Partial reinforcement and conditioned taste aversion: No evidence for resistance to extinction

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Abstract

The partial reinforcement extinction effect (PREE) is the observation that, following training in which a response is followed by reward on only a subset of trials, the response is more resistant to extinction following the total removal of reward than it is after training in which reward is presented on all trials. The PREE is almost ubiquitous in instrumental conditioning procedures but only inconsistently observed in Pavlovian conditioning. In his classic review of animal learning Mackintosh (1974) attributes the bulk of the PREE to generalisation decrement relating to the fact that partial reinforcement typically ensures that acquisition of responding has taken place in conditions similar to that of extinction (e.g. in the absence of the reinforcer). We report here that extinction of a conditioned taste aversion is not retarded by partial reinforcement in terms of either consumption of the taste or hedonic reactions to it (assessed through the analysis of licking microstructure). These results are consistent with Mackintosh's analysis of the PREE and the way in which it might differ between instrumental and Pavlovian conditioning.

Keywords: Taste Aversion, Partial Reinforcement, Extinction, Generalisation Decrement.

The partial reinforcement extinction effect (PREE) is the observation that, following training in which a response is followed by reward on only a subset of trials, the response is more resistant to extinction following the total removal of reward than it is after training in which reward is presented on all trials. The PREE has extensively investigated across many years, mainly within the context of instrumental conditioning (for a review, see Mackintosh, 1974). For some time, this resistance of the conditioned response to extinction after a partial reinforcement schedule has been known to be nearly ubiquitous in instrumental conditioning, but only infrequently observed within Pavlovian conditioning. One implication drawn from this discrepancy is the idea that the PREE potentially differentiates Pavlovian from instrumental conditioning. This is not to say that the PREE has never been observed in Pavlovian conditioning (see for example, Grady, Bowen, Hyde, Totsch, & Knight, 2016; Haselgrove, Aydin, & Pearce, 2004; Pearce, Redhead, & Aydin, 1997; Rescorla, 1999), but that the PREE is far less commonly observed in Pavlovian than instrumental preparations.

The PREE appears to contradict the expectation that the strength of a response should be in direct proportion to the association with reward. That is, if partial and continuous reinforcement produce equivalent associative strength, then they should support equivalent responding, but the PREE confounds this expectation. The continued interest in the PREE has largely stemmed from this conundrum, and a number of theoretical accounts have been offered to explain it. Early accounts include the proposed that partial reinforcement schedule during acquisition increases the difficulty of discriminating the transition to extinction (Mowrer & Jones, 1945) and attributing the PREE to a stronger response tendency in partially reinforced subjects (Denny, 1946; Lawrence & Festinger, 1962). However, Mackintosh (1974, pp. 436-438) persuasively argues that both these accounts proved to be untenable. More recently, alternative theories such as the momentum model (Nevin & Grace, 2000), or quantitative accounts with no associative mechanisms (Gallistel & Gibbon, 2000),

have been proposed. But perhaps the most widely accepted class of theory attributes the PREE to a decrease in generalization decrement (notably, there are several different versions of this proposal). In particular, Amsel (1958, 1992) suggested that partial reinforcement allows animals to form associations between frustration and reward that encourage individuals to respond in the absence of the reinforcer, and Capaldi (1967) stated that nonreinforced trials generate a memory trace which might interfere with preceding and succeeding traces, controlling the response in partial reinforcement schedules. Critically for the present context, it was Nicholas John Mackintosh who proved to be one of the clearest and most influential proponents of this general approach.

In his book of 1974 (see especially pp. 440-443), he considers the explanation of the PREE in terms of generalization decrement; partial reinforcement increases resistance to extinction because it establishes associations appropriate for maintaining the response during extinction, that is, ensures that training has taken place in conditions similar to that of extinction (in particular, in the absence of the reinforcer). Moreover, he suggest that Capaldi's interpretation of this effect in terms of memory trace is indeed a 'useful one' – in a partial reinforcement schedule, responding is reinforced at the moment when the subject still remembers previous non-reinforced trial(s). He also supports the idea of Amsel's frustration state; nonreinforcement is not just an emotionally neutral event, indeed is inhibitory or frustrative, so partially reinforced subjects learn to respond in the presence of the frustration stimuli. Ultimately, these two proposals (Frustration and Sequential theories) both seem applicable to some situations, although perhaps to different degrees depending on the intervals between trials: memory mechanisms may well play a primary role with short intervals between trials (when memory traces of reinforced and non-reinforced trials should be active at the same time), while the emotional learning seems a better fit in studies using

more spaced training (as the frustration-paired stimuli will be present even when the immediate memory traces of non-reinforced trials has decayed).

One of the interesting features of Mackintosh's analysis of the PREE is the suggestion that the difference in prevalence of the effect between instrumental and Pavlovian procedures might not reflect a general difference in learning mechanism, but instead flow from the specific features of the experimental procedures. For example, he notes that the PREE appears to be detected less readily if the response is controlled by very few stimuli: in runway procedures the PREE is larger when a complex or variable set of cues are present and the PREE is less reliable when discrimination learning is required than when it is not (see Mackintosh, 1974, p. 439; Sutherland & Mackintosh, 1971, p. 350). It is also the case that continuous reinforcement results in few stimuli controlling responses while partial reinforcement increase significantly the number of stimuli associated with the reinforcement (McFarland, 1966; Sutherland, 1966; Wagner, Siegel, & Fein, 1967; Waller, 1973). Mackintosh then notes that instrumental and Pavlovian procedures will typically differ in terms of the specificity of learning: in classical preparations, the behaviour of the subject is usually measured immediately before the delivery of the reinforcement and the experimenter has direct control over the exact nature of the stimulus being reinforced; in contrast, there is often a relatively long chain of responses preceding the delivery of the reinforcement in instrumental preparations and the exact behaviour preceding reinforcement is not under experimental control. The fact that classical conditioning experiments normally ensure more specific CS-reinforcement associations than do instrumental preparations may contribute to the lack of a reliable PREE in classical conditioning.

