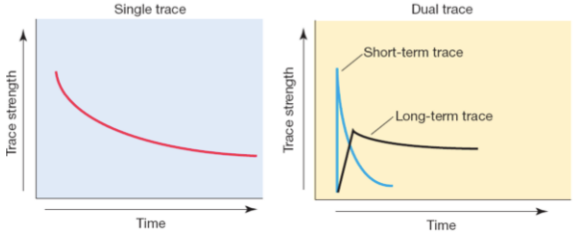
1) What is Memory?

- Memory: draw upon **past experiences** to use in the present
- Memory requires a **structural** or **functional change in the brain**
- Current interests in memory:
    - **Scientific**: cognitive science & neuroscience
    - **Public**: herbal supplements & nootropics (drugs)

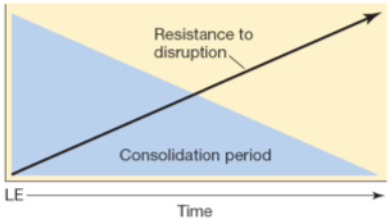
Early Scientific Study

- Ebbinghaus' forgetting curve**: forgetting follows an exponential function; the rate of forgetting occurs rapidly to start with, but slows down over time**
- **Single-Trace Theory**: explains the forgetting curve by assuming that the strength of a single memory declines as a function of time between learning & the retention test
- **Dual-Trace Theory**: explains the forgetting curve results from two memory traces (ST & LT) whose strength decays at different rates



Memory Consolidation

- Memory Consolidation: **following a learning experience (LE), a memory trace is vulnerable to disruption. With the passage of time, resistance to memory disruption increases & the trace becomes more stable due to functional & structural changes in the brain.**
- Consolidation Processes: **processes that stabilise the memory trace**
- Consolidation Period: **time it takes to stabilise the memory trace**



- Ribot's Law: **older memories are more resistant to disruption by traumatic events than newer memories** (first to propose memory consolidation)

Temporal Gradient of Retrograde Amnesia

<u>Active avoidance procedure (Duncan):</u>

- 1) Rats trained on active avoidance procedure (2-compartment chamber: left side = shock; right side = nothing)
- 2) After so many trials, rats showed active avoidance of LEFT SIDE (run out of left side when being put in there)
- 3) Control or ECS (after being taken from the RIGHT SIDE):
    - **ECS**: Rats given electroconvulsive shocks at different intervals after training
    - **Control**: nothing
- 4) 24 hours later: rats put back into left side of chamber

    - Measured active avoidance: how quickly rats run away
        - **Control = Late ECS** (run quickly) **< Immediate ECS** (stay in left side)
- Duncan believed this retrograde amnesia was due to a disruption of memory consolidation (disruption of the reverberatory circuit that underlies memory)
- BUT – alternative explanation:
- Rats who received ECS immediately after training (after being taken from right side):
    - Associate Lside → little shock
    - Associate Rside → ECS (big shock)
- Prefer to be on the left side, show avoidance of right side

<u>Passive avoidance procedure (Campbell):</u>

- 1) Rats trained on passive avoidance procedure (2-compartment chamber: dark side = shock; bright side = nothing)
- 2) After so many trials, rats showed passive avoidance of dark side (stay in bright side when being put in there)
- 3) Groups after training (take from the DARK SIDE):
    - **Retention-control**: nothing
    - **Immersion-control**: immediately placed in water (tests stress of water)
    - **Hyperthermia**: placed in ice cold water at different intervals
        - **Immediately, 5 minutes later, 15 minutes later, 1 hour later**
- 4) 24 hours later: rats put back in 2-compartment chamber
    - Measured passive avoidance: how long rats stayed in bright side
        - **Retention-control** = high passive avoidance of dark side
        - **Immersion-control** = high passive avoidance of dark side
        - **Hyperthermia**:
            - **Immediately:** no passive avoidance of dark side (amnesia)
            - **5 minutes later:** low avoidance of dark side
            - **15 minutes later:** slightly higher avoidance of dark side
            - **1 hour later:** high passive avoidance of dark side
- **Conclusion: retrograde amnesia is induced by disrupted memory consolidation from a stressful event (not merely an association)**
    - In this case, the association was dark side → hypothermia, but the immediate group that should have had the strongest association btw dark side → hypothermia showed no avoidance of the dark side (retrograde amnesia)
- **We can induce retrograde amnesia through stressful events immediately after a learning experience, but not after time passes (evidence of memory consolidation)**
    - There is a temporal gradient for both retrograde memory enhancement & retrograde amnesia: most effective immediately after the learning event (LE)

2) Hormonal Modulation of Memory

- **Endogenous hormone levels signal whether an event was important or not to remember, can either enhance or disrupt memory encoding**
- Adrenal gland: produces hormones during **stress**
    - Medulla → **epinephrine** & **norepinephrine**
    - Cortex → **glucocorticoids** (e.g. cortisol); **mineralocorticoids** (e.g. aldosterone); **sex steroids** (e.g. testosterone)

