Individual differences are more than a Gene x Environment interaction: The role of learning.

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Abstract

Individual differences in behavior are understood generally as arising from an interaction between genes and environment, omitting a crucial component. The literature on animal and human learning suggests the need to posit principles of learning to explain our differences. One of the challenges for the advancement of the field has been to establish how general principles of learning can explain the almost infinite variation in behavior. We present a case that: 1) individual differences in behavior emerge, in part, from principles of learning; 2) associations provide a descriptive mechanism for understanding the contribution of experience to behavior; 3) learning theories explain dissociable aspects of behavior. We use four examples from the field of learning to illustrate the importance of involving psychology, and associative theory in particular, in the analysis of individual differences, these are; i) fear learning, ii) behavior directed to cues for outcomes (i.e., sign- and goal-tracking), iii) stimulus learning related to attention, and iv) human causal learning.

A goal of research into learning is to characterize how behavior changes with experience within and across species. Thorndike's (1898) Law of Effect was an early attempt to characterize the effect of experience on behavior. In offering a general law of how experience contributes to behavior, Thorndike was also giving an account of how an individual becomes unique.

The classic example of Thorndike's method involved cats and an apparatus known as a puzzle box (Thorndike, 1898). The box was a rudimentary cage with latches and gates to afford escape. The cats' dislike of confined space provided a natural motivation to engage in behaviors that might serendipitously lead to release. Thorndike observed that the cats made many false starts but eventually made a response that enabled escape. With repeated exposure to the box, latency to escape decreased. The Law of Effect stated that behaviors preceding any form of 'satisfaction' (e.g., escape) would be reinforced and made more likely on subsequent trials. However, rather than considering this principle as limiting an animal's flexibility to learn, the law only restricts the conditions for learning. Consider that outside the lab, different humans can successfully complete a motivated goal in different ways. They may behave differently but the same Law of Effect strengthens their behaviors.

The goals of this paper are to present the case for the individual differences approach to learning theory. We will argue that (1) learning mediates the influence of genes and environment on behavior and (2) there is complexity, to be explored, within models of learning that can account for diversity in learning. Specifically, we suggest that while genes and environment may contribute to the development of differences in learning, that an individual's phenotype interacts with experience and the memories of experience to further cause individual differences. As such, the study of individual differences in associative learning offers an insight into one of the prime mechanisms contributing to adaptive

behaviors. Further, detailed examination of associative principles, can provide novel insights into the etiology of variability in behavior.

There is considerable complexity within even the simplest models of association and, where differences in learning are observed, it is necessary to isolate the basis of this difference. After all, to understand individual differences is the ultimate *explanandum* for psychology and one that is omitted by a psychological theory that focuses on group differences. We present a case that learning theories, and associative theories in particular, provide a guide to explain how different dissociable aspects of behavior develop.

Because psychology traditionally treats differences as a window into disorders, we will focus broadly on clinically relevant individual differences, considering in turn the etiology of anxiety, addictions, schizophrenia, and depression. Through these examples, we argue that, research has identified relevant individual differences in associative learning. It almost goes without saying that there is considerable work to be done, but we strongly argue that too much work neglects the contribution of learning. Or where learning is acknowledged it is treated simply as a reflection either of genetic or environmental factors. Just as researchers strive to isolate the specific genes contributing to a heritable difference, the study of individual differences in associative learning should seek to isolate specific parameters of learning relevant to differences in behavior.

We start with a general introduction to the role of learning as a mechanism for genetic expression to influence behavior. We set out a simple model of learning and highlight how differences across components of this model can account for a range of individual differences. We also argue that the traditional role of the associative mind (the memories and use of memories of an organism), as reflection or mediating variable between genes and environment (see Figure 1, left panel), is insufficient.

We take an associative perspective on learning for three reasons. The first is that this area of research has existing animal models. Animal models provide powerful tests for the effects of learning in controlled genetic and environmental conditions, conditions that are impossible to control with people. Secondly, this area of research has sensitive tools and experimental designs that are lacking in some other areas. Finally, the associative analysis described is the level of algorithmic analysis necessary to have a mechanistic account of the mind (e.g., Baker, Murphy & Vallee-Tourangeau, 1996).

The Source of Individual Differences

A modern interpretation of individual differences sees them squarely rooted in the interaction between an individual's genes and their environment (Flint, Greenspan, & Kendler, 2010). The interaction between genes and environment is complex and dynamic. This is true for even the simplest of phenotypes. For example, a standard example of a gene x environment interaction, given by Rutter (2010), is the pinkness of flamingos. A diet rich in shrimp and certain plankton will produce the lovely pink hue of the flamingo. The same diet for a mouse will not have the same effect (see the bidirectional arrow in the left panel of Figure 1). Thus, the influence of the environment on a phenotype depends on the genotype.

However, even this interaction is not quite so simple. Heritability is relative; genes depend on the environment to determine expression of the phenotype. Further still, the interaction between gene and environment is dynamic, with the genotype influencing the environment that will influence its expression (Kendler & Baker, 2007). For instance, the Wilson Effect describes the increase in the heritability of IQ with age; monozygotic twins become more, rather than less similar, as they age (Wilson, 1983). This reflects changes in gene expression over the developmental lifespan and the influence that the expression of genotype has on shaping environment (Bouchard, 2013).

Dynamic interactions shift the focus away from finding specific genes or environmental factors and towards identification of the complex interactions (Plomin, DeFries, Knopik & Neiderheiser, 2013). Especially in the context of complex phenotypes, such as differences in human behavior, the early promise of identifying single causal genes has been replaced with a realization we need to understand a complex multi-causal pathway (Rutter, 2010; Kendler, 2005). There is no gene for any behavioral trait but rather, psychological and behavioral traits are the result of a complex multi-causal web of effects reflected in the interaction of gene, mind and environment (Right Panel of Figure 1).

One of the limitations of the analogy of the pink flamingo, when applied to complex behavior, is that the psychological variables that contribute to the cause behavior are not simple reflections of experience. Rather, memories reflect accumulated experience distilled over the lifespan. For instance, initial, innate, differences, such as the speed of learning (e.g., Kaufman, De Young, Gray, Jimenez, Brown & Mackintosh, 2010), can influence learning in a given experience, but this in turn can compound differences in learning about future experiences.

To elaborate one example, while a fear of dogs may involve the simple gene-environment interaction (shown in the left panel of Figure 1), the fear is also a result of *how* an individual learns and *how* that learning has captured the experience with dogs (what we are calling the contents of Mind). Currently an individual's risk for dog phobias might be understood in terms of genetic risk for a negative reaction to a dog encounter if exposed to an environment with aggressive dogs. However, to determine whether someone will develop a phobia requires more than simply understanding the genetic and environmental factors. Rather, there is every sense in which the contribution of previous learning is distinct and has its own causal power to behavior. Further, learning can have effects on environment and the expression of genes, for instance, some forms of memory relate to alternations in gene

expression (see Bronfman, Ginsburg & Jablonka, 2016). As such, we argue that the explanatory power of the gene x environment interaction is enhanced by considering a gene x mind x environment interaction.

The biopsychosocial model of behavior provides a frame of reference for such a tripartite interaction (e.g., Dodge & Pettit, 2003; Engel, 1989; Suls & Rothman, 2004; Jablonka & Lamb, 2014). This model proposes that biological (potentially genetic) factors interact with social (environmental) factors in addition to psychological factors (our associative mind), such that the environment does not always have a direct effect on our emotional state or behavior, but rather, psychological factors, such as how we think about and interpret experiences, can moderate the influence of the environment (e.g., Ellis, 1980). We argue that taking a comparable approach with associative learning will enhance our capacity to explain individual differences in behavior. While both genetic and environmental factors may contribute to differences in associative learning, *how* the environment influences behavior can be influenced by *how* we learn from experience. The etiology of behavior needs to be understood as a Gene x *Mind* x Environment interaction as displayed in the right-hand panel of Figure 1 (see also Kendler, 2005).

The previous focus on genes, environment and their interaction implies somehow that the associative content learnt from experience plays no active role in influencing future behavior. This emphasis mirrors an early behaviorist position that posited that the content of cognitions had no causal role in behavior (i.e., Skinner, 1938, 1945). The strong behaviorist position suggested that behavior could be explained on the basis of an animal's genetically determined behavioral repertoire and the environmental contingencies to which it was exposed (i.e., Skinner). In contrast, we argue that memories for stimuli and processes of association have causal actions (see also, Kirsch, Lynn, Vigorito & Miller, 2004). However,

identifying the nature of these effects requires careful experimentation (e.g., Patitucci, Nelson, Dwyer & Honey, 2016).

Consider this approach to individual differences in perceptual sensitivity to stimuli. Sensitivity to stimuli in the environment can be traced directly to genetic factors, but learning can also have an influence. Visual acuity has a genetic component, and would be expected to enhance or interfere with any memory for a perceived event. However, differences in sensitivity to visual, auditory, olfactory, proprioceptive cues can also be learnt. Consider the ability of the wine connoisseurs' olfactory performance (Bende & Nordin, 1997) or a musician's pitch perception (Micheyl, Delhommeau, Perrot & Oxenham, 2006). While there may be innate differences in sensitivity to taste or pitch, perceptual skills are honed through years of experience and training.

If any clearly traceable genetic difference was likely to provide a test case for the understanding of psychological differences, the easily identifiable genotype differences determining males from females, might be assumed to be a simple starting place. Except for race and intelligence, difference in physical and psychological ability attributable to biological sex is possibly the most studied potential source of individual differences (e.g., Halpern, 2012). Animal learning research has been able to study sex without the confounds of acculturation that mire human research and many sex differences are amenable to a learning analysis.

For instance, sensitivity to color and hue are central to sexual selection and reproductive success in guppies, primates and humans (e.g., Endler & Houde, 1995). Sex-based developmental refinements to the visual processing systems may have their origin in processes of natural selection and be in place from birth or early in development (Bornstein, Kessen, & Weiskopf, 1976; Ling, Hurlbert, & Hurlbert, 2011). However, other differences may emerge later in development as a product of learning.

For example, in the visual system of the female stickleback fish (*Gasterosteus aculeatus*), the retinal cones respond more to light in the red spectrum than those of their male counterparts, reflecting differences in sensitivity to sensory stimuli (e.g., Rowe, Baube, Loew, & Phillips, 2004; Aron & Aron, 1997; Smolewska, McCabe, & Woody, 2006). Genetic differences in wavelength sensitivity can contribute to a behavioral preference that has coevolved with the red wavelength mating signals of males (Rick, Mehlis, & Bakker, 2011). However, differences in responsivity to light may also emerge as a function of experience; literature from different species in different learning paradigms is consistent with an associative interpretation that stimuli that have previously been reliable predictors of a valued outcome increases relative to other stimuli (Baker & Mackintosh, 1979; Le Pelley & McLaren, 2003; Mackintosh, 1973, 1976). Thus, a stimulus (such as the color red) predictive of a valued outcome in a mating context may acquire a higher associability or salience, increasing the rate of future learning. With sticklebacks, Smith et al., (2004) provides evidence that female preference for mates with red throat is a generalized bias from a foraging preference. In the zebrafish (*Danio rerio*) this type of preference is learnable (Spence & Smith, 2008). Simply observing individual differences in sensitivity to light in an adult fish does not isolate the etiology of this difference, it might relate to genetics, previous experience, or current learning environment.

In humans, there are common cultural beliefs about sex differences in preference for color, a visit to a child's clothing store or toy shop will provide the immediate evidence for this assertion. In the West, there is the stereotype that boys prefer blue and girls prefer pink. However, we know that the same colors can be preferred by the opposite sex given different culture-specific environmental exposure (e.g., Al-Rasheed, 2015). While studies of human infants have found little evidence of innate differences in color perception (Bornstein et al., 1976), there is evidence that development contributes to preferences in adults (e.g., Ling et

al., 2011). While these may reflect differences in sensory processing that emerge from physical development, they can equally arise as a result of experiential development. For example, a preference for blue may be the result of specific rewards for choosing blue or may be even more subtle, arising from exposure to blue resulting in elaboration of the mental representation of blueness and second order associations (Mundy, Honey & Dwyer, 2007; McLaren & Mackintosh, 2000).

The example of color preference illustrates that learning from experience can produce differences that not only influence behavior but establish differences in learning which will shape the influence of future experience. However, observing differences in learning does not isolate the cognitive processes that contributes to that difference. To isolate this, we need to look carefully at the parameters that influence learning. As we outline in the four examples below, this is a complex problem, that requires careful manipulation of experimental parameters. We argue that the field of learning has the necessary tools to address this challenge.

What the Standard Learning Model Can Do: Causal Roots to Individual Differences.

One way to develop our understanding of how individual differences in behavior arise, is to test specific parameters of learning. Where two individuals differ in learning, this difference might relate to different parameters of an experience influencing learning. Most models of learning are attempts to describe how a change in behavior or cognition is related to environmental experience. We argue that there is considerable complexity in the parameter space of existing models, capable of accounting for a diversity of learning.

A typical classical conditioning scenario involves learning that a previously neutral stimulus (CS; e.g., brief tone) precedes the presentation of an outcome, or unconditioned stimulus (US; e.g., food; Pavlov, 1927). Through repeated presentation of the CS preceding

the US, the strength of association between the CS and US increases. Variables that influence the rate and strength of associative learning relate to factors specific to the cue (or response), the outcome, and any pre-existing association between the two events (for a review, see Nasser & Delamater, 2016). A mathematical instantiation of the learning process provides a framework for considering the relationship between these variables. For example, the Rescorla-Wagner (1972) model is an associative model that assumes that the change in strength of association is governed by a minimum of three variables; the associability, or learnability, of the cue or CS (α), the associability or motivational significance of outcome, the US (β), and the limit on the strength of the association supported by the US (λ). Change in associative strength is dependent on the strength of the association previously acquired (V), and thus given in Equation 1.

Equation 1: $\Delta V = \alpha * \beta (\lambda - \sum V)$

These variables provide a useful starting point and are common across many other models of association learning (e.g., Hull, 1943; Sutton & Barto 1998; Mackintosh, 1975; Pearce, 1987; Dayan & Abbott, 2001).

An explanation for why two individuals' behavior differs can be reached by assuming differences in any one of the variables (α, β, λ) or their interaction. For instance, the simple presentation of a CS paired with a US might be expected to result in an increment in association between the two. Even without considering their previous experiences, all theories of learning can account for how two different individuals experiencing the same events might learn different amounts. Two individuals might differ with respect to perceptual sensitivity (α) to the cue or motivation for learning about the US (β). Previous experience has an added effect; the effect on associative learning from a single pairing of two events could be small if the individual has already acquired an association (and the gap between λ and V is

small) or large if there has been no prior experience. Generalization of learning from similar stimuli, determined by overlap of elements or perceptual similarity, will influence the associative strength (V) and thus the rate of current learning (e.g., Pearce, 1987; McLaren & Mackintosh 2000; Soto, Gershman & Niv, 2014; Brandon & Vogel, & Wagner, 2000; Gluck, 1991; Bush & Mosteller, 1951).

This means that characterizing how individuals, who come to the lab as fully formed organisms, come to possess their behavioral profiles is extremely complex. In addition to this, as introduced with the stickleback example above, learning is dynamic, such that one learning experience will not only influence associations between CS and US, but will change the parameters for future learning. For instance, experience with a CS as relatively reliable predictor of a US may increase the associability of the CS (α) relative to other stimuli, accentuating future learning (Mackintosh, 1975; Le Pelley 2004; Pearce & Mackintosh 2010).

