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Midazolam amnesia and short-term/working memory processes

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Abstract

We examined whether midazolam impairs short-term/working memory processes. We hypothesize that prior dissociations in midazolam's effects on short-term/working memory tasks and episodic memory tasks arise because midazolam has a larger effect on episodic memory processes than on short-term/working memory processes. To examine these issues, .03 mg/kg of participant's bodyweight of midazolam was administered in a double-blind placebo-controlled within-participant design. Performance on the digit span and category generation/recall tasks was examined. The results of Experiment 1 demonstrated that: (1) midazolam impaired performance on the digit span task; (2) midazolam did not impair performance on the category generation task; (3) midazolam impaired performance on the category recall task; and (4) midazolam's effect on category recall was four times as large as its effect on digit span. The results of Experiment 2 demonstrated that midazolam did not impair digit span performance when the digit span task was administered at a later time. These results suggest that midazolam can impair short-term/working memory processes, but these effects are substantially smaller than midazolam's effect on episodic memory processes. Moreover, they demonstrate that conscious awareness of materials during study is not sufficient to produce episodic memory.

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1. Introduction

Benzodiazepines are well known for producing anterograde amnesia (Curran, 2000; Mewaldt, Hinrichs, & Ghoneim, 1983). The benzodiazepine, midazolam, produces dense anterograde amnesia (Polster, McCarthy, O'Sullivan, Gray, & Park, 1993). This amnesia appears to reflect midazolam's specific effect on encoding processes in episodic memory. To demonstrate this, Polster et al. (1993) administered midazolam prior to study and/or test on a recognition memory task—a standard test of episodic memory. Polster et al. found that midazolam only produced amnesia when injected prior to study. Moreover, there was no evidence that injecting midazolam prior to test reduced the amnesia produced by injecting midazolam prior to study. These results suggest that midazolam amnesia does not reflect impaired retrieval from long-term memory and that it is not a state-dependent effect. In the same vein, Veselis, Reinsel, Feschenko, and Wronski (1997) demonstrated that midazolam amnesia can occur independently of sedation, suggesting that midazolam amnesia is not due solely to general effects on arousal level or motivation. (See Mewaldt et al. (1983) for similar results with other benzodiazepines.)

In considering theoretical explanations of midazolam amnesia, an important question concerns whether administering midazolam impairs short-term/working memory processes (Miyake, 2001). Classical theories of episodic memory (e.g., Raaijmakers & Shiffrin, 1981) assume that encoding in episodic memory relies heavily on short-term/working memory processes. Thus, midazolam's effect on encoding processes in episodic memory may arise because it impairs short-term/working memory processes.

Determining whether midazolam impairs short-term/working memory processes also provides evidence on the role of consciousness in episodic memory encoding. While it is clear that conscious experience of materials during study contributes to episodic memory performance (Jacoby, 1998), this does not imply that consciousness of materials is sufficient to produce episodic memory. If midazolam can impair episodic memory performance without impairing short-term/working memory processes, this would suggest that consciousness of materials during study is not sufficient to produce episodic memory.

At sufficiently high doses, benzodiazepines produce extreme sedation and unconsciousness (Andrade, Sapsford, Jeevarathum, Pickworth, & Jones, 1996). Under these conditions, short-term/working memory processes are necessarily impaired because participants do not attend to presented information. We focus here on the more interesting case in which the dose of midazolam is set so that the associated sedation is minimal. In this case, participants are responsive and can perform a variety of tasks in the midazolam condition, even though they demonstrate dense anterograde amnesia. For example, Hirshman, Fisher, Henthorn, Arndt, and Passannante (2003) demonstrated that participants administered a .03 mg/kg of bodyweight dose of midazolam demonstrated no impairment in a category generation task, even though their later recall of these category items was substantially impaired.

Current evidence on whether midazolam affects short-term/working memory processes is ambiguous. There is substantial prior evidence (Ghoneim & Mewaldt, 1975; Knopman, 1991) that