

The Effect of Patient Beliefs About Treatment Allocation on Outcomes in Clinical Addiction Trials

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Background

In clinical trials participants are told that they have an equal chance of receiving either an active drug or placebo. Which of these they *believe* they have been given can have a profound impact on the way they respond to their treatment during the trial. We asked participants enrolled in a trial testing the efficacy of a cannabis agonist (nabiximols) for treating cannabis dependence¹ what treatment (nabiximols vs. placebo) they believed they had been assigned to, in order to determine if their beliefs predicted their response to treatment over and above their actual treatment.

Results: Actual Treatment predicting Believed Treatment

Table 1. Actual Treatment vs Believed Treatment

		Believed Treatment					
		Week 4		Week 8		Week 12	
		Plac	Nab	Plac	Nab	Plac	Nab
Actual Treatment	Plac	20 (39%)	32 (61%)	16 (43%)	21 (57%)	18 (47%)	20 (53%)
	Nab	7 (14%)	43 (86%)	2 (6%)	31 (94%)	5 (14%)	28 (78%)

Note: Plac = Placebo, Nab = Nabiximols. Shading indicates cells where believed treatment did not match actual treatment.

- The Nabiximols group were 3.8 times more likely to believe they had received nabiximols at week 4 ($p=0.007$; CI 1.5,10.8), 11.8 times at week 8 ($p=0.002$; CI 3.0,79.8), and 5.0 times at week 12 ($p=0.006$; CI 1.7,17.4).
- At all time points **over half of the Placebo group believed they had been receiving nabiximols.**

Discussion

Among the participants who received placebo, those who believed they had received nabiximols used significantly less cannabis than those who believed they had received placebo. This suggests that the belief one has received an agonist drug can reduce illicit drug use even in the absence of the active agent.

Methods

Number of days' use of illicit cannabis in the previous 28 days and beliefs about treatment allocation were measured in research interviews once every four weeks during the 12-week trial. Two analyses were performed at each of three time points (4 weeks, 8 weeks, and 12 weeks). First, how well treatment allocation predicted belief in treatment allocation was assessed by logistic regression. Second, days' use of illicit cannabis (outcome) was regressed on **Actual Treatment** (Received Nabiximols vs Received Placebo) and **Believed Treatment** (Believed Nabiximols vs Believed Placebo) to determine the relative influence of pharmacology and belief on treatment outcomes

Results: Believed Treatment predicting Cannabis Use

- The 2 x 2 regressions were highly unbalanced due to very low numbers in the Received Nabiximols/Believed Placebo group (see Table 1). Therefore days' use was regressed on Believed Treatment at each level of Actual treatment.
- There were no significant differences in cannabis use due to Believed treatment in the Received Nabiximols group.**
- Days' use was lower in the Believed Nabiximols group at all time points. Specifically
 - Week 4:** estimate = -5.3 days; $F_{43}=2.87$; $p=0.093$
 - Week 8:** estimate = -8.4 days; $F_{32}=6.02$; $p=0.016$
 - Week 12:** estimate = -7.2 days; $F_{25}=3.52$; $p=0.064$
 - All time points:** estimate = - 5.2 days; $F_{123}=2.78$; $p=0.006$

Figure 2. Effect of Believed Treatment on Frequency of Illicit Cannabis Use

