

Reinforcement Learning in Children and Adolescents
with Fetal Alcohol Spectrum Disorder (FASD)

by

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B.A., Tufts University, 1997
M.Sc., University of Victoria, 2003

A Dissertation Submitted in Partial Fulfillment
of the Requirements of the Degree of

DOCTOR OF PHILOSOPHY

in the Department of Psychology

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Abstract

Objective: This study examined various dimensions of reinforcement learning in children with Fetal Alcohol Spectrum Disorder (FASD). Specific investigations included (1) speed of learning from reinforcement; (2) impact of concreteness of the reinforcer; (3) comparison of response to two types of shifts in reinforcement; and (4) relationship of reinforcement learning to parent reported social and behavioral functioning.

Participants & Methods: Participants included 19 children with FASD without an intellectual disability, ages 11 to 17, and 19 age- and sex-matched Control participants (11 male, 8 female per group). Each participant completed two novel visual reinforcement learning discrimination tasks (counterbalanced), each administered twice. The first task involved categorical learning followed by either a reversal or a nonreversal shift. The second task involved a computerized probabilistic paradigm (70% contingent feedback) administered using either tokens or points, redeemable for a prize. Parents completed a history questionnaire, the Children's Learning Questionnaire (McInerney, 2007), and the Child Behavior Checklist (Achenbach & Rescorla, 2001).

Results: The Control group demonstrated significantly stronger probabilistic reinforcement learning, although the groups showed similar rates of between-condition

improvement (learning savings). Furthermore, the concreteness of the reinforcer (tokens vs. points) made no significant difference in learning characteristics for either group. In contrast to probabilistic reinforcement learning, there were no significant group differences in categorical discrimination or shift learning. The FASD group demonstrated the age-appropriate pattern of reversals faster than nonreversals, while there was no difference between the two types of shifts in the Control group. A priori identified parent reports were not significantly correlated with task performance when each group was examined separately.

Conclusions: There was no support for the hypothesis that reinforcement learning occurs in a functionally different manner in children with FASD. Rather, reinforcement learning may take longer, paralleling the generally slower speed of all learning in these children, and be more dependent on recent information. This suggests that children with FASD without intellectual disability are able to learn from reinforcement if given sufficient consistent repetition. However, failure of reinforcement learning may occur for a variety of reasons not addressed in this study, including difficulty with transfer of learning or impulsivity.

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Acknowledgements

This research is dedicated to the many families, community organizers, and organizations whose tireless support and dedication made it all possible. I am also unendingly grateful to my friends and family, especially my husband Will, for their unflagging moral support. Thanks as well to my incredibly supportive and helpful academic advisor, Dr. Kimberly Kerns, as well as the rest of my supervisory committee – Dr. Ulrich Mueller, Dr. Clay Holroyd, and Dr. Gina Harrison – for all their advice along the way.

Introduction

Clinical wisdom suggests that children who are affected by prenatal alcohol exposure, even those with intelligence in the average range, do not appropriately alter their behavior in response to consequences. These children seem to make the same mistakes over and over despite being punished for “bad” behavior or rewarded for “good” behavior. This prevailing notion has had a profound impact on advice given to caregivers of individuals with FASD, and yet has received surprisingly little research attention. With this in mind, the current project was designed to investigate reinforcement learning in children and adolescents with Fetal Alcohol Spectrum Disorder (FASD).

This paper will begin with an historical and epidemiological overview of FASD, followed by a review of the neurophysiological and neuropsychological impacts of prenatal alcohol exposure. The next section will provide a brief overview of behavioral conditioning, examine the neuroanatomical and functional substrates of reinforcement learning, and review the human and animal research on prenatal alcohol exposure and reinforcement learning. This will be followed by the rationale, methodology and hypotheses of the current project, prior to presentation of the results and a discussion of the findings in the final sections.

Fetal Alcohol Spectrum Disorder

Diagnostic Criteria

Despite a number of historical references to the detrimental effects of alcohol consumption during pregnancy (Abel, 1999), identification of the *clinical syndrome* associated with fetal alcohol exposure was a relatively recent occurrence (Lemoine, Harousseau, Borteyru, & Menuet, 1968). In a series of now historic papers, Jones and colleagues from the University of Washington coined the term Fetal Alcohol Syndrome (FAS) to describe the specific pattern of malformations associated with prenatal alcohol exposure (Jones & Smith, 1973; Jones, Smith, Streissguth, & Myriantopoulos, 1974; Jones, Smith, Ulleland, & Streissguth, 1973). Early on, researchers realized that there was considerable variation in the physical, cognitive, and behavioral effects of prenatal alcohol exposure. This led to the re-conceptualization of FAS as the most severe end of a spectrum of effects, which came to be referred to under the umbrella term *Fetal Alcohol Spectrum Disorder* (Stratton, Howe, & Battaglia, 1996).

There are currently a number of diagnostic classification systems for FASD, including the recently revised Institute of Medicine (IOM) guidelines (Hoyme et al., 2005), the University of Washington 4-Digit Diagnostic Code (Astley, 2004), the CDC guidelines (Bertrand et al., 2004), and the Canadian guidelines (Chudley et al., 2005). The criteria for a diagnosis of full FAS are similar across systems. First, the individual must display facial dysmorphology in at least two of three areas: (1) short palpebral fissures (eye slits); (2) smooth philtrum (the ridges between the nose and lips); and (3) thin upper lip. Second, there must be growth deficiency, typically defined as less than 10 per cent of average height, weight, or height-weight ratio either at or after birth. Third, there must be evidence of central nervous system (CNS) involvement which may be a known structural abnormality or CNS dysfunction in three or more domains. Finally, FAS must be diagnosed in the context of a confirmed history of prenatal alcohol exposure, although in some cases a diagnosis of FAS without confirmed exposure may be made when all other evidence is present.

Partial FAS (pFAS) requires the same (or slightly less severe depending on the criteria used) facial dysmorphology as FAS with some combination of growth delay and CNS dysfunction, in the context of confirmed maternal alcohol exposure. Alcohol Related Neurodevelopmental Disorder (ARND) is defined as CNS dysfunction with maternal alcohol exposure. Alcohol Related Birth Defects (ARBD) is a term used by the IOM which requires one or more major - or two or more minor - congenital structural deficits with facial dysmorphic features and maternal alcohol exposure.

The University of Washington 4-Digit Diagnostic Code ranks each area on a 4-point Likert scale, with 4 representing the fullest presentation of the feature in FAS, and 1 representing the absence of the feature. Specific guidelines which take into account the scores on each of the four digits allow an individual to be placed within a specific diagnostic category. In addition, this system introduced a few new terms which are used in combination. *Sentinel physical findings* refers to moderate to severe facial dysmorphology or growth deficiencies, *neurobehavioral disorder* refers to possible CNS dysfunction (rank of 2), and *static encephalopathy* refers to probable to definite CNS dysfunction (rank of 3 or 4; Astley, 2004).

Given the wide variety of terminology, and the inconsistency in their application across research studies, this paper will use the term FASD unless a specific diagnosis or category under the spectrum is intended.

Epidemiology

The incidence of FAS in the United States is estimated to range between 0.5 and 2.0 per 1000 births, with a higher incidence of FASD, approximately 1% of live births (May & Gossage, 2001; Sampson et al., 1997). In a review of the literature, Lupton and colleagues estimated the average lifetime cost of an individual with FAS to be approximately \$1.4 million, with a total annual estimated cost to the United States of \$4 billion. Adjusted for current population and inflation, the costs were even higher (Lupton, Burd, & Harwood, 2004).

Neurobiological Sequelae

Alcohol ingested by a pregnant woman is able to cross the placental barrier, and has both direct and indirect teratogenic effects on the developing fetus. Damage can be caused by the alcohol itself, or result from the metabolites of alcohol. The effects are varied, and can include cell death, interference with cellular functions, reduced cell division rate, problems with neuronal migration, and altered gene expression (Goodlett & Horn, 2001).

Prenatal alcohol exposure has also been shown to alter many neurotransmitter systems. The mesolimbic dopamine system is particularly relevant to the current study due to its involvement with the reward system (see the “reinforcement learning” section later in this paper). Prenatal alcohol exposure in rats is associated with decreased concentrations of dopamine in areas which are targets of mesolimbic and other dopamine pathway projections including the cortex, striatum and hypothalamus (Cooper & Rudeen, 1988; Rathbun & Druse, 1985). In the ventral tegmental area (the source of dopamine cell bodies in the mesolimbic and mesocortical dopamine systems), decreased dopamine was found as early as 5 days after birth in animals prenatally exposed to alcohol (Druse, Tajuddin, Kuo, & Connerty, 1990).

Dopamine activity can be categorized as spontaneous (referred to as tonic activity) or evoked by action potentials (referred to as phasic activity). Prenatal alcohol exposure has been demonstrated to impact both tonic (Choong & Shen, 2004a, 2004b;

Shen, Hannigan, & Kapatos, 1999; Xu & Shen, 2001) as well as phasic activity (Choong & Shen, 2004b; Wang, Haj-Dahmane, & Shen, 2006) in rats. In addition, recent research has suggested that the timing of alcohol exposure may alter its impact on the dopamine system. Both early (equivalent to human 1st trimester) and continuous alcohol exposure was associated with decreased striatal dopamine D₂ receptor binding to dopamine synthesis ratio (which leads to a reduction or blunting of the dopamine system), while alcohol exposure limited to mid to late gestation, during the migration and synaptogenesis period, showed the opposite pattern (heightened sensitivity of the dopamine system). Both deviations are noted to be outside what is considered the *optimal range* of dopamine function (Schneider et al., 2005). Dopamine may also be an avenue for intervention. Methylphenidate (Choong & Shen, 2004a) and amphetamine (Xu & Shen, 2001) have both been found to normalize dopamine activity in ventral tegmental neurons, as well as increase D₂ binding sites (S. Randall & Hannigan, 1999) in alcohol exposed rats.

There is also much evidence for an impact of prenatal alcohol exposure on the serotonergic system from both animal (reviewed in Manteuffel, 1996; Sari & Zhou, 2004; Zafar, Shelat, Redei, & Tejani-Butt, 2000; Zhou, Sari, & Powrozek, 2005) and human studies (Riikonen et al., 2005). Other affected neurotransmitters may include GABA (Cuzon, Yeh, Yanagawa, Obata, & Yeh, 2008; J. J. Mitchell, Paiva, & Heaton, 2000; Moore, Quintero, Ruygrok, Walker, & Heaton, 1998), norepinephrine and acetylcholine (reviewed in Manteuffel, 1996).

In addition to changes in the neurotransmitter systems, there is growing evidence that prenatal alcohol exposure causes structural changes in the brain. Recent advances in imaging techniques have allowed a more detailed examination of the brains of alcohol exposed humans, previously available only at autopsy (Spadoni, McGee, Fryer, & Riley, 2007). Prenatal alcohol has been associated with a reduction in overall brain volume (Riikonen et al., 2005; Wozniak et al., 2006), particularly when used in combination with other substances such as cocaine and tobacco (Rivkin et al., 2008). Some of the brain regions which may be specifically impacted include the inferior parietal lobes (Sowell, Mattson et al., 2001; Sowell, Thompson, & Mattson, 2002; Sowell, Thompson et al., 2001), the hippocampus (Willoughby, Sheard, Nash, & Rovet, 2008), the corpus

callosum (Bookstein et al., 2007; Ma et al., 2005; Wozniak et al., 2006), and the cerebellum (Archibald et al., 2001; Sowell et al., 1996).

Another affected area, of particular interest to the current study because of its relationship to the reinforcement system of the brain, is the basal ganglia. Prenatal alcohol exposure has been associated with reduction in the size of the basal ganglia, and in particular, the caudate nucleus (Archibald et al., 2001; Cortese et al., 2006; Mattson et al., 1996). Furthermore, caudate volume was correlated with amount of alcohol consumed during pregnancy (Cortese et al., 2006). In two studies, caudate size was not significantly different between the groups when overall brain size was taken into account (Cortese et al., 2006; Riikonen et al., 2005), while in another study caudate size continued to be significant even after controlling for overall brain size (Mattson et al., 1996).

In addition to the teratogenicity of alcohol, maternal alcohol consumption is frequently associated with other mechanisms which can also harm the developing fetus. Maternal alcohol use may be associated with maternal malnutrition, cigarette or other drug use, pre- or peri-natal stress, and lack of prenatal care, all of which can have an independent or interactive effect on the developing brain. Furthermore, children who are prenatally exposed to alcohol are more likely than their peers to have a number of postnatal risk factors, including multiple home placements, increased likelihood of abuse, etc., all of which can impact functioning. However, it is important to note that exposure to postnatal trauma does not fully account for the cognitive deficits seen in FASD (Henry, Sloane, & Black-Pond, 2007).

Neuropsychological and Psychological Sequelae

FASD is associated with a variety of cognitive, behavioral, social, and emotional problems. Streissguth (1997) provided a framework for understanding the disabilities associated with FASD as either *primary* or *secondary*. Primary disabilities are due to CNS dysfunction the child is born with. In contrast, secondary disabilities are negative outcomes of the interaction between an individual with brain damage and his or her environment. Environmental variables have been found to be extremely important in preventing secondary disabilities in individuals with fetal alcohol exposure. One important protective factor is diagnosis of the full syndrome (FAS) over Fetal Alcohol

Effects (FAE). Early diagnosis (before age 12), and being reared in a nurturing, stable environment are also protective factors (Streissguth et al., 2004).

Much research over the last three decades has been dedicated to identifying the pattern of cognitive and behavioral deficits specific to FASD (the primary disabilities). Such a profile would be useful in diagnosis and intervention with affected individuals, which may in turn help to prevent secondary disabilities. Although progress has been made, the vast inter-individual variability in FASD means the goal of specifying a unique profile has remained elusive. Nevertheless, the following sections will summarize the current knowledge of neuropsychological and psychological functioning (which necessarily will include both primary and secondary disabilities) in children with FASD.

