
Behavioral signatures of Neuroinflammation
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Behavior

- The way in which one acts or conducts oneself, especially toward others
- The way in which an animal or person acts in response to a particular situation or stimulus
- The way in which a natural phenomenon or a machine works or functions
- Collection of movements that fit certain pattern
- Animal, cell, molecule, electron…
- **All behaviors are underlined by biochemical processes**
- **Do all biochemical processes result in the behavior?**
- Level of detection

Why to study behavior

- Academic reasons
- Function of the brain (memory, learning, fear, emotions)
- Psychiatric Diseases (mental health and addiction)
- Diseases that are associated with functions of the brain.

Tests to study behavior in animal models

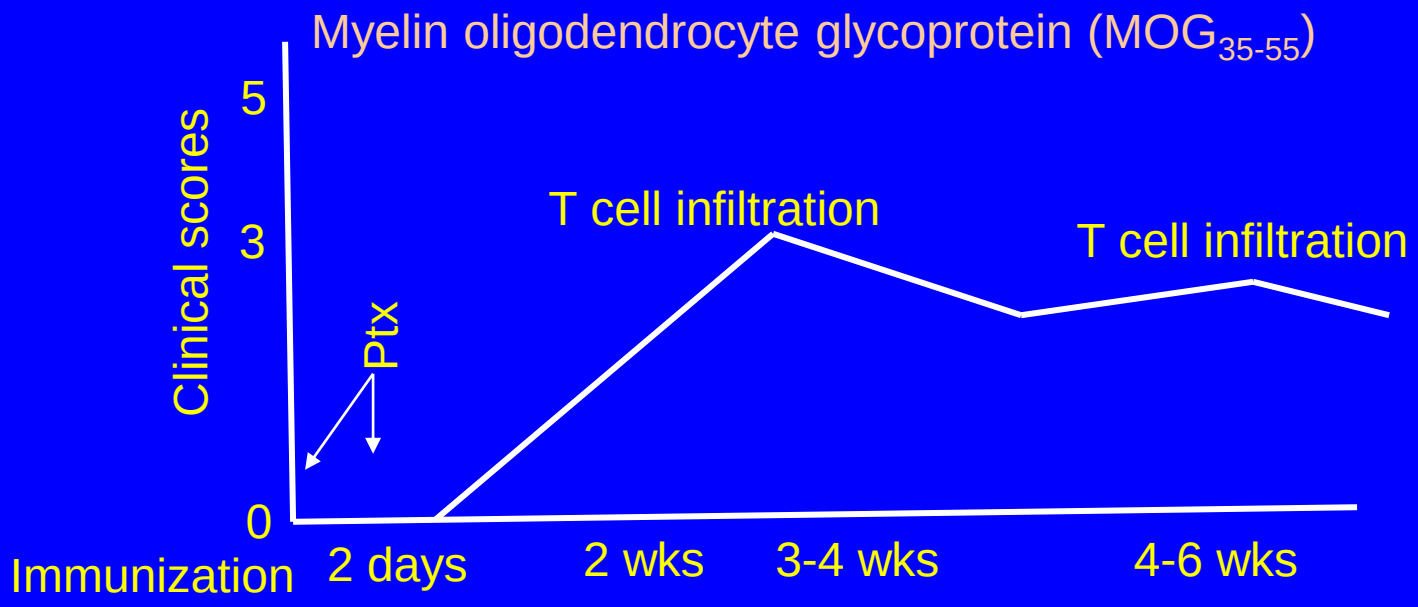
- Anxiety tests, mazes, pain, conditioning
- Majority of experiments evaluate function of a particular brain area, neuronal function, connection
- Tests are directed to evaluate a function of interests
- I propose to implement multi-test approach for neurodegenerative diseases.

