A novel test of conditioned inhibition correlates with personality measures of schizotypy and reward sensitivity

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Abstract

Conditioned inhibition is demonstrated when the meaning of one signal (conditioned stimulus, CS) is qualified by another (conditioned inhibitor, CI). Whilst the CS presented alone reliably predicts the outcome (unconditioned stimulus, US), when presented in conjunction with the CI the otherwise expected US will not occur. Conditioned inhibition has long been established in animal research but there have been difficulties in establishing reliable procedures suitable for use in human research. Such procedures are necessary to investigate disorders in which cognitive inhibitory mechanisms are known to be deficient, e.g., schizophrenia. In healthy participants, individual differences in the tendency to show conditioned inhibition should be related to personality measures of cognitive inhibition. In the present study, this was measured using an automated test procedure, in which visual stimuli predict the occurrence or non-occurrence of a visual outcome US, and BIS/BAS and schizotypy scales. Conditioned inhibition was reliable across two alternative test variants, in which the non-occurrence of the US was specified differently, and was confirmed by summation tests. The level of CI shown was positively associated with BAS Reward Responsiveness but did not correlate significantly with any of the other BIS/BAS scales. Conversely, the level of CI shown was negatively associated with schizotypy. We suggest that this novel conditioned inhibition task should now be applied to investigate a range of disorders that have some basis in dysfunctional inhibitory processes, such as schizophrenia.

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1. Introduction

Inhibitory conditioning tells us when important events, that we would normally expect, will not in fact occur [36]. Conditioned inhibition is demonstrated in discrimination learning procedures in which the meaning of an otherwise excitatory stimulus is qualified by another (by definition inhibitory) stimulus. This effect is well established in animal studies; in the present study, we have developed a new procedure suitable for testing human participants.

Formally, such procedures can be expressed as CS+/(CI, CS)−, where ‘CS’ denotes the conditioned stimulus, ‘CI’ denotes the conditioned inhibitor, ‘+’ means reinforcement with the unconditioned stimulus (US), and ‘−’ means no reinforcement. Demonstration of conditioned inhibition requires setting up two experimental contingencies. Basic training sets up excitatory pairings of the CS and the US; discrimination training introduces trials on which the CI presented together with the CS is unreinforced; the CS presented on its own continues to be followed by the US. Typically, these two contingencies are presented together in a single training stage.

There are many reports of conditioned inhibition in animals [8,32,41], but there have been relatively few successful demonstrations in humans [19]. Thus, this work lags behind the development of other Pavlovian paradigms to test selective learning in human participants [3,13,27,28,43]. Such developments have been critical in allowing translational modelling between human clinical populations and animal work to identify the biological substrates of learning phenomena in which selectivity is key and normal associations are restricted to the most informative predictors of reinforcement [18,25,26,44,45].
What factors are critical for the successful demonstration of conditioned inhibition? One important test is the ‘summation’ test of conditioned inhibition introduced by Rescorla [21,35,39,48]. The inhibitory effects of the CI are measured by presenting it with a CS that is entirely novel or a CS that has never been presented with the CI before (a transfer CS). Thus, the summation test determines whether the CI can counteract the excitatory effects of other CSs. When the summation test is passed, the CS does not result in the expected conditioned response (CR) in the presence of the CI. This test is suitable for training procedures that encourage the use of elemental processing [31,40,47,49]. In the present study, this was achieved by using serial presentation of the stimuli, that facilitates transfer of the CI’s inhibitory properties, and the summation test was therefore applied.

Existing procedures have demonstrated reliable differences in responding to the CS in the presence and absence of the CI [22]. However, there has been little if any demonstration of the transfer of the inhibitory properties of the CI in summation tests [19,33,46,47]. Moreover, whether because of questionable specificity of the inhibitory properties demonstrated [33], or because of failure to transfer inhibitory properties [19,46], current conditioned inhibition procedures, suitable for use with human participants, have proved difficult to identify with the original phenomenon described by Pavlov. Where there have been encouraging results in this respect, to date the procedures have for the most part been aversively motivated. For example, a CI, which inhibited the CR to a CS reinforced by shock US, passed a summation test for both electrodermal responses and subjective expectation judgements [20]. Similarly, Neumann et al. [31] also found a conditioned inhibition effect that passed summation tests with both self-report US expectancy and electrodermal responses in an experiment with shape CSs and an electric shock US when subjects were trained to use an elemental strategy.

