**The local anesthetic phenylethanol modulates transmembrane protein folding**

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The exact mechanism of action of anesthetic is still an open question. While some observations suggest specific anesthetic-protein interactions, nonspecifically induced perturbations of the lipid bilayer have also been proposed to affect the structure and function of membrane proteins indirectly. Here, we have investigated dimerization of the human glycophorin A transmembrane helix (GpA TM) in the presence of the local anesthetic phenylethanol (PEtOH), which is also known as “rose oil”. As a decreased dimerization propensity of the GpA TM was observed in a biological membrane in the presence of PEtOH, TM helix-helix interactions were subsequently studied *in vitro* in model membranes in more detail using fluorescently labeled GpA TM peptides. The results obtained in a detailed FRET analysis indicate that the ability of the GpA TM helix to dimerize decreases with increasing PEtOH concentration. In addition, lipids become significantly more disordered in the presence of PEtOH. The membrane fluidizes and the TM helix dimer dissociates with rates of about 0.60 s-1. Based on our experimental results we suggest that local anesthetics as well as other molecules, which modulate membrane physical properties, can severely influence folding and the structure of membrane proteins, which might subsequently affect TM protein signaling.