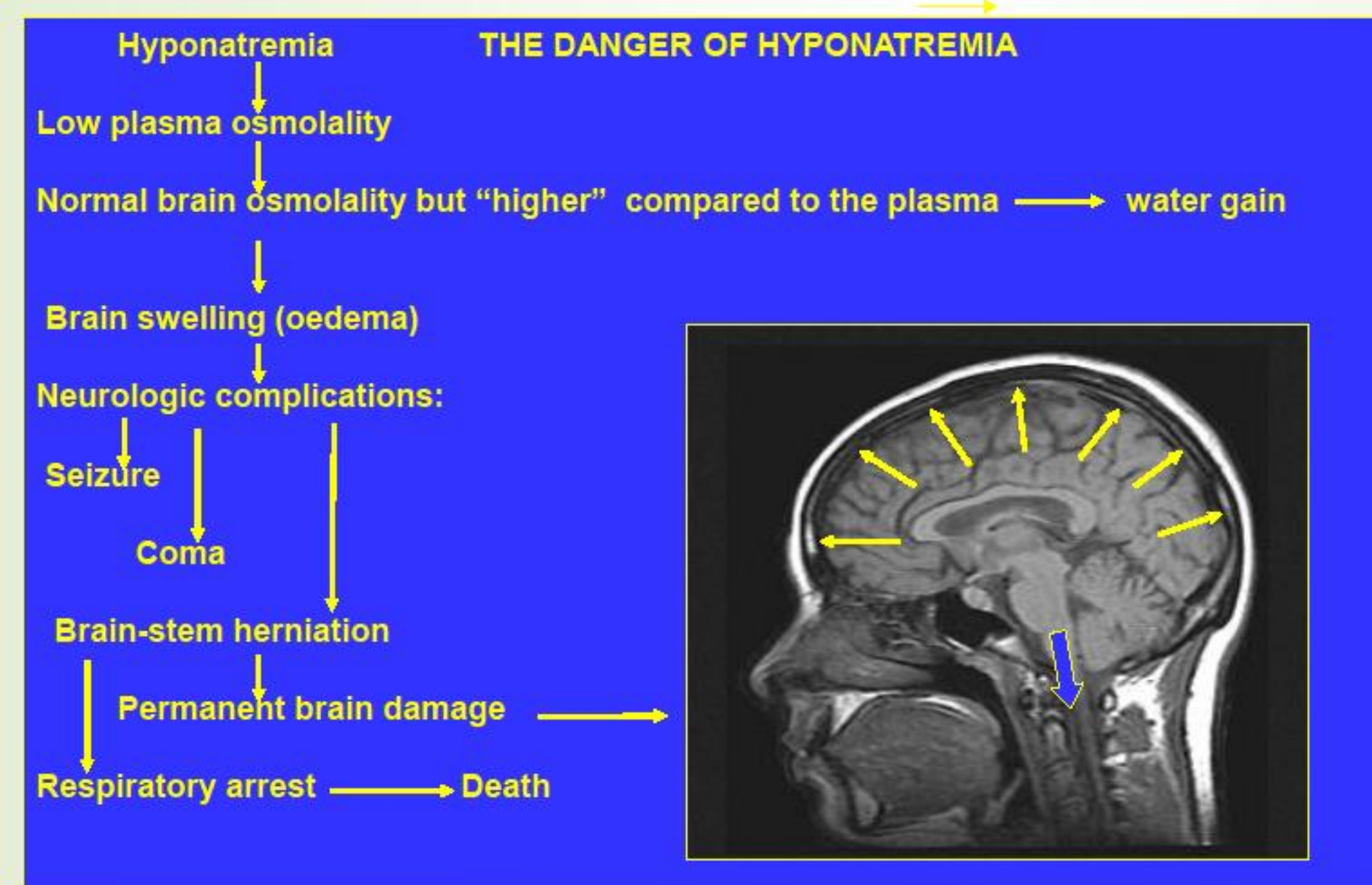
