Sensory Phenotypes

1st ISBS Summer School

St. Petersburg, Russia

May 9th -15th,2008

Sensory input

Taste:

- Gustatory variations in mice can be detected by different choice tests

Touch:

- Ability to respond can be measured by reflexes or by testing mechanical sensitivity with von Frey hairs (Mogil et al., 2001)

Nociception:

- Most common stimulus used for pain research is acute thermal stimulation (e.g. hot water tail-immersion test)
- 129 strain is resistant to nociception and sensitive to antinociception, while C57BL/6 has the opposite characteristics

Vestibular system:

Sensory input

Hearing:

- Mice can hear well above the frequency of human hearing sensitivity
- Can be more sensitive than humans to sudden bursts of noises

Vision:

- Albino strains are more sensitive to bright light and have reduced visual accuity
- Several inbred strains have reduced vision due to the mutations that lead to retinal degeneration

Olfaction

- A very important sense in ethological anxiety tests predator odors
- Marked differences in olfactory sensitivity in some inbred strains have been shown

Voikar, 2006

Example of sensory-motor test battery

1. Visual cliff
2. Auditory startle response
3. Odor orientation/discrimination test
4. Locomotion in the open field test
5. Motor learning and balance in the roto-rod test
6. Pain sensitivity in the hot plate or tail-flick test

Brown et al., 2000

Behavioral effects of visual impairments

Anxiety paradigms – creates appearance of low anxiety

- alternatively, use hole-poke or 2 lever test

Learning and memory – animals appear to have limited learning or spatial abilities

Sight tests

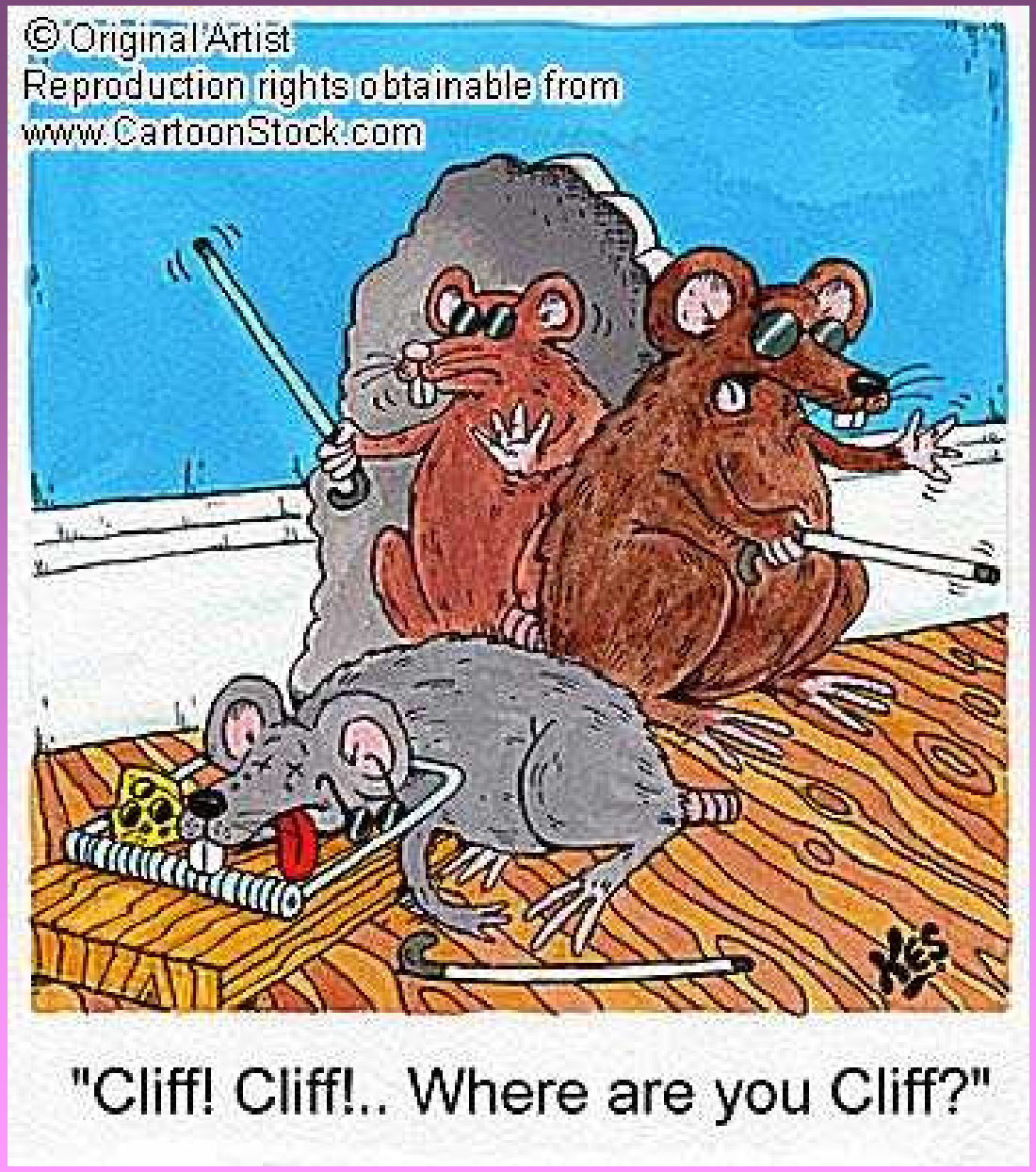
The “Visual Cliff”

- Measures animal’s ability to recognize its surroundings
- Blind mice will go to either side (50%) after being placed in the center.
- Sighted mice have higher percentage of stepping towards the solid side

