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set #11

lecture #:	*date:*	*professor:*
31	Monday, Novemeber 20th	Dr. Martinez
32	Wednesday, November 22nd	Dr. Chacron
33	Friday, November 24th	Dr. Chacron

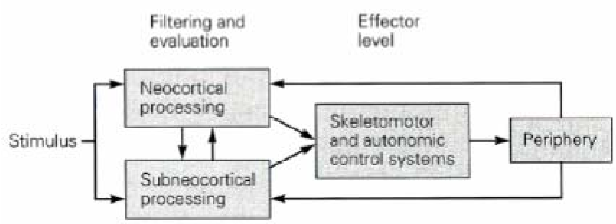
announcements:

- ***Last day of PULS office hours.*** *The PULS office will close for the semester on Tuesday, December 5th, 2006 at 14:00. Come before then to purchase or pickup NTCs, physio-clothing and/or handle any unfinished business with PULS.*
- ***Physiology Ski Trip*** *– Ski all weekend in a condo with 10 of your friends at Mont Ste Anne - Janunary 19-21, 2007 for only $249 – Deadline to sign up is Tuesday December 5th!!!*
- *Good Luck on Finals!*

PLEASE NOTE THE NEXT NTC #12 WILL BE AVAILABLE ONLINE ON ATHENA
http://athena.susonline.net/

This lecture is divided into two parts:

I. **Emotions and Feelings** (Ch. 50)
II. **Motivation and Addiction** (Ch. 51)



I. Emotions and Feelings

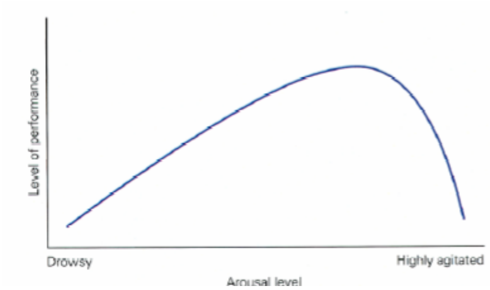
Emotions affect the way we behave, for example in political decision-making, or in our response to a starving child.

We distinguish between the two terms in neuroscience/psychology:

- **Emotion** refers to the *physiological, bodily state* of an organism
  - mediated by a set of peripheral, autonomic, endocrine and skeletomotor responses
  - involves *subcortical* structures.
  - Lie detectors try to sense these physiological changes
- **Feeling** refers to the *conscious sensation* of our emotional state
  - mediated by the cerebral cortext, cingulated cortex and frontal lobe (*cortical* structures).

Emotions affect our arousal level

- High level of arousal increases our level of performance
- Extremely high level of arousal (as in bipolar disease) decreases our efficiency instead
- General arousal refers to the performance of the individual as a whole; specific arousal refers to an area of performance (refers to different stimuli, e.g. sexual arousal)



Development of Theories on Emotions and Feelings

- Up until James and Lange's time, emotions and feelings were thought to trigger physiological changes

James-Lange Theory (1880s)

Feelings occur **after** the cortex receives signals about changes in our physiological state.

- Experimental proof: spinal cord lesion patients (whose cortex don't receive information on physiological state) experience reduction in emotion intensity
- Shortcomings: doesn't explain why emotions are still there after physiological changes stop

↓ improvement

Cannon-Bard Theory (1920s)

Hypothalamus and **thalamus** regulate peripheral signs of emotions and provide the cortex with information.

- Proof: **sham rage** in cats. In cats whose forebrains were sectioned off above the level of the hypothalamus, sham rage response was intact; if forebrain sectioned off below hypothalamus, only isolated elements of the sham rage remained.
- Shortcomings: sham rage in cats don't last very long and aren't real emotional responses (as cats tend to briefly feel anger towards everything.)

↓ improvement

Schachter-Damasio Theory (1960s)

The **cortex** actively *translates* peripheral signals and *constructs* a cognitive response from peripheral signals (much like the cortex constructs vision) in a manner consistent with the individual's expectations social context.

- Prove: A group of individuals were injected with epinephrine and then exposed to annoying or amusing conditions. Individuals who were pre-warned about the side effects of epinephrine associated their arousal (anger/pleasurable feelings) with the drug and showed less arousal.

↓ improvement

Arnold's Theory (current theory)

Emotion is a product of the *unconscious* evaluation of a situation, to be stored in *implicit* memory. **Feeling** is the *conscious* reflection of the unconscious assessment and not a response itself, stored in *explicit* memory.

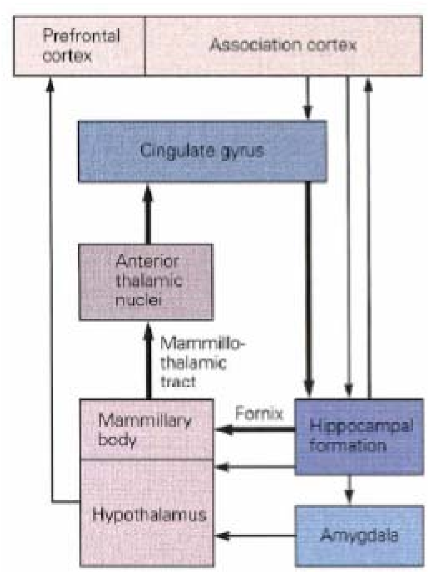
- **Central component** = Cerebral cortex (including cingulated and prefrontal, which evaluates the situation)
- **Coordinating center** = Amygdala (coordinates conscious experience and peripheral expressions)
- **Peripheral component** = Hypothalamus

Hypothalamus (HPT)

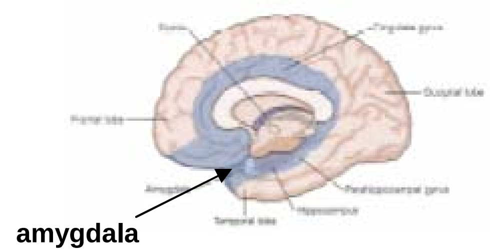
- coordinates the *peripheral (physiological)* expression of emotional states
- lesions of the **lateral HPT** makes animal placid
- lesions of the **medial HPT** makes animal aggressive

Papez Circuit [Figure] * *KNOW DIAGRAM* →

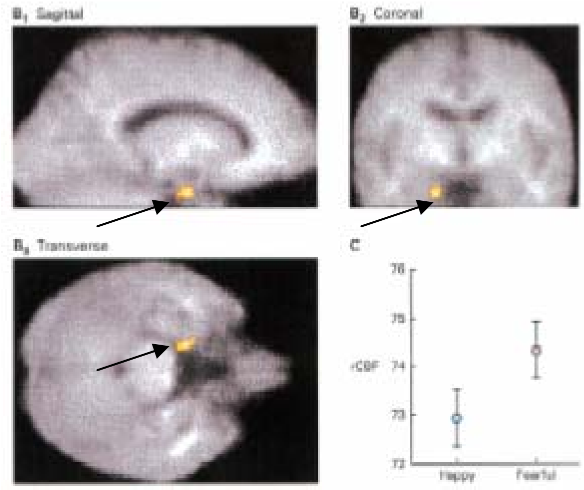
- neural circuit proposed by James Papez in the 1930s to explain emotion in the brain
- **thick lines** indicate the original circuit proposed by Papez:
  - o **hippocampus** was thought to be the main relay-er information to the thalamus and to the cortex (cingulated gyrus)
  - o amygdala was not included
  - o cingulated gyrus in cortex talks to hippocampus about sensory information
- **thin lines** indicate the extension later made by McClean to include the amygdala
  - o the **amygdala** seems to be the structure to coordinate information from cortex to hypothalamus



