

Understanding and measuring pain in animals

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What is pain?

It is not a stimulus

It is a complex percept, a sensory experience, that is colored by emotion.

Pain is an unusual clinical
symptom: You can't see it

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PAIN[®]



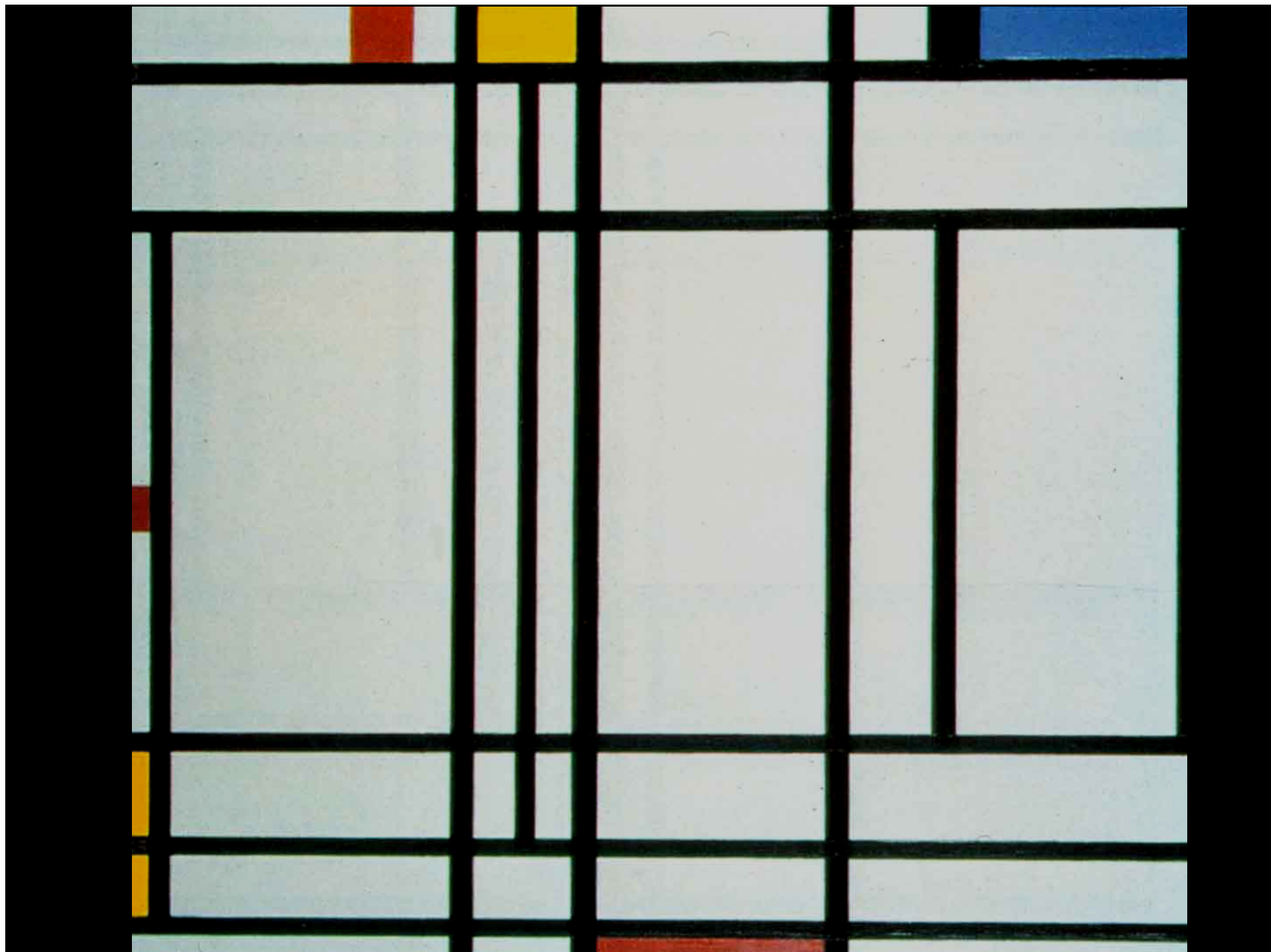
Journal of the IASP

Definition of pain by the International Association for the Study of Pain

"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"

