# Perceptual and memory neural processes underlie short and long-term non-reinforced behavioral change

Rotem Botvinik-Nezer[1,2], Tom Salomon[2] and Tom Schonberg[1,2*]

[1] Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel.

[2] Faculty of Life Sciences, Department of Neurobiology, Tel Aviv University, Tel Aviv, Israel.

* Corresponding author.

**Studies and behavioral interventions have focused on reinforcement and context change as means to influence preferences. Cue-approach training (CAT) has been shown to induce preference changes lasting months, towards items that were merely paired with a neutral cue and a speeded response without reinforcement. We scanned 36 participants with fMRI during a passive viewing task before, after and one month following CAT to study the neural basis of representation and modification of preferences in the absence of reinforcements. We found that enhanced visual processing in the short-term, and memory processes in the long-term, underlie value change. These results show for the first time a change in the neural representation of items in perceptual regions immediately after training and enhanced memory accessibility after 30 days. Our findings emphasize the potential of targeting the process of neural representation to accomplish long-term behavioral change and set the ground for new theories and clinical interventions.**

When faced with a choice between two food items, how do people make a choice? How can choices be affected to promote well-being? Understanding how preferences are constructed and modified is a major challenge in the research of

human behavior with broad implications, from basic science to interventions for long-lasting behavioral change[1,2].

The basic question of how preferences are represented in the brain has been the center of many animal and human studies alike[3–6]. These studies usually involve decisions between different items along several dimensions and are conducted under the assumption that decisions are made based on the comparison of subjective values of each choice alternative[1,3,4]. Previous studies identified a network of brain regions involved in value-based decision-making, mainly the ventromedial prefrontal cortex (vmPFC) and orbitofrontal cortex (OFC), which are considered the regions where values are computed and represented[4,5,7]. The striatum has been implicated in reinforcement learning[8], habit formation[9] and decision-to-motor transform together with the lateral prefrontal cortex[10,11].

The field of decision-making has focused mainly on two types of choice behaviors: Goal-directed (model-based) and habit-based (model-free)[12]. In goal-directed behavior, the value of each available option is computed and the behavior is guided by the potential value of the outcomes. In contrast, habit-based behavior occurs when an action is repeated and reinforced multiple times, omitting the dependency on the potential value of the outcome. These two types of behavior involve reinforcement, either during the evaluation (or learning) of a potential outcome or during the formation of a habit[3]. However, in a novel and unique paradigm for behavioral change, named cue-approach training (CAT)[13], preferences were successfully modified in the absence of external reinforcement.

In the CAT paradigm, the mere association of images of items with a cue and a speeded button-press response leads to preference changes lasting months following a single training session[13,14]. This paradigm putatively affects choices through

automatic processes without external reinforcement[2] and thus allows to obtain novel knowledge on how preferences are represented and affected without external reinforcement or context change. Experiments with CAT commonly consist of three main phases: An evaluation phase to obtain initial subjective preferences for various items, a training phase and a probe phase to evaluate preferences modification with binary choices. During CAT, images of items (originally snack-food items) appear on the screen one by one, and participants are instructed to press a button as fast as they can in response to a delayed cue. Unbeknownst to participants, some of the items are consistently paired with the cue and response (these are termed 'Go items') while the rest of the items are not ('NoGo items'). In a subsequent probe phase, participants choose their preferred item for consumption between pairs of items with similar initial subjective values, in which only one was a Go item, previously paired with the cued button press. Replicated results from multiple samples[13–17] show that participants significantly choose high-value Go over high-value NoGo items. Recently Salomon et al. (2018) demonstrated that CAT can be used to change preferences towards various types of stimuli (i.e. unfamiliar faces, fractal art images and positive affective images) with different types of cues (i.e. neutral auditory, aversive auditory and visual cues)[14], showing that the underlying mechanism of the task is general. Furthermore, preferences' change has been shown to last up to six months following a single training session lasting less than one hour[14], thus endorsing the applicability of CAT as a real-world intervention.

CAT is performed on single items and thus changes preferences of individual items, later manifested in binary choice. Furthermore, its low-level nature, not involving external reinforcement or high-level executive control, provides a unique opportunity to study preference representation and modification in the brain.

Previous studies with CAT were able to predominantly shed light on the neural signature of preference change during choice. Eye-gaze data revealed that during choices, attention is drawn towards Go items more compared to NoGo items even when the Go items were not chosen[13]. Functional MRI results demonstrated an enhanced BOLD signal in the vmPFC during choices of high-value Go items alone and compared to NoGo items[13]. These results indicate enhanced value processing during choices of Go compared to choices of NoGo items, but do not reveal the mechanism of value change in the single item level. A multi-voxel pattern analysis study was also not able to point to differences induced during CAT between Go and NoGo items in perceptual, memory or valuation components[15]. Putatively, functional imaging during training was uninformative as to the source of the value changes occurring during training due to widespread co-activation of the motor and sensory systems during Go items presentations, masking potential differences of Go versus NoGo items. Moreover, no attempt has been made yet to investigate the neural mechanism of the long-term effect of CAT.

Therefore, here we introduce a novel phase to shed light on how preferences toward individual items are represented and modified in the brain. We added a passive viewing task whereby items were presented individually on the screen before and after CAT. During this task, items were individually presented on the screen without any manipulation, while participants performed a sham counting task (Fig. 1b,d). We tested the different neural responses to Go versus NoGo items after training compared to baseline, as well as one month following training compared to baseline. Regions in the brain showing plasticity after training and one month later shed light on the general mechanisms of preference representation in the brain and specifically on how non-externally reinforced training leads to robust long-lasting preference changes.

Overall, current evidence suggests that the immediate behavioral change following CAT might involve attention modification and value enhancement[13,16]. Furthermore, the long-lasting nature of the effect raises the possibility that memory processes are also involved. Therefore, we hypothesized that preferences are highly dependent on attentional and memory-related mechanisms, affecting value representation. In our pre-registered hypotheses (https://osf.io/q8yct/?view_only=360ad8ba027b4a85ab56b1586d6ad6c9), we predicted greater BOLD activity after CAT in response to high-value Go items in episodic memory-related regions in the medio-temporal lobe, top-down attention-related dorsal parietal cortex and prefrontal value-related regions. In addition, we hypothesized we will replicate previous CAT results showing a significant behavioral effect of choosing high-value Go over high-value NoGo items during probe and increased BOLD activity in the vmPFC during choices of high-value Go items[13–18]. Results from this study will help isolate neural representation of preferences that are not based on external rewards and lead to better behavioral change interventions.

