INTERVIEW

Infocop: What motivated you to start investigating antidepressants and the placebo effect?

Irving Kirsch: While still an undergraduate student in psychology, I became fascinated by the degree to which people's beliefs and expectations influenced their experience. I became convinced that the self-confirming effects of expectancies were central to the effects of behavior therapy and was able to confirm that empirically in controlled studies. I then started researching the placebo effect. My first meta-analysis of antidepressants was really aimed at examining the placebo effect. When I saw the results, I was surprised at how small the drug effect (i.e., difference between drug and placebo) was. It was only then that I began to focus on the efficacy of antidepressants.

Infocop: Could you explain what the placebo effect consists of? What is the most surprising finding you have come across with during these years of researching?

I.K.: The placebo effect is that part of the response to a drug (or other medical intervention) that is due to its psychological characteristics, rather than to its chemical composition. The most surprising finding in the placebo literature is our discovery that placebos can be effective even when patients are told that they are being given placebos, as long as this is explained convincingly in the context of a warm therapeutic relationship. See http://dx.doi.org/10.1371%2Fjournal.pone.0015591.

Infocop: Are antidepressants really effective? Do they actually work and to what extend?

I.K.: At most, antidepressants have a meaningful effect for only a small minority of the depressed patients to whom they are prescribed, 10-15% of patients with major depressive disorder. The rest are better off taking a placebo, which produces almost as much improvement, but without the side effects and health risks of antidepressants.

Infocop: Given the results of your research, is it really possible to say that depression is exclusively caused by a chemical imbalance in the brain?

I.K.: Actually, the chemical imbalance theory is as close as close as a theory gets in science to being disproven by the evidence. And here I am not talking only about the results of my research, but that of many others as well. For example, depressed people improve as much on SSREs (selective serotonin reuptake *enhancers* - drugs that decrease serotonin in the brain) as they due on SSRIs (which are supposed to increase serotonin).

SEPCyS: If so many different interventions appear to work on depression (medication, placebo, psychological treatment, sport, buying a pet, etc.),

shouldn't we put into question, first of all, the entity of the diagnosis? That is, if there is a disorder that can be "cured" by anything that has some credibility, aren't we dealing, actually, with a pseudo-diagnosis?

I.K.: Diagnoses for psychological conditions are a problem in general. Depression is a very serious condition, but it may not be an illness at all. It may instead be a normal reaction to life circumstances or a signal that the person is needs to change important aspects of his or her life.

SEPCyS: Is depression an adaptive behavior in a social environment like ours, the so-called developed world? Or are there any other reasons behind it's high prevalence?

I.K.: If used as a signal that something is wrong, leading the person to make changes in life, it can indeed be adaptive. But its high prevalence is also associated with external factors over which people may have little control. We know, for example, that depression is associated with economic hardship and discrimination. Preventing depression requires broad social and economic changes, as well as individual interventions like psychotherapy.

Infocop: What are the implications of these findings both for research and clinical practice?

I.K.: Antidepressants should not be front line treatments for depression. Instead, treatments like physical exercise and psychotherapy should be tried first. If antidepressants are to be used at all, it should only be as a last resort when other treatments have failed to work. As to research, funding needs to be made available for better testing of non-pharmacological treatments for depression.

SEPCyS: Your studies have created certain turmoil in many areas, like the pharmaceutical industry or the medical lobby. What do you think about the impact of your studies and the reaction taken by the American Psychiatric Association?

I.K.: In 1998, when Guy Sapirstein and I first reported that most of the response to antidepressants was due to the placebo effect, the response was disbelief, and our findings were largely ignored. It is gratifying to see that more and more people are taking them seriously and that they have had an impact on health care practices, at least in the UK. Of course, psychiatrists are very resistant to these findings; their livelihood and professional existence is tied to the prescription of psychotropic medication – especially antidepressants.

Infocop: Over the past years, your results have been replicated by many other researchers. Do you think your results are having enough impact on daily clinical practice? Could you further explain why or why not?

I.K.: Medical practice is slow to change. Physicians are still quick to prescribe antidepressants to patients who are mildly depressed, without trying other alternatives. In the UK, they do this despite official treatment guidelines to the contrary.

SEPCyS: Compared with the degree of empirical support that stem from your studies on antidepressants, how do you assess the empirical status of psychological treatments?

I.K.: The short term response to psychotherapy is the same as the short term response to antidepressants, but the long term response is considerably better. Cognitive behavior therapy has been shown to reduce the risk of relapse for as long as six years. Furthermore, psychotherapy does not carry the health risks that are associated with antidepressant use – risks such as sexual dysfunction and mortality. That is why psychological treatments should be the initial treatment choice. If used at all, antidepressants should be a last resort, to be used only when other, less invasive treatments have failed.

SEPCyS: In the current context of economic crisis, do you believe that the current mental health model, based on the prescription of medication from primary care settings and specialized care units is efficient and sustainable?

I.K.: Cost/benefit analyses show that the provision of cognitive and behavioral psychotherapy for depression is cheaper in the long run that medication. That is because these therapies are brief – lasting from 15 to 20 weeks, and their effects are lasting. In contrast, relapse rates are very high when people are taken off of antidepressants. So to keep them from relapsing, they have to be kept on the drugs for years. That is what makes drug treatment more expensive than psychotherapy in the long run.

SEPCyS: According to that, what should be the role of the psychologist in the Mental Health System?

I.K.: Psychologists can provide therapy and/or supervise its provision by other mental health professionals. This is a much better initial approach to treating depression than medication.

Infocop: A recent editorial published by Nature magazine shows that studies to enhance psychological treatments are scandalously under-supported. Why do you think is that?

I.K.: Because there are no large companies that stand to profit from this research and are therefore willing to fund it.