Multiple Sclerosis

- First description of the disease in 14th century
- In 1838 Dr. Charcot connected the symptoms to the pathology of the central nervous system (CNS)
- MS is characterized by appearance of demyelinating plaques throughout the brain and spinal cord
- Approximately **400,000 North Americans** acknowledge having MS, and every week about 200 people are diagnosed. Worldwide, MS may affect 2.5 million
- Autoimmune disorder
- Myelin destruction and neurodegeneration
- Neurological symptoms: fatigue, loss of sensory and motor functions, vision…

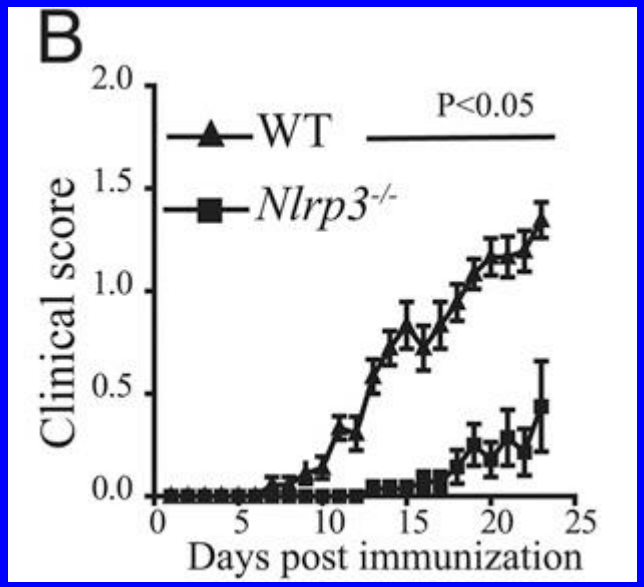
EAE model of MS

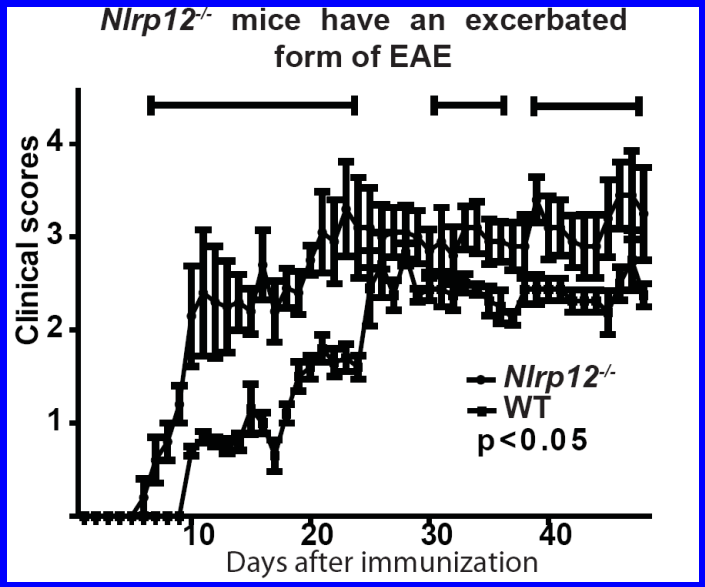
Experimental Autoimmune Encephalomyelitis



0 healthy animal
1 tail dragging on ground constantly
2 tail dragging and locomotor disturbance of at least one hind leg
3 severe hind body paralysis
4 severe locomotor deficiency of front limbs
5 conditions to terminate experiment

Clinical evaluation of the EAE model
Problems of current approaches





- Two experienced and independent observers
- Small number of outcomes
- Short observation period
- Fatigue inducing nature of experiments
- Span of clinical score is very small

Need for a new system

New approach

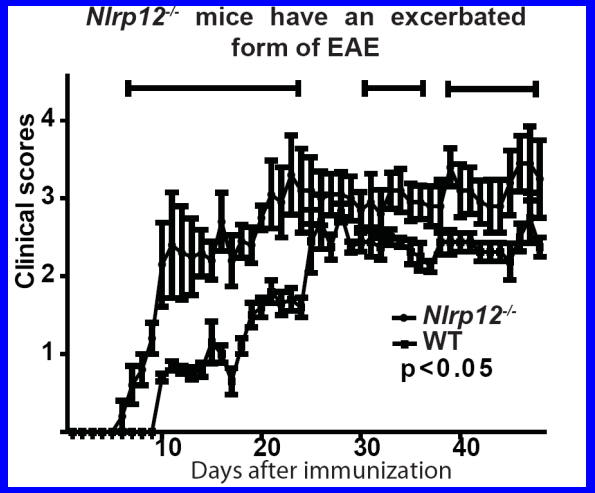
- Automated
- Scans behavior at different time of a day
- Measures multiple outcomes