Amygdala

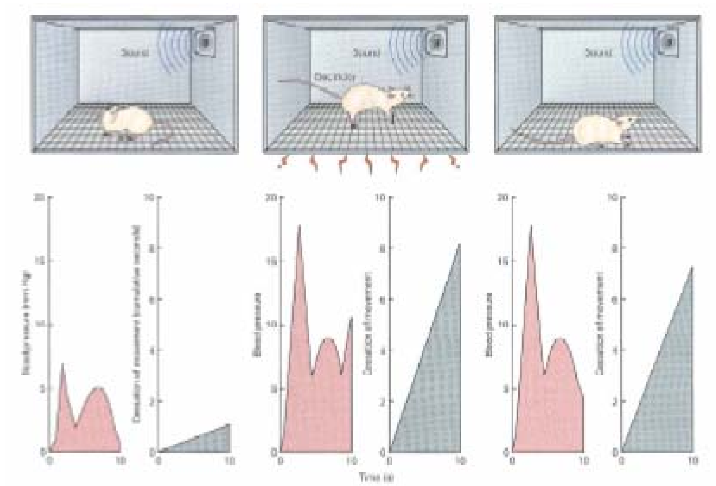


- lesions to the amygdala could be detrimental
- **Kluver-Bucy Syndrome**: removal of the amygdala and hippocampal formation in monkeys causes symptoms:
    - Flattened emotions
    - Increase in sexual behaviour
    - Compulsive tendency to observe and react to every visual stimulus but failure to recognize familiar objects
- **Urbach-Wiethe disease** in humans: calcium deposition in the amygdala
    - Patients cannot process unconscious cues to fear (e.g. facial expression of fear), and are fearless



- **[Figure]** Brain images from an experiment where subjects were shown a continuum of facial expressions
    - Amygdala (arrow) was most active when subjects were judging the facial expression, indicating that it is responsible for emotional responses
    - Amygdala activity was higher for fearful expressions than for happy expressions (shown by graph of regional cerebral blood flow (rCBF))

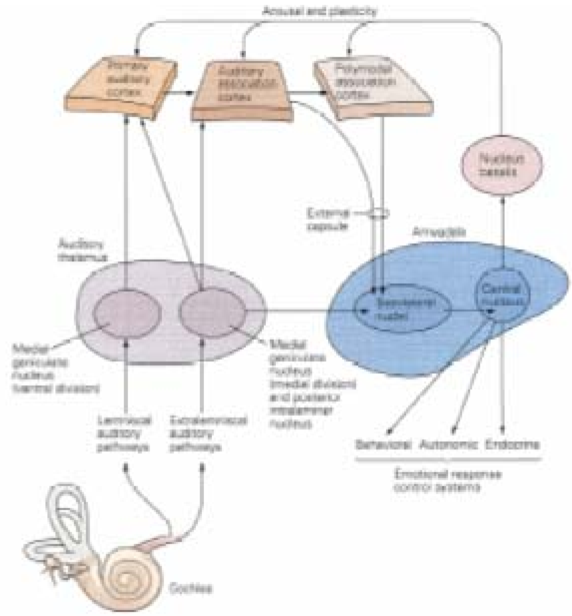
- **Lesions to the amygdala abolishes fear**
    - **[Figure]** The three figures show classical fear conditioning experiments in a rat.



        - Left figure: Simply hearing a sound produces no effects in a rat.
        - Middle: To fear-condition the rat, the same sound is then coupled with a small electric shock to the feet to cause pain to the rat. The rat's blood pressure rises and stops moving after several trials.
        - Right: Later, when the same sound is played alone without electrical shock, the rat's physiological responses to the sound is the same as that for the middle figure, demonstrating fear-conditioning.
    - If the amygdala is lesioned, the rat would not demonstrate fear-conditioning (i.e. doesn't care about shock-related sound)
- Implications: If mechanism for processing fear is abolished in humans, for example, for use in the military soldiers, there can be serious consequences.

Pathways involved in processing emotions

[Figure] Example of the auditory system involved in processing emotions.

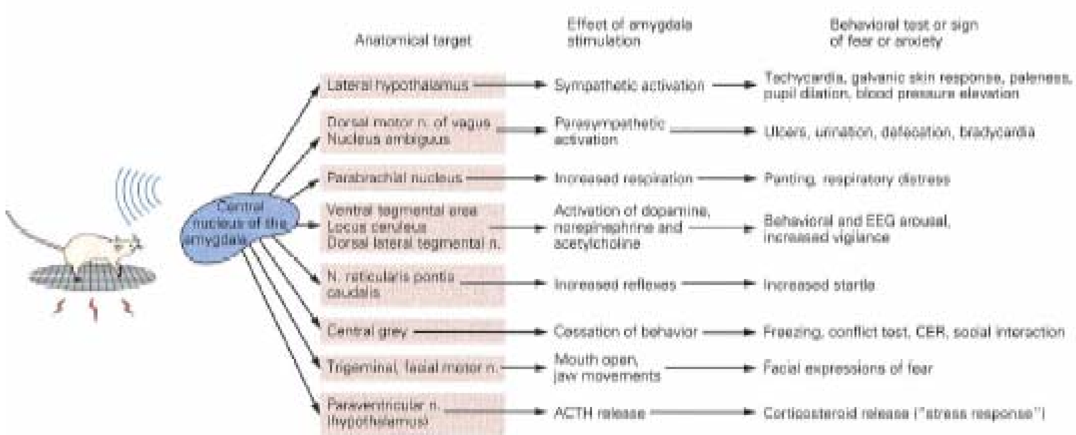


- the auditory sensory information is conveyed to the auditory thalamus
- information goes to the auditory cortex, the auditory association cortex, and polymodal association cortex
- the information is relayed to the amygdala
- the **basolateral nuclei** is the entrance to the amygdala – it receives information from the thalamus and the cortex
- information is relayed to the **central nucleus** of the amygdala where information is integrated – information is sent in *feedback* to cortex, or trigger emotional responses in behaviour, the ANS, or the endocrine system

- *The pathway shows that we don't have to involve a large area of cortex to initiate emotional responses, hence some emotional responses can be unconscious.*

Context Conditioning

- people try to increase contact with environment that have positive stimuli (e.g. drug addicts go to environments where they can experience highs)
- involves amygdala
- lost in Kluver-Bucy syndrome patients



[Figure] The **central nucleus of the amygdala** has many connections to different areas of the brain
- stimulating some of these pathways would trigger specific a physiological response

Other structures involved in emotion

Frontal cortex – behaviour
- lesions here have a **calming effect** on monkeys
- lesions to ventral frontal lobe disinhibits inappropriate behaviour, as in the case of Phineas Gage

Hippocampus – has an indirect role
- contrary to Papez's thinking, where he thought it played a more direct role

II. Motivation and Addiction

Motivation is a set of physiological phenomena that triggers brain to do something.