Perhaps as a product of differences in the reliability of the effect, research on the PREE has tended to focus on instrumental conditioning, mainly in appetitive preparations, with relatively little attention given to the study of PREE in Pavlovian conditioning, especially in

aversive paradigms. The aim of the current study is to explore the possibility of observing a PREE using a conditioned taste aversion (CTA) procedure. CTA is developed when an animal associates a flavour with the gastric illness induced by an emetic drug, and it has been traditionally measured as the decrease in the voluntary consumption of the flavour associated with the state of nausea (Garcia & Koelling, 1967; Nachman, 1970). CTA has been typically considered as an instance of a classical conditioning – the taste is the conditioned stimulus associated to the unconditioned stimulus, namely, the gastric illness – albeit it has been thought to possess "special" characteristics relating to the "fit" between taste CSs and illness-producing USs (see Reilly & Schachtman, 2009 for a review). This characterisation certainly seems appropriate in the context of passive administration of the CS, as often occurs when the taste reactivity (TR) methodology is used (Grill & Norgren, 1978). In this method, the flavour is delivered directly in the animal's mouth through a cannula previously implanted in the oral cavity, and the orofacial and somatic reactions to the CS are recorded. This allows analysing the hedonic reactions to the flavour, which is a reliable measurement of the conditioned aversion (Parker, 2003, 2014). In a standard CTA procedure (where animals are allowed to voluntarily consume the taste CS), the interpretation in terms of Pavlovian conditioning relies on the fact that there is no instrumental contingency between the amount of the CS consumed and the dosage of emetic drug received during the training (indeed, the dose of the US is typically maintained at a constant level despite suppression of consumption of the CS over multiple training trials). Although it is typical to interpret CTA as a consequence of Pavlovian conditioning, some contribution of instrumental behaviours has been suggested because the size of the CTA appears to be larger when training allows for active consumption of the CS as opposed to passive exposure (Fouquet, Oberling, & Sandner, 2001).

The only previous report of partial reinforcement and extinction in CTA is from a conference abstract (Berger, Rubinstein, Ariely, Toicher, & Schuster, 1982) noting no evidence of the PREE. The lack of research here is unfortunate, because the combination of CTA, partial reinforcement, and extinction could contribute both to the examination of the generality of the PREE and to the mechanisms underpinning CTA. With this in mind, the present study examined the effect of partial and continuous CS-US pairings on the acquisition and extinction of a conditioned aversion to a saline solution by using two measurements – the amount consumed and mean lick cluster size (Davis, 1989; Dwyer, 2012). The microstructural analysis of the licking behaviour represents an alternative approach to assess palatability (Davis & Smith, 1992; Dwyer, Boakes, & Hayward, 2008). Rats ingest fluids in sustained runs of licks separated by pauses of varying length (clusters), and the mean number of licks per cluster (lick cluster size) is lawfully related to the nature of the solution ingested, the more palatable the solution the larger the lick cluster size.

Method

Subjects

Forty-eight Lister Hooded male rats, approximately 90 days old and with a mean free-feeding weight of 334 g (range, 282-381 g) at the start of the experiment, were used. Rats were supplied by Harlan, United Kingdom and all procedures reported here where conducted in accordance with the Animals Scientific Procedures Act (1986) requirements for animal experimentation in the UK. The rats were housed in fours under 12hr/12hr light/dark cycle and they had ad lib food throughout the experimental sessions. All experimental manipulations took place during the light phase of the cycle. Before the start of the experiment, rats were moved to water restriction schedule with 60 minutes home-cage access to water per day (given after experimental sessions at approximately 16:00).

Fluids and apparatus

The CS solution was a 1% (w/w) NaCl, and the US solution was lithium chloride (0.15 M LiCl) administered intraperitoneally (i.p.) at a volume of 1 ml/kg of body weight for continuous groups and at 2 ml/kg of body weight for partial groups, thus equating the total amount of LiCl administered across groups.

Training and testing phases took place in a room separated from the holding cages which contained 16 custom-made automated drinking chambers measuring 32 × 15 × 12 cm, with acrylic walls, steel mesh flooring and wire mesh lids. Two 50 ml drinking bottles with metal spouts could be inserted 8 cm apart at one end of each box. A contact sensitive lickometer registered the licks made by rats to the nearest 0.01 s once the bottle was available, and MED-PC software (Med Associates, Inc) controlled the equipment and recorded the data.

Procedure

Animals received two sessions of habituation to the experimental boxes before starting the training phase, during which they had access to a bottle containing water for 10 minutes. Rats were randomly assigned to four groups of 12: Group Partial-paired, Group Continuous-paired, Group Partial-unpaired and Group Continuous-unpaired. On day 3, the first training cycle started. Each of the three training cycles consisted of 4 days (see Table 1). On the first day of each cycle all animals received 10 minutes access to the saline solution: immediately afterwards animals from group Partial-paired were injected i.p. with 2 ml/kg LiCl and animals from group Continuous-paired received 1ml/kg of LiCl. For unpaired groups, the same injections were administered 4 hours after the saline consumption, that is, 2 ml/kg LiCl for Partial-unpaired and 1ml/kg for Continuous-unpaired. The following day all animals received 10 minutes access to a bottle containing water in the conditioning context. On the third day of the cycle, all rats had access to the saline solution and immediately after, animals

from Continuous-paired received an i.p. injection of 1ml/kg LiCl whereas for Partial-paired group was followed by nothing. Four hours later, rats from Continuous-unpaired were injected with 1ml/kg LiCl whereas Partial-unpaired group did not receive injections. On the fourth day all animals had again 10 minutes access to a bottle containing water. After three training cycles were completed, 16 test sessions were performed, in each of these daily sessions animals received 10 minutes access to a bottle containing the saline solution with both consumption and lick data being recorded.