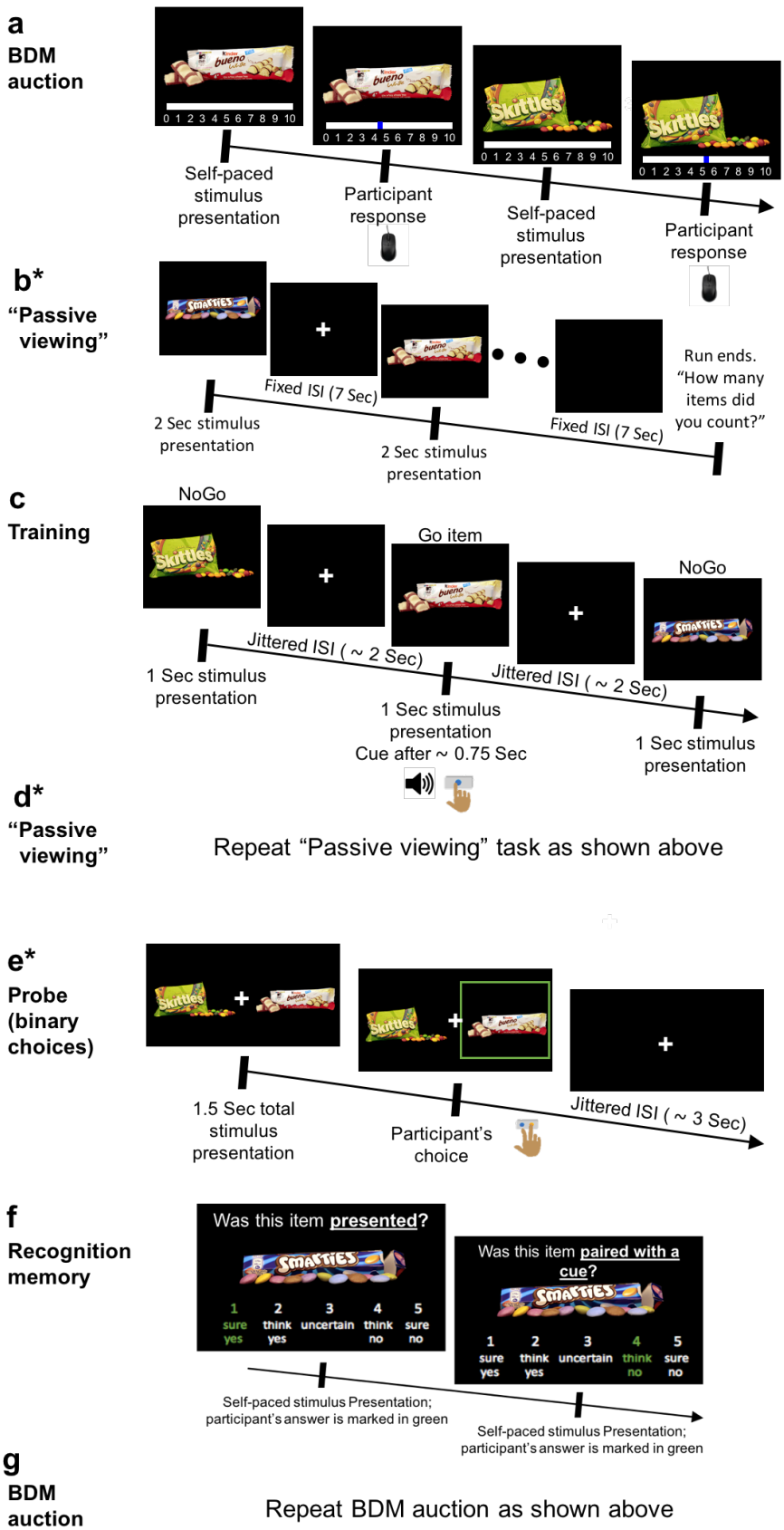
a
BDM auction
0 1 2 3 4 5 6 7 8 9 10
Self-paced stimulus presentation
Participant response
Self-paced stimulus presentation
Participant response
b*
"Passive viewing"
Fixed ISI (7 Sec)
2 Sec stimulus presentation
2 Sec stimulus presentation
Fixed ISI (7 Sec)
Run ends. "How many items did you count?"
c
Training
NoGo
Go item
NoGo
Jittered ISI ( ~ 2 Sec)
Jittered ISI ( ~ 2 Sec)
1 Sec stimulus presentation
1 Sec stimulus presentation
Cue after ~ 0.75 Sec
1 Sec stimulus presentation
d*
"Passive viewing"
Repeat "Passive viewing" task as shown above
e*
Probe (binary choices)
1.5 Sec total stimulus presentation
Participant's choice
Jittered ISI ( ~ 3 Sec)
f
Recognition memory
Was this item presented?
1 sure yes
2 think yes
3 uncertain
4 think no
5 sure no
Was this item paired with a cue?
1 sure yes
2 think yes
3 uncertain
4 think no
5 sure no
Self-paced stimulus Presentation; participant's answer is marked in green
Self-paced stimulus Presentation; participant's answer is marked in green
g
BDM auction
Repeat BDM auction as shown above

***Figure 1.*** *Outline of the experimental procedures. (a) Initial preferences were evaluated using the Becker–DeGroot–Marschak (BDM) auction procedure[19]. (b) "Passive viewing", a new task in which items are individually presented on the screen, while participants passively observe them and perform a sham counting task. (c) Cue-approach training: Participants were instructed to press a button as fast as they could whenever they heard an auditory cue, and before the item disappeared from the screen. Items were presented on the screen one by one. Go items were consistently paired with the cue and button press response, while NoGo items were not. (d) The "passive viewing" task was repeated after training. (e) In the probe task, participants chose their preferred item between pairs of items with similar initial subjective preferences, one Go and one NoGo item. (f) A recognition memory task. (g) The BDM auction was repeated.*
*Procedures performed inside the MRI scanner (during a functional scan) are marked with an asterisk. Stages e-g were performed again in the one-month follow-up session.*

## Results

### Behavioral probe results

***After CAT.*** Participants (N = 36) significantly preferred Go over NoGo items in high-value probe choices (mean = 59.0%, $P$ = 0.002, one-sided logistic regression) and marginally also in low-value probe choices (mean = 56.1%, $P$ = 0.051; Fig. 2). The proportion of Go items choices was significantly higher for high-value compared to low-value items (indicating a differential effect of CAT on preference for stimuli of the two value categories, $P$ = 0.015, one-sided logistic regression). These results were predicted based on previous studies and replicated them[13–15,20].

***One-month follow-up.*** One month following training (mean = 30.26 days, SD = 9.93 days, N = 27) participants significantly chose Go over NoGo items in both high-value (mean = 56.3%, $P$ = 0.032) and low-value (mean = 57.2%, $P$ = 0.026) probe trials. There was no differential effect in this session ($P$ = 0.267).

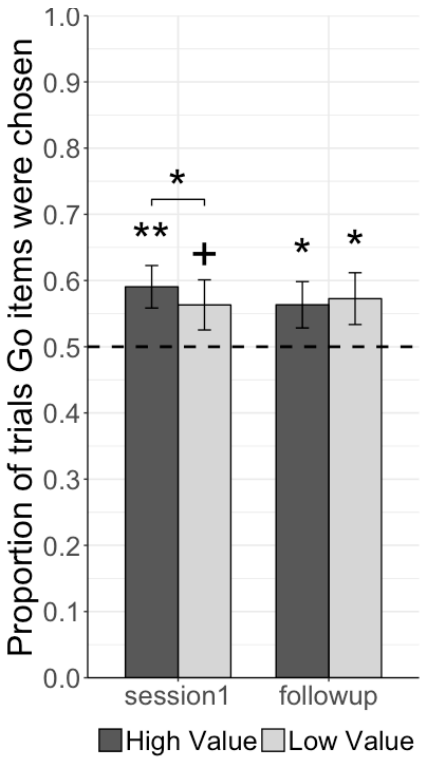


***Figure 2**. Behavioral results of Go choices during probe. Mean proportion of trials in which participants chose Go over NoGo items are presented for high-value (dark gray) and low-value (light gray) probe pairs, for each session (session1 / follow-up). The dashed line indicates chance level of 50%, error bars represent standard error of the mean. Asterisks reflect statistical significance in a one-tailed logistic regression analysis. Asterisks above each line represent proportions higher than chance (log-odds = 0, odds-ratio = 1). Asterisks above pairs of bars represent differential effect between the two value categories; +P < 0.1, *P < 0.05, **P < 0.005.*