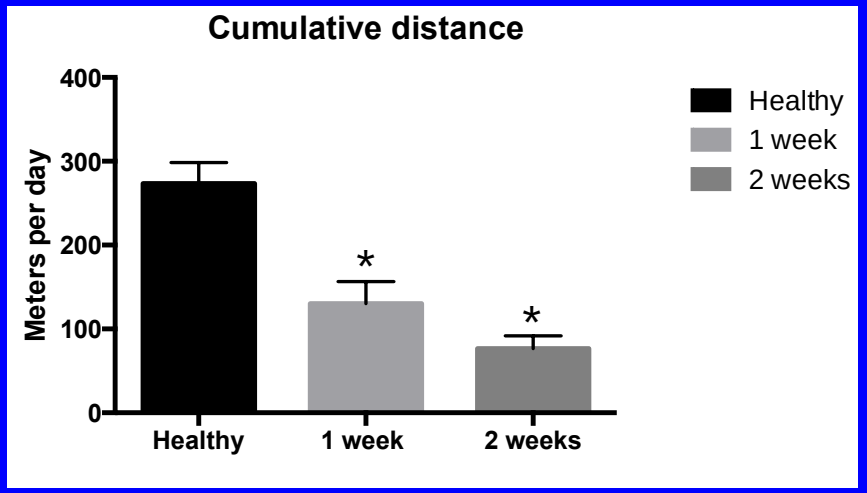
Acquisition analysis system

Array of behaviors

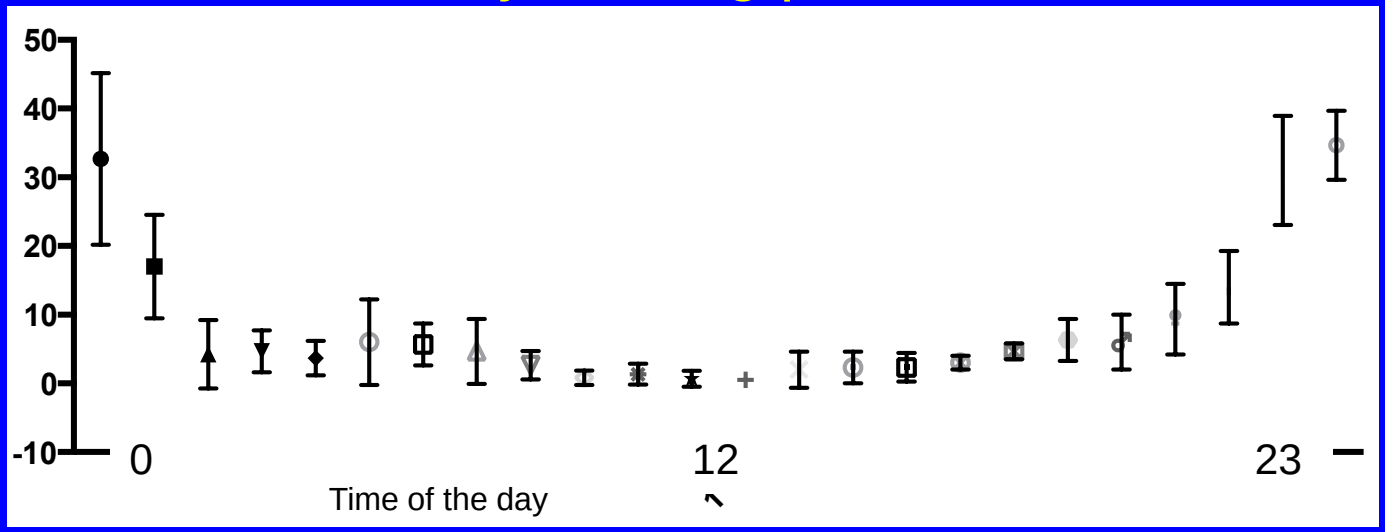
Statistics	Day Bouts	Day Bout Fraction	Day Seconds	Day Time Fraction	Night Bouts	Night Bout Fraction	Night Seconds	Night Time Fraction
Awaken	26	0.077%	73.88	0.103%	26	0.077%	31.68	0.044%
Chew	143	0.422%	162.12	0.226%	370	1.092%	345.84	0.481%
Circle	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Come Down	59	0.174%	17.04	0.024%	127	0.375%	38.04	0.053%
Come Down From Partially Reared	266	0.785%	67.52	0.094%	548	1.618%	139.56	0.194%
Come Down To Partially Reared	73	0.216%	19.32	0.027%	198	0.585%	55.68	0.077%
Dig	5	0.015%	0.92	0.001%	74	0.218%	12.56	0.017%
Drink Spout1	56	0.165%	54.92	0.076%	53	0.156%	40.96	0.057%
Drink Spout2	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Drink Spout3	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Eat Zone1	176	0.520%	508.76	0.708%	299	0.883%	376.32	0.524%
Eat Zone2	74	0.218%	119.96	0.167%	390	1.151%	543.12	0.756%
Eat Zone3	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Forage	10	0.030%	1.52	0.002%	129	0.381%	27.28	0.038%
Groom	132	0.390%	3668.72	5.106%	213	0.629%	9265.32	12.895%
Hang Cuddled	408	1.204%	104.84	0.146%	1668	4.924%	418.64	0.583%
Hang Vertically	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Hang Vertically From Rear Up	44	0.130%	10.80	0.015%	147	0.434%	35.72	0.050%
HangVertically From HangCuddled	271	0.800%	68.44	0.095%	1163	3.433%	294.80	0.410%
