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IS MICE BEHAVIOUR INFLUENCED BY MUSIC?

by

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Budapest
- 2013 -

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INTRODUCTION

Mice are the most frequently used laboratory animals.
They are very adaptive and spread with men from its origin in Asia to all parts over the world.[1]
There are plenty of mice species of which the best known is *Mus musculus*, the house mouse.
Mice are primarily nocturnal active and have a poor vision, which is compensated by hearing and especially their sense of smell.
Their perception evolved from pest, to also pet, and finally element of scientific community.

Most laboratory strains are inbred. There are plenty mouse strains available for different studies. Mutant and transgenic strains can be created by ordinary breeding, transgenic, or knockout.
A milestone in the use of mice as laboratory animals was achieved by Clarence Cook Little. Initially studying the inheritance of coat colour in mice, he bred descendants of siblings with each other and thus created the first inbreed strain of mice, in 1909. Little's interest in neoplastic diseases, which he believed to be best studied using genetics, lead to the assumption that elimination of the great genetic diversity in mice would facilitate this study.[2]
It was found that other constitutional diseases also became established in the various mice genotypes, many of these conditions also present in man.
The sequencing of the mouse genome was completed in 2002, and virtually all genes have human homologs.[3] This provides the option to perform knockout studies which can be translated to humans.
Mice have favourable characteristics to be laboratory animals. They are easy to maintain, and reproduce fast, what is especially important in genetic studies.
The gestation period in mice is 18-21 days, as a general rule, inbred mice tend to have longer gestations periods and smaller litters.[4]
Not only their genetic makeup is utilized, they also serve an important role in behaviour studies, and further uses can be considered. Having a superior sense of smell, they might be used to detect illegal or dangerous substances, such as drugs or explosives.[5]

LITERATURE REVIEW

In the *in vivo* research the use of laboratory mice is inevitable. Therefore their welfare should be as adequate as possible. In this matter we focus on the three R's (Reduction, Replacement, and Refinement). Reduction can only be performed as long as a statistically representative number of test objects are maintained. Replacement is not always possible, because required characteristics cannot be tested otherwise; some strains are specifically bred for this purpose. It has been observed that different strains, even sex, show variable reactions to the same type of enrichment. [6]

Refinement has many possible approached, and is in constant development. Considering enrichment it is not satisfactory if only the direct goals, relating to the animals, are fulfilled, furthermore it is important that these are also practical.[7]

For a normal response in behaviour the housing should be as natural as possible, this can be approached by environmental enrichment. Different levels and forms of environmental enrichment are available, and can be compared among each other.

One option of refinement would be to improve the housing conditions, which can be performed in various ways.

An important aspect in this type of refinement is that the animals continue to use and benefit from the enrichment; also it is not allowed to influence the outcome of experiments in an incalculable direction. In this matter, nesting material is a reliable enrichment.[8]

The availability for nesting material, and also the opportunity for exploration has been agreed to support environmental enrichment, in a 2002 review.[9]

Concerns that improved housing conditions, in female mice, might interfere with test results have been disagreed again in 2004.[10]

Refinement is more problematic in males, as they show increased aggression in structured cages, however also the position of the dominant male was more variable.[11] A later conducted experiment showed similar results. If males are kept under enriched conditions, enough space must be provided.[12]

Nowadays, a large number of different animal models and strains of the same species are available. By using adequate test subjects, the results can be translated to targets, like human cases, production and companion animals. Environmental enrichment is a highly occupied field and accordingly is represented in this action.

Speaking about environmental enrichment, its most popular research area is probably dedicated to learning and the maintenance of mental fitness, in other words, the improvement of the neurological set up, therefore effects of aging and development are often in the centre of observation. A positive effect of environmental enrichment has been accredited in the prevention of "Alzheimer disease". According to a study, environmental enrichment is even more crucial than physical exercise to prevent mental degradation.[13] Using another strain obligated to these studies a positive implication in the reduction of neurodegeneration has been approved if mice were exposed to environmental enrichment in young age.[14] A positive effect has even been confirmed on molecular level.[15]

Another disease in relation to neurodegeneration in which environmental enrichment proved a positive effect is "Huntington's disease".[16] Further successful results have been obtained in mice with ectopia.[17] [18]

In mice models for "Down syndrome" a positive effect was also elicited on their learning progress, although animals of both sex have been equally examined, only females improved significant.[19]

Also studies dedicated to the "Rett syndrome" reflected a positive impact of environmental enrichment.[20]

The before mentioned positive effects in neurodegenerative or developmental diseases are of course also present in healthy mice. Related and further studies, resolving memory and learning, are also conducted and very prominent in healthy individuals.

Apart from results gained in standardised tests, the following findings are based on various physiological parameters, understood to be related to memory, nerve expression, and information delivery, in responsible brain areas. It was already in 1982 suggested that the mammalian brain remains responsive for environmental enrichment up to advanced age, this was mainly attributed to a high level of RNA in cerebrocortical cells. [21] Whereas in the 1982 experiment only male mice were tested, in 2003, using different parameters, it was suggested that enrichment introduced during middle age can reduce age-related impairment in spatial memory in males and females.[22]

Environmental enrichment, in form of social enrichment in young age shows beneficial effect, producing changes in social behaviour and hormones related to learning.[23]

Recent experiments also focus on the action of monoamines, which play an important role in the maintenance and formation of synapses, however in those studies also the negative effect of stress, reducing the amount of the hormones and their transporters, not only influencing the mice itself, but also the physiological set up of its offspring was observed.[24] However, even though environmental enrichment is desirable in all aspects, in 2004 first evidence was reported that different elements of enrichment have a markedly distinct effect.[25]

Accordingly, environmental enrichment has a proven beneficial effect on learning, maintenance and protection of neurological health.

Another field that is in the focus of study, involving the effect of environmental enrichment, is anxiety. In contrast to the aforementioned experiments, conducting neurological health, whereas specific strains for different diseases exist, during anxiety studies strains reacting differently to environmental enrichment become obvious. Behavioural differences in non-enriched mouse strains have already been observed in 1959[26] and 1966.[27] Variations in behaviours related to strains are even more markedly observed under enriched conditions. Contrary to an improved anxiety state under the influence of environmental enrichment, in an experiment comparing two strains, one of them, BALB/c, showed an increased level of anxiety, the other one, C57BL, showed reduced fear.[28] Another strain specific behavioural reaction in relation to anxiety was observed with a C strain, which showed decreased anxiety, while no change was observed in B6.[29] Anxiety often produces stress. Mice exposed to a stress situation under enriched conditions showed a lower corticosterone level compared to the control group, what indicates a beneficial effect.[30]

The beneficial effects of environmental enrichment on anxiety, mentioned before, referring to the cortisone level, and further also immunity, have been confirmed in another study, in 2004.[31]

Anxiety itself also stands in relation to learning processes and its necessity, under enriched conditions an improved memory for contextual fear conditioning was observed.[32]

In the study of effects derived from environmental enrichment continuous studies are conducted and new approaches are tested. For example by changing the fraction of light in the cage, blue light enhanced the stress resistance in mice.[33]

A before mentioned important aspect of environmental enrichment is that it needs to be practical. The vision of mice does not seem to play an important role, but pheromones do.

The mouse eye is of comparably low optical quality and therefore vision is not of primary importance in mice. Even animals with further constricted vision, or even blindness, apart from a longer adaptation period, do not show reduced activity in a novel environment.[34] On the other hand pheromones are of major importance in mice for intraspecies communication. Enrichment needs to be practical, this also includes cleaning protocols, but these have to be assessed to evaluate to which degree the normal signalling is altered.[35] Sexual pheromones are detected by the vomeronasal organ and the main olfactory epithelium. If there is a developmental alteration, or surgical removal, the individuals show abnormal behaviours. It seems that wild-type females need these hormones to repress male behaviour and activate female behaviours.[36]

Another, newer approach in terms of refinement is the application of music. Music, in contrast to noise, is "organized sound" (Edgar Verèse), both influence mice in different ways. Noise is not desired, but always present to some extent. It can "alter endocrine, reproductive and cardiovascular function, disturb sleep/wake cycles, and can mask normal communication between animals" (TURNER et al 2007)[37]. Vacuuming, which is a daily standard procedure in some facilities, produces frequencies audible for mice and could therefore be a source of stress.[38] More shocking results have been obtained while checking the effect of construction noise on mouse gestation and neonatal growth, following which the number of life born pups is decreased and the number of stillborn pups increased.[39]

It is impossible to fully overcome background noise. Even if humans do not realize noise, laboratory animals possibly still do, because they have a different hearing range. Mice cannot hear as low frequencies as humans, but way higher frequencies, up to two octaves higher. Expressed in numbers: mice at 60 dB: 2.3 kHz – 85.5 kHz, versus humans: 31Hz – 8.1 kHz.[40]

The logical approach to limit the disturbance by noise is to overlap it or to substitute it with a more pleasant experience. This more pleasant experience can possibly be found in using exposure to musical stimuli.

Musical exposure has already demonstrated beneficial effects in various fields. Classical music is probably the most established type of music used in refinement. The reason for this is attributed to the beneficial properties of Mozart music, termed “Mozart Effect”. For studies of this effect, the piano sonata, K. 448 is usually used.

The “Mozart effect” was described by Rauscher et al. (1993). It was claimed that after listening to Mozart’s sonata for two pianos (K 448) for 10 minutes, the spatial reasoning skills significantly improved, represented by a spatial IQ score rise of 8 or 9 points. However, the effect did not last for more than 10-15 minutes. The results are still controversially, because not all investigators were able to reproduce these findings.
Although for research Mozart’s double piano sonata K 448 is usually used, also his piano concerto no 23 in A major K 488 has proven to be effective as well, there are probably more compositions which can elicit this desired effect.[41]

The positive effect of Mozart music on spatial memory has been conducted in various studies, other than in the initial experiment, long term exposure was performed in most of the studies. A long-term enhancement of maze learning in mice was attributed to the Mozart effect [42], and also a significant influence on genes in the cortex and hippocampus was observed.[43] Spatial learning and memory in mice was also improved after exposure to the “Liang Zhu violin concerto”.[44]

It is suggested that the “Mozart effect” has an effect on the intracellular signalling pathways, this statement further supports a beneficial effect, therefore might improve learning and memory functions.[45]

However, results obtained after music exposure are not only reserved to learning and memory improvements.
Impressive results were obtained in two studies, with humans, presenting a beneficial effect of Mozart music in epilepsy patients.[46]

Also Mozart music has effectively reduced behavioural and psychological symptoms of dementia in human subjects.[47]

A recent study, 2012, showed a beneficial effect of both opera and classical music in cardiac allograft survival.[48]

A beneficial effect of music exposure was documented in cancer treatment, by effectively reversing the adverse effect of stress on the number and capacities of lymphocytes.[49]

Considering the above described, studies on musical influences to the laboratory animals promise to be fruitful.

