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ISSUES IN FORENSIC CASES ASSOCIATED WITH SELECTIVE SEROTONIN REUPTAKE INHIBITORS

1. There have been a number of cases in which Selective Serotonin Reuptake Inhibitors, SSRIs, have been implicated in criminal defences. The issue being that SSRIs may predispose individuals to exhibit behaviours precipitated by SSRIs as an adverse effect of their therapy.
2. These cases have included motoring offences, shop lifting, robberies, and assaults.
3. Of particular importance have been the cases in which it has been alleged that the SSRIs have precipitated violent behaviour, resulting in at best, criminal assault, and at worst, murder.
4. There have been some cases in which this has been accepted as a defence and others where it appears a crime of specific intent has been reduced to one of basic intent (such as murder to manslaughter) and others where it has been used in mitigation.
5. It appears to be near to impossible to obtain a complete list of these in any one country, notwithstanding the fact that this is clearly a global problem.
6. There have been additional cases in which there have been civil cases brought against the manufactures of SSRIs which have been settled in favour of the claimant as the manufacturer is alleged to have either, at best, not given adequate warning in Product Information and at worst, possibly having information which has not been either analysed or declared to Regulators.
7. It appears to be near to impossible to establish the truth as opposing camps hold their beliefs with religious fervour.
8. The argument against the hypotheses that SSRIs may be implicated is the lack of hard scientific evidence that there is an association between SSRIs and violence. With even less evidence if such an association, if it exists, is causal.
9. There has been created, what has been loosely called the 'Three Legged Defence', being the lack of this published scientific evidence, the association between the diseases for which they

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are used and such behaviour any way, and other factors predisposing to such behaviour demonstrated by the majority of those allegedly affected.

10. Opposing this is the view that SSRIs obviously alter thought and thus behaviour, can probably produce agitation, frustration and dyskinesis, all of which lead to a predisposition violent acts.
11. The people who hold this view also have the opinion that there has possibly, if not probably, been concealment of vital information by the manufacturers of SSRIs as they try to improve the image of this class of compounds. They site the number of cases in which SSRIs are implicated. It has been hard, if not impossible to produce a list of these criminal trials with their outcomes and the reason for such, as well as to produce a list of civil cases with their outcomes.
12. They also point out the increasing regulatory warnings in product literature as evidence of an association.
13. It however has to be considered whether the companies involved to prevent civil claims for possible non-disclosure have agreed to class specific labelling to defend this issue.
14. The paper summarising the issues for those believing that there is a definite association is that by Healy, Herxheimer and Menkes (Antidepressants and Violence: Problems at the Interface of Medicine and Law, PLoS Med. 2006 Sep;3(9):e372).
15. The issues are made more complicated by the fact that these drugs may affect adolescents in different ways and that possibly in adults, and probably in adolescents, there may be a difference in the individual members of the class. Fluoxetine being the only member of the class licensed for use in children in the United Kingdom.
16. There appear to be some important issues to resolve, although it may be impossible to reach a consensus across all interested parties. Those issues are:
    a) Is there an association between SSRIs and violent behaviour including homicide?
    b) Should this association be scientifically sustainable without the need to include suicide in general and violent suicide in particular, in the same group of adverse effects?
    c) If such an association exists, is it causal?

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d) May there be a difference in the association between different SSRIs? i.e. one or more may be associated and one or more may not be.

e) Is there a sub-population of patients more likely to react adversely in this way to SSRIs and can they be identified prospectively?

f) If they have exhibited violent behaviour in the past, is it possible for the SSRI to precipitate it again or make it worse?

g) All the above need to be considered separately in relation to adults, adolescents, and children as product labelling is different in all these groups.

17. If it is scientifically difficult, if not impossible, using usual pharmacoepidemiological and scientific methods to arrive at any conclusions, there still remains the possibility that in individual cases the SSRIs may be involved due to the specific circumstances of the case, the personality of the patient and the adverse effects of the SSRIs.

18. After these issues have been considered, one would have to try to evaluate the effect of simple factors such as age and sex of the patient, dose taken and the time the medicine had been used. It has been suggested that the most likely time is at the start of therapy on dose increase and on withdrawal. Relation to initial and steady state pharmacokinetics has to be evaluated.

