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# Pentobarbital modifies the lipid raft-protein interaction: a first clue about the anesthesia mechanism on NMDA and $GABA_A$ receptors

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**Abstract**

Recent studies have shown that anesthetic agents alter the physical properties of lipid rafts on model membranes. However, if this destabilization occurs in brain membranes, altering the lipid raft-protein interaction, remains unknown. We analyzed the effects produced by pentobarbital (PB) on brain plasma membranes and lipid rafts *in vivo*. We characterized for the first time the thermotropic behavior of plasma membranes, synaptosomes, and lipid rafts from rat brain. We found that the transition temperature from the ordered gel to disordered liquid phase of lipids is close to physiological temperature. We then studied the effect of PB on protein composition of lipid rafts. Our results show a reduction of the total protein associated to rafts, with a higher reduction of the NMDAR compared to the $GABA_A$ receptor. Both receptors are considered the main targets of PB. In general, our results suggest that lipid rafts could be plausible mediators in anesthetic action.

*Keywords:* `Anesthesia, Calorimetry, Lipid membrane, Receptors.`

## 1. Introduction

Recent reports highlight the role of lipid rafts in biological processes. Examples of these are: virus fusion [1], immune modulation [2], cancer [3], Alzheimer disease [4], endocytosis [5], T cell activation [6], and neurotransmitter signalling [7], among many others. Therefore, it seems that the classical fluid mosaic model of Singer-Nicolson fails to describe the cell membrane and to fully explain receptor-effector interactions. Lipid rafts are small (10-200 nm), heterogeneous, highly dynamic, sterol- and sphingolipid-enriched membrane domains able to

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