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Plasticity of Food-related Memories During Reconsolidation

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Abstract

Reconsolidation serves to update and reenforce memories first by reactivation, then followed by retrieval re-stabilization. According to recent discoveries, it is possible to significantly erase maladaptive memories to treat mental disorders through disruption of reconsolidation. As food aversion is becoming a common issue around the world, this study aims to illustrate whether similar process – interfering food-related memories during reconsolidation window – could modify participants' opinions on their aversive food types. In this experiment, a total of 38 participants (n=38) were randomly assigned into experimental group, available for retrieval, and control group without any retrieval, and tested whether their disliked level to their aversive foods (previously identified in questionnaires) altered after watching a short video clip (interference). Greater reduction in disliked rating was observed in experimental group, which suggested that reactivation of memories prior to exposure of interference could weaken consolidated memory. The effect of the initial level of rating and previous exposure experience on the degree of modification was also discussed.

Keywords

Fear memory; Reconsolidation window; Memory retrieval; Food aversion.

1. Introduction

Encoded contents are stored as long-term memory (LTM) after consolidation. However, LTM is not permanent. In fact, it can be constantly being updated through reconsolidation, a process during which memory is destabilized upon retrieval, and restabilized to persist in the brain [1]. After retrieval, memory returns to a vulnerable state during which modification, and even reconstruction becomes available. This period of labile stage immediately after retrieval is referred to as "reconsolidation window". The concept that memories are plastic is important since it allows for adaptivity of readily consolidated memories. Thus, memory reconsolidation could be exploited as a novel therapeutic target for elimination of maladaptive memories underlying psychiatric disorders [1].

The plasticity of memories during reconsolidation window is clinically useful especially in the treatments of psychological disorders related to maladaptive memories such as post-traumatic stress disorder (PTSD). Prolonged exposure therapy, a type of evidence-based treatment for PTSD demonstrates effectiveness, however residual symptoms and relapse remain untreated [2]. Incorporating the concept of memory reconsolidation into currently used evidence-based exposure therapy creates a therapy known as memory reconsolidation therapy (MRT). During MRT, PTSD patients are asked to recall their memories, then followed by a wait period after which the memory becomes liable for modification. The study investigated at three police officers, who were previously diagnosed with PTSD, participating in 12 sessions of MRT, with each session 90-min in length [2]. Results indicated significantly decreased distress levels that

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lasted for over three months. Reduction in trauma symptoms were observed post-therapy in two of the three officers and was maintained over three months in one of the patients.

Drug addiction is a chronic and highly relapsing condition. Drug-seeking behaviour is driven by maladaptive learning processes which store and maintain associative memories. In these memories, drug high is linked to predictive stimuli (e.g. people, places, and paraphernalia) [3]. One prominent cause of high relapse rate in addiction is the exposure to cues that have been previously associated with drugs of abuse [1]. Given the learned association in addiction, the possibility to weaken, or even erase it through disruption of memory reconsolidation has been recognized [3].

Several studies have attempted to study the application of reconsolidation blockade treatments in humans, mostly by bAR antagonist and NMDAR antagonists. Propranolol, a bAR antagonist was studied as an amnestic agent extensively. It was shown that craving in patients were reduced when propranolol was given in conjunction with reactivation of drug-associated memories [4].

Another pharmacological target is NMDAR antagonist which disrupts the reconsolidation of drug memories [5]. Studies have shown that subunit GluN2B mediates the destabilization of methamphetamine-associated memories and GluN2A is critical for the re-stabilization following reactivation [3]. Therefore, it has been exploited that antagonizing GluN2A subunits of NMDAR could potentially maximize the effects of reconsolidation therapy in drug addiction [3].

When someone becomes ill after consuming a meal, there is a propensity to associate the taste to the cause of illness [6]. Therefore, future encounters with the food will evoke negative reactions and as a consequence, the individual will avoid that exposure [6]. However, not all bad tases are aversive. In some cases, a person eats the same food but suffers no such poisoning, instead, breaks out in hives due to an allergic reaction. It is likely that the person will also avoid eating the food, but still appreciates the taste [7]. In this case, the gustatory system signals potential dangers and discourages ingestion (avoidance), but it does not render the taste as disgusting or aversive [7].