19. If evidence cannot be produced directly for the association of violence and murder and SSRIs, one would have to consider if there is evidence that surrogate markers could be used to prove the association, such markers could be changed in thought structure, increasing agitation or dyskinesis. One could then use standard epidemiological techniques to determine if these or other markers are associated with SSRI treatment.

20. One would still have a number of difficulties such as

a) Coding frames and people doing the coding will be different and have different interpretations of individual events. One would have all the problems of trying to summarise and shorten a clinical scenario into a codable event.

b) One would have to come to the opinion as to whether the chosen marker could reasonably predispose to violent acts and murder.

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c) It would have to be determined that by producing these effects the SSRIs created a situation whereby the patient was either unable to know right from wrong and therefore unable to form the specific intent, or that the patient was so driven by the events associated with the surrogate marker that they were physically unable to control themselves.

21. One of the difficulties in interpreting the works published so far have been the different choices in research surveys of surrogate markers and coding strategy as well as the suggestion by some that not all of the available information is in the public domain.

22. Additionally, in epidemiological surveys the data may be confused by alternate paradoxical effects in which there are a group of patients whose risk is made better by SSRIs and a group of patients whose risk is made worse by SSRIs, the overall frequency within the population therefore not changing.

23. Whatever the truth of the above epidemiological evidence, one would still have to consider the effect in an individual case. There does not appear to be a summary in the scientific literature or legal case precedent which summaries those factors which would lead one to find that the drug was responsible or whether the drug was not responsible as there have been with the automatism defence in epilepsy and head injuries.

24. Clearly of importance is the pre-morbid personality and behaviour and in both epilepsy and head injury a guiding fact has been taken to be that the behaviour allegedly due to either of them is out of character for the individual.

25. It would appear to be sensible for such an 'out of character' scenario to be important in the issue of SSRIs as well. This is obviously counter-balanced by the possibility that the SSRI is more likely to precipitate violent behaviour in patients already displaying this behaviour and personality trait as has been suggested for the precipitation of mental health issues with both Roaccutane and some anti malarials.

26. In such a case, one would be looking for a change in frequency of such behaviour after the prescription. One would have to consider whether:

a) The SSRI raised the general level of violence within a person all the time.

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b) Whether the SSRI raised the threshold for a violent episode to a specific precipitating incident as in the former, there could be an increasing number of episodes and in the later, there may only be one episode.

27. The other factors to be taken into account in considering an individual event which may be taken from the cases of epileptic and head injury automatism, would be both an absence of:
    a) Motive
    b) Premeditation
    c) Concealment
28. Individual cases should also be examined for the possibility of post SSRI:
    a) Changes in behaviour
    b) Increasing agitation
    c) Emotional blunting
    d) Dyskinesis
    e) Psychotic symptoms
    f) Withdrawal symptoms
29. It has been suggested by some that all the criteria in the list above are possibly pre-cursors to violent acts, although has not been proven.
30. Other factors in the case would need to be examined in detail and their association with violent acts explored.
31. Of part importance would be other pharmacoactive substances, be they prescribed or illegally obtained.
32. The association between illegal drugs and acts of violence on a physiological and psychological, as opposed to a social basis, is in doubt with conflicting evidence.
33. One has to consider both the long term effects of the substance abuse on personality and behaviour as well as the acute affects while they are intoxicated.
34. The evidence is of differing degree for all the illegal drugs so each would have to be considered in turn on both the frequency of use, the amount used, previous affects and whether acute intoxication was present.

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35. This would have to be considered for cannabis, heroin, cocaine, amphetamines, Ketamine, and other stimulants in turn, as well as alcohol.
36. It is to be hoped that further scientific research will be performed and published to solve the scientific questions on association and causality, as well as regulatory consensus in different countries with hopefully legal consensus with the establishment of criteria on which individual cases can be assessed.
37. In individual cases, it would also need to be considered as to whether the prescription of the drug is in accordance with manufacture's recommendations and whether other therapy, care and management offered to the patient were appropriate.

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