The dimensional view of schizophrenia suggests that the signs and symptoms of the disease are continuous with normality [6,7,30,42]. Many cognitive processes that are dysfunctional in schizophrenia are similarly dysfunctional in individuals scoring highly on schizotypal personality scales. Thus, schizotypy scales displayed should be inversely related.

Beyond schizophrenia, deficient inhibitory learning mechanisms have also been reported in obsessive–compulsive disorder, attention deficit hyperactivity disorder, mania, depression and Tourette’s syndrome. We therefore used an additional personality scale that is not specifically tied to any particular predisposition to disorder to measure activity in the behavioural inhibition system (BIS) and activation systems (BAS) described by Gray [17]. BIS scores were predicted to be positively related to conditioned inhibition. In general terms, both behavioural activation and behavioural inhibition have been argued to influence the development of schizophrenia [14] but the BIS/BAS scale has much wider applicability to a range of disorders of impulse control.

In both experiments, the summation tests measured the generalization of the inhibitory properties of the CI to additional stimuli: a novel stimulus (SN) that did not appear at all in the training phase; and a transfer stimulus (CST) that did not appear with the CI in the training phase. In both experiments it was predicted that conditioned inhibition should be demonstrated as a significant effect of stimulus (i.e., the different stimului combinations presented at test) with US-reinforced stimuli receiving higher expectancy ratings than non-US-reinforced stimuli.

2. Method

This was a visual conditioned inhibition task that depicted scenes in space with large planet CSs and a rocket US. The CI was provided by a grey border on trials on which the CS was not followed by the US, instead there was either an exploded rocket or a blank screen. In addition, there were a number of small distractor planets so that the relationships between the stimuli were not too obvious. Stimuli were presented visually to encourage participants to process them elementally and so promote the demonstration of summation that requires that the CI transfer its inhibitory properties to other excitatory stimuli [31]. In the training phase, participants were required to count rockets. This had two purposes: (1) to provide a level of masking, essential to demonstrate this kind of conditioning effect in humans who otherwise show expectancy effects to the stimuli presented; and (2) to establish rocket presentations as reinforcing.
In Experiment 1, it was possible that rather than the grey border acting as a CI as intended, participants may instead have formed an excitatory association between the grey border and the exploded rocket. Experiment 2 was therefore run as a replication in which instead of presenting an exploded rocket to signify the absence of the US, there was just a background screen. In order to make sure that participants were aware of the absence of the US, the training phase included the instruction ‘Press the space bar to continue’ at the same point in the stimulus sequence where a US could be presented, regardless of whether the rocket did or did not appear. Two variants of the procedure were tested: when an exploded rocket was presented on non-reinforced trials and when the non-reinforcement was designated by the absence of any rocket. The second variant was important to exclude the possibility that the task could be solved using an alternative set of excitatory associations to the exploded rocket stimulus.

2.1. Participants

An opportunity sample of 30 undergraduates (12 males, 18 females) at the University of Nottingham volunteered to participate in Experiment 1, mean age = 21, range 16–38 years. Experiment 2 was conducted on an opportunity sample (18 males, 12 females) that included school students, recently-graduated young professionals and mature professionals, as well as undergraduates, mean age = 24, range 16–48 years. Procedures conformed to the requirements of the relevant Ethics Committee (School of Psychology, University of Nottingham).

2.2. Stimuli and materials

Examples of the stimuli presented are shown in Fig. 1. The program was produced in E-studio and was run through E-prime (Psychology Software Tools Inc., Pittsburgh, US). Both experiments used the same stimuli and procedures except that a background scene replaced the exploded rocket stimulus to signify no US in Experiment 1. Both experiments were conducted on personal computers, each with a standard 17-in. monitor.

