In Press: In "Neurochemical and Behavioral Mechanisms of Alcohol and Opiate Dependence" ed. K. Blum, Academic Press, 1976

ROLE OF PHOSPHATIDYL SERINE IN THE OPIATE RECEPTOR*

L. G. Abood, F. Takeda, and N. Salem, Jr.

Center for Brain Research
and
Department of Biochemistry

University of Rochester Medical Center
Rochester, New York 14642

INTRODUCTION

The molecular nature and configuration of the opiate receptor is a problem under intensive investigation in a number of laboratories (1, 2, 3). Our interest in the problem developed as a result of a finding of others (4) that a proteolipid fraction from brain may be responsible for stereospecific opiate binding observed in various preparations of brain tissue. Upon examining various lipids, proteolipids, and proteins from membranes derived from brain, it was found that phosphatidyl serine (PS),† the major acidic lipid in brain, exhibited stereospecific opiate binding (5). Since the K_d's for the opiate-PS complex and the opiate-tissue complex differed by three orders of magnitude, it was recognized that the binding to PS was nonspecific and different from the high affinity binding to membrane preparations. What interested us was the possibility that PS, in the form of a complex with a membranous protein, may be an important component of the opiate receptor.

In an effort to test this hypothesis a study was undertaken on the effect of added phospholipids on opiate binding. It had been known for many years that exogenous lipids were capable of exchanging with endogenous ones with no apparent alteration in their natural functional or structural characteristics (6). It was demonstrated that the addition of PS to suspensions of synaptic membranes significantly enhanced both high and lower affinity binding, the K_d's without lipid being 1.0×10^{-9} M and those with lipid being 5.0×10^{-10} M and 3.8×10^{-7} M respectively (7). Another observation of interest was that exogenous PE was inhibitory to opiate binding. The present report describes studies aimed at extending the initial findings on the PS-enhancement and to attempt to understand the role of PS and other phospholipids in opiate binding.

---

*This research was supported by USPH grant DA 00464.

†The following abbreviations are used: PS = phosphatidyl serine, PC = phosphatidyl choline, PE = phosphatidyl ethanolamine, PA = phosphatidic acid, PI = phosphoinositides, CTAB = cetyltrimethylammonium bromide, CPC = cetylpyridinium chloride, FSC = cationic "Zonyl" fluorosurfactant (DuPont), SDS = sodium dodecylsulfate, DNDFB = dinitrodifluorobenzene, ^{3}H-DHM = ^{3}H-dihydromorphine.