Understanding “Fear” in Brain

Emotion Circuits in the Brain (LeDoux, 2000)

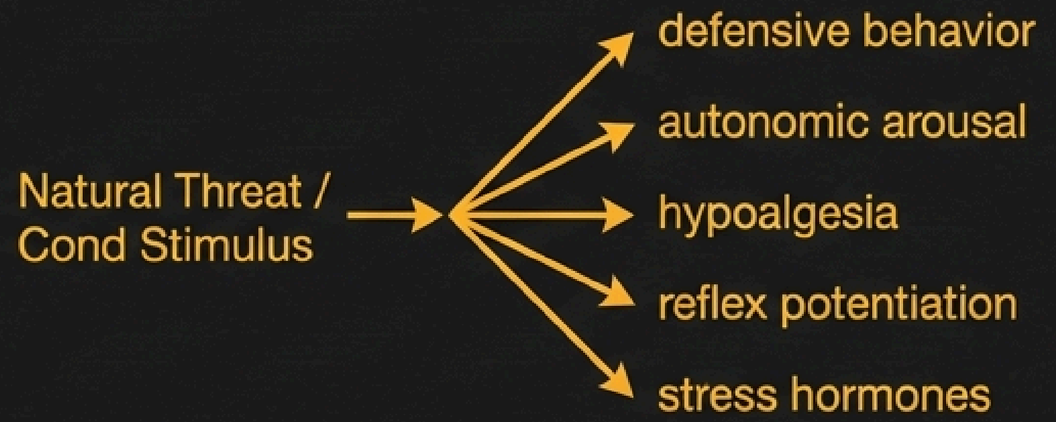
The Conflict: For decades, neuroscience neglected emotion, viewing it as a victim of the “cognitive revolution.” Researchers avoided the topic due to the “dark cloud of subjectivity” surrounding concepts like affect and feelings.

The Pivot: Joseph E. LeDoux (2000) argued that conscious feelings are not required to produce emotional responses.

The Strategy: To make emotion scientifically tractable, research must focus on the neural systems that detect and respond to danger—operationalizing “fear” not as a feeling, but as a survival circuit.

