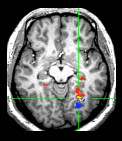
Memory and Awareness in Fear Conditioning



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What is Fear Conditioning?

Information and prediction: Animals use environmental signals to predict the occurrence of biologically significant events. Similar rules apply to learning about pleasant and unpleasant outcomes.

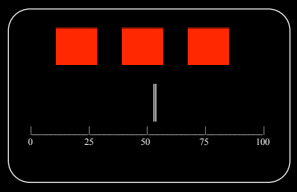
Rapid acquisition: Robust learning can occur with as little as a single paired presentation of stimuli.

Multiple procedures / forms: In addition to simple relations, humans and laboratory animals can learn a variety of complex conditional and higher-order discriminations.

Model system: Currently one of the most popular preparations for neurobiological studies of memory at the behavioral, systems, and cellular level. Basic element of more complex cognitive phenomena.

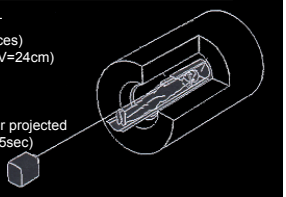
Implicit and explicit processes: Multiple neural systems encode information simultaneously. Processes are anatomically dissociable.

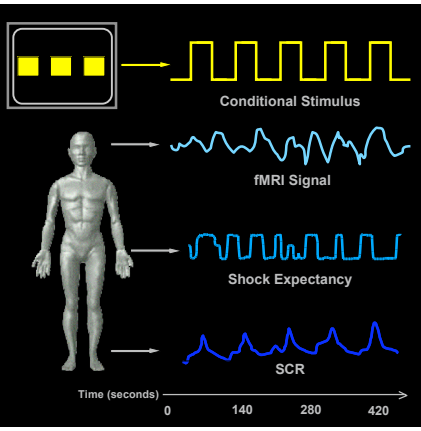
Emotion / affect: "Emotional memory" reflects central and ANS expression mechanisms.



General Imaging parameters:
- ❑ GE Signa 1.5T / Bruker Medspec 3.0T
- ❑ Anatomy: SPGR (124 axial 1.1mm slices)
- ❑ fMRI: EPI (TR=2-3sec, TE=40ms, FOV=24cm)
- ❑ Resolution: 2.0-3.7mm in plane

Behavioral parameters:
- ❑ CS = unique color, shape, and number projected
- ❑ UCS = transcutaneous AC (2-6mA, 0.5sec)
- ❑ GSR, HR & SE in real time
- ❑ Subjective UCS ratings each block





