bstract: Background: Lipid homeostasis and gut flora can be related to many metabolic diseas□es, especially autism. Lipid metabolism in the brain can control neuronal structure and function and can also take part in signal transduction pathways to control metabolism in peripheral tissues, espe□cially in the liver. Impaired phospholipid metabolism promotes oxidative stress and neuroinflamma□tion and is, therefore, directly related to autism. Objective: The effect of propionic acid (PPA) toxicity on lipid homeostasis in the gut-liver-brain axis was evaluated to understand their inter-connection. Cytosolic phospholipase A2 (cPLA2) con□centration and activity was measured in autistic model and protective role of omega-3 (ω-3) and vi□tamin B12 was evaluated. Methods: Animals were divided into five groups: Group I (control group); Group II (autistic model treated with neurotoxic dose of PPA); Group III (treated with vitamin B12 (16.7 mg/kg/day) for 30 days post PPA treatment); Group IV (treated with ω-3 (200 mg/kg body weight/day) for 30 days post PPA treatment; Group V (combined dose of ω-3 and Vitamin B12, for 30 days post PPA treat□ment). Phospholipase A2 activity and protein expression level in the liver homogenate of all the groups was analyzed by western blotting and was compared to brain cPLA2. Results: PPA increased the levels of liver and brain cPLA2. However, independent or combined treatment with ω-3 and vitamin B12 was effective in neutralizing its effect. Moreover, PPA-in□duced dysbiosis, which was ameliorated with the above treatments. Conclusion : This study showed the role of cPLA2 as a lipid metabolism marker, related to PPA-in□duced inflammation through a highly interactive gut-liver-brain axis.