Intellectual ability. Compromised intellectual function is a common finding in FASD research. Four medium to large prospective studies examined IQ in young school-aged children prenatally exposed to alcohol. From these studies, it is evident that the impact of fetal alcohol exposure on intelligence occurs across socio-economic classes and ethnicities (Coles, Brown, Smith, & Platzman, 1991; Howell, Lynch, Platzman, Smith, & Coles, 2006; Russell, Czarnecki, Cowan, McPherson, & Mudar, 1991; Streissguth, Barr, & Sampson, 1990). There is strong support for a dose-response relationship between prenatal alcohol exposure and offspring intellectual functioning, with some evidence that alcohol exposure preferentially affects aspects of attention and working memory. Furthermore, the impact of prenatal alcohol exposure may be particularly strong for children born to mothers over age 30 (J. L. Jacobson, Jacobson, & Sokol, 1996; J. L. Jacobson, Jacobson, Sokol, & Ager, 1998; S. W. Jacobson, Jacobson, Sokol, Chiodo, & Corobana, 2004; Streissguth, Barr, & Sampson, 1990).

Activity, attention, and processing speed. Hyperactivity and inattention are closely associated with FASD. Although problems with attention are a common finding in children with prenatal alcohol exposure, there are some contradictory findings, likely due to the nature of the attention tasks and differences in the populations tested (reviewed in Kodituwakku, 2007; Linnet et al., 2003; Mattson, Riley, Gramling, Delis, & Jones, 1998).

Numerous studies have shown that FASD is associated with slow processing speed in children (Barr, Streissguth, Darby, & Sampson, 1990; Burden, Jacobson, &

Jacobson, 2005; S. W. Jacobson, 1998; S. W. Jacobson, Jacobson, & Sokol, 1994; Mattson, Calarco, & Lang, 2006; Simmons, Wass, Thomas, & Riley, 2002; Streissguth, 1984). Furthermore, slow processing speed may be particularly evident on complex cognitive tasks (Burden, Jacobson, & Jacobson, 2005).

Many (Abel, 1982; Bond, 1981; C. L. Randall, Becker, & Middaugh, 1986; Shaywitz, Griffieth, & Warshaw, 1979; Ulug & Riley, 1983), though not all (Dursun, Jakubowska-Dogru, & Uzbay, 2006; S. Randall & Hannigan, 1999), animal models of FAS have shown that prenatal alcohol exposure is associated with increased activity levels. Hyperactivity is also a common finding in children with FASD. In fact, children with FASD are often diagnosed with comorbid Attention Deficit Hyperactivity Disorder (ADHD; Bhatara, Loudenberg, & Ellis, 2006; Coles, 2001; Fryer, McGee, Matt, Riley, & Mattson, 2007), although some have suggested ADHD of the inattentive type is more common in FASD (Kodituwakku et al., 2006).

Executive functioning. The term “executive functioning” refers to a variety of higher-order mental processes necessary for complex goal-directed behavior and adaptation to environmental changes and demands (Loring, 1999). These processes include planning, self-initiating, shifting from one task to another, working memory, fluency, inhibiting a hasty response and regulating behavior.

Children with prenatal alcohol exposure have been shown to have deficits in various executive abilities including planning (Kodituwakku, Handmaker, Cutler, & Weathersby, 1995; Mattson, Goodman, Caine, Delis, & Riley, 1999), cognitive set-shifting (Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998; Coles et al., 1997; Kodituwakku, May, Clericuzio, & Weers, 2001; McGee, Schonfeld, Roebuck-Spencer, Riley, & Mattson, 2008), fluency (Kodituwakku, Handmaker, Cutler, & Weathersby, 1995; Mattson, Goodman, Caine, Delis, & Riley, 1999; Schonfeld, Mattson, Lang, Delis, & Riley, 2001), and inhibition (Mattson, Goodman, Caine, Delis, & Riley, 1999; Noland et al., 2003). In the area of working memory, deficits have frequently been found on the working memory measures of the Wechsler intelligence tests (Digit Span and Arithmetic; Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998; S. W. Jacobson, Jacobson, Sokol, Chiodo, & Corobana, 2004; Streissguth, Barr, &

Sampson, 1990). In addition, Kodituwakku and colleagues (1995) found that children with FASD performed poorly on complex, but not simple measures of working memory.

Interestingly, Mattson and colleagues found that the performance of children with FASD on a shifting task was not impaired compared to controls (Mattson, Calarco, & Lang, 2006). In this task, participants were presented a mix of auditory (high and low tones) and visual (yellow and blue squares) stimuli in quasi-random order. Participants were asked to alternate between responding to the target visual stimuli (e.g., respond to yellow), and responding to the target auditory stimuli (e.g., respond to low tones) in the absence of corrective feedback. In other words, self-determined correct detection of a target in one modality was the cue to disengage and switch to responding to the target in the other modality. To understand why there was no difference in this study compared to previous studies showing impaired cognitive set shifting, the authors suggest that it is due to either the intermodality nature of the task, or the fact that the cognitive set shifting task typically utilized (Wisconsin Card Sorting Test; WCST) requires shifting in the absence of a cue. However, another difference is in the type of shift. The WCST requires a shift of attention from one aspect of a stimulus to another, while Mattson's task requires continuous reversal of attention between trials. The importance of this distinction and its relevance to the current study will be discussed more in the Reinforcement Learning section.

Many studies which examined executive functioning in children with FASD failed to consider the impact of intellectual ability on executive functioning. However, two studies in adults with FASD suggest that difficulties with executive functioning cannot be completely accounted for by intellectual impairments, as executive abilities were lower than would be expected based on IQ (Connor, Sampson, Bookstein, Barr, & Streissguth, 2000; Kerns, Don, Mateer, & Streissguth, 1997). There is also some evidence that executive deficits persist in children after controlling for IQ (Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998; Schonfeld, Mattson, Lang, Delis, & Riley, 2001).

In addition to the traditional executive functions described here, Zelazo and Müller (2002) described a second type of executive function, which has been called emotion-related, affective, or "hot" executive functioning. Hot executive functioning

requires regulation of motivation, such as the ability to modify behavior in response to changing reinforcement conditions. Hot executive functions are thought to be controlled by the ventromedial prefrontal cortex, which includes the orbitofrontal cortex (OFC). In contrast, “cool” (traditional) executive functioning occurs in decontextualized and abstract contexts. Cool executive functions are thought to be controlled by the dorsolateral prefrontal cortex (Zelazo et al., 2005). One study (Kodituwakku, May, Clericuzio, & Weers, 2001) showed that children with FASD were impaired on a hot executive functioning task (reversal learning) compared to matched controls). This study and a number of related animal studies will be discussed further in the Reinforcement Learning section.

Neuropsychological assessment of executive functions typically takes place in a structured laboratory setting which tends to minimize demands on executive systems. In contrast to such laboratory tests, the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworth, 2000) assesses parent and teacher perceptions of children’s executive functioning in their everyday environment. Two studies by Rasmussen and colleagues have examined the BRIEF in children and adolescents with FASD (Rasmussen, Horne, & Witol, 2006; Rasmussen, McAuley, & Andrew, 2007). Both parent and teacher rated reports showed that the scores of children and adolescents with FASD were elevated (impaired) across the BRIEF subscales. Within parent ratings, there was some inter-scale variation, with the Working Memory subscale emerging as an area of particular difficulty. One study found the Plan/Organize subscale was also problematic (2006), while the other found that Initiate and Inhibit subscales were specific areas of difficulty (2007). Gender differences were also apparent. One study found that parents rated girls with FASD as having significantly more overall executive function impairment than boys (2006). The other study found that this gender difference was limited to the Inhibit subscale (2007) and the Behavioral Regulation Index. It is important to note that on the BRIEF each gender is compared to their respective normative population, so that the difference between genders is relative to gender norms rather than an absolute difference. The authors offer no specific hypothesis to explain the gender difference, though they note there may be a bias among parents of girls, or the results may reflect a more serious level of executive dysfunction in girls.

In summary, there is an overwhelming amount of evidence to support executive function deficits in children with FASD. This includes laboratory measures of executive functioning, as well as parent and teacher rated measures of everyday executive functioning.

Learning and memory. There have been numerous studies examining the impact of prenatal alcohol exposure on learning and memory. One of the earliest such studies was conducted by Streissguth and colleagues (Streissguth, Barr, & Martin, 1983), based on Streissguth's observation that children with prenatal alcohol exposure were slow to habituate to sounds. Habituation procedures assess non-associative learning by measuring the progressive decrease in behavioral response to repeated stimuli. The study included 417 mothers and their newborns who were participating in a longitudinal study on prenatal alcohol use. Using a habituation procedure involving repeated visual or auditory stimuli, infants prenatally exposed to (mostly low levels) of alcohol showed impaired habituation shortly after birth, even after controlling for the effects of nicotine, caffeine, maternal age, nutrition during pregnancy, obstetric medication as well as age and gender of the infant. The effect also held after eliminating the few mothers who reported illegal drug use during pregnancy, or high levels of alcohol use. Habituation scores for infants of the mothers who drank most heavily were 0.75 standard deviations below those whose mothers abstained from alcohol.

Numerous other studies have examined various dimensions of learning and memory in fetal alcohol exposed children using a variety of standardized psychometric tests. An important distinction in this literature must be made between *the ability to acquire new information* and *the ability to recall information following a delay*. Many studies examined learning by using tests that involve multiple presentations of the same material (e.g., word lists, a series of objects). One consistent finding is that children with prenatal alcohol exposure do learn from repetition, although to a lesser degree than do non-exposed controls, so that overall they learn less, even with repetition (Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998; Hamilton, Kodituwakku, Sutherland, & Savage, 2003; Kaemingk, Mulvaney, & Halverson, 2003; Mattson, Riley, Gramling, Delis, & Jones, 1998; Mattson & Roebuck, 2002; J. Pei & Rinaldi, 2004; Rasmussen, Horne, & Witol, 2006; Willford, Richardson, Leech, & Day, 2004).

In contrast to the ability to acquire new information with repetition, assessment of memory is often accomplished by asking children to report information they had learned earlier (delayed recall). Children with fetal alcohol exposure generally recall less than controls. However, most studies have found that this deficit can be accounted for by impaired initial learning. Following a delay, percent retention of initially learned material is generally intact (Kaemingk, Mulvaney, & Halverson, 2003; Mattson, Riley, Gramling, Delis, & Jones, 1998; Mattson & Roebuck, 2002; J. R. Pei, Rinaldi, Rasmussen, Massey, & Massey, 2008; Willford, Richardson, Leech, & Day, 2004). In other words, children with fetal alcohol exposure have difficulty encoding information, but are able to recall the information they did learn following a delay.

Learning and memory are often divided by type of material to be remembered. A common conceptualization is to compare verbal memory (e.g., memory for word lists or stories) to visual memory (e.g., memory for objects or picture scenes, or topographical memory). Most studies which examined both visual and verbal domains found deficits in both (Kaemingk & Halverson, 2000; Kaemingk, Mulvaney, & Halverson, 2003; Mattson & Roebuck, 2002; J. R. Pei, Rinaldi, Rasmussen, Massey, & Massey, 2008; Richardson, Ryan, Willford, Day, & Goldschmidt, 2002). However, one study found impairment in visual but not verbal memory (Uecker & Nadel, 1996), while another found impairment in verbal but not visual memory (Willford, Richardson, Leech, & Day, 2004). In addition, a final set of studies found impaired verbal learning without testing visual learning (Mattson, Riley, Delis, Stern, & Jones, 1996; Mattson, Riley, Gramling, Delis, & Jones, 1998). Impairments in topographical memory have also been noted (Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998; Hamilton, Koditwakku, Sutherland, & Savage, 2003).

A recent study of children evaluated at a Canadian FASD diagnostic clinic highlighted the importance of considering ethnicity when evaluating learning and memory (Rasmussen, Horne, & Witol, 2006). In this study, Aboriginal children scored significantly higher than Caucasian children on measures of visual learning and memory, while Caucasian children scored significantly higher on measures of verbal learning ($n = 24$, approximately 75% Aboriginal). Thus ethnicity differences between various studies may account for some of the variability seen in the literature.

In order for learning to effectively guide behavior in everyday situations, one must be able to take the information or skills learned in one environment and apply them in new environments. This ability is called *transfer of learning* or *generalization*. Although frequently cited as a concern in FASD, transfer of learning has not received much research attention. A recent examination of this topic found parent-reported everyday transfer ability, and one of two novel experimental transfer tasks was significantly impaired in children with FASD compared to controls after controlling for IQ (McInerney, 2007).

In summary, prenatal alcohol exposure is associated with slow learning (encoding), but typically intact retention of learned material. Deficits in learning appear to be a particularly strong finding, evident even in children of light to moderate drinkers (Richardson, Ryan, Willford, Day, & Goldschmidt, 2002; Willford, Richardson, Leech, & Day, 2004). In those studies which have examined the impact of intellectual functioning, IQ does not fully account for these differences (Kaemingk, Mulvaney, & Halverson, 2003; Mattson, Riley, Gramling, Delis, & Jones, 1998). It appears that both visual and verbal forms of learning are impaired, although this finding may be impacted by ethnicity.

Interventions

Clearly, prevention of FASD is the ultimate intervention goal. Until that goal is completely realized, interventions designed to remediate deficits associated with FASD can help to improve the lives of individuals affected by FASD and their families, while reducing the economic burden to society. However, given the inter-individual variation in FASD, and the range of neurological, behavioral, and psychosocial outcomes associated with the disorder, there is not likely to be one single effective intervention.

In the absence of empirically supported intervention approaches, caregivers are likely to rely on standard parenting/teaching approaches. One intervention method which is frequently used with children and adolescents is behavioral therapy, or behavioral modification. Behavioral therapy involves functional analysis of the targeted covert or overt behavior, breakdown of the behavior into small, measurable components, and provision of systematic contingent feedback at each step. It can be applied to specific

problems, such as anxiety or enuresis, or can be used as a general approach to enhancing age-appropriate positive behaviors (i.e. academic achievement, positive social skills).

