Blocking, Overshadowing and Related Concepts

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Synonyms

Attentional learning; Selective learning

Definition

Blocking is a reliable cross species learning effect. It has been studied primarily using classical (Pavlovian) conditioning in which animals come to show their learned anticipation of a biologically significant outcome, typically food or foot shock, through a behavioral conditioned response. This conditioned response often resembles the unconditioned response for the outcome (unconditioned stimulus, UCS) - for example, in Pavlov's original studies, the salivation response to food came to be elicited by a bell, termed the conditioned stimulus (CS), that preceded food delivery. This anticipatory responding allows us to quantify the strength of the conditioned association.

Importantly, classical conditioning is selective to the best predictors of outcomes, raising the possibility that here is a mechanism allowing animals to build up a representation of the causal structure of the environment. In any event, in the absence of selectivity, the learning mechanism would be overloaded and inefficient. The blocking effect, discovered by Kamin in 1968, is an example of selectivity based on the redundancy of a potential CS (B). This redundancy arises because there already exists a reliable CS (A) for the outcome in question (Table 1).

Impact of Psychoactive Drugs

The impact of psychoactive drugs on blocking can only be evaluated with respect to the behavioral controls in place, and these vary from study to study. Blocking in its simplest form is demonstrated in a two-stage procedure: (stage1) present A followed by the UCS; (stage 2) present A in combination with B, followed by the same UCS. Ideally, several controls are needed: For example, because A might be intrinsically more salient than B, the best designs counterbalance the stimulus identities; most importantly, because conditioning to B might be reduced due to competition with A, the stage 2 conditioning is also compared with that seen in a separate group of animals conditioned to the compound. This control group is given equivalent stage 2 training in the absence of any stage 1 pre-training with A. Thus, we can separate out the reduced conditioning to B, which results from direct

cue competition through overshadowing as distinct from the pre-training with A to establish B as redundant. Overshadowing refers to the attenuation of learning to B as a consequence of conditioning in compound with A, relative to a group who are conditioned to B in isolation. The most essential experimental comparison groups to demonstrate blocking and overshadowing are shown in Table 1.

Table 1
Basic design to show a blocking effect (learning in group 2 minus learning in group 1) and overshadowing (learning in group 3 minus learning in group 2). A and B represent the alternative CSs

Experimental group	**Stage 1**	**Stage 2**	**Learning test**
1. Blocking	A → Shock	[A + B] → UCS	Weak conditioning to B
2. Overshadowing		[A + B] → UCS	Moderate conditioning to B
3. Conditioning control		B → UCS	High conditioning to B

Thus, blocking is typically examined together with overshadowing in the same procedure. The fact that the blocking effect is reliably demonstrated over and above the reduction in learning to B produced by overshadowing in the control group suggests that it may rely on additional mechanisms (beyond direct cue competition). At the psychological level, the prior learning in stage 1 is most likely an important factor.

Related Selective Learning Effects

There exist a number of other selective learning phenomena, likely to be related to blocking or overshadowing in terms of underlying mechanisms. Like blocking, latent inhibition is a two-stage procedure in which stage 1 experience reduces subsequent stage 2 conditioning. A variety of mechanisms have been proposed to contribute to this effect (Escobar et al. *2002*; Gray et al. *1991*; Hemsley *1993*; Weiner *2003*). For example, selectivity in learning could arise from changes in the effective salience of less predictive cues or interference between competing associations. Like overshadowing, relative validity procedures show the superiority of one available CS at the expense of another. In this case, the best predictor is established on a probabilistic basis over a number of conditioning trials. All of these selective learning effects reflect competition between the range of experimental cues available, including those provided by the context.

Blocking as an Endophenotype for Schizophrenia

Selective learning effects like blocking have become targets for translational research. Overconditioning to cues that would normally be treated as irrelevant or redundant provides an animal model of disorder. First, when selectivity in learning fails, the animal is flooded with a profusion of potential conditioning cues and aberrant associations will be formed. Second, the neural substrates implicated in selective learning effects point to a key role for the dopamine system known to be dysfunctional in schizophrenia (Gray et al. *1991*; Hemsley *1993*; Kapur *2003*; Weiner *2003*). Furthermore, studies with human participants show that the normal blocking effect is abolished in schizophrenia (Fig. 1). Thus, like impaired latent inhibition, impaired blocking shows excellent

validity, both at the behavioral and the neurochemical level, as an endophenotype for schizophrenic attention deficit (Gottesman and Gould *2003*).