OWN INVESTIGATIONS

MATERIALS AND METHODS

Animals

Data will be collected from 20, specific pathogen-free (SPF), sexually mature, CD1 male mice (body weight, 15-30 g, age 2-5 months); *Mus musculus*, B6; 129S6-Stat 5B). Mice are bred in the Cornell University, Transgenic Mouse Core Facility, (Ithaca, NY). Serology, bacteriology and parasitology evaluation were performed quarterly, at each cage change for sentinel animals exposed to bedding of the subject mice. These mice are part of an Institutional Animal Care and Use Committee-approved research protocol; the principal investigator of that study gave written consent to expose these animals to short-term music exposure and afterwards perform ultrasound recording procedure.

Housing

Mice are in an AAALAC-accredited institution, in polycarbonate individually ventilated cages (IVC) (7 × 11 × 5 in.), on autoclaved ⅛ in. corncob grit (1040; Harlan Teklad, Fredrick, MD). Cages are enriched with nestlets (Ancare, Bellmore, NY) and PVC tubing and placed on a rack (Micro-FLO/Micro-VENT Environmental Rack System, Allentown Caging Equipment Company, Allentown, NJ). Mice are maintained on a 14:10-h light:dark cycle with free access to water through an automated watering system (Edstrom, Waterford, WI) and food (LM 485 Irradiated rat / mouse diet 7912, Harlan Teklad).

Procedures

Mice are to be exposed to music and recordings are taken in an empty cage-changing station (NU 612 Cage Changing Station, NuAire Plymouth, MN), in an open IVC (individually ventilated cage). We use an ultrasound microphone to record vocal emission made by pair of mice before and after the two types of music exposure. Pairs are assigned randomly, forming 10 pairs, resulting in 30 recording (10 × 3), 5 minutes each. In compliance with the IACUC-approved protocol, the mice are neither anaesthetized nor given analgesics for these procedures.

Mice are carried from the next door room, put in the recording cage by pairs (10 × 2), and for 5 min the basal vocalization form taken. After that they are subjected to the 10xMozart, and after that the vocalization registered during the subsequent 5 minutes (after Mozart Vocalization, in the following aMV). In the next 5 minutes there is a break. After that animals (pair after pair) are exposed to the Bach music, and the following 5 minutes the vocalization recorded (in the following after BV). Meanwhile the remaining mice are maintained at 22°C under a dimly lit room with continuous access to food and water except in the registration chamber.

Music

For the energizer music Mozart's Sonata for Two Pianos in D Major, K 448 was chosen. For the relaxing music Bach's Goldberg Variation (BW 988": Aria, var.2, var.3, var.8 and var.10, presented by Glenn Gould) was selected. For exposure the pieces were accelerated to the desired frequencies. The quality was according to the CD-standard (44.1 kHz and 16 bit resolution). For the repeatability, a variant with the dominant "d1" measuring voice of 293.665 Hz was also prepared, by an attenuation of – 6 dB. The Sound Pressure Level (SPL) during the music exposure was 70 dB.

Music exposure - sound recording

In our model, mice are to be exposed to an energizer (Mozart) and relaxing (Bach) music, using an outside Mac Book Pro and a speaker. During data collection, a high quality condenser microphone (USG 116 to 200 UltraSoundGate Kit, Avisoft, Berlin, Germany), protected by a plastic collar, is put in the corner of the IVC, at a distance of 10 to 15 cm from the mice. Recordings will be analysed by using software provided by the manufacturer SASLab Pro, version 4.3, Avisoft) that is sensitive to frequencies as high as 62.5 kHz. A spectrogram analysis is to perform on each recording to determine visually whether any ultrasonic sounds had been heard.

Behaviour scoring

This technique is used to evaluate the chain of behaviour, concentrating on the demobilization (startling) using an arbitrary scale as follows: 0 (no change), 1 (light to moderate) and 2 (intense). Free-running parameters were measured in separate observers.

Statistical analyses

For each trial we score the presence or absence of ultrasound emission immediately after the music exposures was performed. Loudness, duration, and other call parameters are ignored; only presence or absence of ultrasonic emission at any frequency will be used for analysis.

Using $\chi 2$ test for both comparison, we compare the presence of USV during basal, aMV and aBV. If ultrasound vocalization is presence, the spectrogram analysis will be performed by using RAVEN Pro software (TheCornellLab of Ornithology). Differences between group means were assessed using ANOVA followed by Student–Newman–Keuls test for multiple comparisons. An alpha-level of 0.05 is used to define statistically significant.

Ethical approval

The experiment may cause only transient discomfort to the mice. The Cornell Center for Animal Resources and Education CARE (Ethical Committee of Cornell University) approved the protocols.

DEFINITION OF BEHAVIOURAL PARAMETERS

The mice behaviour is evaluated according to: running, sniffing, grooming (itself or other mouse), rearing, digging, eating, and exploration of the ultrasound recording device.

Running

Running involves all actions the mouse performs in locomotion, basically all movements which are associated with a change of location; e.g. climbing.

Sniffing

Since the mice are almost always sniffing, this behaviour is reserved for exploratory behaviour with a limited range of motion.
Sniffing comprises of localised exploration; including the mouse supporting itself at the wall.

Grooming

In rodents, a general pattern of self-grooming cephalocaudal progression is observed as follows: paw licking, nose and face wash, head wash, body wash and fur licking, leg licking, tail/genitals licking and wash.

Resting

The mouse is "motionless". Sleeping is the primary resting behaviour.
A sleeping mouse is either curled up laying on its side, or sitting curled up, with its face into its body.

Rearing

The forelimbs are lifted off the ground, the main body weight is located at the hind part of the mouse, while not being supported.
When it is obviously that the aim is to examine the ultrasound recording device, located in the middle on top of the cage, the time is added to the "exploration of the ultrasound recording device" behaviour.

Digging

The mouse is using its forelimbs to move the bedding, or pushes it past below its body, also using its hind limbs.

Eating

Usually the mouse uses its forepaws to hold food while eating it.

Exploration of the ultrasound recording device

The recording device is located in the centre on top of the cage.

Exploration is performed in various ways, all accredited to this behaviour if the aim is clear, such as climbing on housing elements to get closer to the device and sniff it, raise up towards it, mostly associated with holding on to it.

RESULTS

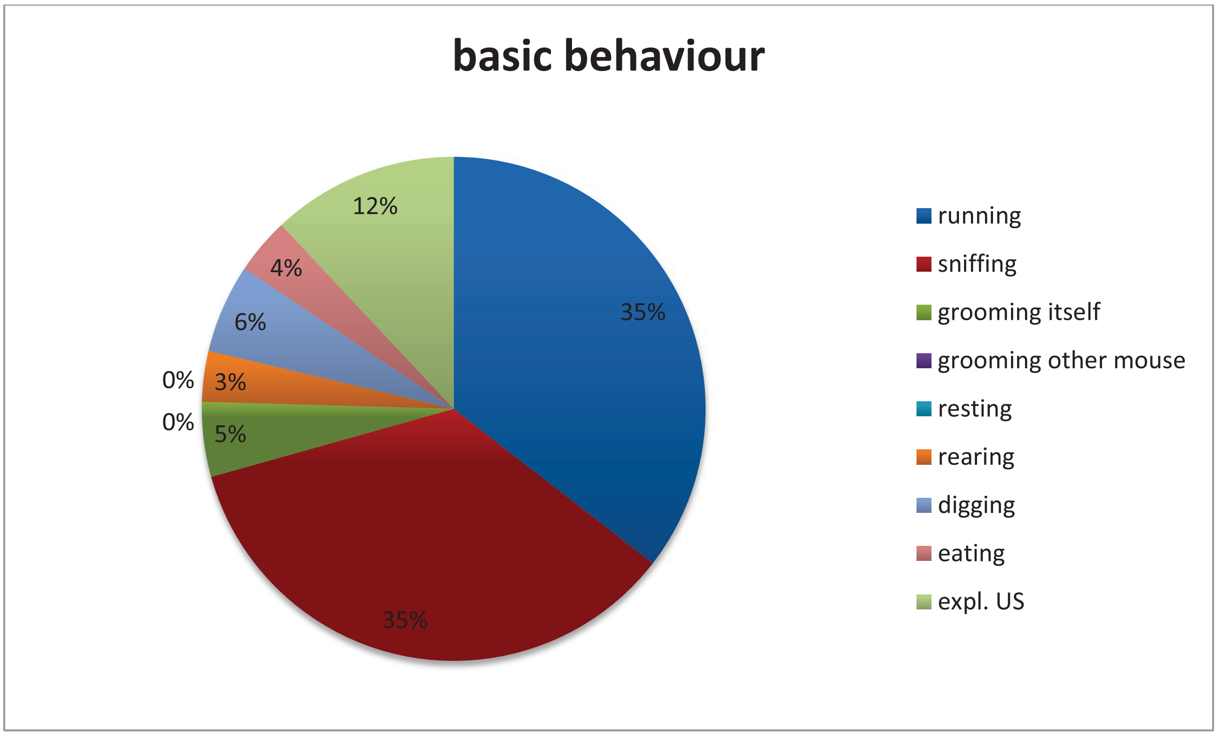


Figure 1: Behaviour of mice before exposure to music, in per cent, rounded numbers

Under normal conditions (absence of music) the mice spend most of the time running (35.50%), closely followed by sniffing (35.15%), exploration of the ultrasound recording device (12.00%), digging (5.70%), grooming itself (4.80%), eating (3.60%), rearing (3.25%), grooming other mouse (0.00%), and resting (0.00%).

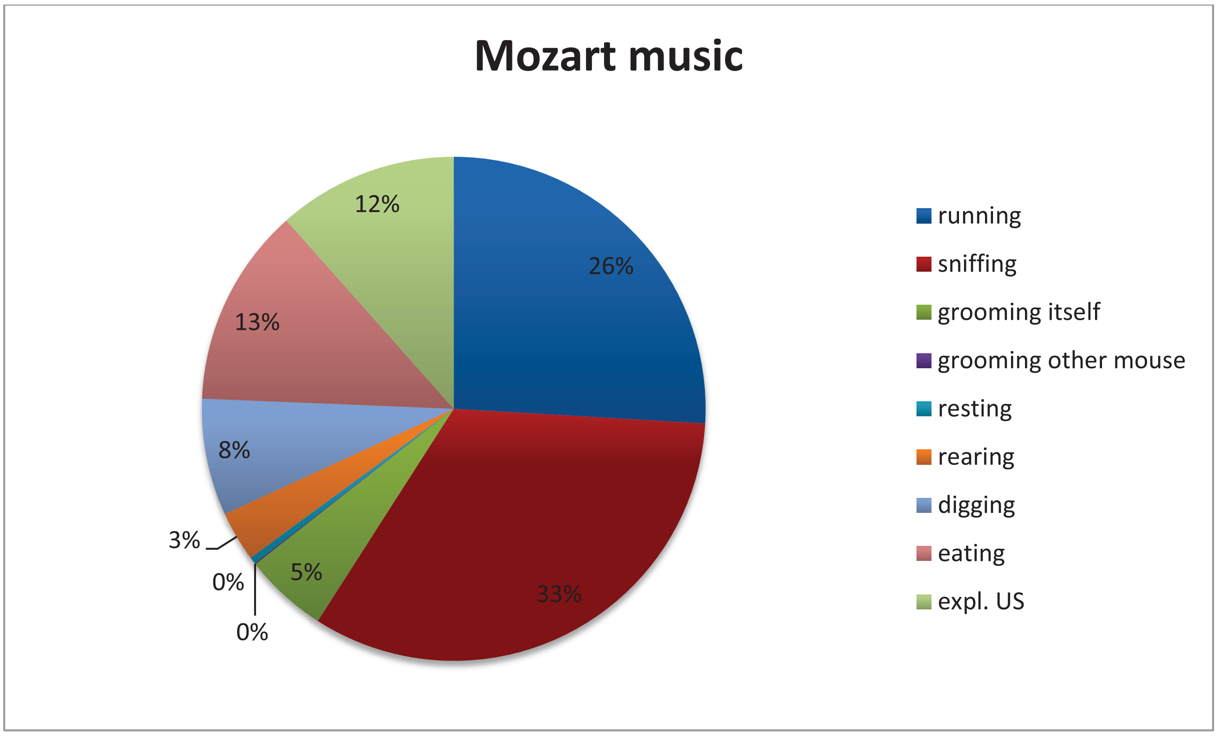


Figure 2: Behaviour of mice during exposure to Mozart music, in per cent, rounded numbers

When the mice were exposed to Mozart music, they spent the highest amount of time sniffing (33.14%), followed by running (25.93%), eating (12.79%), exploration of the ultrasound recording device (11.57%), digging (7.50%), grooming itself (5.36%), rearing (3.21%), resting (0.43%), and grooming other mouse (0.07%).