Data analysis

Consumption was measured by weighing bottles before and after each experimental session. Lick cluster size, the mean number of licks per cluster, was extracted from MED-PC data. A cluster was defined as a series of licks separated by pauses no more than 0.5s interval, a criterion previously used by Davis (1989) and in our previous studies of licking microstructure and taste aversion (Dwyer, 2009; Dwyer, Burgess, & Honey, 2012; Dwyer, Gasalla, & López, 2013). Mixed analyses of variance (ANOVAs) were used to examine the acquisition and the extinction data separately, with between-subjects factors of schedule (partial or continuous conditioning) and treatment (paired or unpaired with LiCl) plus within-subjects factors of acquisition or extinction session. In addition, the last acquisition day (day 3 in the last training cycle) was analysed using schedule and treatment as between-subject factors. All null hypothesis statistical tests reported here used a significance value of $p = .05$.

The analysis of licking patterns requires at least some voluntary consumption. However, some but not all, rats displayed a total suppression of consumption at the beginning of the test period – meaning that lick cluster data was not available for all rats for all extinction sessions. This problem was addressed in two ways: Firstly, missing lick cluster entries were entered as 0 for the analysis of extinction to facilitate the by-session analysis (an

alternative method to address this issue would be to replace missing values with the group mean for that session; 11 replacements were made, mainly on the first extinction trial, and there were no statistical differences between these two methods). Secondly, the first day of extinction on which a rat displayed at least 50 licks was determined, and the extinction data were re-analysed as a function of the eight extinction sessions following reaching that criterion (e.g. if a rat reached this criterion on day 3 of extinction, then the data from sessions 3-10 was analysed; if a rat reached the criteria on day 9 then the data from sessions 9-16 was included) [1].

Critically, in comparing resistance to extinction following partial and continuous reinforcement, it is important to evaluate whether the data provide good evidence for concluding that there is no difference between these treatments. Standard null hypothesis testing methods are ill-suited to this task as a non-significant result does not distinguish between a failure to find evidence for a difference, and evidence against a difference. Therefore, we also report the results of Bayesian analysis methods in order to evaluate the degree of support for the absence of effects of training schedule (and the interactions of this manipulation with other factors). Bayesian tests are based on calculating the relative probability of the null and alternative hypothesis, and the Bayes Factor (denoted as B_{01} when data support the null hypothesis) gives the relative probability for the data under a model based on null hypothesis compared with a model based on some specific alternative model. The resulting Bayes factor can be interpreted as supporting the null or alternative hypothesis (or as giving no conclusive support to for either hypothesis). According to the convention suggested by Jeffreys (1998; see also Rouder, Speckman, Sun, Morey, & Iverson, 2009), a Bayes factor over 3 suggests some evidence to support in favour of the null hypothesis, and

[1] Suppression of voluntary consumption also reduces the exposure to the CS solution. So this re-analysis also helps match animals for CS exposure across the extinction period.

over 10 indicates strong evidence in favour of the null. However, a factor less than 1/3 suggest evidence against the null and less than 1/10 strong evidence against the null hypothesis. Values between 1/3 and 3 constitute inconclusive evidence. Bayesian analysis was conducted using JASP software (JASP Team, 2016; version 0.7.1.12) with Bayes factors for main effects and interactions calculated using the model averaging approach for factorial ANOVA described by Rouder, Morey, Speckman and Province (2012) and Rouder, Morey, Verhagen, Swagman, and Wagenmakers (in press).

Figure 1 about here

Results

Acquisition

Panel A of Figure 1 shows the mean saline consumption over training sessions. ANOVA revealed a significant effect of treatment, $F(1,44) = 198.15$, $p < .001$, session, $F(5,220) = 46.73$, $p < .001$, and a significant interaction between those factors, $F(5,220) = 36.80$, $p < .001$. The schedule factor was not significant, $F(1,44) = 0.82$, $p = .370$, $BF_{01} = 3.419$, but there were significant interactions between schedule and session, $F(5,220) = 6.50$, $p < .001$, schedule and treatment, $F(1,44) = 4.58$, $p = .038$, and schedule, treatment and session, $F(5,220) = 6.14$, $p < .001$. Regarding the schedule by treatment interaction, simple analysis revealed that there was no effect of schedule in unpaired groups, $F(1,44) = 0.76$, $p = .387$, but there was a schedule effect in the paired groups: Group Partial-paired had higher saline intake than group Continuous-paired, $F(1,44) = 4.64$, $p = .037$. Most importantly, ANOVA analysis of the last training session revealed a main effect of treatment, $F(1,44) = 137.52$, $p < .001$, but no effect of schedule, $F(1,44) = 0.09$, $p = .759$, $B_{01} = 3.446$ or treatment and schedule interaction, $F(1,44) = 0.12$, $p = .730$, $B_{01} = 1.030$.

Panel B of Figure 1 shows the mean lick cluster size over training sessions. Mixed ANOVA revealed a main effect of session, $F(5,220) = 14.22$, $p < .001$, treatment, $F(1,44) = 26.29$, $p < .001$ and a significant interaction between them, $F(5,220) = 19.04$, $p < .001$. As in the consumption data, there was no significant effect of schedule, $F(1,44) = 1.37$, $p = .248$, $B_{01} = 3.571$, but there was a significant schedule by treatment interaction, $F(1,44) = 4.52$, $p = .039$ and a session by schedule interaction, $F(5,220) = 2.66$, $p = .023$. Simple main effect analysis of the former interaction revealed an effect of schedule in paired groups, that is, group Partial-paired had a larger mean lick cluster size than Continuous-paired, $F(1,44) = 5.44$, $p = .024$, but schedule had no effect on unpaired groups, $F(1,44) = 0.46$, $p = .502$. A significant interaction of session, schedule and treatment was found, $F(1,44) = 4.89$, $p < .001$. Regarding the analysis performed on the last training session, ANOVA revealed a main effect of treatment, $F(1,44) = 110.52$, $p < .001$, but the schedule effect and the interaction between factors were not significant, $F(1,44) = 1.36$, $p = .250$, $B_{01} = 3.365$, and $F(1,44) = 0.25$, $p = .616$, $B_{01} = 2.375$ respectively. Thus, at the end of the training phase animals that were administered saline solution-LiCl pairings showed an equivalent decrease in both consumption and palatability of the CS flavour regardless of whether they received partial or continuous training schedules.

