

The Hypotheses for the Pathogeny of Drug-Induced Mania and Suicide

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Background

As for 2004, the US and European regulatory agencies began implementing verification programs to assess the influence on suicidal behavior from the use of antidepressants such as SSRIs [1-3]. With the increasing number of cases reported, several newly developed antidepressants were withdrawn from the market, although the mechanisms whereby these drugs can cause suicide remained unclear. It has been posited that some antidepressants may induce anxiety or mania, and thus their use should be cautious [1-3]. On the other hand, since it is possible that the side effects associated with use of these drugs may be individuals rather than all population, we hypothesize that genetic factor may account for drug-induced suicidal behavior [4]. Later, more and more clinical data correspond with our hypothesis [5].

The Presence of Anti-Microbial-Induced Mania

Abouesh's reviewed [6] the phenomenon of rarely occurrences of spontaneous antimicrobial-induced mania. Late, more and more clinical evidence has repeated this phenomenon [7-9], and their mechanisms are still mysteries. It is very similar with our previous hypothesis for antidepressant [4]. Thus we hypothesize some drug-induced toxicological mechanisms and give further explanations.

Hypotheses of the Pathogeny of Drug-Induced Mania and Suicide

In particular, it is feasible that specific genetic polymorphisms affecting the function of the serotonin system (SERT) location is associated with body anxiety which may decide the antidepressant-induced suicidal. Similarly, genetic mutations may exert an influence on the expression of a number of drug-metabolizing enzymes, such as the cytochrome P-450 enzymes that are responsible for the biotransformation of most antidepressants. Polymorphisms of genes controlling these enzymes could also be associated with the presence of various kinds of side effects, including violence and self-harm [10-11]. Future pharmacogenomics and whole-genome genetic association studies [12-13] especially on antimicrobial-induced mania in patients, are needed to confirm our hypothesis.

In considerations of its clinical observations and patients' abnormal episodes, we herein add two more suggestions; (i) rapid recovery from antimicrobial-induced mania after drug withdrawal suggests relative concentrations of drugs in blood is more important for the symptoms of mania. Therefore, we further conclude that genetic mutations of drug metabolizing enzymes, such as cytochrome P450 may play more decisive roles than polymorphisms of mental functioning molecules because such actions will in general elicit complicated genetic consequences and symptoms will last relatively longer; (ii) the higher concentrations of exogenous antimicrobials may trigger the escalated productions of some mania-related factors such as GABA or prostaglandins by overburdened central nerve cells. Our hypotheses could be easily verified by further clinical blood drug concentration tests in patients and be possibly extended to some other similar drug-related mental diseases.

Future Trends

In the future, we can pinpoint more genetic polymorphisms and toxicological mechanisms to explain drug-induced neural toxicity from different angles [14-15]. It is an important area for us to study and shed new light.

References

1. Check E (2004) Drug suicide risks prompt call for FDA action. *Nature* 427: 474.
2. Holden C (2004) Psychopharmacology. FDA weighs suicide risk in children on antidepressants. *Science* 303: 745.
3. Rubino A, Roskell N, Tennis P, Mines D, Weich S, et al. (2007) Risk of suicide during treatment with venlafaxine, citalopram, fluoxetine, and dothiepin: retrospective cohort study. *BMJ* 334: 242.
4. Lu da Y, Lu TR, Ding J (2007) May genetic factors play a role in the risk of antidepressant-induced suicide? *Med Hypotheses* 69: 1380-1381.
5. Brent D, Melhem N, Turecki G (2010) Pharmacogenomics of suicidal events. *Pharmacogenomics* 11: 793-807.
6. Abouesh A, Stone C, Hobbs WR (2002) Antimicrobial-induced mania (antibiomania): a review of spontaneous reports. *J Clin Psychopharmacol* 22: 71-81.
7. Fidan T, Fidan V (2009) Clarithromycin-induced mania in a child. *Int J Clinical Pharmacol Ther* 47: 402-404.
8. Baranowski WJ (2010) Clarithromycin-induced hypomania in a child—a case report. *Acta Psychiatr Scand* 122: 267-268.
9. Tomé AM, Filipe A (2011) Quinolones: review of psychiatric and neurological adverse reaction. *Drug Saf* 34: 465-488.
10. Ingelman-Sundberg M (2005) Genetic polymorphisms of cytochrome P450 2D6 (CYP2D6): clinical consequences, evolutionary aspects and functional diversity. *Pharmacogenomics* 5: 6-13.
11. Taylor S, Stein MB (2006) The future of selective serotonin reuptake inhibitors (SSRIs) in psychiatric treatment. *Med Hypotheses* 66: 14-21.
12. Goldstein DB, Tate SK, Sisodiya SM (2003) Pharmacogenetics goes genomic. *Nature Rev Genet* 4: 937-947.
13. Evans WE, Relling MV (2004) Moving towards individualized medicine with pharmacogenomics. *Nature* 429: 464-468.
14. Lu DY, Lu TR, Zhu PP (2012) How can we Pinpoint Genetic Involvement in Antidepressant-Induced Suicide? *Adv Pharmacoepidem Drug Safety* 1: e101.
15. Lu da Y, Lu TR, Zhu PP (2010) Undesired neural side-effects of a drug, a chemical and genetic interrelated problem. *Cent Nerv Syst Agents Med Chem* 10: 108-112.

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