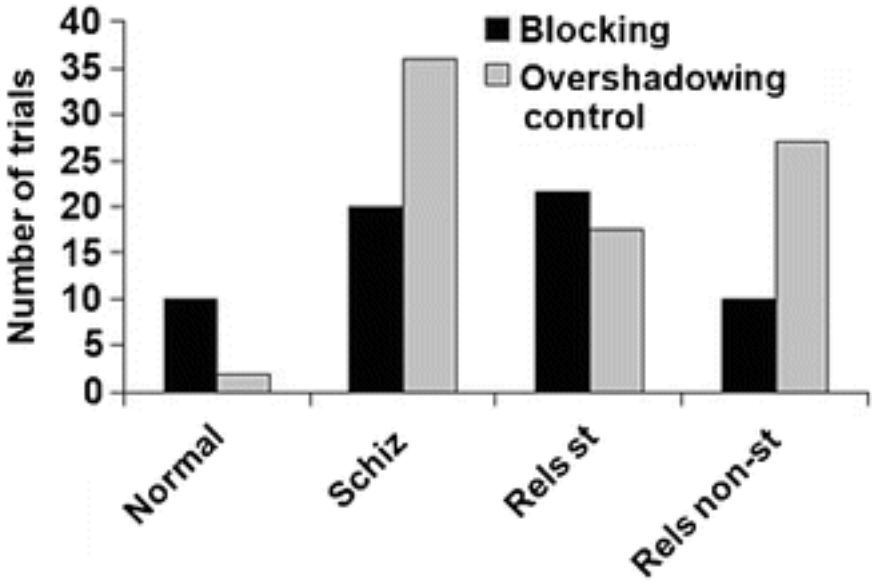

Fig. 1. Blocking in human participants shown in normal participants as an increased number of trials (to the learning criterion) required in the blocking condition relative to the overshadowing controls. This blocking effect was abolished or even reversed in schizophrenic participants (Schiz) and their relatives (Rels), irrespective of levels of schizotypy (st) as measured by questionnaire (Adapted from Jones et al. (*1997*) Behav Brain Res 88:103-114, see text for further details)

Animal Studies of Blocking and Overshadowing

In animals, treatment with indirect dopamine agonists given systemically (typically amphetamine at around 1.5 mg/kg in rats) has been widely reported to abolish blocking. Abolition of the normal blocking effect results in overconditioning, with the consequence that the CS that would normally be treated as uninformative is not blocked from entering into new associations, despite its apparent redundancy (Cassaday and Moran *2010*). In part for practical reasons, because of the need to test for dose-related effects, psychopharmacological studies are not always run with full behavioral controls. In the case of blocking, further reduction in learning produced by the stage 1 pre-training can be a relatively small behavioral effect when compared to that seen in an overshadowing group. In any overshadowing group, conditioning is normally reduced to the stimulus of relatively low intensity; when overshadowing is abolished, by drug treatment, for example, the relatively low-intensity stimulus accrues relatively more associative strength than is seen in the equivalent non-drug-treated group. Amphetamine-induced abolition of overshadowing is not demonstrated under all experimental conditions (Nelson et al. *2011*), and the number of trials may be a critical determinant of sensitivity to drugs (Zelikowsky and Fanselow *2010*). Nonetheless, in some studies, apparent amphetamine-induced abolition of blocking may be confounded by impaired overshadowing under amphetamine. Importantly, patients with schizophrenia have been reported to show impaired blocking, over and above any change in overshadowing (Fig. 1).

With respect to the neural mediation of the systemic effects of amphetamine, dopamine activity in part of the ventral striatum, specifically nucleus accumbens, has been reported to modulate blocking in the absence of any effect on overshadowing in the control group (Fig. 2).