We set out here to work through four examples, considering individual differences in fear learning, differences in behavior to cues for outcomes, differences in learning about cues for outcomes that relate to attention and human causal learning. In these examples, we consider the role of learning in the etiology of individual differences in behavior, how differences in learning develop and summarize the attempts to isolate the basis of such differences in learning.

Example 1: Fear Conditioning and Individual Differences in Anxiety

Enhanced or Deficient Fear Conditioning?

Anxiety is a general feeling of unease experienced from time to time and a common emotional response to situations of threat. Anxiety for a stimulus or environment experienced with aversive outcomes is a common result following fear conditioning. The relationship

between our emotional responses and our aversive experiences provides insights into the etiology of anxiety disorders (Barlow 2002; Mineka & Zinbarg 2006; Mineka & Oehlberg, 1998). However, while it is estimated that up to 95% of people are exposed, at some point in life, to the form of traumatic event that might lead to fear conditioning, only a small minority of trauma survivors develop a clinical disorder (Engelhard et al., 2008). Thus, a stress-diathesis model of psychopathology (e.g., Monroe & Reid, 2009; Monroe & Simons, 1991) is widely invoked to explain how genetic risk, such as threat-related reactivity in specific regions of the brain (e.g., amygdala; Hariri, 2009) or genetic polymorphisms affecting serotonergic and dopaminergic system function (e.g., Gordon & Hen, 2004; Sen, Burmeister & Ghosh, 2004; Lonsdorf, Weike, Nikamo et al., 2009; Londsdorf, Ruck & Bergstrom et al., 2010) may provide an explanation of the individual difference that interacts with experience.

We argue that the gap between experience and the development of anxiety disorders might also be bridged by differences in how individuals learn about aversive events. Further, we suggest that such difference can be captured within the parameters of models of associative learning. It is quite easy to find research that eschews psychologically described quantitative models as explanations for individual differences. For instance, Gershman and Hartley (2015) have argued that associative models provide relatively poor accounts of individual differences in fear conditioning. They propose instead that individuals differ qualitatively, clustering into definable state learners (one-state or two-state), learning either to store acquisition and extinction trials in separate memories or in the same memory, with the difference between these approaches predicted by the individual's prior belief about the structural complexity of the learning environment. Contrary to Gershman and Hartley's position, differences in learning about contexts, integration of cue learning with contexts, and competition between cue and context learning have been accommodated within models of learning (e.g., Rescorla & Wagner, 1972; Murphy, Baker & Fouquet, 2001). We outline here

how careful manipulation of fear conditioning experiments has improved understanding of how individuals differ in fear conditioning. We argue that future work along these lines should enhance our understanding of the parameters, within models of associative learning, that may contribute to individual differences in anxiety.

Fear conditioning can be shown using either simple (single cue S+) or discriminatory (S+, S-) learning procedures. Previously it has been argued that anxiety is related to strong fear conditioning, but this conclusion is based largely on studies using simple conditioning. If we instead consider studies that have used discriminative conditioning, the data suggest a different interpretation, wherein anxiety may be associated with a deficit in the selectivity of learning.

Simple fear conditioning involves pairing a neutral CS with an aversive US, so that the CS comes to signal the US and evoke anticipatory fear for the aversive US (the conditioned response; CR). In a discriminatory fear conditioning paradigm two stimuli are presented during acquisition; one CS is paired with the US (CS+), while another CS is never paired with the US (CS-). The CS- should come to act as a safety signal. The difference in CR elicited by CS+ and CS- is measured.

The discriminatory fear conditioning paradigm makes explicit a discrimination that is implicit in simple fear conditioning. In a simple fear conditioning procedure, participants must learn that the combination of CS and context cues the aversive outcome, while the context presented in isolation acts as a safety signal, cueing the absence of the aversive outcome. Thus, while there is no explicit CS-, participants have to discriminate between the CS+ and the context, which is presented with and without the US. This is arguably a more complex discrimination than that which is presented in the discriminatory fear conditioning procedure.

Individuals with high levels of anxiety show elevated conditioned responses, indicating fear, to the CS- but do not show stronger responses to the CS+ (Duits, Cath, Lissek, Hox, Hamm, Engelhard & Baas, 2015). These results suggest that anxiety relates to impaired discrimination and high levels of generalization between CS+ and CS-; specifically, anxiety may be associated with a *deficit* in the selectivity of associative learning (Lissek, Rabin, McDowell et al., 2009).

While successful fear conditioning leads individuals to learn that the CS predicts the aversive US, a deficit in associative learning deprives individuals of the ability to predict when the US will occur, creating an unpredictable situation and sustaining anxiety (Lissek et al., 2009). Failure to learn a CS-US association may leave the context, in which the CS and US are presented, as the best predictor of the US, resulting in elevated contextual fear conditioning and a chronic state of apprehension (Baas, van Ooijen, Goudriaan, & Kenemans, 2008; Grillon, 2002; Seligman & Binik, 1977; Bouton, 2002). Indeed, sensitivity to the CS-US contingency appears to be closely related to a reduction in context anxiety (Baas et al., 2008; see also Cohen-Kadosh, Haddad, Heathcote, Murphy, Pine & Lau, 2016; Murphy & Baker, 2004).

This is a comparatively new hypothesis for the etiology of anxiety. An earlier meta-analysis of fear conditioning studies, found a relationship between anxiety and strong fear conditioning, observing stronger conditioned responses to CSs in anxious individuals to (Lissek et al., 2005). Rather than simply being interpreted as the consequence of anxiety, researchers had suggested that accentuated fear conditioning might be part of the etiology of anxiety disorders (e.g., Bouton, Mineka, & Barlow, 2001; Wolpe & Rowan, 1988). This incomplete conclusion reflected an over-reliance on simple tests of fear conditioning, which do not provide an opportunity to assess learning with safety signals (Duits et al., 2015). Tests of simple fear conditioning overlook the possible influence of cue competition (Beckers,

Krypotos, Boddez, Effting, Kindt, 2013). Further exploration of individual differences in learning, incorporating more complex and nuanced tests, has already radically changed our understanding of individual differences.

What Causes the Deficit in Discrimination Learning?

Fear conditioning is used as a robust test to assess facets of anxiety (e.g., for review see, Fullana, Harrison, Soriano-Mas, Vervleit, Cardoner, Avila-Parcet & Radua, 2016). However, it is not clear what underlies the deficit in discrimination learning. Even incorporating discriminatory fear conditioning tests, the tasks currently employed to study the relation between learning and anxiety do not readily provide information about *how* individuals differ in learning. We have yet to identify what it is about learning in anxious states that contributes to altered fear conditioning and more importantly, what differences in learning contribute to the development of anxiety. As we set out below, several alternative factors could contribute to reduced discriminatory fear conditioning.

Hypothesis 1: individual differences in the motivational value of the presence (the rate of learning about the US, $\beta_{present}$) and absence (the rate of learning about the absence of the US, β_{absent}) of aversive stimulus (US) could contribute to reduced discriminatory learning. It is quite a common general finding that US absence is less effective than US presence (Wassermann, et al., 1993), indeed some basic learning phenomena require this assumption (Murphy et al., 2001a, 2001b; Wagner, Logan, Hablerlandt & Price, 1968). We might thus extend this idea to make the assumption that individuals differ in the extent of the variation in the motivational value for the presence and absence of aversive US. Particularly high $\beta_{present}$, and low β_{absent}, may result in intact learning about CS+ but impaired learning with the safety signal provided by CS-. In this case, weak discrimination would be the result of normal levels

of generalization combined with reduced ability to learn about the absence of the aversive US.

Hypothesis 2: high levels of generalization between CS+ and CS- would similarly result in poor discrimination. Lissek and colleagues (2009) observe that elevated generalization provides an analogue of symptoms of panic disorder, proposing that conditioned fear to a neutral stimulus, occurring coincident with panic (CS+), generalizes to exteroceptive and introspective stimuli resembling the CS+ (Lissek et al 2009, see also, Bouton et al 2001, Goldstein & Chambless 1978, Mineka & Zinbarg 2006). Elevated generalization may reflect retarded perceptual learning or sustained high levels of attention for many irrelevant features in the learning environment (e.g., McLaren, Kaye & Mackintosh, 1989)

To dissociate these explanations, conditioning paradigms need to assess generalization between stimuli and the motivational value of the outcome. While this may require additional assessments to be conducted alongside tests of conditioning, more precise tests of discriminatory fear conditioning have existed for decades, but are employed infrequently. To give one example, the human conditioned startle-potentiated paradigm measures the magnitude of startle probed during inter-trial intervals to serve as a baseline, from which startle during CS+ and CS- can be compared (Grillon, Ameli, Woods, Merikangas & Davis, 1991). This approach has an advantage over paradigms which simply measure and directly compare responses in the presence of the CS+ and CS-. This differentiates the influence of conditioning with the stimulus and the context. As both stimuli are trained in the same context, the discriminatory learning reflects learning about the stimuli in conjunction with the context and responses to either stimulus may be influenced by contextual fear conditioning. In particular, apparent generalization of responding to the CS-

may reflect responding to the context. It is thus important to measure learning about the context, in addition to the CS+ and CS-.

Beckers and colleagues (2013) further argue that standard tests of fear conditioning provide a poor analogue for anxiety, partially because they focus on the punctate or specific fear experience. To understand how dysfunctional fear conditioning may contribute to the etiology of anxiety, they suggest that ambiguity is crucial. While unpredictable aversive events are a risk factor for anxiety (Seligman & Binik, 1977), many fear conditioning protocols use hedonically strong stimuli with one CS clearly signaling danger, while another clearly signals safety. Addressing this gap, recent studies have considered learning with ambiguous stimuli, assessing the influence of anxiety in tests of blocking (A+, AB+) and protection from overshadowing (C-, CD+; Arnaudova, Krypotos, Effting, Boddez, Kindt & Beckers, 2013; Boddez, Vervliet, Baeyens, Lauwers, Hermans, Beckers, 2012). Future studies may benefit from following this lead and studying learning in conditions of ambiguity.

The Perruchet effect provides a further opportunity to explore individual differences in learning in situations of ambiguity. The effect involves a situation of ambiguity in which participants are exposed to a 50% contingency between a CS and US (originally a puff of air to the eye; Perruchet, 1985; Weidemann, Tangen, Lovibond & Mitchell, 2009). Under conditions of ambiguity, dissociations have been observed between psychophysical indices of anxiety, such as conditioned skin conductance responses, and cognitive measures, such as expectation of the aversive outcome (McAndrew, Jones, McLaren & McLaren, 2012). Such dissociations underline the potential contribution of associative learning to individual differences in anxiety.

Gershman and Hartley's (2015) proposal to abandon an associative approach to account for individual differences in fear conditioning, rests on the fact attention, memory,

motivation, and goals interact with and influence learning. Such interaction does not require us to abandon the associative approach. Rather, following recent suggestions, we advocate continued manipulation of experimental design to further our understanding of the specific learning factors that contribute to anxiety (Beckers et al., 2013).

To summarize this section, gene x environment interactions are invoked to explain individual differences in the development of anxiety. Individuals differ in learning in a fear conditioning procedure, with generalized apprehension associated with failure to learn the CS-US contingency. Differences in *how* individuals learn may interact with genetic and environmental factors to influence the etiology of anxiety. However, the basis of individual differences in fear conditioning has yet to be isolated. Identification of this basis will provide a more precise account of the etiology of anxiety.

Example 2: Sign-tracking and individual differences in addiction

The interest in individual differences in fear conditioning developed from a mismatch between exposure to trauma and development of anxiety. A similar gap is apparent in the addiction literature. Only a very small proportion of individuals exposed to licit or illicit drugs will develop compulsive drug seeking behavior (Belin, Belin-Rauscent, Everitt, Dalley, 2016). However, for individuals who do become addicted, the source of the addiction and associated cues have a powerful hold. The most predictable outcome of the first diagnosis of a drug addiction is relapse (DeJong, 1994). Individuals who have become addicted are unable to shift their thoughts and actions away from the drug and associated stimuli (Flagel, Akil & Robinson, 2009). When addicts encounter stimuli previously associated with the drug, such as drug-related paraphernalia, places, or people, these often instigate renewed drug seeking and / or craving for the drug (for review see, Childress, Hole, Ehrman, Robbins, McLellan & O'Brien, 1993). Stimuli that have acted as a predictive cue for a drug appear to acquire the ability to maintain and instigate drug taking behavior in part because they acquire incentive

motivational properties through classical conditioning (Berridge 2001; Bolles 1972; Toates 1986).

The pairing of a conditioned stimulus (CS) and unconditioned stimulus (US) in classical conditioning can evoke complex emotional and motivational states (Rescorla, 1988). The conditioned response (CR) may include orientation towards, approach of and engagement with the CS (Brown & Jenkins, 1968; Hearst & Jenkins, 1974). Through conditioning, different components of the task (e.g., the CS or the context) may acquire incentive salience, becoming a 'wanted' stimulus (Berridge, 1996). Where stimuli have acquired this new property, they (a) elicit attention and approach behavior (Flagel, Watson, Akil & Robinson, 2008; Hearst & Jenkins, 1974; Peterson, Ackilt, Frommer & Hearst, 1972), (b) can act themselves as conditioned reinforcers of other behavior (Diciano & Everitt, 2004; Williams & Dunn, 1991), and (c) can evoke conditioned motivation, instigating reward seeking or energizing ongoing behavior (Dickinson et al., 2000; Lovibond, 1983; Wyrell & Berridge, 2000).

Individual differences have been observed in the propensity for CSs to acquire incentive salience. Zener (1937) described individual differences in classical conditioning with dogs. As in Pavlov's earlier experiments, a bell was paired with food. However, animals were not restrained. Zener (1937) observed that after training, some dogs responded with an initial glance at the bell, followed by a fixed interest in the food bowl, while other dogs approached the bell. This difference has been described as sign-tracking (i.e., interest in the CS, the bell) vs. goal-tracking (i.e., interest in the location of the US, the food bowl) and has been widely studied in auto-shaping experiments with rats (see Hearst & Jenkins, 1974; Holland, 1980). Individual differences in sign-tracking and goal-tracking have also been reported in human behavior (e.g., Garofalo & di Pellegrino, 2015).

Animals engaging in sign-tracking will approach the CS (the sign), while animals engaging in goal-tracking will approach the location where the US will be presented (the goal). Flagel and colleagues (2009) stress that both sign-tracking and goal-tracking are learned responses conditional on CS-US experience. Once learned, the tendency of sign-trackers to approach the CS remains stable (Flagel et al., 2009). From this perspective sign-tracking looks to be a learned response, which once established will interact with environmental factors to increase risk for addiction. Mapping this onto a gene x mind x environment interaction, genetic disposition and environmental exposure creates the opportunity to sign-track, which once established, moderates the influence of future experiences on behavior.

Why do individuals differ?

Recent research has focused on identifying a neural and genetic basis for sign-tracking (see Patitucci et al., 2016, for discussion). Exploring a genetic basis of sign-tracking, Flagel et al., (2010) compared auto-shaping in rats bred for high (bHR) or low (bLR) locomotor reactivity to a novel environment. Previous research had shown that bHR rats acquire cocaine self-administration more rapidly than bLR rats (Davis, Clinton, Akil & Becker, 2008) and exhibit greater corticosterone response to a mild stress and express lower levels of glucocorticoid receptor mRNA in the hippocampus (Clinton, Miller, Watson & Akil, 2008). Indicating a genetic basis for sign-tracking, Flagel and colleagues (2010) found that bHR rats were more likely to develop sign-tracking than bLR rats.

