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

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

So for our investigation we rely mostly on associative inference paradigms

* 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

And studies have shown the regions and processes involved for different steps of associative inference

* First you need to represent the state a stimulus corresponds to
  + And the other states the stimulus is associated to
  + For instance a rewarded or unrewarded state
  + For this, the OFC seems to play a central role,
    - as its lesion or inactivation strongly impairs this abibilty
  + And functinal imaging as allowed to make a correlation between functionnal connectivity between OFC and hippocampus and performance in this task.
  + Overall, results seem to indicate that this hippo-OFC axis is central to represent and to retrieve the current and associated state
* So as I said before, we are interested in reward and value
  + And if value learning is involved, this recruits the striatum and the dopamine system for reinforcement learning
* If the indirectly associated value seems to be computed along the hippocampus-OFC axis,
  + The connectivity between the striatum and hippocampus seems to also corelates with performance in this tasks
    - Probably to transfer the correct expected value to the striatum
  + Finally there might be a role for the dopamine from the VTA to the hippocampus in facilitating value transfer, but it is not clear
* So 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 couple behavioral stuies indeed showed that pre-existing association seems to improve performance
  + And that people with hippocampal lesion are only able to do the task above chance 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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So in order to investigate that, we are doing an experiment similar to ones done before on associative learning and transitive inference

* 1) association or preconditioning phase, when people are exposed to AB associations and asked to learn them
* 2) reward or conditioning phase, where people learn the link between B and C, with C being a reward
* 3) a last phase where people are asked to make the inference by choosing rewarded A stimulus, indirectly associated with reward

A first analysis is then to use correlation of performance with activation of a region of interest

* And this shows that the hippocampal activity during learning seems indeed to be correlated with later performance
* However, if we use semantically linked AB pairs, because as the link is pre-existing, it shouldn’t be necessary
* And we expect to see less of this correlation, but maybe another region could be predictive

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Another possible analysis is to make use of the stimuli used to measure the association

* For instance by associating a scene and an object as A and B stimuli
  + you can use a localizer trained to differentiate scenes and object
  + and you see if you decode a scene in an object,
    - and if you do it is likely because the two stimulus are now associated
  + so this is a cartoon from a study where they showed that they decoded more and more scenes in objects as learning occured
* for objects and scene that are already semantically associated
  + we expect this effect to appear faster

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Also, as we said before, in order to infer the indirect value

* there seem to be a transfer of state information that involves the OFC, the hippocampus and the striatum
* but as the hippocampus appear not necessary in semantic pairs, we expect less of this connectivity
* and for this connectivity to relate less with performance

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So to sum up we predict

* hippocampal activity and connectivity should be reduced and not correlated with performance for semantically linked paired
* and that the associated stimulus should be reactivated in earlier repetitions for those pairs
* of course we assume there are other regions and processes involved in the associative inference for semantically linked pairs, and some candidates are IFG, EC and PCC

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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 the 3 phases we talked about before: preconditioning, conditioning and probe

* 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 GO but there are 20% of trials that are SS and OO pairs that are no-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 before
  + a simple one back task with repetition of picture of objects and scenes not in the main tasks
* a distractor task between conditioning and probe phase to avoid recency effects
  + really similar
* 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 lets go over the timecourse and design

* the localizer is simple, it’s a block 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 presentation is **organized into 6 runs in which each pair is presented once**
    - this allows to do MVPA
  + the order and ITI are pseudo randomized and optimized for higher power
* For the conditioning phase, it is approximately the same design but for object-reward pairs
* For the distractor, it is basically the same as the localizer
* 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 35minutes, but if you count time for preparation, instruction, etc, it should take 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

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For our analyses

* First we are going to use the phase, the task as a regressor
  + But also the stimuli onset
* The main analysis will be a 2 by 2 ANOVA contrast,
  + in the different phases, we expect different contrasts
* and finally we are going to use classifiers
  + so for the reactivation of associated stimulus, we will first use an univariate classifier based on the localizer
  + but we also want to use multivariate classifiers for more details, and possibly RSA, to understand how and where the association and the transfer are made

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So after basic preprocessing

* for reactivation analysis, it will be within participants so no need to normalize
* but for most of the rest it will be normalized to a standard brain

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
  + in the temporal lobe
* then we create masks from it, and average the beta values in each mask, for each phase, run and category of stimulus
* then we use ANOVAs to asses for changes in classifier output across runs
* the hypothesis being that we will see more classifier output for the associated type
  + so more objects in scene stimulus
  + across runs it should increase
  + and also it should be higher and earlier for semantically linked pairs

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For the second approach we should use representational similarity analysis, RSA

* so in this multivariate approach, we will get the average evoked pattern by category from the localizer
* so we have a average pattern for object and an other one for scene
  + again we limit to the ventral temporal lobe
* then we corralate those with the average evoked activities from different stimuli, across phase, runs, and category
* the hypothesis is the same
  + that the correlation with the opposite pattern is going to increase with run number
  + and it shoould be higher, earlier for semantically linked pairs
* as a control, we check we don’t have the same effect within category, that the similarity of a scene to a scene doesn’t increase across runs

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For hippocampal activity and connectivity

So to detail a bit our prediction and analysis

* we expect, for semantically linked pairs
  + to decode the associated stimulus earlier, and maybe more accurately
  + so either the category (SO) or the stimulus itself, depending on the MVPA ability
* and the second thing we expect on those pairs, is that the learning and decision won’t rely on hippocampus activity and connectivity as much.
  + To see if we confrim lesion results
* But we still have to determine how we will identify the semantic processes involved instead of the hippocampus
  + We could try to see which region better predicts the performance or the reactivation
  + Or we could also look which regions show the highest representational similarity between scene and objects
    - With some candidate ROIs or a searchlight analysis
  + And finally we can also do seed analysis with the striatum, to explore the functional connectivity, and to identify regions that could help with the value transfer

Two hypothesis

* transfer because representation=overlapping
* transfer because state inference