

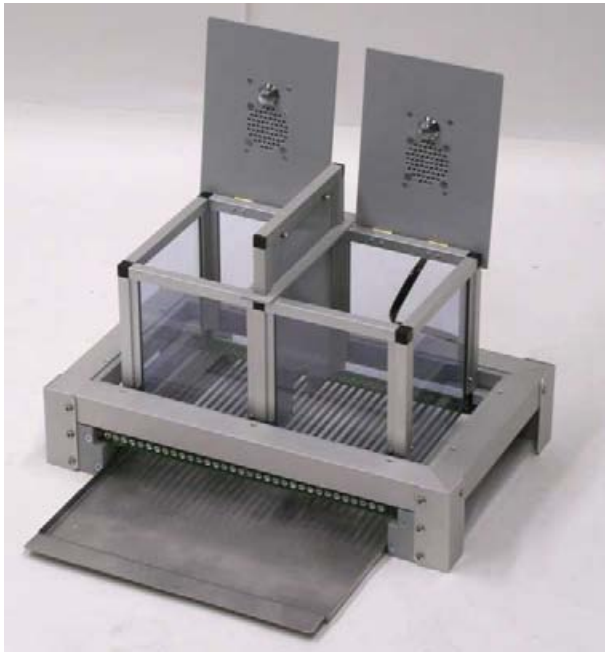
TSE Active Avoidance System

Flexible test system for mice and rats

- Specifications subject to change without notice -

TSE Active Avoidance System

Overview



Mouse test box

The **TSE Active Avoidance System** (“Shuttle Box”) allows active avoidance experiments to be carried out with small laboratory animals.

It consists of the following components:

- up to 4 test boxes for rats or mice
- a control unit
- a special interface (PCI) for IBM compatible PC
- the Active Avoidance software for Windows
- optional housings and other accessories

The test boxes



Mouse frame

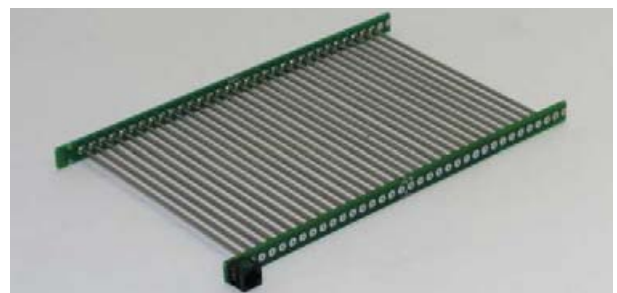
A test box comprises:

- **Base construction - the so-called frame**

The size of this frame depends on the animal species. Animal position is monitored with infra-red light barriers scanned with high frequency. The light is invisible to the animal. Each light-barrier consists of one infra-red transmitting and one receiving sensor. These are mounted into transmitter and receiver strips. Movement is recorded in **one** dimension (X-coordinate).

Light-barriers:	
Mouse:	2 x 7 light barriers - 14mm apart
Rat:	2 x 7 light barriers - 28mm apart

- **Removable stainless steel grid + feces tray**



Mouse grid



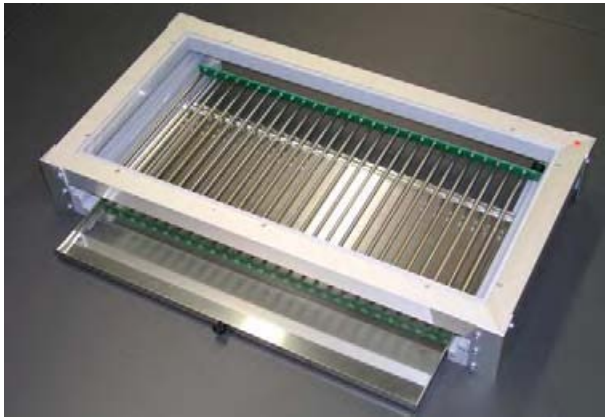
Mouse frame with grid

...for delivering a foot shock (US) of defined duration and intensity. Both halves of the grids are electrically independent units.