Figure 2 about here

Extinction

Panel A of Figure 2 shows the mean saline consumption over all extinction trials. Mixed ANOVA revealed a main effect of session, $F(15,660) = 27.99$, $p < .001$, treatment, $F(1,44) = 93.30$, $p < .001$, but no main effect of schedule, $F(1,44) = 0.46$, $p = .503$, $B_{01} = 2.837$. There was an interaction between session and treatment, $F(15,660) = 17.27$, $p < .001$. Simple effects

analysis revealed that animals that had received saline-LiCl pairings displayed lower consumption than the unpaired controls across all extinction sessions, smallest $F(1,44) = 11.53$, $p < .001$. However, none of the schedule by treatment interaction, schedule by session interaction, and the triple interaction were significant [$F(1,44) = 1.03$, $p = .316$, $B_{01} = 3.355$; $F(15,660) = 0.75$, $p = .728$, $B_{01} > 10$; and $F(15,660) = 1.32$, $p = .179$, $B_{01} > 10$ respectively]. That is, not only was there merely no significant difference between the partial and continuous reinforcement groups across extinction, the large Bayes factors suggest considerable support for the absence of any effect.

Panel B of Figure 2 shows the mean lick cluster size over extinction sessions. Mixed ANOVA revealed a main effect of session, $F(15,660) = 14.35$, $p < .001$, a main effect of treatment, $F(1,44) = 10.68$, $p = .002$ and a significant interaction between them, $F(15,660) = 10.79$, $p < .001$. Simple effects analysis of the interactions revealed an effect of treatment in extinction sessions from 1 to 7, smallest $F(1,44) = 8.03$, $p = .007$, but there was no effect of treatment from extinction session 8 to 16 [largest effect in session 9, $F(1,44) = 3.68$, $p = .062$, and smallest on session 15, $F(1,44) = 0.43$, $p = .838$]. That is, while differences in consumption between paired and unpaired groups persist over extinction, there were no differences between groups in lick cluster size from extinction session 8, and therefore, conditioned changes in lick cluster size extinguished more quickly than consumption changes. Critically, there was no main effect of schedule, $F(1,44) = 1.30$, $p = .260$, $B_{01} = 3.110$, schedule and treatment interaction, $F(1,44) = 0.33$, $p = .566$, $B_{01} = 3.759$, schedule and session interaction, $F(1,44) = 1.29$, $p = .199$, $B_{01} > 10$, or schedule and session and treatment interaction, $F(15,660) = 0.86$, $p = .610$, $B_{01} > 10$. Again, the large Bayes factors for the schedule effect (and its interactions with extinction and treatment) support the conclusion that the partial and continuous groups did not differ in terms of lick cluster size across extinction.

Figure 3 about here

As was noted previously, the analysis of extinction might be compromised by the total suppression of consumption in some animals (both in terms of reducing exposure to the CS and in preventing sufficient lick data being recorded for analysis of cluster sizes). Thus, for each rat, the first session on which they produced at least 50 licks was determined, and extinction re-analysed for the 8 sessions starting at that point (see Figure 3). One animal was removed from this re-analysis because it never produced more than 50 licks in any session. Animals in Group Partial-paired reached this criterion in a mean of 3.16 sessions (SEM 2.62), while the Group Continuous-paired reached it in a mean of 4.54 sessions (SEM = 2.38). Both unpaired groups reach the criterion on the first session– there was a significant effect of treatment $F(1,43) = 31.08$, $p < .001$ (but no effect of schedule nor a treatment by schedule interaction, $Fs(1,43) < 1.81$, $ps > .185$, $B_{01} > 2.441$). For the consumption data, mixed ANOVA revealed a main effect of session, $F(7,301) = 20.65$, $p < .001$, a main effect of treatment, $F(1,43) = 113.34$, $p < .001$, and a significant interaction between them, $F(7,301) = 13.71$, $p < .001$. Simple effects analysis revealed that animals that were injected with LiCl immediately after the saline intake had decreased consumption over all the extinction sessions, lowest $F(1,43) = 6.39$, $p = .015$. Critically, no significant schedule effect was found, $F(1,43) = 1.28$, $p = .265$, $B_{01} = 2.504$, nor were there significant schedule by session, $F(7,301) = 1.31$, $p = .245$, $B_{01} > 10$, schedule by treatment, $F(1,43) = 0.07$, $p = .788$, $B_{01} = 4.255$, or schedule by treatment by session interactions, $F(7,301) = 1.14$, $p = .337$, $B_{01} > 10$. With respect to cluster size, ANOVA revealed, as in consumption, a main effect of session, $F(7,301) = 6.01$, $p < .001$, a main effect of treatment, $F(1,43) = 6.28$, $p = .016$, and a significant interaction between them, $F(7,301) = 8.17$, $p < .001$. Simple effects analysis revealed that pairing a saline solution with the illness induced by the administration of LiCl

produced a decreased in lick cluster size on extinction session 1, 2 and 4, [smallest $F(1,43) = 4.84$, $p = .033$]. However, the effect was not significant on the remaining sessions, largest $F(1,43) = 2.79$, $p = .102$. Importantly, no significant schedule effect was found, $F(1,43) = 0.21$, $p = .649$, $B_{01} = 3.358$, schedule by session interaction, $F(7,301) = 0.99$, $p = .433$, $B_{01} > 10$, schedule by treatment interaction, $F(1,43) = 0.56$, $p = .459$, $B_{01} = 3.906$, or schedule by treatment by session interaction, $F(7,301) = 0.53$, $p = .808$, $B_{01} > 10$. Thus, as with the analysis of the entire extinction period, the large Bayes factors for the schedule effect (and its interactions) are consistent with the absence of any difference between partial and continuous reinforcement across extinction.

In summary, while continuous and partial reinforcement produced equivalent suppression of both consumption and lick cluster size by the end of training, there was no suggestion of greater resistance to extinction following partial reinforcement (if anything, there were hints of faster extinction following partial reinforcement). In addition, the changes in lick cluster size extinguished more quickly and completely than changes in consumption.

