Trauma and the Brain

Trauma in Animals Conference

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SmartDog Training & Behavior

tug-e-nuff Dog Gear

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What is trauma?

- Typically defined as experiencing or witnessing events that are extremely distressing (e.g. sexual assault, abuse/neglect, war, car accident, etc.)
  - Perception is key
  - Not all individuals impacted to same degree – many recover
  - McMillan (2020) – uses term "*potentially* traumatic event" -> individual responses vary
- Trauma can be acute or chronic
- Chronic stress
  - Closely related, trauma often chronic
  - Can experience chronic stress that isn't trauma – still damaging

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Impacts of trauma

Paredes and Morilak, 2019

- Not all trauma = PTSD
  - Range of impact varies
    - Some - no or very mild long-term impact
    - Other mental health disorders related to trauma
    - PTSD is most severe

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Stress

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Stress

- Three components
  1. Triggering event
  2. Disruption or challenge to the status quo
  3. Physiological reaction which includes an increase in stress hormones

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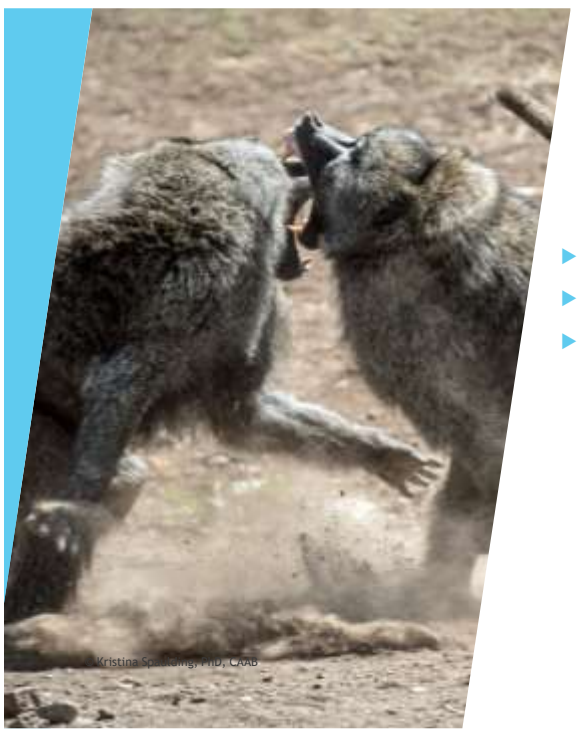

What is the function of stress?

- Adaptive
- Helps the animal survive in the moment
- Preparation for a dangerous environment (developmental stress)

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Physiological response

- Activation of:
  - Sympathetic nervous system
    - Fast (within seconds)
    - Release of epinephrine and norepinephrine
  - Hypothalamic-pituitary-adrenal (HPA) axis
    - Slower (*usually* within 15-30 minutes) (Dickerson and Kemeny, 2004)
    - Release of glucocorticoids
- Combine to produce stress response
  - "Fight or flight"

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The Stress Response

- Immediate energy to critical systems:
  - ↑ Heart rate, blood pressure, respiration
  - ↑ energy in form of glucose
  - ↑ sensory function and memory
  - ↓ pain perception

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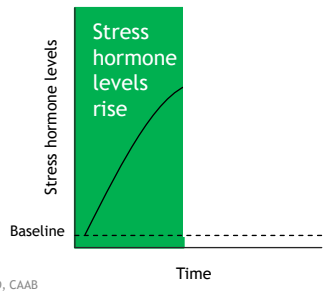
The Stress Response

- Shuts down systems that aren't needed for fight/flight
  - Reproduction
  - Immune system
  - Growth
  - Digestion

In healthy animals…

- Negative feedback brings stress hormone levels back down (to "baseline")