Two types of motivation:

1. **Elementary drive states:** Simple responses, e.g. I eat because I'm hungry
2. **Personal/Social aspirations:** Complex response; sociological associations acquired by experience, e.g. I starve myself because I want to look good

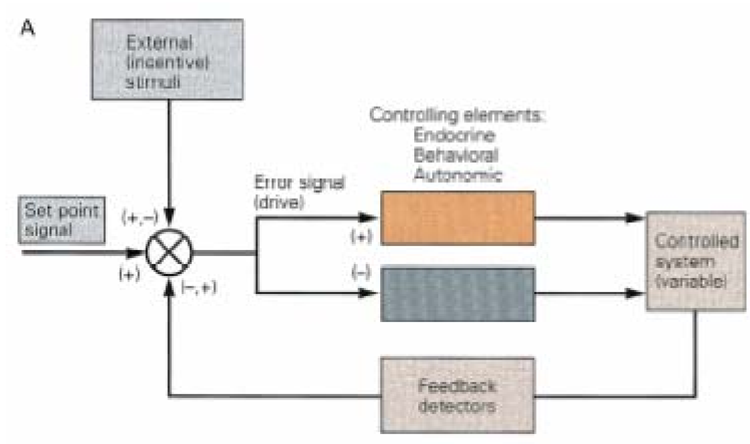
Other factors that affect motivational states:

- **Ecological requirements** of the organism
- **Anticipatory mechanisms** (circadian rhythm)
- **Hedonic factors** (pleasure); e.g. humans will subject themselves to deprivation so to increase pleasure when that deprivation is removed (skipping lunch to enjoy dinner more)

Servomechanism: a control mechanism; a simplistic model we use to help us understand the complex operation behind homeostasis (ie. a negative feedback loop)

Components:

1) **Controlled Variable**: For example, body temperature, food demand
2) **Set Point**: desired value set biologically
3) **Error signal**: generated by integrator when the value of the controlled variable deviates from the set point



* **Temperature regulation** was not covered in lecture; please read it in Kandel's *Principles of Neuroscience*.

FEEDING BEHAVIOUR

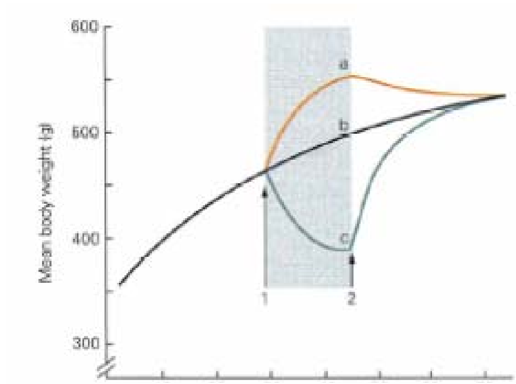
- Body weight is regulated by a set point
- Set point can vary due to stress, palatability of food, exercise, and environmental and genetic factors
- e.g. if I don't like my food, body weight goes down

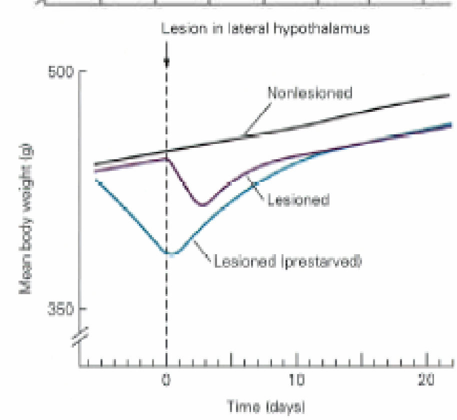
[Figure, top] Rats adjust their food intake to achieve a normal body weight

- shaded region indicates period of time when experimenters interfered with the rat's eating habits
- **group B**: fed normally
- **group A**: over-fed (force-fed); rats lost weight when the force-feeding period was over
- **group C**: under-fed (deprived of food); rats gained weight again
- groups A and C adjusted their body weights to reach the mean weight of the normally-fed rats

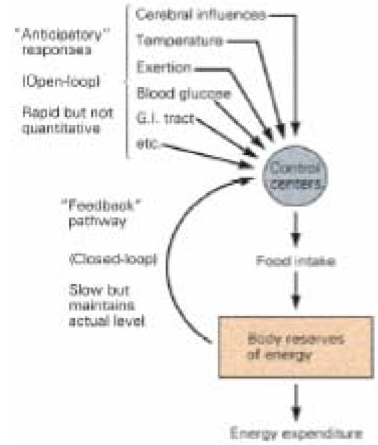
[Figure, bottom] Body weight of rats with lesions to the lateral hypothalamus

- control group was kept on normal diet





- two other groups were lesioned on day 0 and given free access to food
    1) rats that were prestarved prior to lesion started eating right away
    2) rats kept on a normal diet prior to lesion lost weight for a few days before they started gaining weight again
- the experiment proved that a set point was altered, and not a feeding centre



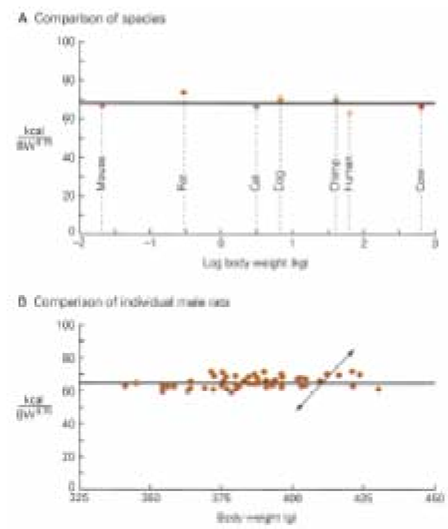
Hypothalamus controls feeding behaviour

- **ventromedial nucleus** of hypothalamus: lesions here cause hyperphagia
- **lateral hypothalamus**: bilateral lesions produces aphagia

Note: These areas affect sensory processing, set points, and dopaminergic pathways; these are not feeding or satiety centers.

Cues control food intake

1. **Short-term cues** regulate size of individual meals
    - cues include blood glucose levels and intestinal hormones such as cholecystokinin
2. **Long-term cues** regulate overall body weight
    - Involves genes such as the *ob* gene, which produces **leptin**
    - **Leptin** is a hormone which suppresses appetite; it suppresses the release of NPY in the hypothalamus
    - **NPY** is a neuropeptide which stimulates feeding behaviour
    - Connecting an obese rat's circulatory system (containing leptin) to a normal rat's circulatory system affects the normal rat's appetite
    - In humans, the feeding behaviour is more complex, and seems to be downstream from the leptin receptors



Daily energy expenditure in different species

- **[Figure, top graph]** shows that if we express the daily energy expenditure in species as **kcal/body weight**, the numbers are fairly constant
- **[Figure, bottom graph]** Shows that metabolic rate goes up with greater food intake, and decreases with less food intake

*** Drinking Behaviour** was not covered in the lecture.

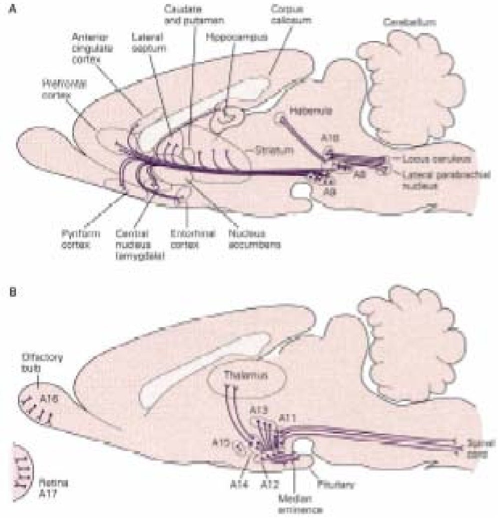
DRUG ABUSE

- Animals can be conditioned to self-administer drugs
    - Rats, given a choice of sugar and cocaine, will choose cocaine

Three mechanisms of addiction:

- **Cocaine** and **amphetamine** act by *blocking* dopamine transporters and thereby increasing dopamine in the **nucleus accumbens**
    - mutant mice missing the dopamine transporter show no response to the administered drugs
- **Nicotine** acts on the presynaptic cholinergic receptors to *enhance* the release of dopamine
- **Mu opiod** agonists act by *inhibiting* GABA neurons that suppress dopaminergic neurons in the ventral tegmental area (ie. removing suppression of dopamine)

[Figure] Dopaminergic pathways in the brain (from Chapter 45 of textbook). Shows some of the neurons affected by drugs.