The Methodology: Pavlovian Fear Conditioning

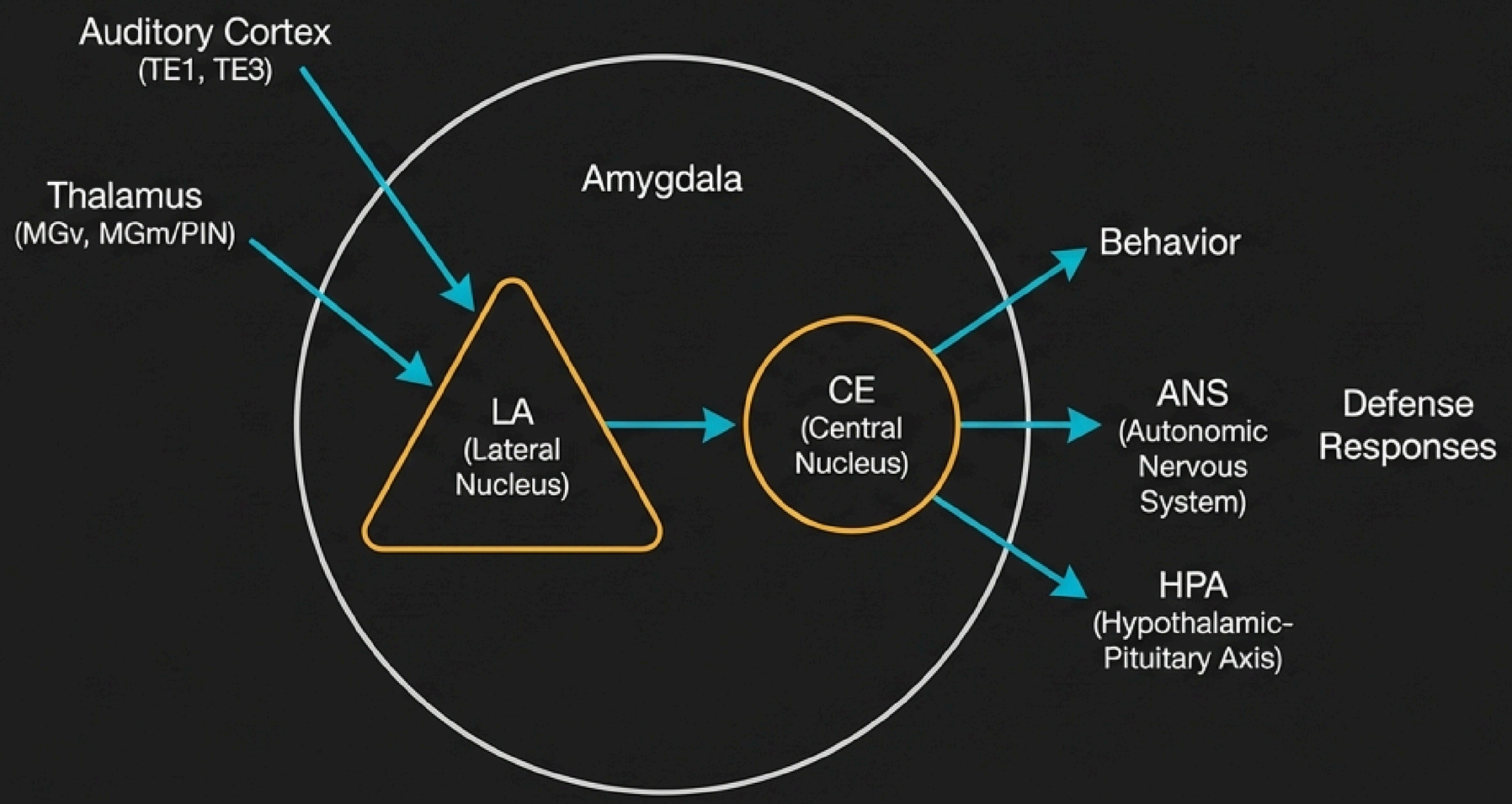
Operationalizing Fear as a Reflex



The Protocol: A neutral Conditioned Stimulus (CS) is paired with a biologically significant Unconditioned Stimulus (US). After temporal pairing, the CS acquires affective properties and elicits innate defense responses—freezing, autonomic arousal, and hormone release—without the need for the US. This mechanism is conserved across phyla, making it the ideal model for mapping circuitry.

The Circuit Revealed: Input and Output

The Amygdala as the Central Processor



- **Sensory Gateway (Input):** The Lateral Nucleus (LA) receives auditory inputs directly from the Thalamus (fast/crude) and the Cortex (slow/detailed).
- **The Controller (Output):** The Central Nucleus (CE) projects to the brainstem to trigger freezing and autonomic activation.
- **The Mechanism: Long-Term Potentiation (LTP) within the LA is the cellular basis of this learning.

The Gaps from the LeDoux Paper

Limits of the Anatomical Map

- **Feeling vs. Function Paradox:** Strictly separates non-conscious survival circuits from conscious "feelings," leaving the interaction between the two unexplained.
- **Neglect of Dimensional Affect:** Heavily focused on categorical "Fear" responses; lacks a framework for "gray areas" like high arousal/neutral valence stimuli.
- **Arousal Locus:** Over-emphasizes the Amygdala as the primary hub, under-representing the role of the Locus Coeruleus (LC-NE) system in driving general physiological arousal.
- **Temporal Resolution:** Describes the structural pathway (High vs. Low Road) but lacks the millisecond-by-millisecond dynamic data of real-time emotional processing.
- **Subjectivity Gap:** Early research avoided the "dark cloud of subjectivity," creating a disconnect between measurable biological reflexes and reported human experience.