Jump	20	0.059%	10.32	0.014%	82	0.242%	41.28	0.057%
Land Vertically	27	0.080%	8.04	0.011%	144	0.425%	38.20	0.053%
No Data	2	0.006%	16.20	0.023%	2	0.006%	1515.00	2.109%
Pause	103	0.304%	885.88	1.233%	58	0.171%	1641.48	2.285%
Rear Up	52	0.154%	12.40	0.017%	76	0.224%	20.32	0.028%
Rear up Full From Partial	128	0.378%	30.96	0.043%	298	0.880%	72.56	0.101%
Rear up Partially	290	0.856%	76.76	0.107%	641	1.892%	171.84	0.239%
Remain Hang Cuddled	534	1.576%	1076.36	1.498%	2176	6.424%	2877.24	4.004%
Remain Hang Vertically	127	0.375%	64.76	0.090%	647	1.910%	313.00	0.436%
Remain Low	2404	7.097%	4494.16	6.255%	3929	11.599%	5485.40	7.634%
Remain Partially Reared	231	0.682%	164.08	0.228%	429	1.266%	287.08	0.400%
Remain RearUp	111	0.328%	50.24	0.070%	295	0.871%	123.76	0.172%
Repetitive Jumping	0	0.000%	0.00	0.000%	2	0.006%	1.96	0.003%
Sleep	30	0.089%	18264.60	25.420%	24	0.071%	10845.24	15.094%
Sniff	277	0.818%	258.56	0.360%	54	0.159%	49.56	0.069%
Stationary	8	0.024%	3.80	0.005%	28	0.083%	11.16	0.016%
Stretch Body	89	0.263%	46.12	0.064%	229	0.676%	137.52	0.191%
Turn	3968	11.714%	1045.32	1.455%	1885	5.565%	504.12	0.702%
Twitch	462	1.364%	1263.56	1.759%	362	1.069%	1001.52	1.394%
Unknown Behavior	1527	4.508%	807.72	1.124%	137	0.404%	93.52	0.130%
Urinate	0	0.000%	0.00	0.000%	0	0.000%	0.00	0.000%
Walk Left	359	1.060%	127.44	0.177%	645	1.904%	196.48	0.273%
Walk Right	396	1.169%	140.56	0.196%	806	2.379%	269.60	0.375%
Walk Slowly	894	2.639%	272.76	0.380%	1737	5.128%	529.28	0.737%