Further research has suggested a role for the neurotransmitter dopamine in sign-tracking. Some research suggests that phasic dopamine serves as a prediction-error signal necessary for learning associations (e.g., Bayer & Glimcher, 2005; Waelti, Dickinson & Schultz, 2001; although see Byrom & Murphy, 2016). While phasic dopamine responses have been observed to shift from US to CS over training (Schultz, 2016), Flagel et al., (2011)

only observed this shift in sign-tracking animals. They argue that dopamine acts selectively, attributing incentive salience to cues for reward in some subjects, for whom reward cues come to powerfully motivate and control behavior. Flagel and Robinson (2017) argue that the difference between sign- and goal-tracking may relate to a difference in dopamine signaling in the core of the nucleus accumbens, an area critical for the attribution of incentive salience to cues for reward. Differences in dopamine transporter expression, associated with faster dopamine uptake in the core of the accumbens, are seen in animals that sign-track (Flagel & Robinson 2017; Signer, Guptaroy & Austin et al., 2016; Flagel et al., 2010; Flagel, Watson, Robinson & Akil, 2007).

Based on this research into the genetic and neural basis of sign-tracking we might draw the conclusion that individual differences in dopamine activity underpins the attribution of incentive salience to CS, leading to sign-tracking and risk for addition. To summarize, sign-trackers have been suggested to be more susceptible to addiction than goal-trackers because they are motivated to seek drugs in the presence of drug-related stimuli (Robinson, Yager, Cogan & Saunders, 2014). This hypothesis is consistent with reports that sign-tracking in rats is associated with a range of factors considered to be a risk for addiction, including action-impulsivity, novelty seeking and low attentional control over behavior (Beckmann, Marusich, Gipson & Bardo, 2011; Paolone, Angelakos, Meyer, Robinson & Sarter, 2013; Belin, Berson, Balado, Piazza & Deroche-Gamonet, 2011; Belin & Deroche-Garmonet 2012; Jentsch & Taylor 1999; Molander, Mar & Norbury et al., 2011; Flagel et al., 2010).

However, these conclusions may be premature. The focus on genes has overlooked the influence that environmental factors can have in the development of sign-tracking. There is evidence that while sign-tracking can develop to discrete visual stimuli, it is unlikely to develop even to localizable auditory stimuli (Davey & Cleland, 1982; Davey, Phillips &

Cleland, 1981; Cleland & Davey, 1983). Further, both the contingency and contiguity between CS and US can influence the development of sign-tracking. For instance, Boakes (1977) demonstrated that changes in the US probability influenced the development of sign-tracking; if only 50% of CS presentations were paired with reward, sign-tracking was more likely to develop than if every CS presentation was paired with reward. Other experiments have demonstrated that increasing the spatial or temporal contiguity between the CS and US, results in a decline in sign-tracking (Brown, Hemmes, De Vaca & Pagano, 1993; Costa & Boakes, 2007; Holland 1980; Silva, Silva & Pear, 1992). The influence of these environmental factors and the role of learning on the development of sign-tracking questions the prominence of simple biological or genetic predispositions.

Further, while links have been made between dopamine and incentive salience, Flagel and colleagues (2009) outline that the difference between sign-trackers and goal-trackers is not a difference in attribution of incentive salience, but a difference in where incentive salience is attributed. In sign-trackers, incentive salience is attributed to the CS. In goal-trackers incentive salience is attributed to the spatial location in which the US is presented, or to the wider contextual cue for the US. Saunders and Robinson (2012) identified that while sign-trackers may be at elevated risk of relapse in the presence of discrete drug cues in the environment, goal-trackers showed greater context-conditioned hyperactivity and context-induced reinstatement of drug seeking than sign-trackers. This suggests that for goal-trackers, the context has acquired incentive salience, so that contextual cues motivate behavior (Robinson et al., 2013).

Robinson and colleagues (2013) suggest that psychological processes govern the difference between sign-tracking and goal-tracking. Mapped onto our gene x mind x environment model, this suggestion highlights the potential role of the mind in mediating the interactive influence of genes and environment. Considering possible differences in the

mechanisms of learning, Di Feliceantonio and Berridge (2012) note that sign-trackers attend to the CS predicting the occurrence of the US. Where the CS is a reliable predictor of the US, the CS will be the most reliable predictor of the US, but may not be the last stimulus encountered before consuming the US. Sign-trackers are thus using contingency over contiguity. By contrast the goal-trackers are attending to the location in which the US is delivered. This is much less informative; as this stimulus is always present, it should be associated with the presence and the absence of the US. However, the precise location where the US is delivered is always the last thing seen before the reward, so while there is a low contingency between this stimulus and the US, there is high contiguity. Di Feliceantonio and Berridge (2012), thus suggest that contiguity remains important for controlling learning for goal-trackers. This distinction between the effects and relevant importance of contiguity over contingency is echoed in the distinction between model free and model based learning on the basis of evidence in which local experience for instances is more or less relevant than an extracted generalization from continuous experience. Model based learning makes assumptions about how the experience is incorporated (e.g., Quinlan, 1993).

Where then, would sign-tracking fit into our concept of a gene x mind x environment interaction? Is sign-tracking an endophenotype for addiction? For a behavior to be classed as an endophenotype, it must be heritable, must not be state dependent and must segregate with the related behavioral phenotype within families (Gottesman & Gould, 2003). To classify sign-tracking as an endophenotype implies that it is a facet of learning that is an intermediate step between a genetic factor and a complex phenotype. This would rule out possible environmental factors influencing sign-tracking.

It is notable that compared to the exploration of the genetic basis of sign-tracking, less research has considered the, potentially relevant, environmental factors. This is curious as early studies indicated that sign-tracking was dependent on the CS-US contingency and

contiguity (e.g., Boakes 1977; Brown et al., 1993; Hearst & Jenkins, 1974; Holland 1980). Recent work has focused on using the distinction between sign-tracking and goal-tracking as an animal model to develop our understanding of the role of dopamine in reward learning. In this respect, research in sign-tracking draws parallels to the work in latent inhibition (as discussed below), where, rather than exploring the environmental and behavioral parameters necessary to induce latent inhibition, research has moved to focus on understanding individual differences and its neural basis.

As illustrative of the ambiguity around the importance of sign-tracking for individual differences in addiction, a recent study of sign-tracking provides evidence to argue that the general distinction between sign- and goal-tracking is inaccurate as the tendency to sign- or goal-track is US specific (Patitucci et al., 2016). Patitucci and colleagues found that goal-tracking was dependent on the value of the reinforcers, such that individual differences in sign- and goal-tracking were not consistent across different CS-US relationships.

Novel experimental designs, using eye-tracking to assess value-modulated attentional capture, provide an opportunity to explore the relationship between sign-tracking and addiction in humans. Le Pelley, Pearson, Griffiths and Beesley (2015) observed that participants are more likely to look at a distractor that signals the availability of high reward as compared to one that signals the availability of low reward, even when looking at the distractor led to the omission of the reward. This suggest that Pavlovian signals of reward elicit automatic attentional capture. Of relevance to sign-tracking and addiction, greater reward-modulated attentional capture is associated with greater risk of illicit drug exposure, particularly in those with less cognitive control (Alberta, Copeland, Pearson, Watson, Wiers & Le Pelley, 2017; Wiers, Boelema, Nikolaou & Gladwin, 2015).

There are parallels to be drawn between sign-tracking and other learning effects discussed in this paper. For example, in the distinction between sign- and goal- tracking we

see a difference in the attribution of incentive salience to discrete or contextual cues. In relation to anxiety, we outlined a difference in the acquisition of discrete CS-US associations compared with context-US associations. This parallel deserves attention in future research as addiction is frequently co-morbid with anxiety (Grant et al., 2004).

In summary, individual differences in sign-tracking may contribute to the risk for developing addiction, interacting with environmental and genetic factors in a gene x mind x environment interaction. The focus on identification of the genetic and neurobiological basis of sign-tracking may frame individual differences in learning as purely genetic, removing any necessity to consider the independent causal status of sign-tracking. However, we suggest that it is too early to draw such a conclusion as environmental factors and individual differences in the value ascribed to environmental factors such as the US in particular, have some influence over sign- and goal-tracking. The next steps here might be to consider whether genetic and environmental factors interact to induce sign-tracking and isolate specifically, in terms of associative processes, how sign- and goal- tracking differ.

Example 3: CS Processing Effects, Schizotypy and Schizophrenia

Schizophrenia is characterized by attentional abnormalities that impact learning, for instance, reduced selective attention and an inability to tune out irrelevant stimuli (Frith, Stevens, Johnstone, & Crow, 1979; McGhie & Chapman, 1961) or use contextual information to guide processing (J. A. Gray, Feldon, Rawlins, Smith, & Hemsley, 1991; Hemsley, 1987; Patterson, 1987). A deficit in selective learning, such as a heightened tendency to learn about irrelevant stimuli, may be part of the etiology of schizophrenia, contributing to delusions and hallucinations (J. A. Gray et al.,). While this definition appears to specify individual differences in learning (attentional abnormalities), there remains considerable disagreement about the causal basis of schizophrenic-related differences in learning.

Individual differences in relation to schizophrenia and, more often, trait measures relating to schizophrenia (e.g., schizotypy; Claridge & Broks, 1984; Mason, Claridge, & Jackson, 1995) have been observed in a range of CS focused effects, as summarized in Table 1, and illustrated in Figure 2. In referring to CS focused effects we are considering effects such as blocking, overshadowing, latent inhibition and learned relevance.

Blocking and overshadowing are instances of stimulus selection effects and demonstrate that the association between CS and US does not depend simply on the characteristics of the CS, its correlation with the US or even past experience with the CS. Rather, blocking and overshadowing suggest that learning may be affected by the nature of the other CSs present at the same time and prior experience with co-presented CS (Mackintosh, 1975; Pavlov, 1927; Kamin, 1969).

Deconstructing Latent Inhibition

Latent inhibition and learned relevance demonstrate that prior experience influences the rate at which learning occurs with a given CS. Latent inhibition shows that exposure to a stimulus in the absence of a US can retard subsequent performance acquiring a CS-US association (Ginton, Urca, & Lubow, 1975; Lubow & Moore, 1959). The learned relevance effect demonstrates that prior experience can also influence the associability of stimuli; learning with a CS that has been a relatively reliable predictor of an outcome will proceed at a greater rate than learning with CS that has previously been a poor predictor of the outcome (Baker & Mackintosh, 1979; Bennett, Wills, Oakeshott, & Mackintosh, 2000; Le Pelley & Schmidt-Hansen, 2010; Mackintosh, 1975).

Schizophrenia-associated disruptions in CS focused learning effects have provided support for the *Aberrant Salience* hypothesis of schizophrenia, with the proposal that

individual differences in these effects relate to how stimuli capture attention (Kapur, 2003). Schizophrenia has been described as a disorder arising from the misattribution of salience; neutral or irrelevant stimuli are treated as salient, leading to the formation of inappropriate associations contributing to cognitive noise (Kapur, 2003; Corlett, Honey, & Fletcher, 2007; Jensen, Willeit & Kapur, 2008). While genetic and environmental factors may contribute to aberrant salience, their impact on learning may multiply the detrimental effect, with dysfunctional mechanisms of learning contributing to the development of hallucinations and delusions. However, the observation of individual differences in CS focused effects does not isolate the facets of learning that are important. There remain alternative accounts for the causal basis of individual differences in learning. This is, in part, because there are alternative explanations for CS focused learning effects. To provide an example, we outline the alternative hypotheses for the stimulus pre-exposure effect, sometimes referred to as latent inhibition.

Latent inhibition is an effect of retarded learning following simple stimulus pre-exposure (Ginton, Urca, & Lubow, 1975; Lubow & Moore, 1959). Tests of the effect involve two phases. In Phase 1, a stimulus is pre-exposed without pairing with a US. A CS-US association is then trained in Phase 2. There are many examples of individual difference in latent inhibition (e.g., Baruch, Hemsley & J.A., Gray, 1988a, 1988b; N.S. Gray, Fernandez, Williams, Ruddle & Snowden, 2002). While this is a simple protocol, there are alternative accounts of the apparent retardation of learning in Phase 2 and individual differences in this effect.

Attention-based hypotheses propose that experience with a stimulus in the absence of a paired outcome results in a reduction of subsequent attention directed to that stimulus slowing subsequent learning (e.g., Mackintosh, 1975; Pearce & Hall, 1980; Pearce & Mackintosh, 2010). Different attentional accounts of CS associability modulation have been

developed, though hybrid models have integrated these perspectives (Le Pelley, 2004; Pearce & Mackintosh 2010). Mackintosh's (1975) model of selective attention describes a reduction in associability for stimuli that do not reliably predict a meaningful outcome. Thus, in latent inhibition, repeated exposure to a stimulus that does not predict a relevant outcome results in a decrease in attention to that stimulus, as the irrelevance of the stimulus is learned (Mackintosh, 1975). Pearce and Hall (1980) posited that repeated presentation of a stimulus can render the stimulus less surprising, reducing associability. Thus, in latent inhibition, because the stimulus has been pre-exposed, it is expected and thus captures less attention. The hybrid approach recognizes that the associability of a stimulus may change because of its previous relative predictive validity and repeated presentation (Le Pelley, 2004; Pearce & Mackintosh 2010). From this perspective, disruptions in latent inhibition can be related to individual differences in CS associability or modulation of CS associability. Failure to update CS associability based on experience would result in the absence of the latent inhibition effect, as observed in high levels of schizotypy and schizophrenia.

While widely accepted to explain individual differences in latent inhibition, the attention-based hypotheses do not account for data showing that pre-exposure to the stimulus influences future *performance* rather than *learning*. For instance, the latent inhibition effect can be disrupted by presentation of the US in a different context (Kaspow, Catterson, Schachtman & Miller, 1984), the passage of time between Phase 1 (pre-exposure) and Phase 2 (CS-US training; e.g., Kraemer, Randall & Carbary, 1991, Hall & Minor, 1984) and 'extinction' of the context present in Phase 1 (Baker & Mercier, 1982; Grahame, Barnet, Gunther, & Miller, 1994; but see also, Hall & Minor, 1984; Zalstein-Orda & Lubow, 1995). According to the comparator hypothesis, proposed by Miller and Matzel (1988), which assumes that an association between the CS and the context formed during Phase 1 interferes

with the expression of the CS-US association, deficits in latent inhibition reflect an inability to learn about or use context information.

Further Oberling, Gosselin and Miller (1999) also showed that deficits in latent inhibition reflect an impaired ability to acquire associations with contextual stimuli. There are similarities between this proposal and Cohen and Servan-Schreiber's cognitive model (1992) of schizophrenia which focuses on problems with memory, assuming that individuals with schizophrenia correctly process contextual information at training, but are unable to maintain this information over time and use it to inhibit inappropriate responses. Therefore, disruptions in latent inhibition might also reflect a deficit in ability to express CS-context associations or activate the comparison mechanism that would use CS-context associations to influence current performance (Escobar, Oberling & Miller, 2002). Thus, there are several association-based hypotheses, outlining a range of different causes of individual difference in latent inhibition.

Far from being a simple effect, the source of individual differences in latent inhibition remains controversial. From the attentional perspective, differences reflect the allocation or modulation of attention. From an interference perspective, differences have been considered to reflect either the ability to learn about contexts, the ability to remember learning with contexts or the ability to use learning with contexts to influence current performance.

Future work with humans needs to clarify the contribution of attention and interference to individual differences in learning. We highlight here two studies that have taken a different approach to isolating the causal basis for individual differences in learning in relation to schizotypy.

Approaches to Isolating the Causal Basis for Individual Differences.