Although there has been no research on the effectiveness of behavioral interventions in children with FASD, caregivers of individuals with FASD are often advised against relying on rewards and punishments to control behavior. For example, the following are quotes from two different brochures on FASD:

Traditional behavior management techniques and traditional reward systems including tokens, stickers, money and star charts do not work. For these approaches to be effective, the child must understand the concept of “future earning” and have the impulse control to change his behavior for the future. A child affected by FASD does not have this ability. (Region 6 Edmonton and Area Child and Youth with FASD Sub-Committee, 2004, p. 12)

Because of the organic brain damage, using consequences or punishing behaviours does not work. Faulty memory and the inability to generalize information means that each situation is new to her, even if the same thing happened 15 minutes ago. ("Trying differently: A guide for daily living and working with FAS and other brain differences, 2nd edition", 2002, p. 8)

This type of advice is typically part of an education program that attempts to re-conceptualize or *reframe* the behavioral and cognitive problems associated with FASD as a mismatch between an individual with organic brain damage and an environment with unreasonable values and expectations. The goal is to recognize and accommodate the individual's needs by changing the environment in order to prevent secondary behaviors (tantrums, withdrawal, loss of self-esteem, frustration, etc.), and further prevent secondary disabilities (depression, trouble with the law, etc.). As with the quotes above, the arguments for this approach typically rely on outlining the primary behavioral characteristics of FASD. In this case, problems with learning, impulsivity, and transfer of learning are cited as the basis for rejecting consequence-based interventions. However, it is surprising that there is not any substantial research to directly investigate this premise, especially given its widespread use in dealing with behavioral concerns. The following section will summarize the available research on reinforcement learning in both humans and animals exposed to prenatal alcohol. First, however, it will review the basics of

classical and operant conditioning, including the brain areas involved and neurological substrates.

Reinforcement Learning

Thorndike's Law of Effect states,

Of the several responses made to the same situation, those which are accompanied or closely followed by satisfaction to the animal, other things being equal, will be more firmly connected with the situation, so that when it recurs, they will be more likely to recur; those which are accompanied or closely followed by discomfort to the animal will, other things being equal, have their connection with the situation weakened so that, when it recurs, they will be less likely to recur. (Thorndike, 1911)

The term *operant conditioning* was first coined by Skinner (1938) to refer to behavior, such as described by Thorndike, which can be modified by its consequences. Skinner was the first to differentiate operant conditioning from what had previously been described as classical or respondent conditioning. Classical conditioning is based on the principle that certain stimuli elicit automatic or "unconditioned" responses without any previous learning. In contrast, operant conditioning, a term first coined by Skinner (1938), refers to the modification of voluntary behavior by its consequences. Following the work of Skinner and other early behaviorists, a number of reports in the 1950s demonstrated that the principles previously outlined in animals were also valid in humans. In the 1960s and 1970s, practical applications of operant conditioning procedures were reported in various populations previously seen as resistant to treatment (e.g., individuals with autism, severely psychotic individuals). Since that time, behavior modification procedures have been applied in a wide variety of fields (e.g., medicine, psychiatry, education, social work) with both clinical and non-clinical populations, including child behavior management.

Reinforcement learning is a type of behavioral conditioning which involves discovering the actions or choices which yield the most reward and the least punishment using a trial and error process. It involves exploring a variety of actions, and learning over time the actions that appear to be best (Sutton & Barto, 1998). Learning from reinforcement contingencies requires the ability to acquire a mental representation of the value of stimuli, predict the occurrence of rewards and punishments, use those predictions to select the most adaptive response for a particular circumstance, and shift

responses as contingencies change. Extensive animal research, human lesion/disorder studies, and human neuroimaging studies have begun to identify specific brain regions and neurochemical systems involved in these functions.

The mesolimbic dopamine system and related brain areas have been repeatedly identified as playing a key role in reinforcement learning. The mesolimbic dopamine system has its origin in the ventral tegmentum of the midbrain and connects with the nucleus accumbens in the striatum (part of the basal ganglia). A closely associated pathway is the mesocortical dopamine pathway, which links the ventral tegmentum to the cerebral cortex, particularly the frontal cortex (Bozarth, 1991; Haber & Fudge, 1997).

The mesolimbic dopamine system is theorized to be involved in learning to predict reinforcement contingencies (Schultz, 1998, 2006). Learning these contingencies is necessary in order to predict future contingencies, and therefore adapt behavior to maximize rewards. Dopamine cells have an intrinsic, baseline level of firing associated with tonic levels of dopamine in the synaptic space. When an individual makes a response that leads to an unexpected reward, there is a transient (phasic) burst of dopamine. On the other hand, unexpected punishment leads to a transient dip in dopamine firing. Once the individual learns to predict the rewards and punishments, the phasic change in dopamine is elicited by the conditioned stimulus (the point when reinforcement is *predicted*) rather than the presentation of the reward or punishment itself. Any changes to the previously learned reinforcement contingency would create a reward prediction or temporal difference error, associated with phasic dopamine changes at the time of feedback or reinforcement (Ljungberg, Apicella, & Schultz, 1992; Schultz, Apicella, & Ljungberg, 1993).

In reinforcement learning, contingencies may be fixed (consistent) or probabilistic (associated with a degree of uncertainty). Under everyday circumstances, the relationship between a stimuli and a contingency is often probabilistic in nature. A child must learn not to approach a bully on the playground, even if sometimes the bully may smile or ignore the child when approached. Sometimes good behavior is praised, but sometimes it is ignored or even punished. In a research setting, probabilistic learning is often assessed through a discrimination task. A stimulus or series of stimuli are associated with a certain percentage likelihood of reward and/or response cost. For example, in a probabilistic

simultaneous visual discrimination task, a pair of stimuli (X and Y) is presented together over multiple trials. On 70% of trials, stimulus X is rewarded, while on 30% of trials, stimulus Y is rewarded. Non-rewarded trials may be associated with response cost, or may be neutral (no reward or response cost). Respondents must learn which stimulus is overall the best choice, and choose it every time to maximize reward. Using the theory of temporal difference errors, probabilistic learning would be associated with a temporal difference error on each trial, as the outcome is always uncertain. Or, if the task is sufficiently learned and understood, a temporal difference error may only occur on the less frequent non-rewarded trials.

A study in healthy adult humans demonstrated the importance of dopamine in probabilistic reinforcement learning. Pessiglione and colleagues (Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006) found that adults who were administered L-DOPA (a dopamine agonist) showed improved choice of high-probability rewards (choosing the option that had an 80% chance of earning money) compared to subjects who consumed haloperidol (a dopamine antagonist). However, neither drug increased the frequency of avoiding low-probability loss (avoiding the option that had a 20% chance of losing money) nor did the drugs impact reaction time or subjective rating of mood. Furthermore, fMRI scans during this task revealed the importance of the striatum in reinforcement learning - a high level of activity in the ventral striatum was positively correlated with the occurrence of reward prediction errors.

Parkinson's disease, which is a condition associated with dopamine depletion in the basal ganglia, provides a clinical model for the examination of the function of dopamine in reinforcement learning. Frank and colleagues (Frank, Seeberger, & O'Reilly, 2004) tested patients with Parkinson's disease both on and off dopamine-enhancing medication. They found, as predicted, that patients off medication were impaired at probabilistic learning from positive feedback, presumably because low levels of dopamine made it difficult to learn from phasic bursts of dopamine. In addition, these same patients showed enhanced learning from negative feedback presumably because low levels of dopamine facilitate the phasic "dips" in dopamine associated with negative feedback.

Another type of reinforcement learning important for the current study is categorical discrimination learning. In this type of learning, decisions or actions are guided by the classification of events or objects into different categories. When presented with novel or distinct objects, the ability to categorize allows us to respond to those objects in a similar manner to known objects with which they share certain features. For example, an unfamiliar fruit may still be easily categorized as “fruit.” Categorical discrimination is frequently assessed using simultaneous visual discrimination tasks. In this type of task, the respondent is presented with two objects or pictures which each vary along two binary-valued dimensions (e.g., shape, color). They must learn to respond to one aspect of one dimension (e.g., always respond to blue stimuli, not red) while ignoring the other dimension (e.g., shape).

There is a long history of research into categorical discrimination learning. Since the 1960s, there has been considerable debate between those who support the notion that young children perform this task using qualitatively different modes of learning compared to adults (H. H. Kendler & Kendler, 1975; T. S. Kendler, 1979), and others who have theorized that the underlying mechanisms are the same (Zeaman & House, 1974). Despite the extraordinary amount of attention given to this question, there has been surprisingly little consensus on the topic. A recent re-conceptualization of the debate posits that there are two neurologically distinct competing systems in category learning. Which of these systems is used depends on the type of task (Ashby, Alfonso-Reese, Turken, & Waldron, 1998). The first system is rule-based, and dominates when the relevant rule is easy to verbalize. Use of this system involves explicit hypothesis testing supported by working memory and executive attention. Neuroimaging studies suggest that this system primarily relies on the anterior cingulate cortex, the prefrontal cortex, the medial temporal lobe, and the head of the caudate nucleus. The second system is an implicit, procedural based learning system which learns rules incrementally in the absence of an easily verbalizable rule. Research suggests that this system relies on the tail of the caudate nucleus and connected visual cortical areas (reviewed in Ashby & Maddox, 2005; Nomura & Reber, 2008). Evidence suggests that preschoolers tend to rely more on the nonverbal system, whereas adults are biased to rely on the verbal system

(unless the verbal system is taxed with a simultaneous task, or the nonverbal system is consistently reinforced; Ashby et al., 1998).

According to Frank and Claus' (2006) computational simulations, the striatal basal ganglia dopamine system is sufficient to make appropriate choices based on frequencies of positive and negative reinforcement. However, a more complex model, which includes the OFC, is required when recent changes in reinforcement must be kept on-line in order to override the prepotent response tendencies established by the striatal basal ganglia system. This is especially important as reinforcement contingencies change. When the current response set is no longer rewarded, some type of shift in response is required. Mental flexibility, or the ability to shift focus, is typically conceptualized as a form of executive, or higher-level attention (Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991; Posner & Petersen, 1990; Sohlberg et al., 2003). A number of studies have found that this type of switching ability increases in early childhood to near-adult levels by age 10 (Chelune & Baer, 1986; CShu, Tien, Lung, & Chang, 2000; Huizinga & van der Molen, 2007; Levin et al., 1991; Rosselli & Ardila, 1993). Frank and Claus described the importance of the OFC in this aspect of reinforcement learning as a "top-down, goal-directing biasing on the decision outputs" (p.314). This model is supported by animal research studies such as Winocur and Eskes' study (1998) which showed that lesions to the caudate nucleus (located within the basal ganglia) were associated with impairments in learning the basic stimulus-response associations, while lesions to the prefrontal cortex impaired performance when the response learning or response selection requirements were more difficult, requiring strategic processing (e.g., learning to press the lever opposite to a light rather than next to a light).

In addition to the OFC, the anterior cingulate cortex (ACC) is theorized to be important in responding to shifts in environmental stimuli. Holroyd and Coles proposed that the role of the ACC is to utilize the reward prediction error generated by the midbrain dopamine system to assist in the selection of a new response when the current response is not working. According to this theory, information is transmitted to the ACC through a temporal difference error signal carried by the dopamine system. These errors are generated when a human makes an error on a task. The ACC uses these error signals to guide the most appropriate motor response (Holroyd & Coles, 2002).

There is a large body of literature to support the existence of two dissociable forms of shifting which are reliant on distinctly different brain mechanisms. Categorical discrimination tasks are particularly useful for examining these different types of shifts. An *affective* shift involves changing the affective value of stimuli. For example, reversal learning involves completely reversing the items' reinforcement values, with the relevant dimension remaining the same (e.g., switch from "blue is correct, red is incorrect" to "red is correct, blue is incorrect"). In contrast, an *attentional* (nonreversal) shift involves shifting of selective attention from one dimension or aspect of a stimulus to another. For example, this type of shifting involves changing the reinforced dimension from one dimension (e.g., shape, "squares are correct") to another dimension (e.g., color, "red items are correct"). A visual example of these types of shifts can be found in Appendix A.

Dias and colleagues (Dias, Robbins, & Roberts, 1996) found a double dissociation in that lesions to the OFC impaired reversal shifting but not nonreversal shifting in monkeys, while lesions to the dorsolateral prefrontal cortex showed the opposite pattern. Studies with humans are supportive of this dissociation, as individuals with ventrolateral/OFC lesions have been shown to be impaired on reversal learning, while individuals with dorsolateral prefrontal cortex or other non-ventral injuries were not impaired on reversal learning (Fellows & Farah, 2003; D. G. Mitchell et al., 2006; Rolls, Hornak, Wade, & McGrath, 1994). These deficits were typically found in the context of intact visual discrimination reinforcement learning.

The distinction between these types of shifts has also been demonstrated by studies which modulate the ascending monoamine neurotransmitter systems. Depletion of catecholamines (including dopamine) using 6-hydroxydopamine lesions to the prefrontal cortex in monkeys was associated with impaired nonreversal set shifting, but not reversal set shifting (Roberts et al., 1994). In contrast, serotonin may be particularly important in reversal shifting. Marmosets whose prefrontal cortex was depleted of serotonin showed perseverative responding when required to reverse responses, although discrimination and retention were not impaired (Clarke, Dalley, Crofts, Robbins, & Roberts, 2004). A follow-up study further showed that nonreversal set shifting was not impaired with serotonin depletion (Clarke et al., 2005).

Another study showed that acute administration of norepinephrine-enhancing medication in healthy adults did not impact probabilistic discrimination learning or reversal learning. However, acute administration of serotonin-enhancing medication impaired probabilistic discrimination learning and reversal learning. The authors suggested that this latter paradoxical result may be accounted for by autoreceptor feedback which temporarily reduced serotonin following the acute dose, or may be due to an “inverted U” function, such that both serotonin under- and over-activity impair this type of learning (Chamberlain et al., 2006).

Certain task variables have been shown to impact the speed at which one learns to successfully shift. Nonreversal shifts take more trials to learn compared to reversals (Esposito, 1975; H. H. Kendler & Kendler, 1975; T. S. Kendler, 1983, 1995; Tighe & Tighe, 1978; Wolff, 1967). Sirois and Shultz (1998) note that while this pattern is seen in adults and children older than 10 years, it is not clearly seen in preschool age children, who tend to show equal performance in the two tasks (Esposito, 1975; Wolff, 1967).

