(P > 0.05). Thus, our findings indicate that CRF neurotransmission within the IC is involved in anxiogenic-like and cardiovascular responses caused by stress, and this control is site-specific along the rostrocaudal axis of the IC.

Declaration of Interest Statement

None

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PARALLEL SYMPOSIUM
PARALLEL SYMPOSIUM 35: NEUROBIOLOGY OF STRESS: SEX DIMORPHISMS, STRESS RESILIENCE AND NEUROCHEMICAL AND NEUROIMMUNE MECHANISMS
13-09-2023 10:05 - 12:05

NEUROIMMUNE TARGETS TO ENHANCE RESILIENCE TO A HYPERVIGILANT PHENOTYPE IN FEMALES

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Stress-related disorders such as post-traumatic stress disorder are prevalent world-wide and disproportionately affect females. One hallmark symptom of this disorder is hyperarousal and hypervigilance, regulated in part by an exaggerated locus coeruleus (LC)-norepinephrine system. Recent evidence points towards heightened neuroimmune signaling in response to stress as a mechanistic factor underlying this behavioral dysfunction. Previous experiments in our lab determined that social stress, specifically vicarious witness stress (WS), leads to development of a hypervigilant phenotype and increased neuroimmune signaling within the LC-norepinephrine system of females. Importantly, proinflammatory cytokines activate LC neurons, ultimately promoting downstream norepinephrine release. We have identified that decreasing IL-1β expression via microglial cell knockdown in the LC blocks the hypervigilant behavioral and autonomic response to WS. Taken together, these studies determined if increased neuroimmune signaling may be a critical factor eliciting increased susceptibility to social stress-evoked behavioral dysfunction. This study used a chemogenetic DREADDs techniques with a virus engineered to target microglia (AAV-CD68-Gi) to evaluate the functional and behavioral impact of transiently blocking microglial activity within the LC during WS exposure on subsequent hypervigilance-related outcomes. First studies aimed at validating the selectivity and efficacy of the DREADD virus to inhibit microglia were conducted. Next, rats were injected with either CNO to activate the DREADDs virus or vehicle one hour prior to stress. These studies concluded that DREADD-mediated microglial inhibition prevents the emergence of the hypervigilant burying behaviors both during stress and in response to the stress context. Further, as predicted, the DREADD-mediated inhibition of microglial cells was confirmed to suppress neuronal activity of noradrenergic cells in the LC as confirmed with cfos immunohistochemistry. In all, these experiments identified stress-evoked LC microglial activation as a key factor mediating hypervigilant burying behavior in females and may provide a novel treatment target for the prevention of stress-related pathologies

Declaration of Interest Statement

None

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PARALLEL SYMPOSIUM
PARALLEL SYMPOSIUM 35: NEUROBIOLOGY OF STRESS: SEX DIMORPHISMS, STRESS RESILIENCE AND NEUROCHEMICAL AND NEUROIMMUNE MECHANISMS
13-09-2023 10:05 - 12:05

HIPPOCAMPUS SELECTIVE INACTIVATION THROUGH DAUN02 METHOD IN MALE AND FEMALE C-FOS TRANSGENIC RATS AND STRESS-INDUCED ADAPTATION RESPONSES

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Aim

Present work used Daun02 inactivation method in c-Fos lacZ transgenic rat in order to evaluate the effect of ventral hippocampus (VH) on behavioral responses related to repeated chronic stress (CRS) in male and female rats. Daun02 is substrate of β-galactosidase that catalyses Daun02 into daunomycin, causing neuronal inactivation. Methods: Guide cannulas were implanted into the VH of male and female c-Fos LacZ transgenic rats. We submitted rats to acute restraint stress (RS, 2 h/day for 1 day) or CRS (2 h/day for 21 days) and studied the effect of vehicle or Daun02 microinjection into the VH on RS or CRS-induced anxiety- (elevated plus maze-EPM and open field-OF) and depressive-like (forced swimming test-FST and splash test-ST) responses observed, respectively, 24 and 48 h after the last stress session.

Results

RS or CRS caused no anxiety-related effect observed in EPM and OF tests in both gender of lacZ animals. However, bilateral microinjection of Daun02 into the VH promoted an anxiogenic-like effect observed in EPM in chronically stressed female rats. Furthermore, CRS but not RS caused an increase in grooming time in both gender

of lacZ animals. In the FST, RS did not cause any change in the analyzed parameters (swimming, climbing and immobility times) in lacZ male rats. However, RS caused an increase in climbing time and a reduction in immobility time in female rats and both responses were reverted in Daun02-treated animals. CRS caused an increase in immobility time in lacZ male rats and a reduction in immobility time in lacZ female rats and both responses were reverted in Daun02-treated animals.