Photo: LBN, Korea University, Seoul, Korea

Human visual cliff test

encarta.msn.com

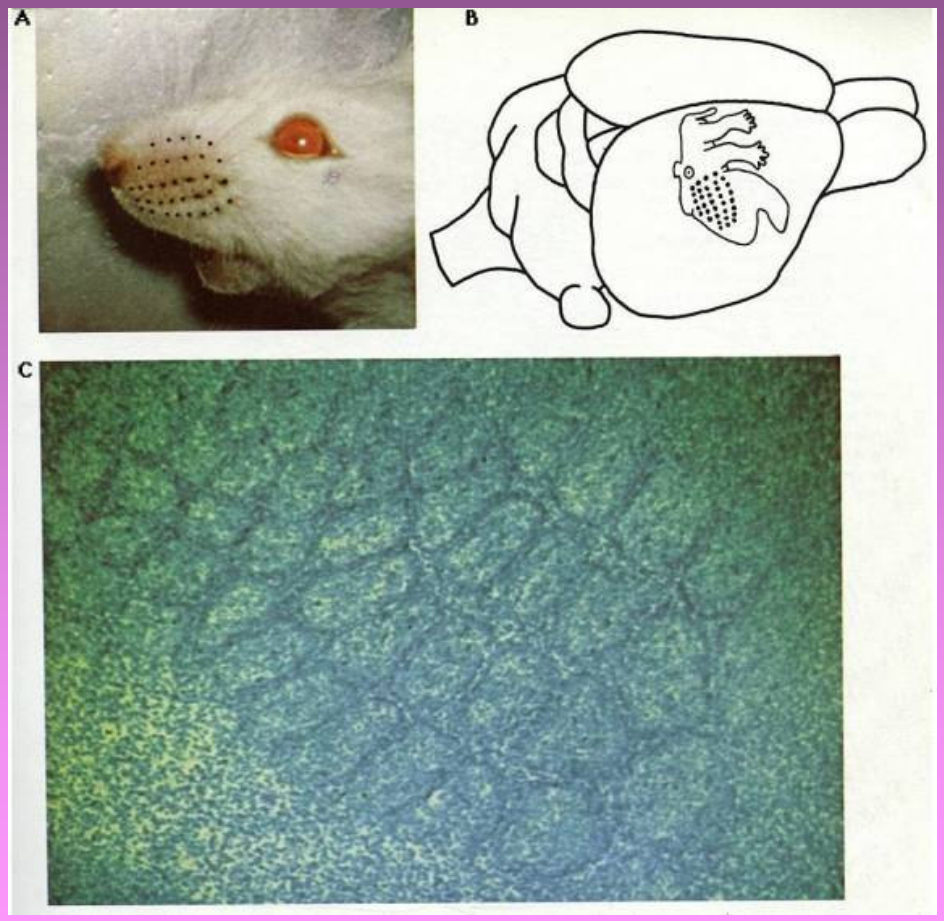

© Original Artist
Reproduction rights obtainable from
www.CartoonStock.com
"Cliff! Cliff!.. Where are you Cliff?"

Whiskers

- Composed of dead cells growing from a follicle
- First appear in embryo at 12 days-old
- Grow around 1mm per day
- Triggers nerves that send messages to the brain
- Used for sensory inputs

Ratbehavior.org

Neurophysiology of whiskers



- (A) spatial arrangement
- (B) the corresponding matrix of cell rings in the somatosensory cortex
- (C) Actual barrels from layer IV

Blakemore, 1977

Whiskers

Barbered whiskers:

- If removed, navigation and sensory abilities are impaired for 8-11 days
- If shortened, will experience impairment for 7-10 days
- The rodent's brain will compensate, so there is no permanent damage
- Alter responses in anxiety testing paradigms (due to either impaired tactile sense and/or ↑ anxiety)

Ratbehavior.org

Sensorimotor system in facial areas

Tests:

- Palpebral reflex (eyelids closed when touched)
- Ear twitch
- Whisker response

Behavioral effect of hearing loss

Can present difficulties for certain tests:

1) Fear conditioning. Measures learning and memory of a specific auditory stimulus

