the first independent study to offer a quantitative analysis of the issue; no other studies exist with which our results can be compared."

By now many experts are questioning whether it can be said that the benefits of SSRIs outweigh their risks or whether they have any benefits at all. According to Dr Peter Breggin, another well-known expert on SSRIs, and author of, *The Antidepressant Factbook*, "study after study has confirmed that antidepressants typically perform only a little better than sugar pills."

"In some studies," he notes, "antidepressants actually turn out to be less effective than the lowly sugar pill."

He also points out that "if depression is a product of our conflicts, stressful life experiences, and stifled choices, a drug would have no direct effect on treating it."

Another expert in the field, and author of, *The ADHD Fraud*, Dr Fred Baughman, says, "we have the "disease-ing" of emotional and behavioral problems—of life's problems with never a mention that the causes can be found in every-day life difficulties—things people can and must be helped with."

He says when people get help in solving their work problems or marital and family problems or financial problems their "mental illness" is often gone in a day.

"The drugging psychiatry-pharmaceutical cartel," Dr Baughman warns, "is too anxious to "disease" and "disable" those with real-life problems and the emotional symptoms they beget."

Dr Healy has said that most patients diagnosed with mild or moderate depression would be better characterized as suffering from "community nervousness." And although he views the condition as a real disorder, he says that it "could be due to a host of different factors such as overwork, stress, and constitutional deficits. But clinicians everywhere are diagnosing depression because that's what they have a treatment for."

"The Prozac story," he writes in the book, *"Let Them Eat Prozac,"* is one of a "wholesale creation of depression on so extraordinary and unwarranted a scale as to raise grave questions about whether pharmaceutical and other health care companies are more wedded to making profits from health than contributing to it."

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