Conclusion

Results show that VH participate in the neural pathway which is involved with behavioral responses observed during stress in both gender of rats differently. Financial Support: The State of São Paulo Research Foundation (FAPESP # 2018/04899-1; 2021/00148-4; 2021/04572-5; 2021/06709-8;2023/00306-4).

Declaration of Interest Statement

None

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PARALLEL SYMPOSIUM
PARALLEL SYMPOSIUM 35: NEUROBIOLOGY OF STRESS: SEX DIMORPHISMS, STRESS RESILIENCE AND NEUROCHEMICAL AND NEUROIMMUNE MECHANISMS
13-09-2023 10:05 - 12:05

ADOLESCENT STRESS CONFERS RESILIENCE TO TRAUMATIC STRESS LATER IN LIFE: ROLE OF THE PREFRONTAL CORTEX

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Adolescence is associated with terminal differentiation of neural pathways linked to emotional processing. Stress exposure impinges on ongoing developmental processes, in some cases predisposing stress-related pathologies, in others, resilience to later adversities. Here, we tested whether chronic stress exposure in adolescence would affect responses to a single prolonged stress (SPS) later in life, a manipulation linked to generation of PTSD-related symptoms. In these studies, male and female rats were exposed to chronic variable stress throughout late adolescence (d45-60), received SPS 5 weeks later, followed by assessment of emotional memory (contextual and cued fear conditioning) one week later. A separate group of animals was used to test the impact of the chronic stress-SPS model on prefrontal cortical electrophysiology. Our data indicated that SPS produced robust impairment of extinction learning in male rats, consistent with observations seen in PTSD. Reinstatement of freezing following a reminder shock was enhanced in males. Both effects were blocked by exposure to chronic stress in adolescence. Females had mild extinction impairments and reinstatement deficits, which were again blocked by adolescent stress. Behavioral effects of SPS effects were linked to reduced infralimbic (IL) cortex Fos staining in males, whereas in females, Fos staining was increased in central amygdala in females. Changes in Fos induction were prevented by adolescent stress, suggesting different neurocircuits involved in generating resilience in the two sexes. Finally, SPS caused marked decrements in infralimbic cortex excitability in males, an effect that was again blocked by adolescent stress exposure. Our data indicate that adolescent stress can impart resilience to the effects of traumatic stress on neuroplasticity and behavior in both males and females. These data suggest a possible mechanism affording behavioral resilience to traumatic stress in animals exposed to adversity in adolescence.

Declaration of Interest Statement

None

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PARALLEL SYMPOSIUM
PARALLEL SYMPOSIUM 36: MITOCHONDRIAL REDOX SIGNALING IN COGNITION: AN ENERGY MATTER
13-09-2023 10:05 - 12:05

TRISOMY 21 AND ABERRANT REDOX HOMEOSTASIS: A SYNERGISTIC PATH TO NEURODEGENERATION

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Down Syndrome (DS) is the most common genetic disorder due to the abnormal triplication of chromosome 21 (trisomy21) resulting in a variety of pathological conditions of DS subjects. Among these, individuals affected by DS show with ageing the accumulation of oxidative damage associated with defects of the proteostasis network (1). DS is currently considered a human genetic model of early onset Alzheimer disease (AD). The talk will discuss the role of trisomic genes which, directly and indirectly, contribute to the occurrence of an aberrant redox-phenotype and how it contributes to the dysfunction of several cellular functions (2). Among these, we hypothesize that redox dysregulation is closely linked to metabolic defects, including reduced glucose metabolism, energy production and aberrant insulin signaling. Alteration of energy metabolism significantly contributes to accelerate the onset of Alzheimer like neruodegeneration, including amyloid and Tau neuropathology, in DS individuals. References: 1) Barone E, Head E, Butterfield DA, Perluigi M. HNE-modified proteins in Down syndrome: Involvement in development of Alzheimer disease neuropathology. FRBM 2017;111:262-269. doi: 2) Insulin resistance, oxidative stress and mitochondrial defects in Ts65dn mice brain: A harmful synergistic path in down syndrome. Lanzillotta C et al. FRBM. doi: 10.1016/j.freeradbiomed.2021.01.042.

Declaration of Interest Statement

None

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