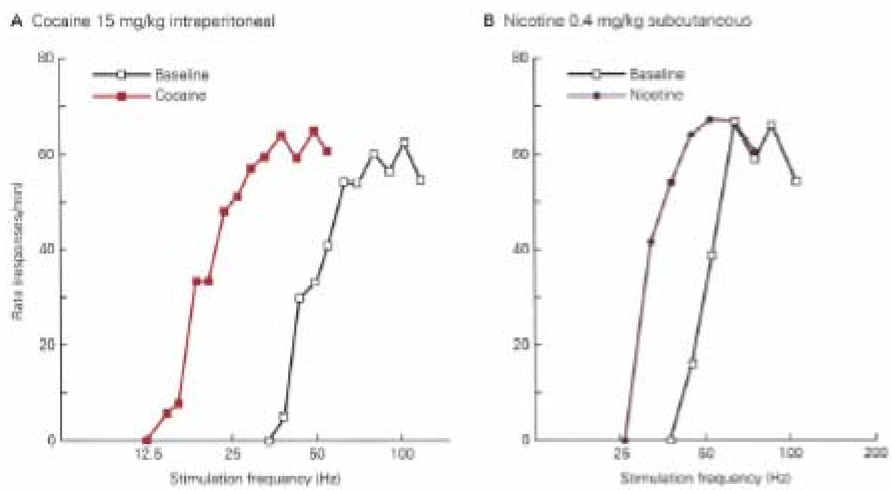


Dopaminergic neurons in the human brain are divided between:

1) **Substantia nigra,** giving rise to the nigrostriatal pathway (affected by Parkinson's disease)
2) **Ventral tegmental area,** giving rise to the <u>mesocorticolimbic projections</u>

- **Nucleus accumbens** has a core and shell
    - <u>Shell</u>: strong connections to the limbic system and hypothalamus. Very sensitive to addictive drugs.

[Figure] Cocaine and nicotine affect the rate of electrical-self stimulation.



- The graphs show that drugs enhance the pleasure produced by electrical brain stimulation.
- The electrical stimulation produces the same effect as a drug of abuse's effect in the brain, producing pleasure.
- The x-axis is the frequency of the electrical stimulation used by the mice, the y-axis shows the corresponding response in the animal's brain
- Taking the drugs shifts graph the left, meaning that a less frequent (less potent) stimulation is necessary to produce the same effect in the animal's brain. Hence, drugs <u>potentiate the effects of the stimulation</u>.
- If you stop consuming the drug, there are **withdrawal effects**, because the dopaminergic pathway has been affected.

<u>Some terms:</u>

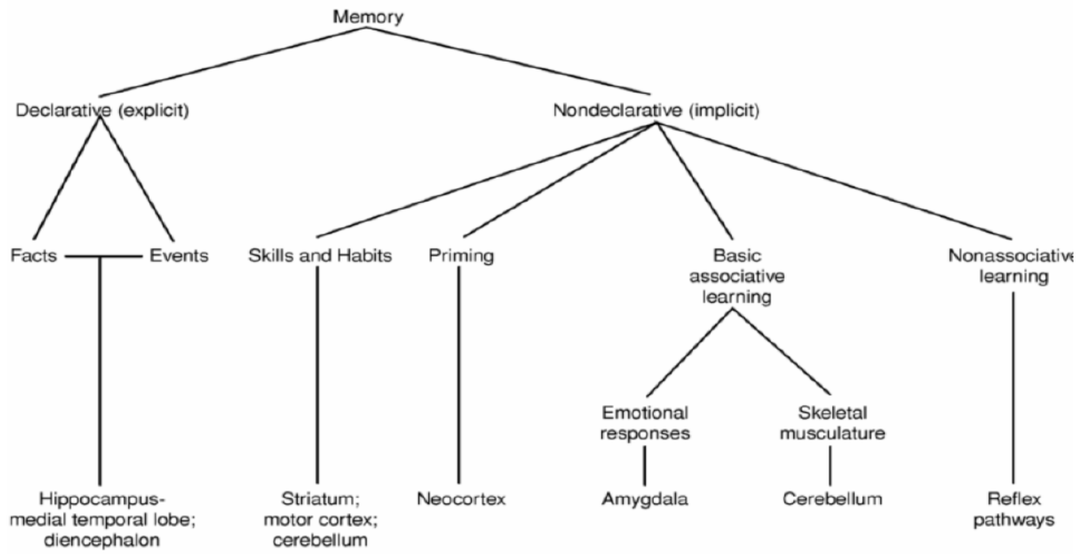
- **Tolerance:** Progressive adaptation to the dosage that produces euphoria
- **Dependence:** negative visceral consequences of withdrawal of the drug
    - dependence can also occur in the *absence* of dopaminergic mechanisms

REPRESENTATION OF SPATIAL INFORMATION IN THE HIPPOCAMPUS

- New Professor: Dr. Chacron
- Will be diving deeper into Martinez's information of memory

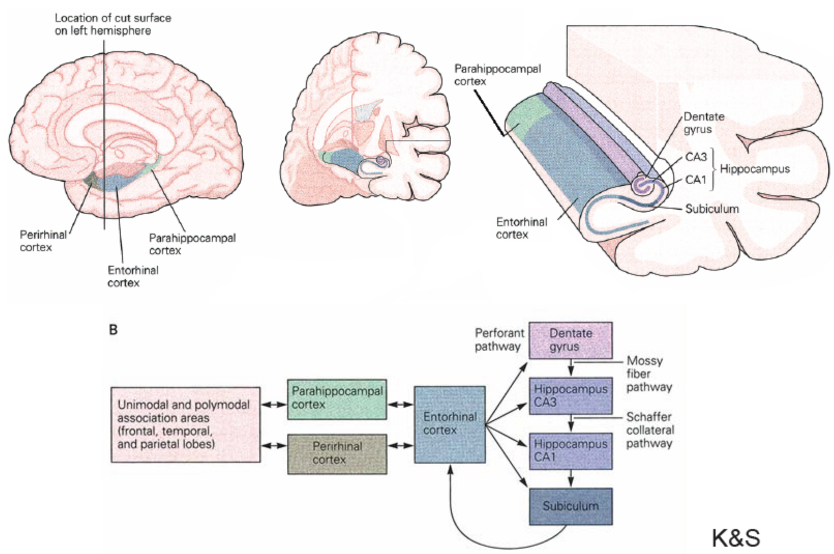
REVIEW OF HIPPOCAMPUS AND MEMORY

- Note the **Taxonomy of Memory:**



  - ***Declarative:** facts and events or **Nondeclarative:** skills and habits*
  - ***Associative moving:** i.e. associating a sound with a specific movement*
  - ***Non-associative:** habituation, sensitization*