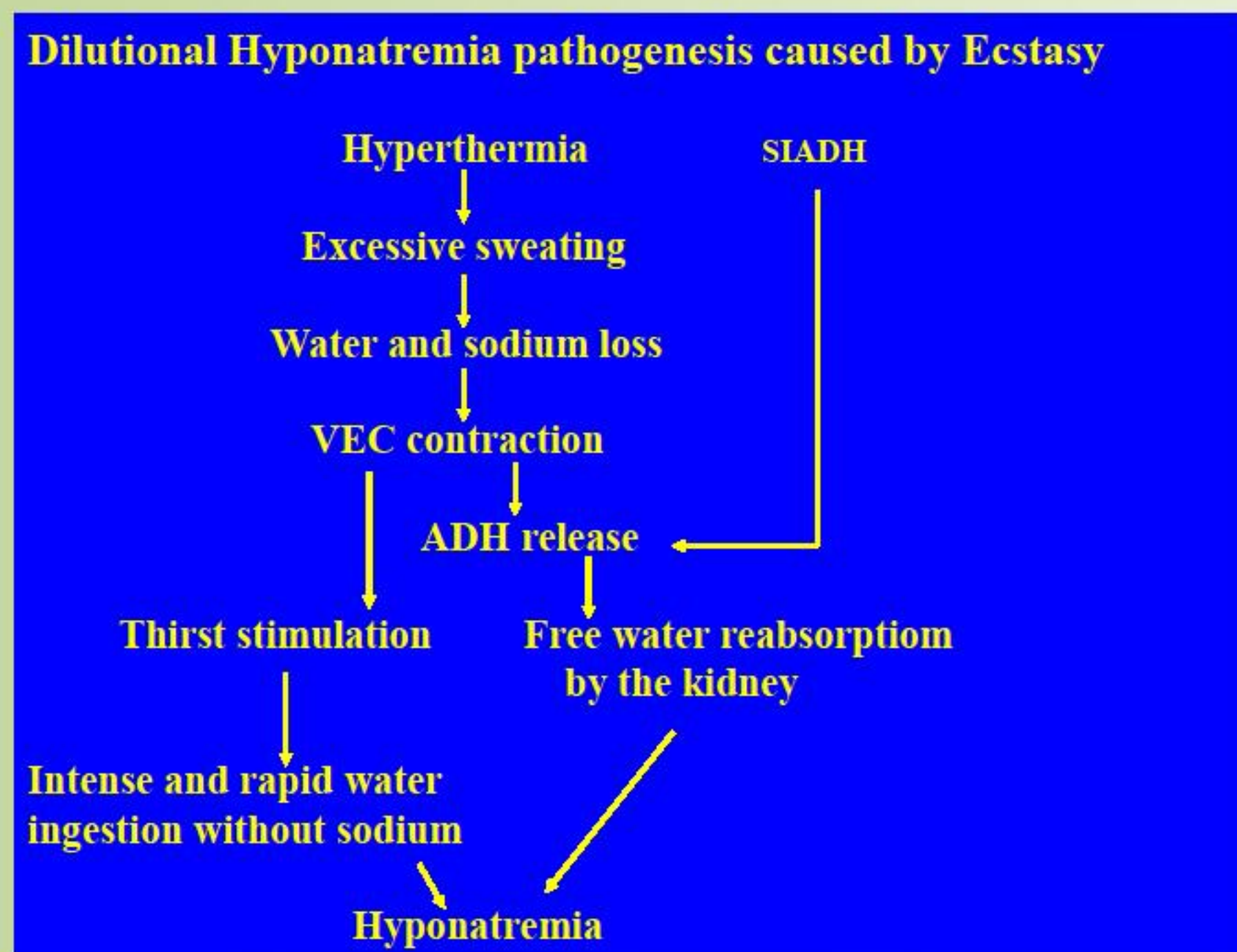