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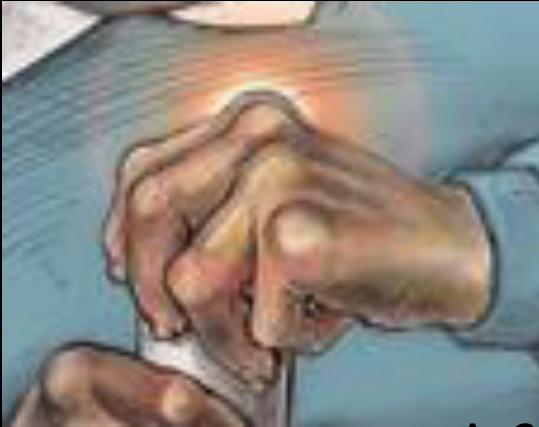


Dimensions of the pain percept

Sensory-Discriminative

Stimulus features:

Location, Modality, Intensity

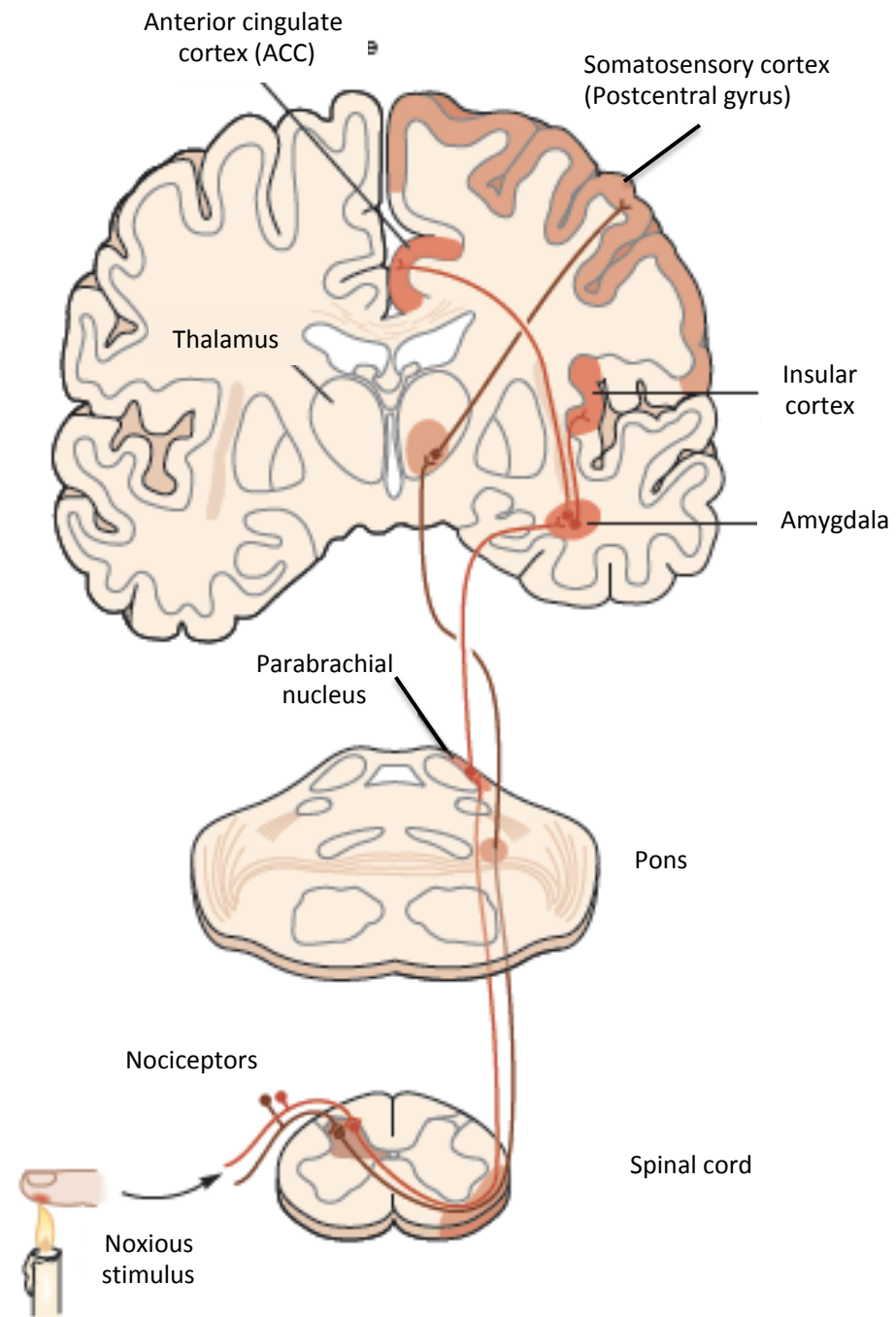


Affective-Motivational

How unpleasant or upsetting is the pain?

What will I do about the pain?





How can we measure pain?
Is there a pain biomarker?

What is a biomarker?

Fever: Temperature

Heart attack: EKG

Cancer: CAT scan/biopsy

Epilepsy: Seizures/EEG

For pain: There is, as yet, no biomarker.

But, humans can talk; so, we ask them.

For example.....

The McGill Pain Questionnaire

Group	Words
1	Flickering, Pulsing, Quivering, Throbbing, Beating, Pounding
2	Jumping, Flashing, Shooting
3	Pricking, Boring, Drilling, Stabbing
4	Sharp, Cutting, Lacerating
5	Pinching, Pressing, Gnawing, Cramping, Crushing
6	Tugging, Pulling, Wrenching
7	Hot, Burning, Scalding, Searing
8	Tingling, Itchy, Smarting, Stinging
9	Dull, Sore, Hurting, Aching, Heavy
10	Tender, Taut (tight), Rasping, Splitting
11	Tiring, Exhausting
12	Sickening, Suffocating
13	Fearful, Frightful, Terrifying
14	Punishing, Grueling, Cruel, Vicious, Killing
15	Wretched, Blinding
16	Annoying, Troublesome, Miserable, Intense, Unbearable
17	Spreading, Radiating, Penetrating, Piercing
18	Tight, Numb, Squeezing, Drawing, Tearing
19	Cool, Cold, Freezing
20	Nagging, Nauseating, Agonizing, Dreadful, Torturing

But, animals cannot talk. So how can we assess whether it is experiencing pain?

Reflex response to a mechanical stimulus



Problem: The presence of a reflex withdrawal is not indicative of pain

How then can the animal communicate
to you about its pain experience?