Two personality measures were given to all participants. These were a 55-item schizotypal traits questionnaire, the STQ developed by Claridge and Brooks [6,7]. This questionnaire is comprised of STA and STB subscales to distinguish schizotypal and borderline personality, respectively [6,7]. In addition, we administered the BIS/BAS questionnaires [5,17]. The BIS/BAS measure has four subscales to measure functioning in these two systems: BIS, BAS drive (BAS-D), BAS fun seeking (BAS-FS) and BAS reward responsiveness (BAS-RR) [5].

2.3. Procedure

This was the same for both experiments. The training phase consisted of 90 stimulus sequences. The aim of the study was masked by the requirement to press the spacebar whenever a rocket appeared and to count the number of (intact) rockets presented. There were 15 cycles of 6 stimulus sequences: CSA+, CSB+, CST+, [CI, CSA]−, [CST, CSB]− and −−−−−, ‘+’ signifies reinforcement with intact rocket US; −−−−− signifies no reinforcement, i.e., presence of the exploded rocket in Experiment 1 or the background screen in Experiment 2; the letters designate the different planet CSs (see Fig. 1). The ‘minus’ (−−−−−) stimulus presentations were simply entirely unpredicted presentations of the exploded rocket, included to ensure that presence of the rocket US was predicted by a planet CS and not by the absence of the CI. Thus, there were a total of 45 reinforced trials and up to 45 intact rockets should have been counted. An example stimulus sequence is shown in Fig. 2. This procedure was completed in approximately 45 min.

The test phase consisted of 45 stimulus sequences, 5 cycles of 9 randomly presented stimulus sequences: CSA+, CSB+, CSN+, CST+, [CI, CSA]−, [CI, CSB]−, [CI, SN]−, [CST, CSB]− and −−−−−. The procedure for each stimulus presentation in the test phase followed that of the training phase until the presentation of the US, where instead a question mark was presented, indicating that participants had to rate the likelihood (on a scale of 1–9) of the presentation of an intact rocket by pressing a number key on the keyboard. They were instructed that pressing ‘1’ indicated that they were sure the rocket would appear (instead of the US); pressing ‘9’ indicated that they were sure that the rocket would not appear, and pressing ‘5’ indicated that they were not sure either way. Following their decision, a rocket (intact or exploded) could be presented, as applicable, in the test phase this was not followed by distracter planets. The US continued to be presented in the test phase so that conditioned responses did not simply extinguish.

Participants had the opportunity to ask any questions regarding the use of the scale before the test phase began. The generalization of inhibitory properties (reflected in participants’ expectancy scores) from the CI to the compound stimulus sequences with the novel and transfer stimuli in the test phase would constitute the summation test of conditioned inhibition. As in the training phase, the order of the stimulus sequences within the cycles was random in the test phase.

Finally, participants were given as much time as they needed to complete the two personality questionnaires. The only difference in procedure between Experiments 1 and 2 was in how the US was specified (see above).

2.4. Design and analysis

Analysis of variance (ANOVA) was run in a repeated measures design with two factors: stimulus type, of which there were nine levels (see Table 1); and trial, of which there were five levels. The dependent variable was participants’ expectancy scores (for appearances of the intact rocket) which were on a scale of 1–9. Planned comparisons (t-tests at $p \leq 0.05$) were conducted further to...
examine the effect of stimulus type. For these tests, scores were summed over reinforced and non-reinforced presentations, i.e., an average for each stimulus combination was calculated from all five test trials.

We further tested the importance of how non-reinforcement was specified by analyzing for replication effects when the results of Experiments 1 and 2 were combined. For this test, a three-way (9×5×2) mixed analysis of variance was conducted on expectancy scores for rocket appearance. The independent variables were stimulus type, trial and procedural variant (replication).

Next, the two sets of data from Experiments 1 and 2 were pooled to test for the relationship between conditioned inhibition and the personality measures in use. For this we used a conditioned inhibition ratio that was calculated by dividing the average expectancy score for non-reinforced stimulus presentations by the average expectancy score for reinforced stimulus presentations. Thus, conditioned inhibition is indicated by a ratio less than one, and the absence of conditioned inhibition by a ratio greater than or equal to one.