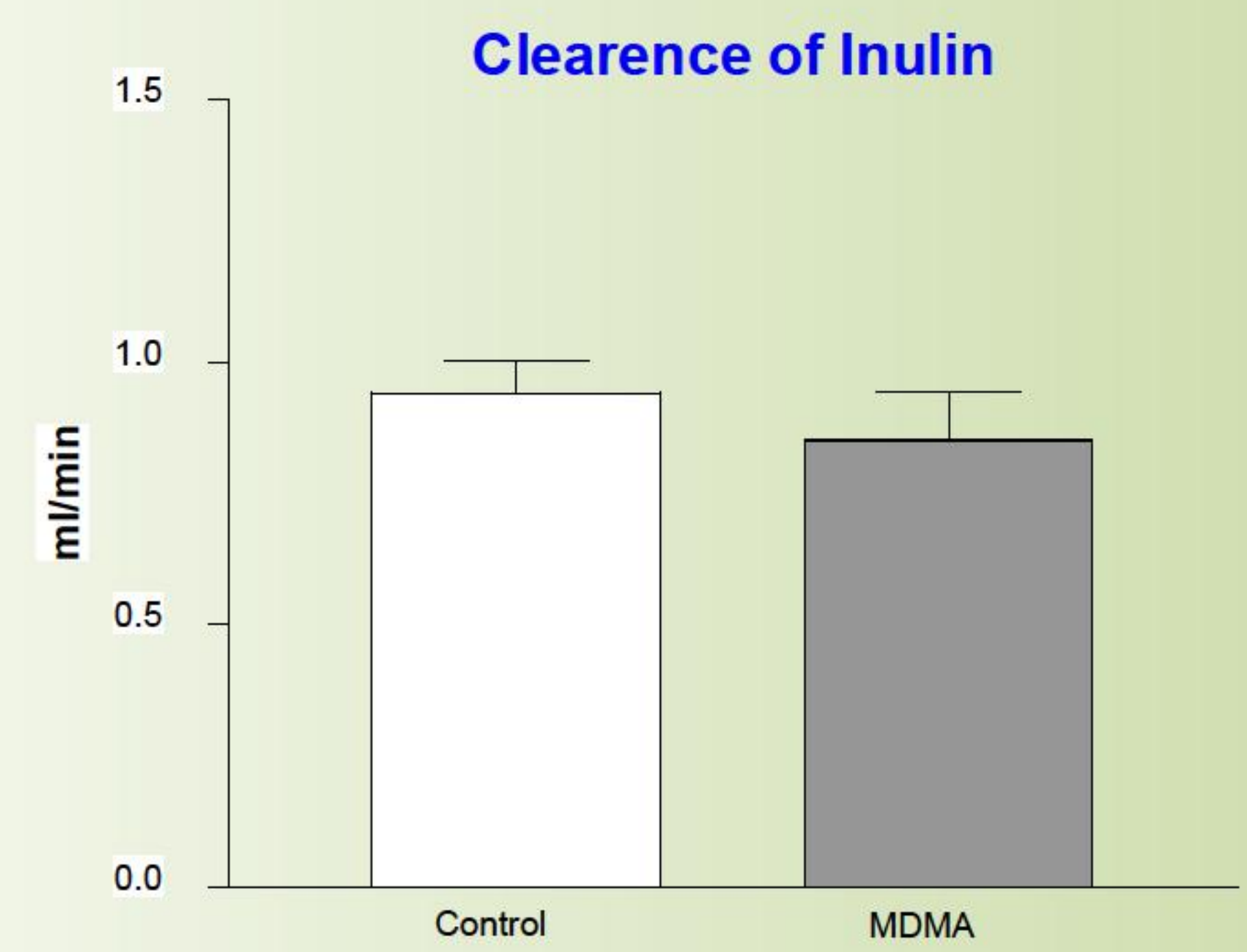