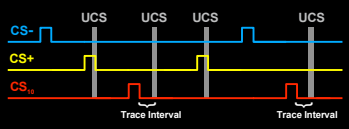
Data Analysis

• Delay vs. Trace Conditioning

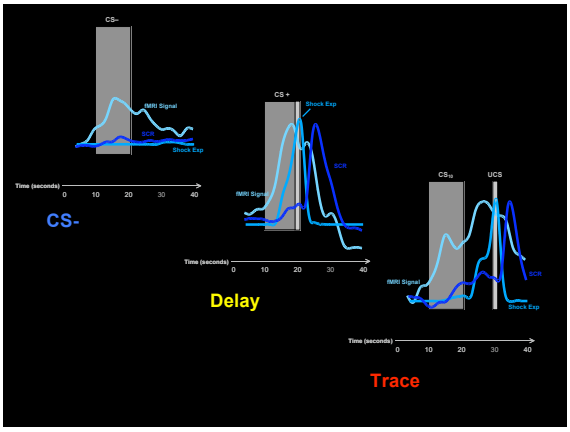
• Discrimination and Reversal

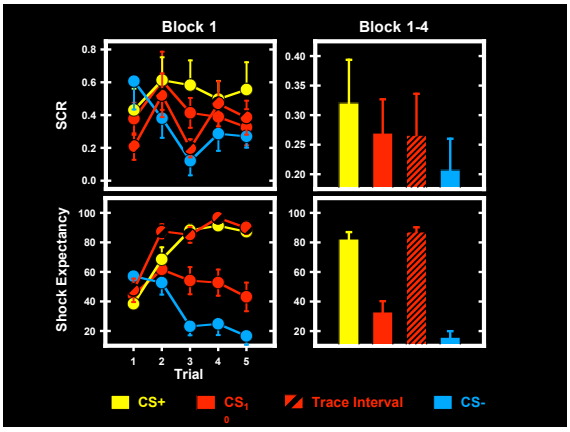
• Complex Discriminations

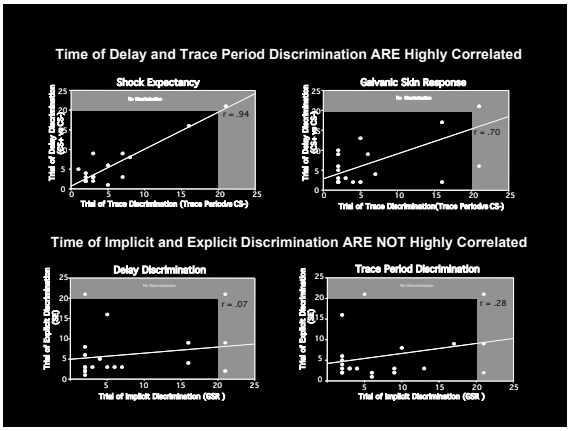
Trace Conditioning Procedure

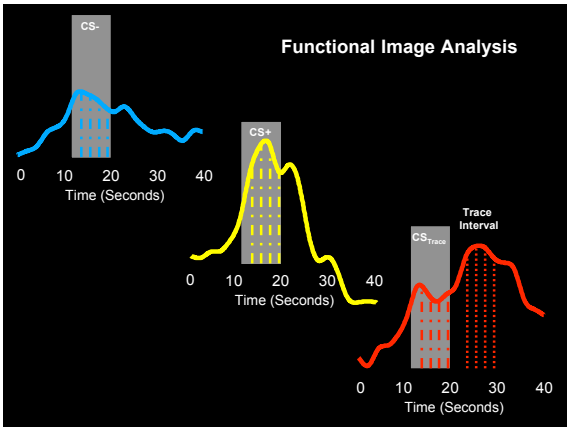


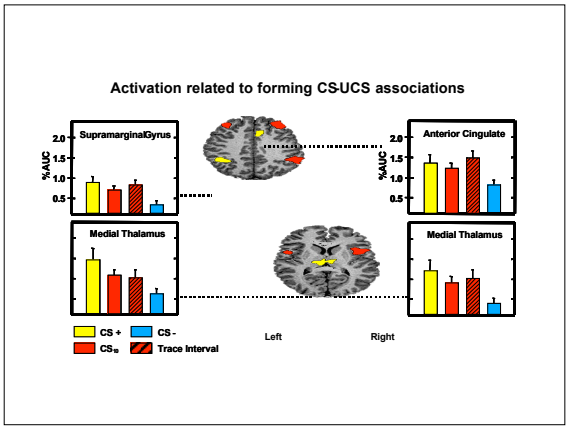
Subjects:	N=17 (9 female), 18-43 yrs, right handed.
Training:	Within-subjects, Blocks of 5 trials each CS x 4 blocks. Block=680s, CS=10s, UCS=0.5s, ITI=30s, Trace=10s
Imaging:	3 Tesla, TR=2s, TE=27.2msec, FOV=24cm, Flip=90deg

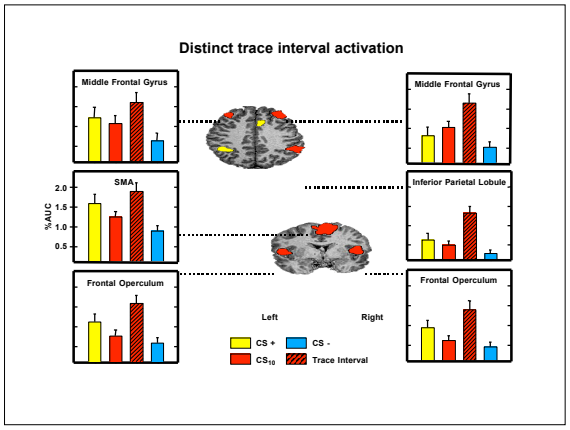

CS-
fMRI Signal
SCR
Shock Exp
Time (seconds)
0 10 20 30 40
CS-
CS +
Delay
CS10
UCS
Trace

