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Optimisation of ketamine-xylazine anaesthetic dose and its association with changes in the dendritic spine of CA1 hippocampus in the young and old male and female Wistar rats

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Abstract

Background: A combination of ketamine-xylazine (K-X) is frequently used for anaesthesia in rats. Sex and age affect this cocktail dosage. Ketamine causes a hypnotic effect by blocking NMDA receptors located on the dendritic spine of the CA1 region.

Objectives: The present study aimed to find the optimal dosage of K-X and its association with the changes in dendritic spine number of the CA1 region for aged and young rats of both sexes.

Methods: We injected 150–4 mg/kg of K-X in young and 100–2 mg/kg in aged Wistar rats intraperitoneally and recorded the onset time and duration of anaesthesia and death percentage. Then, animals were sacrificed, brains removed, cut and after Golgi-Cox staining, the total number of dendritic spines on CA1 was estimated.

Results: The findings showed that the onset time of anaesthesia lasted longer and its duration lasted shorter, and the number of mature spines decreased with aging, but sex caused no significant effect. The death percentages in young groups comprise 20% and in the aged groups were lower: 5% in males and 0.0% in females.

Conclusions: It seems 100–2 mg/kg of K-X is an optimal dose in aged rats and retains an association with reduction of the mature dendritic spine of CA1.

KEYWORDS
aging, anaesthesia, CA1 region, dendritic spine, ketamine, xylazine

1 | INTRODUCTION

The combination of ketamine and xylazine is widely used in anaesthesia for laboratory animals (Richardson & Flecknell, 2005). Ketamine is a glutamate n-Methyl-D-aspartate antagonist that causes proper anaesthesia and analgesia (Whipe et al., 1982). There are some advantages, such as different routes of administration, high safety and the possibility of being combined with other drugs such as xylazine (Gaertner, 2008). Xylazine is an α2-adrenergic agonist with analgesic, sedative and muscle-relaxant properties (Giroux et al., 2015). Ketamine-xylazine (K-X) combination is given collectively by numerous ways of administration, such as intraperitoneal and intramuscular, providing enough surgical anaesthesia time and also it is good pain relief in rats (Buitrago et al., 2008). Administered anaesthetic doses are very different in the literature, with 40–260 mg/kg for ketamine and 5–39 mg/kg for xylazine in intramuscular injection and 75–100 mg/kg for ketamine and 10 mg/kg for xylazine in intraperitoneal injection (Dittmar et al., 2004).

that 7-month-old mice had a lower number of spine than 5-month-old. It seems that different brain areas exhibit differing levels of synaptic turnover during development (Roberts et al., 2010).

In addition, spines are substrates for synaptic transmission and they can affect the possible contacts between neurons (Tackenberg et al., 2009). It is reported that changes in the shape and size of dendritic spines are correlated with the strength of excitatory synaptic (Hotulainen & Hoogenraad, 2010). So, it seems that in old rats because of the lower mature spine and might less NMDA receptors, the dosage of K-X for induction of anaesthesia is lower than for young ones. Certainly, more studies on molecular mechanisms are needed.

5 | CONCLUSION

In conclusion, this study shows that the high intraperitoneal dosage of K-X (150–4 mg/kg) should not be recommended for anaesthesia in young (2–3 months) Wistar rats, and the intraperitoneal injection of 100–2 mg/kg of K-X dose could be the optimal dose and route in the male and female aged (18–20 months) Wistar rats. Also, it seems that the reduction of the mature spines of CA1 in old rats has associations with a lower dose of K-X dosage and less duration anaesthesia time.

AUTHOR CONTRIBUTIONS

Narges Sotoudeh: Investigation; methodology; writing-original draft. Mohammad Reza Namavar: Funding acquisition; project conception, design, and supervision; data analysis; writing-review & editing. Both authors read and approved the final manuscript.

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ETHICAL STATEMENT

It is emphasised that this article has not been submitted to any other journals for publication. It is acknowledged that both authors have contributed significantly and agree with the contents of the manuscript. The authors are affiliated with Shiraz University of Medical Sciences is an academic place of education and research. Animal procedures were conducted under the National Institutes of Health's Guide for Care and Use of Laboratory Animals and the Animal Research: Reporting in Vivo Experiments (ARRIVE) guiding principle and approved by the Ethics Committee of Shiraz University of Medical Sciences (SUMS, Ethical code: IR.SUMS.REC.1397.77).

CONFLICT OF INTEREST

The authors declare they do not have any known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

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PEER REVIEW

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