**Imaging results**

Behavioral results with snack food items from previous studies[13–15] and from the current study demonstrated a consistent differential pattern of the change of preferences across value level: Preferences modifications were more robust for high-value compared to low-value items. Therefore, in our imaging results, we chose to focus on the functional changes in the representation of high-value items, which had more dominant behavioral modification effect. We further tested two kinds of relations between the behavioral effect and the neural response: *Modulation across items*, meaning that the change in activity was stronger for items that were later more

165 preferred during the subsequent probe phase (within-participant first-level parametric
166 modulation); and *correlation across participants*, meaning that the change in activity
167 was stronger for participants that later showed a stronger behavioral effect quantified
168 as higher ratio of choosing high-value Go over high-value NoGo items (between-
169 participants group-level correlation). Finally, for a subset of three pre-hypothesized
170 and pre-registered regions (vmPFC, hippocampus and superior parietal lobule) we
171 performed a small volume correction (SVC) analysis (see online methods).
172 Untresholded images of all contrasts presented here can be found on NeuroVault[21]
173 (https://neurovault.org/collections/TTZTGQNU/)
174

175 **Passive viewing imaging results**

176 To investigate the functional changes in the response to the individual items following
177 CAT, we scanned participants with fMRI while they were passively viewing the items.
178 Participants completed this task before, after and one month following CAT (N = 36;
179 follow-up N = 27).

180 ***After CAT*** *(Fig. 3, for description of all activations see Supplementary Table 2).* BOLD
181 activity while passively viewing high-value Go compared to high-value NoGo items
182 was increased after compared to before CAT in the left and right occipital and temporal
183 lobes (Fig. 3a), along the ventral visual processing pathway[22].

184 Results of the SVC analyses revealed enhanced BOLD activity during passive viewing
185 of high-value Go items after compared to before CAT in the vmPFC (Fig. 3b).

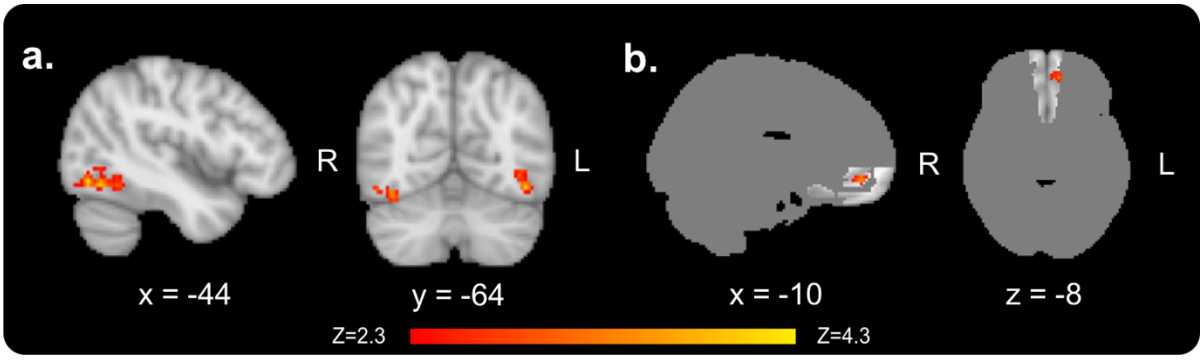


***Figure 3.*** *fMRI results from the passive viewing task after compared to before CAT. (a) Enhanced BOLD activity in bilateral occipito-temporal regions, for high-value Go compared to high-value NoGo items (whole-brain analysis). (b) Enhanced BOLD activity in the vmPFC in response to high-value Go items (Small volume corrected results; the mask used is presented on a dark grey brain silhouette). For description of all activations see Supplementary Table 2.*

***One-month follow-up*** *(Fig. 4, for description of all activations see Supplementary Table 3).* Comparison of the BOLD activity in response to high-value Go items in the follow-up compared to before CAT did not reveal significant clusters with whole-brain correction. However, similar to the short-term change, BOLD activity in the vmPFC was found to be enhanced with SVC analyses (Fig. 4a). In addition, BOLD activity in the left orbitofrontal cortex (OFC) in response to high-value Go items was positively modulated by the choice effect across items in the follow-up compared to before CAT (whole-brain analysis; Fig. 4b). SVC analyses revealed that BOLD activity in response to high-value Go items in the right anterior hippocampus was positively modulated by the choice effect across items in the follow-up compared to before training (Fig. 4c), while BOLD activity in response to high-value Go minus high-value NoGo items in the right SPL was negatively correlated with the choice effect across participants in the follow-up compared to before training (Fig. 4d).

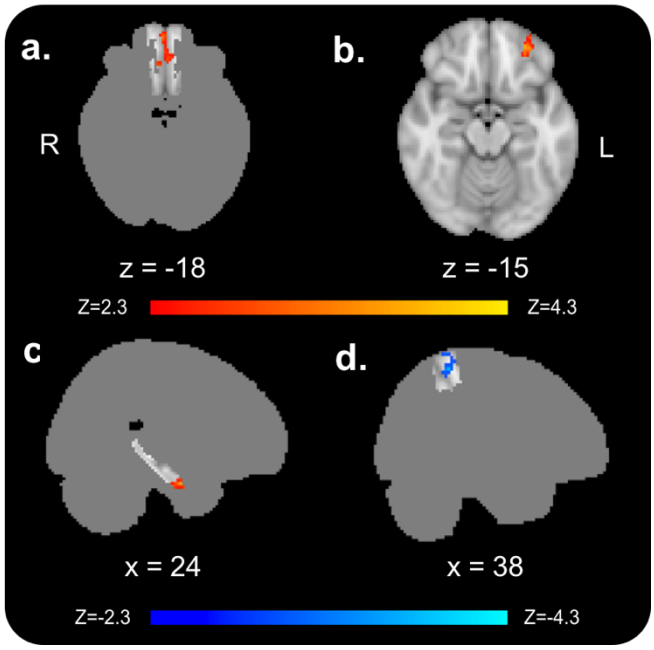


***Figure 4.*** *fMRI results from the passive viewing task in the one-month follow-up compared to before CAT. (a) Enhanced BOLD activity in response to high-value Go items in the vmPFC (small volume corrected). (b) BOLD activity in response to high-value Go items in the left OFC was positively modulated by the choice effect across items (whole-brain analysis). (c) BOLD activity in response to high-value Go items in the right anterior hippocampus was positively modulated by the choice effect across items (small volume corrected). (d) BOLD activity in response to high-value Go minus high-value NoGo items in the right SPL was negatively correlated with the choice effect across participants (small volume corrected). The masks used for the small volume correction (SVC) analyses are presented on a dark grey brain silhouette. For description of all activations see Supplementary Table 3.*

Inspection of the uncorrected results (z > 2.3) revealed increased visual enhancement for high-value Go compared to high-value NoGo items in the follow-up compared to before CAT, in visual regions similar to the ones found to be enhanced after CAT. However, these clusters did not exceed statistical significance following whole-brain cluster correction and were not preregistered; therefore, we did not perform an SVC analysis for these regions.

226 **Probe imaging results**

227 To investigate the functional response during choices, we scanned participants with
228 fMRI while they completed the probe (binary choices) phase, as was done in previous
229 studies[13,15]. Participants completed the probe task after CAT (N = 33) as well as in the
230 one-month follow-up for the first time (N = 25).

