Effects of Sub-Chronic Anabolic Steroids Exposure on Cocaine Conditioning and Anxiety-Like Behaviors in Adult Male Rats

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INTRODUCTION

➢ Addiction to substances is a health problem that causes major health and social concerns and affects the lives of millions.[1] Addiction has been defined as a behavioral disorder mediated by neurobiological changes in the brain[1] and is characterized by: (1) Compulsion to seek and take drug, (2) Loss of control in limiting intake, and (3) Emergence of a negative emotional state during the absence of the drug in the body[4] in spite of harmful consequences.

➢ Anabolic-androgenic steroids (AAS) are used by a considerable proportion of the athlete community to enhance physique and performance.[6] For decades, elite athletes have used AAS to improve performance. Most AAS users are not competitive athletes, but simply individuals who want to look leaner and more muscular.[2]

➢ Recent survey has estimated that people who abuse AASs also tend to abuse psychotropic drugs such as cocaine, heroin, amphetamine, and 3,4-methylenedioxymethamphetamine (MDMA) or ecstasy[3,5] and these drugs can contribute to produce agressivity behavior. [5]

OBJECTIVES

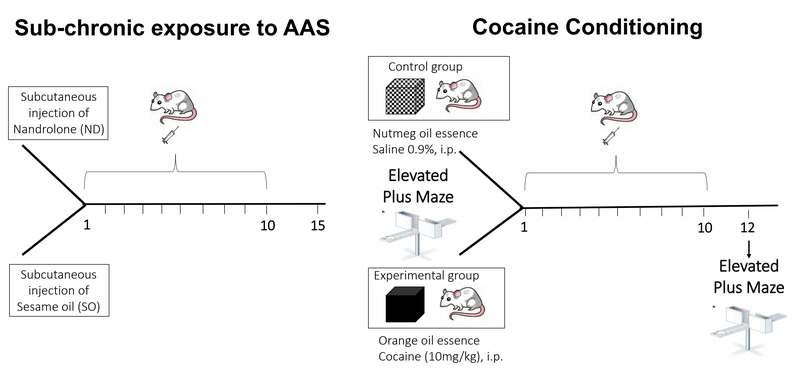
➢Evaluate the effects of subchronic exposure to AAS in adult male rats on anxiety-like behaviors triggered by cocaine cues and changes in size of specific internal organs (heart, adrenal glands, testes) of male adult animals.

➢Characterize the changes in expression of androgenic receptor (AR) and dopaminergic receptor 1 (D1) within the brain, adrenal glands and heart of male adult rats following subchronic exposure to AAS and environmental-elicited cocaine conditioning.

HYPOTHESIS

➢ Subchronic administration of AAS will potentiate the anxiogenic responses triggered by cocaine cues, induce changes in the size of all the selected organs and increase expression of AR in the heart, adrenal glands and NAc. In addition, D1 receptor will be up-regulated within the NAc of adult rats treated with AAS and cocaine treatments.

METHODS



RESULTS

Elevated Plus Maze (EPM)

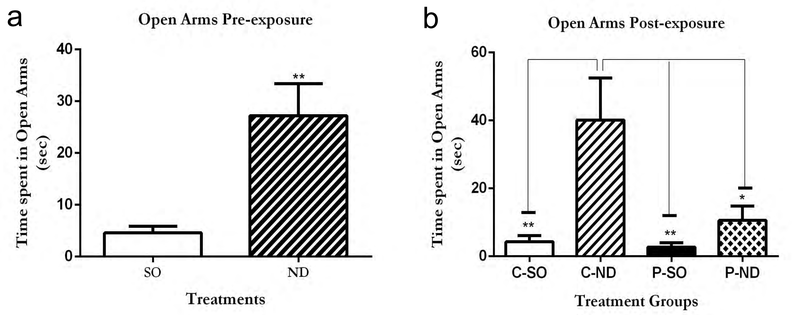


Figure 1 - Anxiety state of male rats pre-exposed and post-exposed to the environment-elicted cocaine conditioning. (a) There is a statistical significant difference between both SO and ND groups (n=11) on the time spent in open arms before placed in the conditioned environment. **(b)** Time spent in closed arms is increased significantly between the control (ND) and cocaine-paired groups compared to control (SO) groups, and cocaine-paired (ND) decreased significantly versus cocaine-paired (SO) (n=7) in post exposure time in the environment cocaine conditioning. (* p<0.05, ** p<0.01)

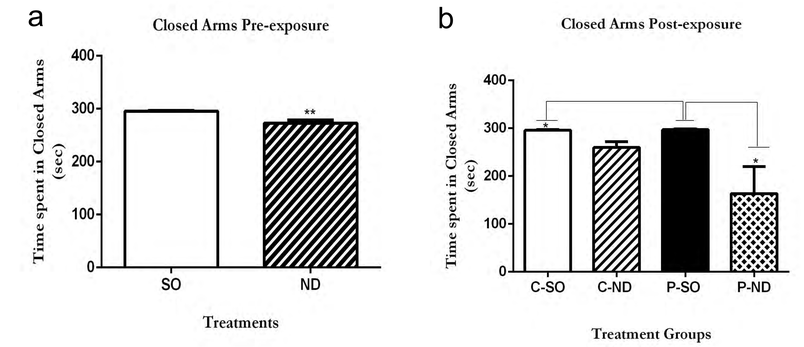


Figure 2 - Anxiety state of male rats pre-exposed and post-exposed to the environment-elicted cocaine conditioning. (a) There is a significant increase of the time spent in open arms between both SO and ND groups (n=11) before running within the conditioned environment. Nevertheless, **(b)** demonstrates that the control (SO) and cocaine-paired groups exhibited a significant reduction of the time spent in open arms compared to control (P-ND) groups (n=7) after exposure to the environment cocaine conditioning. (* p<0.05, ** p<0.01)