Bridging the Gap: In Vivo Human Recording

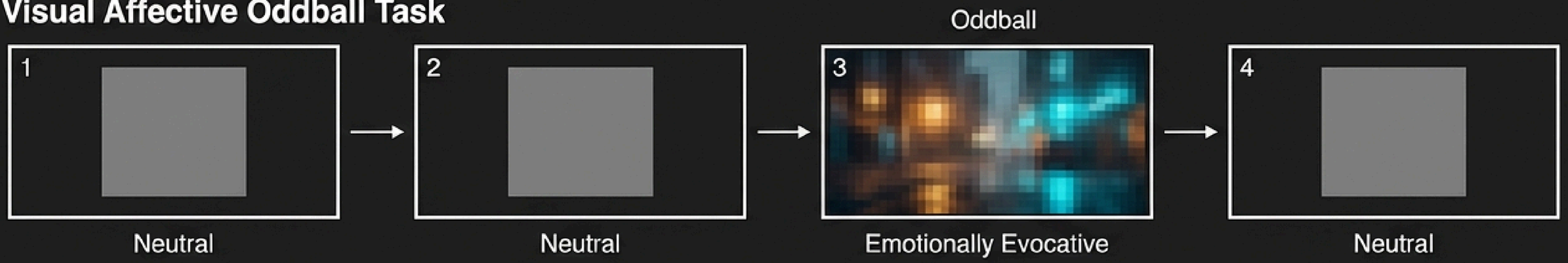
Noradrenaline tracks emotional modulation of attention (Bang et al., 2023)

- **The Breakthrough:** Bang et al. demonstrate that electrochemical estimates of sub-second neuromodulator dynamics can be obtained in humans.
- **The Setting:** The study utilized Epilepsy Monitoring Units (EMU), utilizing depth electrodes already implanted for clinical seizure monitoring.
- **The Target:** Electrodes were located in the Amygdala, allowing for direct comparison between animal models and human experience.

Capturing the Signal: Methodology

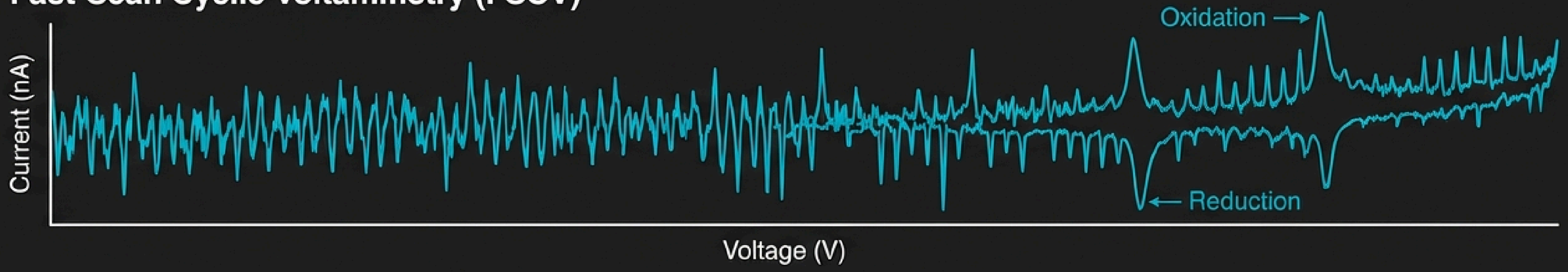
Visual Affective Oddball Task & Fast-Scan Cyclic Voltammetry

Visual Affective Oddball Task



The Measurement: Fast-Scan Cyclic Voltammetry (FSCV) applies a rapid voltage ramp to the electrode to measure the oxidation and reduction of specific chemicals.
The Innovation: A signal prediction model, trained on in vitro data, isolated Noradrenaline (NA) signatures from the noisy brain environment.

Fast-Scan Cyclic Voltammetry (FSCV)