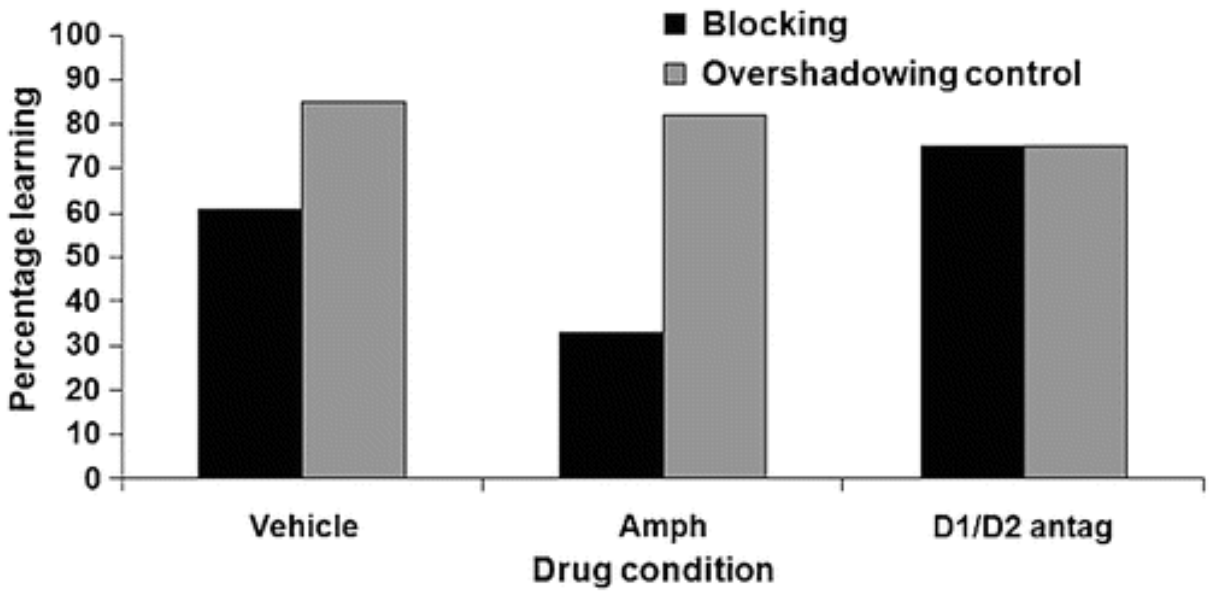

Fig. 2. Blocking shown as a low percentage of baseline learning in a contextual fear conditioning procedure. The comparison group controls for overshadowing by context which it can be seen was unaffected by any of the drug treatments. Blocking was increased by injection of amphetamine in nucleus accumbens and decreased by combined D1 and D2 receptor antagonism produced either by injection of cis-(z)-flupenthixol or combined treatment with SCH23390 and sulpiride. In isolation, SCH23390 and sulpiride were without effect, suggesting that a combined action at dopamine D1-like and D2-like receptors mediates amphetamine effects on blocking (Adapted from Iordanova et al. (*2006a*) Eur J Neurosci 24:3265-3270, see text for further details)

Similarly, the evidence for a pivotal role of nucleus accumbens and related structures is overwhelming in the case of latent inhibition (Gray et al. *1991*; Weiner *2003*). However, it is important to note that the nucleus accumbens is a heterogeneous structure and opposing effects of drug treatments and lesions can be seen in relation to very small differences in the laterality of the cannula placement (Nelson et al. *2011*). Moreover, the evidence with respect to the neural substrates of other selective learning phenomena is patchy, in part because of the poor selectivity of the lesion methods used to date. Techniques in neuropsychopharmacology such as lesions selective to dopamine and precisely targeted microinjection studies are required to delineate the underlying substrates of blocking, overshadowing, and related effects. To date, the role of dopamine has been an understandable focus for pharmacological studies, principally of latent inhibition, though also of blocking and other selective learning effects, due to the fact that established antipsychotics are dopamine antagonists. For example, there is evidence for differential behavioral effects in directly comparable latent inhibition and overshadowing procedures, in relation to dose of amphetamine and laterality of injection placement (Fig. 3; Nelson et al. *2011*). Based on the known effects of serotonergic treatments on latent inhibition (Weiner *2003*), serotonin would similarly be expected to modulate blocking and related effects. However, with few exceptions (Iordanova et al. *2006b*, see below), the effects of localized treatments with non-dopaminergic drugs have been little investigated to date.