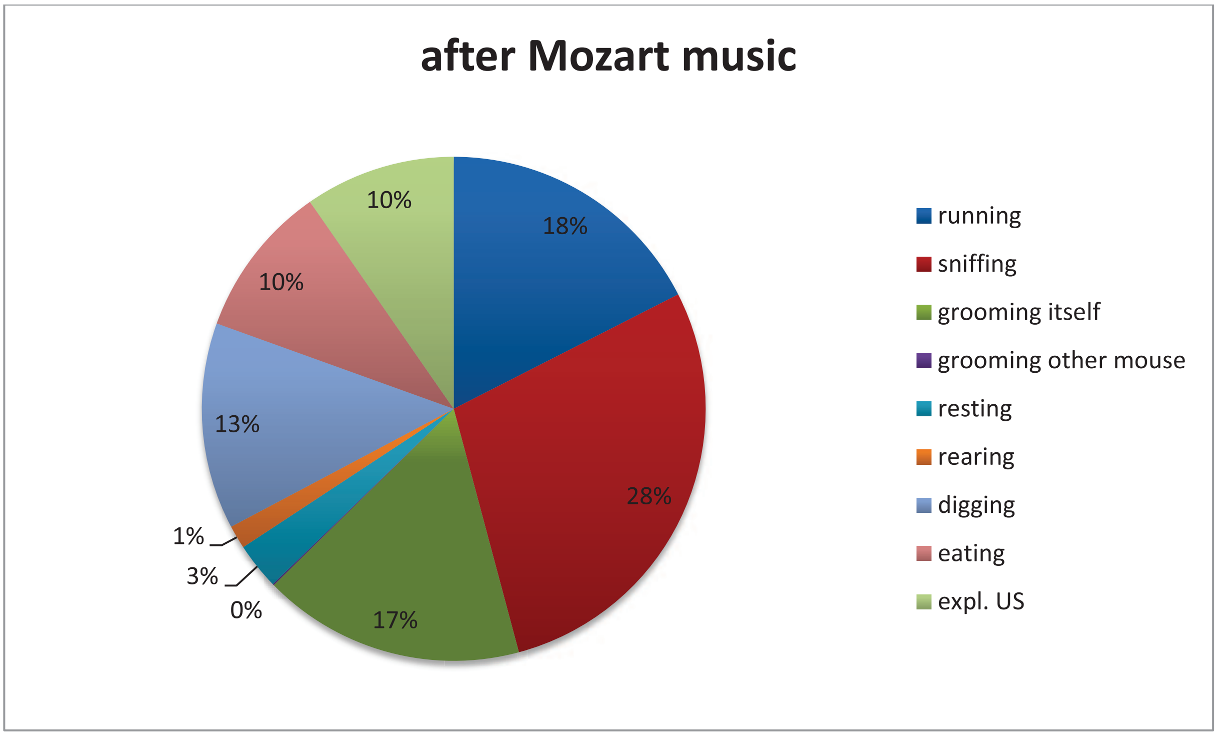


Figure 3: Behaviour of mice after exposure to Mozart music, in per cent, rounded numbers

After the exposure to Mozart music the behaviour was accordingly: sniffing (28.33%), followed by running (17.50%), grooming itself (16.83%), digging (13.25%), eating (9.83%), exploration of ultrasound device (9.67%), resting (3.00%), rearing (1.50%), and grooming the other mouse (0.08%).

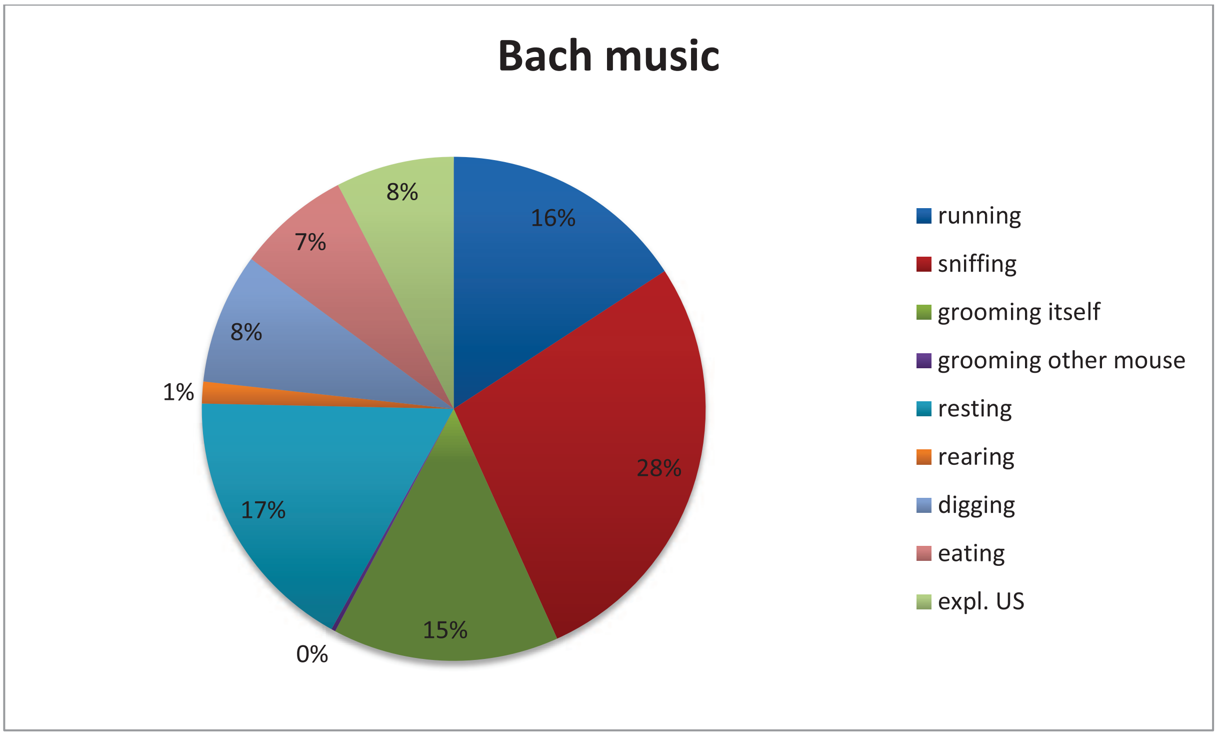


Figure 4: Behaviour of mice during exposure to Bach music, in per cent, rounded numbers

While exposed to Bach music, the mice spent most of the time sniffing (27.47%), followed by resting (17.27%), running (15.80%), grooming itself (14.53%), digging (8.40%), exploration of ultrasound recording device (7.60%), eating (7.27%), rearing (1.40%), and grooming the other mouse (0,27%).

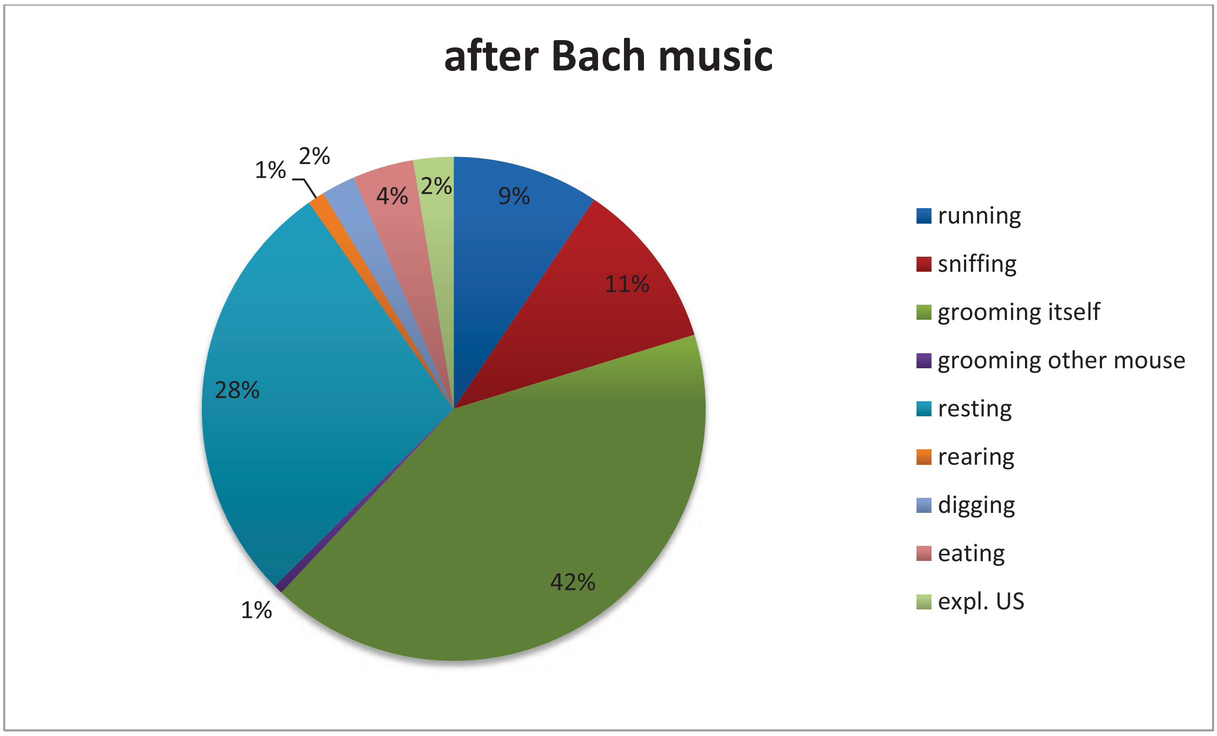


Figure 5: Behaviour of mice after exposure to Bach music, in per cent, rounded numbers

In the time period after the exposure to Bach music, the mice spent most of the time grooming itself (41.75%), followed by resting (27.67%), sniffing (10.83%), running (9.42%), eating (3.93%), exploration of ultrasound device (2.58%), digging (2.17%), rearing (1.08%), and grooming the other mouse (0.58%).

