Results
A dose-dependent systemic physiological change, alterations of mouse behavioral patterns and indications of neuronal death was observed upon chewing tobacco treatment. Oral SLT administration reduced the horizontal ambulatory activity and induced anxiolytic function. *In vivo* studies have given certain insights into mechanistic neuronal cell death. Concurrent with the neuronal death pattern, differentiated neuronal cell culture model of PC12 and SH-SY5Y were employed to underpin the SLT induced threats. SLT reduced the oxidative phosphorylation and aerobic glycolysis as determined by the diminution of ATP production and basal respiration. There was breakdown of mitochondrial health and structure with concomitant membrane potential drop along the increasing SLT doses. The involvement of mitochondria and its downstream factors were further confirmed by immune-blot, flowcytometry and microscopic techniques. Hallmark apoptotic signals like leakage of cytochrome *c* was observed after 24hr (6mg/ml) SLT treatment. We observed time dependent increase of t-Bid levels and down-regulation of Bid gave significant protection from cell-death upto 72hr in neurons and NG pretreatment significantly reduced (1.49X) t-Bid expression. Bid authoritatively mediated mitochondrial membrane permeabilization and subsequent cytochrome *c* release leading to apoptosis, neurotoxicity and neurodegeneration. In protective studies, citrus flavonoid NG ameliorated the challenges of SLT mediated systemic stress responses particularly on neuronal cells.
Conclusion
The present study is a comprehensive, in-depth report portraying the fatal effects of SLT identifying some specific clues of neurodegeneration. Another bright side of the work was identification of role of NG against the prevention of SLT mediated perils.

B 06-45
An experimental study of mental activity in healthy individuals using simple and complex sensorimotor reaction times to various visual stimuli
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Introduction
Studies have shown that first-year medical students, experience psychological stress and, in some cases, mental illness due to new environments and stressful study regimes, which negatively affect their ability to study, academic performance, and full participation in life (1, 2).
Methods
An experimental study was conducted on first and next (2-3) year medical students, out of which 17 were males and 21 females. Participants were exposed to two randomized order simulated virtual tasks that differed in their demand levels. Some derivative indices - correct answers in percent (CA%), reaction sustainability (RS), and functional ability level (FAL) of mental activity were calculated based on the simple and complex reaction time measures (SSMRT, CSMRT) (3-5).
Results
No significant difference in mental activity between the two genders in 2-3 year medical students, except for CA% in the males' group (p=0.044) during CSMRT which indicates that males are able to concentrate better; There were significant differences in parameters of SSMRT (FAL p=0.001) and CSMRT (RS p=0.007; FAL p=0.007) between first-year males and females; Significant differences were found also in parameters of SSMRT (RS p=0.012; FAL p=0.016; CA% p=0.001) and CSMRT (RS p=0.009; FAL p=0.013; CA % p= 0.014) between first and next-year medical students in the females' group and significant differences in the males' group only in CA% (p=0.049) of SSRT.
Conclusion
Independent of gender, in 2-3 year medical students the sensorimotor and cognitive abilities are almost the same. The better mental performance parameters in the male group of first-year students can be explained only by the presence of certain stress in the female group, which can be related to the difficulty adapting to new environments and stressful learning regimes of the medical universities. In addition, male students are able to concentrate better compared to females on acute visual stress. Our results contribute to a better understanding of the psychophysiology of mental activity and further demonstrate how a virtual model can be used to investigate acute cognitive stress effects.

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B 06-46
Changes in total choline levels in heart tissues of vagotomized rats.
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Introduction
Several mechanisms are identified for peripheral sympathetic–parasympathetic interactions on cardiac regulation thus understanding the factors affecting main neurotransmitter acetylcholine levels is crucial. Our previous studies showed that different types of vagotomy may affect cardiac function distinctly. This study was designed to evaluate different branches of acute vagotomy that may distinctly affect the levels of acetylcholine levels released from vagus nerve endings which

might be responsible for the contralateral vagus over-activity causing hemodynamic parameters (1).