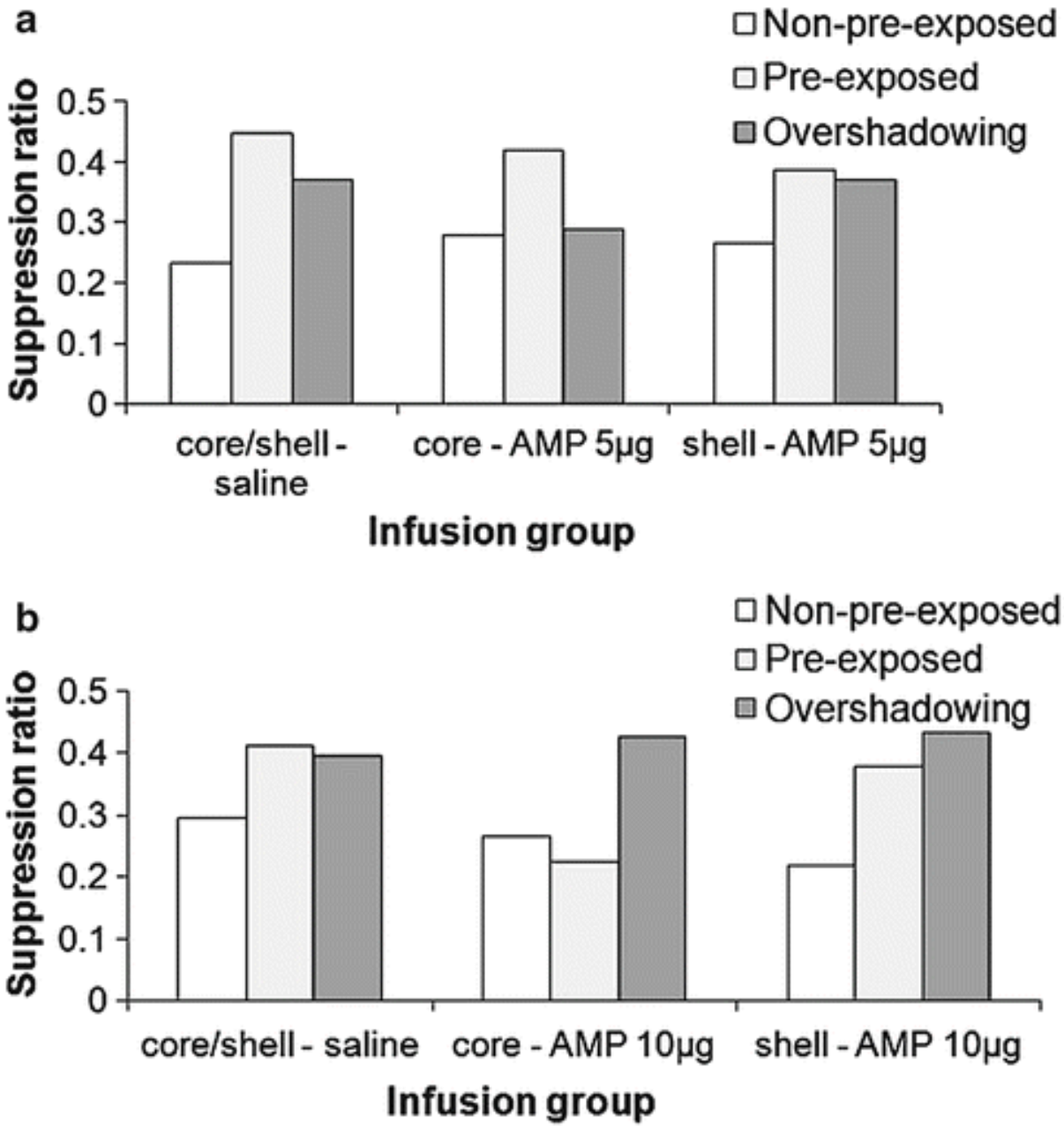

Fig. 3. Learning is shown as suppression ratio scores (low ratio score = strong conditioning; high ratio score = weak conditioning). Latent inhibition is shown as higher suppression ratio scores in pre-exposed compared to non-pre-exposed groups. Overshadowing is shown as higher suppression ratio scores in overshadowing compared to the same (non-pre-exposed) control group. These effects were measured following injection of saline and (**a**) 5 µg amphetamine or (**b**) 10 µg amphetamine in either the core or shell subregions of the nucleus accumbens. Overshadowing was nonsignificantly attenuated after 5 µg amphetamine in core. Latent inhibition was significantly attenuated after 10 µg amphetamine in core (Adapted from Nelson et al. (*2011*) J Psychopharmacol 25:1649-1660, see text for further details)

Blocking and Prediction Error

The blocking effect has been targeted, to understand the biological basis of attentional abnormality, to a large extent without a full consideration of its underlying psychological mechanisms. This situation