-Can use contextual test instead of cued

2) Prepulse inhibition. Measures response to a startling sound

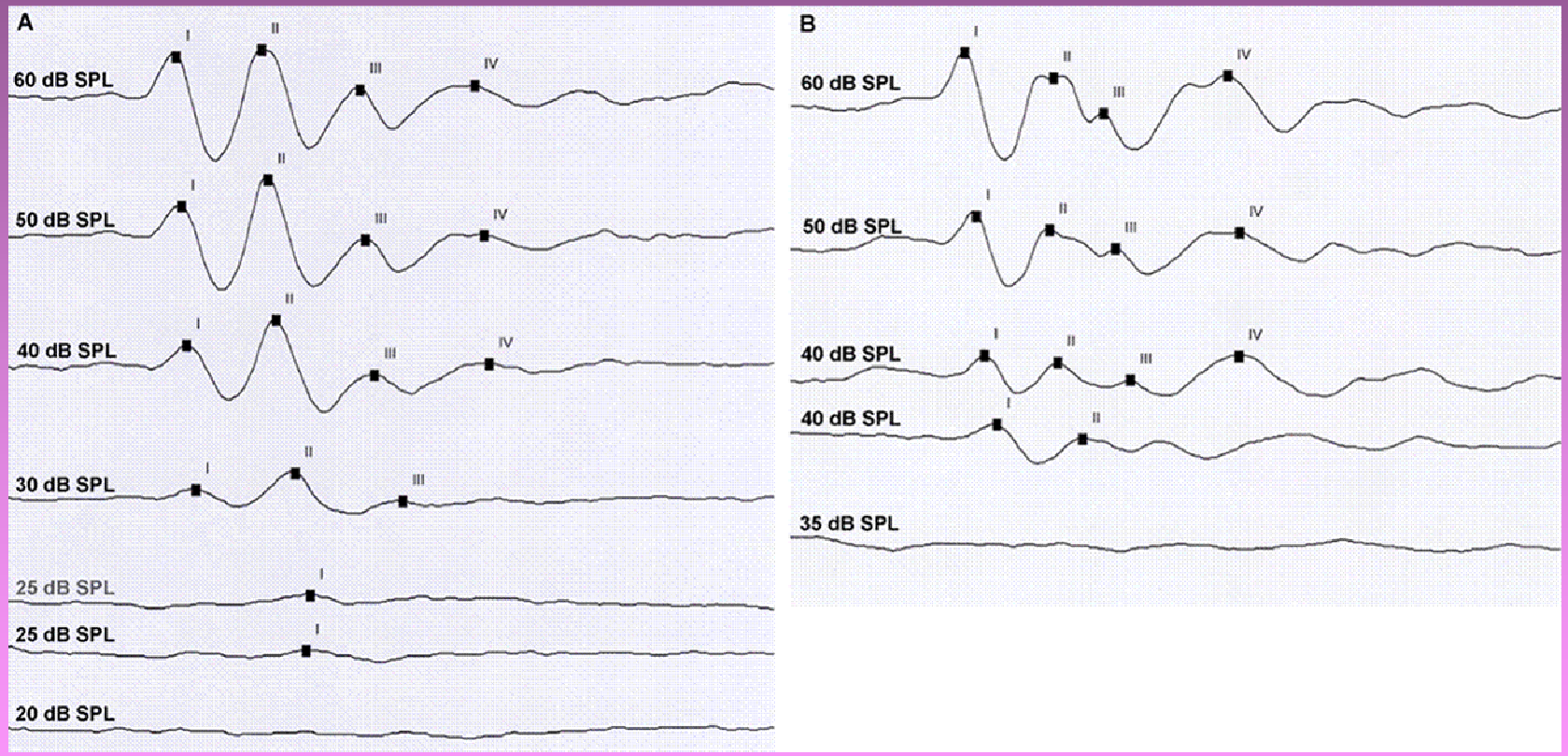
-Use alternative stimuli (air puff vs. noise)

Pletnikov, 2006

Auditory brain stem response

Wild type mouse

VDR-/- mouse



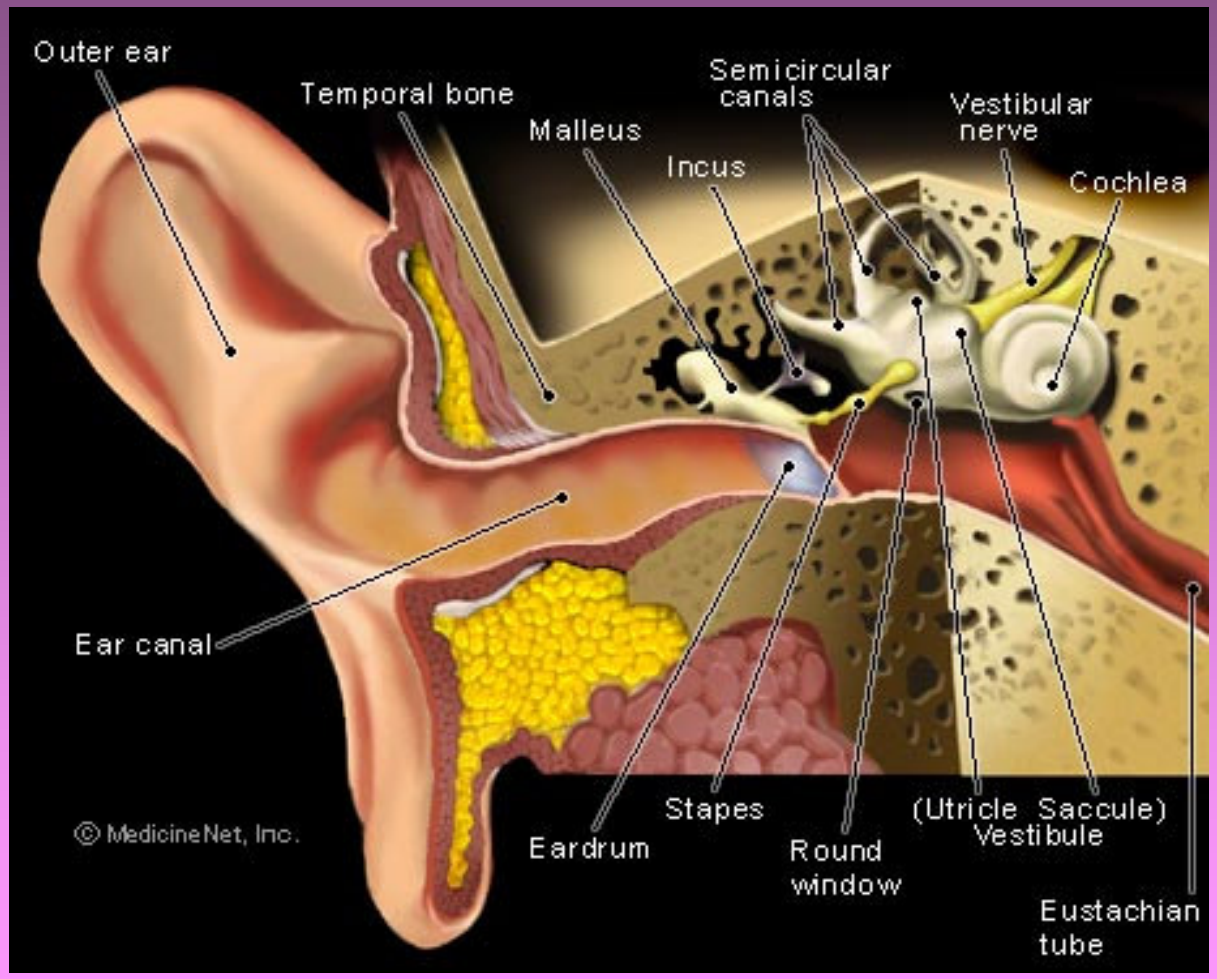
Brain wave activity in the auditory centers of the brain is recorded in response to a series of clicks. The ABR test indirectly estimates the level of hearing in the peripheral auditory system (middle ear and inner ear).

