ual characteristics included initial amplitude of responses to test stimulation and HFS, the magnitude of early and late LTP. Period of 5-20 min after HFS was considered as early LTP, and the period 25-60 min after HFS - as late LTP. All indices were normalized relative to the control distribution. Correlation analysis revealed that though the data from males and females had common area of regression, they were differently distributed. The slices of females subjected to neonatal NPS were more apt to synaptic depression and, as a result, deficit of synaptic depolarization in response to HFS. That was the main limiting factor for LTP induction both in males and females, however, a large part of male slices demonstrated less or no effect. No LTP impairment could be detected in the slices with normal background activity. Significant positive correlation between LTP performance and amplitude of CA3-CA1 responses at stimulus intensity used for HFS confirms that LTP deficit is associated with initial synaptic depression in the slices of male rats subjected to NPS. After controlling these factors, comparison of late LTP revealed improved maintenance. Yet full LTP development in the slices of male NPS group was often associated with the generation of multiple spikes (epileptiform-like discharges). We suggest that hippocampal synapses matured in the milieu affected by NPS become more vulnerable to excitotoxicity in response to strong activation. In both male and female groups this effect was attenuated in concert with synaptic depression and LTP deficit. This may suggest neuroprotective role of synaptic depression, in particular, since we did not find gross NPS-induced disturbances in learning and memory. Overall, the disturbances ranged from synaptic depression of background activity to the other extreme which may be associated with excitotoxic damage. Considering the effects of NPS described by [4], we hypothesize that variations in inhibitory transmission maturation may be responsible for gender-related differences in hippocampal pathology.

Disclosure statement: This work was supported by the Russian Science Foundation (grant #14-25-00136).

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doi: 10.1016/j.euroneuro.2018.11.354

P.244 Effects of ketamine and tiagabine in mice exposed to single prolonged stress protocol, a mouse model of posttraumatic stress disorder

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Today, a growing occurrence of traumatic events, e.g. acts of terrorism, traffic incidents and usage of firearms, is reported. Worldwide probability of experiencing the above mentioned events could reach over 50%. Posttraumatic stress disorder (PTSD) is a psychiatric condition, following such experiences. Literally, it may develop in 1/3 of trauma participants. According to WHO, this problem concerns about 4% of worldwide population. Current therapy comprises mainly benzodiazepines, antidepressants and several coadjuvants, but it is ineffective in 70% of patients [1]. Hence, novel therapeutic paths in PTSD are urgently required.

In PTSD individuals, an abnormal excitation of amygdala is reported. Due to this, the prevalence of anxiety, fear and intrusive memories are enhanced. In amygdala complex, two neuronal populations are distinguished: excitatory glutamatergic neurons and inhibitory GABA-ergic interneurons, respectively [2]. In our study we assumed, that the balance in amygdala could be restored by decreasing excitatory activity of glutamatergic neurons via NMDA receptors antagonism, or by increasing GABA-ergic transmission. In order to evaluate this hypothesis, we have studied the activity of ketamine and tiagabine in a mouse model of PTSD induced with the use of single prolonged stress protocol (SPS) [3].

For this purpose, a potential antidepressant-like activity (forced swim test, FST) [3], a potential anxiolytic-like activity (four plate test, FPT) and contextual fear conditioning (CFC) were assessed in CD-1 mice [4]. To further investigate this issue, the analysis of mouse ultrasounds vocalizations was performed. Aside from acute-treated groups (1 h before each test: ketamine 25 mg/kg, tiagabine 10 mg/kg or saline, i.p.), two pretreated groups were involved (administration of ketamine or tiagabine 24 h and 1 h before SPS). Statistical analysis was done using GraphPad Prism Software (two-way analysis of repeated measures ANOVA, followed by Bonferonni's multiple comparison test).