Discussion

One of the most studied determinants of the performance over extinction has been the schedule of reinforcement in acquisition. The PREE is well established over a wide range of instrumental conditions; however, the effects of partial reinforcement have received little attention in the CTA literature. The current study demonstrates that extinction of CTA is not retarded by partial reinforcement during acquisition in terms of either consumption or palatability of the CS. It is worth noting that Mackintosh (1974) suggests that while large rewards increase the rate of extinction after continuous reinforcement, they retard extinction after partial reinforcement. Indeed, the PREE increases proportionally with the increase of the magnitude of the reward (Gonzalez & Bitterman, 1969; Likely, Little, & Mackintosh, 1971;

Ratliff & Ratliff, 1971). Here, we used a larger dose of LiCl in the partial reinforcement group, which should have promoted a PREE thus further emphasising the lack of an observed effect on extinction. In line with our results, one previous conference paper reported no evidence of increased resistance to extinction after partial reinforcement using a CTA paradigm (Berger et al., 1982). In that study, animals were trained to drink a sweet solution prior to a LiCl injection under a continuous reinforced schedule or reinforced only in the 60% of the trials (matching number of reinforcements or number of trials). There were no evidence of resistance to extinction after partial reinforcement. Taken together, the current experiment and the previous conference report provide no evidence for the PREE in CTA, and suggest that the failure to observe a PREE effect in CTA is reliable.

We will now consider the implications of our current results, firstly for the question of whether CTA reflects instrumental or Pavlovian processes, and then for Mackintosh's analysis of the PREE as the product of generalisation decrement. As noted previously, studies of classical conditioning have failed to demonstrate a consistent PREE, unlike those using instrumental conditioning. Although the learning occurring in CTA has been suggested to contain instrumental components (Revusky & Garcia, 1970) because the intake response (or eating) is reinforced in the presence of a particular discriminative stimulus, there are strong reasons supporting an interpretation of CTA as classical conditioning. Rats are able to develop CTA to flavour without its ingestion (Bellingham & Lloyd, 1987; Bures & Buresova, 1989; Cloutier, Cross-Mellor, Kavaliers, & Ossenkopp, 2011; Domjan & Wilson, 1972) and there is typically no instrumental contingency between the intake response and the outcome (if any contingency does exist it is essentially negative: consumption decreases but the intensity of the gastric illness normally remains unaltered). Given that PREE is almost always observed in instrumental conditioning but relatively infrequently in Pavlovian preparations

the failure to see a PREE effect in CTA is also consistent (at least probabilistically) with the idea that CTA may be best categorized as an instance of classical conditioning.

That said, it is possible that CTA might reflect multiple processes, including both instrumental and Pavlovian components. For example, Fouquet et al. (2001) examined the differential effect of the method of fluid delivery, active (i.e. voluntary consumption) vs. passive (i.e. oral infusion), on CTA (see also Wolgin & Wade, 1990). In brief, they found that the expression of the CTA was stronger for the actively conditioned animals when an active test was later used which they explained in terms of contextual modulation provided by the intraoral cannula (for a related analysis of the potential context effects of oral infusion vs free consumption in the context of latent inhibition see, López et al., 2010). Critically, they suggest that an instrumental process might be the determinant factor in mediating this context effect. In the Pavlovian tradition, the CS are typically of low biological significance, however, in CTA the CS typically possess incentive value (e.g. because they are palatable fluids provided to water-restricted animals). In a CTA paradigm, the consumption behaviour is first reinforced with a flavoured fluid and then, the incentive value of the flavour is reduced by the administration of the emetic drug. They proposed that the CTA can be defined in terms of an instrumental contingency (self-generated activity → fluid) followed by a Pavlovian contingency (flavour → gastric illness). This might suggest that responses reflecting self-generated activity leading to fluid consumption should be more likely to show the PREE than responses reflecting the devaluation of the flavour by pairing with illness. This possibility does not seem to be consistent with the current results. Here, we assessed both intake of the CS solution (which would be sensitive to self-generated activity resulting in consumption), and the microstructure of the licking behaviour (which is sensitive to the hedonic response to the flavour). Neither measure showed a PREE, although the extinction of the change in lick cluster size reflecting hedonic responses was faster overall than the extinction in fluid intake.

The relatively rapid extinction of hedonic responses compared to intake measures is entirely consistent with previous studies examining the extinction of palatability (Baird, St John, & Nguyen, 2005; Cantora, López, Aguado, Rana, & Parker 2006; Dwyer, 2009; Dwyer et al., 2013). Our previous analysis of the more rapid extinction of hedonic responses as opposed to intake measures relied on the distinction between preparatory responses (which include approach to the site of a CS) and consummatory responses (which are directly influenced by hedonic properties of the CS) (see Dwyer et al., 2013). Thus, while there may be multiple components to learning underpinning CTA, it does not appear that any of them are obviously subject to the PREE effect.

As an aside, it should be noted there is a recent demonstration of instrumental effects in CTA (Li, Hsiao, & Li, 2013). This elegant experiment shows that when two tastes are followed by LiCl, if the LiCl dose is based on the amount consumed of only one of them, then only consumption of the contingent taste is suppressed and consumption of the non-contingent taste gradually increases (despite both tastes being presented in the same Pavlovian relationship with LiCl). Thus it remains an open question as to whether a PREE might be more apparent when an instrumental schedule is explicitly imposed on a CTA procedure.

Turning to the question of how the PREE might best be analysed, the lack of PREE in CTA appears to be entirely consistent with Mackintosh's analysis of the PREE as a consequence of generalisation decrement. That is, the PREE is obtained when partially reinforced animals have been reinforced for responding under conditions similar to those controlling responding in extinction, and the CTA procedure does not appear to reflect this type of situation. Considering first the factor of memory trace: Mackintosh noted that when animals are trained on a variable pattern of reinforced and nonreinforced trials, the memory trace of preceding trials can be regarded as forming part of the set of events available for

association with the reinforcer on subsequent trials. Since memory traces decay over time, the trace of the previous trials must be active on rewarded ones to influence learning. Both typically, and in the current study, CTA procedures are arranged such that the trials are widely spaced in time and therefore, the trace of a nonreinforced trial is unlikely to be particularly active on subsequent rewarded trials. Thus, the memory traces active during partially reinforced training in the current study (or CTA more generally) would not be more like those in extinction than the traces active during continuously reinforced training. However, the presence of long ITIs does not entirely prevent the PREE: while several studies have showed decreased resistance to extinction after partial reinforcement using long ITIs (Capaldi, Berg, & Sparling, 1971; Mackintosh, 1970; Sheffield, 1949; Weiner, Feldon, & Bercovitz, 1987) it has also been demonstrate that the PREE is still obtained with extended (24hrs) gaps between trials (e.g. Weinstock, 1958).