Anatomical structure

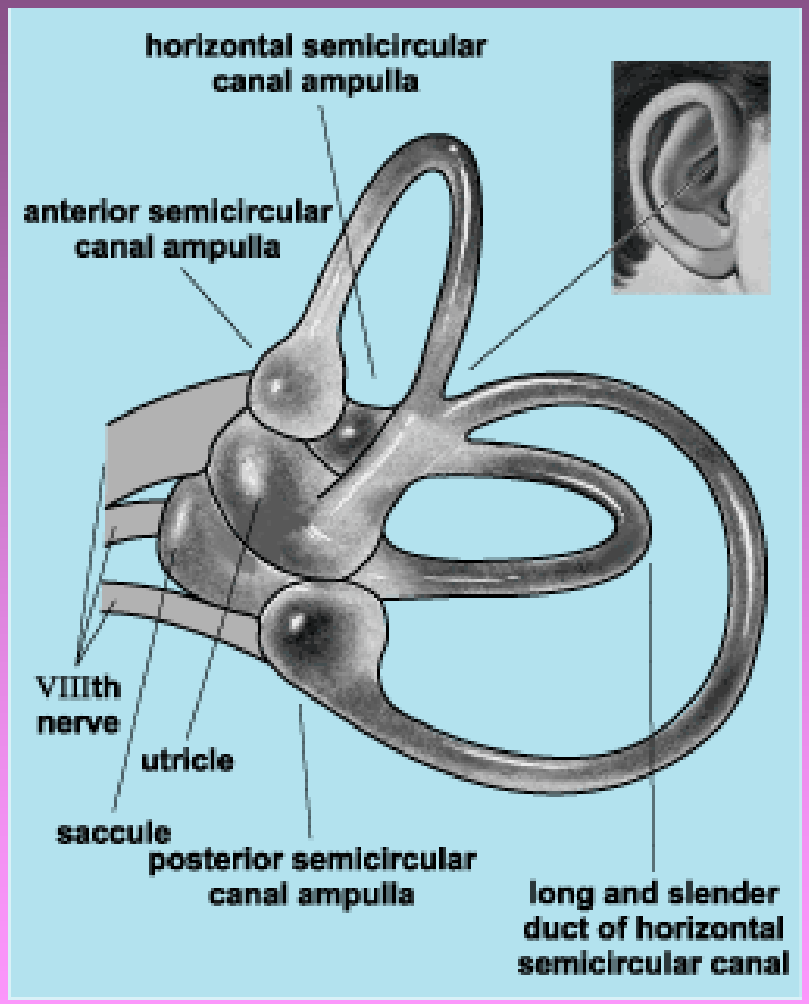
Outer ear - ear canal.

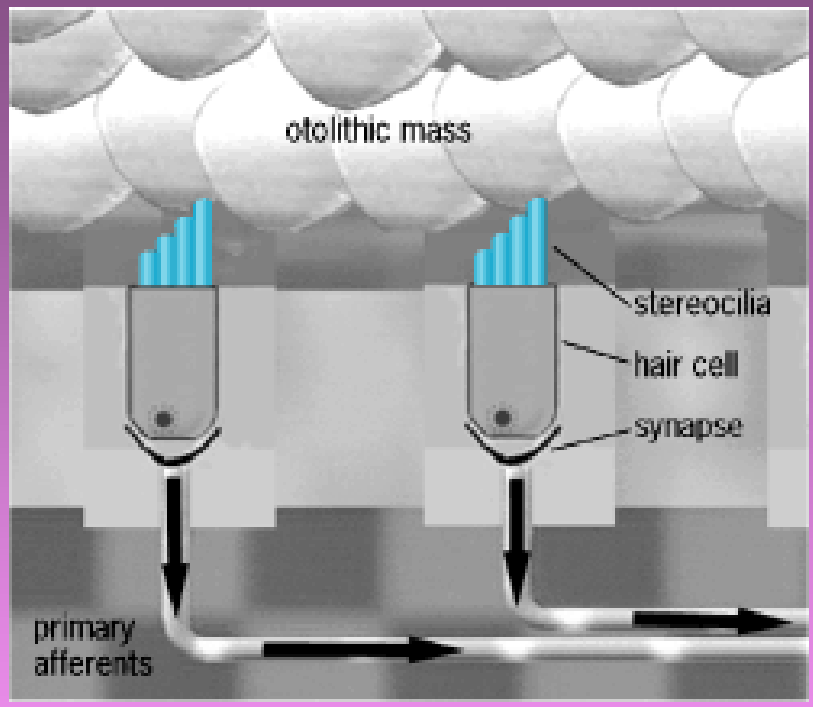
Middle ear - eardrum (tympanic membrane) and the hammer (malleus), anvil (incus), and stirrup (stapes). Connects to the back of the throat by the Eustachian tube.