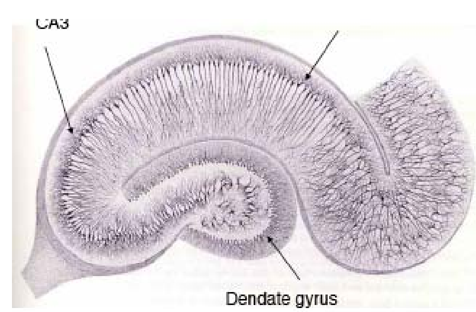
- **Hippocampal Anatomy**



K&S

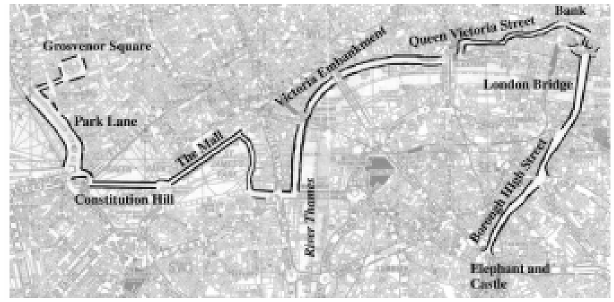
  - *Note location of the enterorhinal cortex*
  - ***Aside:*** CA stands for "rams horn" in another language
  - Input from the **entrohinal cortex** to the **dendate gyrus**
  - Dendate gyrus **granule cells** make **mossy fiber connections** into CA3 **pyramidal cells**
  - CA3 **pyramidal cells** make contact to CA1 **pyramidal cells** through **Schaffer collaterals**
  - Project to cortex and feedback

- **The Hippocampus**
  - There are two sections of the hippocampus, the **right** and the **left**
  - Lesions of the **right hippocampus** affects **spatial memory**
  - Lesions of the **left hippocampus** affects **words, objects, or people**

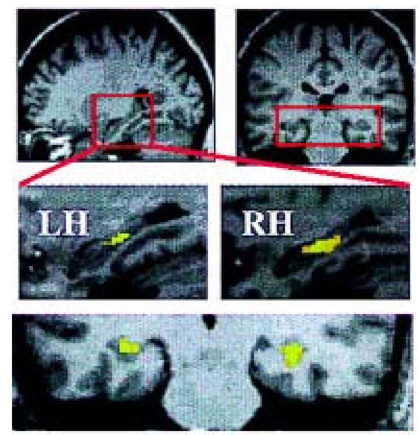


EVIDENCE FOR THE ROLE OF THE HIPPOCAMPUS IN SPATIAL LEARNING

- Some professions require the use of more spatial memory than others
- This is seen most notably in taxi drivers, who require a large amount of spatial knowledge for navigating through the city
- There is one specific study that has examined the correlation of spatial memory to the hippocampus through the use of taxi drivers [*link on WebCT*]



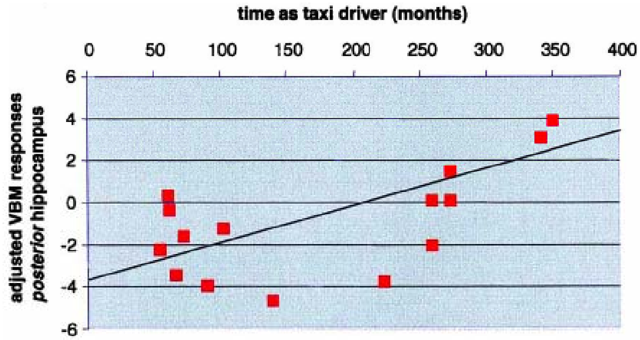
- **1.** See outline of map: was gathered by information from a taxi driver who was sitting on a chair, blindfolded → he was **not** driving, this recall was from memory
    - o Therefore, the driver was able to maintain the correct spatial knowledge of the city to get from point A to point B without needing visual cues.
    - o ***Note:*** London taxi drivers must undergo two years of training and then pass a final exam, much of it using questions such as these
    - o **Take-Home Point:** taxi-drivers have good spatial memory



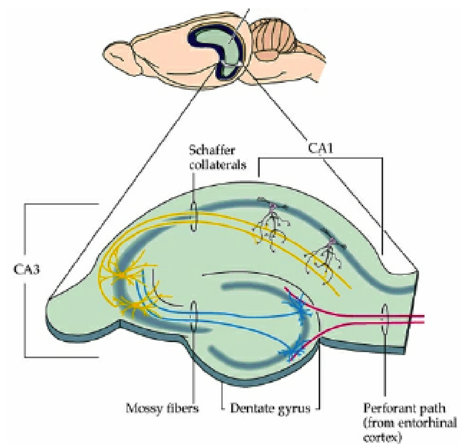
- **2.** Examined fMRIs of London Taxi drivers hippocampi
    - o Use **fossil based morphology** [explained in the paper], but it essentially is used to *estimate the volume of grey matter* present in a given location
    - o Therefore, using this technique Maguire et al. compared the size of the hippocampi in control subjects versus the taxi drivers
        - The taxi drivers were shown to have a much larger volume of grey matter when activated for spatial purposes
    - o Furthermore, although the right hippocampus is involved with spatial information, taxi drivers must remember the names of streets, so the left hippocampus was seen to be larger as well during activation
    - o **Take-Home Point:** the posterior sections of both the right and the left hippocampus are larger in taxi drivers than in control subjects. Therefore, there is most probably a link with these areas and spatial memory

- **3.** Examining cross-sectional areas of the hippocampus shows that **the net volume of the hippocampus is constant**
    - o However, in both the left and the right hippocampus, the **posterior** portion is significantly larger in taxi drivers than in the control subjects where as the **anterior** portion is significantly smaller
        - This claims that it is the posterior portion of the hippocampus that regulates the spatial and verbal memory required to be a taxi driver [*it was not mentioned what the anterior hippocampus is involved in*]
    - o **Take-Home Point:** the total volume of the hippocampus is conserved, but the posterior regions will grow at the expense of the anterior regions.