INTRODUCTION

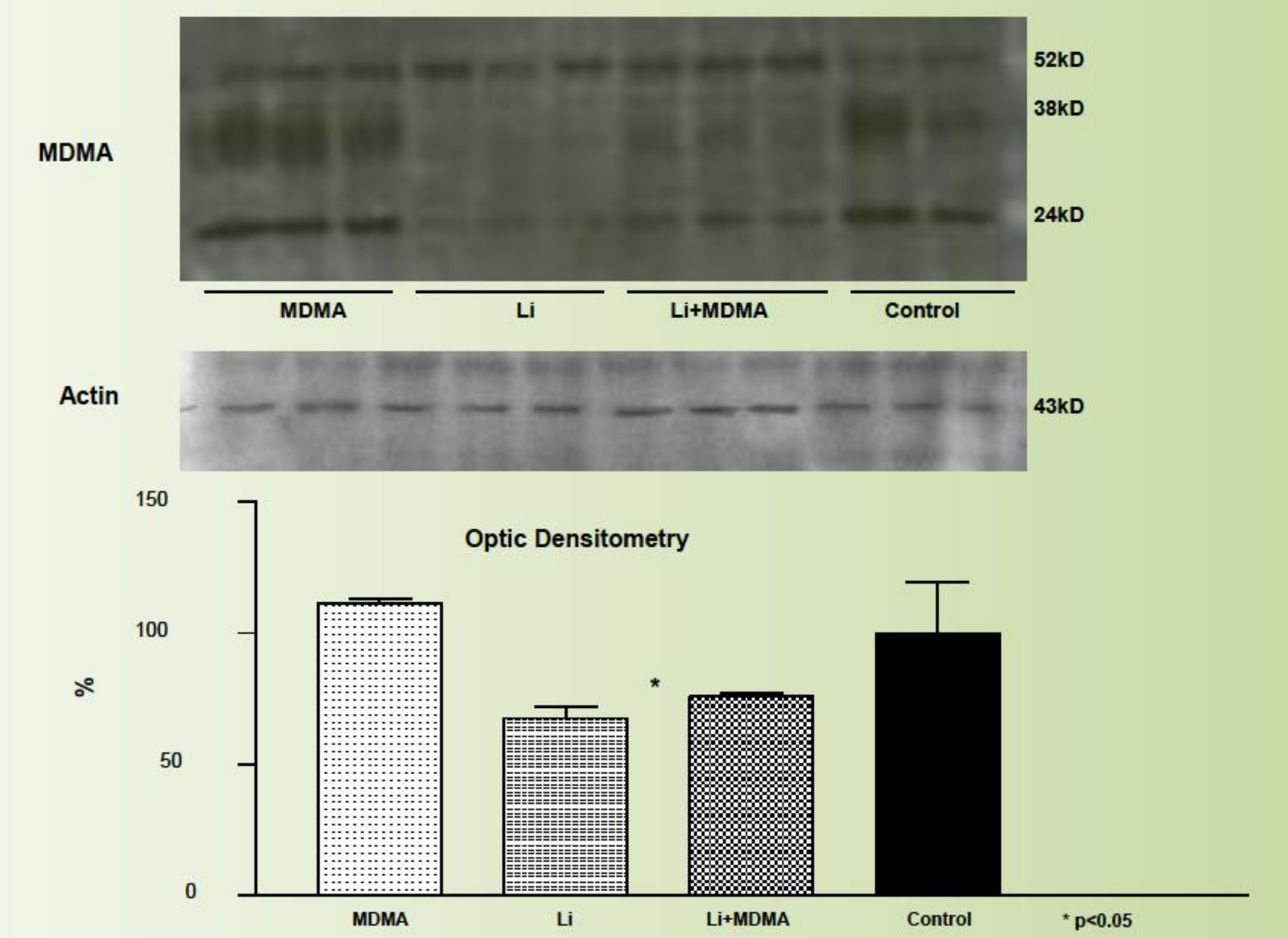
3,4-Methylenedioxymethamphetamine (MDMA or Ecstasy-Ec) is an amphetamine derivative popularly used as a recreational drug of abuse mainly among young people, due its psychotropic properties. However, Ec also produces tachycardia, hyperthermia, high blood pressure, strong sudoresis, intense thirst, multisystemic toxicity, oxidative stress and also an inappropriate antidiuretic hormone secretion. The intense thirst, together with the vasopressin effect, induces a high ingestion of free water, leading to acute hyponatremia, which frequently could cause death.