To account for the reversal/nonreversal age difference, Sirois and Shultz proposed the *spontaneous overtraining* theory (1998), which suggests that older children and adults spontaneously provide themselves with extra training through mental rehearsal. They argue that spontaneous rehearsal effectively provides more learning trials. Preschoolers do not get the benefit from this extra training, presumably because of their still-developing rehearsal mechanisms (i.e., internal speech, working memory). To test their hypothesis, Sirois and Schultz conducted a study where adults were required to do a verbal distracter task (counting down by 3's) while simultaneously participating in a series of shifting tasks. They found that, like preschoolers, distracted participants showed equal speed of learning in the reversal and nonreversal conditions (Sirois & Shultz, 2006). Also, like preschoolers (Coles 1973, 1976), distracted participants were highly variable. On the flip-side, previous research has found that when preschoolers overlearn the tasks (are given 20 extra trials past the learning criterion), they look like adults - reversal is faster than nonreversal - and more children are able to reverse (Eimas, 1967; Shepp & Adams, 1973; Tighe & Tighe, 1966; Wolff, 1967). In fact, this overtraining reversal effect can also be seen in adults, where extra trials in the discrimination learning

phase leads to increased speed of reversal learning compared to a standard amount of training (Reid, 1953).

Sirois and Shultz's interpretation is mostly consistent with Ashby and colleagues' theory of competition between verbal and implicit systems in that young children likely rely more on an implicit system. Overtraining and mental rehearsal strengthen their reliance on the verbal system. In contrast, verbal distraction in adults weakens reliance on the verbal system, forcing increased reliance on the implicit system, thereby making older respondents appear more like young children.

In summary, there is strong evidence that specific brain areas and neurological systems are involved in various aspects of reinforcement learning. It is with this evidence in mind that the discussion now turns to the impact of prenatal alcohol exposure on classical and operant conditioning.

Classical Conditioning and Fetal Alcohol Exposure

There is evidence from both human (Coffin, Baroody, Schneider, & O'Neill, 2005; S. W. Jacobson et al., 2008) and animal research (Brown, Calizo, & Stanton, 2008; Green, Rogers, Goodlett, & Steinmetz, 2000; Stanton & Goodlett, 1998) that children with FASD are impaired in eyeblink conditioning, a classically conditioned procedure that depends on cerebellar-brainstem circuitry. Classical fear conditioning in fetal-alcohol affected animals has shown equivocal results (Caul, Fernandez, & Michaelis, 1983; Weeber, Savage, Sutherland, & Caldwell, 2001).

Operant Odor & Taste Conditioning in Animals with Fetal Alcohol Exposure

Newborn rats (as well as humans) have an innate ability to learn to associate odors with positive and negative stimuli. This allows, for example, the extremely adaptive ability of animals to learn to associate tactile stimulation with the smell of their mother. Young rats prenatally exposed to alcohol show deficits in both appetitive and aversive olfactory conditioning, with intact stimulus recognition. Adult rats, however, learned aversions as well as control animals (Barron, Gagnon, Mattson & Kotch, 1988).

In addition to smell, rats also acquire conditioned taste aversions (e.g., if a food makes you sick, avoid it in the future). Although not yet developed at postnatal day 5, the beginning of this ability is evident in normal mice by day 10 (Riley, Barron, Driscoll, & Chen, 1984). By day 15, prenatally alcohol exposed pre-weanling rats show significantly

less pronounced taste aversion compared to controls, with those animals exposed to higher levels of prenatal alcohol demonstrating larger deficits (Driscoll, Riley, & Meyer, 1985; Riley, Barron, Driscoll, & Chen, 1984). This dose-response relationship is also apparent in young post-weanling rats (Riley, Lochry, & Shapiro, 1979).

Operant Position/Spatial Discrimination Conditioning in Animals with Fetal Alcohol Exposure

Although classical conditioning studies support fetal alcohol exposed animals generally learning the cues associated with a fearful situation, a number of studies have found that young and adult fetal alcohol exposed rats are impaired in active and passive avoidance behavior based on these cues. In these studies, alcohol exposed animals were slow to learn to run to the other side (or stay on the same side) of the apparatus in response to a tone in order to avoid a shock (Abel, 1979, 1982; Bond & DiGiusto, 1978; C. L. Randall, Becker, & Middaugh, 1986; Shaywitz, Griffiths, & Warshaw, 1979). One exception is a study by Riley and colleagues (Riley, Lochry, Shapiro, & Baldwin, 1979), who found that animals exposed to no, moderate or high levels of prenatal alcohol all successfully learned to go down one of two arms of a maze in response to a tone to avoid a shock. However, when the animals were required to reverse their response, and go down the other arm to avoid the shock, there was a significant difference between the groups, with a linear trend showing higher alcohol exposure was associated with increased difficulty learning the reversal.

Thomas and colleagues (Thomas, Weinert, Sharif, & Riley, 1997) found that adult rats which were exposed to a single high dose of alcohol on postnatal day 6 were slower compared to controls to learn to swim to the correct arm of a 2-arm maze where they were rewarded with escape. These animals also had significant difficulty when the rewarded arm was reversed. Furthermore, analysis of the types of errors showed that alcohol exposed animals made significantly more repeated entrances into the wrong arm (within single trials), suggesting that the deficit may be better accounted for by difficulty with inhibiting perseverative responses rather than with position discrimination. Interestingly, this deficit was significantly attenuated in animals that had been given a dose of an N-methyl-D-aspartic acid (NMDA) receptor agonist 24 hours after the acute

alcohol administration, supporting the notion that NMDA receptor-mediated excitotoxicity may contribute to ethanol's toxic effects on the developing brain.

In a similar escape task, pre-weanling male rats (not females) exposed to alcohol throughout gestation were impaired on learning the discrimination. In addition, no animals (using different animals from the same litters) were impaired at maturity (Lee, Haddad, & Rabe, 1980). In contrast to other studies, none of the alcohol exposed rats showed reversal deficits.

Appetitive 2-arm maze discrimination was examined in 10 day old pre-weanling rats exposed to alcohol throughout the last two thirds of gestation. These animals learned to crawl to one arm of the maze where they were rewarded with 30 seconds of dry suckling on an anesthetized dam. When they learned the correct arm to criterion, the rewarded arm was reversed on the next set of trials. Of those animals which learned to criterion both in the acquisition and reversal sets, those exposed to prenatal alcohol were significantly slower to learn both the discrimination and reversals (Anandam & Stern, 1980).

Operant Behavioral Response Conditioning in Animals with Fetal Alcohol Exposure

Other researchers have examined conditioned simple and complex behavioral responses in alcohol exposed animals. Mihalick and colleagues (Mihalick, Crandall, Langlois, Krienke, & Dube, 2001) found that adult rats exposed to alcohol throughout pregnancy were not impaired when learning to make a different response for each of two different auditory stimuli, nor were they impaired when the previously learned stimuli were changed to novel sounds, even in the context of a multi-step response requirement and a shifting series of sounds to discriminate. It is important to note, however, that the sounds were not repeated, and therefore the animals did not need to inhibit a prepotent response to familiar stimuli. In order to examine whether alcohol exposed animals were impaired when required to inhibit a prepotent response, the authors used a reversal paradigm. Reversal paradigms require animals to inhibit the previously learned reinforcement contingencies while learning new contingencies (e.g., previously rewarded stimuli are now punished, and previously punished stimuli are now rewarded). In this reversal task, stimuli consisted of a tone and a click (with rewarded and non-rewarded associations counterbalanced). Once the animal met the learning criterion, the

reinforcement contingencies in the next session were reversed (with reversals continuing for a maximum of 30 sessions). There was a nearly significant trend for alcohol exposed animals to take longer to discriminate the first tone/click, suggesting that this was a somewhat more difficult task than the previous successive discrimination task. Once the discrimination was acquired, alcohol exposed animals took significantly longer than control animals to meet the first reversal learning criterion. Interestingly, this deficit was associated with neuronal cell loss in the medial prefrontal cortex.

In an experiment with adult mice prenatally exposed to alcohol from gestational days 5 to 17 (Gentry & Middaugh, 1988), reinforcement changed from a fixed ratio of 1 (FR1 – one lever press for one reward) to subsequent sessions which increased the number of responses required for a reward, and varied the pattern of responses required. The pattern included: FR20, FR100, FR20, extinction, followed by a multiple-schedule reinforcement which continually alternated within single sessions between FR5 and a differential reinforcement of other behavior (DRO) condition where the animal was reinforced for every 15 seconds following a tone without a lever press. This study found deficits in alcohol exposed animals across conditions. A later study by the same authors showed that prenatal alcohol exposure during gestational days 12 to 17 was sufficient to produce the same effect. The authors suggested that prenatal alcohol exposure during this critical time impacts the developing mesolimbic dopamine reward system (Middaugh & Gentry, 1992).

Riley and colleagues also found that young post-weanling rats prenatally exposed to alcohol throughout gestation were impaired on a gradually increasing fixed ratio reinforcement paradigm (from FR2 to FR33). Furthermore, they found a dose-response relationship between percent of ethanol-derived calories delivered to the mother and impairment on the tasks (Riley, Shapiro, Lochry, & Broida, 1980). In support of the dose-response finding, a more recent study with guinea pigs exposed to low-level alcohol exposure throughout gestation showed that these animals were not impaired on a similar task (increasing from FR1 to FR33; Hayward et al., 2004). The alcohol exposed guinea pigs did, however, show increased responding on extinction. Another study with a similar increasing FR procedure showed that a moderate level of alcohol in combination with cocaine, but not moderate alcohol intake alone, led to impaired performance on an

increasing fixed ratio schedule (Segar, Klebaur, Bardo, & Barron, 1999). In this study, alcohol was only administered during the early postnatal stage (equivalent to human third trimester).

Similarly, adult rats prenatally exposed to high levels of alcohol throughout gestation and nursing were less efficient responders to a series of changing continuous, fixed ratio, and differential reinforcement of low rate (DRL - where the animals were required to respond only every 10 or 15 seconds) reinforcement conditions. Animals exposed through nursing alone were less efficient in only the fixed ratio schedule (J. C. Martin, Martin, Sigman, & Radow, 1977). In this study, as well as in another study with adult rats (Driscoll, Chen, & Riley, 1980), an initial fixed ratio schedule was changed to a DRL schedule. Under DRL, animals with prenatal alcohol exposure initially received more rewards than controls (due to their low level of lever presses). However, with practice, controls surpassed the performance of the alcohol exposed group. This was also evident when a cue light was illuminated to indicate when reinforcement was available (Driscoll, Chen, & Riley, 1980).

Operant Conditioning in Humans with FASD

There have been two studies of reinforcement learning in fetal alcohol exposed humans. In an early study of newborn infants, Martin and colleagues (J. Martin, Martin, Lund, & Streissguth, 1977) conducted two operant conditioning paradigms. The first required the newborn to learn to turn their head to one side following a tone, in order to receive a two-second access to a sugar solution. The second task required the newborn to suck 10 times on a nonnutritive nipple within a 30-second period in order to receive access to the reward solution. Both tasks were followed by extinction. Only those babies who showed any upward learning slope were included in the analyses. Similar results were found for both paradigms. The interaction between alcohol and nicotine intake was the most predictive of operant learning (as measured by perseveration on a non-reinforced response during extinction). Higher levels of alcohol combined with higher levels of nicotine consumption resulted in the poorest operant learning, whereas cigarette smoking alone was associated with better performance (perhaps due to faster motor responses).

In the second study, Kodituwakku and colleagues (2001) compared 20 children and adolescents (ages 7 to 19) with confirmed prenatal alcohol exposure (10 had a diagnosis of FAS, while the others had prenatal alcohol exposure without an FAS diagnosis) to non-clinical age, sex, and ethnicity matched controls on a successive visual discrimination conditioning task. Although not reported in the paper, personal communication with Kodituwakku (July 13, 2007) revealed that children were requested (if medically advisable) to be off psychostimulant medication for 24 hours prior to the study. In this study of successive visual discrimination and shifting, two abstract designs (fractal images) were presented one at a time, and the children earned points for clicking on the rewarded design (S+) or for not clicking on the losing design (S-), while also losing points for clicking on S- or not clicking on S+. The alcohol exposed group was significantly slower to learn the discrimination.

Once the participant learned the contingencies (as measured by nine of ten correct responses in a single block), the contingencies were reversed without warning. The contingencies were reversed up to three times, or to a maximum of 30 trials. There was a significant group difference between the FASD and control group in the rank-transformed mean number of reversals learned ($t(38) = 3.947, p < 0.0001$). Since both controls and children with FASD made proportionally more errors of commission than omission, the deficit was not simply due to greater impulsivity in the FASD group.

After the reversal task, the extinction phase was initiated. New images were presented and participants again had to learn to respond to S+ and not respond to S-. Interestingly, participants in the FASD group showed a marked improvement in speed of learning the contingencies, while children in the control group performed approximately at the same level as previously (likely a ceiling effect). This suggests that the children with FASD likely *learned* from their experience in the first task, and were able to apply that knowledge to the new task as the demands were the same and only the stimuli differed.

Once the participants learned the contingencies associated with the new images to criterion, both stimuli became S- in the extinction phase. The number of trials required to learn the extinction criterion was comparable between the groups, although the alcohol exposed group had significantly more variation in number of trials than the control group.

Given this improvement in performance between tasks, the authors hypothesized deficits observed in this study were due to *deficient (slow) processing skills*, rather than problems with perseveration per se. To support this hypothesis, they cite evidence from their own and other studies which show that participants with FASD are slower than controls on measures of information processing speed.

Kodituwakku and colleagues (2001) also examined conceptual/attentional set shifting (nonreversal) learning using the WCST in addition to reversal learning. Converting scores from both the WCST and the experimental task to standardized z-scores showed that the FASD group was not *more* impaired in reversal shifting (number of the 3 reversals successfully acquired in 30 trials on the experimental task) compared to WCST set shifting (number of the six WCST categories acquired in 120 trials), although both types of shifting were significantly impaired compared to controls. However, the group difference in number of reversals acquired remained significant even after controlling for nonverbal IQ and WCST score, suggesting that these two types of shift were not entirely interchangeable. It should be noted, however, that direct comparison between the WCST and the reversal learning task is problematic: the WCST is a more complex task (four response options instead of two; requires categorical conceptualization along three dimensions), and it involves corrective feedback without earning points as in the reversal task.

Interestingly, in this study, parent-reported behavior problems were predicted by problems with reinforcement learning. Specifically, a combination of three variables, WCST perseverative errors, omission errors in reversal learning, and extinction variability accounted for 50% of the variability in the parent rated Personal Behavior Checklist.