may soon be remedied in that blocking has recently assumed prominence as a tool to investigate the neural basis of prediction error. Prediction error is fundamental to normal associative learning because it provides the basis on which to learn when there is a discrepancy between what is expected and what actually occurs. Thus, uncertainty is an important factor in determining attention in learning, and dominant learning theories propose that new learning requires that an association is not already at full strength. Positive prediction error generates excitatory conditioning; negative prediction error generates inhibitory conditioning (Fig. 4).

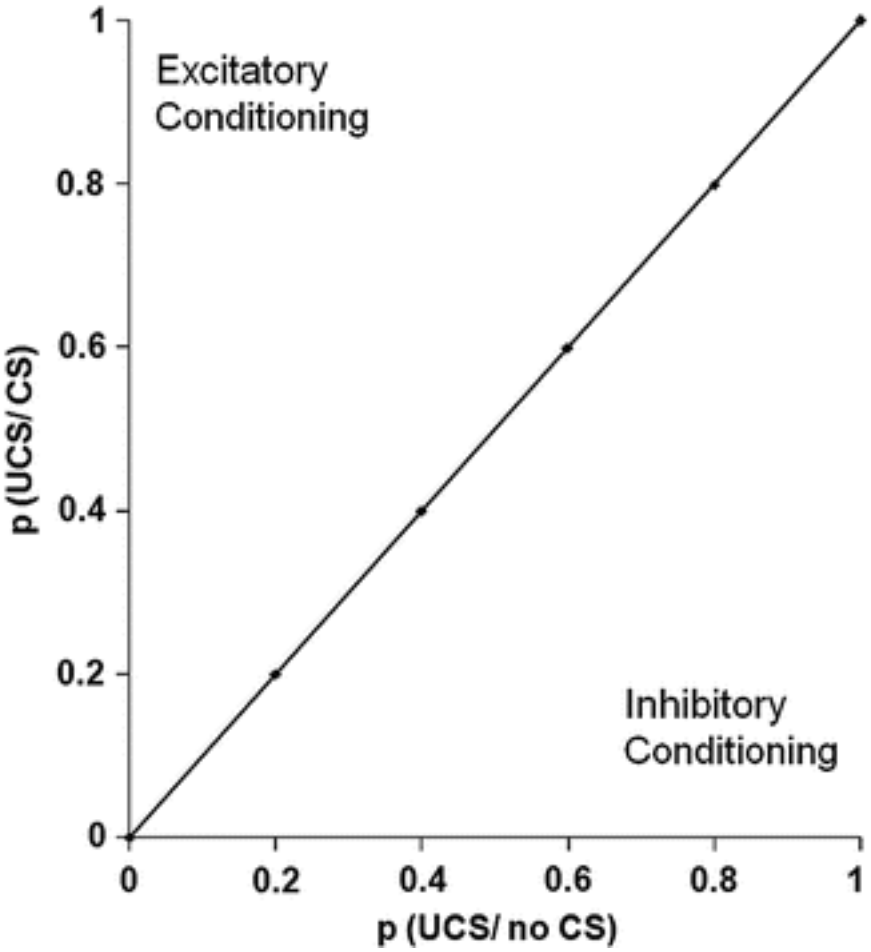

Fig. 4. Positive prediction error when the probability (*p*) of the UCS is increased on presentation of the CS in question generates excitatory conditioning. Negative prediction error when the probability of the UCS is decreased on presentation of the CS in question generates inhibitory conditioning. When *p*(UCS/CS) = *p*(UCS/no CS) along the diagonal trend line, there can be no new learning