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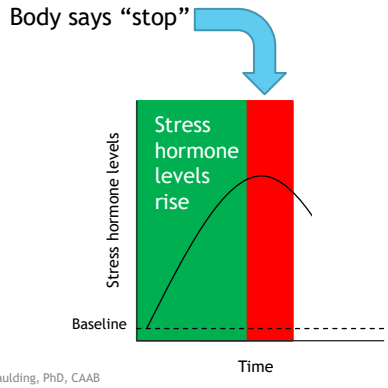

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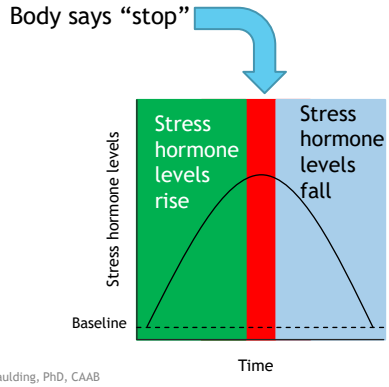
In healthy animals…

- Negative feedback brings stress hormone levels back down (to "baseline")
- Prevents negative effects of stress hormones



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When things go wrong

- Chronic stress and developmental stress
  - Negative feedback loop malfunctions
  - Stress system becomes dysregulated
  - Brain becomes less flexible
  - Decreased ability to cope

Impacts of chronic stress

- Partial list
  - Decreased growth
  - Decreased immune function
  - Reproductive issues
  - Slower healing
  - Gastrointestinal problems
  - Increased fear and anxiety
  - Impaired learning
  - Impaired social skills
  - Decreased wellbeing
  - Early death

Post-traumatic stress disorder (PTSD)

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PTSD criteria in humans (DSM 5)

- Exposure to trauma
- "Intrusion" – nightmares, flashback, physiological reactions to triggers (1+)
- Avoidance of trauma stimuli (1+)
- Cognitive/mood changes (2+)
- Changes in arousal/reactivity – e.g. aggression, hypervigilance, enhanced startle, attentional issues, sleep issues) (2+)
- > 1 month duration
- Impairs function
- Ruled out medical

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Do animals experience trauma and PTSD?

- Rodent models
  - Attempt to produce PTSD-like symptoms in order to "model" in humans
  - Most of symptoms seen in rodents
    - Not all in one model (Whitaker *et al.*, 2014; Deslauriers *et al.* 2018)
    - May not be quite the same in animals as in humans (or…just difficult to "manufacture" a specific mental health disorder)
  - Rodents show similar patterns of development and prevalence (Verbitsky et al. 2020; McMillan, 2020)

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Do animals experience trauma and PTSD?

- Other evidence – some symptoms consistent with PTSD
  - Wolf-exposed cattle (Cooke *et al.*, 2017)
  - Earthquake survivors (dogs) (Yamamoto, 2003)
  - Handful of other reports in a variety of species (see McMillan 2020 for review)

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Human vs. animal symptoms

Human symptom	Corresponding animal-model symptom
Intrusions	Fear extinction
Avoidance	Avoidance
Changes to cognition/mood	Spatial memory, valence, anhedonia
Aggression/arousal	Aggression/arousal

Fenster et al. 2018

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PTSD symptoms in nonhuman animals

- ✓ Exposure to trauma
- ✓ "Intrusion" – nightmares?, flashbacks?, physiological reactions to triggers
- ✓ Avoidance of trauma stimuli
- ✓ Cognitive/mood changes
- ✓ Changes in arousal/reactivity – e.g. aggression, hypervigilance, enhanced startle, attentional issues, sleep issues)
- ✓ > 1 month duration
- ✓ Impairs function
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Trauma and PTSD in nonhuman animals

- Do they experience it?
  - Trauma – all evidence points to yes
  - PTSD
    - More difficult to categorize – cannot access subjective experience
    - Different species -> different perception of world
    - Probably can't say PTSD in human sense
  - Separate symptoms and diagnosis
    - Can and do experience many of *symptoms*
    - Focus of rest of talk

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Trauma and the Brain

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Conrad, 2008; Lupien et al. 2009; Toffanin et al. 2011

