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THE SAHLGRENSKA ACADEMY
INSTITUE OF NEUROSCIENCE AND PHYSIOLOGY

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Announcement - scholarship at undergraduate/advanced level

The Department of Pharmacology, Institute of Neuroscience and Physiology, hereby announces a vacant scholarship at undergraduate/advanced level in Addiction medicine.

Training plan
Subject:
Investigations of the effect of tirzepatide on drug-related responses in male and female rodents

Background:
Alcohol use disorder (AUD) is characterized by craving and loss of control [1]. AUD is considered one of the most serious public health problems worldwide, as it contributes to both mortality and morbidity. It also causes devastating social, economic, and personal consequences [2]. To date, a few medications are approved to treat AUD, and their efficacy is limited. The lack of effective treatments is a global challenge, and additional treatment options are needed for this heterogeneous disorder. The mechanisms underlying AUD are complex and involve social, environmental, psychological, genetical, and neurobiological factors making it essential to identify these factors for comprehensive understanding and effective intervention. **The overall aim of the present project is to understand the neurobiological contribution and thereby identify novel treatment options for addiction.**

Recent advances in animals and humans reveal that the gut-brain axis plays a role in AUD processes. While peptides of the gut-brain axis such as ghrelin, GLP-1, and amylin are well-known to control feeding [3], our team was the first to demonstrate that these peptides regulate both natural and artificial rewards (Fig 1) [4]. Specifically, our research revealed that GLP-1R agonists, which are currently approved for the treatment of diabetes and obesity, reduce alcohol consumption, suppress the rewarding properties of alcohol, prevent the motivation to consume alcohol as well as relapse drinking. [5, 6]. Given that our research has established that gut-brain peptides like GLP-1 constitute a novel target for addiction, we now hypothesize that a combination of gut-brain peptides synergistically prevents addiction while introducing fewer side effects. Successfully, a combination of traditional addiction medications has been tested for the treatment of AUD, where the combination of varenicline and bupropion prevents relapse drinking of alcohol in rats [7]. Moreover, naltrexone together with either varenicline or bupropion reduces alcohol consumption in rats [8, 9]. This approach also holds for the treatment of obesity where the combination of either agonist at AMYR and GLP-1R [10, 11] or a drug targeting receptors of both GLP-1 and glucose-dependent insulinotropic polypeptide (GIP; Tirzepatide)[12] synergistically reduces body weight in obese rats. However, the impact of tirzepatide on responses associated with alcohol remains unknown.

Purpose:

The specific aim of the present project is to explore the impact of tirzepatide on alcohol-induced locomotor stimulation in male mice.

Method:
Adult male NMRI mice will be used. Alcohol and other addictive drugs activates the mesolimbic dopamine system causing a locomotor stimulation; alcohol responses are tentatively associated with reward in humans (for review see (9)). Open field boxes (42 x 42 x 20 cm; Med Associates Inc; Georgia, Vermont, USA) will be used. Activity will be measured by 16x16 infrared beams located at two different levels. At the initiation of the test, the mice will be allowed 60 minutes to habituate to the open field boxes that are ventilated, dim lit (3 lux) and sound-isolated. Thereafter, they will receive treatment and their behavior will be monitored for the following 60 minutes. Distance traveled, stereotypic counts, vertical counts, and average velocity are recorded in each experiment. The first experiment aims to define doses of tirzepatide that do not alter motor behavior *per se*. Therefore, different doses of tirzepatide will be injected and the mice's motor behavior will be measured. Then, the impact of tirzepatide (three different doses) on alcohol- and drug-induced locomotor stimulation will be explored. Thus, the male mice will be treated with tirzepatide and then injected with alcohol or other addictive drugs (nicotine, cocaine, opiods). All necessary equipment and resources will be provided by the department.

Work plan/scedule:

Week 1: training with supervisor; Week 2-7: Running experiments; Week 8: Summary of data and learning outcome

Learning outcome:
The student will learn the basics in addition research and will be familiarized with preclinical addiction methods. The student will through seminars and presentation of obtained results learn more about the addiction theories. The student will be trained in laboratory work and working as a researcher. The scholarship covers living expenses and is not coverage for work conducted at the University of Gothenburg.

Period
2024-11-25 to 24-12-31

Financing
1 payment of 18 750 SEK. A total of 18 750 SEK for the whole period. The project is possible to conduct by two students in collaboration (i.e. 2 periods per person).

If you require any further information, please contact Elisabet Jerlhag Holm, elisabet.jerlhag@pharm.gu.se, supervisor.

Application
To apply please fill out the form "Scholarship application" and send it to Elisabet Jerlhag Holm, elisabet.jerlhag@pharm.gu.se, supervisor.

Please attach a copy of:

CV
Letter of motivation
Registration certificate

Closing date 2024-11-17