

Project working title: Comparing reinforced versus non-reinforced effects of behavioral change

Authors: Shiran Oren, Tom Schonberg

Affiliation: Tel Aviv University

A. Hypotheses

Despite the critical need for ways to change people's value-based decision making to be healthier and adaptive, most current interventions rely on cognitive effort or external reinforcement, and fail to last in the long term (Christiansen, Bruun, Madsen, & Richelsen, 2007; Higgins, 1995; Jeffery, 2000; Judith J. Prochaska, Kevin Delucchi, 2004; Pan S. Li C., Zhao M., 2012; Wing, R. R., Venditti, E., Jakicic, J. M., Polley, B. A., & Lang, 1998).

Recently, a novel method employing non-reinforced learning was presented (Schonberg et al., 2014). This method, named the Cue Approach Task (CAT), is composed of three main parts: 1. A WTP procedure, in order to obtain participants' subjective rating (Becker, G. M., DeGroot, M. H., & Marschak, 1964) 2. A training phase, in which all the items are presented one by one, some of them consistently coupled with a cue (Go items). Participants are instructed to press a button once they detect the cue. 3. A probe phase, in which the change in preferences due to the training is examined via controlled pre-task equal valued comparisons between the Go items and the items that appeared in the training phase without a cue ('no-go' items). This task shows promise for long-term maintenance of behavioral change, with effects lasting up to 6 months so far (Salomon et al., 2017), and calls for further examination.

Here, we propose to investigate the behavioral and neural impacts of using reinforced versus non-reinforced cues in behavioral change towards snack food items, both immediately and up to one year after the experimental intervention.

We hypothesize that the effect of non-reinforced learning will decay slightly over time, but will still last in the long-term, while the effect of the reinforced training will be similar to the non-reinforced training immediately after training, but will decay sharply over time due to the removal of the reinforcing reward.

B. Methods

1. Participants

Sixty participants will participate in each group (120 overall). We predict ~25% dropout rate over the year, thus expect ~45 participants in each group for the final one year follow-up.

2. Apparatus

Stimulus presentation will be done using Matlab and Psychtoolbox 3 (Brainard, 1997; Pelli, 1997).

3. Stimuli

The stimuli data set is composed of 60 Israeli snack food items, presented on a black background. All snacks are available at main marketing stores in Israel and cost no more than 10 NIS (equal to 2.7\$).

4. Procedure

We will perform the CAT procedure while participants are inside the MRI scanner. The experiment will include five imaging sessions across one year. Participants will be randomly divided into two groups: non-externally reinforced (CAT) and externally reinforced group (Pavlovian cue CAT: PC-CAT). In the first session, Participants will undergo the full CAT experiment (Schonberg et al., 2014). The only difference between the two groups will be the cue during the training phase. For the PC-CAT group, the cue will be a number from the range of 21-24 (i.e.: "+21", "+23"), indicating a future winning. Participants will be informed that at the end of the experiment one trial will be selected and they will win the amount shown (21-24 NIS

equal to 5.7-6.5\$) as a bonus. The cue for the regular CAT group will be "***". After 1, 3, 9 and 12 months, we will invite all participants for a follow-up imaging session, and perform the probe phase followed by a memory task, in order to see if the effect of the CAT or the pavlovian cue had lasted.

3.1. Experiment

All sessions will be held in the imaging center at Tel-Aviv University.

Session 1: full CAT experiment

1. BDM: ~15 minutes, outside the scanner

In order to obtain the participant initial subjective preference for 60 snacks, we will use the BDM procedure (Becker, G. M., DeGroot, M. H., & Marschak, 1964). Each snack will be presented and rated 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 subject will enter the scanner--

2. Response to snacks ~10 minutes

Forty snacks will be chosen from the BDM, according to their subjective ratings (items ranked 3-22 and 39-58 from the sorted-by-preference ranking list of each subject). 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 were single or plural. In each trial, an item will be presented for 2s, followed by fixed ITI of 7s. Each run will start with 2s of pre-run fixation, and finish with 7s post-run fixation completion to the last run fixation. There will be 2 runs, each run will present all 40 items. Thus, each item will be presented twice in the task, resulting in 80 trials over 2 runs. Items will be presented in a random order, randomized for each run and subject.