The data were processed by using multiple ANOVA (**an**alyse **o**f **va**riance).

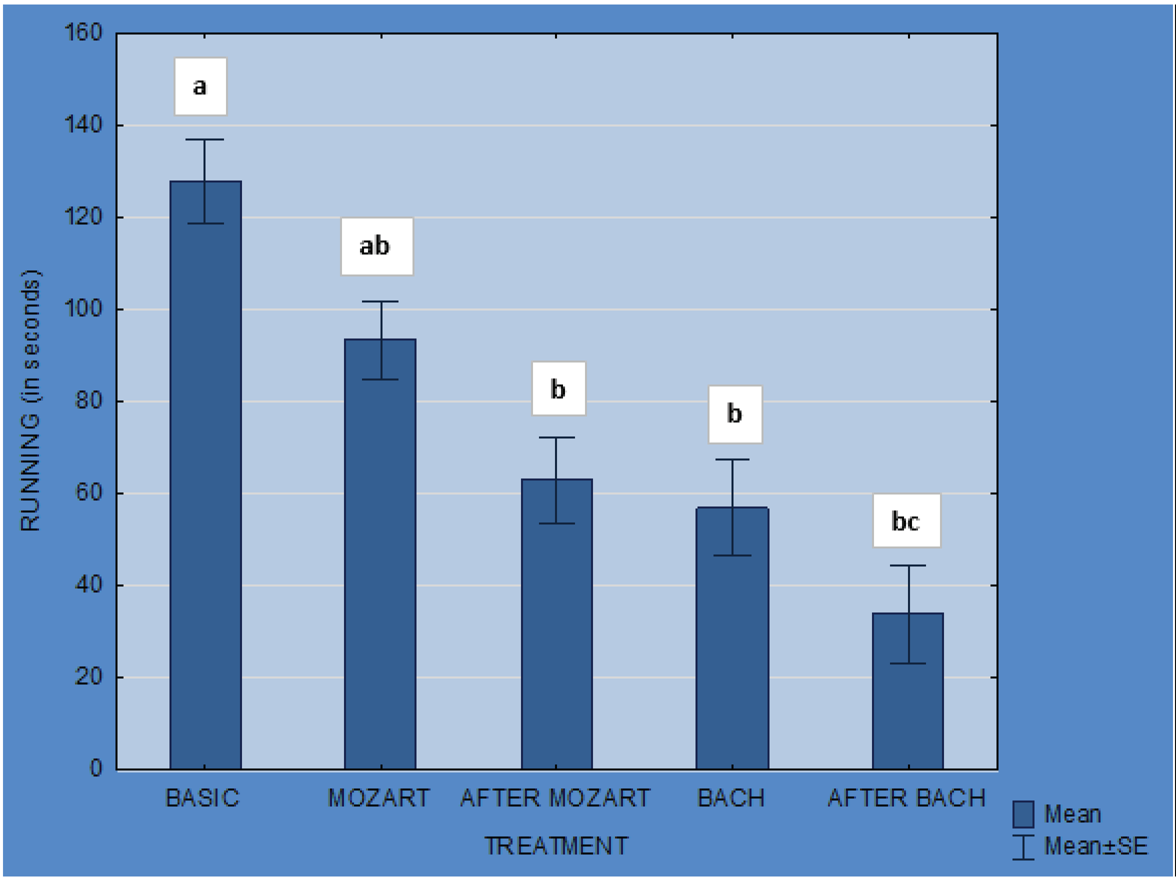


Figure 6: Means and Standard Errors of running behaviour in seconds, values having different upper case letter are significantly different.

Table 1: Means and Standard Errors of running, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *running*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	40.32±9.02	**BB**		0.09	0.00	0.00	0.00
MOZART	37.91±8.48	**MM**	0.09		0.17	0.06	0.00
AFTER MOZART	41.55±9.29	**AM**	0.00	0.17		0.99	0.21
BACH	46.20±10.33	**BM**	0.00	0.06	0.99		0.44
AFTER BACH	47.26±10.57	**AB**	0.00	0.00	0.21	0.44	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent running during the different sections. The highest amount for running was observed during the basic evaluation followed by the other sections in consecutive order. There was a significant decrease in running in-between the basic behaviour and the after Mozart music treatment.

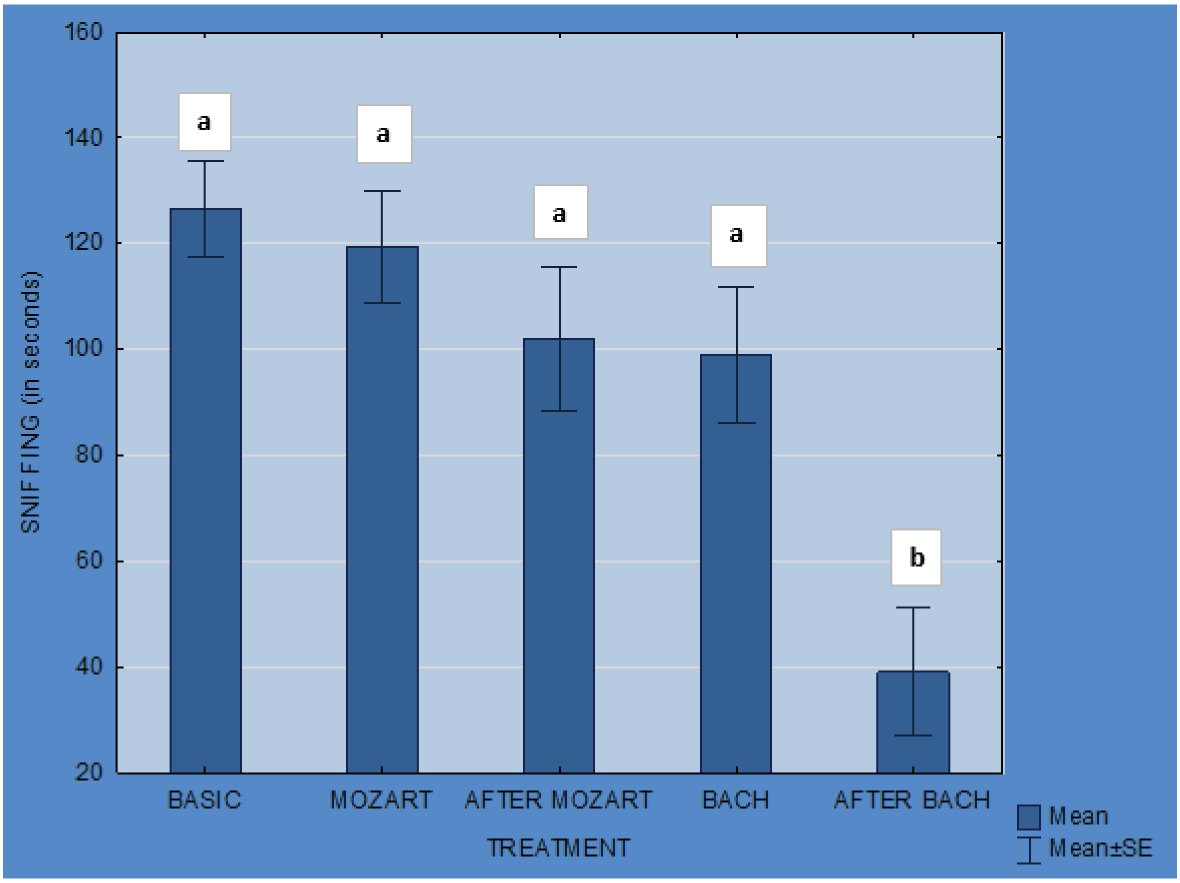


Figure 7: Means and Standard Errors of sniffing behaviour in seconds, values having different upper case letter are significantly different.

Table 2: Means and Standard Errors of sniffing, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: ***sniffing***	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	41.35±9.25	**BB**		0.99	0.58	0.46	0.00
MOZART	46.86±10.48	**MM**	0.99		0.84	0.74	0.00
AFTER MOZART	61.53±13.76	**AM**	0.58	0.84		1.00	0.00
BACH	57.27±12.81	**BM**	0.46	0.74	1.00		0.00
AFTER BACH	53.93±12.06	**AB**	0.00	0.00	0.00	0.00	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent sniffing during the different sections. The amount of sniffing behaviour gradually decreases until a significant drop following the Bach music, during the after Bach treatment.

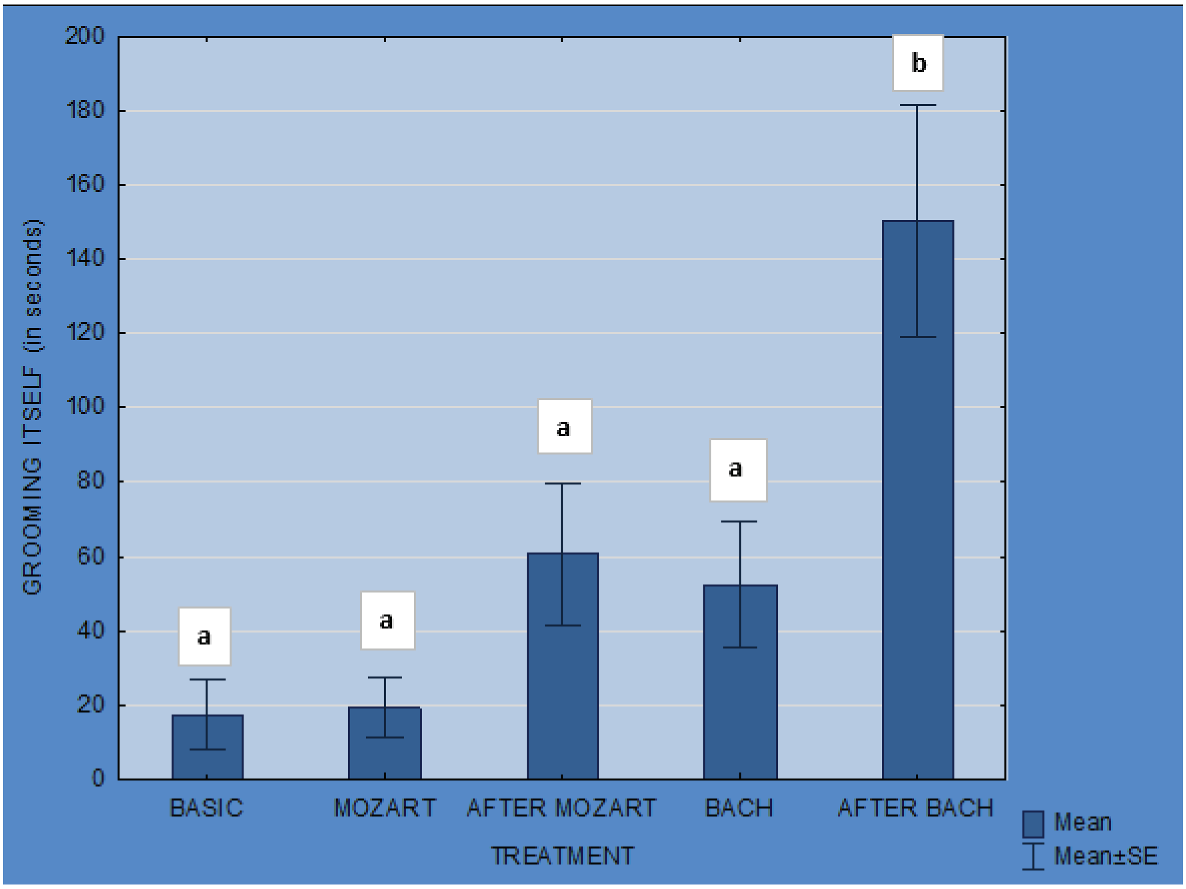


Figure 8: Means and Standard Errors of grooming itself behaviour in seconds, values having different upper case letter are significantly different.