Combining tests of associative learning is one approach to developing understanding of individual differences. For instance, Haselgrove and Evans (2010) tested the assumption that individual differences in attentional effects may reflect differences in selective learning, and specifically the implementation of a summed error term in learning. Selective learning is seen in blocking, where a CS-US association is not acquired when the CS is novel and trained in compound with a CS that has already predicts the paired US (e.g., Kamin, 1969; Le Pelley, Oakeshott & McLaren, 2005). Individual differences in blocking have been reported, with blocking attenuated or abolished in individuals with schizophrenia (e.g., Jones Hemsley, Ball and Serra, 1997; Jones Hemsley & Gray, 1992; Moran, Al-Uzri, Watson & Reveley 2003). While this difference has been attributed to the selectivity of learning, variance in both the selectivity of prediction error and attention could account for differences in blocking. To provide a more precise test of the non-selective learning hypothesis, Haselgrove and Evans (2010) combined a test of blocking with a test of asymmetrical learning.

In contrast to blocking, asymmetrical learning, summarized in Table 1, reflects the absence of a selective error term. The the change in associative strength of stimuli trained in compound is assumed to be governed by the associative strength of each stimulus (Haselgrove & Evans 2010). Rescorla (2001) had previously observed that if two stimuli are trained as equivalent predictors of a US (A+ and C+) and two stimuli are trained as predictors of the absence of the US (B- and D-), prior to A and B being paired with the absence of the US (AB-), initial training will influence the rate of conditioning in compound. This should only occur if the error term for each of the stimuli trained in compound can change independently. The effect of initial training on compound training can be assessed by testing the compounds AD and BC. Rescorla found that responding was weaker for AD than BC, despite their equivalent associative histories. This asymmetry suggests that more is learnt about A than B during the AB- training, indicating a non-selective prediction error.

While blocking is dependent on a summed error term, and hence selective learning, asymmetrical learning is dependent on the absence of such a summed error term. Therefore, to the extent that individuals show a blocking effect, and importantly, the selective learning assumed to underpin this, they would *not* be expected to show asymmetrical learning (Rescorla & Wagner, 1972; Haselgrove & Evans, 2010). Individuals with high levels of introverted anhedonia (a negative schizotypy trait; Claridge & Broks, 1984; Mason et al., 1995) failed to show blocking but demonstrated asymmetrical learning (Haselgrove & Evans, 2010). The combination of tasks narrows the range of explanations for individual differences, providing of one approach to improve our understanding of individual differences.

However, on its own this study has not provided overwhelming evidence that individual difference in CS focused effects, such as blocking, relate to the selectivity of prediction error. It is important to acknowledge the range of different CS focused effects that are relevant for this question. Schizotypy relates to individual difference in latent inhibition, learned relevance, and overshadowing, as well as blocking. The logic of Ockham's razor suggests that we should expect a common causal mechanism to underpin these disruptions. In which case, it is important to assess whether differences in the selectivity of prediction error provides a complete account for other CS focused effects.

Alternative explanations for individual differences in CS focused effects

There are also alternative explanations for CS focused effects in human learning that do not presume a role for selective prediction error or selective attention. For example, De Houwer, Vandorpe and Beckers (2005) argued that blocking in human learning can result from participants drawing higher level inferences of the form “cues A and B together cause the outcome to occur with the same probability as does cue A alone; this implies that cue B is

not a cause of the outcome." From this approach, individual difference in blocking may reflect individual difference in inferential reasoning rather than attention (e.g., Garety, Hemsley & Wessely, 1991; Mitchell et al., 2009; Sellen, Oaksford & Gray, 2005), which itself may involve a complex form of associative generalization.

Schizotypy-related differences in learning, have also been studied using complex configural discriminations (e.g., Haddon, George, Grayson, McGowan, Honey and Killcross, 2011). Individuals with high levels of introverted anhedonia are impaired solving a biconditional discrimination, suggesting an inability to treat the co-occurrence of stimuli as a unique configuration. The biconditional discrimination (AX+, AY-, BX-, BY+) requires participants to learn about multiple co-occurring stimuli (Byrom & Murphy, 2016; Saavedra, 1975). Thus, this finding of individual difference in biconditional discrimination mirrors, Cohen and Servan-Schreiber's (1992) suggestion that cognitive deficits observed in schizophrenia reflect a dysfunction of unitary a *cognitive context* mechanism, resulting in an inability to maintain or use task setting information to guide ongoing behavior. Such impaired ability to use task setting information might relate to negative symptoms in particular (e.g., Thoma, Zoppelt, Wiebel, & Daum, 2007).

Differences in the extent to which individuals use configurations of cues may still reflect differences in attention. Attentional breadth, a cognitive trait related to emotional arousal (Fredrickson, 2001), relates to an ability to solve configural discriminations such as negative patterning and biconditional discriminations (Byrom & Murphy 2014; 2016, 2017; see also McDonald et al. 1998, for an evaluation of the hippocampus in these tasks). Thus, while differences in ability to learn about multiple co-occurring stimuli may relate to some underlying ability to maintain or use task setting information, these differences may be related to attention. Further work is necessary here to clarify this relationship.

In summary, individual differences in learning may interact with genetic and environmental factors to cause symptoms of schizophrenia. In this respect differences in learning may be a key component of the etiology of schizophrenia. Individual differences in learning have been taken as support for the aberrant salience hypothesis of schizophrenia, supporting the assumption of differences in attention. However, it is far from clear that individual differences in CS focused effects, such as latent inhibition, should be attributed to attention alone. Further work is necessary to isolate the mechanisms underpinning CS focused effects and thus the causal basis of individual differences in such effects.

Example 4: Individual Differences in Contingency Learning and Depression.

As with anxiety and addiction, discussed above, gene x environment models are used to explain the etiology of depression. Heritability rates for depression are estimated between 40% and 50%, suggesting a substantive genetic contribution to risk for depression (Lohoff, 2010). Further, specific candidate genes have been investigated, including the serotonin transporter gene (Caspi, Hariri, Holmes, Uher, & Moffitt, 2010), the Brain-Derived Neurotrophic Factor (BDNF) gene (Hashimoto, 2010) and the Tryptophan Hydroxylase gene (Zill, Baghai & Ackenheil, 2004; for review see, Wray et al., 2012). Diathesis-stress theories develop the gene x environment model suggesting that stress interacts with a potential predisposition leading to psychopathology (Monroe & Reid, 2009; Monroe & Simons, 1991). However, the mechanism by which any of these genes interacts with environmental factors to increase risk for depression remains unclear. For instance, while the short allele of the serotonin transporter gene appears to influence sensitivity to the environment, heightening sensitivity to stress, how this translates into a depressed state is not clear (Caspi et al., 2010, see also Dayan & Huys, 2008).

We have already argued that (1) both genetic and environmental factors contribute to the development of differences in learning, and that (2) once established, differences in learning interact with genetic and environmental factors to increase risk. In the context of depression, the well-established effect of learned helplessness supports these hypotheses, providing an illustration of environmental factors (experience) establishing a stable difference in learning, which creates an independent risk factor. Learned helplessness describes an approach to learning, developed through experience of aversive events that an individual has no control over (Seligman, 1972). Learned helplessness has been observed in species as diverse as honey bees (Dinges, Varnon, Cota, Slykerman & Abramson, 2017), dogs (Seligman, 1972) and humans (Hiroto & Seligman, 1975). Here an environmental factor contributes to establishing a specific approach to future learning, creating individual differences in causal reasoning. Once established, learned helplessness will shape the subsequent influences of the environment on behavior, in a gene x mind x environment interaction (Abramson, Seligman, & Teasdale, 1978; Seligman, 1972; see also Maier & Seligman, 2016).

Further, individuals differ in their risk for developing learned helplessness; increased sensitivity to a lack of causal control may increase the risk for developing learned helplessness. Alloy and Abramson (1979) identified this difference as *depressive realism*, which sets up a pathway to develop and maintain depression, with a self-reinforcing cycle. Individuals who are better able to learn about their lack of causal control are more likely to learn that they are helpless, increasing their risk for depression (Alloy & Abramson, 1979).

Alloy and Abramson (1979) identified individual differences in the accuracy of mapping contingency judgements to this normative measure. Specifically, participants were told that over a set of discrete trials they could test whether their actions caused a given outcome. In a zero-contingency task, programmed so that the outcome happened equally

often in response to and in the absence of the participants' actions, non-depressed participants tended to overestimate the contingency between action and outcome, while individuals with mild symptoms of depression accurately judged the zero contingency (see also, Yarritu, Matute, & Luque, 2015; Yarritu, Matute, & Vadillo, 2014).

A normative measure of the contingency between action and outcome (ΔP), describes the strength and direction of a contingent relationship in terms of the difference between the probability of the outcome occurring following an action, P(o|e) and the probability of the outcome occurring in the absence of the action (i.e., effect), P(o|~e), as shown in Figure 3 (Allan, 1980). Judgements of control are broadly sensitive to manipulations of the statistical contingency between an action and an outcome (e.g., Baker, Murphy, Vallee-Tourangeau, 1996; Shanks, 1987; Wasserman, Elek, Chatlosh & Baker, 1993). However, normative calculations of ΔP can remain unchanged while the probability of actions and outcomes are manipulated. In contrast to this some participants appear to be sensitive to shifts in these probabilities, altering judgements of causal control with changes in the probability of outcome or action independent of changes in contingency (Blanco, Matute & Vadillo, 2011; Murphy, Vallee-Tourangeau, Msetfi & Baker, 2005; Vallee-Tourangeau, Murphy, Drew, & Baker, 1998; Vallee-Tourangeau, Payton & Murphy, 2008).

Why do individuals differ in judgements of control?

The observation of a difference in contingency judgement alone, does not itself provide insight into how this difference occurs However, with careful manipulation of the parameters influencing judgements of causal control, we are closer to understanding why individuals differ in their perception of contingency. Several factors may be relevant to individual differences in judgments of control, including; differences in the speed of learning,

sensitivity to the context, time perception and activity rates. Some of these factors may arise as a product of learning and all influence learning, potentially explaining individual differences in judgements of causal control.

Speed of Learning: One source of difference is perhaps the speed at which individuals learn. We know that the speed of contingency learning task is related to personality (e.g., openness-to-experience predicting performance Kaufman et al., 2010; Shanks, Lamberts, & Goldstone, 2005). Slow learning is more resistant to recent trial experience which, in an uncorrelated situation, is liable to misdirect the perceiver. Much like a difference between goal- and sign- tracking, with slow learning, the strong memory for the most recent event may override the long-term likelihood relation.

Sensitivity to the Context: Low mood is associated with poor maintenance of contextual information (Msetfi, Murphy, Kornbort & Simpson, 2009). Competition with contextual cues can have powerful effects on learning (Baker et al., 1996; Baker et al., 2000; Murphy et al., 2005). Msetfi and colleagues (2005) showed that individual differences in judgments of causal control, seemingly related to depressive symptoms, were themselves related to context learning. Msetfi et al., manipulated the probability of outcomes occurring (outcome density; the rate at which outcomes occur in a given learning period) and the inter-trial interval (ITI; the time gap between events), observing that individual differences in judgements of causal control were strongest with a high probability of outcomes occurring and long ITIs (Msetfi et al., 2005; Msetfi, Wade, & Murphy, 2013). The ITI provides experience of the background context in the absence of actions or outcomes. In terms of ΔP and the matrix in Figure 3, the ITI is equivalent to a cell D trial. Incorporating this into a normative calculation of contingency increases the contingency between action and outcome (or CS and US in a Pavlovian case). In terms of associative learning, exposure to the ITI provides experience of the *context* in the absence of the outcome, reducing the strength of

association between context and outcome and thus competition between the context and action for associative strength. Thus, through its influence on cue competition, reduced context processing can explain differences in judgements of causal control.

Supporting the hypothesis that individual differences in contingency judgements relates to cue competition, Msetfi and colleagues (2005) found that manipulation of competing cues influenced learning. Individuals differed in contingency judgements only in conditions with a long ITI. Non-depressed individuals judged that they had control of the outcome, an effect that reflects extinction of the context-outcome association, boosting the action-outcome association. The absence of this effect in depressed individuals suggests that they were insensitive to the information occurring in the ITI or that this experience of the combination of context and no outcome did not influence their action-outcome association. This study suggests that differences in contingency learning, increasing risk of learned helplessness, relate to the influence of context learning on cue competition.

While the role of context processing provides insight into how individual differences in judgements of causal control develop, differences in context processing need explaining. The ITI contains (a) the absence of action, (b) the absence of outcome, (c) the absence of stimuli and (d) the presence of the context. Differences in processing any of these components can explain differences in learning causal control. We do not propose that it is simple to identify individual differences in such learning. Indeed, research thus far suggests that differences in several different factors interact to influence learning.

Time Perception, Attention, and Activity Rates: While there is some evidence of a relationship between low mood and altered time perception (Kornbort, Msetfi & Grimwood, 2013), other studies suggest that apparent differences in time perception reflect ability to maintain attention (Msetfi, Murphy & Kornbort, 2012). Activity rates both influence causal learning and may be influenced by causal learning, in a mutually reinforcing relationship

(Byrom, Msetfi & Murphy, 2015). While some studies suggest that accurate judgements of causal control may arise due to low activity rates associated with low mood (Blanco, Matute, Vadillo, 2012), there is also evidence of high activity rates in individuals with low mood (Byrom et al., 2015). Changes in time perception, attention and activity rates could all contribute to differences in context processing and thus judgements of causal control, or may influence the perceived and actual components of a causal judgement experience, directly altering the perception of causal control.

Summary

To summarize, we wish to highlight several points. Individual differences in a simple effect of contingency learning may arise from a complex array of different and interacting factors. Where individual differences are observed, it is necessary to explore the factors underlying the individual differences and experiments need to manipulate parameters to begin to isolate the factors contributing to individual differences in learning. As illustrated in this example, these factors may relate directly to learning, or other cognitive factors, such as perception of time. It will only be in studying the interaction between parameter manipulations and individual differences that we can provide a comprehensive understanding of the mechanisms contributing to individual differences in learning. It is also clear that these behavioral effects are not simple consequences of a gene x environment interaction.

It will not have escaped the observant reader that there is a mismatch between how we envisage the study of depressive realism informing understanding of the etiology of depression and the current evidence base. We started this section by suggesting that individual differences in contingency learning could contribute to risk for depression, specifically, enhanced ability to identify a zero-contingency relationship between actions and

outcomes would accentuate the development of learned helplessness, establishing a learning framework that would increase risk for depression. While we believe that individual differences in contingency learning will interact with genetic and environmental factors to contribute to risk for depression, the studies outlined above have all assessed how depression or low mood influences learning. Thus, we cannot state with any confidence that differences in contingency learning contribute to the etiology of depression, rather than arise as a result of depression. This is illustrative of an important gap in the research into individual differences in associative learning; if our understanding of individual differences in associative learning is to enhance our understanding of the etiology of differences in behavior, we need to be studying the development of difference.

Conclusions

We began this paper by situating animal learning and learning theory with the study of individual differences. We have argued that: 1) principles of learning are also principles of individual differences; 2) principles of learning provide a mechanism for understanding the contribution of the psychological to behavior; 3) learning theories, far from being too simplistic, provide a guide for how to explain different dissociable aspects of behavior.

We have argued for a gene x mind x environment interaction. Differences in learning, which might be established through the interaction of genetic and environmental factors, have an independent causal power, interacting with both genetic and environmental effects. The differences in learning that we have described extend beyond endophenotypes, being influenced by both genetics and environment. As such, we argue that the role of the mind in the interaction of gene and environment needs careful consideration as more than just part of the pathway through which genes exert an effect on phenotype.