231 ***After CAT*** *(Fig. 5, for description of all activations see Supplementary Table 4).* BOLD
232 activity was stronger during choices of high-value Go compared to choices of high-
233 value NoGo items in bilateral visual regions and bilateral central opercular cortex and
234 Heschl's gyrus (Fig. 5a). In addition, BOLD activity in the striatum while choosing high-
235 value Go compared to high-value NoGo items after CAT was negatively correlated
236 with the choice effect across participants (the ratio of choosing high-value Go items
237 during probe; Fig. 5b) and negatively modulated by the choice affect across items (Fig.
238 5c). SVC analysis revealed that BOLD activity in the right SPL while choosing high-
239 value Go items after CAT was negatively correlated with the choice effect across
240 participants (Fig. 5d) and negatively modulated by the choice effect across items (Fig.
241 5e).

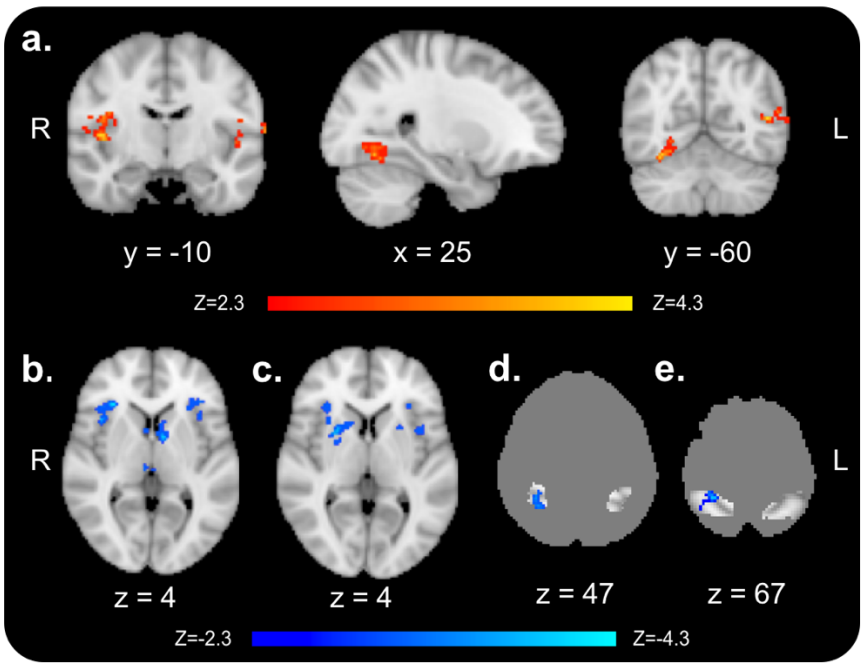


***Figure 5.*** *fMRI results from the probe task after CAT: (a) Enhanced BOLD activity during choices of high-value Go compared to choices of high-value NoGo items in bilateral visual regions and bilateral central opercular cortex and Heschl's gyrus (whole-brain analysis). (b) BOLD response negatively correlated with the choice effect across participants and (c) negatively modulated by the choice effect across items, during choices of high-value Go over high-value NoGo items in the striatum as well as other regions (whole-brain analysis). (d) BOLD response negatively correlated with the choice effect across participants and (e) negatively modulated by the choice effect across items, during choices of high-value Go compared to high-value NoGo items, in the right SPL (small volume corrected). The masks used are presented on a dark grey brain silhouette. For description of all activations see Supplementary Table 4.*

***One-month follow-up*** *(Fig. 6, for description of all activations see Supplementary Table 5).* BOLD activity in the precuneus, bilateral superior occipital cortex and bilateral middle and superior temporal gyrus while choosing high-value Go items in the follow-up was positively modulated by the choice effect across items (Fig. 6a). BOLD activity in the precuneus/posterior cingulate cortex (PCC) and right post-central gyrus while choosing high-value Go items in the follow-up was positively correlated with the choice effect across participants (Fig. 6b).

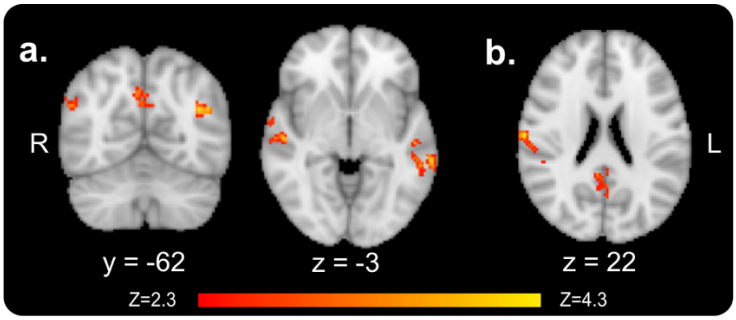


***Figure 6.*** *fMRI results from the probe task in the one-month follow-up: BOLD activity during choices of high-value Go items (whole-brain analyses) was (a) positively modulated by the choice effect across items in the precuneus, bilateral superior occipital cortex and bilateral middle and superior temporal gyrus and (b) positively correlated with the choice effect across participants in the precuneus/posterior cingulate cortex (PCC) and right post-central gyrus. For description of all activations see Supplementary Table 5.*

## Discussion

Research of value-based decision-making and behavioral change mainly focused on reinforcement and context change as means to change preferences[3,23,24]. The cue-approach training (CAT) paradigm has been shown to change preferences using the mere association of a cue and a speeded button response without external reinforcement. The paradigm is highly replicable with dozens of studies demonstrating the ability to change behavior for months with various stimuli and cues[13–18]. The behavioral results obtained in the current study replicated previous studies, demonstrating enhanced preferences towards high-valued cued (high-value Go) compared to high-valued non-cued (high-value NoGo) items following CAT[13–18]. Importantly, CAT utilizes low-level associations to induce long-term change of preferences at the item level, without external reinforcement or high-level self-control mechanisms, and thus it provides a unique opportunity to study how preferences are represented and modified in the brain at the individual item level in the absence of reinforcement. Here we introduced a new passive viewing task to study the functional

286 plasticity of the response to single items before, after and one month following CAT,
287 in order to deepen our understanding of the neural mechanisms involved in non-
288 reinforced preferences modification, both in the short and in the long term.
289 Prior to data analysis, we predicted and preregistered that the underlying neural
290 mechanisms will involve memory, attention and value-related brain regions. We found
291 enhancement of visual processing for Go compared to NoGo items after training
292 during passive viewing. We show for the first time that activity in high-level visual
293 processing occipito-temporal cortex is related to subjective values without rewards. By
294 recording eye-gaze from a sub-group of our participants during this task, we found that
295 enhanced activity in occipito-temporal visual cortex was probably not the result of
296 longer gaze duration on paired items (see Supplementary Data). Activity in low and
297 high-level visual regions was previously shown to be related to value, but this activity
298 was related to past rewards and not to subjective values[25].
299 We also found evidence for enhanced BOLD response in the vmPFC for cued items,
300 after CAT and in the one-month follow-up, indicating a long-lasting value change
301 signature[26,27] of individual items not during choice. These results reveal for the first
302 time an item-level value change during passive viewing[25,26], in accordance with
303 previous findings of enhanced activity in the vmPFC during binary choices of more
304 preferred high-value Go items[13,15]. In addition, this is the first time, to the best of our
305 knowledge, that such enhancement in value-related prefrontal regions is found one
306 month following a behavioral change paradigm.
307 In the follow-up session, we further found that the long-term behavioral change was
308 related to plasticity in memory, attention and value-related brain regions. In addition to
309 the enhancement of activity in the vmPFC described above, the change in BOLD
310 response to the cued Go items in the left OFC and right hippocampus was positively