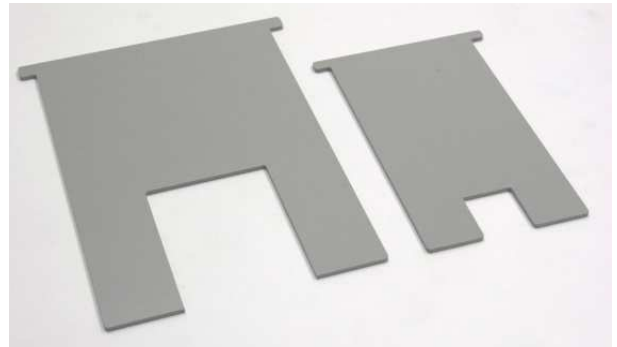
Grid specification:	
Mouse:	Bars 4mm diameter, 8.9mm distance*
Rat:	Bars 6mm diameter, 19.5mm distance*

* between rod centers

A removable feces tray is placed below the sensor frame.



Rat frame with rat grid and feces tray underneath



■ Active Avoidance arena



Rat arena

The arena is placed inside the sensor frame. It is equipped with clear walls.

Arena size:	
Mouse:	Total 280 x 155 x 160mm (LxWxH) compartment width 140mm
Rat:	30 x 205*mm (LxWxH) width 242mm

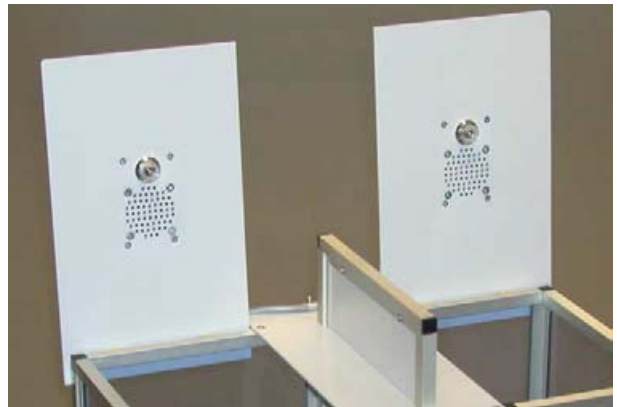
* 270mm optional

The arena is divided into 2 compartments by a dividing wall. In the stand-alone Active Avoidance configuration this divider is an open gate.

An automatic door that is opened and closed by the software is used in the combination system Active & Passive Avoidance (see *Options*).

Gate size:	
Mouse:	37 x 40mm opening (WxH)
Rat:	90 x 115mm opening (WxH)

The gate has a rectangular shape. The arch-shaped gates that are shown in some of the pictures are not available any longer.



Each compartment is equipped with its own lid. The lids feature a software-controlled light (constant illumination). Each lid also contains a loudspeaker to deliver a stimulus sound (1 sound channel).

The animal is placed in the selected compartment from above.

Other components

The **control unit** provides the connection between the boxes and the PC. It contains the electronics for the location sensors and for controlling the stimulus components. The standard unit controls up to 4 boxes and features:

- Power source for stimulus lights
- 2 shocker channels. The microprocessor controlled current generator with integrated current flow detector ensures that the current is applied with a high degree of accuracy. Amplitude is software-adjustable in steps of 0.1mA (max. 3.1mA), pulsating or constant.
- An audio generator for generating a stimulus sound (fixed amplitude and frequency), switched on/off by the software during the experiment.

The **control interface** (PCI slot) is designed to be built into an IBM-compatible computer. The control unit is connected to this interface.

The **software** controls the system and records, analyzes and stores the measuring data.

An IBM compatible computer is required to run the system. Suitable operating systems are Windows 98, 2000 and XP.

We can supply a complete system including the computer ready for use!

Options

- The standard height of the rat compartment is 205mm. For larger rats a height of 270mm is available on request.
- The compartments can also be divided by a hurdle that can be electrically stimulated. A software upgrade and an additional shocker channel is required here.
- The standard shocker allows adjustment of the shock amplitude in steps of 0.1mA. If smaller steps are required the shocker is available with a maximum amplitude of 1.5mA – this allows steps of 0.05mA to be applied.
- The standard low-intensity light integrated into the box lids can be exchanged for stronger lamps whose intensity can be manually adjusted by the user (increased aversiveness).