We acknowledge that many different factors influence individual differences in learning, including differences in attention, memory, and motivation. However, this is not a cause to abandon the associative model. What we must abandon is the idea that ‘mind’ is a veridical expression of experience, or a simple mediator of the real and prime gene x environment relation (see Figure 1). There is complexity enough within learning models to account for diversity in learning. What is needed are careful manipulations of experimental parameters to isolate the causal basis of individual differences in learning.

Throughout we have looked at various learning effects. These tend to be examined in isolation. We bring these together here because there are comparable threads of research across fear conditioning, sign-tracking and latent inhibition. Consideration of overlapping components of learning, should advance our understanding of individual differences in these effects. For instance, the distinction between learning about diffuse and discrete cues is apparent in individual differences in fear conditioning and sign-tracking. Differences in the ability to use contexts to cue appropriate performance and judgements have been proposed to account for individual difference in latent inhibition and judgment of control. Despite these overlaps, different mechanisms are proposed to explain individual difference in these effects in a way that lacks parsimony when individual differences in learning are considered in the whole.

The history of animal learning offers another important lesson on the study of individual differences. Skinner’s behaviorist program eschewed the study of behavior in terms of differences between groups and even the development of an overarching theory (Skinner, 1938, 1945). In this, Skinner was interested in individual differences; his proposal was that each individual animal provided a unique, N=1, object of study and analysis. He also thought that cognitions and the contributions of an individual animal’s mind (which was

unobservable) to behavior, was beyond the scope of 20th century science. As we continue into the 21st century this challenge has become part of modern psychological study.

More generally, the analysis of human medicine and psychology are recognizing that over-general rules of scientific analysis are insufficient to account for individual variability. For instance, cancer treatment is not a single causal event, but rather a treatment of cancer may be as unique as the individual patient. To diagnose and treat any individual may require understanding their unique genetic, environmental as well as psychosocial background (e.g., Kerry et al., 2012; Murphy, Byrom & Msetfi, 2017). The so called 'person-centered' medical movement is accompanied by a revaluation of the value of Randomized Control Trials and group statistical analyses as the most respected source of evidence based medicine (Kerry et al.,). Such radical thinking may require a similar radical response in psychology, an analysis of both group and individual, not just society or environment, but individual. Ultimately, if psychology is to provide an account of the human and animal condition we need our theories to describe how an individual's learning experience comes to shape their behavior.

References

Abramson, L. Y., Seligman, M. E., & Teasdale, J. D. (1978). Learned helplessness in humans: critique and reformulation. *Journal of Abnormal Psychology, 87*(1), 49-74.

Al-Rasheed, A. S. (2015). An experimental study of gender and cultural differences in hue preference. *Frontiers in psychology, 6*, 30.

Albertella, L., Copeland, J., Pearson, D., Watson, P., Wiers, R. W., & Le Pelley, M. E. (2017). Selective attention moderates the relationship between attentional capture by signals of nondrug reward and illicit drug use. *Drug and alcohol dependence*, 175, 99-105.

Allan, L. G. (1980). A note on measurement of contingency between two binary variables in judgement tasks. *Bulletin of the Psychonomic Society, 15*, 147 - 149.

Allan, L. G., & Jenkins, H. M. (1980). The Judgement of Contingency and the Nature of the Response Alternatives. *Canadian Journal of Psychology-Revue Canadienne De Psychologie, 34*(1), 1-11.

Alloy, L. B., & Abramson, L. Y. (1979). Judgment of contingency in depressed and nondepressed students: sadder but wiser? *Journal of Experimental Psychology: General, 108*(4), 441-485.

Arnaudova, I. B., Krypotos, A., Effting, M., Boddez, Y., Kindt, M., & Beckers, T. (2013). Individual differences in discriminatory fear learning under conditions of ambiguity: a vulnerability factor for anxiety disorders? *Frontiers in psychology, 4*.

Aron, E. N., & Aron, A. (1997). Sensory-processing sensitivity and its relation to introversion and emotionality. *Journal of Personality and Social Psychology, 73*(2), 345.

Baas, J. M., van Ooijen, L., Goudriaan, A., & Kenemans, J. L. (2008). Failure to condition to a cue is associated with sustained contextual fear. *Acta Psychologia (Amst), 127*(3), 581-592.

Baetu, I., Baker, A.G., Darredeau, C. & Murphy, R.A.(2005). A comparative approach to cue competition with one and two strong predictors. *Learning and Behavior*, 33, 160-171.

Baker, A. G., & Mackintosh, N. J. (1979). Preexposure to the CS alone, US alone, or CS and US uncorrelated: Latent inhibition, blocking by context or learned irrelevance? *Learning and Motivation, 10*(3), 278-294.

Baker, A. G., & Mercier, P. (1982). Extinction of the context and latent inhibition. *Learning and Motivation*, 13(4), 391-416.

Baker, A.G. & Msetfi, R.M., N. Hanley and Murphy, R.A., (2011). Sadly not wiser. In L. Hogarth & M. Haselgrove (Eds.) *Clinical applications of learning theory*. Hove: Psychology Press.

Baker, A.G., Murphy, R.A.& Vallée-Tourangeau, F. (1996). Associative and normative models of causal induction: Reacting to versus understanding cause. In D.R.Shanks, K.J.Holyoak & D.L.Medin (Eds.), *The Psychology of Learning and Motivation*, Vol. 34, (pp. 1-45) San Diego, CA: Academic Press.

Baker, A.G., Murphy, R.A., Vallée-Tourangeau, F. & Mehta, R. (2001). Contingency learning and causal reasoning. In R.R.Mowrer & S.B.Klein (Eds.), *Handbook of Contemporary Learning Theories*. (pp. 255-306) Hillsdale, NJ: Lawrence Erlbaum Associates.

Baker, A.G., Vallée-Tourangeau, F. & Murphy, R.A. (2000). Asymptotic judgment of cause in a relative validity paradigm. *Memory & Cognition, 28, 466-479.*

Bannerman, D. M., Bus, T., Taylor, A., Sanderson, D. J., Schwarz, I., Jensen, V., Hvalby, O., Rawlins, J.N.P., Seeburg, P.H., & Sprengel, R. (2012). Dissecting spatial knowledge from spatial choice by hippocampal NMDA receptor deletion. *Nature neuroscience, 15*(8), 1153-1159.

Bannerman, D. M., Sprengel, R., Sanderson, D. J., McHugh, S. B., Rawlins, J. N. P., Monyer, H., & Seeburg, P. H. (2014). Hippocampal synaptic plasticity, spatial memory and anxiety. *Nature reviews neuroscience., 15*(3), 181-192.

Barlow, D. H. (2002). *Anxiety and its disorders: The nature and treatment of anxiety and panic*. Guilford press.

Baruch, I., Hemsley, D. R., & Gray, J. A. (1988a). Differential performance of acute and chronic schizophrenics in a latent inhibition task. *The Journal of Nervous and Mental Disease, 176*(10), 598-606.

Baruch, I., Hemsley, D. R., & Gray, J. A. (1988b). Latent inhibition and “psychotic proneness” in normal subjects. *Personality and Individual Differences, 9*(4), 777-783.

Bayer, H. M., & Glimcher, P. W. (2005). Midbrain dopamine neurons encode a quantitative reward prediction error signal. *Neuron*, 47(1), 129-141.

Beckers, T., Krypotos, A. M., Boddez, Y., Effting, M., & Kindt, M. (2013). What's wrong with fear conditioning? *Biological psychology*, 92(1), 90-96.

Beckmann, J. S., Marusich, J. A., Gipson, C. D., & Bardo, M. T. (2011). Novelty seeking, incentive salience and acquisition of cocaine self-administration in the rat. *Behavioural brain research*, 216(1), 159-165.

Belin, D., Belin-Rauscent, A., Everitt, B. J., & Dalley, J. W. (2016). In search of predictive endophenotypes in addiction: insights from preclinical research. *Genes, Brain and Behavior*, 15(1), 74-88.

Belin, D., Berson, N., Balado, E., Piazza, P.V. & Deroche-Gamonet, V. (2011) High-novelty-preference rats are predisposed to compulsive cocaine self-administration. *Neuropsychopharmacology* 36, 569–579.

Belin, D., & Deroche-Gamonet, V. (2012). Responses to novelty and vulnerability to cocaine addiction: contribution of a multi-symptomatic animal model. *Cold Spring Harbor perspectives in medicine*, 2(11), a011940.

Bende, M., & Nordin, S. (1997). Perceptual learning in olfaction: professional wine tasters versus controls. *Physiology & Behavior*, 62(5), 1065-1070.

Bender, S., Muller, B., Oades, R. D., & Sartory, G. (2001). Conditioned blocking and schizophrenia: a replication and study of the role of symptoms, age, onset-age of psychosis and illness-duration. *Schizophrenia Research, 49*(1-2), 157-170.

Bennett, C. H., Wills, S. J., Oakeshott, S. M., & Mackintosh, N. J. (2000). Is the context specificity of latent inhibition a sufficient explanation of learned irrelevance? *The Quarterly Journal of Experimental Psychology: Section B, 53*(3), 239-253.

Berridge, K. C. (2001). Reward learning: Reinforcement, incentives, and expectations. *The psychology of learning and motivation: Advances in research and theory*, 40, 223-278.

Berridge, K. C. (1996). Food reward: brain substrates of wanting and liking. *Neuroscience & Biobehavioral Reviews*, 20(1), 1-25.

Blanco, F., Matute, H., & Vadillo, M. (2009). Depressive Realism: Wiser or Quieter? *The Psychological Record, 59,* 551-562.

Blanco, F., Matute, H., & Vadillo, M. A. (2012). Mediating role of activity level in the depressive realism effect. *PLoS One*, 7(9), e46203.

Blanco, F., Matute, H., & Vadillo, M. A. (2013). Interactive effects of the probability of the cue and the probability of the outcome on the overestimation of null contingency. *Learning & Behavior*, 41(4), 333-340.

Boddez, Y., Vervliet, B., Baeyens, F., Lauwers, S., Hermans, D., & Beckers, T. (2012). Expectancy bias in a selective conditioning procedure: trait anxiety increases the threat value of a blocked stimulus. *Journal of behavior therapy and experimental psychiatry*, 43(2), 832-837.

Boakes, R. A. (1977). Performance on learning to associate a stimulus with positive reinforcement. *Operant-Pavlovian interactions*, Hillsdale NJ: Erlbaum 67-97.

Bolles, R. C. (1972). Reinforcement, expectancy, and learning. *Psychological Review*, 79(5), 394.

Bornstein, M. H., Kessen, W., & Weiskopf, S. (1976). Color vision and hue categorization in young human infants. *Journal of Experimental Psychology: Human Perception and Performance, 2*(1), 115.

Bouchard, T. J. (2013). The Wilson effect: the increase in heritability of IQ with age. *Twin Research and Human Genetics, 16*(05), 923-930.

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. Psychological bulletin, 114(1), 80.

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological psychiatry*, 52(10), 976-986.

Bouton, M. E., Mineka, S., & Barlow, D. H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Psychological Review, 108*(1), 4.

Bouton, M. E., Rosengard, C., Achenbach, G. G., Peck, C. A., & Brooks, D. C. (1993). Effects of Contextual Conditioning and Unconditional Stimulus-Presentation on Performance in Appetitive Conditioning. *Quarterly Journal of Experimental Psychology Section B-Comparative and Physiological Psychology, 46*(1), 63-95.

Brandon, S. E., Vogel, E. H., & Wagner, A. R. (2000). A componential view of configural cues in generalization and discrimination in Pavlovian conditioning. *Behavioural brain research*, 110(1), 67-72.

Bronfman, Z., Ginsburg, S., & Jablonka, E. (2014). The epigenetics of neural learning. *The Wiley Handbook on the Cognitive Neuroscience of Learning*, 136-176.

Brown, P. L., & Jenkins, H. M. (1968). Auto-shaping of the pigeon's key-peck. *Journal of the experimental analysis of behavior*, 11(1), 1-8.

Brown, B. L., Hemmes, N. S., De Vaca, S. C., & Pagano, C. (1993). Sign and goal tracking during delay and trace autoshaping in pigeons. *Learning & behavior*, 21(4), 360-368.

Bush, R. R., & Mosteller, F. (1951). A Model for Stimulus Generalization and Discrimination. *Psychological Review, 58*(6), 413-423.

Byrom, N. C., & Murphy, R. A. (2014). Sampling Capacity Underlies Individual Differences in Human Associative Learning. *Journal of Experimental Psychology-Animal Learning and Cognition, 40*(2), 133-143.

Byrom, N. C., & Murphy, R. A. (2016). Individual Difference in Configural Associative Learning. *Journal of Experimental Psychology: Animal Learning and Cognition*. 42, 325-335.

Byrom, N. C. & Murphy, R.A. (2016) Learning to predict future events: the role for dopamine. In R.A. Murphy and R.C. Honey (Eds.) *Handbook of cognitive neuroscience of learning*. London: Wiley

Byrom, N. and Murphy, RA. (2017). Cue competition influences biconditional discriminations. *Quarterly Journal of Experimental Psychology: Special Issue for Nicholas J. Mackintosh, XX, XX-XX*

Byrom, N. C., Msetfi, R. M., & Murphy, R. A. (2015). Two pathways to causal control: use and availability of information in the environment in people with and without signs of depression. *Acta psychologica,* 157, 1-12.

Caspi, A., Hariri, A. R., Holmes, A., Uher, R., & Moffitt, T. E. (2010). Genetic sensitivity to the environment: the case of the serotonin transporter gene and its implications for studying complex diseases and traits. *Focus, 8*(3), 398-416.

Chase, H., Crockett, M.J., Msetfi, R.M., Murphy, R.A., Clark, L., Sahakian, B.J. & Robbins, T.W. (2011) 5-HT Modulation by Acute Tryptophan Depletion of Human Instrumental Contingency Judgements depends on Baseline Depression Score. *Psychopharmacology, 213, 615-623.*

Childress, A. R., Hole, A. V., Ehrman, R. N., Robbins, S. J., McLellan, A. T., & O'Brien, C. P. (1993). Cue reactivity and cue reactivity interventions in drug dependence. *NIDA research monograph*, 137, 73-73.

Claridge, G. S., & Broks, P. (1984). Schizotypy and hemisphere function—I: Theoretical considerations and the measurement of schizotypy. *Personality and Individual Differences, 5*(6), 633-648.

Cleland, G. G., & Davey, G. C. (1983). Autoshaping in the rat: The effects of localizable visual and auditory signals for food. *Journal of the experimental analysis of behavior*, 40(1), 47-56.

Clinton, S., Miller, S., Watson, S. J., & Akil, H. (2008). Prenatal stress does not alter innate novelty-seeking behavioral traits, but differentially affects individual differences in neuroendocrine stress responsivity. *Psychoneuroendocrinology*, 33(2), 162-177.

Cohen, J. D., & Servan-Schreiber, D. (1992). Context, cortex, and dopamine: a connectionist approach to behavior and biology in schizophrenia. *Psychological Review, 99*(1), 45.

Cohen Kadosh, K, Haddad, A.D.M., Heathcote, L. Murphy, R.A., Pine, D. & Lau, J. (2015). High trait anxiety during adolescence interferes with discriminatory context and learning. *Neurobiology of Learning and Memory, 123*, 50-57.

Corlett, P. R., Honey, G. D., & Fletcher, P. C. (2007). From prediction error to psychosis: ketamine as a pharmacological model of delusions. *Journal of Psychopharmacology, 21*(3), 238-252.

Costa, D. S., & Boakes, R. A. (2007). Maintenance of responding when reinforcement becomes delayed. *Learning & behavior*, 35(2), 95-105.