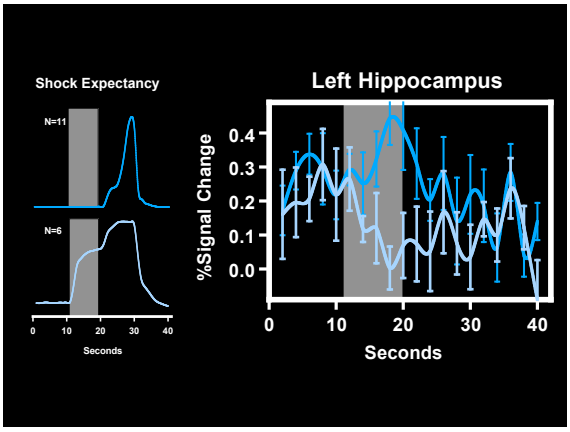

Block 1
Block 1-4
SCR
Shock Expectancy
Trial
CS+
CS1
0
Trace Interval
CS-

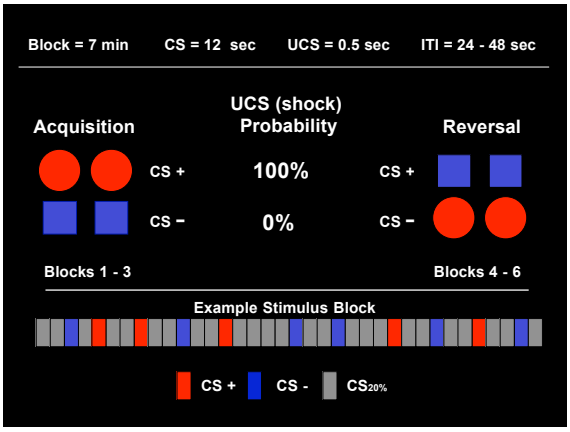

Time of Delay and Trace Period Discrimination ARE Highly Correlated
Shock Expectancy
Galvanic Skin Response
r = .94
r = .70
Time of Implicit and Explicit Discrimination ARE NOT Highly Correlated
Delay Discrimination
Trace Period Discrimination
r = .07
r = .28

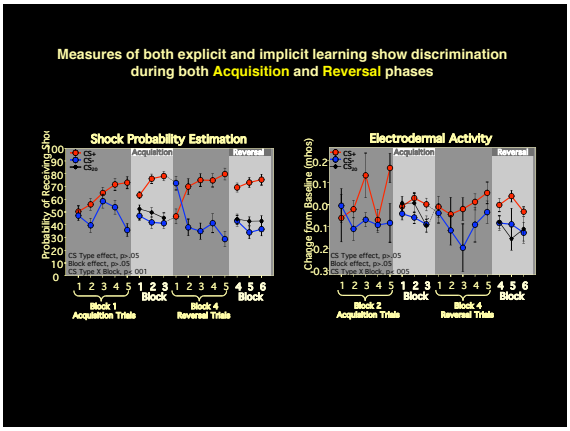

CS-
Functional Image Analysis
Time (Seconds)
CS+
Trace Interval
CS Trace

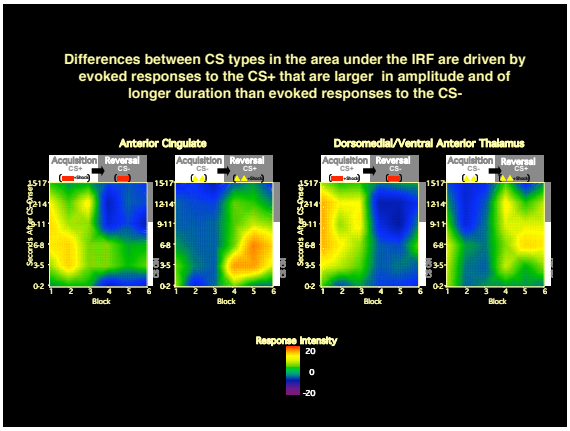

Activation related to forming CS-UCS associations
SupramarginalGyrus
Anterior Cingulate
Medial Thalamus
Medial Thalamus
%AUC
CS +
CS -
CS10
Trace Interval
Left
Right