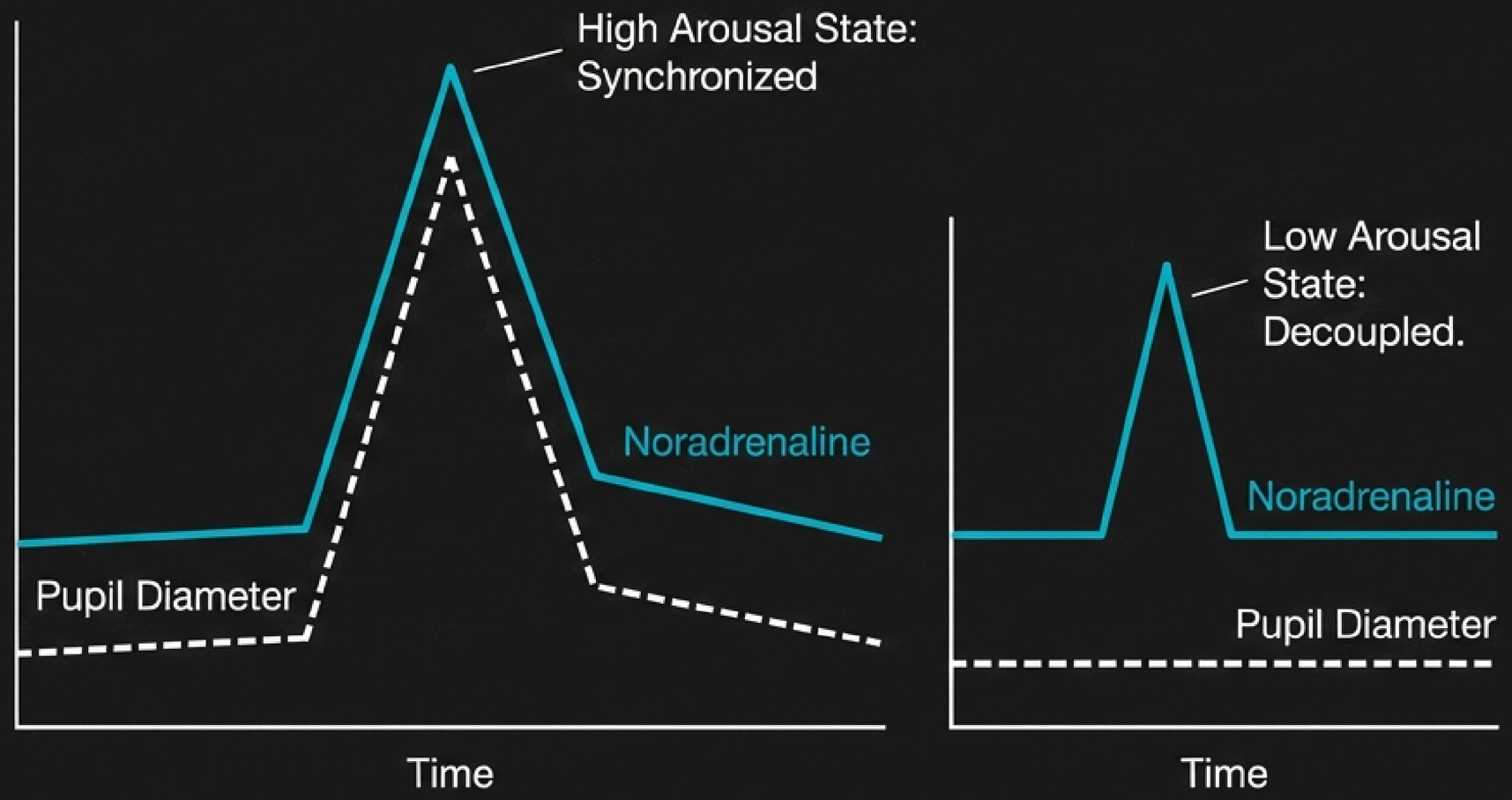


The Chemistry of Attention

Noradrenaline Dynamics and State-Dependent Coupling

Primary Finding: Noradrenaline (NA) levels in the amygdala track the emotional modulation of attention.

Pupil Coupling: Pupil dilation is a proxy for NA, but this coupling is state-dependent. The correlation exists only during high-arousal states.



Advanced Signal Analysis: Matlab-Generated Data Visualization

C: > Users > Dell > Downloads > Cog nwueo data

pupil_data3.m × behavioru_ana.m × behavioru2_ana.m × Bang2023_Behavioral_Replication.m ×