311 modulated by the choice effect across items, meaning that activity in these regions
312 was stronger while viewing Go items which were chosen more during the subsequent
313 probe phase.
314 We suggest that the functional changes in the bilateral occipito-temporal visual regions
315 reflect modifications in the representation of the paired items[28–30], following the low-
316 level association of visual images with auditory cues and motor responses during
317 training. The bottom-up enhanced perceptual processing and representation of paired
318 items led to enhanced value-related processing, reflected as enhanced activity in the
319 vmPFC, and thus to choices of these items over non-paired items[25]. The bottom-up
320 enhanced short-term perceptual processing enhancement affected the encoding and
321 accessibility of paired items and their related associations in memory for the long-term.
322 This suggests why in the one-month follow-up, visual processing was enhanced to a
323 lesser extent, while memory-related processes drove the long-term behavioral effect.
324 In addition to these results, the change in BOLD response in the long-term (follow-up
325 greater than before CAT) in the right SPL was negatively correlated with the choice
326 effect across participants; i.e. participants with overall greater behavioral change
327 demonstrated reduced change of BOLD response to high-value Go items in this
328 region. Although the SPL was one of our pre-hypothesized regions, we expected a
329 positive relation between the behavioral effect and the change of activity in this region.
330 This finding might indicate less involvement of top-down attention mechanisms during
331 passive viewing of Go compared to NoGo items[31].
332 We further compared BOLD response during choices of paired versus non-paired
333 items during the probe phase. BOLD response was enhanced mainly in visual and
334 auditory related regions in the occipital and temporal lobes. This strengthens the
335 finding of enhanced perceptual processing of paired items during passive viewing by

336 indicating that visual, as well as auditory processing, are also enhanced during choices
337 of paired over non-paired items. These findings suggest that bottom-up processing is
338 putatively driving the short-term enhanced preferences towards Go items.
339 Furthermore, activity in the right SPL during choices of paired items was negatively
340 modulated by the choice effect across items as well as negatively correlated with the
341 choice effect across participants (though in a more posterior and inferior region),
342 indicating that top-down attentional mechanisms were less involved during choices of
343 Go compared to choices of NoGo items[31]. Activity in the striatum, a region known to
344 be involved in reinforcement learning and habit-based learning[9,32], was also negatively
345 correlated with choices of paired over non-paired items, both in a parametric
346 modulation across items (mainly in the right putamen) as well as a correlation with the
347 behavioral effect across participants (mainly in the left caudate). These findings
348 potentially suggest that cue-approach training shifted the process of goal-directed
349 decision-making during binary choices to be more automatic and based on non-
350 reinforced mechanisms. Although previous studies included fMRI during the probe
351 phase, this is the first study with CAT to observe this effect in the striatum and thus it
352 remains to be replicated in future studies[13,15]. In the follow-up session, choices of
353 paired compared to non-paired items were related to enhanced BOLD activity in the
354 precuneus and posterior cingulate cortex (PCC), which have been related to episodic
355 memory retrieval (and are also considered to be part of the default mode network)[33–
356 37], for participants that had a stronger behavioral effect and for items toward which
357 preferences were more enhanced. This again demonstrates the central role of
358 memory processes in the long-term behavioral change.
359 Overall, results obtained from the fMRI data during binary choices showed a similar
360 pattern to those obtained during passive viewing: Enhanced perceptual processing in

361 the short-term and involvement of episodic memory processes in the long-term. We
362 were not able to replicate previous results of enhanced activity in the vmPFC during
363 choices of paired items, modulated by the number of choices of each item during probe
364 (modulation across items)[13,15]. These previous results were found for high-value Go
365 items when the group's behavioral effect of choosing high-value Go over high-value
366 NoGo items was significant but weak relative to other samples (study 3 in Schonberg
367 et al., 2014[13]). Similar results were found for choices of low-value Go compared to
368 choices of low-value NoGo items when the behavioral effect was strong for high-value
369 items and weak for low-value items[15]. Therefore, a possible explanation for the lack of
370 replication of these findings in the current study is that this contrast of modulation
371 across items depends on the variance of the choice effect across items, which seems
372 to be smaller here compared to previous samples that found this effect.
373 Related to this potential issue of variance is the fact that the CAT effect is a group
374 effect. Not all participants choose paired over non-paired items following training, and
375 there is a considerable variance across participants. In addition, training is performed
376 on the individual item level, and thus preferences are affected only for some but not
377 all paired items. The CAT effect at the one-month follow up was relatively weak. This
378 might explain why our findings immediately after CAT were found in contrasts testing
379 for main effects across all high-valued paired items, whereas results from the one-
380 month follow-up were obtained mainly in parametric modulation of choices across
381 items (within participants). Since the long-term behavioral effect was weaker than the
382 effect in the short-term, the variance across items was larger and enabled us to find
383 differences in the response to different items in the follow-up session.
384 The behavioral change of preferences in the one-month follow-up was relatively weak
385 in the current study, although the behavioral effect was found to last for up to six

386 months in previous studies[13,14]. This may be a side-effect of the new passive viewing
387 task which was completed before, after and one month after training. In this task, items
388 are presented on the screen without cues or motor responses. The task is completed
389 three times before the follow-up probe (choice) phase, which might cause partial
390 extinction of the item-cue pairing established during training. In accordance with the
391 marginally significant behavioral follow-up effect, the visual enhancement during
392 passive viewing of paired compared to non-paired items was also present in the one-
393 month follow-up (but only with $z>2.3$ uncorrected), but did not exceed statistical
394 significance following cluster-based correction for multiple comparisons.
395 Our results suggest that in the short-term, perceptual processing is enhanced beyond
396 all paired items, while in the long-term, the effect persists only for some of the items,
397 and thus the overall behavioral effect is weaker and the neural changes are for specific
398 items, these that elicited stronger response in memory-related regions, and not for all
399 paired items. Furthermore, in the follow-up session we also found a negative
400 correlation between the change of activity and the behavioral effect across participants
401 (a group level correlation) in the parietal lobe. Since this correlation is not item-specific,
402 but participant-specific, it informs us about the neural changes that were stronger for
403 participants that were more affected by CAT.
404 Up until the current study it was not clear what is the mechanism underlying the CAT
405 effect, unexplained by current value-based decision-making theories. How are
406 preferences represented in the brain and why such a simple training changes them for
407 the long-term? Based on the findings of the current study, we suggest that low-level
408 association-based paradigms, such as CAT, affect the neural representation of
409 targeted individual items and draw bottom-up attention (manifested in previous studies
410 with eye-gaze during binary choices[13]) towards them (although probably less top-down

411 attention). In the short-term, the enhanced bottom-up processing of individual Go
412 items leads to enhanced preferences towards them when a fast binary choice is
413 required (and with less top-down attention during these choices). In the long-term,
414 enhanced perceptual processing and attention affected encoding and accessibility of
415 these items in memory. During choices, positive associations in favor of the more
416 accessible paired items accumulates faster to choices[38].
417 A previous influential review proposed a framework for studying the neurobiology of
418 value-based decision-making[3]. They divided the decision-making process into five
419 main computations: Representation, valuation, action selection, outcome evaluation
420 and learning. Regarding the representation stage, they stated that "unfortunately, little
421 is known about the computational and neurobiological basis of this step". Previous
422 research of the representation stage has mainly focused on reinforcement learning
423 (e.g. Wilson and Niv, 2012[39]). Our findings emphasize the importance of the
424 representation stage and the necessity of studies investigating the representation of
425 choice alternatives and its relation to preferences. Moreover, our findings with CAT
426 highlight the potential of utilizing this process in order to accomplish long-term
427 behavioral change. Finally, they highlight the importance of memory in the
428 construction and modification of preferences[38,40].
429 Gaining knowledge on the representation stage of decision-making and on non-
430 reinforced change of preferences has great potential as a fruitful path for new theories
431 relating neural mechanisms such as perceptual processing, memory and attention to
432 preferences. It also holds great promise for new long-term behavioral change
433 interventions based on automatic mechanisms, which might improve the quality of life
434 for people around the world.