In FST both ketamine (24 h after SPS:$p<0.0001$; 14 days after SPS:$p<0.0001$; 21 days after SPS:$p<0.0001$; 28 days after SPS:$p<0.05$) and tiagabine (24 h and 7, 14, 21, 28 days after SPS: $p<0.0001$) revealed activity, however tiagabine was much more effective. In the ketamine-pretreated group a delayed onset of depressive-like features was observed (14 and 21 days after SPS:$p<0.01$). In FPT only tiagabine was active (48h and 8 days after SPS:$p<0.0001$, 22 and 29 days after SPS:$p<0.01$). In ketamine-pretreated mice, 48 h after SPS, a significant reduction in anxiety was observed ($p<0.001$). In CFC, 22 days after SPS, both tiagabine ($p<0.0001$) and ketamine ($p<0.05$) significantly reduced freezing behavior. Although, 29 days after SPS, this effect persisted only in tiagabine-treated group ($p<0.001$).

Our study reports antidepressant-like activity of ketamine and both anxiolytic and antidepressant-like effect of tiagabine in a mouse PTSD model. Moreover, tiagabine via significant reduction of freezing behavior in CFC might hinder intrusive memory recall. We did not report significant effects of pretreatment with tiagabine, or ketamine. However, it is worth mentioning, that ketamine-pretreated group presented a delay in developing depressive-like features associated with mouse PTSD model. Hence, enhancing GABA-ergic activity appears to be more beneficial when compared to glutamatergic attenuation to alleviate PTSD-like symptoms in mice.

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doi: 10.1016/j.neuropharm.2016.10.019

P.245 Early and late-life stress and longitudinal telomere length in old twins

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Introduction: It has often been proposed that stress in the form of stressful life events and childhood trauma can have detrimental effects on health outcomes, including age-related disorders such as cardiovascular disease and dementia [1,2]. Moreover, stress has been associated with direct effects on markers of biological aging; including greater levels of inflammation and telomere shortness or shortening [3,4]. So far several studies have shown that there is an association between stressors and leukocyte telomere length(LTL) [5], but it is unclear whether stressors can also lead to accelerated LTL shortening.

Aim: Therefore in the current study we will examine the effect of early-life stressors and late-life stressors on longitudinal LTL with a follow-up time of 25 years.

Methods: In the Swedish Adoption Twin Study of Aging (SATSA) we assessed early-life environment and late-life stressful events in 543 participants (mean age 68.4 and 40% men). LTL was measured using qPCR up to 5 separate LTL measurements. Longitudinal analyses were conducted using latent growth curve modeling in the whole cohort corrected for lifestyle factors and depressive symptoms. A two slope model was used, that was centered on the median age at baseline (69.3 years). Additionally we examined discordant twin pairs to investigate in detail the effects of early- and late-life stressors on longitudinal LTL.

Results: Our main finding is that participants who reported both higher levels of early- and late-life stressors showed a steeper LTL decline after the age of 69.3 years old than participants who reported only early life stressors, only late-life stressors or no stressors. Within participants with high early-life stress, late-life stress was associated with decline on LTL with increasing age (slope 1: B=−0.002, p=0.10; and slope 2: B=−0.013, p=0.04), whereas in participants with low early-life stress, late-life stress was not related to LTL (slope 1: B=0.004 p=0.47; and slope 2: B= 0.003 p =0.56). Main effects of either early or late-life stressors alone on shorter LTL were not observed when we looked in the total cohort; however when we zoomed in on discordant monozygotic twin pairs we found that early-life stress has a significant impact on accelerated LTL decline over time (both before and after the age of 69.3), whereas no significant decrease in LTL for late-life stressors was observed. See table 1 for the results of the discordant twin pairs.

Discussion and conclusion: Our findings in an older population suggest that particularly early-life stressors have a long-lasting effect resulting in accelerated LTL decline. Accelerated shortening of telomeres is thought to be a proxy for accelerated aging and there is evidence that shorter telomeres are associated with mortality.

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doi: 10.1016/j.euroneuro.2018.11.356