emotional disorders and neurodegenerative diseases. In this sense, the aim of the present study was to use A2a receptor knockout (KO) mice with complete and specific inactivation of the A2a receptor [3] as an endophenotype model of schizophrenia. To achieve this goal, we performed different behavioural paradigms to assess emotional, social and cognitive alterations in adult (3–6 months) male KO and wild-type (WT) littermates. Nesting and social interaction tests were used to evaluate social behaviour, tail suspension test constituted a measure for despair-like behaviour and object recognition test and passive avoidance paradigm were used to evaluate cognitive alterations. Our results showed a depressive like-response in KO mice seen by an increase in the immobility time in the tail suspension test (WT vs. KO, $n = 14$; $p < 0.01$). KO animals also exhibited poor social interaction skills, evaluated by following (WT vs. KO, $n = 13–14$; $p < 0.01$), oral sniffing (WT vs. KO, $n = 13–14$; $p < 0.001$), genital sniffing (WT vs. KO, $n = 13–14$; $p < 0.001$) and fighting (WT vs. KO, $n = 13–14$; $p < 0.05$) behaviours, although no differences were observed in the nesting test (WT vs. KO, $n = 14$; n.s.).

Finally, both cognitive tests showed learning alterations in KO animals.

Either the object recognition test, a task dependent on the hippocampal formation (WT vs. KO, $n = 14–15$; $p < 0.01$) and the passive avoidance paradigm, a test dependent on the PFC and the amygdale (WT vs. KO, $n = 9–10$; $p < 0.05$) showed learning and memory deficits in KO mice. All together, our results indicate that A2a KO mice exhibit many typical negative and cognitive hallmarks of schizophrenia and propose these animals as a new mouse model of the disorder.

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P.1.h.010 Early life influences on emotional reactivity, social behaviour and neuroinflammation

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Early life experiences play a key role in shaping brain and behavior.

Different mouse models of early life adversity, such as 'maternal separation with early weaning' (MSEW) [1] have been developed in an attempt to elucidate the neurobiological substrate of emotional disorders.

In MSEW, pups are separated from the dam various hours per day between postnatal day (PD) 2–16 and are weaned earlier on PD 17. On the other hand, social environmental enrichment has emerged as a protective factor that diminishes the vulnerability to psychopathologies. Recently, a model called 'communal nest' (CN) has been proposed as social enrichment. In CN, three females combine their pups, sharing care-giving behavior, and pups are weaned on PD 25 [2]. The aim of the present study was to evaluate the effects of these early rearing manipulations and the 'standard nesting condition' (SN) on the emotional reactivity, social behavior and the neuroinflammatory response of male and female adolescent offspring CD1 mice. Indeed, recent findings have suggested a link between depression and an increased inflammatory response [3]. Thus, at PD30 mice were subjected to a wide range of tests to assess locomotor activity, anxiety- and depressive-like responses (elevated plus maze, tail suspension test and saccharin test), and social behavior (nesting test and social interaction test). Additionally, microglial activation was assessed by inmunofluorescence in the hippocampus which is an important brain area implicated in emotional responses. The results showed a hypolocomotor phenotype in MSEW male (MSEW vs. SN $n = 16–23$; $p < 0.05$). Additionally, MSEW and CN mice exhibited increased levels of anxiety on the elevated plus maze (Male: MSEW vs. SN $n = 16–19$; $p < 0.05$; CN vs. SN $n = 16$; p=n.s.

Female: MSEW vs. SN $n = 15–14$; $p < 0.01$; CN vs. SN $n = 15–16$; $p < 0.05$). In the tail suspension test, MSEW mice showed the highest percentage of immobility. (Male: MSEW vs. SN $n = 25–34$; $p < 0.001$; CN vs. SN $n = 25–31$; $p < 0.01$. Female: MSEW vs. SN $n = 30–32$; $p < 0.001$; CN vs. SN $n = 31–32$; p=n.s). MSEW mice also showed significantly lower preference to saccharin solution over water (Male; MSEW vs. SN $n = 7–8$; $p < 0.05$; CN vs. SN $n = 7–8$; p=n.s. Female: MSEW vs. SN $n = 7–8$; $p < 0.05$; CN vs. SN $n = 7–8$; p=n.s). No differences were observed either in the nesting test or in the social interaction test. Finally, immunofluorescence studies showed higher activation of hippocampal microglia in females from MSEW and CN groups. (Females; MSEW vs. SN $n = 3$; $p < 0.01$; CN vs. SN n= 3; $p < 0.05$). Our results suggest that MSEW is a good model to study; i) emotional alterations after early life adverse events and ii) the link between emotional disorders and neuroinflammation. Additionally, the present results cannot confirm the protective role of CN because mice subjected to this rearing condition pointed out increased anxiety and despair behavior in the EPM and TST tests respectively.

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P.1.h.011 Studies on the effects of some Bidens tripartita extracts on psychomotor abilities in rats

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Adaptogens are naturally occurring substances found in rare plants, which appear to increase the body's ability to adapt to stress [1]. Bidens tripartita a flowering plant from the genus Bidens, family Compositae, subfamily Asteroideae was widely used in traditional medicine for its antiseptic, anti-inflammatory,

antioxidant, astringent, diuretic, febrifuge, narcotic and sedative effects [2].

The aim of our study was the experimental researches on the effects of two extracts of Bidens tripartita plant in a behavioral model in rats.