The interrelationship between the level of conditioned inhibition shown and the personality measures in use was explored by Pearson’s correlation, 1-tailed where the direction of the difference was predicted a priori, otherwise 2-tailed.

Finally, prior studies investigating the relationship between schizotypy and performance on learning and attentional tasks such as latent inhibition have indicated that high schizotypal individuals (defined as those scoring equal to or above the group median) have compromised inhibitory processes [27,29]. We therefore analysed the present data in this way for the critical STA scale.

3. Results

3.1. Experiment 1

Conditioned inhibition was clearly demonstrated. There was a significant main effect of stimulus type (F_{8,928} = 4.52, p < 0.001), see Fig. 3A. Reinforced stimuli (CSA+, CSB+, SN+ and CST+) produced higher expectancy scores than on the corresponding non-reinforced trials ([CI, CSA]−, [CI, CSB]−, [CI, SN]− and [CI, CST]−). All of the relevant (planned) comparisons were significant: for each of stimuli A, B, N and T, the

Table 1

<table>
<thead>
<tr>
<th>Training phase</th>
<th>Test phase</th>
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<tbody>
<tr>
<td>CSA+</td>
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<td>CSB+</td>
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<td>CST+</td>
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<tr>
<td>[CI, CSA]−</td>
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<td>[CI, SN]−</td>
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See Fig. 1 for stimuli. A ‘+’ indicates that the rocket was presented and a ‘−’ indicates that the rocket was not presented, with the exploded rocket being shown in Experiment 1 and a blank screen in Experiment 2.
reinforced expectancy score was higher than the correspond-
ing non-reinforced expectancy score for presentations of that
same stimulus with the CI ($t_{29} \geq 2.04, p < 0.05$). As would be
expected, the average expectancy score on the minus trials was
also significantly lower than the overall average on reinforced
trials, as there was by definition no particular corresponding po-
sitive stimulus ($t_{29} = 2.84, p < 0.01$). It was therefore appro-
piant to average over the positive and negative stimulus sequences
(see Fig. 3B).

To test whether the expectancy scores of the US on reinforced
and non-reinforced stimulus presentations were overall differ-
ent to the neutral point (‘not sure either way’, an expectancy
score of 5), two one-sample $t$-tests were carried out to com-
pare expectancy scores to the neutral point of 5. The mean expec-
tancy score for reinforced stimulus presentations was 5.73,
which was significantly greater than 5 ($t_{29} = 4.31, p < 0.001$).
The mean expectancy score for non-reinforced stimulus pre-
sentations was 4.55, which was also significantly less than 5
($t_{29} = 2.87, p < 0.01$). This means the presentation of the condi-
tioned inhibitor clearly reduced participants’ expectancy that a
US presentation would follow.

3.2. Experiment 2

Conditioned inhibition was here demonstrated when the
absence of the US was signified by the presentation of the
background screen in the absence of any rocket. There were sig-
nificant main effects of stimulus type ($F_{3,92} = 2.06, p < 0.05$),
trial ($F_{4,329} = 3.84, p < 0.01$). In this experiment, there was also an
interaction between stimulus type and trial ($F_{12,329} = 1.45,
p = 0.05$). This arose because there was some variation in the
size of the conditioned inhibition effect from one trial to the
next. Fig. 4A shows the data averaged over trials for compari-
son with Experiment 1.

Again reinforced stimuli (CSA+, CSB+, SN+ and CST+) for the most part produced higher expectancy scores than non-
reinforced stimuli ([CI, CSB]+, [CI, CSA]+, [CI, SN]–, and [CI, CST]–). This difference was not significant for the pre-
trained stimuli A and B ($t_{29} = 1.79$ and 1.09, respectively). How-
ever, it was clear for stimuli T and N ($t_{29} = 2.10$ and 3.34, $p < 0.05$
and $p < 0.005$, respectively, confirming that the summation test
was again passed. In contrast with Experiment 1, the average expec-
tancy score on the minus trials was not significantly lower than the overall average on reinforced trials in Experiment 2 ($t_{29} = 1.18$) probably because the blank screen was a much less
effective event than the exploded rocket on the minus trials. We
again averaged over the reinforced and non-reinforced stimulus
presentations, as before, for direct comparison with Experiment 1 (see Fig. 4B).

