The neuronal activity of single DA cells was recorded by standard extracellular recordings from the VTA and SNc in anaesthetised SD rats. Lorcaserin was administered in cumulative doses (5-640 μg/kg, i.v.) fashion. In the antagonism experiments, the 5-HT_{2C}R selective antagonist SB242084 (200 μg/kg, i.v.) was given 5 min before lorcaserin. The effect of lorcaserin (3-10 mg/kg) on extracellular monoamine and metabolite levels were measured using online microdialysis and the tissue levels of DA and metabolites were assessed using HPLC.
Results showed that lorcaserin (n=10) significantly reduced ($p<0.05$) the firing rate of DA neurons of the VTA when compared to controls (saline, n=10). However, lorcaserin had no significant effect on the firing rate of SNc DA neurons (n=10). Preliminary results in microdialysis experiments confirmed the lack of effect of lorcaserin on striatal dopamine release.
5-HT_{2C}Rs are involved in the 5-HT mediated inhibition of the DA function. Moreover, this data shows that the 5-HT_{2C}R-mediated inhibition is specific to the mesocortical limbic dopaminergic system rather than to the nigrostriatal system. In addition, this study suggests lorcaserin as a potential drug in the treatment of compulsive behaviours and drug abuse by preferentially inhibiting the VTA DA system.

P12.11
TEMPORAL STRUCTURE OF THE MUSCULAR DYSTROPHY X-LINKED MOUSE BEHAVIOR TESTED IN OPEN FIELD
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Duchenne muscular dystrophy (DMD) is a severe X-linked recessive disease where the cytoskeletal protein dystrophin is not expressed in muscle as well as in the nervous system. The dystrophin deficient mdx (muscular dystrophy X-linked) mouse is genetically comparable to the human form of DMD and it is the most used animal model. Despite the importance of the central deficits of the DMD (e.g. deficits in cerebellar circuitry has been observed) only little information has been obtained, until now, on the behavioral structure of this mouse strain.
To shed light on this matter, 2 different groups of mice, 5 wild type (WT) and 5 mdx were tested for 10 min in open field (OF) and their behavior recorded using a digital camera. Both quantitative and T-pattern analyses (TPA) were applied. TPA is a multivariate technique based on the assessment of critical relationships among the events in the course of time.
Quantitative analysis shows a total of 1073 events for WT mice whereas 1657 for mdx mice with an increase in walking activities and vertical explorations for the last group; in addition a reduction in static activities was observed as well. Concerning TPA, WT mice show 26 different T-patterns while mdx mice show 153 different T-patterns. As to WT mice, mean occurrences ± SE of T-patterns are 101.27 ± 16.55 with a mean length ± SE of 2.54 ± 0.13; as to mdx mice, mean occurrences are 30.33 ± 4.87 and mean length 10.42 ± 0.52.
These preliminary results suggest that the behavior of the two strain of mice tested in the OF apparatus has a complex structure characterized by close interrelationships occurring sequentially and with significant constraints on the interval lengths separating them. In comparison with WT, mdx mice show a different behavioral organization with a more articulated structure of the temporal patterns. Present study sheds light, for the first time, on specific temporal features of behavior in an animal model of DMD.

P12.12
EPILEPSY AND AUTISM COMORBIDITY: ROLE OF *GAIN-OF-FUNCTION* DEFECTS OF Kir4.1 CHANNELS
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Dysfunctions of the astrocytic inwardly-rectifying potassium channel Kir4.1 (*KCNJ10*) result in impaired control of extracellular K+ in the brain contributing to pathogenic mechanisms underlying Autism-Epilepsy Phenotype (AEP), a condition where seizures (or EEG abnormalities) and Autism Spectrum Disorders (ASD) coexist.
To define the role of Kir4.1 variants in AEP, we sequenced *KCNJ10* in a sample of affected individuals, and performed genotype-phenotype correlations. The effects of mutations on channel activity, protein trafficking, and astrocyte function, were investigated in *Xenopus laevis* oocytes, and in human astrocytoma cell lines. An *in vivo* model of the disorder has also been explored by assessing locomotor behaviour, EEG recordings, and two-photon brain imaging of *kcnj10a* morphant zebrafish overexpressing the mutated human *KCNJ10*.
Germline heterozygous *KCNJ10* variants were found in about 5% of affected children, mainly displaying epileptic spasms and sensory processing dysregulation. All pathogenic variants revealed *gain-of-function* defects when investigated on *in vitro* cell systems. Kir4.1 mutations also recapitulated the main disease phenotype when transiently modelled *in vivo* in zebrafish embryos.
Our findings confirm that variants in *KCNJ10* deserve attention in autism-epilepsy, and provide insight into the molecular mechanisms of autism and seizures, as well as into the role of astrocyte dysfunction in abnormal synaptic transmission and electrical discharge underlying the disorder. Further work on zebrafish models is now ongoing to get larger phenotype assessments and high-throughput drug screenings, to allow focusing studies in transgenic mammalian models while seeking for new drugs for children with autism-epilepsy comorbidity.

P12.13
THE FAAH INHIBITOR NF1245 SHOWS ANTIEPILEPTIC EFFECTS IN TWO RAT MODELS OF EPILEPSY
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