Inner ear (labyrinth) - the semicircular canals and vestibule for balance, and the cochlea for hearing.



http://www.medicinenet.com/vestibular_balance_disorders/page2.htm, 2008

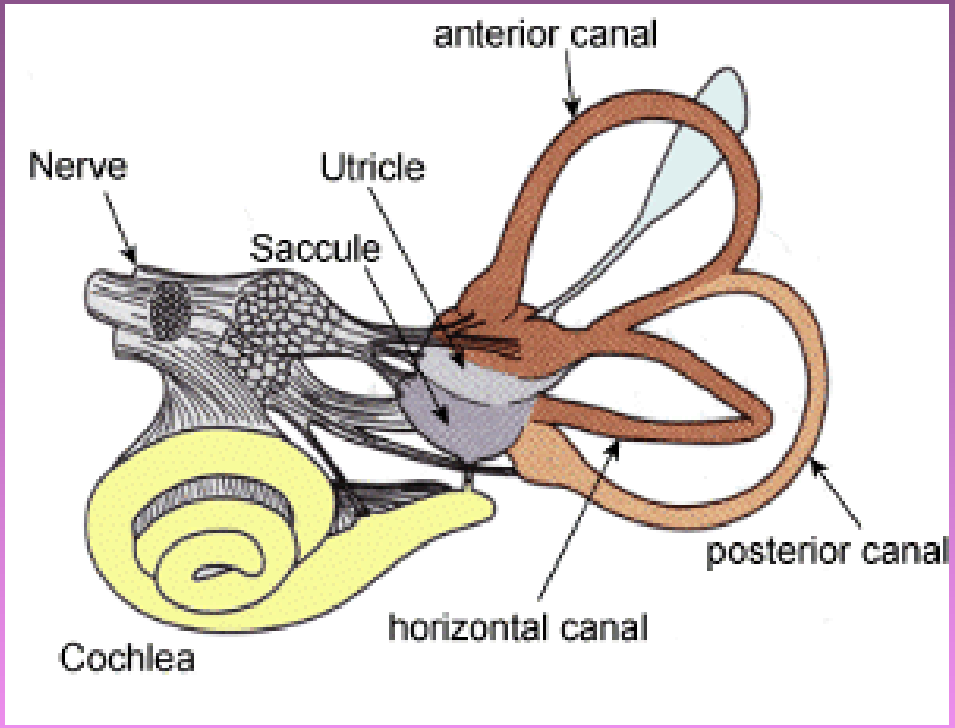




Otolithic macula at rest.

Answers.com, 2008

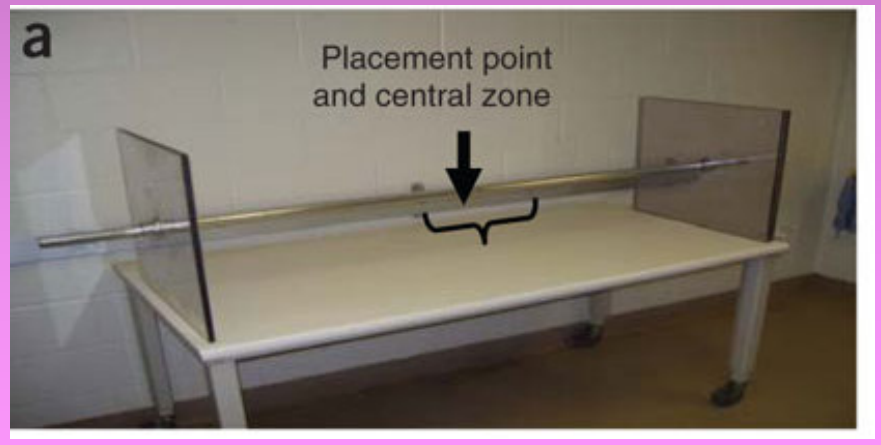
Human Labyrinth



- i) the **cochlea** (yellow) - peripheral organ of our auditory system
- ii) the **semicircular canals** (brown) - transduces rotational movements
- iii) the **otoliths** (in the blue/purple pouches) - transduce linear accelerations