A thorough review of the FASD literature revealed no other studies of involving reinforcement learning, the impact of contingencies, or the effectiveness of a token economy. Given this dearth of research, useful information may be gathered from examining a population with significant overlap with FASD – Attention Deficit Hyperactivity Disorder (ADHD). As discussed previously, children with FASD are frequently co-diagnosed with ADHD. Multiple lines of evidence suggest that ADHD is strongly associated with dysfunction of the midbrain dopamine system and associated

frontal striatal brain systems (DiMaio, Grizenko, & Joobar, 2003; Faraone et al., 2005; Levy & Swanson, 2001), systems also implicated in FASD. Given the association of ADHD with the dopamine system, it is not surprising that theoretical accounts of ADHD frequently highlight aberrant response to reinforcement (reviewed in Luman, Oosterlaan, & Sergeant, 2005).

Work by Holroyd and colleagues (Holroyd, Baker, Kerns, & Mueller, 2008) suggests that children with ADHD may be more positively responsive to *in-hand* monetary reinforcement, and that this difference may be mediated by the midbrain dopamine system. In this study, physically receiving earned monetary reward halfway through the task increased the reward-related electrophysiological responses in the ADHD group, but decreased the same response components in the control group. This study suggests that the concreteness or tangibility of a reinforcer may affect those with ADHD differently than controls. Given that children with FASD typically have difficulty with abstract concepts, they also may be impacted by the tangibility of the reinforcer.

Summary

A review of the effects of prenatal alcohol exposure on reinforcement learning reveals some commonalities as well as some remaining questions. First, there is strong evidence from animal research for deficits in reinforcement learning in young animals prenatally exposed to alcohol. Some deficits appear to improve with age (Barron, Gagnon, Mattson, Kotch et al., 1988; Lee, Haddad, & Rabe, 1980) suggesting the possibility of a developmental delay, rather than a permanently damaged system. As with a number of other functional and structural effects of prenatal alcohol exposure, there is strong evidence to support a dose-response relationship, such that a higher level of exposure is associated with increased deficits. In other areas, animal research has been somewhat contradictory; not all studies have found deficits in reinforcement learning. Examination of the types of tasks which are impaired versus those that are intact can help elucidate the problem. Some studies show decreased response rates in alcohol exposed animals when very high or very low rates of response (e.g., lever press) are required, while other studies show increased levels of responding (e.g., lack of extinction). This suggests deficits in reinforcement learning are not simply due to *hypo-* or *hyper-*activity. Interestingly, Kodituwakku's operant reinforcement study (2001) in humans with FASD

was concordant with this assertion. A relatively strong finding is that prenatal alcohol exposure is associated with impairment on tasks where the contingencies are altered in such a way that inhibition of a previously learned contingency is required (reversal tasks, extinction, fluctuating reward systems). Some, but not all, studies suggest this impairment is found in the absence of deficits in reinforcement learning. Finally, much of the rich history of research in animals has yet to be translated to research with humans.

Goals and Hypotheses

The goal of this study was to examine various aspects of reinforcement learning in children and adolescents with FASD. Although there is ample evidence that prenatal alcohol exposure impacts the reinforcement systems in animals, evidence in humans is scarce. Therefore, this study was intended to be exploratory, examining reinforcement learning from a variety of angles and perspectives. This study can be broadly divided into three parts. The first part examined probabilistic reinforcement learning including the potential impact of the concreteness of the reinforcer. The second part investigated categorical discrimination reinforcement learning and shifting (reversal versus nonreversal). The third part addressed parent reports of behavioral and social functioning and examined the relationship between these reports and reinforcement learning.

Part 1: Probabilistic Learning and Concreteness of Reinforcers

Modifications to the basic probabilistic learning task allow for the exploration of various aspects of reinforcement learning. One such aspect is the nature of the reinforcers. In Kodituwakku's (2001) study, participants earned points which were displayed on the screen (but were not redeemable for money or prizes), and heard a pleasant or unpleasant sound depending on the accuracy of their response. This is a method frequently employed in computerized experimental tasks. In order to increase the reliance on the dopamine reinforcement system, the current study assigned *value* to the reinforcers in that they were tied to a prize at the end.

The current study examined the impact of concreteness of reinforcement on a probabilistic learning task (utilizing a simultaneous visual discrimination paradigm) in two conditions, one in which points were shown on the computer screen during the task and the other in which actual tokens were physically given/taken away during the task.

Hypothesis 1: Given the consistent finding in the literature that individuals with FASD are slower to learn, there is strong support for the hypothesis that participants with FASD in the current study will overall be slower than controls to learn from reinforcement contingencies (i.e., they will have a lower overall score). In addition to overall learning, *learning savings* was examined by comparing performance in the first and second conditions (between-condition learning), while *speed of learning* was examined by comparing performance in the first half of the tasks to performance in the second half of the tasks (within-condition learning). It was hypothesized that the FASD group would have both slower within- and between-condition learning compared to the Control group. This would support an abnormal process of reinforcement learning, rather than simply deficient processing skills as suggested by Kodituwakku and colleagues (2001).

Hypothesis 2: Given the fact that tokens and points are essentially *worth* the same amount, it was hypothesized that participants in the Control group would show no difference between the two conditions. However, it was unclear from available evidence how children with FASD would respond to Points versus Tokens. Due to the difficulty children with FASD frequently have with abstract concepts such as mathematics (Burden, Jacobson, & Jacobson, 2005; Coles et al., 1997; Goldschmidt, Richardson, Stoffer, Geva, & Day, 1996; Howell, Lynch, Platzman, Smith, & Coles, 2006; Kopera-Frye, Dehaene, & Streissguth, 1996), it was possible that they may respond better to concrete, in-hand reinforcement contingencies compared to the more abstract points on the screen. On the other hand, given the accumulating evidence that prenatal alcohol exposure may be associated with dysfunction in the mesolimbic dopamine reinforcement system, the FASD group may have been expected to show poorer performance in the Tokens condition compared to the Points condition. This could occur if the Tokens condition represents a more salient reinforcer (more immediately recognized, attended to, and understood) than the more abstract “Points on the screen” condition.

Part 2: Discrimination Learning and Shifting

Reversal and nonreversal shifting in individuals with FASD was explored through categorical discrimination and shift learning tasks developed for this study. Each task

began with discrimination learning, followed without warning by shift learning (either reversal or nonreversal).

Hypothesis 1: Given the consistent finding in the literature of slower learning in individuals with FASD, there is strong support for the hypothesis that participants with FASD in the current study would be slower than controls to learn from reinforcement contingencies in the discrimination and shifting conditions. If the FASD group were to be significantly slower in the first, but not the second discrimination and reversal, this would support Kodituwakku and colleagues' (2001) hypothesis that deficits in the FASD group are due to slow (rather than deficient) processing skills (i.e., they improve with practice).

Hypothesis 2: Consistent with the long history of shift research, it was hypothesized that the Control group would show reversal bias (faster reversal shift learning compared to nonreversal shift learning). Similar to the response pattern of preschoolers, it was further hypothesized that the FASD group would not show a significant difference between the two types of shifts.

Hypothesis 3: Given the strong support from animal research that prenatal alcohol exposure is associated with impaired shifting, it was hypothesized that the FASD group would be slower than the Control group to learn to shift, even after accounting for their speed of initial discrimination learning. However, if deficits in shifting could be fully accounted for by deficient processing (as proposed by Kodituwakku et al., 2001), there would no group differences in shifting once initial discrimination learning was accounted for.

Hypothesis 4: Both discrimination learning and probabilistic learning are visual discrimination tasks that involve learning which of two responses is correct based on reinforcement. As such, it was hypothesized that there would be a significant correlation between a participant's score in discrimination learning and their score in probabilistic learning.

Part 3: Parent Reports

Hypothesis 1: It was hypothesized that probabilistic learning, discrimination learning and shifting would be significantly correlated with parent-reported Aggressive Behavior, Rule-breaking Behavior, and Social Problems on the CBCL and with transfer

of learning as assessed by the CLQ, such that lower (more impaired) task scores would be associated with a higher level of behavior/social/transfer problems.

Method

Participants

Power Analysis

It is typical for neuropsychological studies looking at clinical populations to yield large effect sizes. A review of 66 clinical neuropsychology studies found a large mean effect size of 0.88 (Bezeau & Graves, 2001). This suggests that clinical studies, even with small sample sizes, often have sufficient power to detect these typically large effect sizes. Indeed, the majority of studies (excluding longitudinal studies) which examine cognitive functioning in individuals with FASD are quite small, with sample sizes of 10 to 25 participants per group.

For the current study, the best estimate of expected effect size for the discrimination learning section of this study comes from Kodituwakku and colleague's (2001) visual reinforcement learning paradigm. In this study, the alcohol exposed group was significantly slower to learn the discrimination ($t[38] = 3.898, p < 0.0001$). Using the formula for calculating a Cohen's d effect size from a t -score¹ (Cohen, 1988), the effect size is large ($d = 1.26$). A similar effect size could be calculated for the number of reversals completed ($t[38] = 3.947, p < 0.0001$). Assuming a power level of 0.80 and an alpha of 0.05, the total number of required participants to detect this large effect size in a two-tailed independent groups t -test is 11 per group (calculated using G*Power 3; Faul, Erdfelder, Lang, & Buchner, 2007). However, given that analysis in the Kodituwakku study was conducted using rank-transformed data (reducing the variability and therefore increasing the effect size), in order to increase the power of the current study and reduce the likelihood of making a Type II error, the recruitment goal for this study was 18 participants per group. The final analysis included 19 participants per group. With this sample size, power was 0.96 for detecting the large effect size from Kodituwakku and colleague's study, and 0.66 for detecting a standard large effect size (.80) for a two-tailed design.

¹ Cohen's $d = (\text{Mean group 1} - \text{Mean group 2}) / \text{pooled standard deviation}$
 where pooled standard deviation (sd) = $\sqrt{[(sd_1^2 + sd_2^2) / 2]}$

Recruitment

Participants (both FASD and Controls) were recruited by (1) contacting families who previously participated in research studies in Dr. Kerns' laboratory; (2) distributing information and fliers to physicians, psychologists, and other professions who were likely to have contact with individuals with FASD, including advertisement on appropriate email listserves; (3) distributing information/fliers throughout Victoria and the surrounding areas in locations frequented by families including community centers, grocery stores, and parenting web sites; (4) personal contact with parent groups, sports team coordinators, and programs that serve youth; and (5) classified advertisements in local newspapers.

Inclusion/Exclusion Criteria

As previously discussed, there is some evidence from the animal literature that deficits in reinforcement learning due to prenatal alcohol exposure attenuate in adulthood. Therefore, children and adolescents (rather than adults) were the target of this study. Furthermore, this study was limited to older children and adolescents (age 11 to 17) as shifting ability is generally believed to reach adult levels by around age 10 (as discussed in the Reinforcement Learning section).

To participate in the study, children in the FASD group were required to have a pre-existing diagnosis on the fetal alcohol spectrum. If they were diagnosed using the University of Washington 4-Digit Diagnostic Code system (Astley, 2004), participants were required to have a prenatal alcohol exposure rank of 3 or 4. In addition, current guidelines for assessment in Canada recommend "evidence of significant prenatal exposure to alcohol at levels known to be associated with physical or developmental effects, or both" (Chudley, et al., p. 5). Rank of 4 indicates high risk levels of alcohol ingestion, while rank of 3 indicates confirmed exposure at levels less than a rank of 4 or unknown levels of exposure. In addition, there must have been either some evidence for the facial features associated with fetal alcohol exposure (rank of 2, 3 or 4) or some indication of CNS dysfunction (rank of 3 or 4).

Facial features were not required because extrapolation from mouse models suggests that alcohol exposure must occur in weeks 3 to 4 of gestation to cause the characteristic facial features of FAS in humans (Sulik, 2005). Therefore, diagnosis cannot

rely solely on analysis of facial features because although the features are fairly specific to prenatal alcohol exposure (Hoyme et al., 2005), in many cases of prenatal alcohol exposure facial features will be normal.

If diagnosed with another criteria set, the following diagnoses were acceptable for inclusion in the study: FAS, (CDC, IOM, Canadian guidelines), pFAS (IOM, Canadian guidelines), ARBD (IOM), and ARND (IOM, Canadian guidelines). Caregivers were asked to confirm the diagnosis, either by reference to the written diagnostic report or verbal consultation with the diagnostician. Given the inclusion criteria, it is clear that all participants had some confirmed prenatal alcohol exposure, but the levels of exposure were not consistent across the FASD participants and not all participants were exposed to high levels of alcohol.

Participants were pre-screened for general suitability for the study (e.g., age, diagnostic status, exclusionary criteria) using a brief phone consultation with their parent or guardian. Exclusionary criteria for the FASD group included: visual impairment, hearing impairment, mental retardation, moderate to severe traumatic brain injury, stroke, psychotic disorder, bipolar disorder, drug addiction, and specific neurodevelopmental disorders including Fragile X syndrome, cerebral palsy, and autism. Testing sessions were conducted at the University of Victoria, in the participant's home, or in a community setting convenient to the family (e.g. library, FASD Resource Centre). Prior to the testing session, written informed consent was obtained from all participants and their parent or legal guardian (please see Appendix B).

Participants in the Control group were chosen to match the FASD group based on sex and age. Exclusionary criteria for the Control group included all of the previous conditions, as well as teratogenic medication or street drugs consumed during pregnancy, three or more standard alcoholic drinks consumed per week anytime during pregnancy (or the month prior to pregnancy recognition), unknown fetal alcohol exposure, suspected or confirmed diagnosis of ADHD, learning disability, epilepsy, and any known neurological or psychiatric disorder including anxiety or mood disorders. Furthermore, any participant (in either the FASD or Control group) who was found during testing to have both a verbal and performance IQ below 70 was excluded. This cutoff was

important in order to ensure that participants could understand and follow task instructions.

Individuals with FASD are often co-diagnosed with ADHD and some are treated with psychostimulant medication (O'Malley, 2007). Psychostimulant medication is fast-acting, and many parents take their children off medication for short periods of time (school vacations, weekends etc.). Due to its impact on the dopamine system, participants were requested to have been off psychostimulant medication for at least 24 hours prior to testing. Parents were asked to consult with their child's physician in this regard, and if medication could not be discontinued for the study, they were still allowed to participate (a similar procedure as Kodituwakku et al., 2001).