## Methods

**Data sharing.** Behavioral data and codes are available at the Open Science Framework: https://osf.io/ts7b5/?view_only=c867c80179264ae5874af3d26ec39914. Imaging data is available in Brain Imaging Data Structure (BIDS) format[41] at OpenNeuro: https://openneuro.org/datasets/ds001417. Unthresholded statistical images are available at NeuroVault[21]: https://neurovault.org/collections/TTZTGQNU/.

**Participants**. Forty healthy right-handed participants took part in this experiment. The sample size was chosen before data collection and pre-registered during data collection (https://osf.io/kxh9y/?view_only=4476c6fd74a84f0eb5a893df7e46700a). We initially planned to collect n = 35 participants based on previous imaging CAT samples and based on predicted 10% attrition for the one-month follow-up. However, during data collection we realized attrition rates are higher than expected, thus the planned sample size was increased to n = 40 (before exclusions and attrition), and re-pre-registered. The total number of participants included in the final analyses of the first session is 36 (19 females, age: mean = 26.11, SD = 3.46 years). Twenty-seven participants completed the follow up session (15 females, age: mean = 26.15, sd = 3.44 years).

*Exclusions.* A total of four participants were excluded: One participant due to incompletion of the experiment, one based on training exclusion criteria (7.5% false alarm rate during training) and two participants with incidental brain findings.

All participants had normal or corrected-to-normal vision and hearing, no history of eating disorders or psychiatric, neurologic or metabolic diagnoses, had no food restrictions and were not taking any medications that would interfere with the experiment. They were asked to refrain from eating for four hours prior to arrival to the

460 laboratory[13]. All participants gave informed consent. The study was approved by the
461 institutional review board at the Sheba Tel Hashomer Medical Center and the ethics
462 committee at Tel Aviv University.
463
464 **Stimuli**: Sixty color images of familiar local snack food items were used in the current
465 experiment. Images depicted the snack package and the snack itself on a
466 homogenous black rectangle sized 576 x 432 pixels (see Supplementary Table 1;
467 Stimuli dataset was created in our lab and is available online at
468 http://schonberglab.tau.ac.il/resources/snack-food-image-database/). All snack food
469 items were also available for actual consumption at the end of the experiment.
470 Participants were presented with the real food items at the beginning of the experiment
471 in order to promote incentive compatible behavior throughout the following tasks.
472
473 **Experimental procedure:** The general task procedure was similar to previous studies
474 with CAT[13,14]. In order to test for functional changes of the neural response to the
475 individual items following CAT, we added a new passive viewing task before, after and
476 one month following training.
477 First, we obtained the subjective willingness to pay (WTP) of each participant for each
478 of the 60 snack food items using a Becker-DeGroot-Marschak (BDM) auction
479 procedure, performed outside the MRI scanner (see Fig. 1a,g)[19,42]. Then, participants
480 entered the scanner and completed two "passive viewing" runs while scanned with
481 fMRI (see Fig. 1b,d), followed by anatomical and diffusion-weighted imaging (DWI)
482 scans. Afterwards, participants went out of the scanner and completed cue-approach
483 training (CAT) in a behavioral testing room at the imaging center (see Fig. 1c). They
484 then returned to the scanner and were scanned again with anatomical and DWI. Then,

485 they were scanned with fMRI while performing two more runs of the “passive viewing”
486 task and four runs of the probe phase, during which they chose between pairs of items
487 (see Fig. 1e). Finally, participants completed a recognition task outside the scanner
488 (see Fig. 1f), during which they were presented with snack items that appeared in
489 previous parts of the experiment, as well as new items, and were asked to indicate for
490 each item whether it was presented during the experiment and whether it was paired
491 with the cue during training. As the last task during the first day of scanning, they again
492 completed the BDM auction to obtain their WTP for the snacks.
493 *Follow-up session*. Approximately one month after the first day of the experiment,
494 participants returned to the lab. They entered the scanner, were scanned with
495 anatomical and DWI scans and completed two “passive viewing” runs as well as
496 another probe phase (without additional training). Finally, participants completed the
497 recognition and BDM auction parts, outside the scanner.
498 Anatomical and diffusion-weighted imaging data were obtained for each participant
499 before, immediately after and one month following training. Analyses of diffusion data
500 are beyond the scope of this paper.
501
502 *Initial preferences evaluation* (see Fig. 1a,g). In order to obtain initial subjective
503 preferences, participants completed a BDM auction procedure[19,42]. Participants first
504 received 10 Israeli Shekels (ILS; equivalent to ~2.7$ US). During the auction, 60 snack
505 food items were presented on the screen one after the other in random order. For each
506 item, participants were asked to indicate their willingness to pay (WTP) for the
507 presented item. Participants placed their bid for each item using the mouse cursor
508 along a visual analog scale, ranging from 0-10 ILS (task was self-paced). Participants
509 were told in advance that at the end of the experiment, the computer will randomly

510 generate a counter bid ranging between 0 - 10 ILS (with 0.5 increments) for one of the
511 sixty items. If the bid placed by the participant exceeds the computer's bid, she or he
512 will be required to buy the item for the computer's lower bid price. Otherwise, the
513 participant will not be allowed to buy the snack but gets to retain the allocated 10 ILS.
514 Participants were told that at the end of the experiment, they will stay in the room for
515 30 minutes and the only food they will be allowed to eat is the snack (in case they
516 "won" the auction and purchased it). Participants were explicitly instructed that the
517 best strategy for this task was to indicate their actual WTP for each item.
518
519 *Item selection***.** For each participant, items were rank ordered from 1 (highest value) to
520 60 (lowest value) based on their WTP. Then, 12 items (ranked 7-18) were defined as
521 high-valued items to be used in probe, and 12 items (ranked 43-54) were defined as
522 low-valued items to be used in probe. Each group of twelve items (high-value or low-
523 value) was split to two sub groups with identical mean rank. Six of the 12 items were
524 chosen to be paired with the cue during training (Go items; training procedures are
525 described in the following sections), and the other six were not paired with the cue
526 during training (NoGo items). This allowed us to pair high-value Go and high-value
527 NoGo items, or low-value Go with low-value NoGo items, with similar initial WTPs, for
528 the probe binary choices. To maintain 30% frequency of Go items during training
529 (similar to previous studies with CAT[13–15,18]), we used 16 more NoGo items that were
530 also used during training and passive viewing (40 snacks overall; see *Supplementary*
531 *Fig. 1* for a detailed description of all stimuli allocation).
532
533 *Passive viewing* (*see Fig. 1b,d*). The task was performed inside the scanner, while
534 participants were scanned with fMRI. This new task was introduced to evaluate the

535 functional changes in the response to the individual items following CAT. The neural
536 signature of the participants' response to each of the individual items was obtained in
537 three different time points: A baseline measurement before CAT, after CAT and in a
538 one-month follow-up. In this task, participants passively viewed a subset of 40 items,
539 which were presented in the training procedure (see *item selection* section and
540 *Supplementary Fig. 1*). The task consisted of two runs (in each session). On each run,
541 each of the 40 items was presented on the screen for a fixed duration of two seconds,
542 followed by a fixed inter-stimulus interval (ISI) of seven seconds. Items were presented
543 in random order. To ensure participants were observing and processing the presented
544 images, we asked them to perform a sham task of silently counting how many items
545 were of snacks containing either one piece (e.g. a 'Mars' chocolate bar) or several
546 pieces (e.g. a 'M&M' snack) in a new package. At the end of each run, participants
547 were asked how many items they counted. Task instructions (count one / several)
548 were counterbalanced between runs for each participant. The time elapsed between
549 the two runs before training and two runs after training was about two hours (including
550 cue-approach training, anatomical and diffusion weighted scans before and after
551 training and time to exit and enter the scanner).