Electrophysiological studies show the pivotal role of dopamine as a neurochemical substrate of prediction error (Schultz *2006*; Schultz and Dickinson *2000*). Blocking was the key paradigm that drove our understanding of associative learning in terms of prediction error: the stage 1 pre-training means that the UCS is fully predicted by the time that the competing cue is introduced in stage 2. Thus, there can be no prediction error and thus no additional conditioning to the redundant cue. However, prediction error can be systematically manipulated by changing the UCS delivered. If the UCS is other than expected, unblocking occurs. This can take the form of additional excitatory conditioning to the additional CS if the UCS is more than expected (e.g., a higher intensity foot shock is delivered in upshift unblocking) or inhibitory conditioning to the additional CS if the UCS is less

than expected (e.g., a lower intensity of foot shock is delivered in downshift unblocking). Electrophysiological studies have confirmed that some of the same populations of dopamine neurons that show increased activation subsequent to the presentation of "more than predicted," show depressed neuronal firing after presentation of inhibitory stimuli that signal "less than predicted" (Schultz *2006*). These neurons show no change in neuronal firing when there is zero prediction error, in other words when things remain "as expected." Such a case is provided in the blocking procedure. Pre-training with CS A normally blocks learning about CS B because the prediction error is small. The standard blocking procedure is readily adapted to study the neural bases of excitatory and inhibitory learning (Fig. 4) by manipulating the UCS delivered (Table 2).

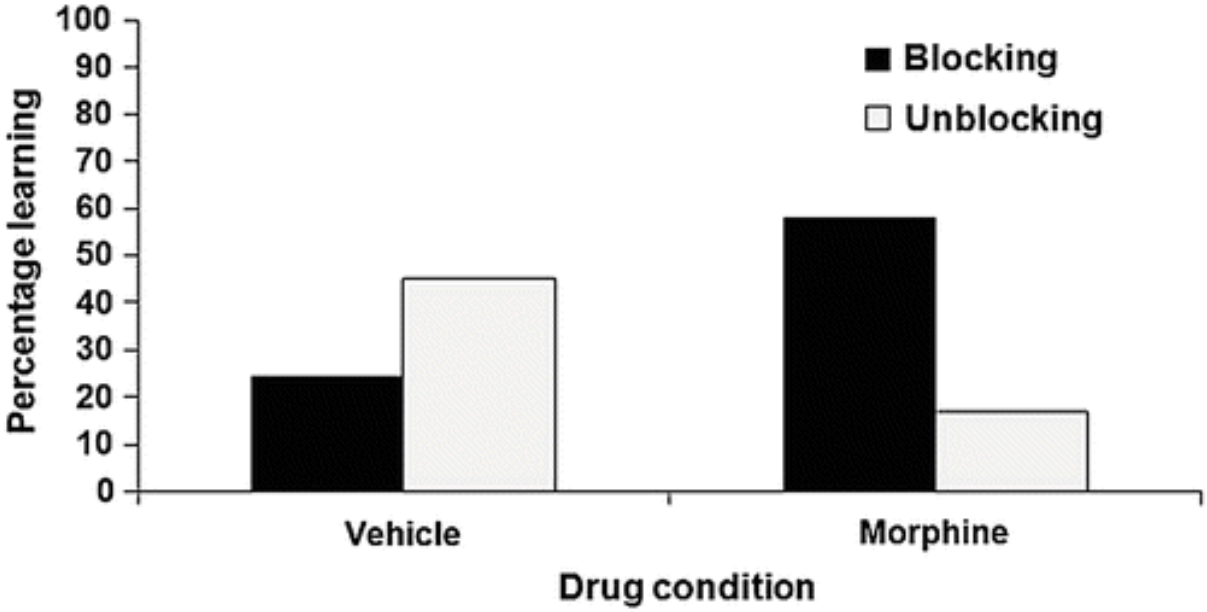

Fig. 5. Blocking shown as a low percentage of baseline learning in a fear conditioning procedure. Unblocking was produced by halving the UCS (shock intensity) and was demonstrated as relatively increased percentage learning. The control level of learning was around 50 %. Blocking and unblocking were affected in opposite ways by injection of opioid compounds in nucleus accumbens (Adapted from Iordanova et al. (*2006b*) J Neurosci 26: 4036-4045, see text for further details)