Characteristics of the Final Sample

A total of 39 participants (20 in the FASD and 19 in the Control group) participated in the study. Three children under age 11 who were siblings of participants were also tested, but not included as part of the final study. One participant (from the FASD group) was eliminated due to low IQ, leaving 19 participants per group. Participants in the Control group were matched as closely as possible with participants in the FASD group by sex and age. Each group consisted of 11 boys and 8 girls. The age of participants ranged from 11.2 to 17.5. The mean age of the groups was not significantly different (*see Table 1*; $t(36) = -0.190, p = 0.85$). In the Control group, 18 participants lived with at least one biological parent, while 1 participant lived with adoptive parents. In the FASD group, 3 participants lived with a biological parent, 5 lived with adoptive parents, 9 with foster parents, and 2 with grandparents. Of these, all lived in their current family home for 2 or more years, with all but 4 in the same home for 8 or more years. Table 1 provides an overall description of participants in the study.

The parent-reported ethnicity composition of the two groups was different. Most notably, there was a larger number of Aboriginal children (including those noted to have both Aboriginal and Caucasian heritage) in the FASD group ($n = 13$) compared to the Control group ($n = 1$). The groups also differed in their mean intellectual function, with controls showing significantly higher FSIQ ($t(36) = 6.19, p < .001$). Furthermore, those with partial or full FAS had a significantly lower FSIQ ($m = 80.3, sd = 7.8$) compared to those with ARND or ARBD ($m = 91.8, sd = 9.2; t(17) = -2.950, p < .01$).

Table 1
Participant Demographic Features

	FASD	Control
Age in years (Mean [SD], Range)	14.0 (1.8), 11.7-17.5	13.8 (1.7), 11.2-17.5
Gender ratio (male: female)	11:8	11:8
K-BIT-2 FSIQ (Mean [SD], Range)	85.1 (10.1), 69-107	107.2 (11.9), 88-132
Ethnicity (number of children)		
Aboriginal	10	1
Black	0	1
Caucasian	6	17
Aboriginal & Caucasian	3	0

In the FASD group, there were a range of diagnoses on the fetal alcohol spectrum. This included 6 participants with FAS, 4 with pFAS, 7 with ARND, 1 with ARBD, and 1 with static encephalopathy and sentinel physical findings (who met study criteria under the Washington Diagnostic Code). The majority ($n = 15$) were diagnosed by a multi-disciplinary team, while the remaining were diagnosed by a pediatrician.

Six participants in the FASD group normally took psychostimulant medication, and four of these also normally took Risperidone, an antipsychotic medication (commonly used to help control aggressive behavior). Most parents were hesitant about disrupting medication schedules, therefore all but one of the participants were tested on their regular medications (see Table 2).

Table 2

Number of FASD Participants Taking Medication by Diagnostic Status

Diagnosis	Psychostimulants		Antipsychotics	
	Regularly	During Testing	Regularly	During Testing
Fetal Alcohol Syndrome	2	2	2	2
Partial Fetal Alcohol Syndrome	1	1	0	0
Alcohol-Related Neurodevelopmental Disorder	2	1	2	1
Alcohol-Related Birth Defects	0	0	0	0
Static Encephalopathy & Sentinel Physical Findings	1	1	0	0

*Materials**Probabilistic Reinforcement Learning Task*

In this computerized task, the participant was required to learn which stimulus within a pair of stimuli was associated with a higher probability of earning rewards. The stimuli consisted of two pairs of abstract multi-colored squares (see Appendix C). The squares measured 3.5 by 3.5 centimeters. They were presented in the center of the computer screen with a 3.5 centimeter space between the stimuli.

For each participant, one of the stimuli in each pair was randomly assigned to be “correct”. The task was presented in 12 blocks of 10 trials each, for a total of 120 trials. Within each block, on 70% of the trials, choosing the correct stimulus was rewarded with earning one point or token, while on 30% of the trials, choosing the correct stimuli was punished by losing one point or token. Also within each block, the “incorrect” stimulus was punished by losing one point or token on 70% of the trials, and rewarded by earning one point or token on 30% of the trials.

The pairs were presented in semi-random order, with no more than two in a row of the same pair. Within each pair, stimuli were presented with equal frequency on the left and on the right. There was a 500 millisecond inter-stimulus interval between trials

during which the result of the previous trial was presented. Positive feedback consisted of seeing the phrase “You won 1 point (or token),” along with a pleasant sound. Negative feedback consisted of seeing “You lost 1 point (or token),” along with an unpleasant sound. There were no negative scores during the task (the score never goes below zero). If a loss occurred when the participant had no points or tokens to lose the response was: “You have no points (or tokens) to lose.” The participant was required to click “OK” to begin the next trial.

The first task was preceded by a 40-trial practice task with a single pair of unique stimuli. The practice task was always conducted with points, although these points did not count towards the final tally. Following the practice, the examiner discussed the task with the participant, ensuring they understood the task. Immediately following the practice trial, the participant began either the points or the tokens condition. In the points condition, the participant earned and lost points, which accumulated on the screen in a running tally. In the tokens version, the participant earned and lost tokens, which were distributed by the examiner into a small box lid situated next to the mouse. In each condition, the participant was given 5 points or tokens to start. Half of the participants were assigned to begin with the points condition, while the other half were assigned to begin with the tokens condition. Assignment of an image pair to a particular task was counterbalanced so that half of the participants were assigned pairs 1 and 2 in the tokens condition, while the other half of the participants were assigned pairs 1 and 2 in the points condition. Between the two conditions, participants completed a subtest from the IQ test.

Task instructions, presented before the practice trial, alerted participants to the probabilistic nature of the task:

You will see two pictures on the screen at the same time. Pick one of the pictures, and then the computer will tell you if you’re right or wrong. If you’re right, you’ll earn a point/token. If you’re wrong, you’ll lose a point/token. On each turn, one picture is right, and one is wrong. As you play, you’ll start to see that one of the pictures is a better choice than the other. But it’s complicated because sometimes the one that is better actually makes you lose a point/token. And sometimes the one that is not as good actually makes you earn a point/token. Try to figure out which pictures are the best choices so you get the most points/tokens at the end. When you figure out the correct ones, then choose them every time, even

if they are sometimes wrong. Also, it doesn't matter which side of the screen you see the picture on (e.g., there is no left-right-left-right type of patterns).

The primary outcome score for this task was the percentage of trials on which the correct stimulus was chosen. A number of supplemental scores were calculated to provide a more meaningful analysis of performance. In addition to an overall score, percent correct was also calculated separately for the first and second halves of the task, so that the change in performance over time could be examined. Mean reaction time was calculated as the time (in milliseconds) taken to choose a stimulus (disregarding the first trial). Finally, feedback sensitivity - a concept described by Chamberlain and colleagues (2006) - was calculated as the overall likelihood that the participant switched from a correct to an incorrect response after receiving misleading negative feedback for that particular image pair.

Reinforcement Learning and Shifting Task.

This simultaneous categorical visual discrimination task was presented in a spiral bound booklet (22 x 13 cm), with one trial per page. On each page, one pair of stimuli was presented. The stimuli were presented in 5 x 5 cm square boxes, with a 5 cm space between the boxes. The location of each stimulus (right versus left) within each pair was varied throughout the task. Pairs were presented in a pre-arranged, semi-random order, with no more than 2 in a row of any given pair. Stimuli varied along two dimensions (either number of shapes/type of shape or color/size). There were two versions of this task. Each condition consisted of two parts: pre-switch learning, and post-switch learning (see Appendices D, E). Participants were required to learn to respond to one attribute of one dimension (e.g., always respond to large stimuli) while ignoring the other dimension (e.g., color). Following 8 in a row correct, or 8 out of 9 correct with an initial run of at least 3 correct, the rule switched without warning.

In condition A, where the type of switch was reversal, the participant learned to respond to previously non-rewarded stimuli. In this condition, rewards were initially given for responses to stimuli with two of the same shape (attend to number while ignoring shape). Following the switch, rewards were given for switching to responding to stimuli which were presented alone (continue attending to number, but switch to the

opposite stimuli). In condition B, where the post-switch task was nonreversal, participants were initially rewarded for responding to color (blue). The switch involved learning to respond to the other dimension (choose the larger stimulus, while ignoring color).

Participants were given 5 tokens at the outset of each condition. Verbal feedback was provided following each trial. In addition, participants earned one token for each correct response and lost one token for each incorrect response. The tokens earned or lost on each trial were immediately put in, or taken out of a box lid by the examiner.

A short practice test with unique stimuli preceded the first condition. The practice test involved initial discrimination only (i.e., there was no shift). Tokens were used in this task, but participants were informed that they did not count towards the final tally. If the participant had difficulty learning the discrimination in the practice test, the examiner helped by asking the participant how the pictures were different from each other. On the practice test, all participants were asked to verbalize how they figured out the pattern.

The learning score was the primary outcome measure. This score was calculated as the trial number of the last error made before reaching the run that met the learning criterion (or the last error before discontinuation if the learning criterion was not met). In the nonreversal shift, the learning score did not include initial consecutive ambiguous errors². In order to assess for loss of sustained attention, two separate scores were calculated. A participant was scored as having made an *attentional slip* if they completed a series of eight correct responses, interspersed with one incorrect response (8 out of 9 correct). Attentional slips were only counted if there were at least 3 initial correct responses, in order to reflect true attentional lapses rather than a situation where they have not yet learned the correct set. Another measure of sustained attention was *failure to maintain set* errors. A participant was scored as having made a failure to maintain set error if they completed 5 consecutive correct responses followed by one or more incorrect responses (but did not complete the set). Finally, perseverative errors were the number of unambiguous consecutive errors made where the participant continued to

² This type of error would occur on the relatively rare occasion when the first item (or consecutive series of items) after the shift was correct according to both the discrimination and the shift criteria. Therefore, the participant would not have yet received a cue indicating a shift in contingencies. This type of error would only occur on the nonreversal shifting task as the reversal shifting task involves a complete reversal of contingencies.

respond using the same criteria for discrimination when they are supposed to shift (e.g., continued to respond to large stimuli despite consistent negative feedback).

IQ Testing

All participants were administered the Kaufman Brief Intelligence Test – Second Edition (K-BIT-2; Kaufman & Kaufman, 2004) as a measure of intellectual functioning. This three-subtest test measures both verbal and nonverbal intelligence and takes about 20 minutes to complete. The verbal component included Verbal Knowledge (60 items testing receptive vocabulary and general knowledge about the world) and Riddles (48 items testing verbal comprehension, reasoning, and vocabulary knowledge). The nonverbal component was Matrices (46 items testing nonverbal observation and problem solving skills). Outcome scores included Verbal IQ, Nonverbal IQ, and a Full Scale IQ (FSIQ) Composite, all standardized based on the participant's age.

Parent Reports

Parents were asked to complete a developmental history questionnaire designed specifically for this project (see Appendix F), the multiple choice portion of the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), and the Children's Learning Questionnaire (CLQ; see Appendix G; Michel, McInerney, & Kerns, 2007). The CBCL is a standardized screening measure for children and adolescents ages 6 to 18 for assessing social-emotional and behavioral problems. Parents were asked to rate 113 items based on how true each item was for their child now or within the past 6 months on a Likert scale (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true). The composite scales of interest (standardized based on age and gender) were Aggressive Behavior, Social Problems, and Rule-Breaking Behavior. The CLQ is a 22-item questionnaire designed to assess caregiver's perceptions of a child's transfer of learning abilities in everyday life as well as the variables important for transfer to occur, such as inhibitory control and flexibility. Items are rated on a Likert scale (0 = never; 1 = rarely; 2 = sometimes; 3 = often). In addition to the overall raw score, one individual item from the CLQ was coded for analysis due to its specific reference to the overall research question ("Makes the same mistake over and over.")

Design and Procedure

Compensation

Before testing began, participants were told that if they earned “enough” tokens & points, they would be given their choice of one of the large prizes rather than a small prize. The amount required for a large prize was deliberately withheld to ensure that all participants gave their fullest effort throughout the tasks. The large prizes consisted of one of the following: (1) art set (colored pencils and oil pastels); (2) set of 3 blank journals; or (3) \$10 store gift certificate. Small prizes consisted of one of the following: (1) mini memo pad; (2) pencil; or (3) deck of cards. When testing was complete, all participants were given their choice of a large prize, regardless of the number of tokens and points earned. Parents were reimbursed for the cost of bus fare, or parking, as appropriate.

Order of Tasks

Testing typically lasted about one hour. The order of tasks was counterbalanced so that half of the participants completed the probabilistic learning task first, while the other half completed the reinforcement learning and shifting task first. In addition, within the reinforcement learning task, half of the participants completed the nonreversal shifting condition first, while the other half completed the reversal shifting condition first. In the probabilistic learning task, half of the participants completed the points condition first, while the other half completed the tokens condition first. The image pairs used were also varied, so that half of the participants received one image set in the points condition, while the other half received that same set in the tokens condition. The three subtests of the K-BIT-2 were administered between the four experimental tasks. K-BIT-2 subtests were administered in the standardized order (Verbal Knowledge, Matrices, Riddles).

Results

Summary of Statistical Analyses

Results will be discussed in three parts. The first section will present results from the probabilistic learning task. The next section will present results from the discrimination and shift learning reinforcement task. The final section will present results from the parent reports and their relationship to the experimental tasks.

