

Results of neurogenesis on Ts65Dn\*GAD67-GFP treated with placebo and  $\alpha 51A$  will be presented.

**Conclusions:** Our study confirmed that at early life stage, neurogenesis in the hippocampal dentate gyrus is reduced in trisomic mice. Nevertheless, injection of  $\alpha 51A$  was not able to correct that deficit. Thus early postnatal inhibition of GABA transmission in Ts65Dn mice is not sufficient to restore normal levels of neurogenesis. This lack of effect could be due to the complex activity of GABA that switches from excitatory to inhibitory early after birth.

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#### P.1.h.022 Brain histamine depletion enhances motor sequences complexity of mice tested in open field: new insights from temporal pattern analysis

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**Background:** Tourette Syndrome (TS) has been classically related to dopaminergic dysregulation of Basal Ganglia circuitry [1]. However, the identification of a rare autosomal dominant form of TS, linked to a mutation of the key-enzyme for Histamine (HA) synthesis (1-Histidine decarboxylase, Hdc), has shed light on a putative involvement of this monoamine on the pathophysiology of tic and related disorders and fostered the development of coherent animal models [2]. Although HA-deficient rodents display markedly increased tic-like stereotypies following amphetamine administration, neither underlying nor predisposing differences in the open field test have been reported in quantitative measurements of their baseline behaviour, compared to controls [3].

**Aim:** To investigate, by means of multivariate Temporal Pattern Analysis, the effect of an acute HA depletion on the temporal organization of behavioural motor sequences of mice tested in the open field.

**Methods:** We employed 10 adult HA deprived CD1 mice tested for 5 minutes in the open field and 10 controls (Ctrl). Histamine

Deprivation (HD) was obtained via i.c.v. administration of 5 $\mu$ g alpha-fluoromethylhistidine ( $\alpha$ FMH), a suicide inhibitor of Hdc, 24 hours before the test. Ctrl group received i.c.v. injections of saline. Experiments were recorded, and video files were stored in a PC for the following hand-made coding process. To this purpose an ethogram encompassing nine behavioural components was employed. Temporal Pattern Analysis was carried out as it represents a refined tool to determine whether two or more behavioural components occur sequentially and with statistically significant time intervals, even in the absence of evident motor stereotypies. These sequences are named temporal patterns [4].

**Results:** An average number for subject of 229.7 (HD group) and 238.8 (Ctrl group) behavioural components were detected. Quantitative analyses with T-test for unpaired samples showed no difference between the two groups in both durations and frequencies of each component of the ethogram. However, by means of Temporal Pattern Analysis, the HD group revealed an evident increase in the complexity of the repeated temporal patterns compared to the Ctrl group. We found 34 patterns of different composition occurring, comprehensively, 3654 times in the HD group. Significantly, the Ctrl group showed 17 different patterns occurring 2157 times. In addition, HD was associated with patterns encompassing up to 11 behavioural components, whereas Ctrl with patterns limited to 4. Most of the detected patterns represent vertical and horizontal exploratory activity. Fourteen specific patterns were found in both groups. Among these, five represent sequences of grooming activity.

**Conclusion:** HD seems to be related with a general enhancement of pattern complexity in number and structure. Our results suggest that HA could exert an inhibitory modulation on the expression of specific temporal patterns characterizing mice behavioural phenotype in the open field. This study is in line with recent data suggesting a putative role of HA in the pathophysiology of tics and related disorders [5]. HA dysfunction within the CNS could result in a reduced motor selectivity and thus facilitate the appearance of stereotypies under dopamine stimulation. Further analyses are underway in our laboratories.

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