552 *Cue-approach training* (see *Fig. 1c*)**.** Training was performed outside the scanner. The
553 training task included the same 40 items presented in the passive viewing task. Each
554 image was presented on the screen one at a time for a fixed duration of one second.
555 Participants were instructed to press a button on the keyboard as fast as they could
556 when they heard an auditory cue, which was consistently paired with 30% of the items
557 (Go items). Participants were not informed in advance that some of the items will be
558 consistently paired with the cue, or the identity of the Go items. The auditory cue
559 consisted of a 180ms-long sinus wave function. The auditory cue was heard initially

750ms after stimulus onset (Go-signal delay, GSD). To ensure a success rate of around 75% in pressing the button before stimulus offset, we used a ladder technique to update the GSD. The GSD was increased by 16.67ms following every successful trial and decreased by 50ms if the participant did not press the button or pressed it after the offset of the stimulus (1:3 ratio). Items were followed by a fixation cross that appeared on the screen for a jittered ISI with an average duration of two seconds (range 1-6 seconds). Each participant completed 20 repetitions of training, each repetition included all 40 items presented in a random order. A short break was given following every two training repetitions, in which the participants were asked to press a button when they were ready to proceed. The entire training session lasted about 40-45 minutes, depending on the duration of the breaks, which were controlled by the participants.

**Probe** (see *Fig. 1e*). Probe was conducted while participants were scanned with fMRI. The probe phase was aimed to test participants' preferences following training. Participants were presented with pairs of items that had similar initial rankings (high-value or low-value), but only one of the items in each pair was associated with the cue during training (e.g. high-value Go vs. high-value NoGo). They were given 1.5 seconds to choose the item they preferred on each trial, by pressing one of two buttons on an MRI-compatible response box. Their choice was highlighted for 0.5 second with a green rectangle around the chosen items. If they did not respond on time, a message appeared on the screen, asking them to respond faster. A fixation cross appeared at the center of the screen between the two items during each trial, as well as during the ISI, which lasted on average three seconds (range 1-12 seconds).

The probe phase consisted of two blocks. On each block, each of the six high-value Go items were compared with each of the six high-value NoGo items (36 comparisons), as well as each of the six low-value Go items with each of the six low-value NoGo items. Thus, overall there were 72 pairs of Go-NoGo comparisons (each repeated twice during probe, once on each block). In addition, on each block we compared each of two high-value NoGo items versus each of two low-value NoGo items, resulting in four probe pairs that were used as “sanity checks” to ensure participants chose the items they preferred according to the initial WTP values obtained during the BDM auction. Each probe block was divided to two runs, each consisted of half of the total 76 unique pairs (38 trials on each run). All pairs within each run were presented in a random order, and the location of the items (left/right) was also randomly chosen. Choices during the probe phase were made for consumption to ensure they were incentive-compatible. Participants were told that a single trial will be randomly chosen at the end of the experiment and that they will receive the item they chose on that specific trial. The participants were shown the snack box with all snacks prior to the beginning of the experiment.

**Recognition** (see *Fig. 1f*). Participants completed a recognition task, were the items from the probe phase, as well as new items, were presented on the screen one by one and they were asked to indicate for each item whether or not it was presented during the experiment and whether or not it was paired with the cue during training. Analysis of this task is beyond the scope of this paper.

**One-month follow–up session.** All participants were invited to the follow-up session approximately one month after training. A subset of 27participants returned to the lab

609 and completed the follow-up session. They were scanned with anatomical and
610 diffusion protocols, completed two passive viewing runs and performed another probe
611 while scanned with fMRI protocols, similar to the first session. In the follow-up session,
612 the probe included the same pairs as the probe of the first session, presented in a new
613 random order. Afterwards, participants completed another session of the recognition
614 task and a third BDM auction, both outside the scanner in the testing room.
615
616 **Behavioral analysis of the probe phase**. Similar to previous studies using cue-
617 approach task[13,14], we performed a repeated-measures logistic regression to compare
618 the odds of choosing Go items against chance level (log-odds = 0; odds ratio = 1) for
619 each trial type (high-value / low-value). We also compared the ratio of choosing the
620 Go items between high-value and low-value pairs. These analyses were conducted
621 for each session separately.
622
623 **MRI acquisition.** Imaging data were acquired using a 3T Siemens Prisma MRI
624 scanner with a 64-channel head coil, at the Strauss imaging center on the campus of
625 Tel Aviv University. Functional data were acquired using a T2*-weighted echo planer
626 imaging sequence. Repetition time (TR) = 2000ms, echo time (TE) = 30ms, flip angle
627 (FA) = 90°, field of view (FOV) = 224 × 224mm, acquisition matrix of 112 × 112. We
628 positioned 58 oblique axial slices with a 2 × 2mm in plane resolution 15° off the anterior
629 commissure-posterior commissure line to reduce the frontal signal dropout[43], with a
630 space of 2mm and a gap of 0.5mm to cover the entire brain. We used a multiband
631 sequence[44] with acceleration factor = 2 and parallel imaging factor (iPAT) = 2, in an
632 interleaved fashion. Each of the passive viewing runs consisted of 180 volumes and
633 each of the probe runs consisted of 100 volumes. In addition, in each scanning session

634 (before, after and one month following training) we acquired high-resolution T1w
635 structural images using a magnetization prepared rapid gradient echo (MPRAGE)
636 pulse sequence (TR = 1.75s, TE = 2.59ms, FA = 8°, FOV = 224 × 224 × 208mm,
637 resolution = 1 × 1 × 1mm for the first five participants; TR = 2.53s, TE = 2.88ms, FA =
638 7°, FOV = 224 × 224 × 208mm, resolution = 1 × 1 × 1mm for the rest of the sample.
639 Protocol was changed to enhance the T1w contrast and improve registration of the
640 functional data to the standard space).
641
642 **fMRI preprocessing**: Raw imaging data in DICOM format were converted to NIfTI
643 format with dcm2nii tool[45]. The NIfTI files were organized according to the Brain
644 Imaging Data Structure (BIDS) format v1.0.1[41]. Preprocessing of the functional
645 imaging data was performed using fMRIprep version 1.0.0-rc8[46], a Nipype[47,48] based
646 tool. Each T1 weighted volume was corrected for bias field using
647 N4BiasFieldCorrection v2.1.0[49] and skull stripped using antsBrainExtraction.sh v2.1.0
648 (using OASIS template). Cortical surface was estimated using FreeSurfer v6.0.0[50].
649 The skull stripped T1 weighted volume was coregistered to skull stripped ICBM 152
650 Nonlinear template version 2009c[51] using nonlinear transformation implemented in
651 ANTs v2.1.0[52]. Functional data were motion corrected using MCFLIRT v5.0.9[53]. This
652 was followed by co-registration to the corresponding T1 weighted volume using
653 boundary based registration with nine degrees of freedom, implemented in FreeSurfer
654 v6.0.0[54]. Motion correcting transformations, T1 weighted transformation and MNI
655 template warp were applied in a single step using antsApplyTransformations v2.1.0
656 with Lanczos interpolation. Three tissue classes were extracted from the T1 weighted
657 images using FSL FAST v5.0.9[55]. Voxels from cerebrospinal fluid and white matter
658 were used to create a mask in turn used to extract physiological noise regressors