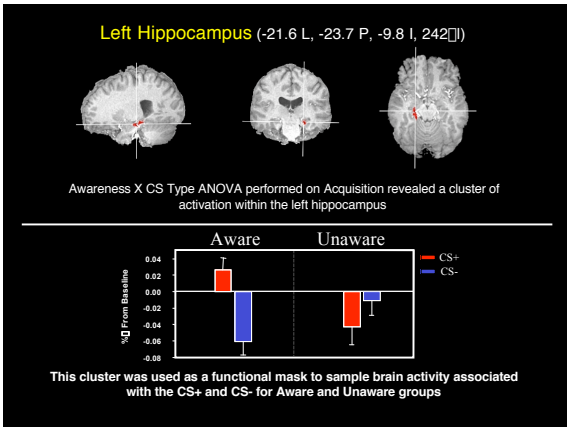

Distinct trace interval activation
Middle Frontal Gyrus
Middle Frontal Gyrus
SMA1
Inferior Parietal Lobule
Frontal Operculum
Frontal Operculum
%AUC
Left
Right
CS +
CS -
CS10
Trace Interval

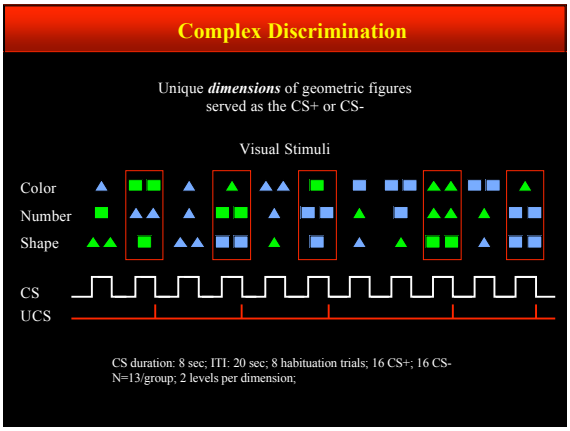

Shock Expectancy
N=11
N=6
0
10
20
30
40
Seconds
Left Hippocampus
%Signal Change
0.4
0.3
0.2
0.1
0.0
0
10
20
30
40
Seconds


Block = 7 min
CS = 12 sec
UCS = 0.5 sec
ITI = 24 - 48 sec
Acquisition
UCS (shock) Probability
Reversal
CS +
CS –
100%
0%
CS +
CS –
Blocks 1 - 3
Blocks 4 - 6
Example Stimulus Block
CS +
CS -
CS20%

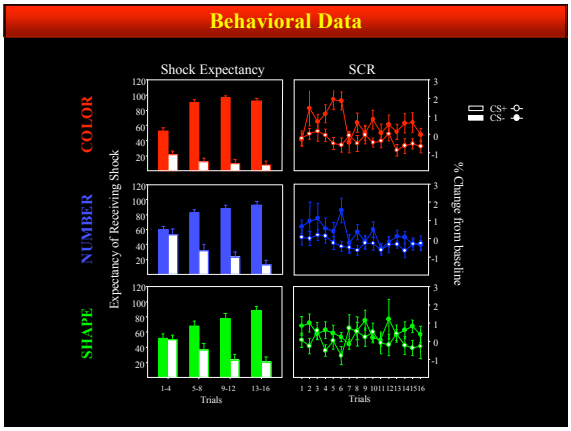

Measures of both explicit and implicit learning show discrimination during both Acquisition and Reversal phases
Shock Probability Estimation
Electrodermal Activity
Acquisition
Reversal
Block
Block 1 Acquisition Trials
Block 4 Reversal Trials
Block 2 Acquisition Trials
Block 4 Reversal Trials


Differences between CS types in the area under the IRF are driven by evoked responses to the CS+ that are larger in amplitude and of longer duration than evoked responses to the CS-
Anterior Cingulate
Dorsomedial/Ventral Anterior Thalamus
Acquisition
Reversal
Block
Response Intensity
20
0
-20

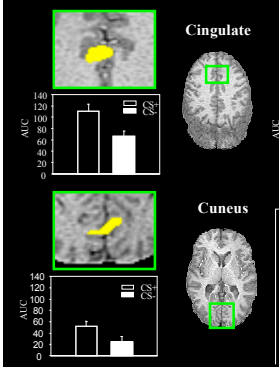

Left Hippocampus (-21.6 L, -23.7 P, -9.8 I, 242)
Awareness X CS Type ANOVA performed on Acquisition revealed a cluster of activation within the left hippocampus
Aware
Unaware
CS+
CS-
This cluster was used as a functional mask to sample brain activity associated with the CS+ and CS- for Aware and Unaware groups