- The control unit can be equipped with controls to adjust the sound amplitude and to select a frequency between 2...20kHz.
- A noise channel can be added to the system to apply continuous background noise with adjustable amplitude during the experiment. The noise is switched on and off by the user with a toggle switch on the control unit front panel.
- An air puff set can be included into the setup. Air puffs can then be used as an alternative to foot shock. A software upgrade is required to operate the air puff.



Air puff module



Air delivery modules
(to be mounted on the side of the arena)

- The box can be operated in a sound attenuating housing, featuring:
- removable front door with integrated window that can be closed if not used,
- house light, switched on and off manually,
- ventilator in the side wall,
- sliding floor plate for easy removal of test box.



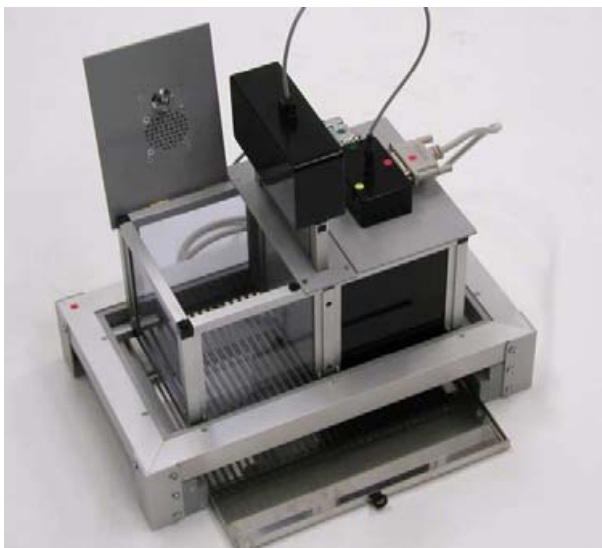
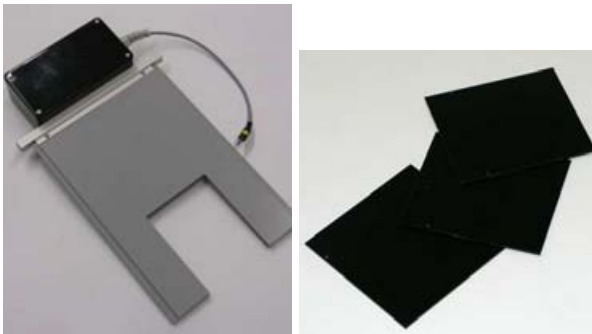
Housing

- More than 4 boxes can be controlled on request.

If you are interested in these options please contact us.

System extensions – other systems

- The system is also available as combination system rat & mouse. In this system a large base frame allows to use large rat as well as small mouse arenas. The light-beam density corresponds to the rate version here.
- The Active Avoidance system can be easily configured for standard Passive Avoidance experiments by exchanging the clear acrylic walls on one side for dark walls which are permeable for infra-red light. An automatic door is also required here.

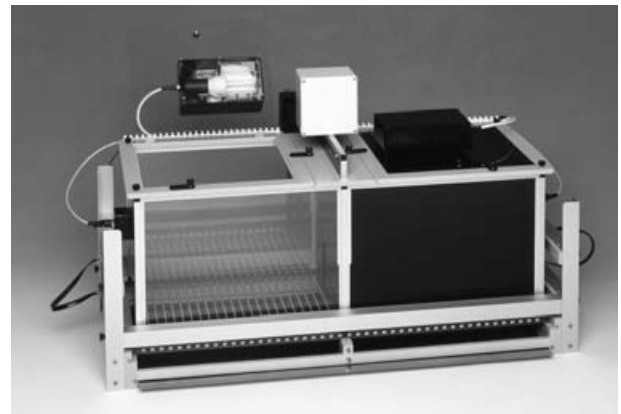


Passive Avoidance BASIC Mouse

- For **"Step-Down" Passive Avoidance** experiments a platform is available that is placed into the bright compartment of the Passive Avoidance arena.

If you are interested in these system extensions please contact us.