Material and Method: The vegetable product used for the study was obtained after maceration and extraction in alcohol. Flowers's powder was dissolved in absolute chloroform, re-extracted and filtered. After a complete dryness the product was extracted by the addition of ethanol then evaporated. The extracts chemical composition was determined [3]. The retained dose of extracts from Bidens tripartita administered was 1/20 of lethal dose 50 (LD50). The experiment was carried out with white male Wistar rats (200–250g) distributed into 3 groups of 7 animals each treated intraperitoneally as follows: **Group I (Control):** distilled water 0.1 ml/10g weight; **Group II (coded BT-alcoholic):** 200 mg/kbw alcoholic extract from Bidens tripartita; **Group II (coded BT-aqueous):** 250 mg/kbw aqueous extract from Bidens tripartita; The substances psycho-motor abilities were tested in the LE-8811 Actimeter device (Panlab) in order to investigate the both global motor behavior and the number of escape attempts. Rats were placed on the cage device and each movement produced a signal caused by variation in inductance and capacity of the apparatus resonance circuit. Horizontal or vertical activity was defined as the total number of beam interruptions during two minutes interval. The data were presented as mean ± standard deviation of mean and significance was tested using SPSS for Windows version 13.0 and ANOVA method. The p-values less than 0.05 were considered statistically significant comparing with those of control group.

Experimental protocols were implemented according the guidelines of our University Committee for Research and Ethical Issues.

Results: In the alcoholic and aqueous extracts of Bidens tripartita there were identified different active principles such us: tannins, anthracene derivatives, triterpenes, coumarins, antocyanosides, respectively: anthracene derivatives, antocyanosides, flavonoids, coumarins, saponosids, tannins, proteic compounds, polysaccharides. In our experimental conditions both alcoholic (200 mg/kbw) and aqueous (250 mg/kbw) extract from Bidens tripartita determined a reduction of rats horizontal movements, statistically significant ($p < 0.05$) comparing with control group. The alcoholic extract from Bidens tripartita intraperitoneal injection, resulted in a statistically significant ($p < 0.05$) decreasing of rats vertical movements in Actimeter test. The aqueous extract from Bidens tripartita administration produced a decreasing of vertical movements, but not significant compared to control group.

Conclusions: These results reflects a significant diminution of the number of escape attempts, exploratory and self-maintenance spontaneous behavior after alcoholic extract of Bidens tripartita treatment, which could correspond somehow to sedation in humans.

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Disclosure statement: The authors thank AMPOSDRU for financial support of the research in the project 'Inter-university partnership for increasing the medical doctoral research quality and inter-disciplinarity through doctoral scholarships – DocMed.net' (POSDRU/107/1.5/S/78702).

P.1.h.012 Changes in alpha(1D)-adrenergic receptor expression and working memory of female mice with selective glucocorticoid receptor ablation

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Noradrenergic system consists of relatively small number of neurons located mainly in locus coeruleus (LC) and several other small hindbrain nuclei. LC is the principal site for brain synthesis of noradrenaline and sends projections to almost entire brain, including most cortical areas.

Noradrenergic innervation of prefrontal cortex (PFC) is implicated in modulation of working memory (WM) and attention through the noradrenaline action on alpha(1)- and alpha(2)-adrenergic receptors (AR). Noradrenergic system is also involved in an immediate response to stressful stimuli which enhance noradrenaline release. This neurotransmitter modulates the hypothalamic–pituitary–adrenal (HPA) axis activity. HPA axis is engaged in adaption to long term stress by employing corticosteroids acting on glucocorticoid receptors (GR). Moreover, the effects of stress on both noradrenergic system and WM show gender dependent differences [1][2].

The aim of this study was to investigate the role of GR in noradrenergic neurons in context of noradrenergic receptors system in PFC and functioning of WM in female mice.

The study was carried out on fmale mice lacking GR selectively in noradrenergic neurons (GR^{DBHCre}) and generated in Cre/loxP system by crossing mice hosting the Cre-recombinase under the dopamine beta-hydroxylase (DBH) promoter with animals harboring the floxed GR gene.

To investigate possible abnormalities in noradrenergic signaling in PFC of GR^{DBHCre} mice, quantitative real-time PCR with TaqMan probes for all existing alpha(1)-, alpha(2)-AR subtypes and beta-AR subclasses was performed. We found that changes in expression of mRNA were limited to alpha(1D)-AR subtype that was downregulated by 49% in mutant animals ($p < 0.05$). Since it was reported that mice lacking alpha(1D)-AR exhibit WM impairments [3], we investigated if GR^{DBHCre} may develop similar abnormalities due to the decreased alpha(1D)-AR expression observed in these mutants.

To assess WM performance we used spontaneous alternation paradigm in Y-maze on female GR^{DBHCre} mice, 12 weeks of age. Mice were placed in Y-maze for 5 minutes and scored for: number of successive entries to all three arms (SAP), alternating entries between two arms (AAR), and returns to the same arm (SAR). Mutant animals showed the decrease in percent of SAP (59% vs 36%, $p < 0.01$, for control and mutant animals respectively) that indicates their WM impairment, however, the increase in number of AAR and SAR was statistically insignificant.

Our results show that GR in noradrenergic neurons is important for maintaining of proper noradrenergic signaling in PFC of female mice. Furthermore, the observed changes in alpha(1D)-AR may contribute to the WM deficiency.

Impairment of WM observed both in GR^{DBHCre} and in mice lacking alpha(1D)-AR is somewhat controversial in light of