Another factor identified by Mackintosh as contributing to generalisation decrement in PREE is the range of stimuli/events potentially associated with the reinforcer – for example, instrumental responding typically occurs in relatively unconstrained situations (e.g. a runway or a box with a lever) where any aspect of the situation might control responding. However, when the control of responding is focused on a smaller set of cues (e.g. by examining discrimination learning based on explicit cues) then the reliability of the PREE is greatly diminished (see Mackintosh, 1974 p. 439). In the current study, training trials with the flavour CS were interspersed with water-only trials, ensuring that it was the CS, and not the general environment of the experimental apparatus or the consumption of fluid generally, which controlled responding[2]. As the flavour of the CS was entirely consistent between training and extinction for both partially and continuously reinforced groups then there would

[2] Moreover, if the context was controlling the response, this should be observable in consumption on water trials. However, there was no effect of schedule for paired groups on water consumption over training trials, $F(1,22) = 0.978$; $p = .334$, $B_{01} = 2.063$.

be little opportunity to other cues (which might differ between the partial and continuous groups) to control responding.

Finally, it remains the case that the animals should be able to form an association between any cues which are elicited when reinforcement is expected but absent and the outcome. Although this idea was originally developed in the context of frustration responses to the omission of reward Amsel (1958, 1992), it is entirely consistent to apply it to any internal state created by the omission of either positive or negative outcomes (see for example Pearce et al., 1997). In the current situation, both the partial and continuously reinforced animals received experience of the apparatus without the induction of nausea on the water alone trials, and so both would have the opportunity to form associations between these contextual cues and any emotional state produced by non-reinforcement. Thus, to the degree emotional responses elicited by the absence of illness could be associated with subsequent induction of illness, this could occur in both partially and continuously reinforced animals thus obviating the possibility of this mechanism contributing to a PREE in the current experiment.

Returning to the relationship between the PREE and instrumental and Pavlovian conditioning, Mackintosh's own analysis is typically nuanced and informative. Firstly, he notes that the many procedural factors which contribute to the PREE (e.g. ITI, number and distribution of reinforced and non-reinforced trials) are often very different between Pavlovian and instrumental situations, and so any firm comparison of PREE between instrumental and classical responses would require more direct matching of conditions than has typically been the case. Secondly, he notes that Pavlovian responses might be particularly closely tied to the stimuli which elicit them, and thus be relatively impervious to interference from external events (including the memory traces of prior outcomes). As such, the potential difference in PREE between instrumental and Pavlovian conditioning might not rest in some

general difference in learning mechanism, but instead derive mainly (if not completely) from the specifics of the learning situation. Indeed, the analysis of the current experimental parameters in terms of the ITI and presence of water-alone sessions, is a reminder that factors already identified as contributing to the reduction of PREE in instrumental conditioning are present in this (and other) putatively Pavlovian procedures. In contrast, at least some of the reports of the presence of the PREE in Pavlovian preparations involve training parameters that might elicit a reduction in generalisation decrement (e.g. relatively short ITIs and designs which do not afford learning about cues created by the omission of reinforcement in the continuously reinforces conditions – see Haselgrove et al., 2004; Pearce et al.1997). Thus, while the absence of reliable PREE effects might well provide a functional distinction between Pavlovian (including CTA) and instrumental procedures in practice, this may be contingent on the specifics of the procedures rather than a reflection of a difference in learning mechanism itself.

In summary, we demonstrate here that extinction of CTA in terms of either consumption or palatability is not retarded by partial reinforcement in acquisition. Although Mackintosh never considered the question of partial reinforcement and CTA himself, the current results are entirely in line with his general theoretical analysis of the PREE effect as generalisation decrement as well as his comments on the ways in which the PREE might differ between instrumental and Pavlovian procedures. Thus, the current results illustrate some of the properties of CTA learning, but perhaps more importantly, they also remind us of the deep legacy of Nick Mackintosh's writing and the contemporary relevance of his theoretical analysis of learning and conditioning processes.

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Conflict of interest

The authors declare that they have no conflict of interest, financial or otherwise, related to this work.

Figure 1. Mean intake of saline solution (A) and lick cluster size (B) during acquisition phase for all groups. Error bars represent the standard error of mean (*SEM*).

Figure 2. Mean saline solution consumption (A) and lick cluster size (B) over the 16 extinction trials. Error bars represent the standard error of mean (*SEM*).

Figure 3. Mean saline solution consumption (A) and lick cluster size (B) over first 8 extinction trials once the "minimum engagement" criterion of 50 licks/session was met. Error bars represent the standard error of mean (*SEM*).

Table 1. Design of experiment

Group	3 x Training cycle				16 x Test
	Day 1	Day 2	Day 3	Day4	
Partial-paired	NaCl → 2 ml/Kg LiCl	water	NaCl → nothing	water	NaCl
Continuous-paired	NaCl → 1 ml/Kg LiCl		NaCl → 1 ml/Kg LiCl		
Partial-unpaired	NaCl // 2 ml/Kg LiCl		NaCl // nothing		
Continuous-unpaired	NaCl // 1 ml/Kg LiCl		NaCl // 1 ml/Kg LiCl		

Note. Groups paired were administered an i.p. LiCl injection immediately after drinking a saline solution, meanwhile unpaired groups were injected 4 hours after the saline consumption. On Day 3 in each training cycle, partial groups did not received the ip LiCl injection. Saline solution was presented at 1% (w/w) for 10 minutes.

Figure 1.