Answers.com, 2008

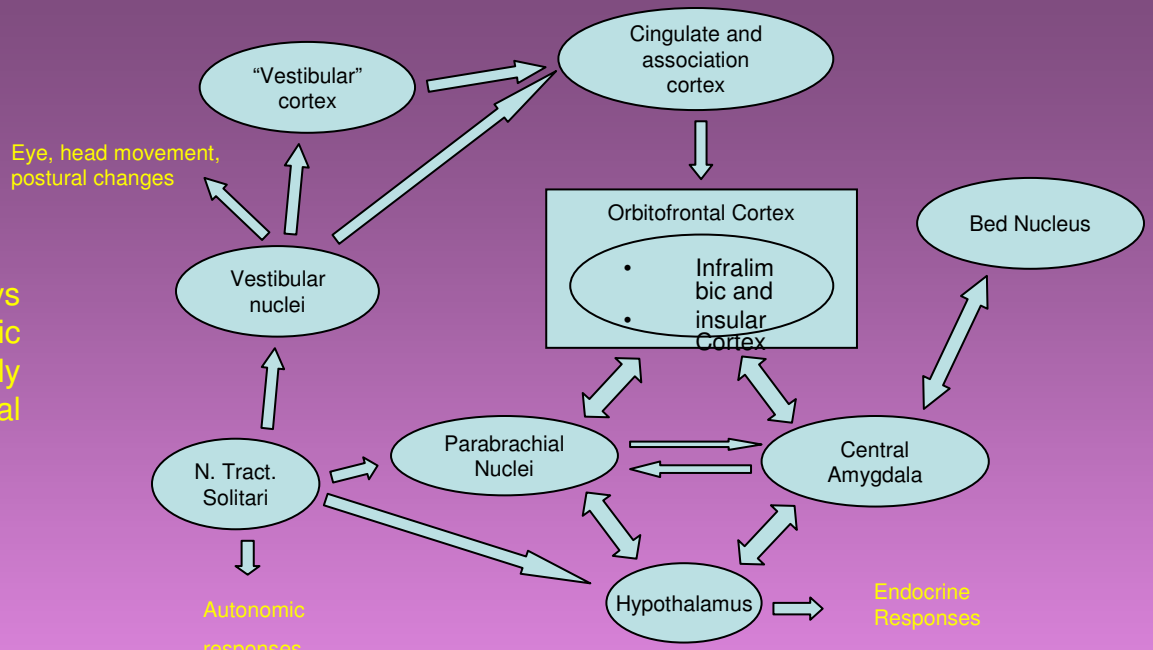
Measuring balance



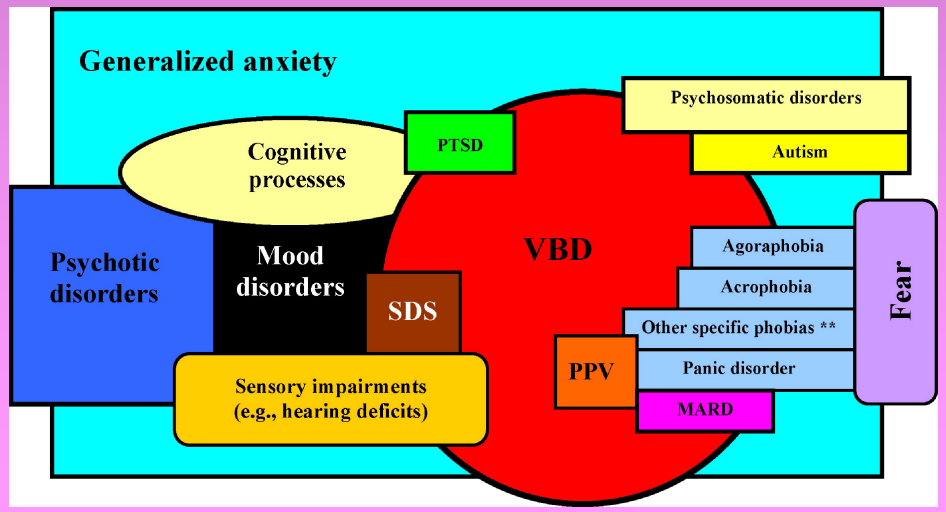
Top photos: Neurodetective International, 2008
Lower: Kalueff et al., 2007

Targeting anxiety-vestibular interplay

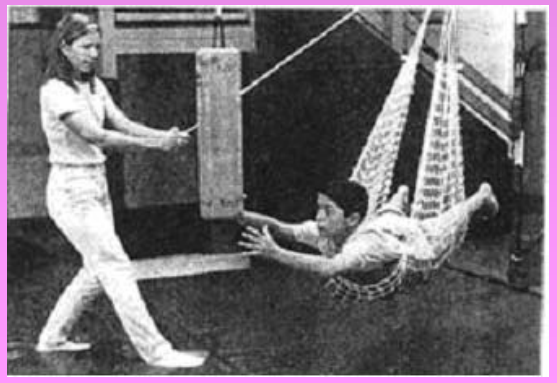
Neural circuits are shared by pathways that mediate vestibulo-autonomic interactions and anxiety, thereby directly linking balance disorders with emotional disorders (Balaban et al., 2000)



