ELSEVIER

LETTER TO THE EDITOR

# Effects of Scopolamine on Human Brain Glucose Consumption

Results recently published by Molchan et al. (1994) on the effects of scopolamine on human brain glucose consumption differ in several respects from our earlier findings (Blin et al., 1991, 1992, 1993, 1994a, 1994b). Because Molchan et al. (1994) did not address these differences, it may be useful to attempt to reconcile their observations with ours.

The methods used by Molchan et al. (1994) were generally similar to ours. However, we administered drug and placebo on different days to blinded subjects in random order, and analyzed the data using repeated measures ANOVA and $t$ tests corrected for multiple comparisons. We found that in six individuals administered scopolamine, their metabolic values showed significant variation by region ($p < .001$, ANOVA) (Blin et al., 1994a). After adding three more subjects ($n = 9$) ($p < .0001$, ANOVA), the result held (Blin et al., 1994b). The effect of scopolamine was a metabolic increase (compared with the placebo), affecting whole brain values (14–16%) as well as all regions of the cerebral cortex (ranging from 10% in the prefrontal cortex to 21% in the occipital cortex). The scopolamine-induced changes correlated with the effects of physostigmine measured in the human brain (Blin, 1992, 1994a) as well as with the effects of scopolamine and physostigmine measured in the rat brain (Blin 1993, 1994b).

In the work by Molchan et al. (1994), the volunteers were studied twice during a single day, and scopolamine was administered just before the second scan. Since the second dose of ($^{18}$F)2-fluoro-2-deoxy-D-glucose (FDG) was infused two hours after the first FDG injection, residual radioactivity had to be removed from the second scan before calculating glucose consumption. Differences between the two scans were analyzed using paired $t$ tests, without correcting for multiple comparisons. In six out of the 60 examples analyzed, the authors observed a significant decrease in regions of the frontal and occipital cortex, and an increase in regions of the parieto-occipital or middle temporal cortex. Scopolamine produced no significant alteration in whole glucose consumption.

This lack of global effect as well as the magnitude and distribution of the small regional variations found with scopolamine by Molchan et al. (1994) do not fit with the relatively large scopolamine effects observed in our studies. Several factors may contribute to these discrepancies. Molchan et al. did not randomize the order of scopolamine administration between the first and the second scan. Moreover, they did not use a scopolamine placebo, and thus their subjects were not blinded. Their lack of controlling for the order of administering the scopolamine could be particularly important because, in our data, the order had a clear effect ($p = .003$) and because the effects of scopolamine might be masked by the correction of residual radioactivity. Therefore the lack of controlling for placebo effect and blind condition, the residual radioactivity, or the order effect could explain the lack of clear effects of scopolamine in Molchan et al. (1994).

Jerome Blin, M.D., Ph.D.
University of Louvain
Brussels, Belgium

Tom Chase
Experimental Therapeutics Branch
National Institutes of Health
Bethesda, Maryland

## REFERENCES

Blin J, Ownby JH, Gupta S, Giacometti KR, Giuffra ME, Mouradian MM, Chase TN (1991): Effect of scopolamine


Published 1995 by Elsevier Science Inc.
655 Avenue of the Americas, New York, NY 10010

0893-133X/95/$9.50
SSDI 0893-133X(95)00022-6

on brain glucose consumption in humans. J Cereb Blood Flow Metab 11(suppl 2):S875

Blin J, Giuffra ME, Ownby JH, Giacometti KR, Mouradian MM, Gillepsie M, Piercey MF, Chase TN (1992): Physostigmine and scopolamine effects on glucose metabolism measured with positron emission tomography (PET) in human brain. Neurology 42(suppl 3):714P

Blin J, Ray CA, Piercey MF, Ownby JH, Giuffra ME, Bartko JJ, Mouradian MM, Chase TN (1993): Comparison of physostigmine and scopolamine effects on regional cerebral glucose metabolism in rats and humans. J Cereb Blood Flow Metab 13(suppl 1):S576

Blin J, Piercey MF, Giuffra ME, Mouradian MM, Chase TE (1994a): Metabolic effects of scopolamine and physostigmine in human brain measured by positron emission tomography. J Neurol Sci 123:44–51

Blin J, Ray C, Piercey M, Bartko JJ, Mouradian MM, Chase TN (1994b): Comparison of cholinergic drug effects on regional brain glucose consumption in rats and humans by means of autoragraphy and positron emission tomography. Brain Res 635:196–202

Molchan SE, Matochik JA, Zametkin AJ, Szymanski HV, Cantillon M, Cohen RM, Sunderland T (1994): A double FDG/PET study of the effects of scopolamine in older adults. Neuropsychopharmacology 10:191–198