We also provide a new type of Passive Avoidance systems (ADVANCED) that – in contrast to the basic system – it allows movement to registered in 3 dimensions: X- and Y-coordinate for detailed information about exploratory behavior, Z coordinate for vertical activity (rearing). Other features are: High-intensity lamp ensuring a high level of aversiveness, comprehensive analysis tables and graphs for detailed analysis of exploration (parameters include inactivity time, speed, rearing and jumping events). Please note that this system cannot be converted into an Active Avoidance test system.



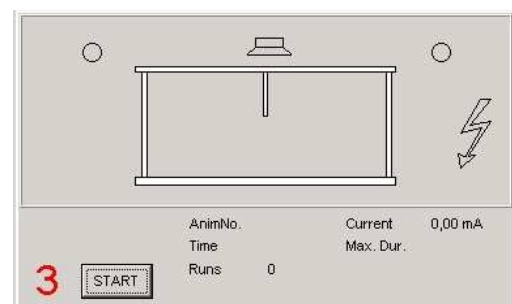
Passive Avoidance "Advanced"

Experimental procedure

A test proceeds according to the following pattern:

- box selection and test preparation,
- test procedure and
- subsequent data analysis.

Box selection & experiment preparation



Trial monitor (before the start)

Only 1 box is shown as an example

Experiments in the available boxes can be run at different times – they are controlled independently from one another. Each box has its own separate run control.

Before an experiment is started all the parameters which describe the experiment and the animal and which determine the experimental procedure are defined for each box.

An animal is described by providing the following information:

Animal No. / Group / Strain / Age / Weight

An experiment is described by providing the following information:

Trial No. / Exp. No. / Code / Operator / Comment / Substance / Dosage

Some entries are obligatory - they can later be used for filtering the stored data files.

Descriptive entries

A *Parameter Definition* button opens an additional window in which all the information which determines the trial procedure is entered.

Parameter definition

Trial Start Conditions: At the start of the trial, the **light** will be switched on in the compartment that is marked here. This can be either the region of the box into which the animal is to move (target area) or the compartment in which the animal is located (start area). The other

compartment remains dark. If required a **sound** stimulus can be output in parallel.

Current Settings: After the defined time has elapsed (see below) the foot shock (aversive stimulus) is applied with a preset amplitude. The amplitude is entered here (“E-Stimulus”). Until a reaction takes place the current is increased by the offset amplitude – if defined in the entry field “Offset-Stim.”. The current can be selected to be constant or pulsating.

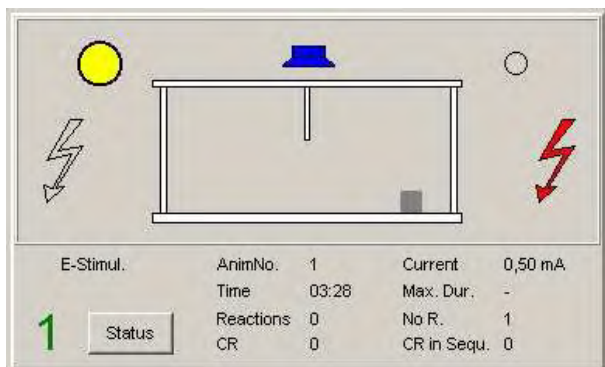
Time Settings: The following settings determine the course of the experiment.

Habituation	Resting time before the first intertrial period starts.
Latency E-Stim.	Time from trial start until the E-stimulus is switched on.
Latency Offset-Stim.	Time from trial start until automatic switch on of offset stimulus – if defined.
Max. Duration	Time from trial start until all stimuli are switched off for the case in which the animal did not transfer into the other compartment. This time therefore corresponds to the maximum trial length. The entry has to be larger than Latency Offset-Stim. If the animal reacts by changing the compartment, the trial is terminated immediately. All stimuli are switched off and the experiment is continued with an intertrial interval.
Minimum Rest	This entry is only important when the intertrial interval has been selected to be variable. It defines a minimum resting time between trials.
Intertrial Interval	Time between trial end and the start of the next trial. The intertrial interval (ITI) must be at least the time entered under Minimum Rest. The ITI can be constant or variable: Constant: The ITI corresponds to the entered time. Variable: The ITI results from the time ± X% of this value (e.g. ITI = 30 sec and X=50%: the value could be anything in the range from 15 sec to 45 sec.) If the animal changes compartments in the ITI then the ITI period is restarted.
Detection center not active	If this option is activated the center detection of the animal is deactivated.