This study aims to target the first type of aversion and to discover whether interference of reconsolidation could weaken previously learned aversive responses. By assigning participants into retrieval group (experimental) and non-retrieval group (control), the effect of introducing cues – in the form of video clips – during reconsolidation window is demonstrated.

It was hypothesized an overall decrease in the mean value of aversion level in both groups. However, degree of changes in control group should be less than experimental group across all food choices. Participants rated higher on the scale at the beginning might exhibit less degree of changes in aversion level compared to those rated lower. Aversive responses in participants who have tried their selected food previously might exhibit less changes than those who have not.

2. Methods

A pre-test questionnaire, shown in Table 1. consisting a total of 8 questions were provided to participants beforehand.

Responses from a total of 72 participants were collected. All of the participants were from China, with most of them between the age of 17 to early twenties and only a few in their fifties.

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Table 1. Questionnaire before test

Please identify your gender F/M
What is your age?
Please identify the last 4 digits of your phone number.
Which part of China are you from?
Do you dislike any of the food listed below? Y/N Durian LiuZhou rice noodle Sashimi Mushrooms Animal offal Peppers/bow peppers/green peppers
If your answer to Q5 is yes, please rate your selected food on a scale of 1-5 (5=most disliked, 1=least disliked).
If your answer to Q5 is no, please list any of your disliked food here and rate them on a scale of 1-5 (5=most disliked, 1=least disliked).
Would you like to be participated in future online experiment that may involve a short 5min video meeting? Y/N

Five kinds of food most commonly chosen (durian, rice noodle, sashimi, mushrooms and animal offal) in the questionnaire were selected for further experiment. Thirty-eight participants labelled at least one of the food choices were selected. Among these participants, 10 of them were assigned to durian, rice noodle and sashimi each, and four to mushrooms and animal offal each without any repetitions in order to avoid habituation. Within each food choice, participants were allocated randomly into experimental or control group in pairs according to their ratings. For example, a participant rated 5 on durian was assigned to durian control and another participant also rated 5 on durian was assigned to durian experimental. This ensured a balanced contribution of aversion level across the two groups.

All participants were asked to watch a video clip and then rate their aversion level again on the scale of 1-5. The video clips used in this experiment were inspiring but should not promote positive emotion among participants. These clips were taken from cooking blogs demonstrating on how to cook with durian, rice noodle, sashimi, mushrooms and animal offal. Snapshots are shown in Figure 1. They were edited to the same length (45 seconds) and incorporated with same background music. A total of five video clips were prepared, one for each of the tested food.

Figure 1. Snapshots from 5 video clips for durian, LiuZhou rice noodle, sashimi, animal offal and mushrooms

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However, only experimental participants were asked to retrieve a piece of their memories related to their disliked food before watching the video. The memory could be their own experience about having the food, or them watching others eating the food. They were asked to recall on the taste/smell of the food ("Please recall the last time of you having the food or watching others having the food in your mind and recall specifically on the taste/smell"). This step was timed for exactly 30 seconds.

While the experimental group was doing memory retrieval, the control group was asked to complete a simple math test that serves as a distractor for the same duration. In this case, control participants were prevented from naturally recalling on their disliked food to the greatest extent.

Followed by memory reactivation or math test, participants were asked to watch the prepared video clip. Lastly, they were asked to respond to 5 post-test questions, shown in Table 2. All responses were recorded and analyzed in excel sheet.

Table 2. Questionnaire after test

1. Please rate your disliked food on the same scale of 1-5 (with 5 being the most disliked).
2. Did you find a(n) increase, decrease or no change in your aversion level?
3. Have you tried the food before?
4. Have you seen the video clips before?
5. When was the last you had a meal?

3. Results

Collected data was further analyzed by generating graphs from Excel. Then the significance was calculated using a variety of statistical test.