Distance walked a day

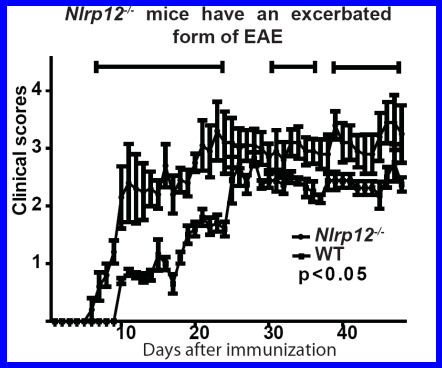




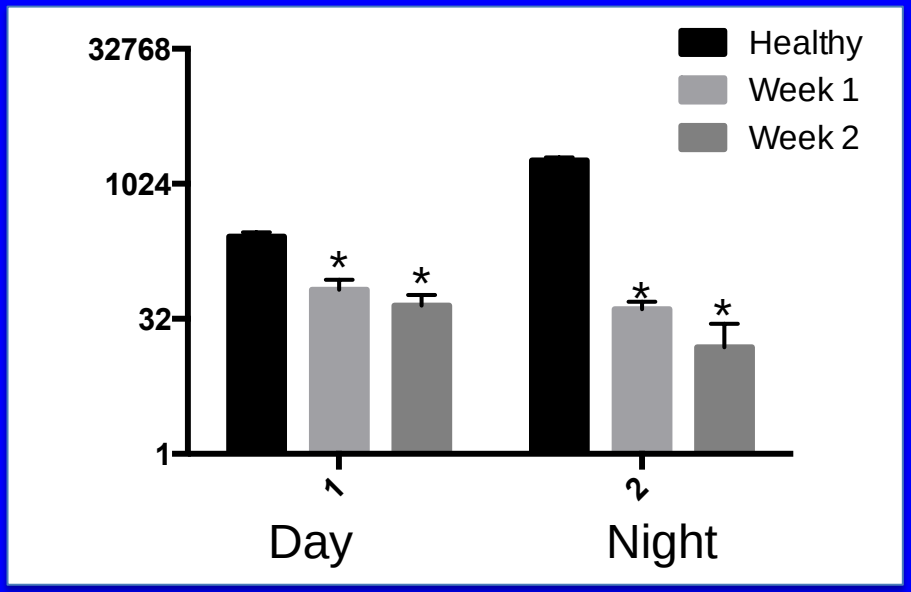
Healthy walking pattern



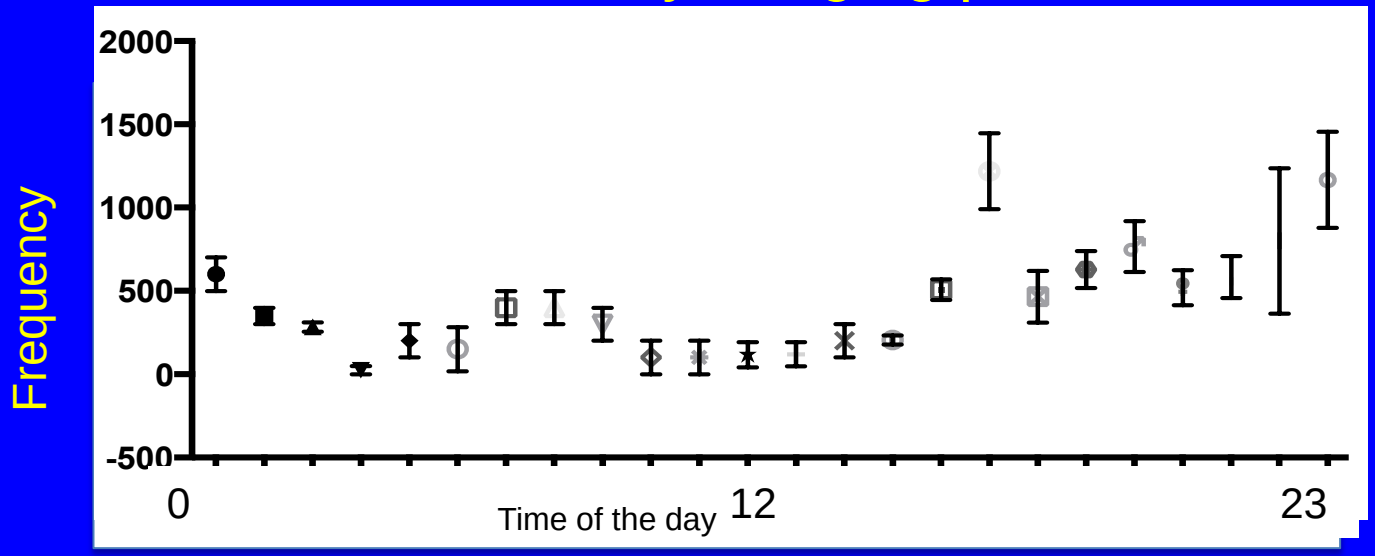
Mice walk significantly less as EAE progresses