Davey, G. C., & Cleland, G. G. (1982). Topography of signal-centered behavior in the rat: effects of deprivation state and reinforcer type. *Journal of the experimental analysis of behavior*, 38(3), 291-304.

Davey, G. C., Phillips, S., & Cleland, G. G. (1981). The topography of signal-centered behavior in the rat: The effects of solid and liquid food reinforcers. *Behaviour Analysis Letters,* 1 (6), 331-337.

Davis, B. A., Clinton, S. M., Akil, H., & Becker, J. B. (2008). The effects of novelty-seeking phenotypes and sex differences on acquisition of cocaine self-administration in selectively bred High-Responder and Low-Responder rats. *Pharmacology Biochemistry and Behavior,* 90(3), 331-338.

Dayan, P., & Abbott, L.F. (2001). *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems.* Cambridge, MA: The MIT Press.

Dayan, P., & Huys, Q. J. (2008). Serotonin, inhibition, and negative mood. *PLoS Computational Biology*, 4(2), e4.

De Houwer, J., Vandorpe, S., & Beckers, T. (2005). Evidence for the role of higher order reasoning processes in cue competition and other learning phenomena. *Learning & Behavior*, 33(2), 239-249.

Dejong, W. (1994). Relapse prevention: an emerging technology for promoting long-term drug abstinence. *International Journal of the Addictions*, 29(6), 681-705.

Di Ciano, P., & Everitt, B. J. (2004). Conditioned reinforcing properties of stimuli paired with self-administered cocaine, heroin or sucrose: implications for the persistence of addictive behaviour. *Neuropharmacology*, 47, 202-213.

Di Feliceantonio, A. G., & Berridge, K. C. (2012). Which cue to 'want'? Opioid stimulation of central amygdala makes goal-trackers show stronger goal-tracking, just as sign-trackers show stronger sign-tracking. *Behavioural brain research*, 230(2), 399-408.

Dickinson, A., Smith, J., & Mirenowicz, J. (2000). Dissociation of Pavlovian and instrumental incentive learning under dopamine antagonists. *Behavioral neuroscience*, 114(3), 468.

Dinges, C.W., Varnon, C.A., Cota, L.D, Slykerman, S. & Abramson, C.I. (2017) Studies of learned helplessness in honey bees (Apsi mellifera linguistica). *Journal of Experimental Psychology: Animal Learning and Cognition*, 43 (2), 147-158

Dodge, K. A., & Pettit, G. S. (2003). A biopsychosocial model of the development of chronic conduct problems in adolescence. *Developmental Psychology*, *39*(2), 349.

Duits, P., Cath, D. C., Lissek, S., Hox, J. J., Hamm, A. O., Engelhard, I. M., Baas, J. M. P. (2015). Updated meta-analysis of classical fear conditioning in the anxiety disorders. *Depression and anxiety*, *32*(4), 239-253.

Ellis, A. (1980). Rational emotive therapy and cognitive behavior therapy: Similarities and differences. *Cognitive Therapy and Research*, 4, 325–340.

Endler, J. A., & Houde, A. E. (1995). Geographic variation in female preferences for male traits in Poecilia reticulata. *Evolution*, 456-468.

Engel, G. L. (1989). The need for a new medical model: a challenge for biomedicine. *Holistic Medicine*, *4*(1), 37-53.

Engelhard, I. M., van den Hout, M. A., & McNally, R. J. (2008). Memory consistency for traumatic events in Dutch soldiers deployed to Iraq. *Memory*, 16(1), 3-9.

Escobar, M., Oberling, P., & Miller, R. R. (2002). Associative deficit accounts of disrupted latent inhibition and blocking in schizophrenia. *Neuroscience & Biobehavioral Reviews*, 26(2), 203-216.

Flagel, S. B., Akil, H., & Robinson, T. E. (2009). Individual differences in the attribution of incentive salience to reward-related cues: Implications for addiction. *Neuropharmacology*, 56, 139-148

Flagel, S. B., Watson, S. J., Akil, H., & Robinson, T. E. (2008). Individual differences in the attribution of incentive salience to a reward-related cue: influence on cocaine sensitization. *Behavioural brain research*, 186(1), 48-56.

Flagel, S. B., Robinson, T. E., Clark, J. J., Clinton, S. M., Watson, S. J., Seeman, P., Phillips, P.E., & Akil, H. (2010). An animal model of genetic vulnerability to behavioral disinhibition and responsiveness to reward-related cues: implications for addiction. *Neuropsychopharmacology*, 35(2), 388.

Flagel, S. B., Watson, S. J., Robinson, T. E., & Akil, H. (2007). Individual differences in the propensity to approach signals vs goals promote different adaptations in the dopamine system of rats. *Psychopharmacology*, 191(3), 599-607.

Flagel, S. B., Clark, J. J., Robinson, T. E., Mayo, L., Czuj, A., Willuhn, I., Akers, C.A., Clinton, S.M., Phillips, P.E., & Akil, H. (2011). A selective role for dopamine in stimulus-reward learning. *Nature*, 469(7328), 53-57.

Flagel, S. B., & Robinson, T. E. (2017). Neurobiological basis of individual variation in stimulus-reward learning. Current Opinion in Behavioral Sciences, 13, 178-185.

Flint, J., Greenspan, R. J., & Kendler, K. S. (2010). *How genes influence behavior*: Oxford University Press.

Fredrickson, B. L. (2004). The broaden-and-build theory of positive emotions. *Philosophical transactions-royal society of London series b biological sciences*, 1367-1378.

Frith, C. D., Stevens, M., Johnstone, E. C., & Crow, T. J. (1979). Skin conductance responsivity during acute episodes of schizophrenia as a predictor of symptomatic improvement. *Psychological medicine, 9*(1), 101-106.

Fullana, M. A., Harrison, B. J., Soriano-Mas, C., Vervliet, B., Cardoner, N., Àvila-Parcet, A., & Radua, J. (2016). Neural signatures of human fear conditioning: an updated and extended meta-analysis of fMRI studies. *Molecular psychiatry*, 21(4), 500-508.

Garety, P. A., Hemsley, D. R., & Wessely, S. M. R. C. (1991). Reasoning in deluded schizophrenic and paranoid patients: biases in performance on a probabilistic inference task. The Journal of nervous and mental disease, 179(4), 194-201.

Garofalo, S., & di Pellegrino, G. (2015). Individual differences in the influence of task-irrelevant Pavlovian cues on human behavior. *Frontiers in behavioral neuroscience*, 9, 163.

Gershman, S. J., & Hartley, C. A. (2015). Individual differences in learning predict the return of fear. *Learning & behavior*, 43(3), 243-250.

Ginton, A., Urca, G., & Lubow, R. E. (1975). The effects of preexposure to a nonattended stimulus on subsequent learning: Latent inhibition in adults. *Bulletin of the Psychonomic Society*, *5*(1), 5-8.

Gluck, M. A. (1991). Stimulus-Generalization and Representation in Adaptive Network Models of Category Learning. *Psychological Science* 2(1): 50-55.

Goldstein, A. J., & Chambless, D. L. (1978). A reanalysis of agoraphobia. *Behavior Therapy*, 9(1), 47-59.

Gordon, J. A., & Hen, R. (2004). Genetic approaches to the study of anxiety. *Annual Review of Neuroscience*, 27, 193-222.

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: etymology and strategic intentions. *American Journal of Psychiatry*, 160(4), 636-645.

Grahame, N. J., Barnet, R. C., Gunther, L. M., & Miller, R. R. (1994). Latent inhibition as a performance deficit resulting from CS—context associations. *Animal Learning & Behavior*, 22(4), 395-408.

Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, S. P., Dufour, M. C., Compton, W., Pickering, R.P., & Kaplan, K. (2004). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the national epidemiologic survey on alcohol and related conditions. *Archives of general psychiatry*, 61(8), 807-816.

Gray, J. A., Feldon, J., Rawlins, J. N. P., Smith, A. D., & Hemsley, D. R. (1991). The neuropsychology of schizophrenia. *Behavioral and Brain Sciences, 14*(1), 1-19.

Gray, N. S., Fernandez, M., Williams, J., Ruddle, R. A., & Snowden, R. J. (2002). Which schizotypal dimensions abolish latent inhibition? *British Journal of Clinical Psychology, 41*(3), 271-284.

Gray, N. S., Hemsley, D. R., & Gray, J. A. (1992). Abolition of latent inhibition in acute, but not chronic, schizophrenics. *Neurology Psychiatry and Brain Research, 1*(2), 83-89.

Gray, N. S., Snowden, R. J., Peoples, M., Hemsley, D. R., & Gray, J. A. (2003). A demonstration of within-subjects latent inhibition in the human: limitations and advantages. *Behavioral Brain Research, 138*(1), 1-8.

Grillon, C. (2002). Associative learning deficits increase symptoms of anxiety in humans. *Biological Psychiatry, 51*(11), 851-858.

Grillon, C., Ameli, R., Woods, S. W., Merikangas, K., & Davis, M. (1991). Fear-potentiated startle in humans: Effects of anticipatory anxiety on the acoustic blink reflex. *Psychophysiology*, 28(5), 588-595.

Haddon, J. E., George, D. N., Grayson, L., McGowan, C., Honey, R. C., & Killcross, S. (2011). Impaired conditional task performance in a high schizotypy population: Relation to cognitive deficits. *Quarterly Journal of Experimental Psychology, 64*(1), 1-9.

Haddon, J. E., George, D. N., Grayson, L., McGowan, C., Honey, R. C., & Killcross, S. (2014). Extreme elemental processing in a high schizotypy population: Relation to cognitive deficits. *The Quarterly Journal of Experimental Psychology*, 67(5), 918-935.

Hall, G., & Minor, H. (1984). A search for context-stimulus associations in latent inhibition. *The Quarterly Journal of Experimental Psychology*, 36(2), 145-169.

Halpern, D. F. (2012). *Sex differences in cognitive abilities*: Hove: Psychology press.

Hariri, A. R. (2009). The neurobiology of individual differences in complex behavioral traits. *Annual review of neuroscience*, 32, 225-247.

Haselgrove, M., & Evans, L. H. (2010). Variations in selective and nonselective prediction error with the negative dimension of schizotypy. *Quarterly Journal of Experimental Psychology, 63*(6), 1127-1149.

Hashimoto, K. (2010). Brain-derived neurotrophic factor as a biomarker for mood disorders: an historical overview and future directions. *Psychiatry and clinical neurosciences, 64*(4), 341-357.

Hearst, E., & Jenkins, H. M. (1974). Sign-tracking: The stimulus-reinforcer relation and directed action. *Psychonomic Society.*

Hemsley, D. R. (1987). An experimental psychological model for schizophrenia. *Search for the causes of schizophrenia*, *1*, 179-188.

Hiroto, D. S., & Seligman, M. E. (1975). Generality of learned helplessness in man. *Journal of personality and social psychology*, 31(2), 311.

Holland, P. C. (1980). Influence of visual conditioned stimulus characteristics on the form of Pavlovian appetitive conditioned responding in rats. *Journal of Experimental Psychology: Animal Behavior Processes*, 6(1), 81.

Hull, C.L. (1943). *Principles of Behavior: An Introduction to Behavior Theory*. New York: Appleton-Century-Crofts.

Jablonka, E., Lamb, M. J., & Zeligowski, A. (2014). *Evolution in four dimensions, revised edition: Genetic, epigenetic, behavioral, and symbolic variation in the history of life*. MIT press.

Jensen, J., Willeit, M., Zipursky, R. B., Savina, I., Smith, A. J., Menon, M., Crawley, A.P., & Kapur, S. (2008). The formation of abnormal associations in schizophrenia: neural and behavioral evidence. *Neuropsychopharmacology, 33*(3), 473-479.

Jentsch, J. D., & Taylor, J. R. (1999). Impulsivity resulting from frontostriatal dysfunction in drug abuse: implications for the control of behavior by reward-related stimuli. *Psychopharmacology,* 146(4), 373-390

Jones, S. H., Gray, J. A., & Hemsley, D. R. (1992). Loss of the Kamin blocking effect in acute but not chronic schizophrenics. *Biological Psychiatry, 32*(9), 739-755.

Jones, S. H., Hemsley, D., Ball, S., & Serra, A. (1997). Disruption of the Kamin blocking effect in schizophrenia and in normal subjects following amphetamine. *Behavioral Brain Research, 88*(1), 103-114.

Kamin, L. J. (1969). Predictability, surprise, attention and conditioning. In B. A. Campbell & R. M. Church (Eds.), *Punishment and Aversive Behavior* (pp. 279-296). New York: Appleton-Century-Crofts.

Kasprow, W. J., Catterson, D., Schachtman, T. R., & Miller, R. R. (1984). Attenuation of latent inhibition by post-acquisition reminder. The Quarterly Journal of Experimental Psychology, 36(1), 53-63.

Kaufman, S. B., De Young, C. G., Gray, J. R., Jimenez, L., Brown, J., & Mackintosh, N. (2010). Implicit learning as an ability. *Cognition, 116*(3), 321-340.

Kendler, K. S. (2005). “A gene for…”: the nature of gene action in psychiatric disorders. *American Journal of Psychiatry, 162*(7), 1243-1252.

Kendler, K. S., & Baker, J. H. (2007). Genetic influences on measures of the environment: a systematic review. Psychological medicine, 37(05), 615-626.

Kerry, R., Eriksen, T. E., Lie, S. A. N., Mumford, S. D., & Anjum, R. L. (2012). Causation and evidence-based practice: an ontological review. *Journal of Evaluation in Clinical Practice*, *18*(5), 1006-1012.

Kirsch, I., Lynn, S. J., Vigorito, M., & Miller, R. R. (2004). The role of cognition in classical and operant conditioning. *Journal of Clinical Psychology*, 60(4), 369-392.

Kornbrot, D. E., Msetfi, R. M., & Grimwood, M. J. (2013). Time perception and depressive realism: judgment type, psychophysical functions and bias. *PloS one*, 8(8), e71585.

Kraemer, P. J., Randall, C. K., & Carbary, T. J. (1991). Release from latent inhibition with delayed testing. *Animal Learning & Behavior*, 19(2), 139-145.

Kruschke, J. K. (2001). Toward a unified model of attention in associative learning. *Journal of Mathematical Psychology*, *45*(6), 812-863.

Le Pelley, M. E. (2004). The role of associative history in models of associative learning: A selective review and a hybrid model. *Quarterly Journal of Experimental Psychology Section B*, 57(3), 193-243.

Le Pelley, M. E., & McLaren, I. P. (2003). Learned associability and associative change in human causal learning. *The Quarterly Journal of Experimental Psychology. B, Comparative and Physiological Psychology*, *56*(1), 68-79.

Le Pelley, M. E., Oakeshott, S. M., & McLaren, I. P. L. (2005). Blocking and unblocking in human causal learning. *Journal of Experimental Psychology-Animal Behavior Processes*, *31*(1), 56-70.

Le Pelley, M.E., Pearson, D., Griffiths, O., Beesley, T., 2015. When goals conflict with values: counterproductive attentional and oculomotor capture by reward-related stimuli. *J. Exp. Psychol. Gen.* 144, 158–171.Le Pelley, M. E., Schmidt-Hansen, M., Harris, N. J., Lunter, C. M., & Morris, C. S. (2010). Disentangling the attentional

deficit in schizophrenia: Pointers from schizotypy. *Psychiatry research*, 176(2), 143-149.