Kalueff et al. 2007, in press

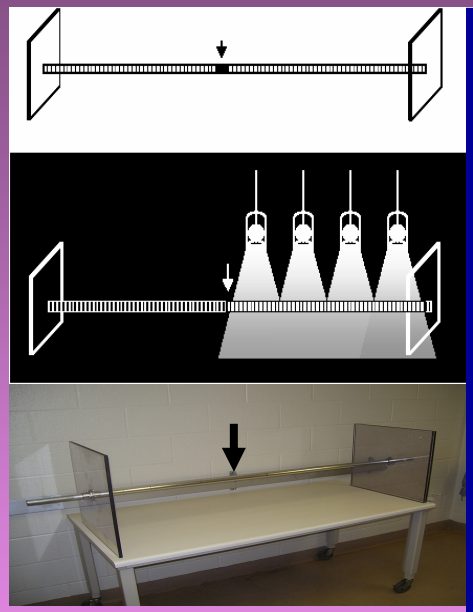


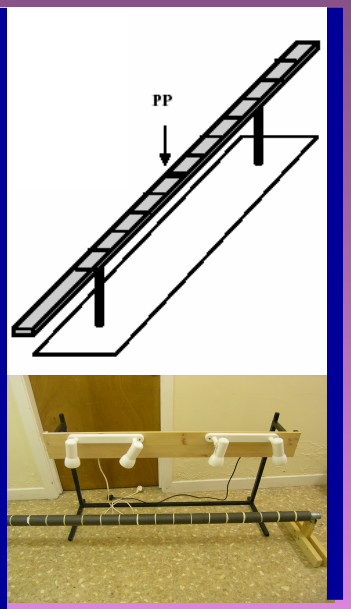
Vestibular therapy of anxiety

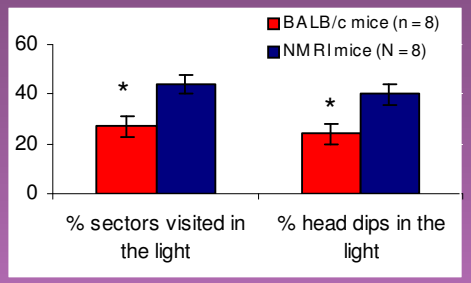


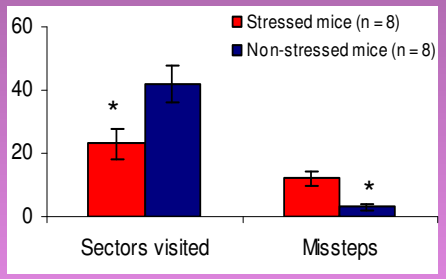
The Suok test of anxiety and balancing

Mouse version **Rat version**









Anxiety (exploration)
Balancing/vestibulation
Motor, neurological functions
Stress-evoked sensori-motor disintegration
Light-dark shifts

Kalueff and Tuohimaa, 2004

Accessibility and advantages:

- High-throughput
- Simultaneous assessment of animal anxiety and balancing
- Short, efficient trials
- Simple, inexpensive apparatus design
- No animal training required

Kalueff, Tuohimaa 2005. The Suok ("ropewalking") murine test of anxiety. Brain Res. Protocols 14, 87-99.
Kalueff et al. 2005. Behavioural characterization in rats using the elevated alley Suok test. Behav. Brain Res. 165, 52-57.
Kalueff et al. 2007. Pharmacological modulation of anxiety-related behaviors in the murine Suok test. Brain Res. Bull., 74, 45-50.
Kalueff et al. Anxiety and otovestibular disorders: linking behavioral phenotypes in men and mice. Behav. Brain Res., in press.

Suok test protocol

1) Transport animals from holding room for 1 hr acclimation in experimental room
2) Place animals individually in the center of the regular or light-dark (snout facing the dark end)
3) Observe behaviors. Sit and remain stationary 2 m away from the apparatus. In light-dark version, assess each area separately and calculate light: dark and light: total indices.

Behavioral measures score:

- Horizontal exploration activity

Kalueff et al., 2008

Olfaction

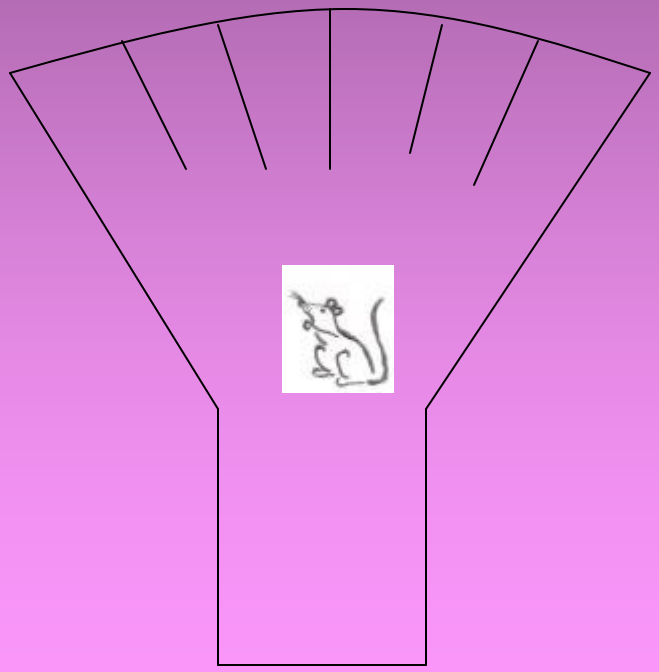
- Plays a major role in rodent's sensory input
- One of their most highly developed senses
- Can measure learning and memory in rodents

www.ananova.com

Crawley, 2000

Olfactory tests

The olfactory discrimination learning apparatus



Staubli et al., 1989

- Chamber delivers various odors at each of 6 holes
- Odors are created by forcing air through water-filled flasks mixed with extracts
- A fan rapidly removes the odors from the testing area
- Floor includes floor plates through which the footshock can be delivered