The mean average of control's aversion level is shown in Figure 2. A slight reduction of 0.264 was observed. Figure 3. demonstrates the change in aversion level of experimental group. Compared to control, the reduction was slightly greater, which was calculated to be -0.473, almost doubled the difference of control.

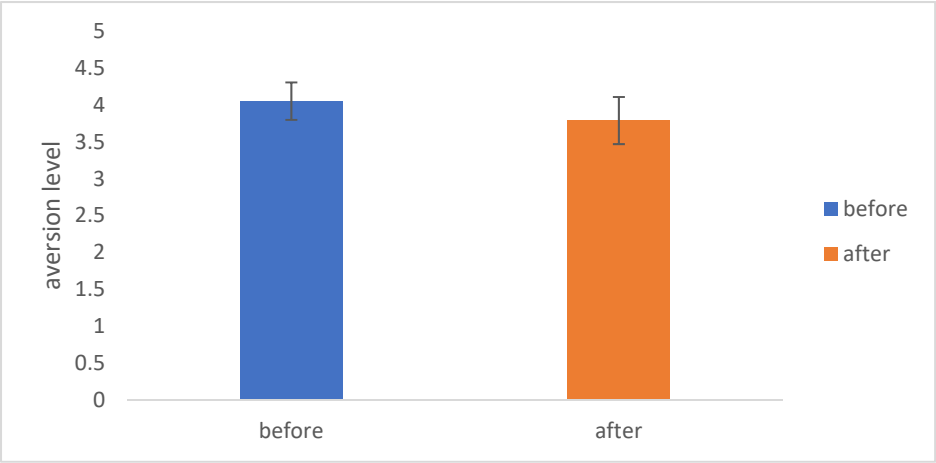

Figure 2. Change in aversion level before and after of control participants

The mean value of control participants before and after watching the video clip was calculated to be 4.053 and 3.789, respectively. The blue bar represents the mean value before the video and the orange bar represent after. Error bars for standard deviation are also shown in the graph. Aversion level on a scale of 1-5 with 5 being the most disliked is shown on y-axis.

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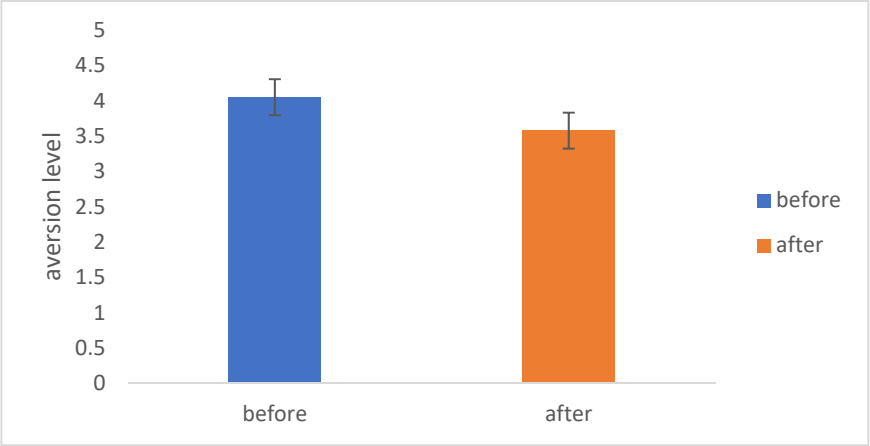

Figure 3. Change in aversion level before and after of experimental participants

The mean value of experimental participants before and after watching the video clip was calculated to be 4.053 and 3.579, respectively. The blue bar represents the mean value before the video and the orange bar represent after. Error bars for standard deviation are also shown in the graph. Aversion level on a scale of 1-5 with 5 being the most disliked is shown on y-axis.

The overall trend in both control and experimental group was decreasing, indicating participants were likely to reduce their disliked level after test. The mean value of aversion differences (after test rating - original rating) was calculated, shown in Figure 4. The greater difference in experimental group (-0.47) illustrates the influence of retrieval on modifying personal opinions. Despite the greater changes observed in experimental group (-0.473) than control group (-0.264), the result did not pass Mann Whitney U, and was found to be insignificant (p-value = 0.327, ns).