RESULTS



Aquaporin 2 Western Blot analysis in IMCD from MDMA and Lithium treated rats



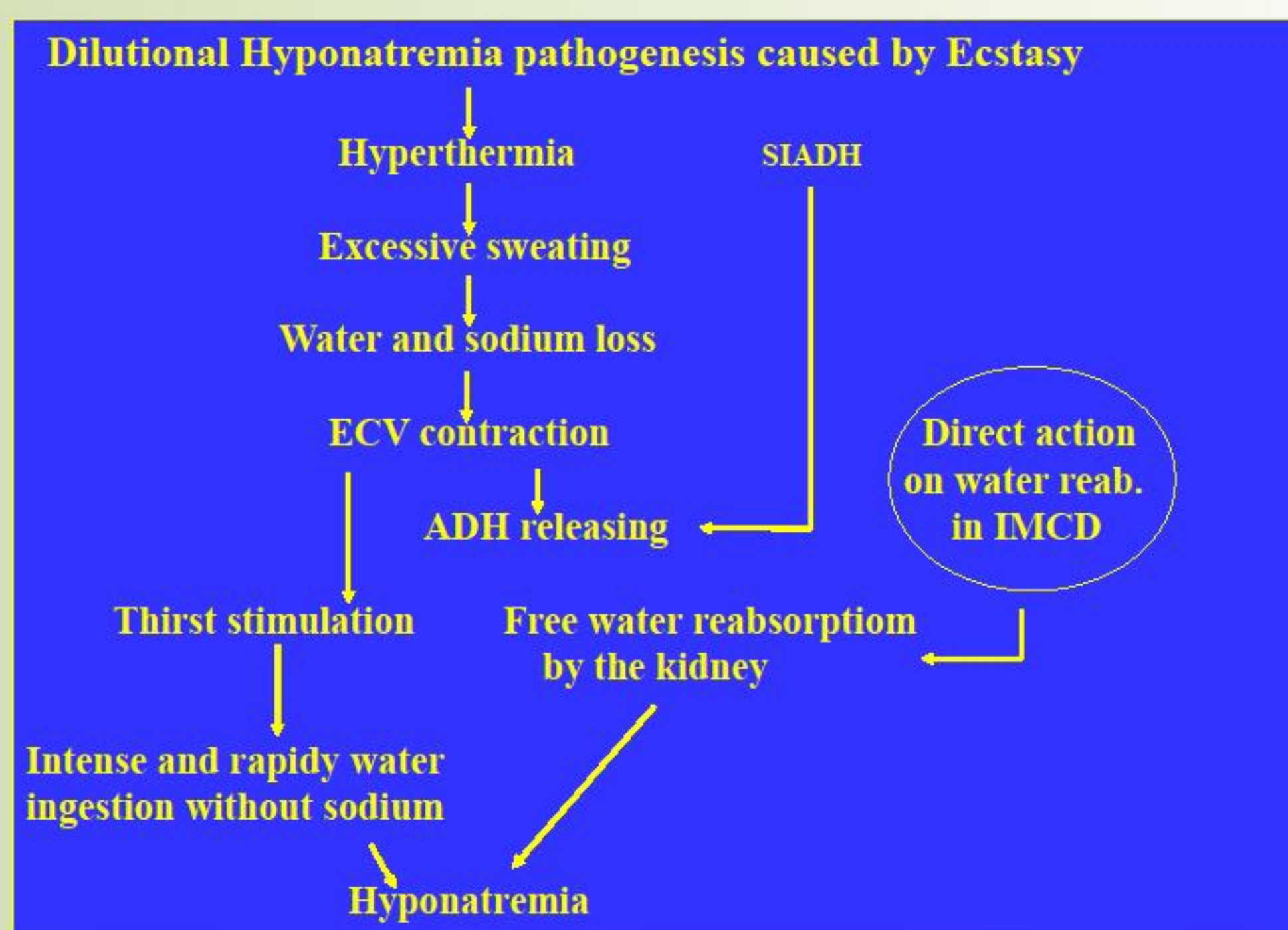
OBJECTIVE

As the hyponatremia is induced rapidly experiments were carried out to investigate a possible effect of the Ec directly on the water transporter in the rat Inner Medullary Collecting Duct (IMCD), measuring the Aquaporin 2 (AQP2) expression. Oxidative Stress (OS) was studied because it has already been reported that Ec can induce the appearance of ROS, causing renal tissue damage. OS was determined by measuring the thiobarbituric acid reactive substances (TBARS) and a reduced form of Glutathione (GSH). To try to decrease the OS, the antioxidant inhibitor N-acetylcysteine (NAC) was used.

Oxidative Stress Protective effect of NAC

	Cont	Group-Ec	Group-Ec+NAC
TBARS	1.92±0.18	2.56±0.11**	1.83±0.19*
GSH	2.71±0.16	1.89±0.10**	3.04±0.12***

n=6 for each groups; * p<0.001xEc, *** p<0.01xEc, ** p< 0.05xCont



METHODS

AQP2 Group – AQP2 expression - rats were maintained on lithium (Li) diet for 5 days to block the Vp action before Ec addition. AQP2 expression was determined by Western Blot techniques in IMCD and measured by densitometric analysis. Ec Group - OS was studied in 6 rats injected i.p. with Ec (10mg/kg), by determining the TBARS (nmoles/24hs) and the GSH (µmol/ml) in the plasma, compared to the control. Ec+NAC Group-OS study in 6 rats previously treated with NAC (added to drinking water- 4.8 mg/L for 5 days) and injected with Ec (Ec+NAC). TBARS and GSH were also determined.

CONCLUSION

Summary and Conclusion- These results showed that the AQP2 abundance was decreased in the presence of lithium but increased in presence of Li+Ec evidencing a proper effect of this drug to increase IMCD water absorption. The increase of water transporter AQP2 expression in the IMCD, demonstrated that there is another mechanism contributing to the rapid hyponatremia that occurs with Ec use. The increase of the TBARS and the decrease of GSH showed an Ec-mediated oxidative stress that was prevented by the previous use of NAC. These results showed that the two effects studied can contribute, at least in part, to a rapid malaise, which in turn can lead to a lethal outcome if not treated correctly and as soon as possible.