To test whether the appearance of the US on reinforced stim-
ulus presentations and non-reinforced stimulus presentations
were given significantly different expectancy scores to the neu-
tral point (‘not sure either way’, an expectancy score of 5),
two one-sample $t$-tests were carried out to compare expectancy
scores with the neutral point of 5. The mean expectancy score for
reinforced stimulus presentations was 5.62, which was signifi-
cantly greater than the neutral point of 5 ($t_{29} = 3.87, p < 0.005$)

Statistically, there was a significant main effect of stimulus
type ($F_{3,1856} = 6.31, p < 0.001$) and an interaction between stim-
ulus type and trials ($F_{12,1856} = 1.61, p < 0.05$). The inter-
action with trials persisted when the stimulus presentations
were averaged over US reinforced and US non-reinforced trials
($F_{4,232} = 4.44, p < 0.005$) and arose because conditioned inhibi-
tion was overall absent on trial 1 and much bigger in magnitude
on trials 3–5. This temporary disruption in the expression of con-
ditioned inhibition was most likely produced by the procedural
changes introduced in the test phase. Importantly, there was no
indication of any effect of replication ($F_{4,316} = 2.20$,
for trials by replication). This means that the conditioned inhi-

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure4.png}
\caption{(A) Expectancy scores (means and standard error bars) for stimulus sequences in Experiment 2. Values below 5 indicate that participants did expect the US to appear, and values of 5 indicate that participants were not sure either way. (B) Average expectancy scores (means and standard error bars) for reinforced and non-reinforced stimuli in Experiment 2. Reinforced sequence: CSA+, CSB+, SN+ and CST+; non-reinforced stimulus sequences: [CI, CSB]+, [CI, CSA]+, [CI, SN]–, [CI, CST]–. ($^{*}p < 0.01$).}
\end{figure}

The mean expectancy score for non-reinforced stimulus presen-
tations was 4.92, which was not in this case significantly less
than the neutral point of 5 ($t_{29} = 0.50, p = 0.62$).

3.3. Comparing results of Experiment 1 and Experiment 2

The combined analysis confirmed that conditioned inhibition
was shown irrespective of the different methods used to specify
non-reinforcement used in Experiments 1 and 2.

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scores measured by the STA subscale of the STQ (Fig. 5. Conditioned inhibition ratio as a function of high and low schizotypy inhibition score and Claridge and Broks’ STQ [7] (greater than or equal to one). The less evidence there was of any conditioned inhibition (loss confirmed that, as predicted, the higher the schizotypy score combined data set of Experiments 1 and 2. Correlational analyses displayed and personality measures using the com-

3.4. Correlations with personality variables

As there was no effect of procedural variant, it was appro-

There was a significant correlation between the conditioned inhibition score and Claridge and Broks’ STQ [7] (r = 0.245, p = 0.03). When the STQ was broken down into its two subscales this correlation was found to arise because of an association with STA scores (for STA, r = 0.241, p = 0.03; for STB, r = 0.185, p = 0.08). The association between conditioned inhibition and STA was further confirmed by the median split analysis. The CI ratio was significantly greater in high versus low schizotypal individuals on STA (F(1,19) = 4.55, p < 0.05), see Fig. 5. The relationship between conditioned inhibition and the BIS and BAS (BAS-D, BAS-FS and BAS-RR) scales [5] was also tested using a 2-tailed Pearson’s r correlation. These correlations were 2-tailed because although BIS scores could be predicted to be positively correlated with the level of conditioned inhibition shown (in which case they should be negatively correlated with the ratio score), there were no firm a priori predictions for the BAS subscales. There was a significant correlation with BAS-RR only (r = −0.30, p < 0.05). None of the other three correlations between the BIS/BAS subscales and conditioned inhibition were significant. Thus, behavioural inhibition as measured by this personality scale was, in the present study, unrelated to the development of conditioned inhibition in an associative learning task. With respect to behavioural activation, BAS-D and BAS-FS were similarly unrelated to the development of conditioned inhibition. BAS-RR is identified as the subscale that moderates the development of conditioned inhibition.