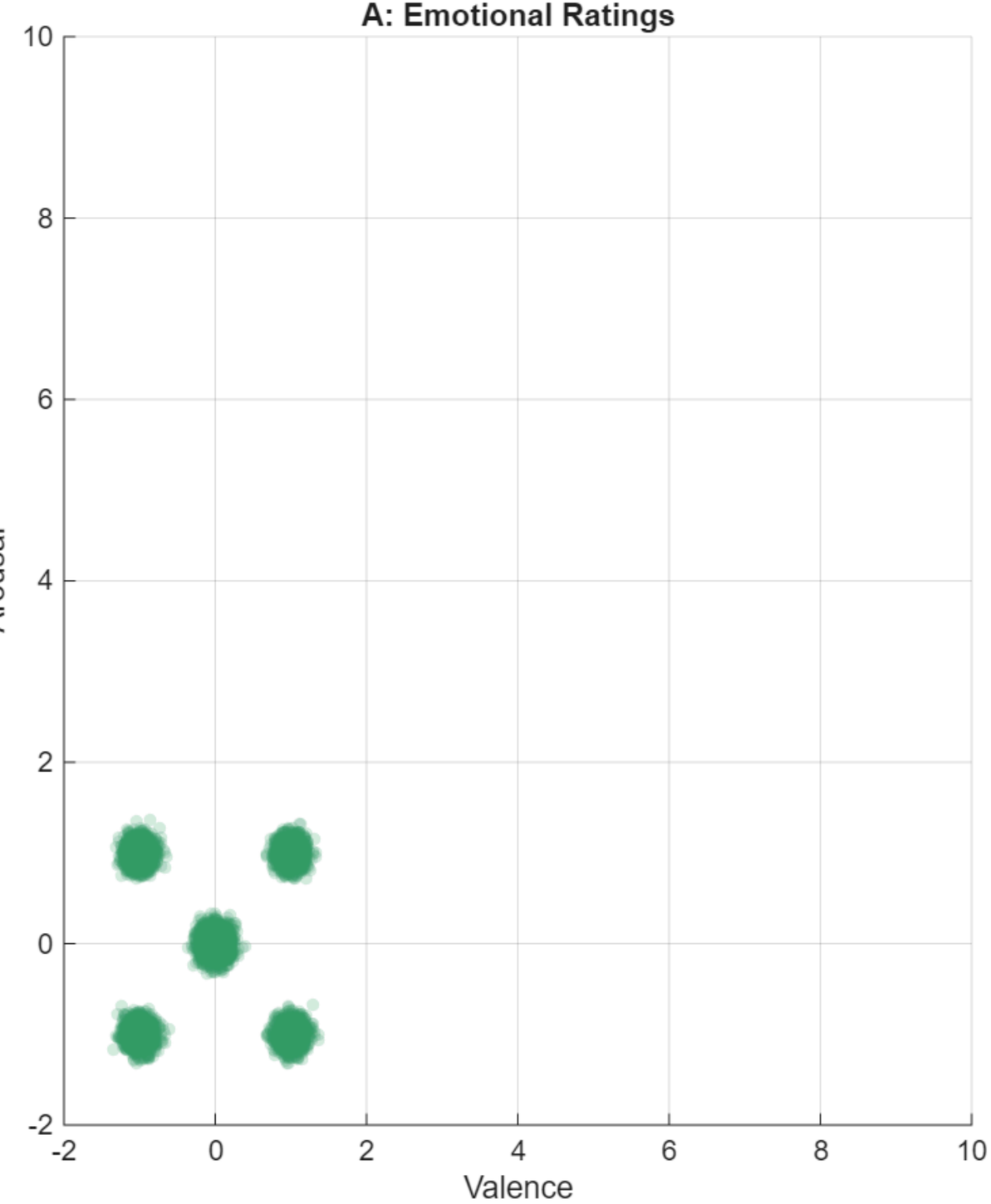
:\Users\Dell\Downloads\Cog nwueo data\behavioru_ana.m