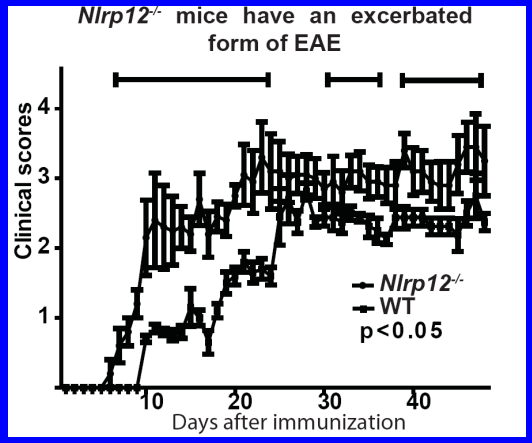
Hanging

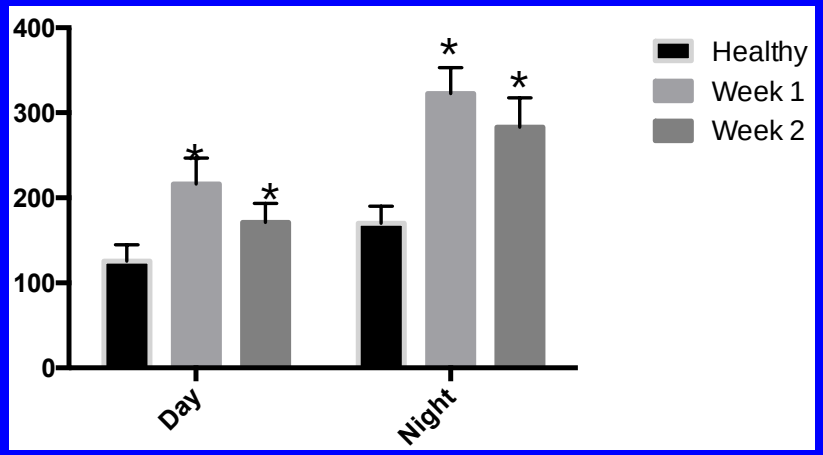


Healthy hanging pattern

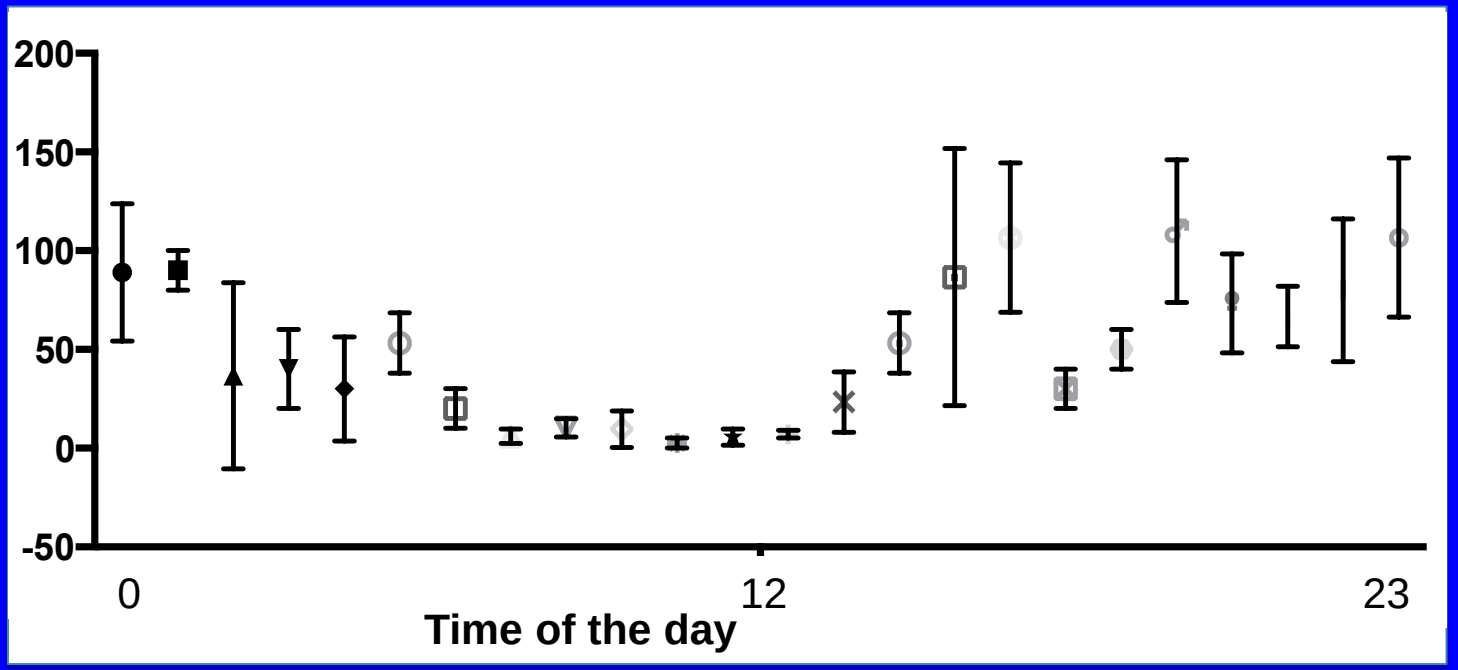


Grooming

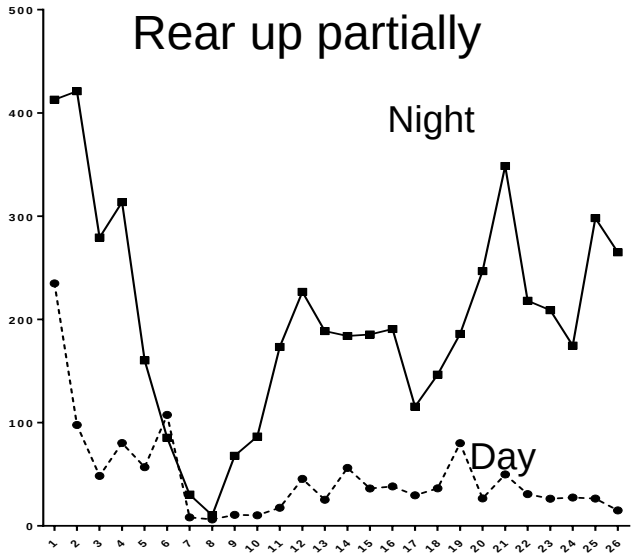


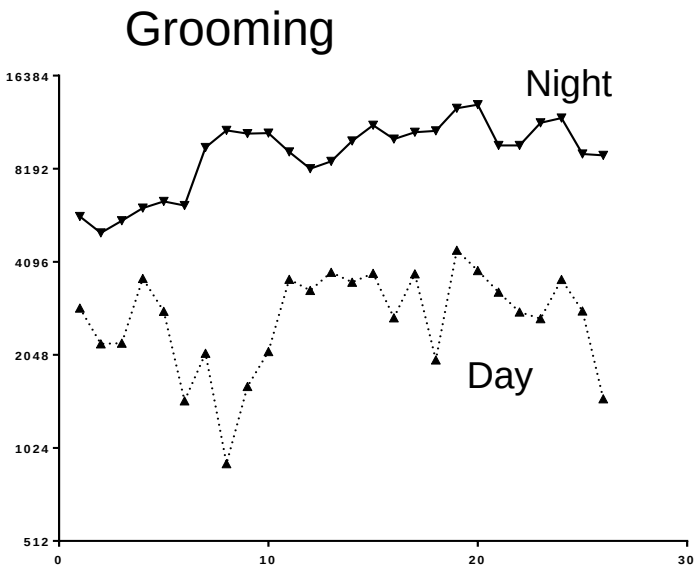