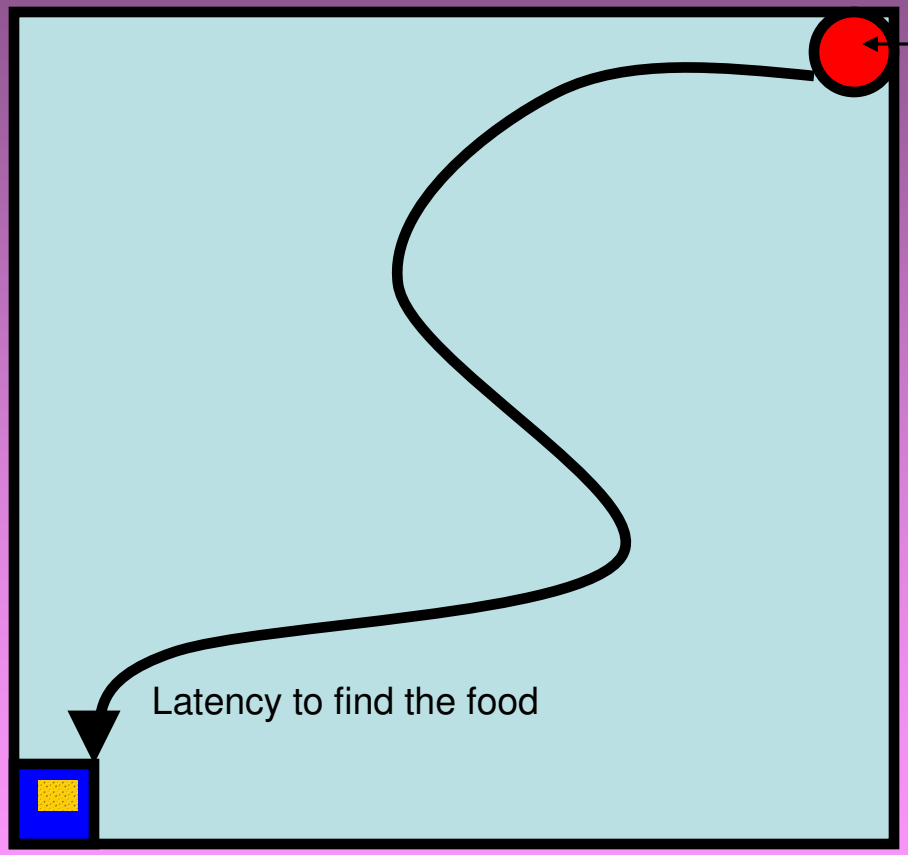
Crawley, 2000

Spatial maze olfactory test protocol

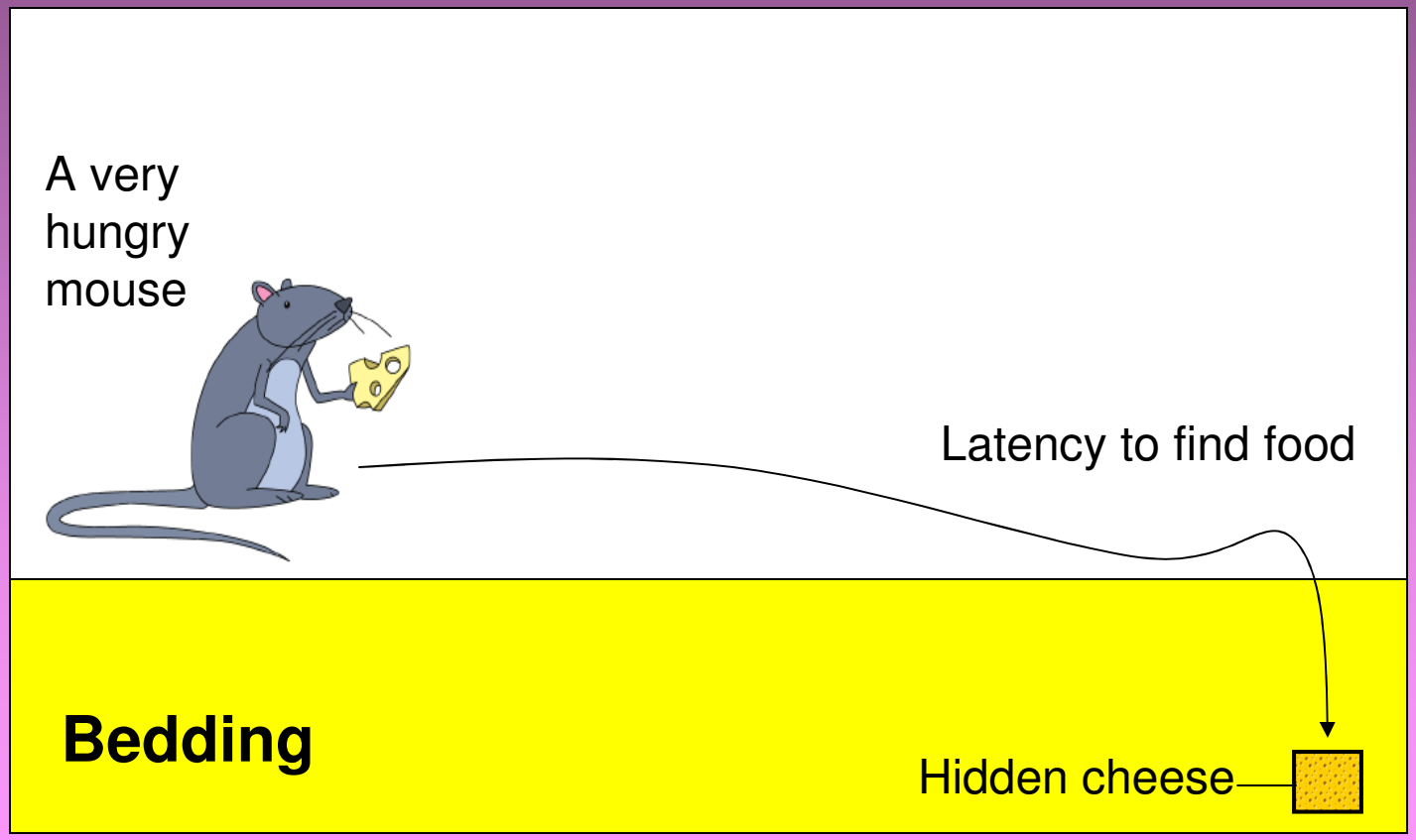
- Used in olfactory learning assessments
- Rodents are trained to choose a specific odor in the maze to receive water reinforcement
- Pairs or triads of odors are used and intervals vary from 1 to 10 minutes
- The position of each odor is randomized
- This is considered a pure olfactory discrimination with no spatial component

Crawley, 2000

Food finding test



Food finding test




© Original Artist
Reproduction rights obtainable from
www.CartoonStock.com
"Can you smell carrots?"