Table 3: Means and Standard Errors of grooming itself, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *grooming itself*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	42.33±9.47	**BB**		1.00	0.49	0.69	0.00
MOZART	35.51±7.94	**MM**	1.00		0.54	0.73	0.00
AFTER MOZART	86.44±19.33	**AM**	0.49	0.54		1.00	0.01
BACH	76.15±17.03	**BM**	0.69	0.73	1.00		0.00
AFTER BACH	140.18±31.35	**AB**	0.00	0.00	0.01	0.00	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent grooming itself during the different sections. A significant higher amount of time grooming itself was observed during the after Bach music section. The highest amount grooming itself was observed during the after Bach treatment, followed by after Mozart, Bach, Mozart, and the lowest amount during the basic behaviour.

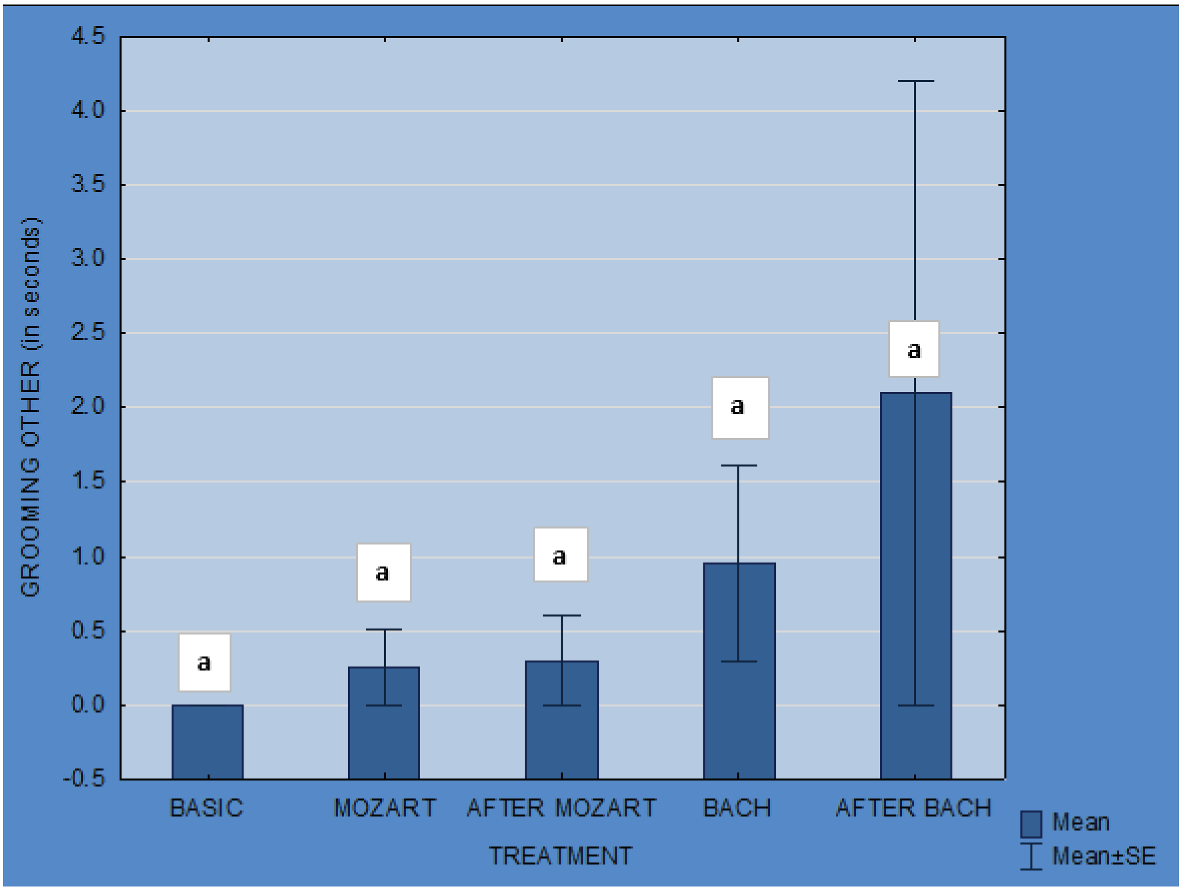


Figure 9: Means and Standard Errors of grooming the other mice behaviour in seconds, values having different upper case letter are significantly different.

Table 4: Means and Standard Errors of grooming other, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: ***grooming other***	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	0.00±0.00	**BB**		1.00	1.00	0.96	0.58
MOZART	1.15±0.26	**MM**	1.00		1.00	0.99	0.69
AFTER MOZART	1.34±0.30	**AM**	1.00	1.00		0.99	0.71
BACH	2.95±0.66	**BM**	0.96	0.99	0.99		0.93
AFTER BACH	9.39±2.10	**AB**	0.58	0.69	0.71	0.93	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was no significant difference in the amount of time spend grooming the other mouse during the different sections. Still, the amount grooming the other mouse is constantly increasing in the subsequent sections.

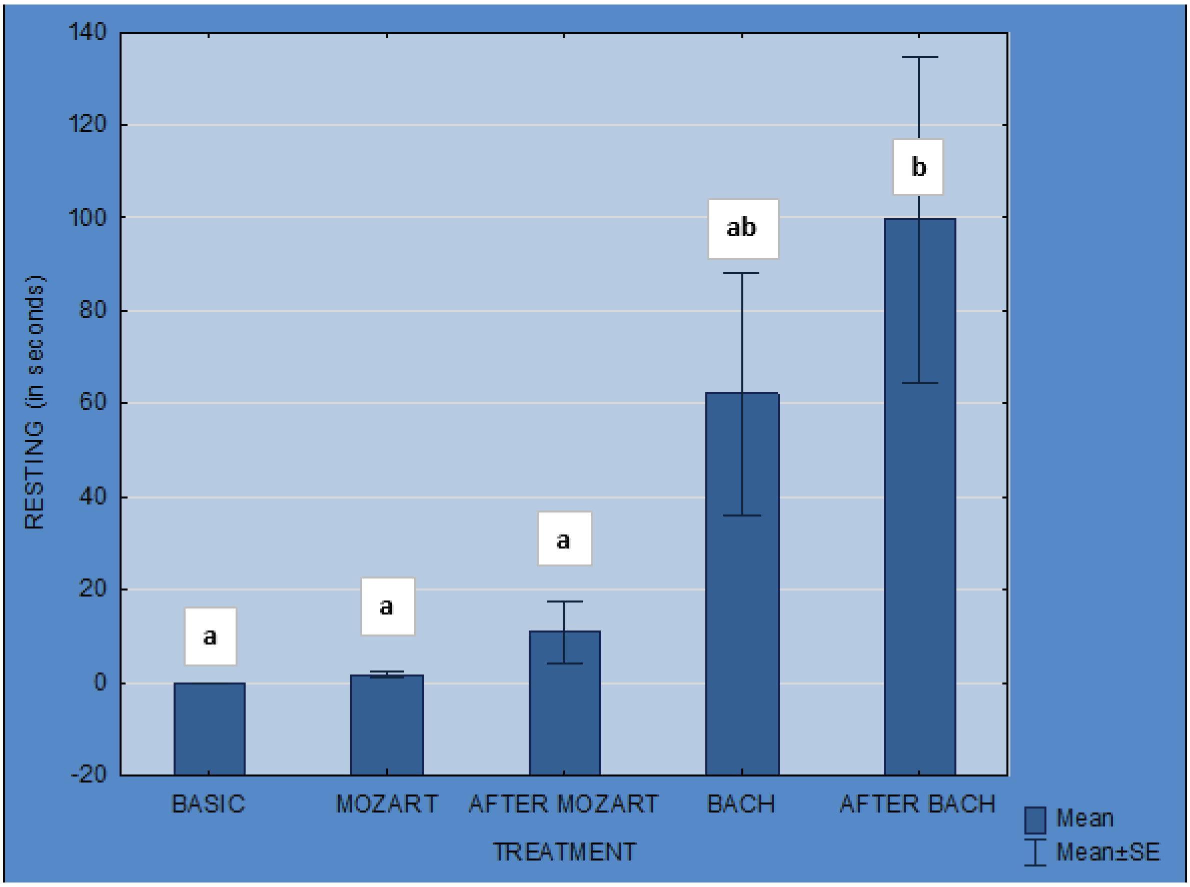


Figure 10: Means and Standard Errors of resting behaviour in seconds, values having different upper case letter are significantly different.

Table 5: Means and Standard Errors of resting, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *resting*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	0.00±0.00	**BB**		1.00	1.00	0.18	0.01
MOZART	2.94±0.66	**MM**	1.00		1.00	0.20	0.01
AFTER MOZART	30.32±6.78	**AM**	1.00	1.00		0.36	0.02
BACH	117.13±26.19	**BM**	0.18	0.20	0.36		0.67
AFTER BACH	156.33±34.96	**AB**	0.01	0.01	0.02	0.67	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent resting during the different sections. The resting behaviour gradually increases in the following sections, showing a significant increase during Bach music and after Bach music.