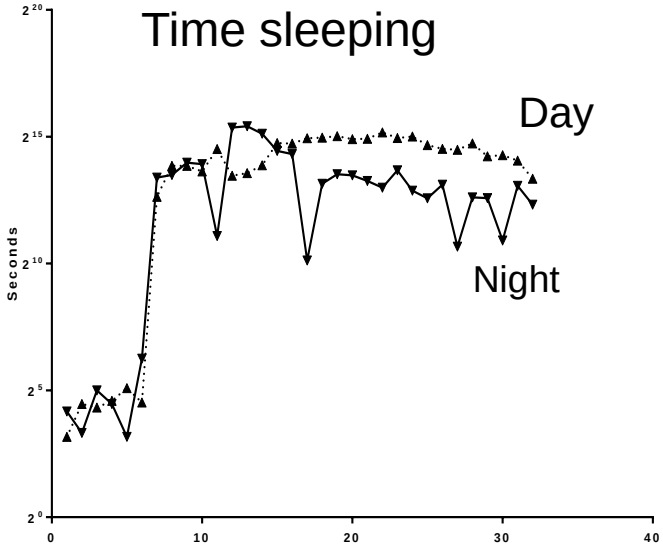
Healthy grooming pattern

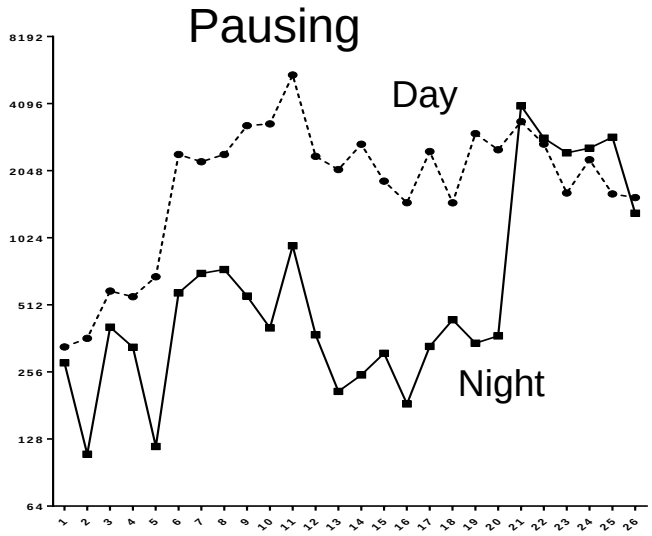


Behavior at night and day in EAE









Patterns at night and day are different in different behaviors

Conclusions

Automated analysis is more sensitive

Tests have to be done the different time of the day

Multiple behaviors are affected during EAE

Multi-parametric behavioral tests are necessary

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