

The thrill is gone -- or is it? Insights from more than 28,000 heavy opioid users.

In a large and ongoing collaborative study with 23andMe (n= 28,802), we have collected data about the initial subjective responses to opioids and how those responses changed during their periods of heaviest use (>1 month of daily or almost daily use). Contrary to our expectations, approximately 50% of users reported no change between their initial subjective response and their subjective response after chronic use. For example, in response to the question "to what extent did you like the way [prescription opioid medications] made you feel overall?" responses were identical for the two time points for about 50% of the research participants. When we divided participants into groups who did or did not self-report opioid use disorder (OUD- vs OUD+), we found that the OUD+ group showed greater changes during their period of heaviest use. Specifically, they showed greater tolerance to both positive (e.g. euphoria) and negative (e.g. dizzy) drug effects. This was most pronounced in individuals who started with higher levels of sensitivity (e.g. extremely, very much), who showed tolerance. Conversely, OUD+ subjects that began with lower levels of endorsement showed greater sensitization, especially to positive subjective effects. Differences between the OUD+ and OUD- groups should be interpreted with caution because the doses used by the OUD+ group may have been larger, leading to greater degrees of tolerance and sensitization. These results challenge key aspects of the allostatic model of addiction, because they identify large numbers of OUD+ individuals who continue to experience hedonic drug effects even during periods of heavy use. Additionally, they identify other OUD+ individuals reporting sensitization to positive drug effects after chronic use.

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