- **4.** The experiment then measure the volume of grey matter as a function of **experience** within the taxi drivers [i.e. the longer you have been a taxi driver correlated with the size of the posterior hippocampus]
    - o In the posterior hippocampus, there is a positive correlation with the time as a taxi driver and the size of the posterior hippocampus
        - It is getting bigger



- In the anterior hippocampus, there is a negative correlation with the time as a taxi driver and the size of the anterior hippocampus
    - It is getting smaller
- Each graph shows no signs of plateauing at a point less that 400 months [approximately 33 years]
    - *Which most likely means that this dominance can be attained at any age and there is no critical period that is required*
- **Take-Home Point:** the size of the posterior hippocampus increases with time if one needs it for spatial memory. Keep in mind that since the size of the hippocampus must stay constant, the anterior portion must be decreasing in size



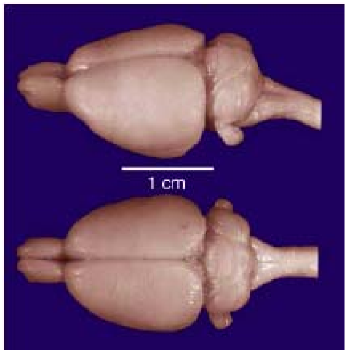
- **Conclusions:** the posterior hippocampi of taxi drivers with extensive navigational experience are larger than those of the control subjects, proving that it must be involved in spatial and verbal learning and memory
    - There is continual neurogenesis in hippocampus of adult humans, it is thought that this neurogenesis underlies the formation of new memories.
    - However, this does not explain the **neural mechanisms** being used

NEURAL ANATOMY

- Used to determine neural components behind mechanisms involved in learning
- *Dendate gyrus → CA3 → CA1 → enterorhinal cortex*

RODENTS AS MODEL SYSTEMS FOR SPATIAL LEARNING

- Rodents show deficits from hippocampal lesions that are similar to those seen in humans
    - ***See movie:***
        - ***1.*** Rat is trained to move around a circular path that contains a food reward at some point in the cycle
        - ***2.*** Food is removed
        - ***3.*** Rat is sent around the path to determine if he notices the absence of the food and can recognize the location it was previously in
            - **With no Lesion:** rat stops and searches at point that previously contained food
            - **With Partial Lesion [to the CA3 region]:** rat fumbles slightly, seemingly knowing like something used to be there, but what? [*seemed like a deja-vu feeling*]
            - **With Full Lesion [to the CA3 region]:** rat has **no** clue what is going on and no retention of what used to be there, if anything
    - **Take-Home Point:** hippocampus is involved in spatial memory

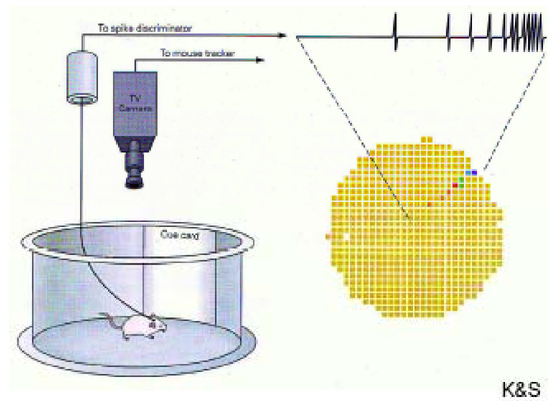


- **The Rodent Brain**
    - Hippocampus anatomy is similar to that of humans

PLACE FIELDS WITHIN RODENTS

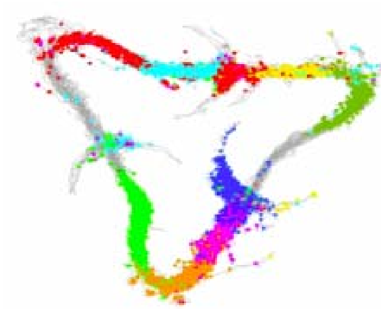
- The question still remains: ***How is spatial information represented and how are new memories formed?***

  - This is determined by recording in vivo from awake, behaving rodents using an array of **tetrodes**, which record action potentials from a variety of neurons and send them to amplifiers which sent the information to computers for processing (can assign APs to different neurons)
    - Tetrodes consist of four wires strung together and inserted within the hippocampus; the wires each contact different neurons, which allows for comparison between locations at a given time
  - Once hooked up to the tetrode, rats are free to move around the environment, **all of which contain spatial cues to determine location** [i.e. a colored panel, a cup, etc]

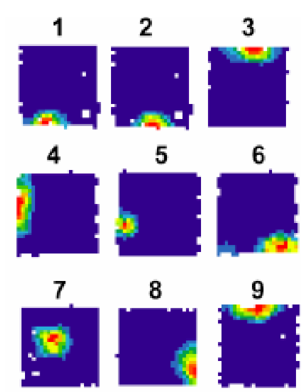


- See Schematic View of Set-up
  - Camera monitors movement while the tetrode coordinates spatial position and action potentials

- **Advantages of the Tetrode Set-Up:**
  - Recording form **large populations**, but from animals whom are **awake, behaving, and moving**
  - Uses a **systems level approach** to reveal the **transformations** that occur in hippocampal circuitry
    - i.e. how spatial location is being encoded with the hippocampus
  - Can understand how these transformations **mediate** complex behavior (i.e. navigation, perception, learning, and memory)
  - ***Can also be implicated in changes in environment: will be discussed next lecture***



- **Experiment 1:**
  - A rat was confined within a maze with food rewards at three locations**.** Once the rat became accustomed to his location, tetrodes where place in the CA1 pyramidal cells to record action potentials as he move around
  - **Results:** the activities of 8 pyrimdal cells were recorded as color coded labels; each time the cell fires, a colored dot corresponding to the neuron that sent it is placed at a spatial position within a diagram of the maze
    - From the results at the right, one can conclude that each individual neuron fires at specific markers within the environment
      - The location where firing occurs is termed a **place field**
  - *In addition, note that hippocampal cells have a low spontaneous firing rate, so if they do fire, it is to encode a specific stimuli*
  - **Note** that although each point was recorded from the same tetrode the neurons being record from cover most of the spatial area
  - **Take-Home Point:** hippocampal neurons each encode for a specific location within the environment present and are activated when present in that environment

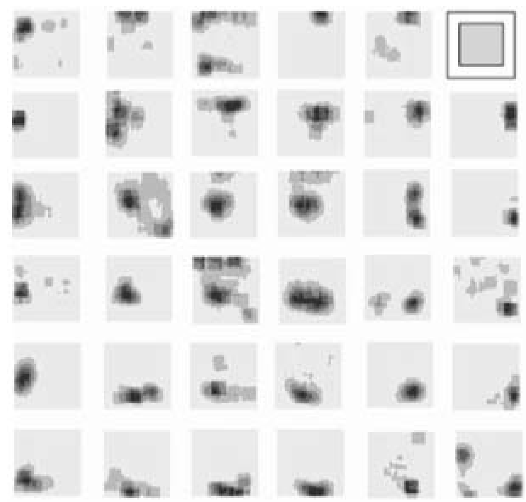


- **Experiment 2:**
  - Can quantify place fields in different ways, other than dots representing action potentials
  - Here, we are recording from 9 different neurons in CA1 and frequency of firing intervals are recorded as different colors [i.e. 5-6 action potentials/sec results in red coding]

- Recorded as a function of location, it can again be seen that these place fields *cover most of the environment* the rat is in
- **Take-Home Point:** CA1 pyramidal cells are location dependent

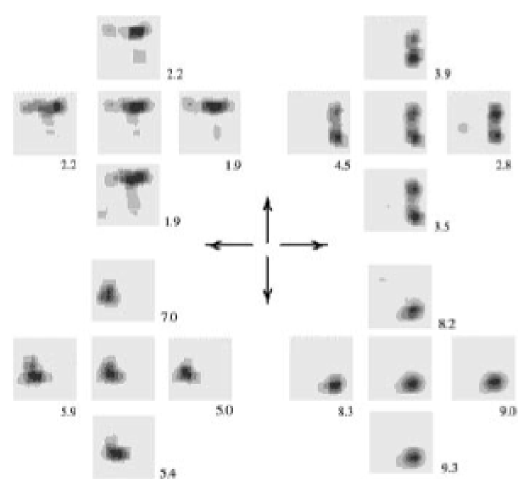
- **Experiment 3:**
  - The upper right hand box shows the environment the rat was present in
  - Recorded from tetrodes, place cells have been ordered with respect to the distance from the tetrode
  - **Results:**
    - **1.** Proves place fields will cover most of the sensory environment

i.e. it has elsewhere been shown that it only requires 130 neurons to encode spatial position over the entire environment present in at 1cm/sec resolution