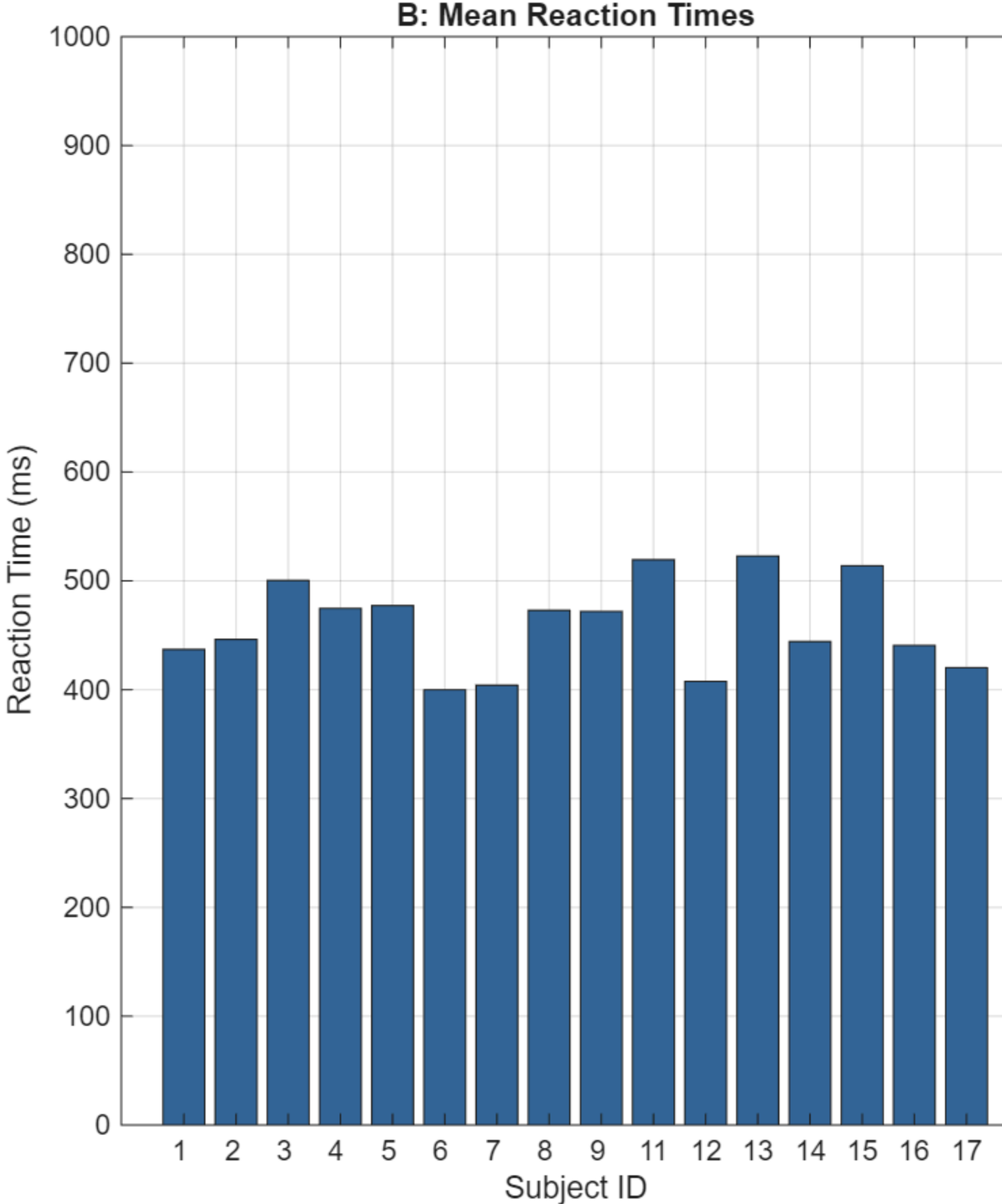
```
n_sbj = 17;
all_valence = [];
all_arousal = [];
subjects_found = 0;

fprintf('Analyzing Behavioural data for 17 subjects...\n');

for i = 1:n_sbj
    fileName = sprintf('HC_%03d.mat', i);

    if exist(fileName, 'file')
        try
            % We load the file into a temporary structure 'S'
            % This is safer than loading directly into the workspace
            S = load(fileName);

            % Check if the 'data' variable exists inside the file
            if isfield(S, 'data')
                all_valence = [all_valence; S.data.valence(:)];
                all_arousal = [all_arousal; S.data.arousal(:)];
                subjects_found = subjects_found + 1;
                fprintf('Successfully loaded Subject %d\n', i);
            end
        catch
            % If Subject 10 is broken, this will catch the error and keep going
            fprintf('!! Warning: Could not open %s (File may be corrupted). Skipping...\n', fileName);
        end
    else
        fprintf('Note: %s not found. Skipping...\n', fileName);
    end
end
```