4. Discussion

A conditioned inhibition effect was demonstrated in both ver-
sions of the task tested and confirmed by summation tests. The fact that conditioned inhibition was shown irrespective of how the absence of the US was indicated is consistent with the poss-
sibility that the exploded rocket and the entirely absent US were processed in the same way. The complete omission of a stimu-
lus to represent non-reinforcement may be preferable as it stays faithful to conditioned inhibition as described by both Pavlov and the later Rescorla–Wagner theory [33]. In terms of individ-

4.1. Conditioned inhibition was clear irrespective of how the UCS was specified

In Experiment 1, as would be expected, participants reported a higher expectancy when the US was programmed to appear than when it was not, demonstrating apparent excitationary and inhibitory learning, respectively. Furthermore, the inhibitory properties of the grey border CI were transferred to a novel stim-

4.2. What learning processes were involved?

The summation test was passed in these experiments. Serial presentation of stimuli was used to encourage elemental pro-
cessing and this may have promoted the demonstration of con-
ditioned inhibition. Whilst there are studies that have shown
CI without actively encouraging participants to process stimuli elementally [20], almost all other studies that have shown CI in humans and passed a summation test [39], have involved a stage which encouraged elemental processing of the to-be-conditioned stimuli [31].

A debate beyond the scope of this study concerns whether associative learning of the kind demonstrated here involves implicit or explicit cognitive processes. It has been argued that ‘humans may use abstract rules to solve discrimination problems that rats solve by associative learning’ [24,47]. However, there is also widespread evidence to support the formation of associations between stimuli in human Pavlovian conditioning without awareness [34].

It is likely that the masking procedure used in the present study would have served to promote a task solution based on implicit learning, but in order to differentiate between implicit and explicit learning, different measurements of the conditioned response would need to be used. Autonomic reactions, including electrodermal, vasomotor, cardiac and startle responses, can be measured as an alternative to self-reported US expectancy. In situations where autonomic responses are found in the absence of self-reported awareness of associative rules, implicit learning can be assumed.

4.3. Conditioned inhibition and personality characteristics

The relationship between the level of conditioned inhibition shown and the personality measures of schizotypy and BIS/BAS was tested using averaged ratio scores. The fact that the conditioned inhibition ratios were lower (showing the development of conditioned inhibition) on the reinforced as compared to the non-reinforced stimulus presentations in the absence of the US, for all the different types of stimulus presentation, confirmed that the transfer and novel stimulus presentations could be grouped with the reinforced stimulus presentations in the presence of the US for this analysis.

We have shown the predicted relationship between conditioned inhibition and schizotypy. Individuals scoring highly on a schizotypy measure, in particular the STA, show significantly lower inhibition indicated by higher CI ratio scores. This suggests that conditioned inhibition as measured using this task may indicate how conditioned inhibition might contribute impulsive responding. In any event, mesolimbic dopamine would provide a very plausible underlying substrate for effects mediated through both reward sensitivity and schizotypy [14,18,44,45]. This issue could be directly addressed with follow up drug studies, e.g., using amphetamine. Further work will also be necessary to determine how conditioned inhibition is moderated by additional individual differences, such as age and gender, as has been investigated in other selective learning tasks such as Kamin blocking [10] and LI [27].

4.4. Conclusions and implications

In the present study, a non-aversive procedure to show conditioned inhibition has been reliably demonstrated and confirmed by summation test. In normal participants, we find an association between conditioned inhibition performance and established measures of schizotypy and reward sensitivity. This novel task uses visual attentional learning and provides a reproducible test of conditioned inhibition, with good construct validity in terms of how the effect is moderated by key individual differences variables. Procedures such as these are essential to explore the clinical implications of conditioned inhibition and its dysfunction.

The relationship between increased conditioned inhibition and BAS-RR could be relevant to our understanding of a wide range of disorders including substance misuse, binge eating, and socially disordered behaviour in general, as well as schizophrenia. In particular, the likely relevance of the present task to our understanding of schizophrenia was confirmed by the inverse relationship between the level of conditioned inhibition displayed and schizotypy.

Acknowledgement

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