Le Pelley, M. E., & Schmidt-Hansen, M. (2010). Latent inhibition and learned irrelevance in human contingency learning. In R. E. Lubow & I. Weiner (Eds.), *Latent inhibition: Cognitions, neuroscience and applications to schizophrenia* (pp. 94-113).

Le Pelley, M. E., Schmidt-Hansen, M., Harris, N. J., Lunter, C. M., & Morris, C. S. (2010). Disentangling the attentional deficit in schizophrenia: pointers from schizotypy. *Psychiatry Research, 176*(2-3), 143-149. doi: 10.1016/j.psychres.2009.03.027

Ling, Y., Hurlbert, A., & Hurlbert, A. C. (2011). Age-dependence of colour preference in the UK population. *New Directions in Colour Studies*, 347-360.

Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., & Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: a meta-analysis. *Behavior Research and Therapy*, *43*(11), 1391-1424.

Lissek, S., Rabin, S. J., McDowell, D. J., Dvir, S., Bradford, D. E., Geraci, M., Pine D.S., Grillon, C. (2009). Impaired discriminative fear-conditioning resulting from elevated fear responding to learned safety cues among individuals with panic disorder. *Behavior Research and Therapy, 47*(2), 111-118.

Lonsdorf, T. B., Weike, A. I., Nikamo, P., Schalling, M., Hamm, A. O., & Öhman, A. (2009). Genetic gating of human fear learning and extinction possible implications for gene-environment interaction in anxiety disorder. *Psychological science*, 20(2), 198-206.

Lonsdorf, T. B., Rück, C., Bergström, J., Andersson, G., Öhman, A., Lindefors, N., & Schalling, M. (2010). The COMTval158met polymorphism is associated with symptom relief during exposure-based cognitive-behavioral treatment in panic disorder. *BMC psychiatry*, 10(1), 99.

Lohoff, F. W. (2010). Overview of the genetics of major depressive disorder. *Current psychiatry reports, 12*(6), 539-546.

Lovibond, P. F. (1983). Facilitation of instrumental behavior by a Pavlovian appetitive conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes*, 9(3), 225.

Lubow, R. E., & Moore, A. U. (1959). Latent inhibition: the effect of nonreinforced pre-exposure to the conditional stimulus. *Journal of Comparative and Physiological Psychology, 52*, 415-419.

Lubow, R. E., Weiner, I., & Schnur, P. (1981). Conditioned attention theory. *Psychology of learning and motivation, 15*, 1-49.

Lubow, R. E. (1989). *Latent inhibition and conditioned attention theory*. Cambridge University Press.

Mackintosh, N. J. (1973). Stimulus selection: Learning to ignore stimuli that predict no change in reinforcement. In R. A. Hinde & J. Stevenson-Hinde (Eds.), *Constraints on Learning: Limitations and predispositions*, Oxford: Academic Press (pp. 488).

Mackintosh, N. J. (1975). Theory of Attention - Variations in Associability of Stimuli with Reinforcement. *Psychological Review, 82*(4), 276-298.

Mackintosh, N. J. (1976). Overshadowing and stimulus intensity. *Animal learning & behavior*, 4(2), 186-192.

Maren, S., Phan, K. L., & Liberzon, I. (2013). The contextual brain: implications for fear conditioning, extinction and psychopathology. *Nature Reviews Neuroscience, 14*(6), 417-428.

Mason, O., Claridge, G. S., & Jackson, M. (1995). New scales for the assessment of schizotypy. *Personality and Individual Differences, 18*(1), 7-13.

McAndrew, A., Jones, F. W., McLaren, R. P., & McLaren, I. P. L. (2012). Dissociating expectancy of shock and changes in skin conductance: an investigation of the Perruchet effect using an electrodermal paradigm. *Journal of Experimental Psychology: Animal Behavior Processes*, 38(2), 203.

McDonald, R. J., Murphy, R. A., Guarraci, F. A., Gortler, J. R., White, N. M., & Baker, A. G. (1997). Systematic comparison of the effects of hippocampal and fornix-fimbria lesions on acquisition of three configural discriminations. *Hippocampus, 7*(4), 371-388.

McDonald, R. J., & White, N. M. (1993). A triple dissociation of memory systems: hippocampus, amygdala, and dorsal striatum. *Behavioral neuroscience, 107*(1), 3.

McLaren, I. P., Kaye, H., & Mackintosh, N. J. (1989). An associative theory of the representation of stimuli: applications to perceptual learning and latent inhibition. In R.G.M. Morris (Eds.), *Parallel Distributed Processing: Implications for psychology and neurobiology*, (pp. 102 – 130) Oxford University Press.

McLaren, I. P. L., & Mackintosh, N. J. (2000). An elemental model of associative learning: I. Latent inhibition and perceptual learning. *Animal Learning & Behavior*, 28(3), 211-246.

McGhie, A., & Chapman, J. P. (1961). Disorders of attention and perception in early schizophrenia. *British Journal of Medical Psychology*, *34*(2), 103-116.

McGregor, A. (2016). The relation between spatial and nonspatial learning. In R. A. Murphy & R. C. Honey (Eds.), *The Wiley Handbook on the Cognitive Neuroscience of Learning*. Chichester: Wiley.

Miller, R. R., & Matzel, L. D. (1988). The comparator hypothesis: A response rule for the expression of associations. *Psychology of Learning and Motivation, 22*, 51-92.

Micheyl, C., Delhommeau, K., Perrot, X., & Oxenham, A. J. (2006). Influence of musical and psychoacoustical training on pitch discrimination. *Hearing research*, 219(1), 36-47.

Mineka, S., & Oehlberg, K. (2008). The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders. *Acta psychologica, 127*(3), 567-580.

Mineka, S., & Zinbarg, R. (2006). A contemporary learning theory perspective on the etiology of anxiety disorders: it's not what you thought it was. *American psychologist*, 61(1), 10.

Molander, A.C., Mar, A., Norbury, A., Steventon, S., Moreno, M., Caprioli, D., Theobald, D.E., Belin, D., Everitt, B.J., Robbins, T.W. & Dalley, J.W. (2011) High impulsivity predicting vulnerability to cocaine addiction in rats: some relationship with novelty preference but not novelty reactivity, anxiety or stress. *Psychopharmacology* 215, 721–731.

Monroe, S. M., & Reid, M. W. (2009). Life stress and major depression. *Current Directions in Psychological Science, 18*, 68-72.

Monroe, S. M., & Simons, A. D. (1991). Diathesis-stress theories in the context of life stress research: implications for the depressive disorders. *Psychological Bulletin, 110*(3), 406.

Moran, P. M., Al-Uzri, M. M., Watson, J., & Reveley, M. A. (2003). Reduced Kamin blocking in non paranoid schizophrenia: associations with schizotypy. *Journal of Psychiatric Research, 37*(2), 155-163.

Msetfi, R.M., Kornbrot, D., Matute, H. & Murphy, R.A. (2015) The relationship between mood state and perceived control in contingency learning: Effects of individualist and collectivist values. *Frontiers in Psychology: Psychopathology.*

Msetfi, R.M., Kumar, P., Harmer C. & Murphy, R.A (2016). SSRI enhances sensitivity to background outcomes and modulates response rates: A randomized double blind study of instrumental action and depression, *Neurobiology of Learning and Memory*, 131, 76-82.

Msetfi, R. M., Murphy, R. A., Simpson, J., & Kornbrot, D. E. (2005). Depressive realism and outcome density bias in contingency judgments: The effect of the context and intertrial interval. *Journal of Experimental Psychology-General, 134*(1), 10-22.

Msetfi, R. M., Murphy, R. A., Kornbrot, D. E., & Simpson, J. (2009). Impaired context maintenance in mild to moderately depressed students. *The Quarterly Journal of Experimental Psychology*, 62(4), 653-662.

Msetfi, R.M., Murphy, R.A. and Kornbrot, D. (2012). Effect of mild depression on time discrimination. *Quarterly Journal of Experimental Psychology*. 65, 632-645.

Msetfi, R.M., Murphy, R.A. & Kornbrot, D. (2012). Dysphoric mood states are related to sensitivity to temporal changes in contingency**.** Special Issue on Causality and Time, *Frontiers in Perception Science*. 3, 368.

Msetfi, R. M., Wade, C., & Murphy, R. A. (2013). Context and time in causal learning: contingency and mood dependent effects. *PLoS ONE, 8*(5), e64063.

Msetfi, R. M., Byrom, N.C., & Murphy, R. A. (Under review), To Neglect or Integrate Contingency Information from Outside the Task Frame, that is the question! Effects of Depressed mood, *Acta Psychologica*.

Mundy, M. E., Honey, R. C., & Dwyer, D. M. (2007). Simultaneous presentation of similar stimuli produces perceptual learning in human picture processing. *Journal of Experimental Psychology: Animal Behavior Processes*, 33(2), 124.

Murphy, R.A.& Baker, A.G. (2004). A role for CS-US contingency in Pavlovian conditioning. *Journal of Experimental Psychology: Animal Behavior Processes, 30*, 229-239.

Murphy, R.A., Byrom, N. & Msetfi, R. (2017) The problem with explaining symptoms: The origin of biases in causal processing, European Journal for Person Centred Healthcare.

Murphy, R.A., Baker, A.G. & Fouquet, N. (2001). Relative validity effects with either one or two more valid cues in Pavlovian and instrumental conditioning. *Journal of Experimental Psychology: Animal Behavior Processes*, 27, 59-67.

Murphy, R.A., Baker, A.G. & Fouquet, N. (2001). Relative validity of contextual and discrete cues. *Journal of Experimental Psychology: Animal Behavior Processes*, 27, 137-152.

Murphy, R. A., Vallée-Tourangeau, F., Msetfi, R., & Baker, A. G. (2005). Signal-outcome contingency, contiguity and the depressive realism effect. In A.J., Wills (Eds.) *New directions in human associative learning*, (pp.193-219). NJ: Lawrence Erlbaum Associates.

Nasser, H. M., & Delamater, A. R. (2016). The determining conditions for pavlovian learning: psychological and neurobiological considerations. In R. A. Murphy & R. C. Honey (Eds.), *The Wiley Handbook on the Cognitive Neuroscience of Learning* (pp. 7 - 47). Chichester: Wiley.

Oberling, P., Gosselin, O., & Miller, R. R. (1999). Latent inhibition in animals as a model of acute schizophrenia: A reanalysis. In M. Haug & R.E. Whalen (Eds.) *Animal models of human emotion and cognition* (pp. 87 – 102). Washington, DC, US: American Psychological Association.

Paolone, G., Angelakos, C. C., Meyer, P. J., Robinson, T. E., & Sarter, M. (2013). Cholinergic control over attention in rats prone to attribute incentive salience to reward cues. *Journal of Neuroscience*, 33(19), 8321-8335.

Patitucci, E., Nelson, A.J.D., Dwyer, D.M. & Honey, R.C. (2016). The Origins of Individual Differences in How Learning Is Expressed in Rats: A General-Process Perspective. *Journal of Experimental Psychology: Animal Learning & Cognition*, 42, 313-324.

Patterson, T. (1987). Studies toward the subcortical pathogenesis of schizophrenia. *Schizophrenia Bulletin, 13*(4), 555.

Pavlov, I. P. (1927). *Conditioned Reflexes*. Oxford: Oxford University Press.

Pearce, J. M., & Hall, G. (1980). A Model for Pavlovian Learning - Variations in the Effectiveness of Conditioned but Not of Unconditioned Stimuli. *Psychological Review, 87*(6), 532-552.

Pearce, J.M. (1987). A model for stimulus generalization in Pavlovian conditioning. *Psychological Review*, 94, 61-7.

Pearce, J. M., & Mackintosh, N. J. (2010). Two theories of attention: A review and a possible integration. In C.J. Mitchell & M.E. Le Pelley (Eds.) *Attention and associative learning: From brain to behaviour*, (pp. 11-39), Oxford University Press.

Perruchet, P. (1985). A pitfall for the expectancy theory of human eyelid conditioning. Pavlovian *Journal of Biological Sciences*, 20, 163–170.

Peterson, G. B., Ackilt, J. E., Frommer, G. P., & Hearst, E. S. (1972). Conditioned approach and contact behavior toward signals for food or brain-stimulation reinforcement. *Science*, 177(4053), 1009-1011.

Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderheiser, J. (2013). *Behavioral genetics.* Palgrave Macmillan.

Rescorla, R. A. (1988). Pavlovian conditioning: It's not what you think it is. *American Psychologist,* 43(3), 151.

Rescorla, R. A. (2001). Unequal associative changes when excitors and neutral stimuli are conditioned in compound. *Quarterly Journal of Experimental Psychology Section B-Comparative and Physiological Psychology, 54*(1), 53-68.

Rescorla, R. A., & Wagner, A. R. (Eds.). (1972). *A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement*: Appleton-Century-Crofts.

Rick, I. P., Mehlis, M., & Bakker, T. C. M. (2011). Male red ornamentation is associated with female red sensitivity in sticklebacks. *PloS one, 6*(9), e25554.

Robinson, T. E., Yager, L. M., Cogan, E. S., & Saunders, B. T. (2014). On the motivational properties of reward cues: individual differences. *Neuropharmacology*, 76, 450-459.

Rowe, M. P., Baube, C. L., Loew, E. R., & Phillips, J. B. (2004). Optimal mechanisms for finding and selecting mates: how three spine stickleback (Gasterosteus aculeatus) should encode male throat colors. *Journal of Comparative Physiology A, 190*(3), 241-256.

Rutter, M. (2010). Gene–environment interplay. *Depression and anxiety, 27*(1), 1-4.

Saavedra, M. A. (1975). Pavlovian compound conditioning in the rabbit. *Learning and Motivation, 6*(3), 314-326.

Saunders, B. T., & Robinson, T. E. (2012). The role of dopamine in the accumbens core in the expression of Pavlovian-conditioned responses. *European Journal of Neuroscience*, 36(4), 2521-2532.

Schmidt-Hansen, M., Killcross, A. S., & Honey, R. C. (2009). Latent inhibition, learned irrelevance, and schizotypy: assessing their relationship. *Cognitive Neuropsychiatry, 14*(1), 11-29.

Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science*, 275(5306), 1593-1599.

Schultz, W. (2016). Dopamine reward prediction-error signaling: a two-component response. *Nature Reviews Neuroscience*. 17, 193-195.

Seidel, R. J. (1959). A review of sensory preconditioning. *Psychological Bulletin, 56*(1), 58.

Seligman, M. E. (1972). Learned Helplessness. *Annual Review of Medicine, 23*(5), 407-&.

Seligman, M. E., & Binik, Y. M. (1977). The safety signal hypothesis. In H. D. H. M. B. Hurwitz (Ed.), *Pavlovian-operant interactions* (pp. 165-187). Hillsdale, NJ: Erlbaum.

Sellen, J. L., Oaksford, M., & Gray, N. S. (2005). Schizotypy and conditional reasoning. *Schizophrenia Bulletin*, 31(1), 105-116.

Sen, S., Burmeister, M., & Ghosh, D. (2004). Meta-analysis of the association between a serotonin transporter promoter polymorphism (5-HTTLPR) and anxiety-related personality traits. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 127(1), 85-89.

Shanks, D. R. (1987). Acquisition functions in contingency judgment. *Learning and Motivation*, 18(2), 147-166.

Shanks, D. R., Lamberts, K., & Goldstone, R. L. (2005). Implicit learning. *Handbook of cognition*, 202-220.

Silva, F. J., Silva, K., & Pear, J. J. (1992). Sign-versus goal-tracking: effects of conditioned-stimulus-to-unconditioned-stimulus distance. *Journal of the experimental analysis of behavior*, 57(1), 17-31.