Stress response system

- Extreme or chronic stress -> dysregulation of HPA axis
  - Impaired production of neurons
  - Loss of existing neurons
  - Decrease in dendritic branching (important for communication between neurons)
- Damage to hippocampus, prefrontal cortex
- Increased activity in amygdala

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Intrusive symptoms – strong physiological responses

- Emotional regulation/inhibition
  - Amygdala – experience of fear
    - Lesion amygdala -> no fear (LeDoux et al. 1984)
    - Trauma/chronic stress -> increased activity
    - "Hyper-conditioning" (Pittman, 1988)
  - Prefrontal cortex – inhibits amygdala (Milad and Quirk, 2016)
    - Trauma/chronic stress -> decreased prefrontal cortex activity -> increase amygdala activity
    - Impairment in "top down" regulation of memories -> leads to repeated re-experiencing

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Extinction

- What is extinction?
- Decoupling of stimuli and fear
  - Example:
    - Learned that tone predicts shock
      - Tone -> fear
    - Present tone repeatedly without shock
      - Tone ≠ fear

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Intrusive symptoms – failure of fear extinction

- PTSD patients have difficulty maintaining extinction memories
  - Can still acquire them – but they don't last
  - Extinction does *not* erase existing memories – inhibits them
  - Decreased PFC activity -> impaired inhibition
  - Trauma/chronic stress -> decreased hippocampus activity -> lose input regarding context
    - Overgeneralization
    - Cannot distinguish what is safe

Bonne *et al.*, 2004; Sherin and Nemeroff; 2011 Milad and Quirk, 2016; Fenster, 2018: McMillan, 2020

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Avoidance

- Avoidance prevents extinction because never experience stimuli
- In humans:
  - More avoidance when
    - High hippocampal reactivity to context
    - High hippocampal reactivity to fear-related stimuli
    - High amygdala and hippocampus activity during extinction
  - Avoidance is closely related to fear

Sripada *et al.* 2013; Fenster *et al.* 2018

Passive vs. active avoidance

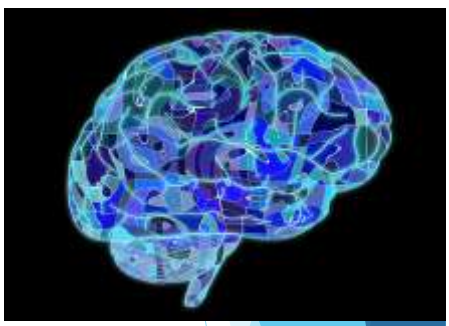
- Two types of avoidance
  - Passive – e.g. freezing
  - Active – e.g. flight – run from one side of cage to another to avoid shock
- Both are problematic if overused
- Passive response appears to be worse
  - Poorer stress coping/greater physiological response to stress (Ollef et al. 2005, Wood *et al.* 2015)
  - Associated with stress-related mental health disorders (Paredes and Morilak, 2019)

Passive vs. active avoidance

- Passive
  - Midbrain -> amygdala -> freezing, fear
  - Add control -> inhibits midbrain -> inhibits amygdala -> decreased freezing/fear
- Active/passive responses appear to inhibit each other
- New hypothesis: amygdala "gates" decisions about approach/avoidance
  - Current model may be too simplistic
  - Not just about fear -> may inhibit behavioral engagement
    - Allows for decision-making in relation to potential threats

