Sir,—We read with interest the study by Takada and colleagues [1] on the effects of midazolam and flunitrazepam on the release of dopamine from rat striatum.

Recently, we postulated that benzodiazepines may reduce the synthesis, release and postsynaptic effect of dopamine centrally [2]. This action at the chemoreceptor trigger zone is a possible mechanism for the antemetic effect of benzodiazepines [2]. Analysia mediated by benzodiazepine binding to the GABA-A receptor complex may also contribute to the antemetic effect by reducing the psychic input to the vomiting centre [2].

The study by Takada and colleagues [1] supports the hypothesis that benzodiazepines reduce dopamine release centrally. However, they suggest that the effect is mediated by benzodiazepine binding to the GABA-A receptor complex, causing inhibition of dopaminergic neuronal activity. The reason given for this conclusion is that the benzodiazepine effect on dopamine release was abolished by flumazenil.

It has been shown that flumazenil is also an adenosine antagonist [3]. Benzodiazepines block the re-uptake of adenosine and some of their central effects may be explained by an increased adenosine action [3]. Adenosine, a central neuromodulator, has been shown to inhibit nigrostriatal dopamine release by an adenosine-A_{1}-receptor mediated effect [4].

The alternative explanation for the reduced release of dopamine after administration of midazolam and flunitrazepam is that benzodiazepines block the re-uptake of adenosine, causing an adenosine-mediated reduction in dopamine release [2]. This effect can be blocked by flumazenil acting as an adenosine antagonist.

The regional differences in the effects of midazolam and flunitrazepam found by Takada and colleagues [1] may reflect the differing activities of the drugs on adenosine neuromodulation, the GABA-A receptor complex or both. Obviously, further studies are required to clarify this problem.

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