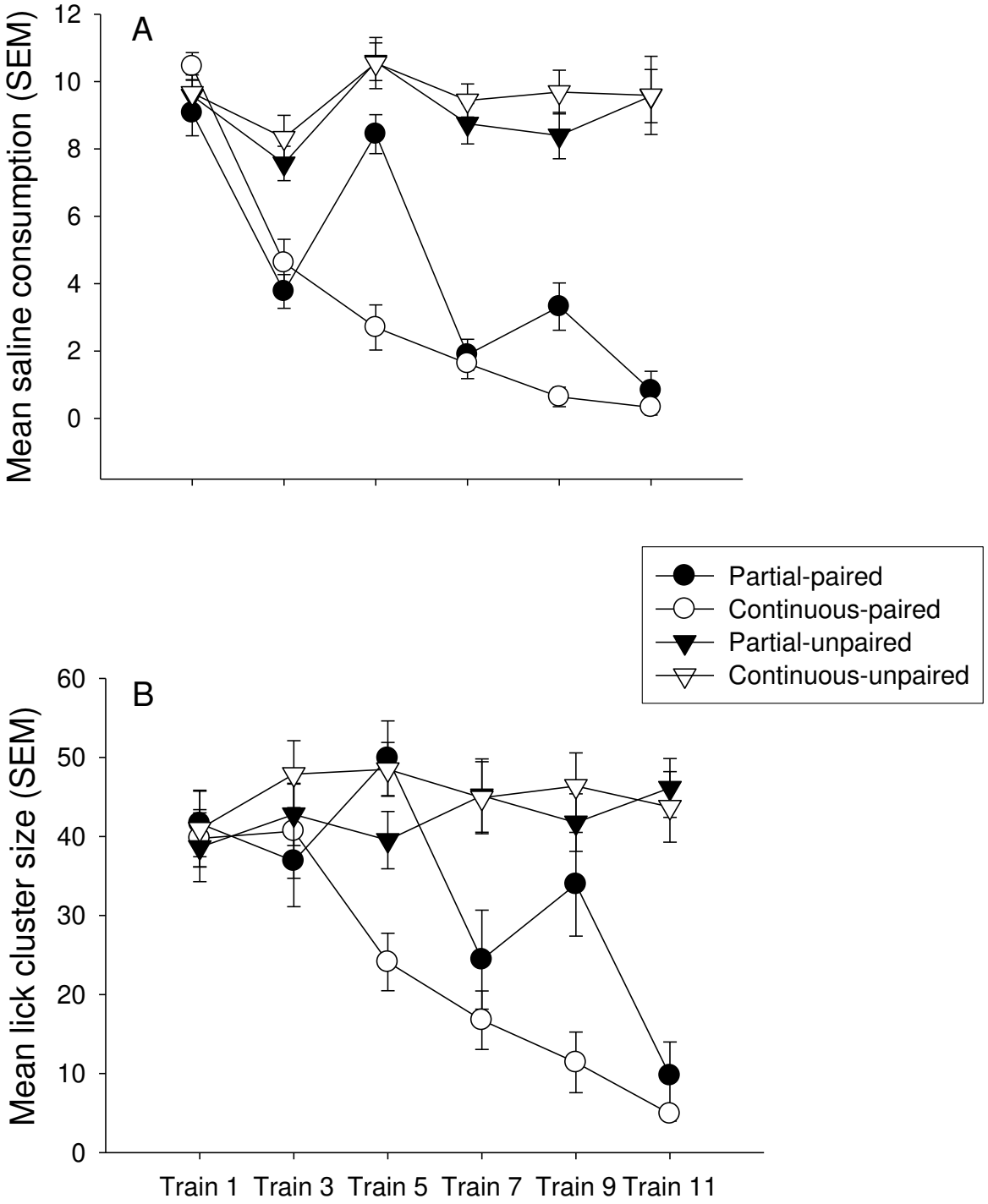

A
Mean saline consumption (SEM)
12
10
8
6
4
2
0
B
Mean lick cluster size (SEM)
60
50
40
30
20
10
0
Train 1
Train 3
Train 5
Train 7
Train 9
Train 11
Partial-paired
Continuous-paired
Partial-unpaired
Continuous-unpaired

Figure 2.