Maier and Seligman, 2016; Paré and Quirk, 2017; Fenster, 2018

Impaired cognition

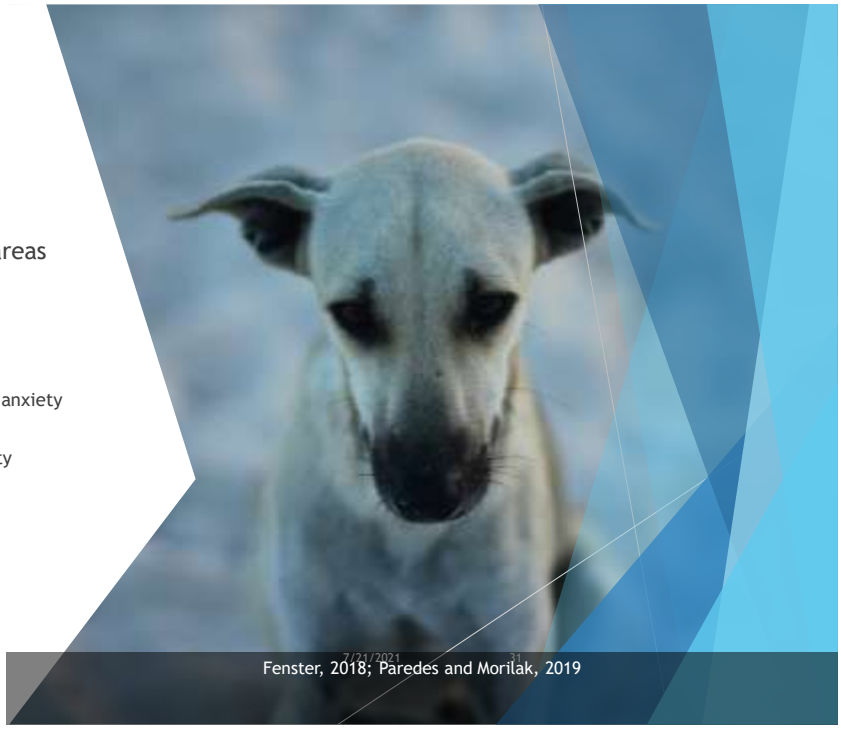


- Some aspects not well understood
- Memory issues
  - Primarily in declarative memories – facts, episodic memory
    - Unclear how this manifests in nonhuman animals
  - Nonhuman animals show:
    - Decreased attention
    - Impaired short-term memory
    - Decreased behavioral and mental flexibility
  - Related to changes to hippocampus, frontal cortex

Shansky et al., 2006; Fenster, 2018

Persistent negative mood

- Again, involves several brain areas
- Again, issues with emotional dysregulation
  - Decreased activity in PFC:
    - Decreased inhibition of fear/anxiety through amygdala
    - Decreased cognitive flexibility
    - Decreased impulse control



Fenster, 2018; Paredes and Morilak, 2019

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Fenster, 2018

Neurons and mood

- Very little is known about this
- *Groups* of neurons in many brain areas seem to respond to *both* pleasant and unpleasant cues
  - Individual neurons??
    - Tried to switch neurons from one valence to the other (Redondo *et al*. 2015)
      - Worked in hippocampus - context
      - Not in amygdala

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Neurons and mood

- Role of emotional state
  - Reynolds and Berridge (2008)
    - Activated neurons in nucleus accumbens in two contexts
      - Stressful environment (unfamiliar, bright lights and Iggy Pop)
      - Home environment (familiar, dark, quiet)
    - Effect of activation varied
      - Stressful environment – 90% of neurons -> fear
      - Home environment – 90% of neurons -> appetitive (eating) behavior
    - The results "suggest that a stressful context can influence the range of…behaviours available to an organism. A similar mechanism may help to explain how trauma can alter the range of [emotional] experience available to individuals with PTSD" – Fenster, 2018
  - **One study - still under investigation!

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Reward processing

- Also appears to be impacted by PTSD
  - Decreased interest in pleasurable activities
  - Unable to feel positive emotions
  - Less responsive to reward
- Two components – both may be impaired
  - Seeking – approach/dopamine
    - May be changes to dopamine neurons
  - Consumption – hedonic pleasure/opioids
- Many brain areas involved including:
  - Ventral tegmental area, amygdala, parts of prefrontal cortex

Fenster et al. 2018

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Arousal and reactivity

- In terms of PTSD, includes:
  - Increased vigilance
  - Increased startle
  - Irritability/aggression
  - Risk-taking
  - Decreased concentration
  - Sleep issues
  - Emotional dysregulation

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What might this look like?