3. Training: ~30 minutes

All items will be presented one by one. Some of the items will be coupled with a cue (Go items). The remaining items will not be associated with a cue (NoGo 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 proportion of Go out of all items is 0.3. this proportion also remains for the distribution of high and low value items, such that there are 6 high value & 6 low value Go items. The training will have 480 trials, divided to 6 runs. Each run will have 2 repetitions of the 40 items, resulting in 12 repetitions for each item. Each item will be presented for 1s, followed by jittered ITI of ~2s. The timing for the cue appearance after the item presentation will be calculated by a step-wise procedure, in order to obtain 75% of successful button presses during the 1.5s from item onset. Each run will start with 2s of pre-run fixation, and finish with 6s post-run fixation completion to the last run fixation.

4. Repeated response to snacks ~10 minutes

As explained above in '2.'

5. Anatomical scans: ~7 minutes

MPRAGE, FLAIR

6. Probe: ~15 minutes

Similar-valued comparisons between the Go items and NoGo items (the items that appeared in the training phase without visual cue will be presented). The 12 NoGo items are chosen such that they have the same mean rankings of Go items (for each of the high and low value groups). For instance, if the ranking of the high Go items is 7, 10, 12, 13, 15, 18, the ranking for nogo' items will be 8, 9, 11, 14, 16, 17. there are 2 such assignments for Go and NoGo items, counterbalanced across participants. 36 high value and 36 for low value comparisons will be presented twice, concluding to 144 trials, separated to two runs. Each binary choice will be presented for 1.5s, followed by ITI fixation of jittered ~3.5s. The participant's response will be indicated by a green square around the chosen item, for 1.5s minus RT. If the subject did not respond in time, the writing "You must respond faster!" will appear for 0.5s, followed by ITI fixation of jittered ~2.5s. Each run will start with 2s of pre-run fixation, and finish with 6s post-run fixation completion to the last run fixation.

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

7. Memory: ~5 minutes

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 rate on a scale of 1-5 if that item appeared in the experiment, and if it was associated with a cue. This part will include 96 trials (24 'old' + 24 'new' snacks, 48 trials for each question). Each question will be presented for 3s. Participants' responses will be indicated by a green square around the chosen answer, for 3 seconds minus reaction time. If the participant did not respond in time, the writing "You must respond faster!" will appear for 0.5s.