Complex Discrimination
Unique dimensions of geometric figures served as the CS+ or CS-
Visual Stimuli
Color
Number
Shape
CS
UCS
CS duration: 8 sec; ITI: 20 sec; 8 habituation trials; 16 CS+; 16 CS-
N=13/group; 2 levels per dimension;

Behavioral Data

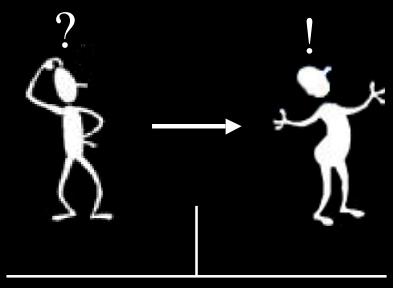


Imaging Data: CS+ versus CS-



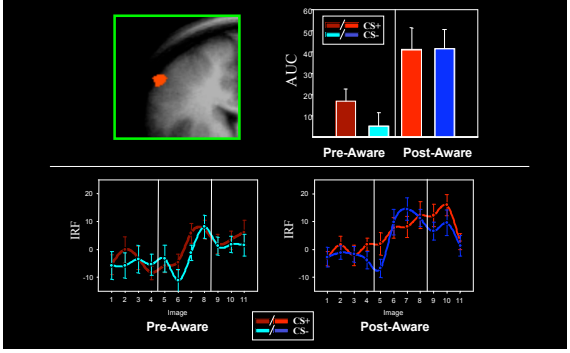
Regions that demonstrate increased responding to the CS+ relative to the CS- regardless of category group. These contingency-related effects in sensory and motivational systems are similar to those previously reported.

Development of Task Awareness



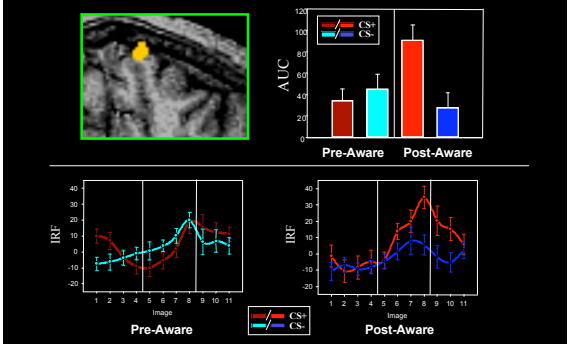
Awareness (main effect)

R. Middle Frontal Gyrus



Awareness x CS Type

L. Primary Somatosensory Cortex

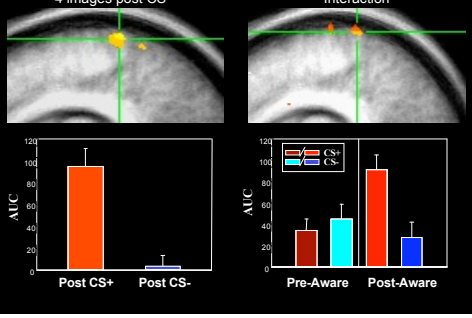


Shock UCS

Contrast ($p < 0.001$):
4 images post CS+ versus
4 images post CS-

UCS "Expectancy"

Contrast ($p < 0.01$) :
CS Type x Awareness
Interaction



Conclusions:

- Organisms exposed Pavlovian procedures simultaneously learn the explicit relationships between stimuli, encode the nature of the signaled outcome, and express affective / emotional reactions that do not depend on explicit awareness.
- Delay and trace fear conditioning are acquired at similar rates. Activity maps during trace interval periods support a "working memory" interpretation. MTL regions may contribute to accuracy or timing on trace trials.
- Brain activity patterns differ within subjects when comparing the periods before and after explicit contingency awareness. Specifics of MTL contributions to awareness remain unclear.

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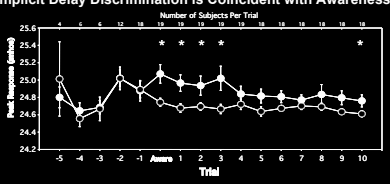
Implicit Delay Discrimination is Coincident with Awareness



Implicit Trace Discrimination Occurs After Awareness