Methods

The experimental study was approved by the local Ethics Committee for Animal Experimentations. 12-16 weeks old male Wistar rats (288,6 ± 34,23 g, n=40) were used for experiments to eliminate the effect of the menstrual cycle on HRV parameters. Animals were randomly divided into five groups (each n=8): sham, right vagotomy, left vagotomy, bilateral vagotomy, and atropine. During the experimental procedure right, left, or bilateral vagotomy was performed. In the sham-operated group, the right and left vagal nerves were exposed and fixed, but no incision was made. In the Atropine group, vagal innervation was chemically prevented with Atropine Sulfate (5 mg/kg, i.p.). After the experiments rats were sacrificed with urethane (1.5 g/kg, i.p.). Totalcholine/acetylcholine levels in heart tissues of experimental groups were measured by a commercially available kit according to the manufacturer's instructions by spectrophotometer. One-way analysis of variance (ANOVA) with Tukey test for multiple comparison tests was used for statistical analysis. $p<0.05$ was accepted statistically significant.

Results

Total choline/acetylcholine levels were significantly higher only in right vagotomy group compared to sham (10,09 ± 6,964 nM, $p<0.001$) and bilateral vagotomy groups (12,00 ± 3,588 nM, $p<0.01$). The levels were not statistically differs between Atropine-treated group (8,720 ± 1,923 nM), left vagotomy group (10,24 ± 4,951 nM) and in right vagotomy group (22,05 ± 4,494 nM).

Conclusion

Asymmetrical vagal innervation produces change in acetylcholine release in heart tissues. Our data showed that acute right vagotomy significantly increased the total choline levels. Together with our previous findings, this data showed that right vagotomy may induce compensatory hemodynamic recovery through contralateral vagus overactivity along with the enhancement of total choline/acetylcholine levels in heart tissue (2).

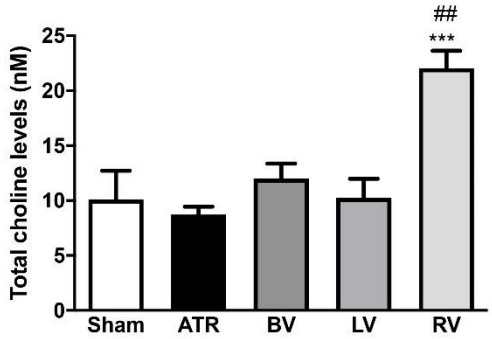

Figure 1
Total choline levels in heart tissues in groups of Sham, Atropine, Bilateral Vagotomy, Left Vagotomy and Right Vagotomy.

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B 06-47

An examination of the activity of the ubiquitin-proteasome system during brain ageing and in Parkinson's diseased patients.

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We are grateful to The Neuropsychopharmacology Research Group at the Department of Pharmacology of the University of the Basque Country (UPV/EHU) that supplied the human post-mortem samples used in the ageing brain cohort studies (https://www.ehu.eus/en/web/neuropsicofarmacologia/aurkezpena), and the Parkinson's UK Brain Bank, Imperial College London, that supplied the Parkinson's disease brain tissue and matched control subjects.

Introduction

The global population is rising and so is the number of patients living with neurodegenerative diseases (NDDs). Approximately one million people are affected by NDDs in the UK, and 50 million people worldwide suffer from dementia. The accumulation of intra- or extra-cellular protein deposits is a histopathological hallmark of a number of NDDs. Reduced activity of the ubiquitin-proteasome system (UPS) may be one of the molecular mechanisms that could lead to reduced clearance of potentially toxic protein aggregates. To examine this further, the activity of the UPS was quantified in *post-mortem* tissue in the brains of a cohort of aged individuals (n = 40, age range 23-93 years) and from brain regions of Parkinson's disease (PD) patients (n = 11) and controls (n = 10).

Methods

The activity of theUPS was quantified using a fluorometric assay for the chymotrypsin-like activity of the 20S proteasome. Protein profiling was also performed using denaturing polyacrylamide gel electrophoresis to detect the accumulation of protein aggregates.

Results

UPS activity did not change significantly between samples from the ageing brain cohort or between brain regions from PD patients vs controls ($p > 0.05$). Protein profiling revealed cytoskeletal protein reductions during ageing with reduced α- and β-tubulin expression in brains of individuals of ≥60 years of age, and there were differences in cytoskeletal protein expression between PD brain samples and controls.

Conclusion

Collectively, our results suggest that the ATP-dependent chymotrypsin-like activity of the UPS is stable in the ageing brain and for PD patients, but that molecular changes to the cytoskeleton are present.