Table 2

Basic comparison groups to show unblocking due to upshift when the UCS is more than expected (**UCS**) and downshift when the UCS is less than expected (ucs). A and B represent the alternative CSs

Experimental group	**Stage 1**	**Stage 2**	**Learning test**
Blocking	A → UCS	[A + B] → UCS	Weak conditioning to B
Upshift unblocking	A → UCS	[A + B] → **UCS**	Excitatory conditioning to B
Downshift unblocking	A → UCS	[A + B] → ucs	Inhibitory conditioning to B

Thus, blocking and unblocking variants provide target tasks to identify the neuropharmacological substrates of prediction error, for example, using microinjections into the nucleus accumbens (Fig. 5). Moreover, analysis of blocking from an associative learning theory perspective has identified the same underlying neural substrates that are the target of translational studies of blocking as an endophenotype for schizophrenia. At the behavioral level, abnormalities in the processing of

prediction error may be the cause of the formation of inappropriate associations in schizophrenia. In other words, studies of prediction error, known from electrophysiological studies to depend on the dopamine system, also further our understanding of dopaminergic disorders such as schizophrenia. Deficits in blocking, seen both in schizophrenia and under amphetamine, represent a paradigm instantiation of abnormalities in the processing of prediction error. Future studies of the relevant neural substrates of prediction error should include, but are not restricted to, those identified in blocking procedures. Downstream from these Pavlovian effects, abnormal processing of prediction error has been linked to abnormalities of action, including drug addiction where overconditioning in hyper-dopaminergic or glutamatergic states could promote cue-driven relapse because of the increased representation of drug-related cues (Schultz and Dickinson *2000*; Freeman et al. *2013*).

Advantages and Limitations of Blocking and Overshadowing

Latent inhibition, now well established as a model for schizophrenia, shows the predicted sensitivity to psychoactive drugs, and human participants with schizophrenia show impaired latent inhibition (though this demonstration depends on medication status). Similarly, there is good evidence for impairments in blocking in schizophrenia; hence, blocking provides a potential animal model in which to assess the effects of psychoactive drugs, for example, to distinguish the role of dopamine D1 and D2 receptor families in this aspect of attentional learning, as distinct from overshadowing (Fig. 2). Much of this work has yet to be done, in part because reliable parameters to demonstrate blocking can be difficult to establish. An additional disadvantage in the use of blocking arises because a fully controlled study necessitates the use of an overshadowing comparison condition and overshadowing may itself be affected by some of the same drug treatments. Future studies should address this confound. However, overshadowing remains of interest in its own right as a procedure to present stimuli that should normally show reduced salience for learning, to test for overconditioning to weak cues in hyper-dopaminergic states (Cassaday and Moran *2010*; Gray et al. *1991*; Kapur *2003*; Nelson et al. *2011*).

In principle, blocking has an additional attraction in that it relates an issue of fundamental importance in normal associative learning, namely, the role of surprise, encapsulated in the study of prediction error. Through unblocking manipulations, we can study the liberation of attention by surprise and drug effects thereon. However, the reliable demonstration of unblocking can require extensive behavioral pilot work. Moreover, attention is only half the story in that successful associative learning should reflect the direction of change when the outcome is more or less than expected. Aficionados have noted that inhibitory learning is not consistently demonstrated in aversively motivated downshift unblocking procedures - on the contrary, a weaker UCS than expected can result in excitatory conditioning to the additional CS B (Fig. 5), whereas this learning should theoretically be inhibitory (Fig. 4; Table 2).

Cross-References

Aminergic Hypotheses for Schizophrenia
Animal Models for Attention
Attentional Bias to Drug Cues Classical (Pavlovian)
Conditioning Cognitive Enhancers
Latent Inhibition
Psychiatric States Antipsychotic Drugs

Schizophrenia
Schizophrenia: Animal Models
Translational Research

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