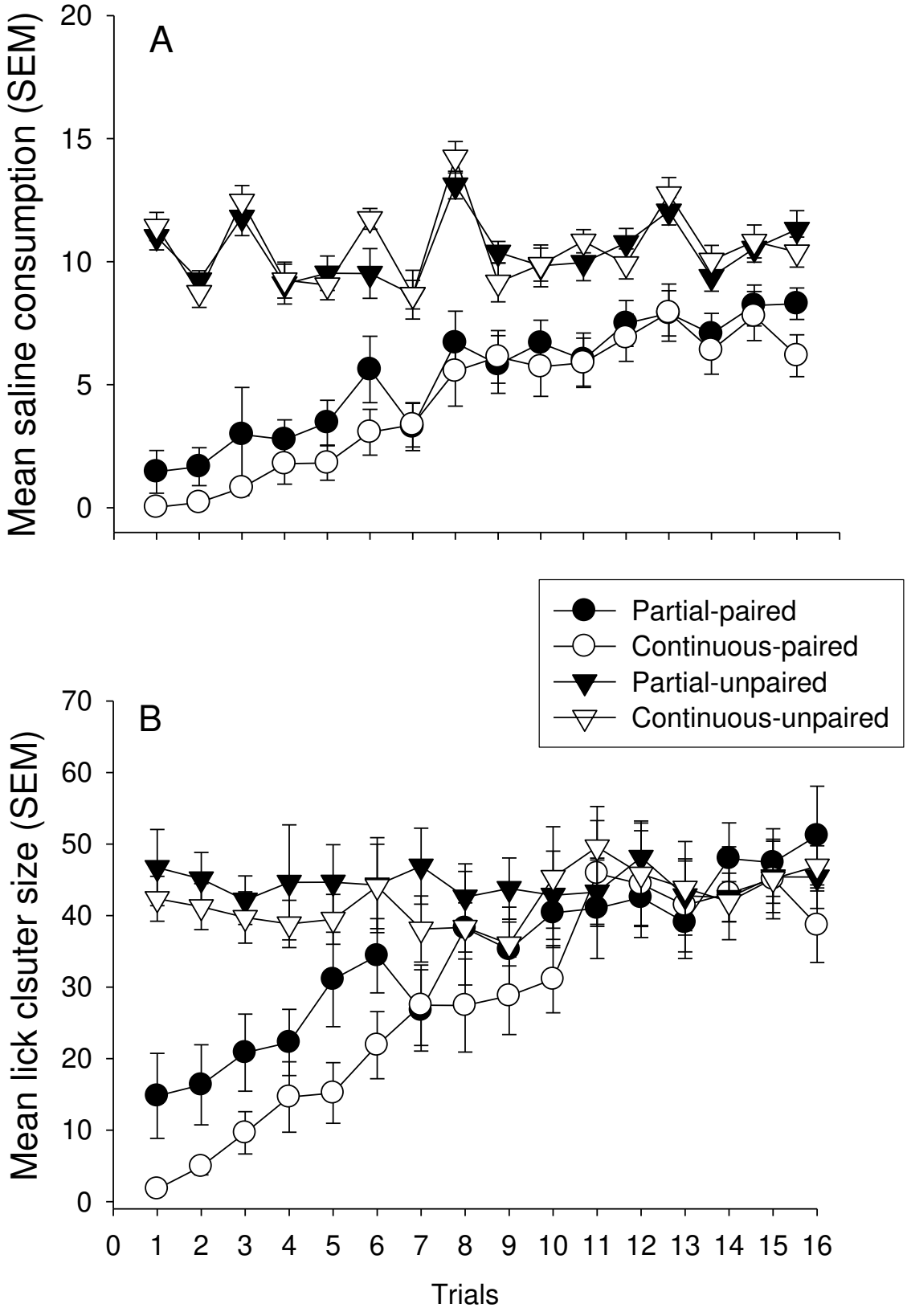
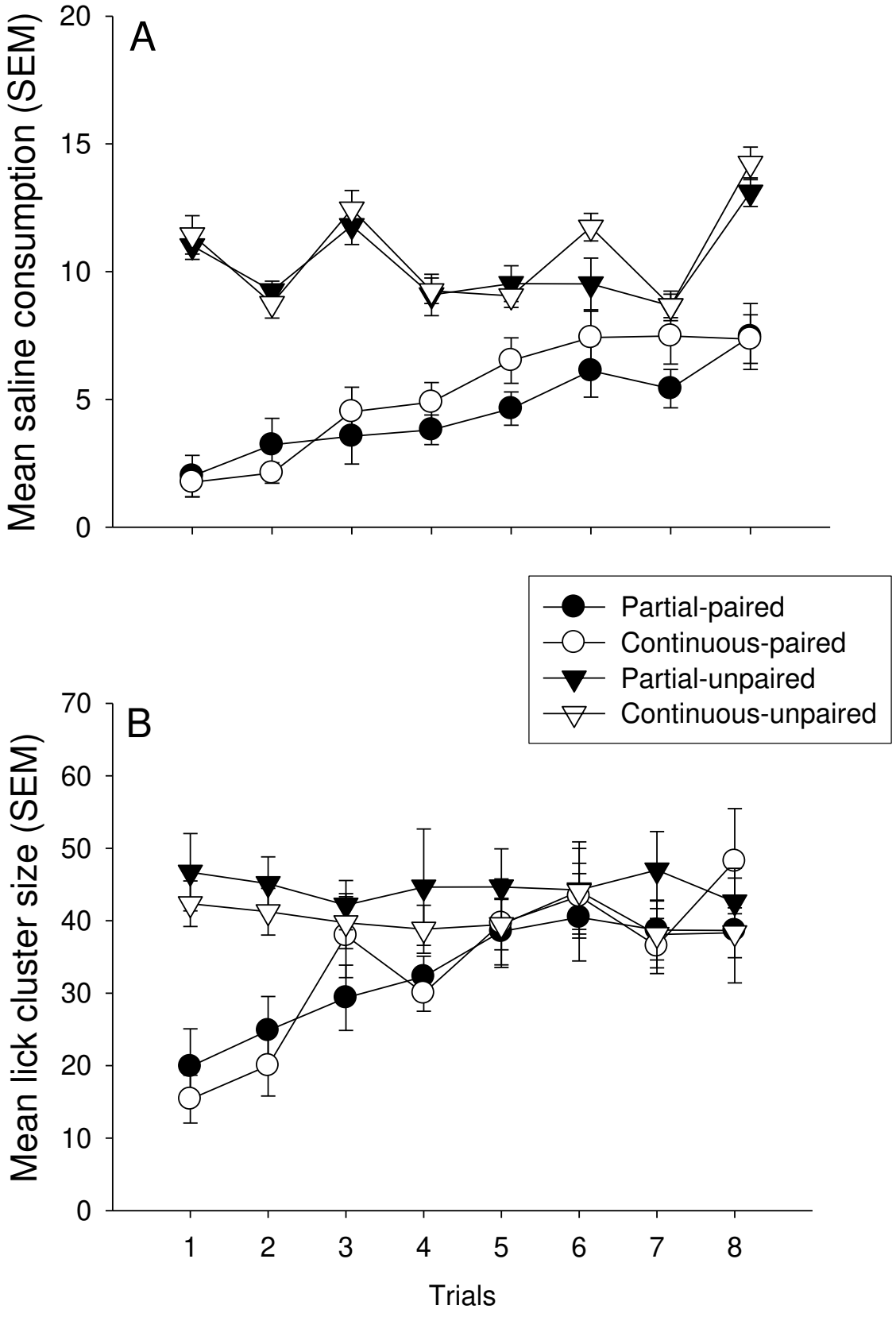

A
Mean saline consumption (SEM)
20
15
10
5
0
Partial-paired
Continuous-paired
Partial-unpaired
Continuous-unpaired
B
Mean lick clsuter size (SEM)
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Trials

Figure 3.


A
B
Mean saline consumption (SEM)
Mean lick cluster size (SEM)
Trials
Partial-paired
Continuous-paired
Partial-unpaired
Continuous-unpaired
0
5
10
15
20
30
40
50
60
70
1
2
3
4
5
6
7
8

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