Termination criterion: A session is terminated after a preset duration, a preset number of trials, a preset number of reactions (avoidance + escape reactions) or after a preset number of conditioned reactions (avoidance reactions; in total or successive).

“No Reaction Message”: If the animal does not transfer between compartments a warning message may be output after a certain number of trials without reactions.

The running experiment



When all the parameters have been entered the animal is placed in the box. The experiment is started with a mouse-click.

The trial monitor shows all relevant information about the status of the trial. The location of the animal is represented by a square which alters its position when the animal moves (left, right, center). If loudspeaker, light, and E-stimulus are activated then the corresponding symbols are highlighted in color.

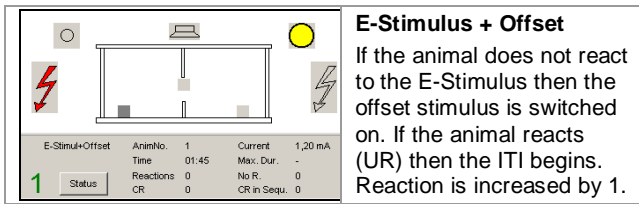


Below the display of the box the following information is output:

- name of the active phase
- animal number
- amplitude of the current in mA
- actual trial time
- maximum duration of the active phase
- number of reactions (avoidance and escape)
- trials without reaction
- number of conditioned reactions (avoidance reactions)
- number of successive conditioned reactions

Example of the experimental sequence:

Trial Monitor	Description
	<p>Habituation</p> <p>The animal is placed in one of both compartments and the experiment is started. The habituation time follows – if defined. No stimuli are given in the habituation phase.</p>
	<p>Intertrial (ITI)</p> <p>The intertrial phase follows.</p>
	<p>Stimulus Phase</p> <p>When the ITI is finished the stimuli are activated. The activated elements are highlighted in color. In the example shown light has been selected in the target area.</p> <p>If the animal reacts by changing into the other compartment (here: the bright side) this is a conditioned reaction (CR). The trial is terminated, the stimuli are switched off and the ITI starts. Reactions, the sum of conditioned and unconditioned reactions, is set to 1; CR is set to 1 as well as CR in Sequ. (not shown).</p>
	<p>E-Stimulus</p> <p>If the animal does not react to the stimuli, then the foot shock is given. If the animal reacts now (unconditioned reaction = UR) then the trial is terminated, the stimuli are switched off and the ITI starts. Reactions is incremented by 1; CR in Sequ. is set to 0 (not shown).</p>



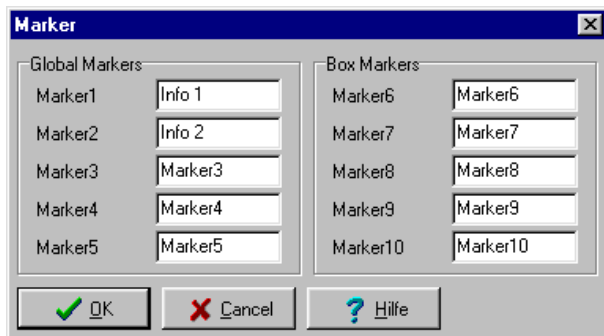
E-Stimulus + Offset

If the animal does not react to the E-Stimulus then the offset stimulus is switched on. If the animal reacts (UR) then the ITI begins. Reaction is increased by 1.

While the E-stimulus is being applied it is possible to manually change the amplitude of the current.

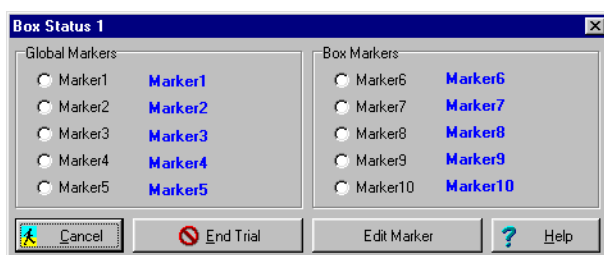
Event markers

While the experiment is being carried out so-called event markers can be set by the user in order to document particular events that are of importance for the test procedure.