- *It is still being investigated why we then have so many millions of neurons encoding this*
- **2.** There is no topography organization
  - i.e. recordings from neighbouring cells are just as likely to encode 2 areas that are close to eachother as 2 that are far
- ***From examining representations of place cells, one should be able to determine the animals location in space***
- **Take-Home Point:** there is no topographic map placed on the hippocampus

- **Experiment 4:**



  - To make sure that the hippocampus is actually encoding spatial location, it is important to prove that **selectivity should not depend on the direction the rat is moving**
  - To the right: shows results from four different place cells
    - The center of each module combines the output of each direction the rat is moving where the four outer squares are recording spatial location while the rat is moving in each of the four main directions
    - No difference in placefields in one direction of mouse movement vs other directions
  - **Results and Take-Home Point:** there is **no** directional selectivity

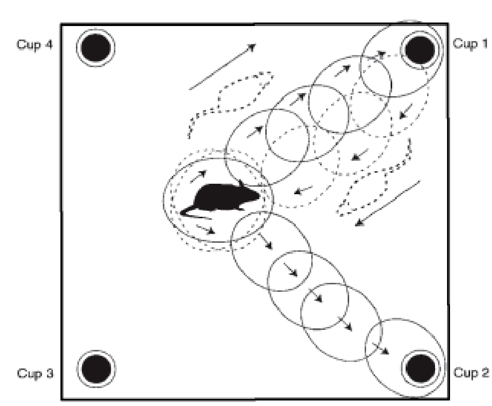
- **Experiment 5:**
  - For place fields to be used for learning and memory, they must stay constant over time
  - Using the previous experimental set-up [tetrodes, environment markers, etc] allows for recording from the same neurons over extended period of time
  - The rats firing rate was recorded over four sessions, each with a specific number of days between sessions
    - ***Note: the recording of the same neuron was ensured***
  - **Results:** firing pattern is similar in structure throughout the sessions
    - Stability is essential for memory and therefore, by the cells remembering features and location within an environment, stability is ensured

- o **Take-Home Message:** place fields are stable over time
  - *However, if the subject is removed from the environment for a long enough period of time, place fields can be re-mapped: discussed in following lectures*

TAKE HOME MESSAGES:
- Today we talked about **implicit memory**
- The hippocampus is divided into **right** and **left hemispheres**, each which coordinate different properties
  - o The left, posterior lobe of the hippocampus is likely involved in **spatial memory and learning**
- The hippocampus lobe remains a **constant volume** of grey matter, but specific sections may become dominant based on the needs of occupation
  - o Size of the divisions of the hippocampus are **proportional to experience and time** is has been used, while maintain constant volume
- Flow of neural information follows the following pathway:
  - o ***Dendate gyrus → CA3 → CA1 → enterohinal cortex***
- Rats and humans are similar in their anatomical divisions
- **Tetrode** set-ups are useful in determining the action potentials of numerous neurons during a given time in a given space while the animal remains active and awake
- **Place Fields:**
  - o Encode for a specific location and firing is dependent on that location
  - o Contain no topographic map
  - o Cover all space
  - o Are directionally independent
  - o Are stable over time [if stimulus remains]

  - o ***However, place cells and spatial memory rely on both internal and external cues from the environment***
    - *This will be discussed in future lectures*

SUMMARY
- CA1 pyramidal cells used a **distributed representation** to encode a specific spatial position
  - o Need recordings of a population of neurons to infer location
    - i.e. recordings from a tetrode
- No topographic organization
  - o Cells recorded from the same tetrode are not necessarily near each other in real space
- **Omnidirectionality** ensures **coding** of place or location
  - o Cells do not depend on direction of movement for encoding
    - *Other cells in caudate nucleus code for direction and velocity*
  - o Required for memory retention
- **Stability** of place fields is **critical** for memory retention
  - o Place fields are stable over time
  - o Once formed, remain the same for the duration one is exposed to the specific environment



Important Notes: for the experiments to be true, the environments require visual cues [i.e. red board, cup], the rat requires a set amount of time to become accustomed to his environment and develop place cell coding, and regardless of the connections made, if the rat is removed from the environment for an extended period of time, place fields ca be re-written

Sensory Control over Place Fields in the Hippocampus

Summary from last lecture:

- London taxi drivers: Overall volume of hippocampus remained the same, but posterior hippocampus grew at expense of anterior area because of the increased need for spatial navigation.
- Model System (rodents): Recording of CA1 pyramidal cells, firing of neurons correlated to rat's spatial position.
- Pyramidal cells are spatially selective, encode the location of animal in the environment.
- Place fields are direction insensitive and cover all of space.
- Using a tetrode, one records only a few pyramidal cells located close together. However, one can record most of the environment the animal is in, so no topographic organization exists.

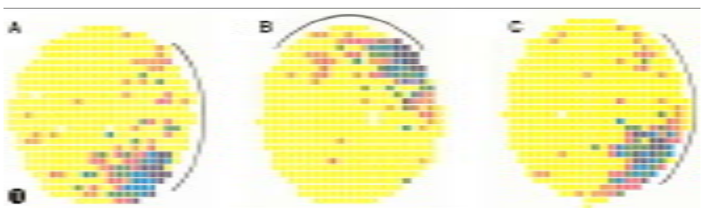
<u>A Cognitive Map</u>: created by both the external landmarks in the environment and the internal compass of an animal.
In different situations, either the external landmarks or the internal compass will be dominant for navigation.

Experiment:
Rat is placed in an enclosed environment (closed box with a cue card used for reference).
Rat has been pre-trained for months to adapt and forage in this particular environment for food.

Note: These manipulations can be done either with or without the animal's knowledge, this of course changing the effect on place fields

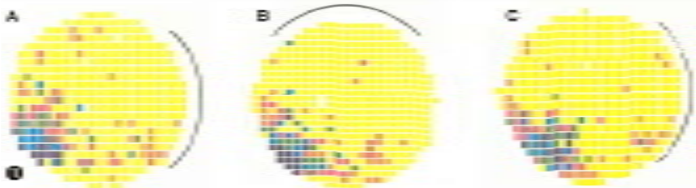
<u>Manipulation #1A:</u>
- Rotation of cue card without the animal's knowledge. (Rat rotated on motor and blinded at a sub-vestibular velocity).
- Animal trained that cue card is located on left hand side, the card is moved by 90 degrees counter clockwise.
- Place Field moved in relation to cue card moving, so external cues dominate in this instance.
- rotation of place fields occur when landmark positions are rotated without the animal's knowledge

Standard Rotation 90° CCW Standard



<u>Manipulation #1B:</u>
- In this case the rat is aware of the cue card being moved, so the place fields do not change position in relation to the movement of the cue card. Domination of internal compass in this case, since the external cue is deemed unreliable (as it is moving) for navigation by the rat.
- remapping of place fields does nto occur when landmark's positions are rotated in the animal's presence