659 using aCompCor[56]. Mask was eroded and limited to subcortical regions to limit overlap
660 with grey matter, and six principal components were estimated. Framewise
661 displacement (FD)[57] was calculated for each functional run using Nipype
662 implementation. For more details of the pipeline using fMRIprep
663 see http://fmriprep.readthedocs.io/en/1.0.0-rc8/workflows.html. We created confound
664 files (tsv format) for each scan (each run of each task of each session of each
665 participant), with the following columns: standard deviation of the root mean squared
666 (RMS) intensity difference from one volume to the next (DVARS), absolute DVARS
667 values, voxelwise standard deviation of DVARS values and six motion parameters
668 (translational and rotation, each in three directions). We added a single time point
669 regressor (a single additional column) for each volume with FD value larger than 0.9,
670 in order to model out volumes with extensive motion. Scans with more than 15%
671 scrubbed volumes were excluded from analysis, resulting in one excluded participant
672 from the analysis of the first session's probe task.

673 **fMRI analysis.** Imaging analysis was performed using FEAT (fMRI Expert Analysis
674 Tool) v6.00, part of FSL (FMRIB's Software Library)[58] v5.0.10.

675 *Univariate imaging analysis - passive viewing:* The functional data from the passive
676 viewing task were used to examine the functional changes underlying the behavioral
677 change of preferences following CAT in the short and long-term. We used a general
678 linear model (GLM) with 13 regressors: Six regressors modelling each item type (high-
679 value Go, high-value NoGo, high-value sanity, low-value Go, low-value NoGo and low-
680 value sanity); six regressors with the same onsets and duration, and a parametric
681 modulation by the mean-centered proportion of trials each item was chosen in the
682 subsequent probe phase (the number of trials each item was chosen during the

683 subsequent probe divided by the number of probe trials including this item, mean-
684 centered) and one regressor for all items with a parametric modulation by the mean-
685 centered WTP values acquired from the first BDM auction. These 13 regressors were
686 convolved with the canonical double-gamma hemodynamic response function, and
687 their temporal derivatives were added to the model. We further included at least nine
688 motion regressors as confounds, as described above. We estimated a model with the
689 above described GLM regressors for each passive viewing run of each participant in
690 a first level analysis.
691 In the second level analysis (fixed effects), runs from the same session were averaged
692 and compared to the other session. Two second level contrasts were analyzed
693 separately: after compared to before CAT and follow-up compared to before CAT.
694 All second level analyses of all participants from after minus before or from follow-up
695 minus before CAT were then inputted to a group level analysis (mixed effects), which
696 included two contrasts of interest: One with the main effect (indicating group mean)
697 and one with the mean centered probe effect of each participant (the demeaned
698 proportion of choosing Go over NoGo items during the subsequent probe in the
699 relevant pair type, i.e. either high-value, low-value or all probe pairs). The second
700 contrast was used to test the correlation between the fMRI activations and the
701 behavioral effect across participants (correlation with the behavioral effect across
702 participants).
703 All reported group level statistical maps were thresholded at $Z > 2.3$ and cluster-based
704 Gaussian Random Field corrected for multiple comparisons at the whole-brain level
705 with a (corrected) cluster significance threshold of $P = 0.05$[59].
706 Since we only found a behavioral effect for high-value items (similar to previous cue-
707 approach samples with snack food items[13,14]), we focused our analyses on the

contrasts for high-value items: high-value Go items, high-value Go items modulated by choice and high-value Go minus high-value NoGo items.

*Univariate imaging analysis - probe:* Imaging analysis of the probe data was similar to previous imaging studies with CAT[13,15]. We included 16 regressors in the model (in addition to at least nine motion regressors), based on the initial value of the probe pair (high / low) and the choice outcome (participant chose the Go / NoGo item), resulting in four regressors (high-value chose Go / high-value chose NoGo / low-value chose Go / low-value chose NoGo) without parametric modulation; the same four regressors with a parametric modulation across items by the mean-centered proportion of choices of the specific item during the entire probe phase; the same four regressors with a parametric modulation by the WTP difference between the two presented items; one regressor for all "sanity-check" trials; one regressor for all missed trials; and two regressors accounting for response time differences (one regressor with a modulation of the demeaned response time across trials for each value category).

Since our behavioral effect was stronger for high-value items (similar to previous cue-approach samples with snack food items), we focused our analysis on the contrasts for high-value chose Go, high-value chose Go modulated by choice and high-value chose Go minus high-value chose NoGo. Similar to analyses of the passive viewing task, we estimated a first level GLM for each run of each participant. We then averaged the four runs of each probe (after / follow-up) of each participant in a second-level analysis. Finally, we ran a group level analysis as described above, with one contrast for the mean group effect and one contrast for the demeaned probe effect across participants (correlation with the behavioral effect across participants).

732 Some of the probe runs were excluded from the imaging analysis because one of the
733 regressors was empty or because the parametric modulator of Go item choices was
734 zeroed out, resulting in a rank-deficient design matrix. This happened, for example,
735 when a participant chose high-value Go over high-value NoGo items on all trials of a
736 specific run. Participants who did not have at least one full valid block (out of two probe
737 blocks, each probe including one presentation of each probe pair) without any empty
738 regressors or zeroed modulators for Go items, were excluded from the probe imaging
739 analysis (i.e. not included in the second level analysis of the specific participant). In
740 order to minimize the number of excluded runs and participants, we did not exclude
741 runs or participants due to a zeroed modulator of NoGo items choices, but rather
742 decided not to use the contrasts including modulation by choice of trials where NoGo
743 items were chosen. Overall, one participant was excluded from the imaging analysis
744 of the probe from both the after and follow-up sessions and two more were excluded
745 each from one of the sessions, based on regressors causing rank-deficient matrices
746 (in addition to the one participant that was excluded from the first session due to
747 excessive motion, as described above). Thus, a total of 33 (out of 36) participants
748 were included in the imaging analysis of the probe after training (out of which for 28
749 participants no run was excluded, for four participants one run was excluded and for
750 one participants two runs- one block- were excluded), and 25 (out of 27) participants
751 were included in the imaging analysis of the follow-up probe (out of which for 21
752 participants no run was excluded and for four participants one run was excluded).
753

754 <u>Small volume correction (SVC) analysis - passive viewing:</u> We pre-hypothesized (and
755 pre-registered) that value, attention and memory-related regions will be involved in the
756 behavioral change following CAT: Prefrontal cortex, dorsal parietal cortex and medial-

temporal lobe, respectively (https://osf.io/6mysj/). Thus, in addition to the whole-brain analyses described above for the passive viewing and probe task, we ran similar group level analyses once for each of these pre-hypothesized regions (bilateral hippocampus, bilateral SPL and vmPFC), with a mask containing the voxels which were part of the region. All masks were based on the Harvard-Oxford atlas (see *Supplementary Fig. 2*), anatomical regions for the vmPFC mask were based on those used in previous CAT papers[13,15].

**Pre-registration of analysis plan**. Our analysis plan was pre-registered (https://osf.io/x6hsq/?view_only=d3d59209e1704f97bc044b7aa6eb6fd2) prior to final full analyses.

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**Author contributions**

R.B.N. and T.Sc. designed the experiment, R.B.N. and T.Sa. collected the data, R.B.N., T.Sa. and T.Sc analyzed the data, and R.B.N., T.Sa. and T.Sc. discussed the results and wrote the paper.

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