Event markers can be defined *before* the start of the experiment and *while* the experiment is being carried out. 2 categories of markers are available:

- 5 global markers: during the experiment they apply simultaneously to all active boxes.
- 5 box-specific markers characterize events which only affect individual boxes: they are allocated to one specific box only.



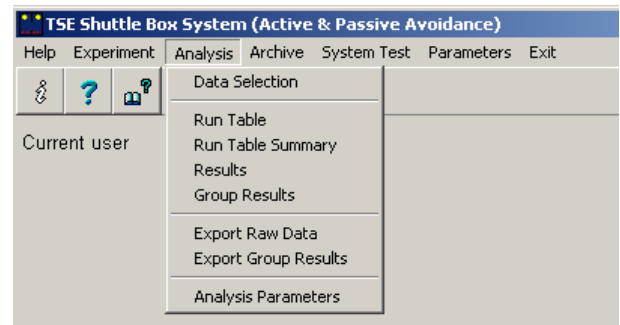
The event markers appear in the analysis tables and export files.

End of trial

The trial is ended automatically when the termination criterion has been reached. A trial can also be ended manually by the operator.

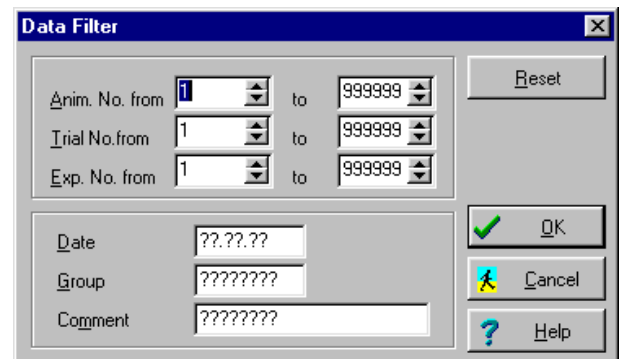
As long as boxes are still active the trial monitor cannot be closed. When the test has been completed in all boxes the trial monitor can be closed and analysis can be performed.

Analysis



The analysis of stored trial data is carried out in two stages.

The first step is to select the data to be used in the analysis (*Data Selection*). The data records can be preselected with the aid of a filter in which parameters defined during test preparation are used for filtering criteria; this makes handling of even large amounts of data easier.



Data can then be listed as:

- **Run table**, a chronological list of the course of the experiment.
- **Results table** that displays calculated results.
- In a group analysis experiments can be compared with each other (**Group Results**).
- Data can be stored in the form of ASCII-compatible files for further processing with statistics programs such as EXCEL (**Export**).

Run table

The run table provides a chronological list of the events in the box. The table has the following columns:

01:00:0 End of Habituation
 02:00:0 Stimulus
 02:01:0 E-Stim. const. 0,40 mA
 02:02:6 Transfer left
 02:02:6 Unconditioned Reaction
 03:02:6 Stimulus
 03:03:3 Transfer right
 03:03:3 Cond. Reaction
 04:03:3 Stimulus
 04:04:3 E-Stim. const. 0,40 mA
 04:08:3 E-Stim. Offset 0,60 mA
 04:13:3 No Reaction
 04:49:2 Transfer left
 04:49:6 Transfer right
 04:50:4 Transfer left
 04:51:0 Transfer right
 04:51:7 Transfer left
 05:13:3 Stimulus
 05:14:1 Transfer right
 05:14:2 Cond. Reaction

Cond. Reaction 6
 Uncond. Reaction 4
 No Reaction 25
 Transfers during Habituation 3
 Intertrial Transfers 12
 Mean Latency Cond. React. 0,71 s
 Mean Latency Uncond. React. 1,81 s

The following parameters are listed:

Total number of conditioned reactions (=avoidance)
Total number of unconditioned reactions (=escape)
Total number of trials without reactions (No R)
Total number of transfers during habituation
The number of transfers during the intertrial period
Mean reaction time conditioned reactions
Mean reaction time unconditioned reactions

Time	Time at which event
Event	Description of the event (max. 2 columns) - End of <i>Habituation</i> phase - <i>Stimulus</i> onset - <i>E-Stim.</i> + type of current (<i>const.</i> or <i>pulsating</i>) + amplitude in mA - <i>E-Stim.</i> + <i>Offset</i> + total amplitude in mA - <i>Transfer</i> + direction of transfer (into <i>right</i> or <i>left</i> compartment) - <i>Reaction</i> (unconditioned, conditioned or no reaction) - <i>Trial End</i>

Group analysis

In the group analysis results table the results from several experiments are gathered together in order to make a direct comparison possible.

