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REPLY

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# Incentive-sensitization and drug 'wanting'

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We commend Zernig et al. (2003) for trying to incorporate incentive-sensitization concepts into traditional behavioral pharmacology. However, their present formulation suffers from three crucial misunderstandings. Zernig et al. (2003) said that we "propose that increased drug consumption is not due to tolerance but to *sensitization* to the drug's reinforcing effect or ... an increase in drug 'wanting'". Then, they presented an alternative explanation. It is difficult to defend a position one never took in the first place, but that is the position we find ourselves.

The initial error Zernig et al. (2003) made regarding incentive-sensitization was to say that drug reinforcement roughly corresponds with what we have called drug "wanting". "Wanting" is a short-hand term for the process of incentive salience attribution, not reinforcement (Robinson and Berridge 1993, 2000, 2003; Berridge and Robinson 1998). To equate reinforcement with "wanting" badly distorts the concept of incentive salience and incentive-sensitization theory. We have said it before and we say it again: drug reinforcement does NOT correspond to drug "wanting".

In our initial paper on this topic (Robinson and Berridge 1993), we included a glossary of terms, including reinforcement, incentive salience and "wanting". That glossary defined reinforcement in the standard Skinnerian way, as "a purely behavioral and descriptive term for the relationship between the occurrence of a stimulus and changes in the subsequent probability of a behavior" (see p. 281 for the full entry). By contrast, we have consistently defined "wanting" in terms such as, "it is the process of incentive salience attribution that transforms the sensory features of ordinary stimuli or, more accurately, the neural and psychological representations of stimuli, so that they become especially salient stimuli, stimuli that "grab the attention", that become especially attractive and wanted, thus eliciting approach and guiding behavior to the goal. It is incentive salience that determines the value of incentives" (Robinson and Berridge 2000, p S105).

These are obviously very different concepts. We have gone to considerable lengths to distinguish incentive salience from reinforcement, and have pointed out limitations of Skinnerian reinforcement, even arguing that "behaviorist reinforcement should not be mistaken to be an explanation of either drug-taking or addiction in either a physiological or psychological sense" (Robinson and Berridge 2000, p S93; Berridge and Robinson 2003).

Zernig et al. (2003) made their second error about incentive-sensitization when they said that we claim incentive-sensitization to be manifest by an upward shift in a cocaine dose–response rate curve. It could be, but we have never said this, because we do not believe an upward shift (or a shift in any direction) in a cocaine dose–response rate curve *necessarily* indicates sensitization to anything. If anyone else has said it, we think they might misunderstand incentive-sensitization theory.

The kinds of dose–response rate functions discussed here are simply the wrong instrument to properly test incentive-sensitization, because they do not specifically measure changes in incentive processes. The rate of drug self-administration is susceptible to influence by too many other processes distinct from incentive salience, such as S-R habit effects, tolerance effects, hedonic effects, cognitive effects, aversive effects, and other effects of drugs. Shifts in dose–response rate functions could be due to changes in any of these processes, making them ambiguous to interpret (Wyvell and Berridge 2000; Berridge and Robinson 2003; Robinson and Berridge 2003).

To measure incentive salience separately from other effects, it is necessary to use paradigms that more specifically probe it alone, such as Pavlovian conditioned incentive procedures (e.g., Cardinal 2002; see for discussion Wyvell and Berridge 2000, 2001; Berridge and

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Robinson 2003; Robinson and Berridge 2003). Importantly for incentive-sensitization theory, Pavlovian conditioned motivational responses have been shown to sensitize (Cardinal 2002). Indeed, sensitization of Pavlovian motivational processes might be responsible for the facilitatory effects of past drug treatment on the acquisition of drug self-administration behavior (Piazza et al. 1989; Horger et al. 1990), conditioned place preference (Lett 1989) and progressive ratio responding (Mendrek et al. 1998; Lorrain et al. 2000), even though those are not specific tests for incentive motivation. As we recently said (Robinson and Berridge 2003, p 41–42), "the evidence for sensitization of drug reward pursuit ... is compatible with the incentive-sensitization view of addiction, but it is not conclusive, because it could be alternatively explained by changes in a number of other components of reward or learning (Wyvell and Berridge 2000; Cardinal et al. 2002)." "In order to test whether sensitization can *specifically* enhance incentive salience or "wanting" triggered by reward cues (S–S associations), it is necessary to design experiments so as to exclude alternative explanations." We then go on to explain how.

Finally, Zernig et al. (2003) asked, 'why do addicts escalate their dose?', and they answered that it is due to tolerance to the rate-decreasing effects of cocaine (including aversive effects). Although incentive-sensitization could conceivably lead to dose escalation, their view actually sounds similar to an alternative view we expressed long ago. We wrote a decade ago that addicts may "increase dose to achieve the more intense (and more desirable) subjective effects produced by larger doses. They are able to do this only because tolerance develops to the *aversive* 'side effects' of drugs. That is, addicts increase their dose because they can, without the dire negative effects experienced by naive users. Doses that might be unpleasant, or even life-threatening, in inexperienced users, are 'tolerated' by experienced users because of tolerance to many of the drug's negative effects, including effects on the autonomic nervous system" (Robinson and Berridge 1993, p 275). This sounds very similar to the "new" view advocated by Zernig et al. (2003), and so we come full circle. Tolerance to aversive effects did not exclude a role for incentive-sensitization in addiction in 1993, and it does not exclude incentive-sensitization now. These two concepts are not mutually exclusive explanations for the same phenomenon. They are explanations for different phenomena and are quite mutually compatible.

We applaud efforts to incorporate incentive-sensitization concepts into operant behavioral pharmacology, but we close with a fervent wish for fewer errors in the future. To paraphrase the great American poet, Robert Frost (from "The Fear of Man"):

"May we in our brief bolt across the scene
Not be misunderstood in what we mean."

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