Conditioning Cues

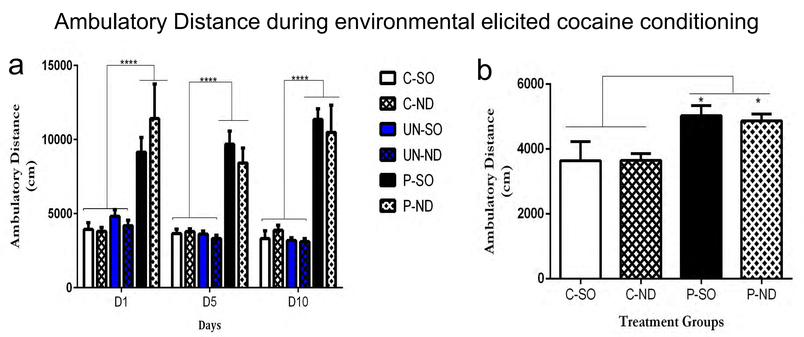


Figure 3 - Ambulatory Distance (AD) during environmental elicited cocaine conditioning. (a) Cocaine-paired nandrolone (P-ND) and sesame oil (P-SO) animals have demonstrated higher locomotor activity in AD than the control (C-SO & C-ND) and the cocaine-unpaired (UN-SO & UN-ND) animals on all days. (**b)** In test day (D12), we only considered the control (SO & ND) and cocaine-paired (SO & ND) groups and we have observed that there was a significant difference amongst all different groups. (*p<0.05, ****p<0.0001)

RESULTS (CONT.)

Organ Weight

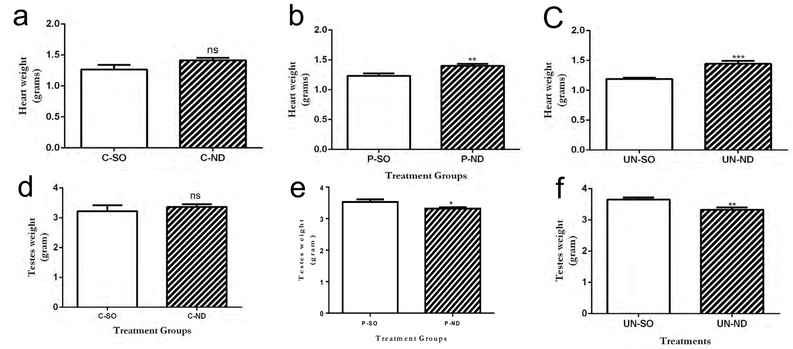


Figure 4 - Size of different organs of animal groups which have received ND or SO treatment. There is no significant difference between both C-SO and C-ND groups (n=11) in the heart size **(a)** or testes size **(d)**, but there is a significant increase in the heart and testes size of P-ND **(b, e)** and UN-ND **(c, f)** compared to P-SO (*p<0.05,**p<0.01, n=11) and UN-SO (***p<0.001, n=11) respectively.

Dopaminergic (D1) and androgenic (AR) receptors expression

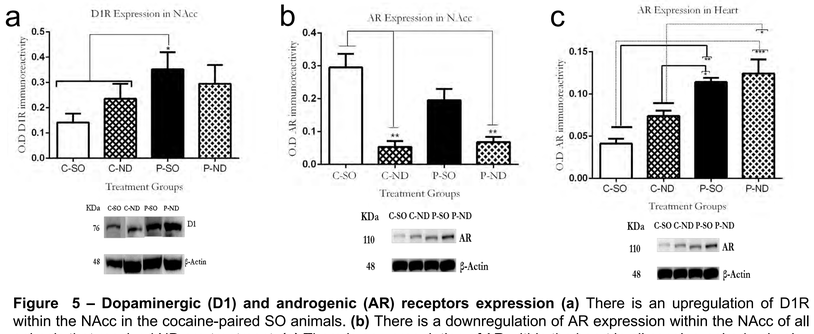


Figure 5 – Dopaminergic (D1) and androgenic (AR) receptors expression (a) There is an upregulation of D1R within the NAcc in the cocaine-paired SO animals. **(b)** There is a downregulation of AR expression within the NAcc of all animals that received ND pre-treatment. **(c)** There is an upregulation of AR within the heart in all cocaine-paired animals.

CONCLUSIONS

➢This study suggests that previous exposure of AAS subchronically in adult male rats after post-exposition to environment-elicited cocaine conditioning increase the anxiety state .

➢Pre-exposure to AAS subchronically leads to morphologic changes in heart of adult male rats.

➢Future studies aim at examining the effects of AAS subchronically pre-exposure in adulthood on the hormonal profile of corticosterone and expression of androgen receptors within the heart.

ACKNOWLEDGMENTS

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