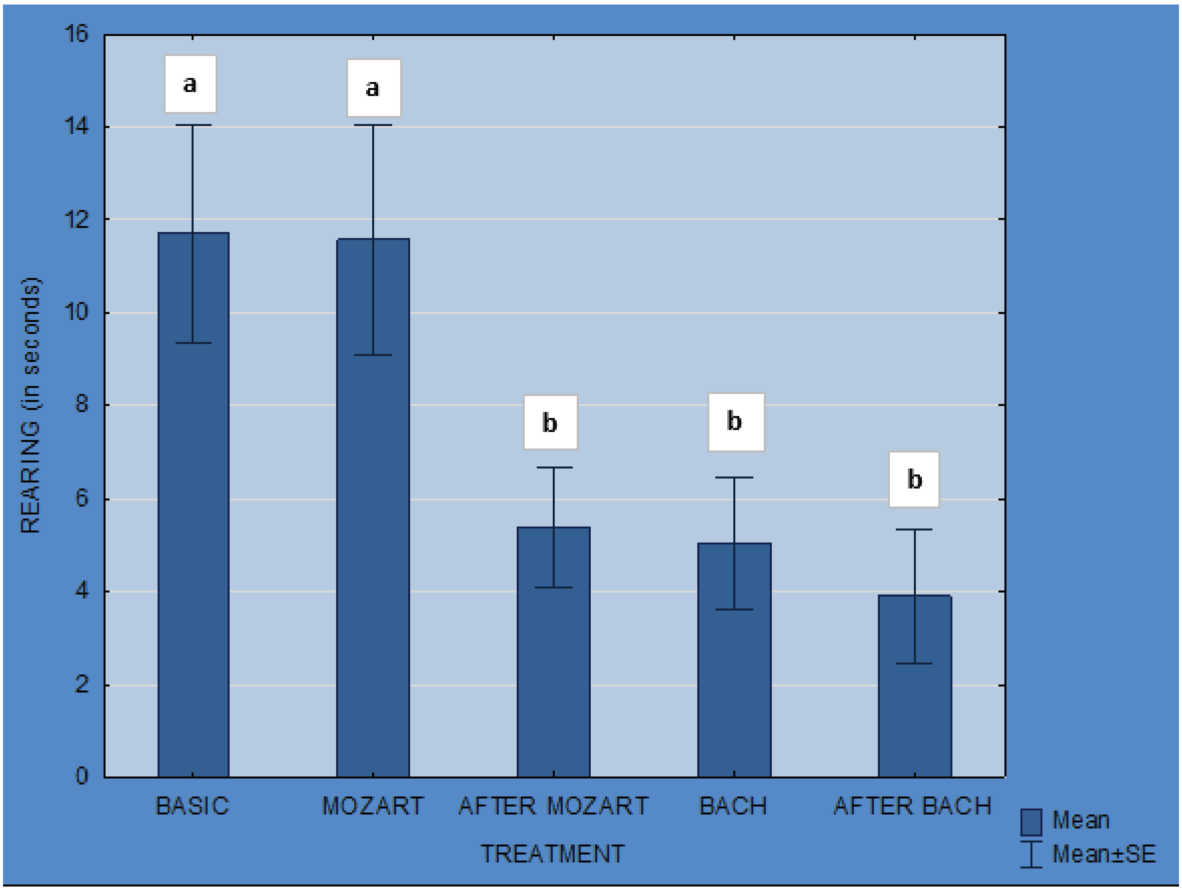


Figure 11: Means and Standard Errors of rearing behaviour in seconds, values having different upper case letter are significantly different.

Table 6: Means and Standard Errors of rearing, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: ***rearing***	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	10.50±2.35	**BB**		1.00	0.13	0.09	0.03
MOZART	11.05±2.47	**MM**	1.00		0.14	0.11	0.04
AFTER MOZART	5.81±1.30	**AM**	0.13	0.14		1.00	0.98
BACH	6.32±1.41	**BM**	0.09	0.11	1.00		0.99
AFTER BACH	6.54±1.46	**AB**	0.03	0.04	0.98	0.99	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent rearing during the different sections. The time spent rearing constantly decreases, but is maintained at similar level during the basic behaviour and Mozart music, followed by a significant decrease during the after Mozart treatment, to regain a new, lower level showing no great time variation.

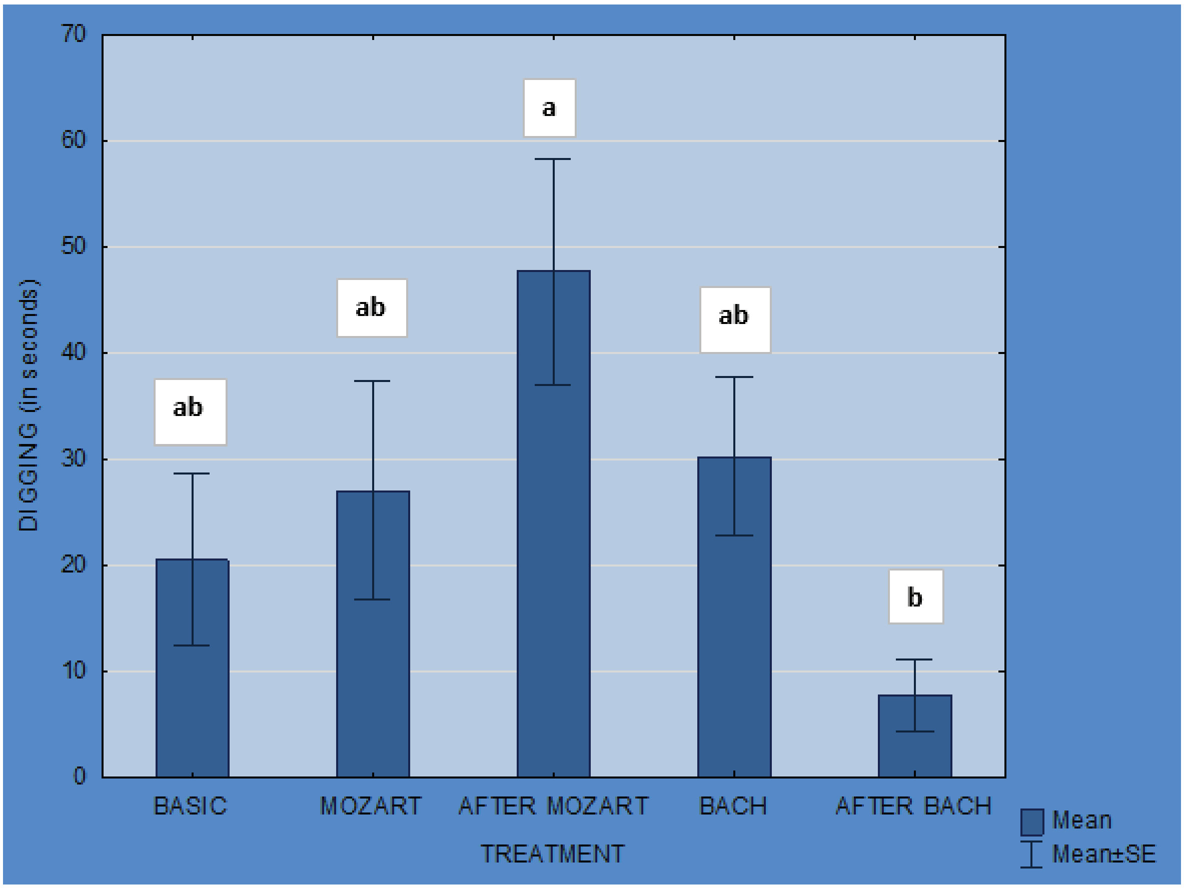


Figure 12: Means and Standard Errors of digging behaviour in seconds, values having different upper case letter are significantly different.

Table 7: Means and Standard Errors of digging, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *digging*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	36.28±8.11	**BB**		0.98	0.16	0.92	0.82
MOZART	45.84±10.25	**MM**	0.98		0.41	1.00	0.49
AFTER MOZART	47.62±10.65	**AM**	0.16	0.41		0.58	0.01
BACH	33.26±7.44	**BM**	0.92	1.00	0.58		0.33
AFTER BACH	15.22±3.40	**AB**	0.82	0.49	0.01	0.33	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent digging during the different sections. The amount of time spent digging shows a pyramid-like development including all sections subsequently, while showing a significant increase during the after Mozart music, and a significant decrease during the after Bach music section.

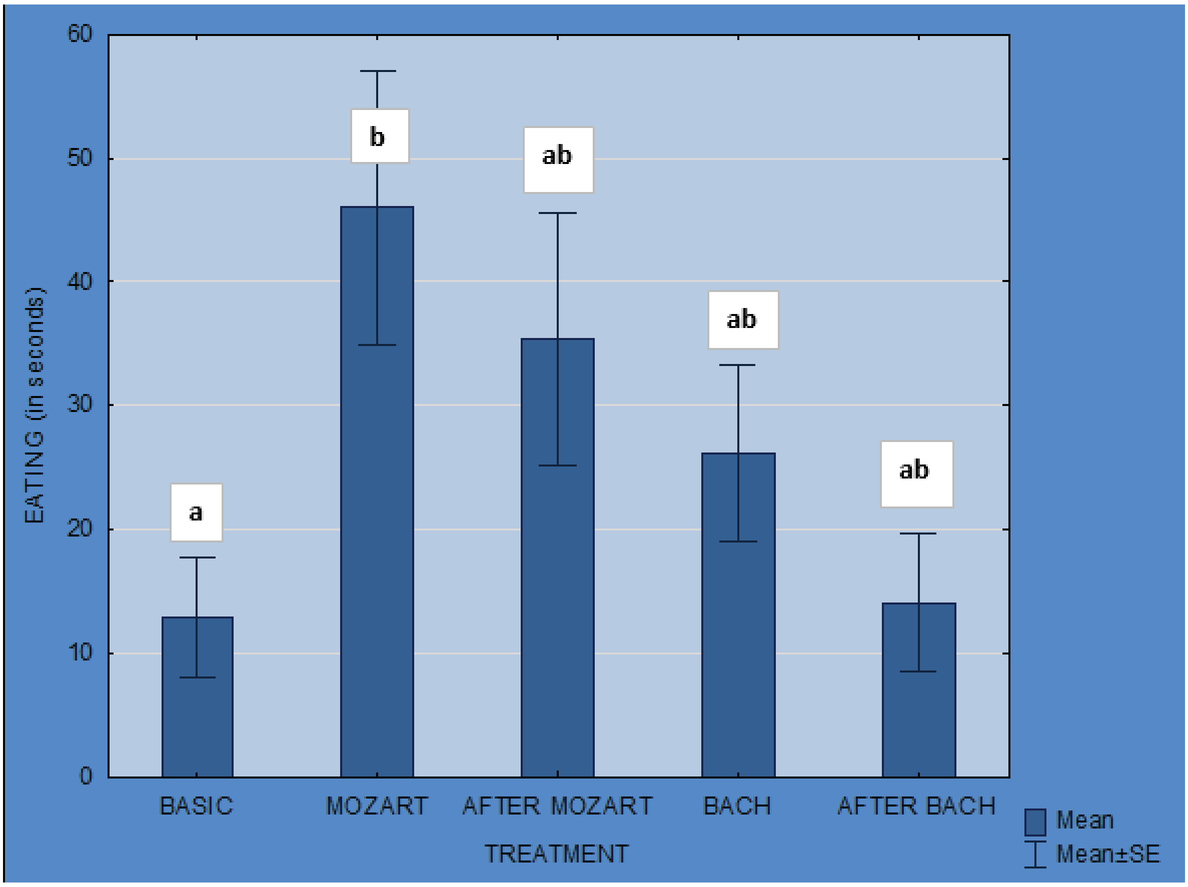


Figure 13: Means and Standard Errors of eating behaviour in seconds, values having different upper case letter are significantly different

Table 8: Means and Standard Errors of eating, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *eating*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	21.74±4.86	**BB**		0.04	0.30	0.78	1.00
MOZART	49.62±11.10	**MM**	0.04		0.89	0.43	0.05
AFTER MOZART	45.73±10.23	**AM**	0.30	0.89		0.93	0.35
BACH	31.67±7.08	**BM**	0.78	0.43	0.93		0.83
AFTER BACH	26.03±5.60	**AB**	1.00	0.05	0.35	0.83	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent eating during the different sections. The eating behaviour shows a significant increase during the Mozart music treatment, followed by a gradual decrease of eating behaviour.