Group Results

Anim.	Trial	Exp	Date	Start	Hab	CR	UR	NoR	IT	Lat	CR	Lat	UR
4	4	4	10.01.2007	15:47:13	1	0	1	1	2	-	-	1,51	
5	5	5	11.01.2007	13:21:53	3	6	4	25	12	0,71	1,81		

Each line in the table represents *one* record, i.e. one experiment with one animal. The columns have the following meaning:

Anim.	Animal number
Trial	Trial number
Exp	Experiment number
Date	Start date
Start	Start time
Hab	Number of reactions during habituation period
CR	Number of conditioned reactions
UR	Number of unconditioned reactions

Run table summary

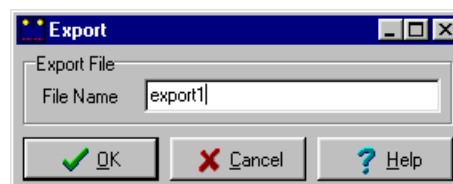
The experiment can also be listed in a summarized table:

No	CR	UR	NoR	T	RT (ms)
0	Habit			3	0
1		E			2610
2	X				650
3			X		0
4	X			5	820
5			X	1	0
6			X		0
7			X		0
8			X		0
9			X		0

Exporting data

In order to use the results for further-reaching statistical calculations in statistics packages or spread sheets (e.g. EXCEL) the system offers the possibility of storing selected tables (run tables and group analysis tables) in the form of special export files.

Various settings can be made for the export before carrying out the export itself.



The file name is defined by the user. The file is in the dBase-compatible CSV-format; this is supported by all professional statistics package.

No	Each line represents one run (ITI + stimulus period). Run no. 0 ist the habituation period
CR	Conditioned reaction
UR	Unconditioned reaction (E = E-Stimulus; A = Air Puff)
NoR	No reaction
T	Number of reactions during the ITI period
RT	Time (in ms) from stimulus onset until reaction of the animal
No	Each line represents one run (ITI + stimulus period). Run no. 0 ist the habituation period
CR	Conditioned reaction

Results table

The results table calculates some result parameters for each data record selected.

Partial list of users - Active & Passive Avoidance System

- Altana Pharma AG, Barsbüttel, Germany
- AstraZeneca R&D Södertälje, Södertälje, Sweden
- Charité - Universitätsmedizin Berlin, Berlin, Germany
- Charles University in Prague, Prague, Czech Republic
- Ecole Polytechnique Federale de Lausanne - EPFL, Lausanne, Switzerland
- Evotec Neurosciences AG, Zürich, Switzerland
- Heinrich-Heine-Universität, Düsseldorf, Germany
- Leibniz-Institut für Neurobiologie, Magdeburg, Germany
- Medizinische Hochschule Hannover - MHH, Hannover, Germany
- Medizinische Universität Graz, Graz, Austria
- Merck Research Laboratory, Rahway, NJ, USA
- NISAD Neurosc.Inst.Schizophrenia & Allied Disord., Darlinghurst Sydney, NSW, Australia
- Otto-von-Guericke-Universität Magdeburg, Magdeburg, Germany
- Purkyne Military Medical Academy, Hradec Kralove, Czech Republic
- Suven Life Sciences Limited, Hyderabad, India
- University of Hawaii, Honolulu, HI, USA
- University of Tartu, Tartu, Estland
- Vrije Universiteit Amsterdam, HV Amsterdam, The Netherlands
- Westfälische Wilhelms-Universität Münster, Münster, Germany

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TSE Systems is a leading supplier of sophisticated research instrumentation in the global life science market. Our focus is on providing the total customer solution, with modular designs of integrated hardware and software platforms for neuroscience, metabolic and behavioral phenotyping, drug screening and toxicology.

For further information please contact us.

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