Introduction and objectives: Disruption of antioxidant systems and oxidative stress are among the mechanisms of lead toxicity. The glutathione and thioredoxin systems are thiol-dependent systems essential for the cell redox control and antioxidant defense. This study investigated the effects of lead subchronic exposure on the glutathione and thioredoxin systems and its relationship with lead-induced neurotoxicity in rats. Materials and Methods: Rats (n=30) were daily injected (i.p.) with lead acetate (AcPb) for 30 days (0, 1, 5 and 20 mg/kg). At 31st day, rats were subjected to the open field behavior test. One day (24 h) later, the animals were anesthetized to collect blood and euthanized to remove brain, which was dissected in pre-frontal cortex, cerebellum and hippocampus. Blood δ-aminolevulinate dehydratase (δ-ALA-D) and blood lead levels (BLL) were evaluated along with brain thioredoxin reductase (TrxR) and glutathione reductase (GR) activity and histopathological analysis (CEUA/UNOCHAPECÓ/014/2013). The results were analyzed by ANOVA/Tukey. Results and conclusion: BLL of all groups remained within the values established by WHO, even though at 20 mg/kg AcPb these values have been higher than those of other groups. δ-ALA-D inhibition, alterations in the exploratory behavior and histopathological analysis occurred at all doses of lead. TrxR activity increased at 5 and 20 mg/kg in the cerebellum and at all AcPb doses in the pre-frontal cortex. GR activity increased only at 5 mg/kg in the cerebellum and at 20 mg/kg in the prefrontal cortex and hippocampus. In summary, lead induced alterations in the behavior animals even at low levels, which indicates that there is no safe limit for neurotoxic effects of lead. Additionally, the increase of both brain TrxR and GR activity suggest that these thiol-dependent systems are not target of lead toxicity, but are likely to be defense lines against the toxic effects of lead.