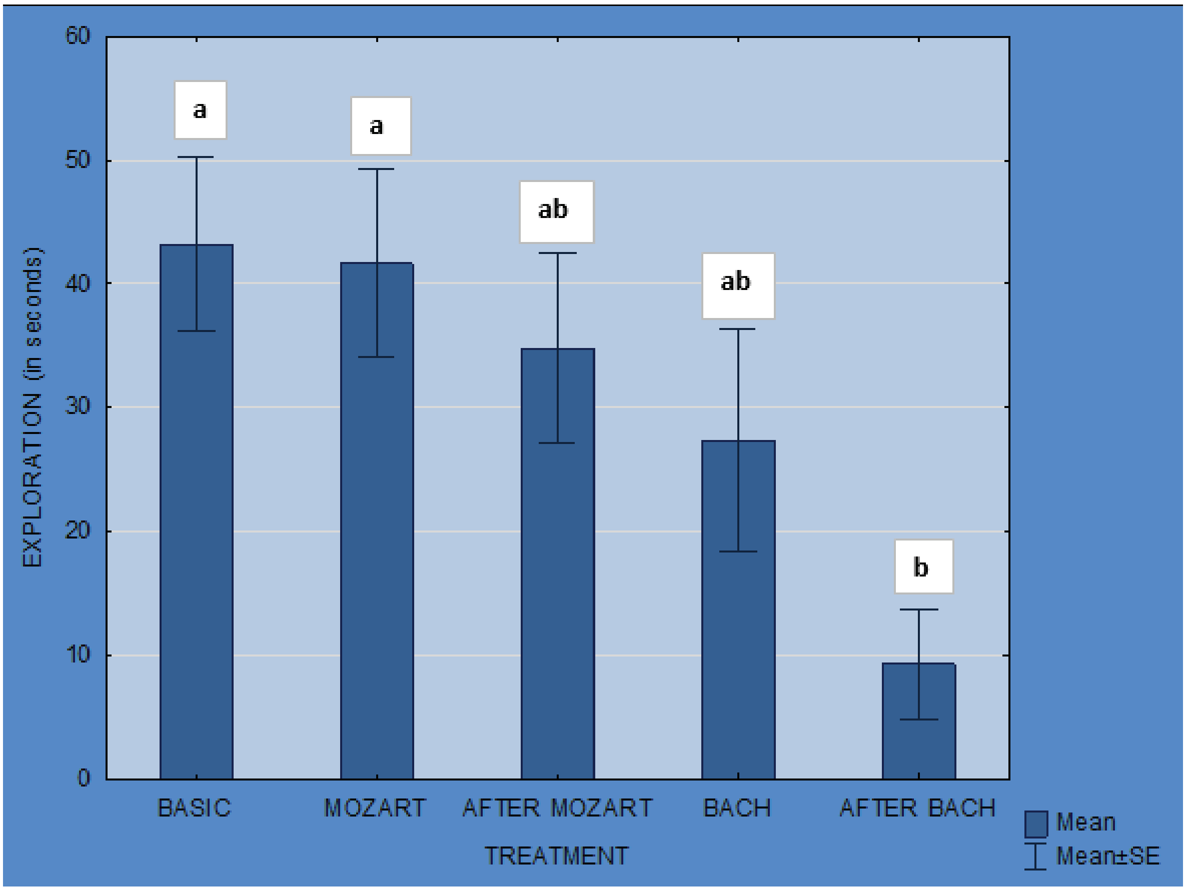


Figure 14: Means and Standard Errors of exploration of the ultrasound recording device behaviour, in seconds values having different upper case letter are significantly different.

Table 9: Means and Standard Errors of exploration of the ultrasound recording device, s. And the significances between the treatments (the marked cells mean significant differences in the level of P<0.05)

Treatment: *exploration*	**Mean ± S.E.**	**P-values**	**BB**	**MM**	**AM**	**BM**	**AB**
BASIC	31.25±6.99	**BB**		1.00	0.93	0.54	0.01
MOZART	34.03±7.61	**MM**	1.00		0.96	0.64	0.02
AFTER MOZART	34.47±7.71	**AM**	0.93	0.96		0.95	0.11
BACH	39.95±8.93	**BM**	0.54	0.64	0.95		0.41
AFTER BACH	19.71±4.41	**AB**	0.01	0.02	0.11	0.41	

Treatments: BB= basic behaviour, MM= Mozart music, AM= after Mozart, BM= Bach music, AB= after Bach

There was a significant difference in the amount of time spent exploring the ultrasound recording device during the different sections. The exploratory behaviour decreases constantly following each section, with a significant decrease during the after Bach music treatment.

DISCUSSION

The results of the experiment can be organised into 3 categories according to their significance; from *non-significant* different (p >0.05), *over significant* different (p <0.05), to *highly significant* different (p <0.001).

Non-significant (p >0.05):

Mentioned percentages in the following sections can be reviewed in “Table 10”, found following the “Conclusion”, on page 32.

The proportion of mice, mentioned in some sections, showing described behaviours in different sections can be found in “Table 11”, on page 33.

a. *Grooming the other mouse*

Time spent grooming the other mouse gradually increases during the subsequent treatments, but does not rise above a ratio of 0.58%. This action was engaged during the Mozart music, and apart from the Bach music treatment, meanwhile two mice groomed their cage mate, only one mouse showed this behaviour during the different treatments. Therefore the highest amount of grooming the other mouse was the result of the action of one sole mouse. Although the grooming the other mouse has a stronger increase during the exposure to Bach music (from 0.08 to 0.27%) and following, music does not seem to have an impact on this behaviour. Only one (momentary two mice) mouse is involved and it does not reach a significant level.

Significant (p <0.05):

b. Resting

The time ratio spend resting constantly increases, not only the time, also the involvement of mice.

The increase is significant during the after Bach music treatment. Resting first appears during the exposure to Mozart music, but on a very small scale (0.43%). The number of mice, five, resting stays the same during the after Mozart music section, but the time ratio raises to 3.00%, however different mice than before, apart from one are involved in this section. During the exposure to Bach music the amount spent, and the number of mice involved, now six, increases further up to 17.27% resting. During the last treatment, after Bach music, we can note involvement of nine mice and a ratio of 27.67%.

There is only a slight variation in the mice involved in resting, apart from three mice the others appear in at least one different treatment as well, furthermore five (out of six) mice observed resting during, or towards the end of, the exposure of Bach music continue to rest, with little or no break, throughout the after Bach music section.

It is possible that music has an influence on the resting behaviour of mice. The ANOVA results and percentage development support the anticipated relaxing properties of the Bach music. However the experiment was not set up in a large enough scale to exclude that those decisive mice would not have rested anyway.

c. *Rearing*

The time spend rearing is constantly decreasing, but can be inflected by error, since it is not always possible to clearly distinguish it from the exploration of the ultrasound recording device behaviour, therefore it is possibly noted there (see definition of behavioural parameters). However, since both behaviours follow a similar trend in a different ratio it should not be of concern.

The time and mice involved in rearing constantly decreases, leading to a significant decrease during the after Mozart music section, and stays on this level, gradually decreasing. It is possible that this behaviour is influenced by music. The initial excitement of the mice, during the basic behaviour, is maintained during the Mozart music which is attributed to be energizing.

d. *Eating*

The eating behaviour shows a significantly increase during the Mozart music treatment, afterwards it constantly decreases. This trend is also accompanied by the number of mice involved in this behaviour during the different treatments.

It is unlikely that the music has an effect on the eating behaviour.

We could argue that the eating is stress induced, since it peaks during the exposure to Mozart music, this is not convincing since the locomotive behaviours (running, eating, rearing etc.) decrease meanwhile.

e. *Digging*

The amount spent digging shows a pyramid-like development along the different treatments. There is a significant increase during the after Mozart section, after which the time spent digging returns to the range as before, and drops significantly during the after Bach music section. The total time amount spent digging is accompanied with the number of mice involved.

It is unlikely that the music has an effect on the digging behaviour. An effect would only be justifiable in relation to the previously high eating behaviour as an attempt to find more food.

f. *Exploration of ultrasound recording device*

The time exploring the ultrasound recording device gradually decreases, leading to a significant decrease during the after Bach music treatment. Even though the time spent exploring the ultrasound device constantly decreases, the number of mice involved increases during the after Mozart section, overall the number of mice involved decreases as well. The exploration seems to be randomly, apart from 2-3 mice that show an on-going intensive interest.

Highly significant (p <0.001)

g. *Running*

The running behaviour constantly decreases. There is a significant decrease during the after Mozart music and the after Bach music treatment. Although the amount spend running constantly decreases the involvement of mice only slightly changes, until the after Bach section during which it abruptly drops, starting during the Bach music (19 to 17), 17 to 11.

h. *Sniffing*

Sniffing behaviour gradually decreases until a significant drop during the after Bach section. Here the change in involvement of mice is even more prominent (see table 11).

i. *Grooming itself*

The time amount grooming itself shows a significant increase during the after Bach section. It is on a low level during the basic behaviour and Mozart music, increases during the after Mozart treatment (16.83%), and decreases again during the Bach music (14.53%); not as low as before; and spikes during the after Bach music (41.75%).

It is possible that the music has an effect on the grooming itself behaviour. The in-between raise, following the exposure to Mozart music may be stress related, however I would assume that this raise is rather random. However, the amount grooming itself during the after Bach music treatment is prominent. Overall the grooming behaviour reflects to be a stress-free, relaxed action.