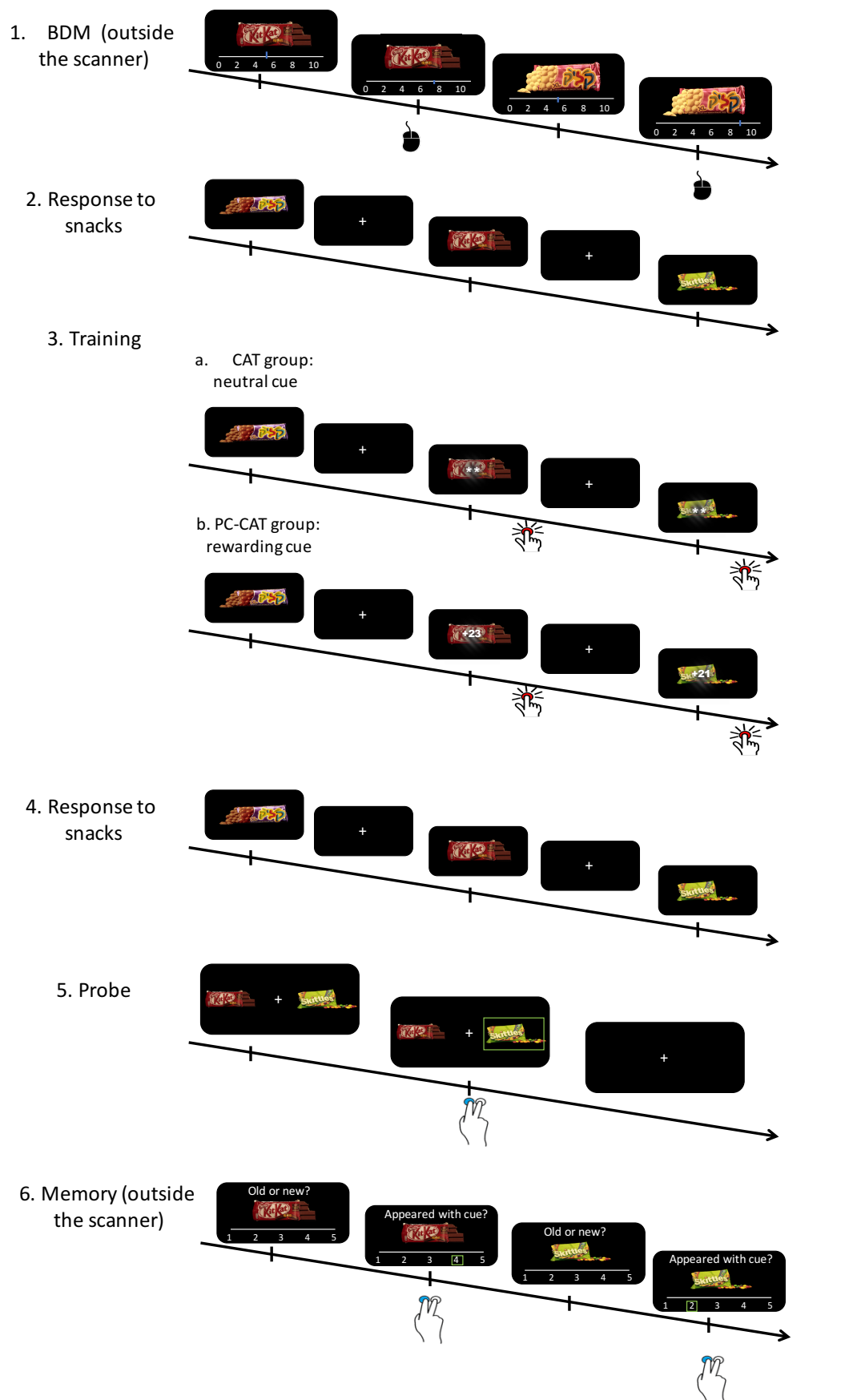
8. Eating questionnaire: ~5 minutes

Participants will be asked to fill out the Adult Eating Behavior Questionnaire (AEBQ, Hunot et al., 2016), translated to Hebrew in our lab.

Sessions 2 to 5: follow-up experiments

These sessions will include imaging scans of a. **response to snacks (2)** b. **probe (6),** 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.

Figure 1. Sequence of Events



5. Critical measures

1. Dependent variables:
 - a. Proportion choices of Go or NoGo item in the probe.
 - b. Remembering if an item appeared in the experiment: accuracy and RT
 - c. Remembering if an item was associated with a cue: accuracy and RT
 - d. Imaging: BOLD response
2. Independent variables:
 - a. Experimental group (2 levels: CAT, Classic; between subject)
 - b. Session number (5 levels: 1-5 session; within subject)
 - c. Item's bid (the index of each item after sorting the BDM bids; within subject)
 - d. Item's type (2 levels: Go, NoGo; within subject)
 - e. Item's value group (2 levels: 'high', 'low'; within subject)

6. Planned sample

1. 120 valid participants (60 in each group) which meet our exclusion criteria (see below) for the first session (numbers in later sessions may be smaller due to drop-out).
2. The data will be collected at Tel Aviv University's imaging center, by Shiran Oren. Participants will be compensated for their participation in the experiment. We will stop collecting data once we reaching 120 valid participants in the first session. We will analyze data for presentations in conferences. participants will be recruited through adds that will be hung in the university and its surroundings, and in social media sites (i.e. facebook groups)

3. Power calculation:

We decided on sample size following power analysis we performed on previous experiments:

1. on data published in Schonberg et al., 2014, minimal n for vmPFC activation during probe is 49 participants.
2. on data from Botvinik-Nezer et al., in prep:
 - Minimal n for OFC activation during response to snacks is 45 participants.
 - Minimal n for Temporal-Occipital activation during response to snacks is 30 participants.

4. Exclusion criteria

We will exclude participants from the analysis if they meet one of the following criteria:

1. BDM: gave less than 1 NIS to more than 40 snacks. This refers only to the first BDM in the first session.
2. Participants will be excluded based on the following behavior patterns during training (indicating task disengagement):
 - a. False alarm greater than 5%. (False alarm is defined as response for a NoGo item during the training phase).
 - b. Miss greater than 10%. (Miss is defined as a Go trial when the participant didn't respond at all (1.5 seconds after image onset).)
3. If at any time during the training phase, the ladder dropped below 200ms.

- a. Ladder – any time the participant fails to respond during the one second image onset of a Go trial, the ladder will drop, each time by 50 ms (starting at 750ms). Each successful Go trial will increase the ladder by 16.67ms. Reaching a ladder below 200ms is an indication that the participant did not respond in many successive trials.
7. Participants will be excluded from participating in the experiment if they do not follow the next conditions:
 - a. Ages 18-40
 - b. Right handed
 - c. Understands Hebrew
 - d. Did not participate in other Schonberg lab's experiments with CAT or snacks
 - e. Normal or corrected to normal vision
 - f. Like snacks, no special dietary restriction (i.e. vegan)
 - g. Compatible to participate in MRI experiment (i.e. no metal in the body, not claustrophobic, no medical condition or regular drugs that affect blood flow (such as SSRI, diabetics), no tattoos in the head region etc.)