Standard Rotation 90° CCW Standard



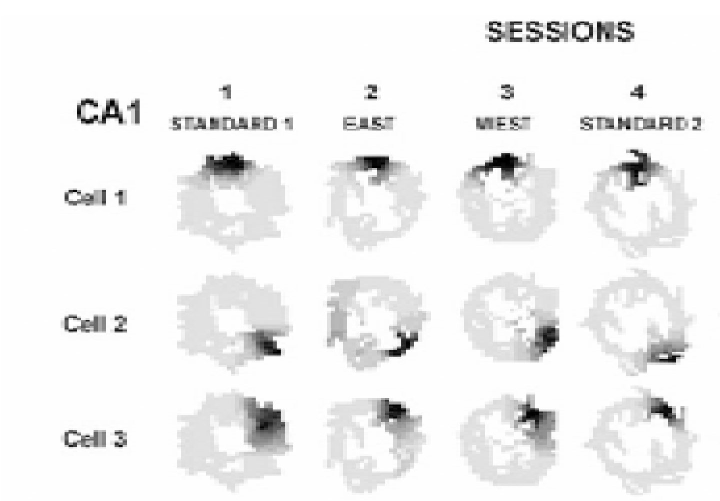
Note: For the remaining manipulations, all were performed without the animal's knowledge.

<u>Manipulation #2: Translations</u>

- animal placed in circular enclosure and retangular enclosure that sit in a larger room
- Several external cues available to the animal for navigation
    - the stability of place firelds allow it to rely on these external cues

Does the distance of these external cues matter?

- You can change various external cues to be closer or farther from the animal, by changing placement of enclosure, to see effect on place fields.
- As the enclosure was moved either East (to the right) or West (to the left), the place fields recorded for three different CA1 cells did not change positions.
    - → Remapping of place fields does not occur when landmark positions are translated.
    - → Place fields are affected by angular positions of external cues, in relation to the enclosure, and not their distances.
- Place fields are sensitive to external cues placement when these do not contradict the animal's self motion cues. (when stationary, animal considers a moving cue to be unreliable.)
    - In cases where the animal is aware of the motion of external cues, its own internal compass will simply take over and the animal will disregard the cues completely.



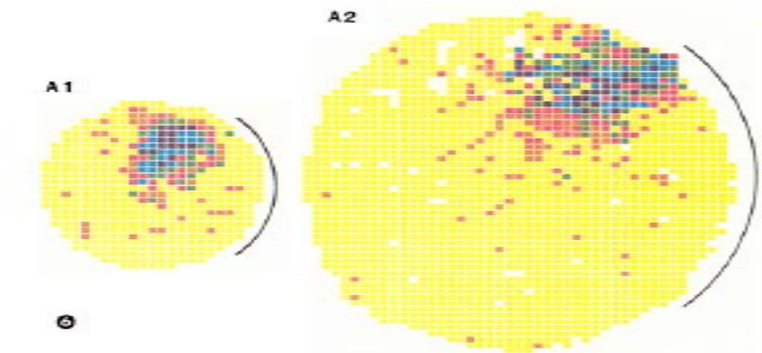
<u>Manipulation #3: Are place fields sensitive to particular shape of external cues?</u>

- Change of width of the cue card.
- Place fields are relatively unaffected, simply the position matters.
    - place fields are largely insensitive to landmark shape

<u>Manipulation #4: Are place fields sensitive to isotropic scaling of environment?</u>

- Isotropic scaling of the environment, by increasing the size of the environment quadruply.

- place fields are largely insensitive to isotropic scaling of the environment
- Location of place fields not affected, however they expand proportionally to the size of the environment.



CONCLUSIONS: place cues are insensitive to both cue shape and isotropic scaling of the environment

Manipulation #5: Are place fields sensitive to novelties in the environment?

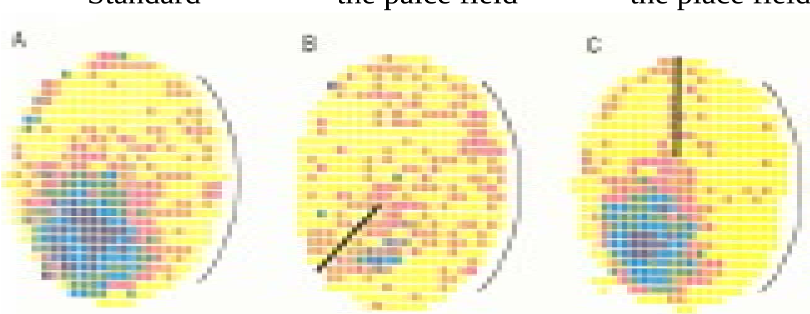
- Removal of cue card from the enclosure.
- The rat becomes very confused (as does not have externa landmark, random remapping occurs in this case. Place fields move to seemingly random locations within the environment. As well place fields may cease to exist, new ones may be created, and some may expand to cover more space.
- when the cue is put back to its original positons, the place field will return to original location → has memory

CONCLUSION: removal of external cues leads to random remapping of place fields

Manipulation #6:

- Placement of a novel object into the enclosure
- The location of the object matters. The place field mapping the location where the object happens to exist will remap. Once the novel object is removed, the place field will return to its original position.
- On the other hand, for place fields not affected by the location of the novel object, one will not see remapping of these.
- So, confusing situations in the environment will cause remapping of place fields, but only if the animal is unaware of the manipulation.

Standard | Novel object inside the palce field | Novel object outside the place field



CONCLUSION: novel objects inside place field leads to remapping

Note: If there are multiple cues present in the enclosure, even if one is removed, remapping of place fields will not occur because there will still be other cues present that can be used for navigation.

Plasticity of Spatial Representations:

How much does animal rely on proximal cues versus distal cues?
Double Rotation Experiments can be performed where one rotates local cues with respect to distal cue and vice versa to see the effect on place fields.
- rat was trained to walk around a circular enclosure with close/local cues on the floor and distal cues on an adjacent wall (both cues help in navigation)

Ex: if local cues are rotated 45 degrees counter clockwise and distal cues 45 degrees clockwise, a 90 degree misalignment occurs in total.
-Confusing situation for the animal, the result is more complex than before.
- Some place fields will rotate along with the local cues and some follow the distal cues.
- Still other place fields remapped, and moved in an unpredictable way.

CONCLUSION: remapping of place fields is dependent on the sensitivity of place fields (some sensitive to both distal and local cues, some one or the other)

Experience Dependent Changes in Place Fields:
In all of the previous experiments, rat was trained to forage in its environment.
- In this case, a rat is trained to run in a stereotyped route, on a linear track.

What happens to place fields?
- If rat is continuously made to run from point A to point B, it is noted that the place fields shift more to the left (towards the starting point), becoming asymmetrical.
    - place fields shift in terms of size and positon

This is called expectation, a change in the plasticity of synaptic connections. The strength of connections between neurons and place fields may have changed and this is what caused the shift in location.

Summary of lecture:

Hippocampal place cells form a distributed representation of sensory space in rats, meaning you have to look at the entire population to determine the animal’s spatial position.
Also, these place cells are environment and experience dependent, so can be influenced by external changes to do with cues or by types of experience such as expectation.

External cues dominate place field remapping, unless they are deemed by the rat to be unreliable and then the internal compass is used.

Primates:
- Experiment: monkeys put in cage, could freely move with implanted electrodes in brain; food placed in various spots in cage
- Results from experiments done with Squirrel Monkeys show that hippocampal place cells also exist in non-human primates as the firing observed was sensitive to the enclosure