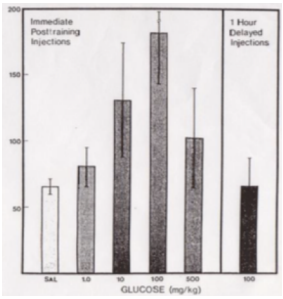
TEMPORAL GRADIENT OF EPINEPHRINE

- 1) Rats trained on lick-suppression procedure (rat is thirsty with no water, rat put near sipper-tube, rat shocked while sipping)
- 2) Over trials, rat shows passive avoidance of sipper tube (latency to drink)
- 3) Injected with saline (control) vs. epinephrine:
    - **Immediately**
    - **10 min**
    - **2hr**
- 4) 24 hours later – rats put back in cage, test latency to drink
    - Immediate: longest to drink (then 10min, then 2 hr, then saline)
- **Conclusion: temporal gradient effect for retrograde memory enhancement by epinephrine (immediate epinephrine = stronger memory)**

Mechanisms of Action for Epinephrine Modulation of Memory

TEMPORAL GRADIENT/INVERTED U SHAPE EFFECT OF GLUCOSE

- 1) Rats trained on lick-suppression procedure (rat is thirsty with no water, rat put near sipper-tube, rat shocked while sipping)
- 2) After experiencing shock, rat will show passive avoidance (longer to sip from tube)
- 3) After training → glucose injections:
    - **Immediate injections:**
        - Saline control group
        - Glucose (1mg, 10mg, 100mg, 500mg)
    - **1-hour delayed injections:**
        - Glucose (100mg)
- 4) 24 hours later: rats put back into cage with sipper tube (measure latency to lick):
    - Saline control group: lowest avoidance (quick to lick)
    - **Immediate glucose groups:**
        - **Inverted U-shape function:**
            - 1mg: low avoidance (= control)
            - 10mg: high avoidance
            - 100mg: highest avoidance (slowest to lick)
            - 500mg: lower avoidance
    - Delayed glucose groups: lowest avoidance (quick to lick)



Effects of Epinephrine

- Increases **glucose release** → enhances memory through this mechanism
- But there is a temporal gradient effect → **glucose only enhances memory immediately after the LE** (due to memory consolidation)

Effects of Glucose on Memory in Humans

Manning et al. (1998) experiment on elderly humans:

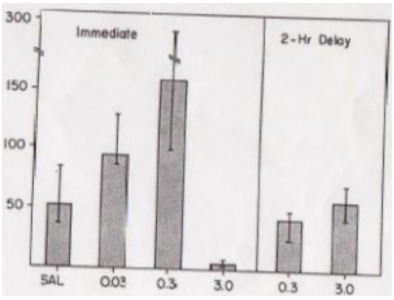
- 1) Ps drink orange juice containing sugar (glucose), or saccharine (no glucose)
- 2) Ps read a story on 2 occasions, 1 week apart
- 3) Prior to reading on one occasion, Ps drank a glucose-infused drink while on the other occasion, Ps drank a saccharin-infused drink
- 4) 1-week later test for memory of each story

- Glucose group > saccharine group (blood glucose levels after drinking glucose)
- Glucose group > saccharine group (items remembered from story)

Effects of ACTH

- **ACTH: produced by pituitary gland & primary effect on the adrenal gland**
- **Increase ACTH → increase cortisol & epinephrine**

TEMPORAL GRADIENT/INVERTED U SHAPE EFFECT OF ACTH



1) Train rats on lick-suppression procedure

- 2) Injection groups:
  - Injected w/ **saline immediately** after training
  - Injected w/ **ACTH immediately** after training
    - **Small dose**
    - **Medium dose**
    - **Large dose**
  - Injected with **ACTH** after **2-hour delay**
- 3) 24 hours later: rats put back into cage with sipper tube (measure latency to lick)
  - **Inverted U-shape function:**
    - Saline: 50sec to lick
    - Small ACTH: 100sec to lick (strong memory)
    - Medium ACTH: 150sec to lick (strongest memory)
    - Large ACTH: 10sec to lick (weakest memory → retrograde amnesia)
      - **Large ACTH disrupted memory**
  - Delayed ACTH: 50sec to lick (no effect)
- **Conclusions**:
  - **Hormones** can be **enhancers** or **disrupters** of **memory**
  - **Effects of post-training exogenous ACTH vary as function of dose and training shock intensity**

Reading: Memory – a Century of Consolidation

- Evidence suggests memory consolidation serves an adaptive function by enabling endogenous processes activated by an experience to modulate memory strength: **emotionally arousing experiences are generally well remembered**
  - Adrenal stress hormones, epinephrine & cortisol, released by emotional arousal, play a key role in strengthening the memory of an experience

3) Stress & Memory in Humans/Effects of Chronic Stress

Effect of Stress & Arousal on Human Memory

Cahill & McGaugh (1996) – PET Scan Experiment:

- 1) Adults saw emotionally-arousing clips (E) or emotionally-neutral clips (N)
- 2) Took a PET scan to measure brain activity while watching clips
- 3) Free recall test 3 weeks later
- Results:
  - **Ratings of film emotionality = E>N**
  - **Number of films recalled = E>N**
  - **E group: +ve correlation right amygdala glucose lvls & no. of films recalled**
    - I.e. more right amygdala glucose = more films remembered