Analysis plan

1. Hypothesis:

We hypothesize that preference change will be influenced by an interaction between group (reinforced versus non-reinforced) and time (0, 1, 3, 9, 12 months). Specifically, we hypothesize that for the non-reinforced group, the effect of preference change will be significant through all sessions, and will show a smaller trend of decay over time than for the reinforced group. For the reinforced group, the effect of preference change will initially be similar to or higher than the non-reinforced group's effect. It will decay more sharply over time up to non-significance in the last session.

We consider the effect of preference change to be reflected in the following measurements:

1. During **probe**: higher probability of choosing Go over NoGo items.
2. During **memory** tasks: Shorter RTs and higher accuracy for Go over NoGo items.
3. **Neural** activity: stronger response for Go over NoGo items in these regions:
 - a. CAT group: significant ROIs from analyses of previous CAT experiments (Schonber et al, 2014; Bakkour et al, 2016), and two additional works that are currently being analyzed (Botvinik-Nezer et al., in prep. ; Salomon et al, in prep.).
 - b. PC group: Reward-related regions: striatum, posterior cingulate cortex (PCC), dopaminergic midbrain (see Bartra, McGuire, & Kable, 2013; O'Doherty, 2004).
 - c. Both groups: Value related region: vmPFC.

2. Planned analyses

Behavioral data:

Probe

- *Will participants choose Go items more than NoGo items?*
- Repeated logistic regression testing choices of Go over NoGo items, with group and time (and their interaction) and item value (high and low) as independent factors. Hypothesis testing will include the interaction and the within-group slopes or the main effects, if the interaction will be significant or not, respectively.

BDM

- *Will the rating of items be different for Go vs. NoGo?*

- Regression of the change in WTP (BDM[2-5]-BDM1) between Go and NoGo items as dependent, with group, session and item value (high and low) as independent factors. Hypothesis testing will include the interaction and the within-group slopes or the main effects, if the interaction will be significant or not, respectively.

Memory task

- *Will Go items be remembered more than NoGo items?*
 - Accuracy:
 - i. Logistic regression for testing accuracy, with by group and time (and their interaction), item association (Go and NoGo) and item value (high and low) as independent factors.
 - ii. To interpret the group*time interaction, a Logistic regression for testing accuracy, item association (Go and NoGo) and item value (high and low) as independent factors, for each session and each group separately.
 - RT:
 - i. Regression for testing response times, with group and time (and their interaction), item association (Go and NoGo) and item value (high and low) as independent factors.
 - ii. To interpret the group*time interaction, a Regression for response times, item association (Go and NoGo) and item value (high and low) as independent factors, for each session and each group separately.

Memory & probe

- *Will better memory for items correlate with choices during probe?*
 - Logistic regression for testing choosing the Go item in probe by **accuracy** for the Go item and inverse accuracy for the NoGo item in the recognition task. Separately for each time point and each group.
 - Logistic regression for testing choosing the Go item in probe by **RT** in the recognition task (for the NoGo item minus Go item). Only for correctly identified items in the recognition task. Separately for each time point and each group.
 - Logistic regression for testing choosing the Go item in probe by **RT** in the **first** recognition task (for the NoGo item minus Go item). Only for correctly identified items in the recognition task. Separately for each time point and each group.

Eye tracking data:

- *Will participant look more at Go items vs. NoGo items?*
 - Regression for testing gaze time per item during probe, with item association (Go and NoGo) and item value (high and low) as independent factors, for each session and each group separately.
- *Will Go items draw more attention than NoGo items?*
 - Logistic regression for whether the first saccades was towards the Go item during the probe, with item value (high and low) as independent factor, for each session and each group separately.

fMRI data:

Response to snacks:

Univariate analysis

- *Will training change neural response while viewing Go vs. NoGo items? Will it be different between the groups?*

- First-level GLM analysis on each of the response to snacks runs with feat (including film autocorrelation modeling), second level GLM analysis on the after (response to snacks [2-6] minus before (response to snacks 1)) images of each subject with feat (fixed effects), and then:
- For each group, analyze the results of the second level with a correction based on Eklund et al.
- Comparing the change of activations between the CAT and Classic groups on the results of the second level with a correction based on Eklund et al.
- Longitudinal effects of sessions 1 to 5 will be analyzed using the SWE SPM toolbox.
- *Will neural response correlate with the initial value of items?*
 - GLM on the response to snacks run before training (response to snacks 1), with WTP from BDM 1 as a regressor, for both group together (since the experiment is identical between the two groups before training).