Silventoinen, K. (2003). Determinants of variation in adult body height. *Journal of biosocial science, 35*(02), 263-285.

Singer, B. F., Guptaroy, B., Austin, C. J., Wohl, I., Lovic, V., Seiler, J. L., Vaughn, R.A., Gnegy, M.E., Robinson, T.E., & Aragona, B. J. (2016). Individual variation in

incentive salience attribution and accumbens dopamine transporter expression and function. *European Journal of Neuroscience*. 34 (5), 662 – 670.

Skinner, B. F. (1938). The behavior of organisms: an experimental analysis. Appleton-Century. *New York.*

Skinner, B. F. (1945). The operational analysis of psychological terms. *Psychological Review, 52*(5), 270.

Smolewska, K. A., McCabe, S. B., & Woody, E. Z. (2006). A psychometric evaluation of the Highly Sensitive Person Scale: The components of sensory-processing sensitivity and their relation to the BIS/BAS and "Big Five". *Personality and Individual Differences, 40*(6), 1269-1279.

Smith, C., Barber, I., Wootton, R. J., & Chittka, L. (2004). A receiver bias in the origin of three-spined stickleback mate choice. *Proceedings of the Royal Society B: Biological Sciences*, *271*(1542), 949.

Spence, R., & Smith, C. (2008). Innate and learned colour preference in the zebrafish, Daniorerio. *Ethology*, *114*(6), 582-588.

Spiers, H., Love, B. LePelley, M, *Gibbs***,** & Murphy, R.A. (2017). Anterior Temporal Lobe Tracks the Emergence of Social Group Stereotypes. *Journal of Cognitive Neuroscience, 29, 530-544.*

Soto, F. A., Gershman, S. J., & Niv, Y. (2014). Explaining compound generalization in associative and causal learning through rational principles of dimensional generalization. *Psychological review*, 121(3), 526.

Suls, J., & Rothman, A. (2004). Evolution of the biopsychosocial model: prospects and challenges for health psychology. *Health Psychology, 23*(2), 119.

Sutton, R. S., & Barto, A. G. (1998). *Reinforcement learning: An introduction* (Vol. 1, No. 1). Cambridge: MIT press.

Thoma, P., Zoppelt, D., Wiebel, B., & Daum, I. (2007). Context processing and negative symptoms in schizophrenia. *Journal of clinical and experimental neuropsychology, 29*(4), 428-435.

Thorndike, E. L. (1898). Animal intelligence: An experimental study of the associative processes in animals. *Psychological Monographs: General and Applied, 2*(4), i-109.

Toates, F. M. (1986). *Motivational systems* (No. 4). CUP Archive.

Vallée-Tourangeau, F., Hollingsworth, L. & Murphy, R.A. (1998). 'Attentional bias' in correlation judgements? Smedslund (1963) revisited. *Scandinavian Journal of Psychology, 39,* 221-233

Vallée-Tourangeau, F., Murphy, R.A. & Baker, A.G. (1998). Causal induction in the presence of a perfect inhibitory cue: Contrasting predictions from the Rescorla-Wagner model and the Pearce model. *Quarterly Journal of Experimental Psychology, 51B,* 173-191.

Vallee-Tourangeau, F., Murphy, R. A., Drew, S., & Baker, A. G. (1998). Judging the importance of constant and variable candidate causes: A test of the power PC theory. *Quarterly Journal of Experimental Psychology Section a-Human Experimental Psychology, 51*(1), 65-84.

Vallée-Tourangeau, F., *Payton, T.,* & Murphy, R.A. (2008). The impact of presentation format on causal inferences. *The European Journal of Cognitive Psychology, 20*, 177-194.

Visscher, P. M., Hill, W. G., & Wray, N. R. (2008). Heritability in the genomics era—concepts and misconceptions. *Nature Reviews Genetics, 9*(4), 255-266.

Waelti, P., Dickinson, A., & Schultz, W. (2001). Dopamine responses comply with basic assumptions of formal learning theory. *Nature*, 412(6842), 43-48.

Wagner, A. R. (1981). SOP: A model of automatic memory processing in animal behavior. In N. E. Spear & R. R. Miller (Eds.), *Information processing in animals: Memory mechanisms*. Hillsdale, NJ: Erlbaum.

Wagner, A. R., Logan, F. A., Haberlandt, K., & Price, T. (1968). Stimulus selection in animal discrimination learning. *Journal of Experimental Psychology, 76*(2), 171-180.

Wasserman, E. A., Elek, S. M., Chatlosh, D. L., & Baker, A. G. (1993). Rating causal relations: Role of probability in judgments of response-outcome contingency. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 19*(1), 174-188.

Weidemann, G., Tangen, J. M., Lovibond, P. F., & Mitchell, C. J. (2009). Is Perruchet's dissociation between eyeblink conditioned responding and outcome expectancy evidence for two learning systems? *Journal of Experimental Psychology: Animal Behaviour Processes*, 35, 169 –172.

Wiers, R.W., Boelema, S.R., Nikolaou, K., Gladwin, T.E., 2015. On the development of implicit and control processes in relation to substance use in adolescence. *Curr. Addict. Rep*. 2, 141–155.

Williams, B. A., & Dunn, R. (1991). Preference for conditioned reinforcement. *Journal of the Experimental Analysis of Behavior*, 55(1), 37-46.

Wilson, R. S. (1983). The Louisville twin study: Developmental synchronies in behavior. *Child development*, 298-316.

Wolpe, J., & Rowan, V. C. (1988). Panic disorder: A product of classical conditioning. *Behaviour Research and Therapy, 26*(6), 441-450.

Wray, N. R., Pergadia, M. L., Blackwood, D. H. R., Penninx, B. W. J. H., Gordon, S. D., Nyholt, D. R., Maclean, A. W. (2012). Genome-wide association study of major depressive disorder: new results, meta-analysis, and lessons learned. *Molecular psychiatry, 17*(1), 36-48.

Wyvell, C. L., & Berridge, K. C. (2000). Intra-accumbens amphetamine increases the conditioned incentive salience of sucrose reward: enhancement of reward "wanting" without enhanced "liking" or response reinforcement. *Journal of Neuroscience*, 20(21), 8122-8130.

Yarritu, I., Matute, H., & Luque, D. (2015). The dark side of cognitive illusions: When an illusory belief interferes with the acquisition of evidence-based knowledge. *British Journal of Psychology, 106*(4), 597-608.

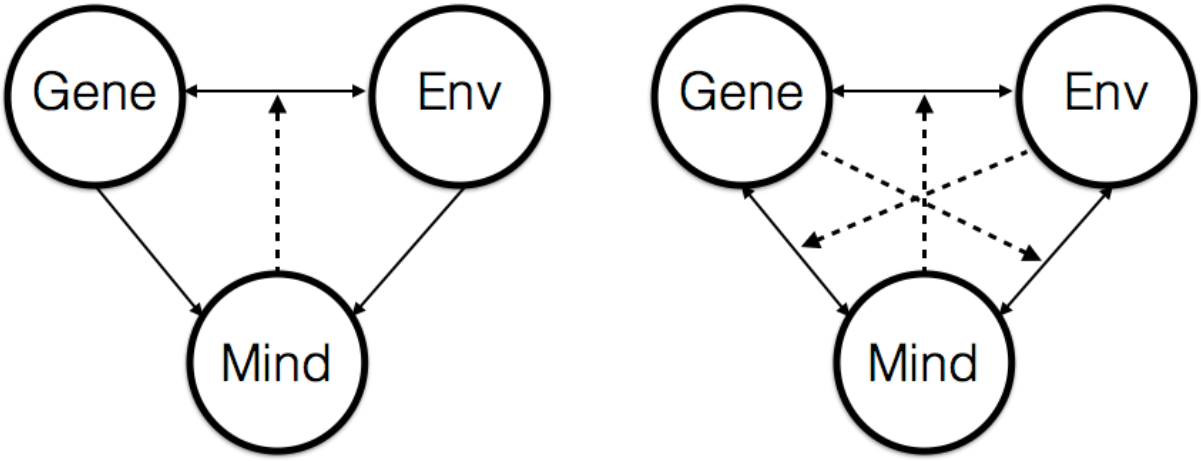
Yarritu, I., Matute, H., & Vadillo, M. A. (2014). Illusion of Control. *Experimental psychology*.

Zalstein-Orda, N., & Lubow, R. E. (1995). Context control of negative transfer induced by preexposure to irrelevant stimuli: Latent inhibition in humans. *Learning and Motivation*, 26(1), 11-28.

Zener, K. (1937). The significance of behavior accompanying conditioned salivary secretion for theories of the conditioned response. *The American Journal of Psychology*, 50(1/4), 384-403.

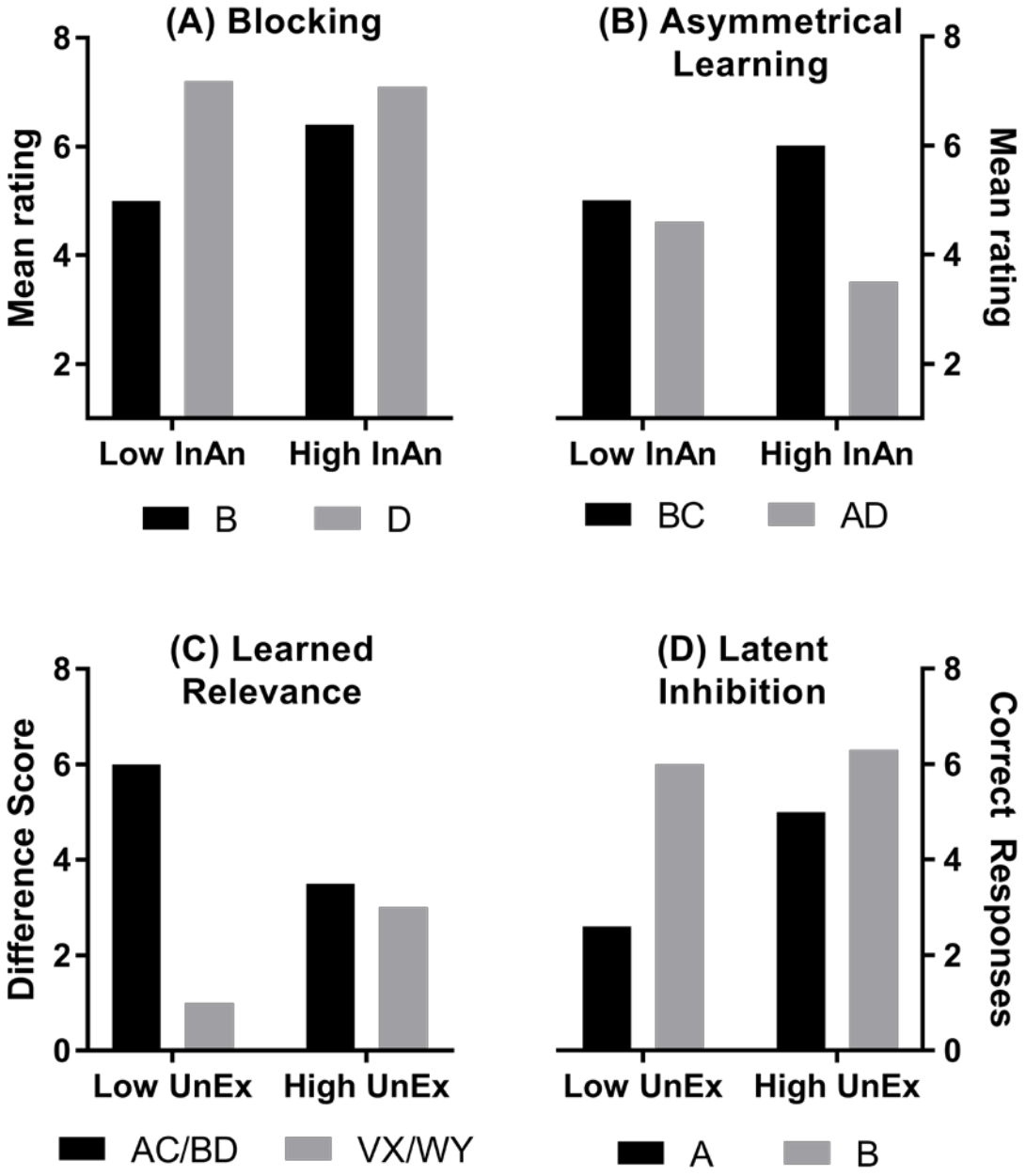
Zill, P., Baghai, T. C., Zwanzger, P., Schüle, C., Eser, D., Rupprecht, R., Moller, H.J., Bondy, B., & Ackenheil, M. S. N. P. (2004). SNP and haplotype analysis of a novel tryptophan hydroxylase isoform (TPH2) gene provide evidence for association with major depression. *Molecular psychiatry, 9*(11), 1030-1036.

Figure 1. Mediation relationships between Genes, Environment, and the Associative Mind.



Traditionally the associative ‘Mind’, a phenotype, is seen to be affected by genes and environment and has a moderating role on the relation between gene and environment but only a weak direct effect. We are proposing that mind can affect gene expression, and environment as well as each one being able to mediate the relation between each separate dyad.

Figure 2: Individual differences in CS processing effects.



Panel A: During test trials participants give B, the blocked cue, a lower rating than D. This effect is abolished in individuals with high scores on the Introverted Anhedonia subscale of the OLIFE (e.g., Haselgrove & Evans, 2010).

Panel B: Following selective learning, individuals are expected to give a comparable rating of the likelihood of a US following either AD or BC (Rescorla, 2001). Individuals with high

scores on the Introverted Anhedonia subscale of the OLIFE do not show evidence of selective learning in this test (Haselgrove & Evans, 2010).

Panel C: Following the design shown in Table 1, Participants rate AC as strongly predictive of O3 and BD as strongly predictive of O4, giving a high discrimination score. VX and WY are rated as weak predictors of O3 and O4 respectively, giving a low discrimination score (see also, Le Pelley & McLaren, 2003). This learned relevance effect is not apparent for individuals with high scores on the Unusual Experiences subscale of the OLIFE questionnaire (Le Pelley, Schmidt-Hansen, Harris, Lunter, & Morris, 2010).

Panel D: Participants are slower to learn with a pre-exposed stimulus than a non-pre-exposed stimulus. This retardation of learning is disrupted in individuals with high scores on the Unusual Experiences subscale of the OLIFE (e.g., Schmidt-Hansen et al., 2009).

Figure 3. Generic contingency matrix showing the relationship between the occurrence of an event and the occurrence of an outcome (e.g., behavior, stimulus).

Occurrence of

The notation a, b, c, d refer to the frequencies of each event-outcome conjunction. The normative model for the one-way relation between them is ΔP. ΔP = a/ (a + b) - c/(c + d) and generates a number between -1 and +1 denoting the strength and direction of the relationship.

Table 1

	Stage 1	Stage 2	Test
(A) Blocking	A +	AB+ CD+	B D
(B) Asymmetrical learning	A+ B- C+ D-	AB-	AD BC
(C) Learned Relevance	AV – O1 AW – O1 BV – O2 BW – O2 CX – O2 CY – O2 DX – O1 DY – O1	AX – O3 BY – O4 CV – O3 DW – O4	AC BD VX WY
(D) Latent Inhibition	A	A+ B+	

Letters refer to different cues. O1 to 4 refer to different outcomes. + refers to the presence of an outcome, - refers to the absence of an outcome. Tests in humans have used the allergist task, or similar cover story, where participants are asked to act as an allergist and identify which foods (represented here by letters) cause an allergic reaction in a fictitious patient e.g., (Haselgrove & Evans, 2010; Le Pelley, Oakeshott, & McLaren, 2005).