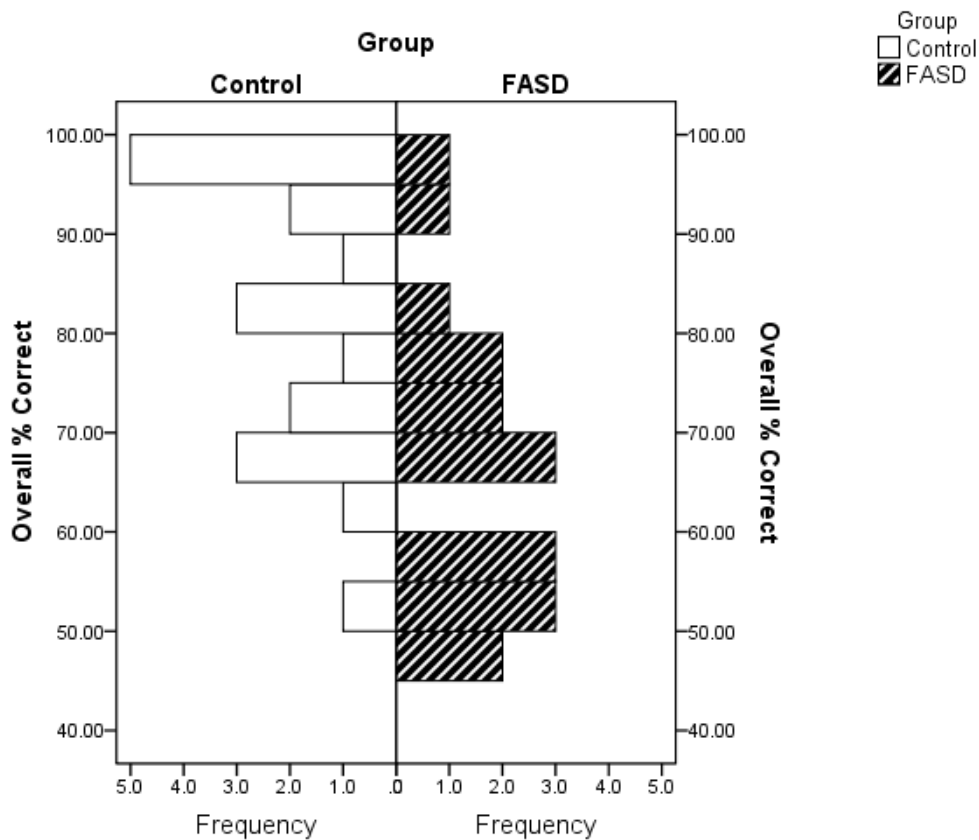
(kurtosis: -1.203; skew: 0.007; *Shapiro-Wilk*: 0.941(37), $p = .05$), it was not sufficiently deviant to violate the model's assumption of normality. A visual representation of overall scores by group is shown in a frequency distribution in Figure 1.

The overall mean score for the total sample was 73.9 ($sd = 16.3$). As hypothesized, the mean score of the Control group ($m = 81.2$, $sd = 14.2$) was significantly higher than the mean score of the FASD group ($m = 66.2$, $sd = 15.0$; $t = 3.128(35)$, $p = 0.004$, $d = 1.03$).

Overall task performance was not significantly correlated with age ($r = -0.033$, $p = 0.848$), and there was no significant difference between the performance of male and female participants ($t(35) = -0.013$, $p = 0.990$). Overall performance was somewhat better in the ARND/ARBD group compared to the pFAS/FAS group but did not reach traditional levels of significance ($t(16) = -2.008$, $p = .062$).

Figure 1

Overall Percent Correct Choices: Frequency of Scores per Group



Speed of Learning & Learning Savings (Hypothesis 1). *Speed of learning* refers to the ability to learn a task through practice (improvement as the task progresses), while *learning savings* refers to the ability to learn from previous experience (performance in the second condition compared to performance on the first condition).

To investigate learning savings, or between-condition speed of probabilistic learning, the score from the first condition administered was compared to the score from the second condition administered (regardless of type of reinforcement). Analysis was conducted using a 2 (Group: FASD vs. Controls) X 2 (Order: 1st probabilistic condition vs. 2nd probabilistic condition) mixed factor repeated measures ANOVA with Group as the between-subjects factor and Order as the within-subject factor. There was no effect of Order ($F(1,35) = 0.17, p = .682$), nor was there an interaction between Group and Order ($F(1,35) = 0.05, p = .821$). Planned comparisons revealed that the groups were significantly different in both the first ($t(35) = 2.819, p = .008$) and second ($t(35) = 2.352, p = .024$) conditions.

Another way of examining learning savings, which takes into account the overall score, is by examined by dividing the between-condition change in score by the total overall score on probabilistic learning: (Condition 2 – Condition 1)/ (Mean of Condition 1 and 2). Learning savings calculated in this way did not differ between the FASD and Control groups, $t(35) = -.154, ns$.

Speed of learning was examined by analysis of the mean difference between the first and second halves of the conditions. Distribution of this new variable was fairly normal (*Shapiro Wilk* ($df = 37$) = .948, $p = .080$; skew = 0.649; kurtosis = -0.123). Both groups showed similar improvement from the first to the second halves of the condition. The Control group showed a significant ($t(18) = -4.141, p = .001$) improvement of 10.4 percentage points ($sd = 10.9$), while the FASD group showed a significant ($t(17) = -4.439, p < .001$) improvement of 8.4 percentage points ($sd = 8.0$). Independent samples *t*-test showed that the group difference in improvement was not significant ($t = 0.609(35), p = .546$).

In order to better characterize performance, each participant was categorized as one of the following: (1) quick learner, defined as one who performed significantly above-chance in both the first 60 trials and the last 60 trials; (2) slow learner, defined as

one who only reached above-chance in the final 60 trials; and (3) non-learner, defined as one who never reached a significantly above-chance level of performance. Using the binomial distribution, for 60 trials, each with a 50% chance of correct response, a participant must have chosen the correct response on 40 or more trials in order to be significantly above chance at $p < .01$ (Lowry). This corresponds to a correct response rate of 67% or higher.

In the FASD group, 8 participants were classified as non-learners, 5 as slow learners, and 5 as quick learners. In the Control group, 2 were classified as non-learners, 5 as slow learners, and 11 as quick learners. In the Control group, one participant scored 69% in the first half, and 61% in the second half (i.e. *learned and lost*), therefore was excluded from this analysis as an anomalous outlier. Pearson's chi-square analysis revealed a nearly significant relationship between group membership and learning status ($\chi^2(2, n = 36) = 5.850, p = .054$).

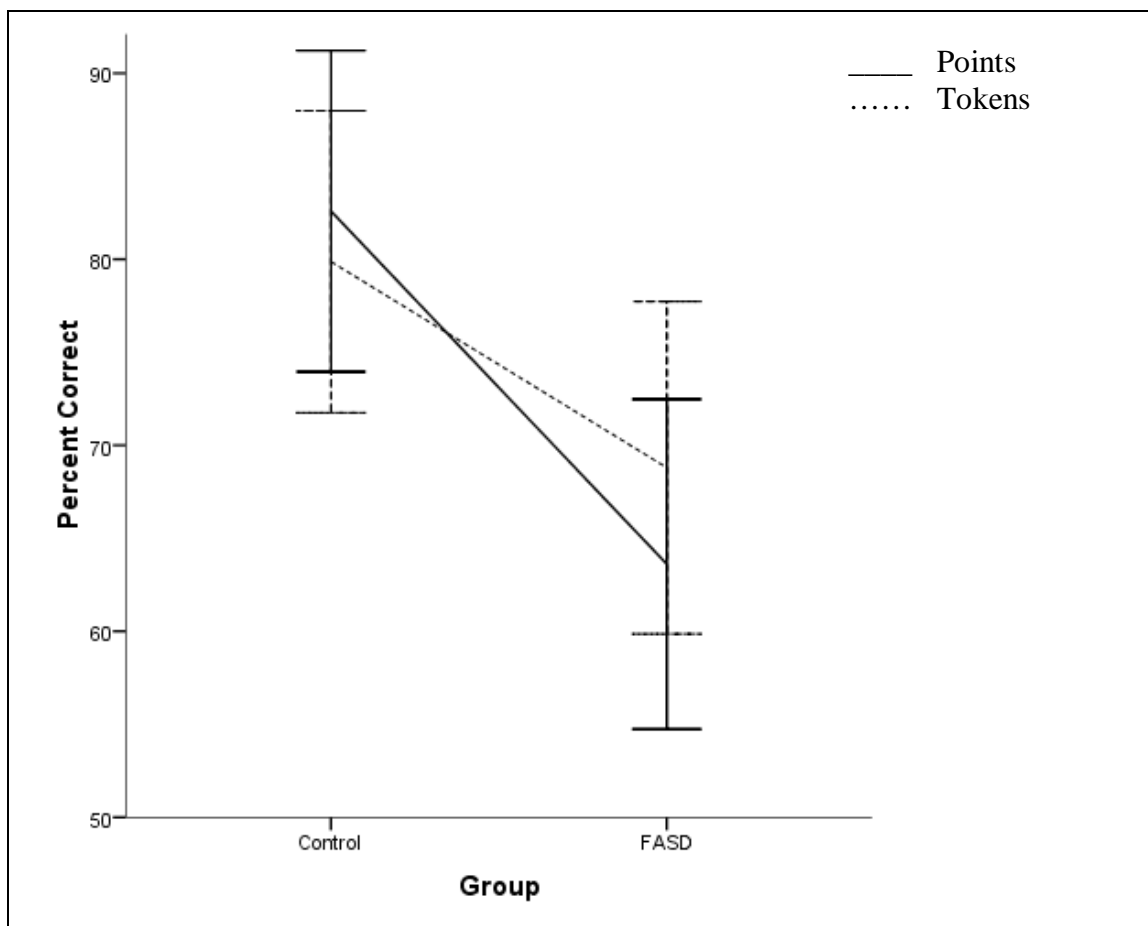
Points Versus Tokens (Hypothesis 2). Probability learning using points and probability learning using tokens were compared to assess whether there was a difference between learning under abstract (points) reinforcers versus more concrete (tokens) reinforcers, both of equal "worth."

To examine this question, a 2 (Group: FASD vs. Controls) X 2 (Condition: Tokens vs. Points) mixed factor repeated measures ANOVA was conducted with Group as the between-subjects factor and Condition as the within-subject factor. The dependent variable was defined as the percent correct choices.

Neither Condition ($F(1,35) = 0.144, p = .707$) nor Condition by Group interaction ($F(1,35) = 1.476, p = .232$) were significant (see Figure 2). As hypothesized, planned comparisons using a dependent samples t-test revealed that the Control group showed no significant difference between the Points and Tokens conditions ($t(18) = 0.592, p = .561$). Contrary to the hypothesis, however, the FASD group also did not show a significant difference between the conditions ($t(17) = -1.127, p = .275$).

Post-hoc independent samples t-test showed a significant mean group difference in the Points condition ($t(35) = 3.228, p = .003$), but failed to reach traditional significance levels in the Tokens condition ($t(35) = 1.935, p = .061$).

Figure 2

Probabilistic Learning: Points vs. Tokens

IQ. Examination of the relationship between IQ and task performance was conducted separately for both groups in order to avoid the possibility of an artificial correlation due to the significant group differences on both variables. When task scores were collapsed across conditions (overall score), each of the IQ composites was significantly positively correlated (Pearson's r) to the overall score (see Table 4).

Interestingly, when examined by order of tasks administered, percent correct on the first (but not second) task performed was significantly positively correlated with Nonverbal IQ and FSIQ in the Control group, as well as Verbal IQ, Nonverbal IQ, and FSIQ in the FASD group.

Table 4

Correlation (r) between IQ and Probabilistic Learning by Group

Condition	FASD			Control		
	FSIQ	Nonverbal IQ	Verbal IQ	FSIQ	Nonverbal IQ	Verbal IQ
First Task	0.855**	0.809**	0.745**	0.536*	0.621**	0.379
Second Task	0.460	0.416	0.421	0.367	0.258	0.377
Points	0.666*	0.570*	0.710*	0.566*	0.685**	0.372
Tokens	0.622**	0.627**	0.435	0.335	0.185	0.388
Overall	0.768**	0.714**	0.683**	0.555*	0.541*	0.464*

* $p < .05$, ** $p < .01$

Reaction Time. Although participants were not requested to respond quickly, analysis of reaction time may prove informative. In computing mean reaction time (MRT) for each condition, the first trial was excluded as instructions were given while this trial was active. A summary of MRT scores can be found in Table 5.

Table 5

Probabilistic Learning Mean Reaction Time (msec) by Group

Condition	FASD		Control	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Tokens	1442.6	464.0	1136.7	343.6
Points	1319.0	569.6	1136.0	489.1
First Task	1512.2	586.5	1175.7	417.4
Second Task	1249.3	409.0	1097.0	424.0
Overall	1380.8	456.4	1136.4	406.3

Repeated measures analysis showed that across groups, there was a significant effect of order, with faster MRT on the second task administered ($F(1,35) = 9.927$, $p = .004$, partial $\eta^2 = .21$), with no significant order by group interaction ($F(1,35) = 2.697$, $p = .110$). Participants in the Control group showed a slightly faster overall MRT compared to participants in the FASD group, although this difference was not significant ($F(1,35) = 2.967$, $p = .094$, partial $\eta^2 = .08$).

Repeated measures analysis also revealed there was no effect of condition on MRT (Tokens vs. Points; $F(1,35) = 0.969$, $p = .332$), nor was there a group by condition interaction ($F(1,35) = 0.948$, $p = .337$). Across groups, overall MRT was significantly negatively correlated with overall task performance, such that slower MRT was associated with poorer task performance ($r = -.375$, $p = .022$).

Response to Misleading Feedback. A trial was defined as providing misleading feedback if the participant chose the correct (most rewarded) stimulus, but received a response cost rather than a reward. *Percent switches following misleading trials* was defined as the percent of misleading trials where the participant switched to the incorrect stimulus on the next trial with the same image pair. The median percent of switches following misleading trials was 8.9 in the Control group (range: 1.4 – 79.8), and 35.8 in the FASD group (range: 3.0- 58.5). Due to the highly skewed nature of the data, the non-parametric Mann-Whitney test was used to examine group differences. This difference was significant ($U = 90.5, N_1 = 18, N_2 = 19, p = .014$).

Within the FASD group, percent switches following misleading trials was significantly negatively correlated with FSIQ ($r_s = -.504, p = .033$). This relationship approached significance in Controls ($r_s = -.447, p = .055$).

The majority ($n = 14$) of the Control group made this type of error on less than 25% of misleading trials. On the other hand, the majority of participants in the FASD group made this type of error on greater than 25 percent of the trials ($n = 14$; see Table 6).

Table 6

Number of Participants Switching Following Misleading Trials by Group

Percent Switches Following Misleading Trials	FASD	Control
0-10	2	10
11-25	2	4
26-50	10	3
51-100	4	2

Image Pairs. In order to ensure the validity of the findings it is important to show that probabilistic learning is of equal difficulty for each of the four image pairs used in this study. Two outliers in the Control group were identified. Both of these individuals scored extremely low on image pair 3 (2%, 13%), while scoring in the high range on all of the other image pairs (86-98%). These were clearly cases of initially choosing (and sticking with) the wrong stimuli rather than random guessing due to lack of learning or inattention. Percent correct by image pair data is presented in Table 7.

