Medical marijuana research

Research in the medical marijuana field is burgeoning as governments consider changing policy in favour of legalizing the marijuana plant *Cannabis sativa*.[1] Like any modern research effort, the gold standard for assessing a new treatment for efficacy compares the treatment to a placebo group. However, controlling for the placebo effects of marijuana may be extremely difficult, and several confounding effects must be considered.

The placebo effect is an improvement in health or behaviour that engulfs a biopsychosocial phenomenon attributable to the placebo and treatment context. On the psychosocial end of the placebo effect spectrum, "the meaning effect" is a similar notion that pertains to the meaning attached to the treatment, as well as the setting and the context of the medical encounter. On the psychobiological end of the spectrum, researchers highlight the central role of expectation, suggestion and conditioning in placebo-related phenomena. New treatments are compared to placebos because placebo effects are very strong — often stronger than the effects of the treatment.

With marijuana, several placebo effects come into play.

Marijuana has a distinct smell and taste, which may elicit classical conditioning responses. Placebo science research holds strong evidence for the effect of classical conditioning related to odour and taste: caffeine-associated stimuli, like the smell and taste of coffee, for example, are shown to increase skin conductance responses and startle eyeblink reflexes in the absence of caffeine. In addition, visual cues associated with smoking marijuana, such as cigarettes, smoke or lighters, may elicit the placebo effect and still remain a factor in even the most well-controlled recent studies.[2,3]

The method of marijuana administration and dose in new trials can carry powerful placebo effects. Will the marijuana be inhaled, injected, or administered topically or sublingually? Placebo science shows that placebo injections work better than placebo pills, and that four placebos work better than two. The strength of the effect of marijuana may differ greatly depending on the method of administration. Medical marijuana research describes several routes of administration, including injecting the psychoactive ingredient delta-9-tetrahydrocannabinol (THC), taking an oral THC capsule or spray, and smoking a marijuana pipe or cigarette. These differing methods of administration will each carry their own placebo effects; grouping such findings together should be avoided.

There is a way to overcome the interference between treatment and placebo effects of marijuana. We can take these lessons from placebo analgesia studies. Studies comparing hidden treatments (e.g., using a computer-controlled infusion machine that is preprogrammed to dispense medication at a desired time) with open administration (where medication is given overtly by a physician or nurse) can eliminate the placebo component. Because patients do not know that the drug is being injected, expectations of a therapeutic response are eliminated. Indeed, a trial conducted by Benedetti and colleagues[4] showed that a cholecystokinin (CCK) antagonist induced stronger analgesia than a placebo, suggesting that it was a good analgesic. However, this conclusion proved to be erroneous, because a hidden injection of the same CCK antagonist was totally ineffective, showing that it had no intrinsic analgesic pharmacodynamic action; instead, it enhanced placebo-activated release of endogenous opioids.[5,6] If similar studies are replicated with THC, researchers may be able to elucidate the pain-relieving properties of marijuana's primary psychoactive ingredient.

The marijuana research field is new. Standardized methods need to be developed so researchers can properly evaluate the effectiveness of this treatment for various disorders. Controlling for the powerful placebo effects of marijuana will bring the scientific community one step closer to identifying which conditions this treatment may be most useful for, and how it is best administered.

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Why conscientious objection merits respect

In his important commentary on respecting conscientious objection to the provision of physician-assisted death (PAD), Dr. Fletcher cites the long-standing tradition of tolerance within the Canadian medical community.[1] We wish to point out several more reasons for respecting conscientious objection to PAD.

First, there is no duty in Canadian law or medical ethics for physicians to provide access to PAD. In the Carter decision, the Supreme Court of Canada explicitly stated that legalizing PAD did not entail a duty on the part of physicians to provide PAD.

Second, physicians frequently decline to offer treatments because they deem them nonbeneficial or harmful.[2] Insofar as all refusals of therapy are ultimately justified by the ethical belief that the goal of therapy is to provide benefit and avoid harm, all treatment refusals are matters of conscience.

Third, the ethical justification of PAD remains debatable because it relies on uncertain metaphysical assumptions about the benefit of death[3–5] and contravenes widely held basic moral intuitions about the inestimable intrinsic value of humans.[6] Because it remains distinctly possible that PAD is unethical, objecting physicians should not be forced to facilitate access to PAD for their patients.

Fourth, physicians are ethically complicit when they deliberately refer a patient for a specific intervention.[7] For