Hippocampal role in the interaction of semantic memory with learning and decision

* We are interested in associative or transitive inference, how it is affected by already existing semantic associations and reward
* Especially since associative inference seems to rely strongly on the hippocampus
  + But not when there are semantic associations

What is associative inference ?

* Simply put, it is the ability to make indirect associations:
  + If you learn A-B and B-C, you can deduce A-C
* You can see how this ability can be useful
  + If the A and B states are neutral but the C is a reward
  + So if you have learned that B leads to a reward
    - You don’t need to re-learn that A also leads to a reward
* It seems straightforward but it involves many processes

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In order to do this, it seems the hippocampus plays a very important role

* Lesions studies and functional imaging studies have shown that hippocampal activity correlates with performance
* Of course also other regions are important, like the Ofc for state representation, and the striatum for learning,
  + But in associative inference task, their connectivity to the hippocampus is also related to learning
* So first, if we consider reward, it involved the dopamine system
  + And this might be relevant to our case, because some studies suggest that there is dopamine innervation to the hippocampus, that might help inference
* Then we want to add a dimension to the picture by considering pre-existing semantic association
  + Meaning that A B and C are semantically linked, for instance, a picture of a garden and a picture of a lawn mower
    - It should make it easier to learn associations and to transfer the value
  + And a behavioral study indeed showed that pre-existing association seems to improve performance
  + And that people with hippocampal lesion are only able to do the task if there is a semantic link
    - So hippocampus necessary for a task that relies on arbitrary associations, but not for one that relies on existing ones

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So we want to better understand the processes behind this facilitation, that doesn’t seem to rely on hippocampal processes

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Now to be able to test our hypotheses we need a simple contrast

* we have a 2 by 2 design, where pairs are either rewarded or not, and semantically linked or not
* we have 4 pairs of each type, so a total of 16 to learn, that is well within the literature range
* also each stimulus of each combination are balanced by familiarity, name accuracy, and inside/outside

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Now for the time course, we have 3 main phases we: preconditioning, conditioning and inference

* where they learn SO pairs
  + - it is a go/nogo task to make sure the participants don’t stop paying attention
    - the SO pairs are NOGO but there are 20% of trials that are SS and OO pairs that are go
* then they learn to predict whether objects are rewarded
  + they have to select the + or – on the screen before the outcome appears
* then they have to predict whether S is rewarded **without feedback**
  + so they really have to do inferences
* But that is not all
* for our analysis we also have a localizer to know which brain region asso w S or O
  + and a distractor task between conditioning and probe phase to avoid recency effects
  + a simple one back task with repetition of picture of objects and scenes not in the main tasks
* and finally a quick memory task outside of scanner, as an additional assurance that they remembered the pairings
  + and basically the pairs are rearranged, and participants are asked to say whether it is a new pairing or not

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So let’s go over the time course and design

* then the preconditioning task has each pair repeated 6 times
  + so the scene, a pause, the object, and a longer pause
  + the order is not a block design but an event related design
    - the order and ITI are pseudo randomized and optimized for higher power
  + the presentation is **organized into 6 runs in which each pair is presented once**
    - this allows to do MVPA
* For the conditioning phase, it is approximately the same design but for object-reward pairs
  + We have several repetitions per runs, because we need more presentations for conditioning to work
* For the distractor/localizer
  + it’s a block design
* For the probe task, they see single images without feedback
  + So you have 2 runs with the 16 scenes presented once in each run
  + Then you have two other runs for the objects
* Then the memory task is done outside of the scanner and takes 4 minutes

So overall it should take 50minutes, but if you count time for preparation, instruction, etc, it should take a bit more than one hour

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No that you are more familiar with the design, I will share with you some behavioral results

* Of course it’s only 4 pilots so it is not really conclusive
* But it appears that there are semantic facilitation, in addition to the reward effect of course
* So this a result for the probe phase for scenes
  + Here we see reaction times by condition
  + And we see they are shorter when the reward is one
  + And that they also are shorter for semantically linked pairs

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Alright, now I summed up the fmri parameters that we have selected with the help of Carlo

* Look slides

So for the regressors it is a basic 2 x 2 design

* For semantic rewarded stimuli, semantic neutral etc…
* And of course counfounding regressors for head motion and physio

To isolate the activations of interest

* we will use regressors for the run numbers, and for the categories of pairs
* so semantically linked or not
* and for the conditioning and inference phase, rewarded or not
* also there will be regressors for the reward stimuli in the conditioning phase

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For the reactivation analysis, we will use two approaches

* first using a classical univariate analysis
* we isolate the areas that are activated by a specific category of stimuli, from the localizer
* then we use ANOVAs to asses for changes in classifier output across runs

For the second approach we should use multivariate decoding

* we train a classifier to differentiate specific scenes and objects
* and see if it can decode the associated stimulus, eg if we feed it an object evoked pattern from the conditioning phase, will it be able to identify the correct associated scene

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For hippocampal activity and connectivity

* we will look at the activity in an hippocampal masks, again averaged by phase/run/category
  + and we again use a 2 x 2 ANOVA
* for the connectivity, we will assess it with PPI;
  + with semantic link or reward as the psychological variable,
    - and signal in the hippocampus as physiological variable

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Finally, we of course have hypotheses for our analysis

* So with the reactivation analysis
  + We expect…
* For the hippocampus analysis
  + …
  + Because maybe not necessary when semantic link
* And we expect the reward effects to change based on the semantic nature of pairs
  + So reward should help inference, especially for not semantic pairs
  + And accordingly, this difference should be modulated by hippocampal activity

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Ok so to recap

* we are using associative inference, also called transitive inference
* a process that implies a transfer of value to make a decision
* and it seems to rely on OFC and hippocampus
  + but not necessarilly as much when there is an already existing semantic link
  + so we want to understand how the inference can be made in this situation
  + and how it interacts with reward
* so for this we will investigate the reactivation of the associated stimulus, in different conditions
* and the hippocampal connectivity with striatum and OFC, and how it changes depending on those conditions
* and we will also try to identify other areas involved