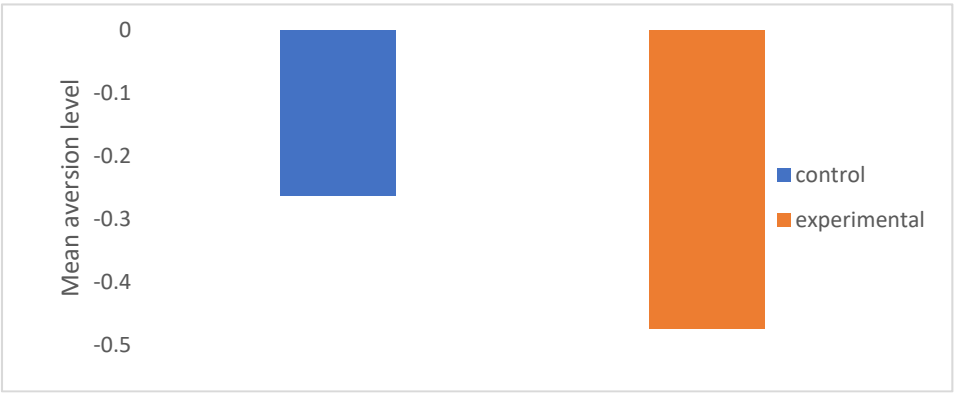

Figure 4. Mean difference of aversion level in control and experimental

The mean value of aversion differences is displayed in the graph. The blue and orange bar represents control and experimental, respectively.

Furthermore, individual variability in control and experimental group was analyzed using dotted graph, shown in Figure 5 and Figure 6, respectively. A wide range of variability was observed in control group. For example, participant 57 rated 3 levels lower than previous rating, which was unexpected. Only 3 of the 19 participants remained unchanged. The results in experimental group varied between participants as well. Four of the participants remained unchanged and the rest changed between 1 to 3 levels.

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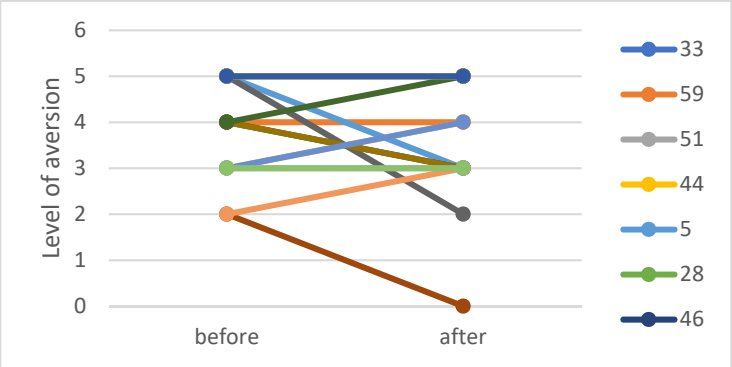

Figure 5. Variability of control participants before and after watching the video

The change in aversion level of each individual in control group is shown in the graph. Each colour represents a participant. Aversion level was measured on the same scale of 1-5 with 5 being the most disliked, shown on the y-axis.

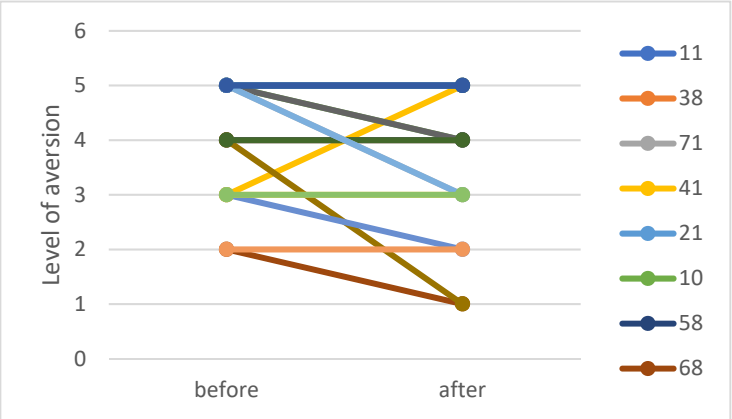

Figure 6. Variability of experimental participants before and after watching the video

The change in aversion level of each individual in experimental group is shown in the graph. Each colour represents a participant. Aversion level was measured on the same scale of 1-5 with 5 being the most disliked, shown on the y-axis.