- Picture reactive/highly anxious dog
  - Scanning
  - Strong reaction to multiple, low-level stimuli
  - Redirection
  - Difficulty calming down
  - Difficulty focusing

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What might this look like?

- Picture reactive/highly anxious dog
  - Scanning - Increased vigilance
  - Strong reaction to multiple, low-level stimuli - Increased startle
  - Redirection/aggression - irritability/aggression
  - Difficulty calming down - emotional dysregulation
  - Difficulty focusing - decreased concentration
- Note: not ONLY caused by previous trauma – several other causes as well.

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Hypervigilance/hyperarousal

- Amygdala
  - Trauma/chronic stress -> increased activity
  - Involved in threat detection
  - Known as fear center, but not totally one-sided
    - May play role in turning fear on and off

Fenster et al. 2018

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Aggression/Impulsive behavior

- Failure of top-down control
- Prefrontal cortex
  - Regulates threat detection (Davidson et al. 2000, Dileo et al. 2008)
    - Potential threat
    - Evaluates context
    - Determines actual threat level
    - Selects appropriate response
  - Regulates emotion, including aggression (Siever, 2008)
    - Amygdala also plays an important role in regulation of emotion

Addressing trauma

Is there hope?

- Pharmacological treatments
  - We already have some (antidepressants/antianxiety meds)
  - More are coming
  - Probably in next couple decades
- Behavioral treatments
  - Impaired extinction
  - Avoidance
  - Mood/cognitive changes
  - Aggression/reactivity

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Impaired extinction and avoidance

- One reason for impaired extinction is extreme avoidance
- In humans: exposure therapy
  - Voluntary exposure to fear-producing stimuli
  - Under guidance of mental health professional
  - Patient is aware of process
  - Distressing
  - Can stop at any time

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Paredes and Morilak, 2019

Exposure therapy

- Increases activation of PFC
- Promotes plasticity in PFC, restores active coping
- Can dramatically reduce PTSD symptoms

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Exposure therapy in nonhuman animals?

- In humans: exposure therapy
  - Voluntary exposure to fear-producing stimuli
  - Under guidance of mental health professional
  - Patient is aware of process
  - Distressing
  - Can stop at any time
- In rodents: Usually modeled with fear extinction
  - Activates PFC
  - Restores cognitive flexibility

Paredes and Morilak, 2019

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Can we do more?

- Extinction is fragile – fear tends to return
- No control
- Counter conditioning => enhanced extinction

Exposure therapy in nonhuman animals?

- Touch the Goblin
  - Place item in open area
  - Reinforce for looking at -> moving toward -> touching item
  - No pressure (including verbal encouragement/luring)
    - Throw treat behind animal
  - Can opt out at any time – adds control
  - Inanimate objects only

Exposure therapy in nonhuman animals?

- In humans: exposure therapy
  - Voluntary exposure to fear-producing stimuli
  - Under guidance of ~~mental health professional~~ trained and credentials behavior consultant
  - Patient is aware of process
  - Distressing
  - Can stop at any time

Paredes and Morilak, 2019

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Mood/cognitive changes

- Dialectical behavior therapy -> "Accumulate positive experiences"
  - Enrichment
  - Exercise
  - Social support
- All also improve ability to cope with stress

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Arousal/reactivity

- Management/reduction of triggers
- Increased control (balanced with safety)
  - Increased animal's ability to cope with stress
  - Limbachia et al. 2021
    - Humans
    - Control over stressor (shock) => decreased activity of threat and anxiety-related brain areas

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All symptoms

- Medication
- The wide-ranging and dramatic changes to the brain justify pharmacological intervention – with a qualified veterinarian

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Summary

- Trauma and chronic stress have dramatic impacts on brain
  - Impact many different brain areas
    - Hippocampus
    - Prefrontal cortex
    - Amygdala
    - Others
  - Impact wide range of functions/behaviors
- Highlights importance of prevention
- Understanding can aid treatment
- Keep an eye on the research

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Thank you!

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