CONCLUSION

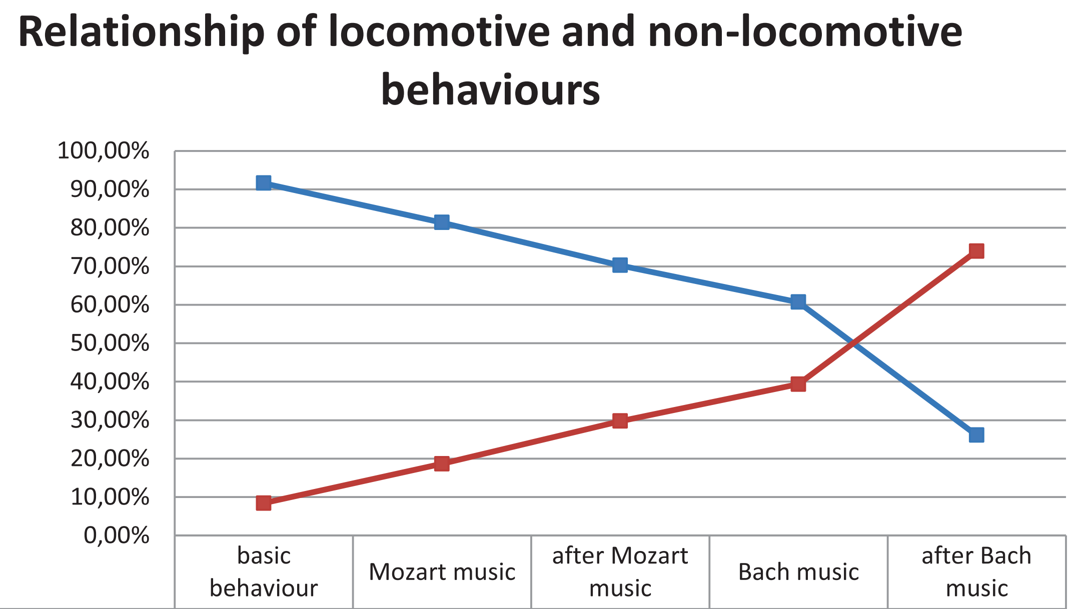
Classical music may contribute to the improvement of the laboratory mice's welfare (3^{rd} "R": Refinement).

The results obtained during this experiment only support the assumption that Bach music can have relaxing properties, no stand out results were obtained in relation to Mozart music, attributed to be energizing.

To assure an effect associated to the musical stimuli further research is required.

Suggestions to secure the results:

- Change the sequence of the different musical stimuli.
- A larger group of test animals is required to rule out that the decisive behaviours have not been displayed by chance.
- If our main focus is to determine the locomotive behaviour; the experiment set-up is sufficient, however to clearly differentiate between the different non-locomotive behaviours a better visualisation is necessary; more angles of observation/ recording, pellucid housing objects.
- Longer exposure times to the musical stimuli.



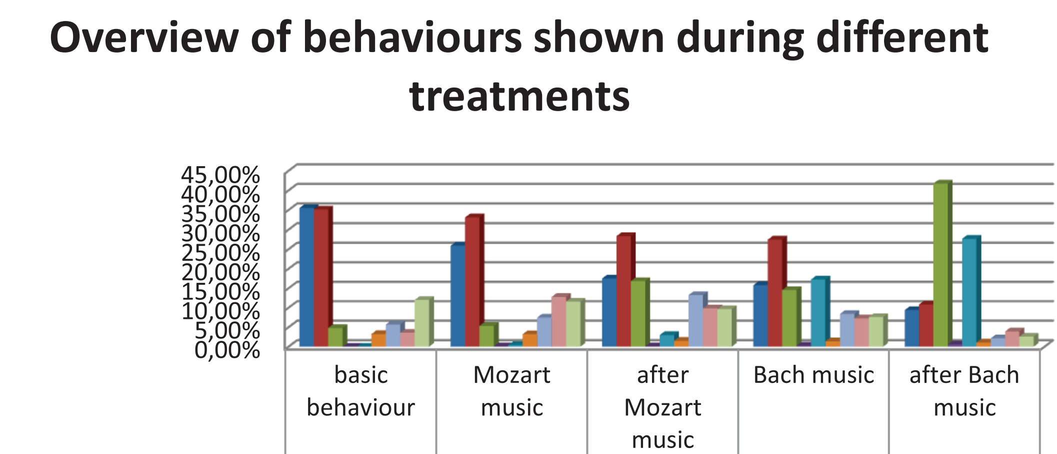
	basic behaviour	Mozart music	after Mozart music	Bach music	after Bach music
locomotive	91,60%	81,36%	70,25%	60,67%	26,08%
non-locomotive	8,40%	18,64%	29,75%	39,33%	73,92%

Figure 15: Relationship of locomotive and non-locomotive behaviours during the different treatments, in per cent

Locomotive behaviours: running, sniffing, rearing, digging, exploration of the ultrasound recording device

Non-locomotive behaviours: grooming, resting, eating

Table 10: Overview of the behaviours displayed during the different treatments, in per cent



	basic behaviour	Mozart music	after Mozart music	Bach music	after Bach music
running	35,50%	25,93%	17,50%	15,80%	9,42%
sniffing	35,15%	33,14%	28,33%	27,47%	10,83%
grooming itself	4,80%	5,36%	16,83%	14,53%	41,75%
grooming other mouse	0%	0,07%	0,08%	0,27%	0,58%
resting	0%	0,43%	3,00%	17,27%	27,67%
rearing	3,25%	3,21%	1,50%	1,40%	1,08%
digging	5,70%	7,50%	13,25%	8,40%	2,17%
eating	3,60%	12,79%	9,83%	7,27%	3,92%
expl. US	12%	11,57%	9,67%	7,60%	2,58%

Table 11: Number of mice showing examined behaviours during different treatments.

	running	sniffing	grooming		resting	rearing	digging	eating	expl. US
active mice			itself	other					
BB	20	20	8 (7/4)	0	0	15 (10/6)	9 (6/4)	7(/6)	20 (16/13)
MM	20 (/19)	20	14 (10/7)	1(0)	5 (1/0)	15 (12/7)	13 (/10)	18 (15/14)	16 (15/14)
AM	19	20	16 (13/11)	1 (0)	5 (3)	12 (4/2)	17 (15/14)	14(12/11)	18 (16/12)
BM	17 (/15)	19	14 (12)	2 (/0)	6	11 (6/2)	14 (13/12)	12 (11/10)	11 (10)
AB	11 (10)	13 (10)	15(/14)	1	9 (8)	7 (4/1)	5	8 (7/6)	8

BB: basic behaviour, MM: Mozart music, AM: after Mozart music, BM: Bach music, AB: after Bach music.

a (b/c):

a= total number of active mice;

b= number of mice active for longer than 6 seconds (if no value= same number as “a”);

c= number of mice active for longer than 12 seconds.

ACKNOWLEDGEMENTS

The authors want to thank Lajos Nagy for the audioengeneering contribution, Dan Lawrence Brown for discussion and critical reading of the manuscript; Mrs. Kiss Józsefné Oláh Edit Margit librarian for excellent assistance. This work was supported by grants from the Fulbright Fund and Cornell University, Department of Animal Science.

ABSTRACT

Is mice behaviour influenced by music?

An effect of music on the behaviour of humans and animals has been shown in different experiments. Already anecdotal reports show that continuous and consistent background music can help to overcome the negative effects of environmental noises in animal facilities. The aim of this study was to evaluate if and to what extent, musical stimuli could influence the behaviour of laboratory mice.

The experiment data was collected, in the form of continuous video and ultrasound recordings, from twenty SPF (specific pathogen free) CD1 male mice, which were randomly paired and put in an open IVC (individual ventilated cage) for the exposure of human music. The mice have been exposed to different musical stimuli, composed for humans and in rodentized, i.e. ten-times faster and higher in pitch version. This paper will focus on the effects of musical stimuli, in human form, on mice, evaluated according to video recordings.

The selected pieces were Mozart's "Sonata for Two Pianos in D Major", K 448 and Bach's "Goldberg Variation" (BW 988": Aria, var.2, var.3, var.8 and var.10, presented by Glenn Gould). First the basic behaviour of the mice was recorded, afterwards the animals were exposed to Mozart, and after a break to the Bach music, followed by another music free interval. In each of the five (basic, Mozart, music-free, Bach and music-free) in human and in "rodentized" version) sections the behaviour was evaluated according to following parameters: running, sniffing, grooming (itself or the other mouse), resting, rearing, digging, eating, possible ultrasound (US) vocalization and exploration of the US microphone. There was no US vocalization.

The ethogram was recorded using millimetre-paper. The evaluation of the results appears to comply with the relaxing qualities attributed to the Bach composition. The locomotion was replaced by resting and grooming during and following the exposure to Bach. It is questionable if Mozart music elicits any effect on the mice. The central locomotive behaviours decrease constantly in comparison to the basic behaviour. However, the eating and digging behaviour reaches its maximum, during and following the exposure to Mozart music.

Exposure to music of laboratory mice may contribute to the improvement of their welfare (3rd "R": Refinement), but the choice of musical background should be chosen cautiously.

ÖSSZEFOGLALÁS

Befolyásolja a zene az egerek viselkedését?

A zene emberi és állati viselkedésre való hatását már több vizsgálat is kimutatta. Több beszámoló is említi, hogy a folyamatos és egyenletes háttérzene segíthet csökkenteni a környezeti zajok okozta stresszt laboratóriumi állatok esetében. Jelen kísérlet célja az volt, hogy megfigyeljük, képes-e a zene befolyásolni a laboratóriumi egerek viselkedését, és ha igen, milyen módon.

A kísérlet során húsz SPF (specific pathogen free), CD1 hím patkány viselkedéséről gyűjtöttek adatot videófölvétel formájában, miközben az állatok ultrahang kibocsájtását is rögzítették. Az állatok a vizsgálat során nyitott, IVC (individual ventilated cage) ketrecekben voltak kettesével elhelyezve. Az egerek különböző zenei ingereknek voltak kitéve, eredeti, emberi fülnek szánt formájában, illetve „rágcsálósított" formában (az egerek hallástartományához igazítva, tízszer gyorsabb és magasabb változatban). Jelen munka az eredeti, „humán" zene hatását vizsgálja. Az adatokat a videófelvételek elemzésével nyerték.

A választott két mű Mozart „D-dúr szonáta két zongorára", K 448 jegyzékszámú darabja, és Bach „Goldberg Variációk", BW 988'': (Ária, var.2, var.3, var.8 és var10) részlete volt, utóbbi Glenn Gould előadásában. Először az állatok zene nélküli alapviselkedését rögzítették, majd az állatok Mozart darabját hallgatták meg. Ez után egy zene nélküli szünet következett, majd a Bach darab meghallgatása, melyet újabb zenementes periódus követett. Mind az öt periódusban a viselkedés az alábbi paraméterek megfigyelésével került rögzítésre: járás, szimatolás, önápolás vagy a másik állat mosdatása, pihenés, ágaskodás, ásás, evés, az esetleges ultrahang-kibocsátás és az ultrahangfölvelő eszköz „fölfedezése". Ultrahangos vokalizáció nem volt mérhető.

Az adatok rögzítése milliméter-papír segítségével történt. Az eredmények alátámasztják a Bach darabnak tulajdonított nyugtató hatást. A korábbi aktív viselkedést felváltotta a pihenés és az önápolás a zene meghallgatása közben illetve utána egyaránt. Kérdéses, hogy a Mozart zene hatással volt-e az egerek viselkedésére, bár a darab hallgatása közben és után is az aktív, mozgással töltött idő csökkent az alapviselkedéshez képest. Ellenben az ásással és evéssel töltött idő ebben a két szakaszban érte el maximumát.

A zene használata a laboratóriumi egerek esetében hozzájárulhat a jóllét fokozásához, mint a harmadik R, a finomítás (Refinement) része, de a lejátszandó darab kiválasztása óvatosságot igényel.

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