pupil_data3.m × behavioru_ana.m × behavioru2_ana.m × Bang2023_Behavioral_

C:\Users\Dell\Downloads\Cog nwueo data\behavioru2_ana.m

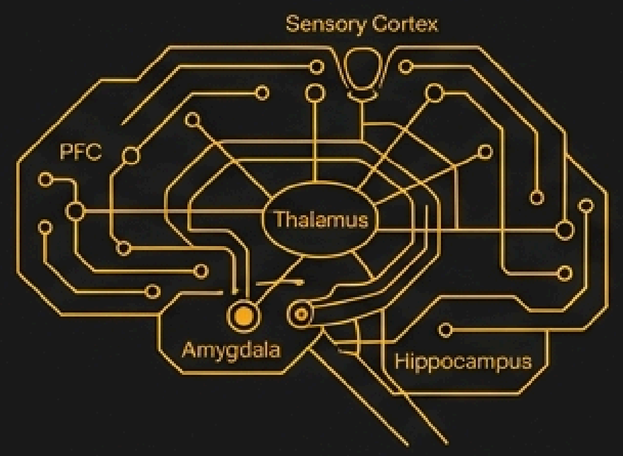
```
fprintf('Generating final combined report...\n');

for i = 1:n_sbj
    fileName = sprintf('HC_%03d.mat', i);
    if exist(fileName, 'file')
        try
            S = load(fileName);
            % 1. Collect Emotion Data
            all_valence = [all_valence; S.data.valence(:)];
            all_arousal = [all_arousal; S.data.arousal(:)];

            % 2. Collect & Filter RT Data
            rt = S.data.reactiontime;
            if iscell(rt), rt = cell2mat(rt); end

            % CRITICAL FIX: Only take RTs between 0.1s and 2.0s
            valid_rt = rt(rt > 0.1 & rt < 2.0);

            if ~isempty(valid_rt)
                subject_means = [subject_means; mean(valid_rt)*1000];
                subjects_list = [subjects_list; i];
            end
        catch
        end
    end
end

% --- CREATE COMBINED FIGURE ---
figure('Color', 'w', 'Position', [100, 100, 1000, 400]);

% Left Side: Emotional Space
subplot(1,2,1);
```

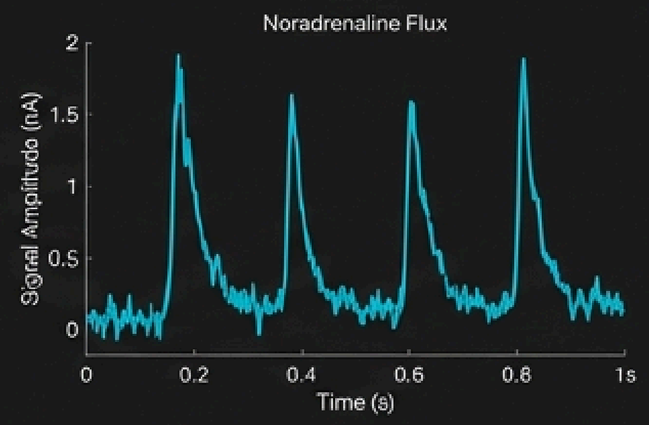

A: Emotional Ratings
Valence
10
8
6
4
2
0
-2
-2
0
2
4
6
8
10


B: Mean Reaction Times
Reaction Time (ms)
Subject ID
1000
900
800
700
600
500
400
300
200
100
0
1 2 3 4 5 6 7 8 9 11 12 13 14 15 16 17

Conclusion

The Evolution of Emotional Neuroscience (2000–2023)





2000: Anatomical Circuits → **2023:** Chemical Dynamics

The Foundation:

LeDoux (2000) established the anatomical validity of fear circuits and LTP as the mechanism of learning.

The Evolution:

Bang et al. (2023) advanced this by measuring the chemical dynamics in awake humans, confirming Noradrenaline tracks emotional attention.

The Future:

We have moved from the “dark cloud” to a proof-of-concept for neuromodulator monitoring monitoring in clinical settings.