Whether rating has an influence on the degree of changes in aversion level was further analyzed using Kruskal-Wallis test that gave a p-value of 0.684, ns.

Using Mann Whitney test, data from participants who have tried the food before was compared to those who have not. The p-value (p-value = 0.133, ns) revealed no significant correlation.

4. Discussion

The experiment was unable to verify the hypotheses. Several unexpected results were observed due to a variety of limitations. The changes in rating of experimental group was expected to be greater than control group. Participants who were asked to recall their memories before watching the video clip were more likely to change their thoughts on their aversive foods. This reinforced the theory that interference provided after memory destabilization was influential in terms of re-organizing an individual's food-related memories. Although greater changes were observed in experimental participants, Mann Whitney U revealed a weak correlation between memory retrieval and degree of changes (p-value = 0.327, ns). Therefore, we failed to conclude a strong association between recall and adaptations in food aversive memories in this experiment.

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It was unexpected that the control participants resulted in great individual variability. Since they were asked to do a math test instead of memory retrieval, they were expected to exhibit minimal changes. However, this was not what had been observed. This could due to various reasons such as small sample size, distraction in the surrounding and accidental memory retrieval and etc.

It was firstly thought that participants having weaker aversive responses were more vulnerable to change. However, this hypothesis did not pass Kruskal-Wallis test (p-value = 0.684, ns).

Furthermore, whether participants had previous experience in tasting their identified food is influential on the result was determined. The Mann Whitney test revealed no significant correlation between previous experience and the result (p-value = 0.133, ns).

5. Conclusion

The failure of leading to significant results might due to a variety of limitations. To begin with, since the experiment was done in a two-week period, it was limited in terms of available data collected. This resulted in a fairly small sample size, with only 19 participants in each group. Enlarging the sample size in future experiments may produce significant results since individual variability could be balanced.

All measurement recorded in the experiment (e.g. ratings of disliked level before and after the video) were entirely subjective. This could be another reason leading to insignificant outcomes. It might be possible to measure some biological changes such as heart rate, dilation of pupil, and facial expressions in addition to subjective reflections in a follow-up experiment. Since emotions can be revealed through facial expression, by recording the contraction of facial muscle of the participants, more reliable results should be obtained. Categorization of emotions is beyond the six basic emotions. There are consistent and differential facial muscle articulations (a.k.a. AUs) associated with each emotion category. For example, the contraction of frontalis resulting a visible rising of the inner section of eyebrows is AU1, only seen in several emotions. It is possible that participants were unable to distinguish clearly between two slightly different feelings (e.g. disgust and curious disgust), thus unable to report their dislike accurately. However, recordings of facial expressions should provide more reliable data that reflects participants' internal emotions.

Homeostatic mechanisms involving neuronal circuits in the hypothalamus and brainstem, as well as satiety and hunger signaling in the peripheral regulate eating behaviours. Reward mechanism regulating hedonic aspects of food intake similar to that seen in drug addiction, is also involved in the regulation of ingestion. Therefore, it is possible that injection of amnesic agent (e.g. bAR or NMDAR antagonist) that had been found effective for treating addiction might lead to prominent modifications in food aversive memories. However, this would require the use of animal models under laboratory settings.

In conclusion, even though a larger degree of changes were observed in memory retrieval group compared to control, the changes were statistically non-significant. However, this experiment was able to give an overview of the potential application of reconsolidation in food aversive memories. Hopefully, future studies with more delicate measurement could reveal promising results of reconsolidation therapy in food aversion.

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