**Comparing pavlovian cues and neutral cues in non-reinforced learning**

The experiment has two between-subject groups (pavlovian cues, neutral cue), and five time points (first session + 1,3,9,12 months after first session).

In the first session, participants will undergo the full CAT experiment (detailed below). The only difference between the two groups will be the cue during the training phase (the sign “+23” vs. “\*\*”). All participants will be recalled 1,3,9 & 12 months later for a follow-up scan.

Fifty five participants will participate in each group (110 overall). We predict ~15% dropout rate over the year, thus expect 45 participants in each group for the final one-year follow-up.

***Experiment design***

**Session 1:** full CAT experiment

1. BDM: outside the scanner

Participants will rank 60 snacks on a scale of 1 to 10. Each snack will be ranked once, with no time limit for each trial. The sorted ratings will be used to determine the rank of the snacks.

--Starting imaging scan, the participant will enter the scanner--

2. Response to snacks

Forty snacks will be chosen from the BDM ranking procedure, according to their subjective rating (items 3-22, 39-58 from the sorted-by-preference ranking list of each participant). All items will be presented twice in a random order, for a total of 80 trials. The purpose of this task is to record the neural activation while the participant passively views the snacks. To ensure that the participant is indeed awake and perceives the items, participants will be instructed to look at the items and count how many pictures had one or several items inside the packaging. Each item will be presented for 1s, followed by a jittered ITI of ~3s (randomly sampled from an exponential distribution range of 1-12).

3. Training:

All 40 items will be presented one by one. Some of the items will be consistently coupled with a cue (‘go’ items). Participants will be instructed to press a button once they detect the cue. Of the forty items in the training, 12 will be ‘go’ items, thus the ratio of ‘go’ and ‘nogo’ items is 0.3. Sixteen runs of all 40 items will be presented. Each item will be presented for 1s, followed by jittered ITI of ~2s randomly sampled from an exponential distribution range of 1-12). The timing for the cue appearance after the item presentation will be calculated by a step-wise procedure, in order to ensure that the participant presses the button up to 1s from the presentation of the item on 75% of the ‘go’ trials.

4. Repeated response to snacks

As explained above in ‘2’

5. Anatomical scans:

MPRAGE, FLAIR

6. Probe:

Controlled similar-valued (based on BDM) comparisons between the ‘go’ items and the items that appeared in the training phase without the visual cue (‘no-go’ items) will be presented. There will be 36 comparisons for the high value range, and 36 for low values. Four runs of 36 trials each will be presented (each unique comparison will be shown twice). Each binary choice will be presented for 1.5s, followed by an ITI fixation of jittered ~3.5s randomly sampled from an exponential distribution range of 1-12). The participant’s response will be indicated by a green square around the chosen item, for 1.5s minus RT.

--Finishing imaging scan, the participant will exit the scanner--

7. Behavioral probe:

For control purposes, 4 sanity (high ‘nogo’ vs. low ‘nogo’) and 8 control (4 high ‘nogo’ vs. high ‘nogo’ + 4 low ‘nogo’ vs. low ‘nogo’) comparisons will be presented. The timing is the same as in the imaging probe detailed above in ‘6’.

8. Memory:

Twenty-four snacks from the probe (12 ‘go’ + 12 ‘nogo’) and twenty-four ‘new’ snacks (which did not appear in the experiment until now) will be shown one by one. The participant will be asked to rate on a scale of 1-5 how he/she is sure that an item appeared in the experiment, and if it was associated with a cue. There will be 96 trials (24 ‘old’ + 24 ‘new’ snacks, 48 trials for each question). Each question will be presented for 3s.

**Sessions 2 to 5:** follow-up experiments

These sessions will include imaging scans of a. **probe (6)**, b. **response to snacks (2)** and c. **anatomical scans (5).** Then, outside the scanner, the participant will perform d. memory (8) and e. BDM (1). The procedures are explained above.

**We would very much appreciate your advice on the following issues:**

1. Design efficiency:
   1. Currently, in all imaging tasks, the ISI (inter stimulus interval, the fixation time between stimuli of successive trials) is a jitter randomly sampled from an exponential distribution with range of 1-12 seconds, with mean of 3 seconds for ‘response to snacks’, 2 seconds for ‘training’ and 3.5 seconds for ‘probe’.
   2. The conditions (i.e. ‘go’/’nogo’, high/low value item) in all parts of the experiment are randomly spread across trials.

The most interesting effect for us is the modulation of choosing ‘go’ versus ‘nogo’ items (based on choices during the probe). Specifically, we hope to find differential activation during ‘response to snacks’, ‘training’ and ‘probe’, for snacks that were chosen versus snacks that were not chosen. This effect will be examined separately for high and low value items, and for ‘go’ and ‘nogo’ items. Since this modulation is determined by the participant’s responses during the probe, we cannot optimize the efficiency for this effect.

Thus, we wonder if we should optimize the design (using optseq for instance or any other tool you recommend) for the conditions we can control (high / low value items, ‘go’ / ‘nogo’ items), or if by optimizing the design for the lesser relevant conditions, we will diminish the power for the most relevant modulation (of which item was chosen in the ‘probe’). In that case, perhaps it will be better to have random (exponential?) jittered fixation as ISIs and random presentation of conditions, instead of controlled design optimization.

1. Analysis:

The general effects we are interested in are:

* 1. Long term effects of the manipulation (changes through-out the 5 time points, within subject)
  2. Differences between the two groups (between subject)
  3. Interaction between them

Is there an analysis model that is optimal for such a large design? (2 groups with 5 time points)

I will need to look into this. The only longitudinal-appropriate model I can think of that I would recommend using is the SWE toolbox in SPM (<https://www2.warwick.ac.uk/fac/sci/statistics/staff/academic-research/nichols/presentations/ohbm2014/Guillaume-SwEtool-OHBM2014.pdf>) I’ll look into it further for the details. It should allow us to calculate these hypotheses over time and I’ll figure out if we can preprocess the data in FSL, but then use SPM for the SWE portion of the model. I’m sure we can, since SPM is a little more flexible about the input.

Other questions I had while reading

* During the portion when they rate do you notice any relationships between ratings and time? Even though the stimuli are randomly ordered, I wondered if some other bias could sneak in. Just curious. You’ve probably looked at this before. I can’t imagine there’s much that could be done about it other than showing the stimuli multiple times and averaging the ratings over stimuli
* As far as efficiency goes, the tasks are all a little bit different not only in terms of ISI, but in what they’re doing (for example, counting). Does that introduce a confound that we will not be able to remove. For example, could response vs training effects actually be counting effects?
* You say the ratio of go to nogo is 0.3, but 12/(40-12) = .43

**Thank you very much! ☺**