One approach: **Place preference**

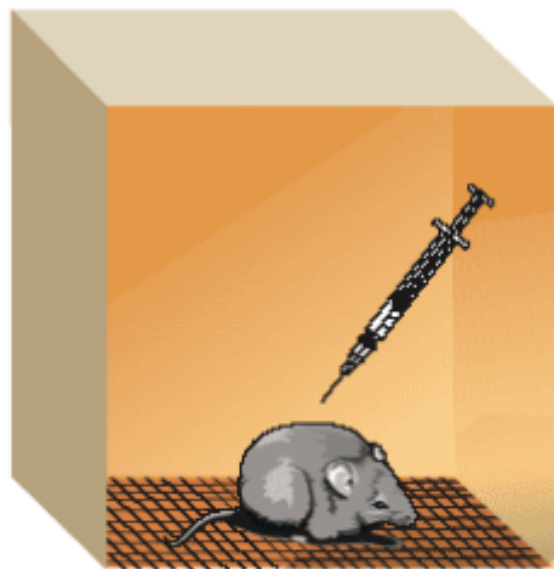
Conditioned Place Preference

TRAINING CHAMBER

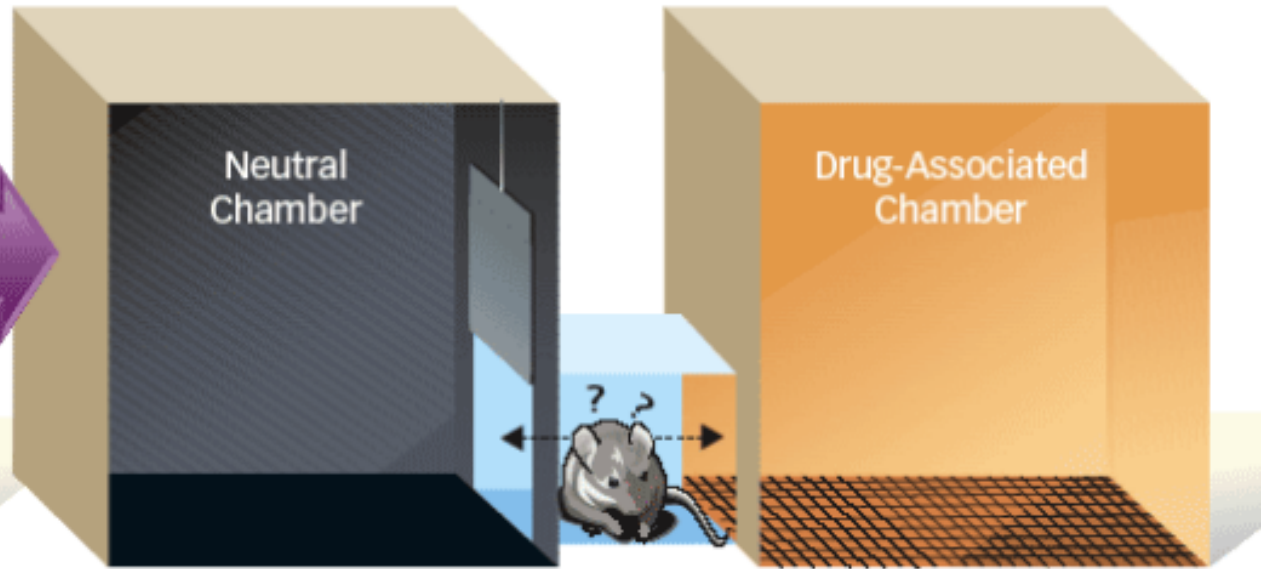


Conditioned Place Preference

TRAINING CHAMBER



TESTING CHAMBERS



So, can we determine whether a brain organoid can experience pain?

No.

However, might a brain organoid
manifest neural activity
patterns indicative of pain?

A possible approach to
answering the question...

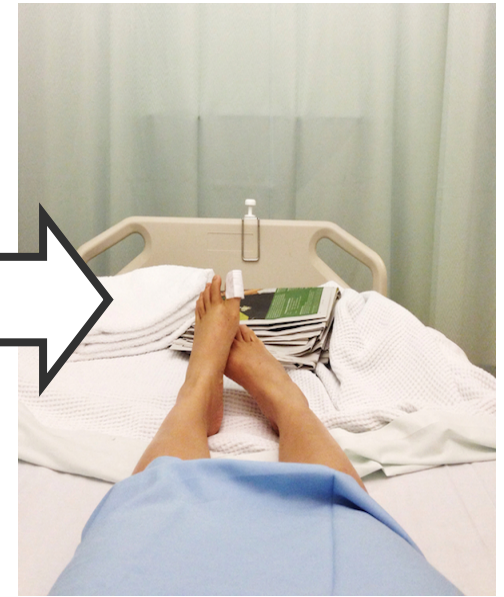
Question: Is there a **subpopulation** of cortical neurons that mediates pain?

