

A vital factor to be considered for any treatment for a psychiatric disorder is the placebo effect. For example, a recent meta-analysis of the effects of anti-depressants concluded that only a small fraction of depressed people, specifically those with the most severe symptoms, were actually getting more benefit from the drug than they would have gotten from a placebo (<http://www.ncbi.nlm.nih.gov/pubmed/20051569>). Even studies questioning this conclusion, and affirming the effectiveness of anti-depressants for all levels of symptoms, still report that many people taking placebos show improvement (<http://www.ncbi.nlm.nih.gov/pubmed/22393205>).

- 1) First, briefly describe meta-analysis statistics and discuss the history of meta-analysis, its application in modern translational science, and the advantages and disadvantages of its use.
- 2) Discuss why placebos may be beneficial in depression and the importance of research design in assessing and comparing pharmacological treatments. *Given your discussion, if a friend told you he was feeling depressed and thinking about trying anti-depressant drug therapy, what would you say to him, and why? (Note—we are **not** asking you to advise him about **which** drug to try, but whether to try drugs at all). Back up your advice with scientific studies and rationale.*
- 3) Discuss what is known about the mechanism(s) of action of SSRIs for treating depression, including a discussion of why several weeks of medication is typically required before symptoms are relieved, despite the fact that elevation of serotonin (or other targeted neurotransmitters) generally occurs immediately. What, if anything, is known about the mechanism(s) by which placebos relieve depression?
- 4) Because some depressed people do not seem to respond to anti-depressant drug therapy, several other treatments have been brought to bear on this disorder. For many years, electroconvulsive therapy (ECT) has been used as a treatment for depression, and more recently deep brain stimulation (DBS), which is increasingly used for the treatment of Parkinson disease, has also been used to treat depression. Compare which brain region(s) are stimulated to relieve symptoms of depression versus Parkinson disease. Describe the research design that you regard as ideal for assessing whether ECT and DBS actually benefit people with depression. As you peruse the literature, have such studies been done? What is your assessment of whether DBS is effective for depression (be sure to cite the studies you find most relevant)? *If your friend was considering DBS for depression, would you encourage him to give it a try? Why or why not?*

For overall evaluation of your answer, the four parts will be equally weighted. The portions in italics are basically asking for your opinion (there is no right or wrong answer, but as a scientist your opinion should be guided by scientific studies or rationale). Asking your opinion on these issues is intended to help you appreciate the challenges of translating research into practice, and this portion of your answer should be less extensive than that addressing the non-italic portions of the question.

Final reminders: be sure to insert page numbers, essay (excluding references) should be 10 -15 pages in length and double spaced. Do not include identifiers of who you are in your essay.