MVPA

- *Will differences in neural response while viewing Go vs. NoGo items dissociate between groups?*
 - Training the algorithm to distinguish between the PC and CAT groups images of the change of response to snacks for Go items vs. for NoGo items (difference of response to snacks [2-6] minus before (response to snacks 1)).
- *Will differences in neural response while viewing Go vs. NoGo items dissociate between learners and non-learners participants?*
 - Training the algorithm to distinguish between participants above and below the median of proportion choices of Go or NoGo item in the probe, by images of the change of response to snacks for Go items vs. for NoGo items (difference of response to snacks [2-6] minus before (response to snacks 1)).
- *Will neural response while viewing the items dissociates Go vs. NoGo items?*
 - Training the algorithm to distinguish between images of the change of response to snacks (difference of response to snacks [2-6] minus before (response to snacks 1)) for Go items vs. for NoGo items.
- *Will neural response while viewing the items dissociates between items that were subsequently chosen?*
 - Dissociate choosing Go: training the algorithm to distinguish between neural response during response to snacks towards items that were subsequently chosen vs. not chosen during probe. We will use separate models for each time point and for each group.
- *Are there distinct neural responses for items that were chosen vs. items that were trained?*
 - *Training two classifiers, to predict 1) Go vs. NoGo items and 2) chosen vs. non-chosen items. These two are intrinsically dependent since Go items are chosen more than NoGo items. Their convergence will indicate if they rely on similar neural systems.*
- *Will neural response while viewing the items in the first session predict subsequent choices in subsequent sessions?*
 - Dissociate choosing Go: training the algorithm to distinguish between neural response during response to snacks [after minus before training] towards items that were subsequently chosen vs. not chosen during probe [2-5]. Separately for each time point and for each group.

gPPI

- *Which functional connectivity patterns are associated with CAT?*
 - Connectivity of change of response to snacks after training (difference of response to snacks [2-6] minus before (response to snacks 1)) for Go items. We will use separate models for each time point and for each group. Seed regions: pre-hypothesized regions & significant regions (up to 10) from the GLM analysis.

Training

Univariate analysis

- *Will neural response change with the progress in training? Will it be different between the groups?*
 - First-level GLM analysis on each of the 6 training runs (each with 2 training repetitions) with feat.
 - Contrast the time variable in second level GLM analysis on the mean of these 6 runs to model the time difference in each subject:
 1. Last 2 runs > First 2 runs
 2. Linear trend model for the 6 runs -3, -2, -1, 1, 2, 3]
 - Group analysis on the results of the second level for each group separately, with a correction based on Eklund et al.
 - Then compare the differences between groups, with a correction based on Eklund et al.
- *Will neural response during training predict subsequent choices?*
 - In the above GLM analysis add a regressor with parametric modulations of choice proportion during probe, in order to identify regions in which activity levels were predictive of future behavior.

MVPA

- *Will neural response during training predict subsequent choices?*
 - Dissociate choosing Go: training the algorithm to distinguish between neural response during training towards items that were subsequently chosen vs. not chosen during probe. Separately for each time point and for each group.

Probe

Univariate analysis

- *Will neural response correlate with choosing Go over NoGo items?*
 - First-level GLM analysis on each of the 2 short-term probe runs with feat, second level GLM analysis on the mean of these four runs for each participant, and then:
 - i. Group analysis on the results of the second level, with a correction based on Eklund et al. Separately for each time point and for each group.
 - ii. Comparing differences between the CAT and Classic groups on the results of the second level, with a correction based on Eklund et al. Separately for each time point.

MVPA

- *Will neural response predict choosing Go over NoGo items?*
 - Training the algorithm to distinguish between trials in which the Go item was chosen vs. trials in which the NoGo item was chosen. Separately for each time point and for each group.

gPPI

- *Which functional connectivity patterns are associated with choosing Go over NoGo items?*
 - Connectivity on each probe (probe [1 -5]), following the above described GLM. Seed regions: pre-hypothesized regions & significant regions from the GLM analysis.

Resting state

- Analyzing 'classical' analysis of resting state, and their stability / reliability within subject over time

General note: We will use a correction based on Eklund et al. with acceptable correction for type 1 error, following Eklund et al. (Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. Proceedings of the National Academy of Sciences, 201602413.)