Probing general general anesthetic mechanisms to answer the question

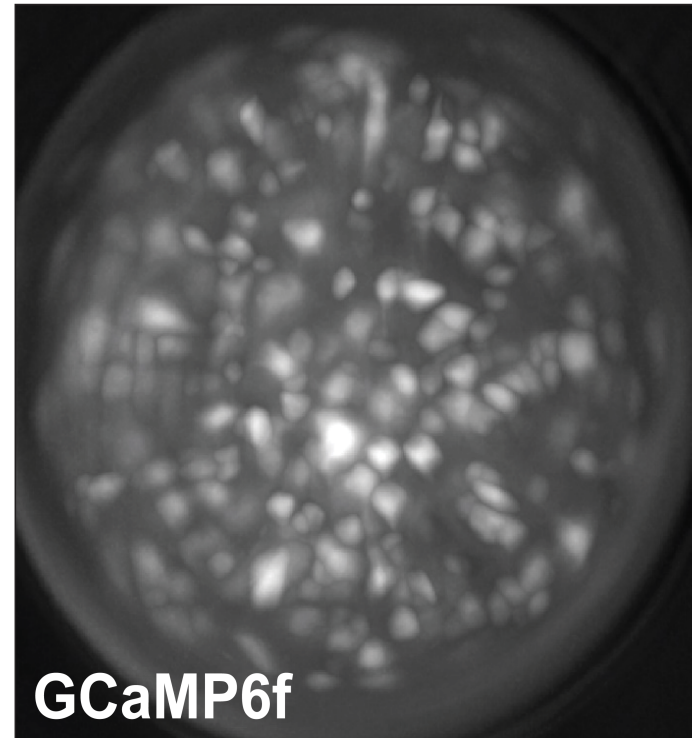
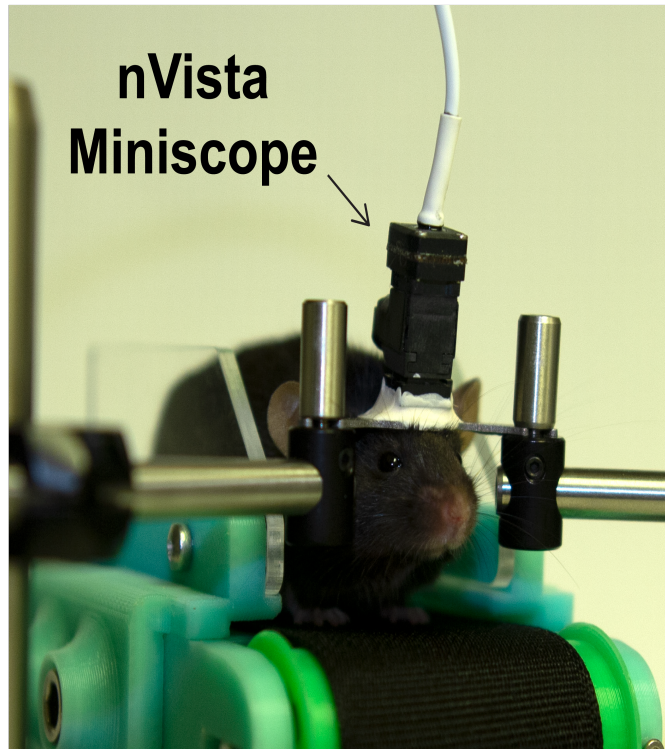
Stages of general anesthesia

Stages of anesthesia

STAGE I	PLANE 1. PRE-ANALGESIA - PRE-AMNESIA
STAGE I	PLANE 2. PARTIAL ANALGESIA - TOTAL AMNESIA
STAGE I	PLANE 3. TOTAL ANALGESIA - TOTAL AMNESIA — LOSS OF CONSCIOUSNESS —
STAGE II	DELIRIUM (ONLY SEEN UPON INDUCTION)
STAGE III	SURGICAL ANESTHESIA
STAGE IV	RESPIRATORY PARALYSIS



Monitoring neural circuit activity in awake and anesthetized mice



This slide will show a video of cortical recordings during isoflurane anesthesia, showing lots of activity followed by concentration dependent suppression of activity and recovery.

So, might a brain organoid
manifest neural activity
patterns indicative of pain?

Perhaps, but not
at this time.

A lingering question about
the molecular make-up of the
brain organoid...the NMDA receptor