To examine the equality of image pairs, a 2 (Group: FASD vs. Controls) X 4 (Condition: Pair1 vs. Pair2 vs. Pair3 vs. Pair4) mixed factor repeated measures ANOVA was conducted with Group as the between-subjects factor and Condition as the within-subject factor. The assumption of sphericity was violated; therefore, a multivariate analysis is reported here. This analysis showed that there was no significant effect of Image Pair ($F(3,31) = 0.942, p = 0.432$), or Image Pair by Group ($F(3,31) = 1.125, p = 0.354$).

Table 7

Probabilistic Learning Percent Correct by Image Pair

Condition	FASD		Control	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Image Pair 1	64.5	21.9	85.1	16.3
Image Pair 2	65.7	17.4	86.4	12.3
Image Pair 3	67.5	20.1	76.2	22.4
Image Pair 4	67.0	15.7	84.5	15.2

Condition and Task Order. To examine the question of whether condition order (beginning with Points versus beginning with Tokens) affected performance, a 2 (Order: Points First vs. Tokens First) X 2 (Condition: Points vs. Tokens) mixed factor repeated measures ANOVA was conducted with Order as the between-subjects factor and Condition as the within-subject factor. With both groups together, there was no significant effect of Condition ($F(1,35) = 0.108, p = .744$), Order ($F(1,35) = 1.097, p = .302$), or interaction of Condition by Order ($F(1,35) = 0.159, p = .692$). Similar results were found with each group examined separately.

Another approach to examining order effects is to look at the broader task order (probabilistic task first vs. discrimination & shift task first). To do this, an independent samples t-test was conducted with the total mean probabilistic learning score (across conditions) as the dependent variable. With both the FASD and Control group examined together, there was no significant impact of task order ($t(35) = -1.315, p = 0.197$). However, when examined individually, task order approached significance in the FASD group ($t(16) = -2.034, p = 0.059, d = .93$), reflecting somewhat higher probabilistic mean scores in the group which completed the probabilistic task first ($m = 73.5, sd = 17.2$) compared to those who completed the reinforcement learning and discrimination task

first ($m = 60.3$, $sd = 10.3$). There was no impact of task order in the Control group ($t(17) = 0.190$, $p = 0.852$). This raises the possibility that prior shift learning may have interfered with probabilistic learning in the FASD group. However, within the FASD group, those who completed the shift learning task first had a lower FSIQ ($m = 81.5$, $sd = 9.5$) compared to those who completed the probabilistic learning task first ($m = 89.6$, $sd = 9.5$), though this did not reach traditional significance levels ($t(17) = -1.77$, $p = 0.093$, $d = .93$). Such spontaneous group differences in IQ may also account for the order effect. Unfortunately the sample size was too small to support a within group comparison of order effects with IQ covaried.

Part 2: Discrimination and Shift Learning

Results from this task consisted of four main variables (Condition A: Discrimination and reversal shift and condition B: Discrimination and nonreversal shift). Examination of the results showed that the data in all four conditions departed significantly from a normal distribution (*Shapiro Wilk* ($df = 38$) range 0.440 to 0.808; $p < .001$ in all conditions). Given that many participants scored at ceiling (0 to 1 errors), there was a positive skew to the data (range 0.916 to 4.767). Three outliers were identified with individual scores greater than three standard deviations from the condition mean. These included two participants from the FASD group (one in condition A discrimination, the other in condition B shift), and one participant from the Control group (condition A shift). The two outliers from the FASD group were both diagnosed with FAS, and had FSIQ scores in the 70s. Neither demonstrated consistently low discrimination and shift learning scores across all conditions. One took 11 trials to learn the discrimination, but given the low variability of the group as a whole, this was considered an outlier. The other took 96 trials to learn to shift, due to the fact he was misled by an initial run of responses which led him to believe the correct responses alternated right-left-right. The outlier from the Control group had a FSIQ of 121, and had no low scores in the other discrimination and shift learning conditions. Observation of his responses suggested he was looking for a complex rather than a simple pattern. All of the outliers eventually learned the correct rule with sufficient repetition.

Examination of the data following removal of outliers revealed improvement across all measures of normality, though significant departure from normality remained

(*Shapiro Wilk* ($df = 35$) range 0.622 to 0.822; $p < .001$ in all conditions; skew range 0.814 to 2.382). Therefore, this section will utilize non-parametric statistical tests (including all outliers).

A summary of median and interquartile range (IQR) of discrimination and shift learning scores can be found in Table 8. All participants successfully learned both discriminations and both shifts within the maximum allowable trials. Data is reported in two formats: (1) order (administered first vs. administered second); and (2) type of task (condition A: Reversal vs. condition B: Nonreversal).

Table 8

Trials to Criterion for Discrimination and Shift Learning by Group

Condition	FASD		Control	
	<i>Median</i>	<i>IQR</i>	<i>Median</i>	<i>IQR</i>
Discrimination Learning				
First	1	0 - 1.5	0	0 - 3.0
Second	1	0 - 2.0	0	0 - 1.0
Condition A	1	0 - 1.0	0	0 - 1.0
Condition B	1	0 - 3.0	0	0 - 3.0
Shift Learning				
First	3	2.0 - 11.8	4	2.0 - 6.0
Second	3	2.0 - 4.0	3	1.0 - 5.0
Reversal (A)	3	2.0 - 3.0	3	2.0 - 7.0
Non-reversal (B)	6	2.0 - 38.0	4	2.0 - 5.0

Across all conditions, participants in the FASD group made 2 attentional slips, and 2 failure to maintain set errors. Participants in the Control group made 5 attentional slips, and 3 failure to maintain set errors.

Overall performance was not significantly correlated with age for any of the four dependent variables (r_s range = -0.219 to 0.243, $N = 38$), and there was no significant difference between the performance of male and female participants (U range = 170.0 to 175.0, $N_1 = 22$, $N_2 = 16$, two tailed, *ns*).

In addition to the main outcome variables above, perseverative errors were also measured for each participant. An error was counted as perseverative if, immediately following the shift, the participant continued to respond to the old rule (e.g., “large”), instead of responding to the new rule (e.g., “blue”). The minimum number of possible

perseverative errors was 1 (the trial following the initial switch). The great majority of participants in both groups made few perseverative errors (see Table 9).

Table 9

Number of Participants Making Perseverative Errors by Group

Number of Perseverative Errors	FASD		Control	
	Reversal	Nonreversal	Reversal	Nonreversal
1 – 2	12	15	14	15
3 – 4	7	3	3	2
5 or more	0	1	2	2

Speed of learning and Learning Savings (Hypothesis 1). How fast a participant learned in a condition was reflected in the main dependent variable (last error prior to learning). Comparing the mean of the two discrimination conditions for each participant, there was no significant group (FASD vs. Controls) difference in speed of learning the discriminations ($U = 137.5$, Mean rank Controls = 17.2, Mean rank FASD = 21.8, $p = .203$, two tailed). There was also no significant group difference in speed of learning the reversal shift ($U = 141.5$, Mean rank Controls = 21.6, Mean rank FASD = 17.5, $p = .244$, two tailed), nor the nonreversal shift ($U = 131.0$, Mean rank Controls = 16.9, Mean rank FASD = 22.1, $p = .145$, two tailed).

Between-condition learning savings in the two discrimination learning conditions was examined using the Wilcoxon Signed Ranks Test. The last error before achieving the learning criterion was used as the dependent variable, comparing the first condition administered to the last condition administered. When the groups were examined separately, there was no significant difference in either the Control group ($z = -1.069$, n Ties = 7, $p = .285$) or the FASD group ($z = -0.089$, n Ties = 7, $p = .929$), nor were there significant differences when both groups were examined in one analysis.

A similar comparison of the two shift learning conditions found that there was no significant difference between the first and the last shift in the Control group ($z = -0.889$, n Ties = 0, $p = .374$), or in the FASD group ($z = -0.903$, n Ties = 6, $p = .367$).

Given this lack of group differences, investigation of the hallmark characteristics of a slow learner may shed light on inter-individual differences. In order to do this, those

participants who performed in the bottom 10% were categorized as slow learners (using controls as the normative group).

The distribution of slow learners across conditions (including those categorized as outliers) is presented in Table 10. One participant in the FASD group was slow to discriminate and slow to shift, but all others represent individual cases. The group differences in the distribution of slow and fast learners failed to reach traditional significance levels ($\chi^2(1, n = 38) = 3.199, p = .074$). There was also no significant difference between fast learners and slow learners in FSIQ ($t(13, \text{equal variances not assumed}) = 0.1359, p = 0.183$) or age ($t(36) = 0.111, p = 0.912$). The relationship between learning speed and parent reports will be examined in Part 3.

Of the 11 participants who were slow to learn in one or more conditions, five made an attentional slip or failure to maintain set error (compared to 5 of 28 in the rest of the sample).

Table 10

Number of Slow Learners by Group

Measure	FASD	Control
Discrimination		
Learning	4	1
Shift Learning		
Reversal	0	1
Non-reversal	5	1

Note: Discrimination A criteria: > 4 errors, Discrimination B criteria: > 3 errors, Reversal shift criteria: > 14 errors, Nonreversal shift criteria: > 21 errors.

Shift type (Hypothesis 2). This analysis compared the number of trials prior to reversal learning to the number of trials prior to nonreversal learning. In the Control group, there was no significant difference between performance in the two shift conditions using the Wilcoxon Signed Ranks Test ($z = -0.020, n \text{ Ties} = 0, p = .984$), but the FASD group showed significantly better scores in the reversal condition ($z = -2.692, n \text{ Ties} = 6, p = .007$), with only one participant in the FASD group showing a better score in the nonreversal compared to the reversal condition.

Shift minus Discrimination (Hypothesis 3). In order to examine whether shifting was significantly impaired after accounting for initial discrimination learning, group differences in shifting were examined with the relevant discrimination learning score

subtracted out. As with the group comparisons of shift performance, there were no significant group differences when discrimination scores were subtracted out in either the reversal task ($U = 140.5, N_1 = 19, N_2 = 19, p = .237$, two tailed), or the nonreversal task ($U = 140.5, N_1 = 19, N_2 = 19, p = .239$, two tailed).

Reinforcement Learning and IQ. In order to examine the relationship between FSIQ and reinforcement learning variables, Spearman correlations (r_s) were calculated between task performance and the three IQ variables (FSIQ, nonverbal IQ, verbal IQ). The groups were examined together as there were no significant group differences in task performance. As seen in Table 11, there were no significant correlations between IQ and trials to learn these tasks, with the exception of verbal IQ and mean discrimination learning.

Table 11

Correlation between IQ and Trials to Learn Discrimination and Shift

Condition	IQ Score		
	FSIQ	Nonverbal IQ	Verbal IQ
Discrimination	-.315	-.242	-.323*
Reversal Shift	.173	.195	.166
Nonreversal Shift	-.226	-.272	-.194
1st Discrimination	-.242	-.149	-.281
2 nd Discrimination	-.170	-.153	-.155
1 st Shift	-.039	-.159	.022
2 nd Shift	.065	.155	.008

* $p < .05$

Order of Tasks. Those who completed the probabilistic learning task prior to completing the discrimination and shift task learned the discrimination task with significantly fewer errors ($U = 95.0, N_1 = 20, N_2 = 18, p = .012$), suggesting prior probabilistic learning may have facilitated discrimination learning, while discrimination and shift learning may have interfered with probabilistic learning. The order of tasks, however, did not impact shift scores for either the reversal shift ($U = 151.5, N_1 = 20, N_2 = 18, p = .393$), or the nonreversal shift ($U = 119.5, N_1 = 20, N_2 = 18, p = .074$). There was also no significant impact of starting with reversal, or starting with nonreversal on either reversal scores ($U = 143.5, N_1 = 20, N_2 = 18, p = .274$) or nonreversal scores ($U = 127.0, N_1 = 20, N_2 = 18, p = .118$).

Relationship between Reinforcement Learning Tasks (Hypothesis 4). The two reinforcement tasks have different demands and were not designed to be directly compared. Therefore, rather than a direct comparison in task performance, this section will compare the distribution of types of learners across tasks. Tables 12 and 13 identify the frequency of being categorized as a fast, slow or non learner in the probabilistic reinforcement task based on whether the participant was a slow or fast learner in the discrimination and shift learning task.

There was no relationship in either group between speed of learning (category membership) in the probabilistic learning task and speed of learning in the discrimination and shifting task (Controls: $\chi^2(2) = 2.291, p = .318$; FASD: $\chi^2(2) = 0.686, p = .710$).

Table 12

Number of FASD Participants Grouped by Learning Speed

Discrimination & Shift Learning	Probabilistic Fast Learner	Probabilistic Slow Learner	Probabilistic Non-Learner
Slow Learner	2	3	3
Fast Learner	5	2	3

Table 13

Number of Control Participants Grouped by Learning Speed

Discrimination & Shift Learning	Probabilistic Fast Learner	Probabilistic Slow Learner	Probabilistic Non-Learner
Slow Learner	3	0	0
Fast Learner	8	5	2

Part 3: Reinforcement Learning and Parent Reports

Parent reports from two participants (in the FASD group) were unavailable due to loss in the mail. T-scores from the a priori CBCL scales of interest (Aggressive Behavior, Rule Breaking Behavior, and Social Problems) are presented in Table 14. T-scores ($m = 50, sd = 10, \text{minimum score} = 50$) are presented for the CBCL. On the CBCL scales, a score less than 67 is considered in the *normal* range, 67 to 69 is considered *subclinical* and 70 or higher is considered to be in the *clinical* range. As the CLQ is an experimental

measure without normative data, raw scores are presented. On each of the scales, independent samples t-tests showed that group differences are significant at $p < .001$.

Table 14

Parent Reported Social and Behavioral Functioning by Group

Scale	FASD		Control		<i>t</i> score (df)
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
CLQ (Raw score)	27.1	9.6	53.4	5.8	3.128 (35)***
CBCL Aggressive	66.0	11.9	53.6	5.6	-3.901 (22)***
CBCL Rule Breaking	66.5	8.1	52.8	4.0	-6.332 (23)***
CBCL Social Problems	68.2	9.7	54.1	5.1	-5.387 (24)***

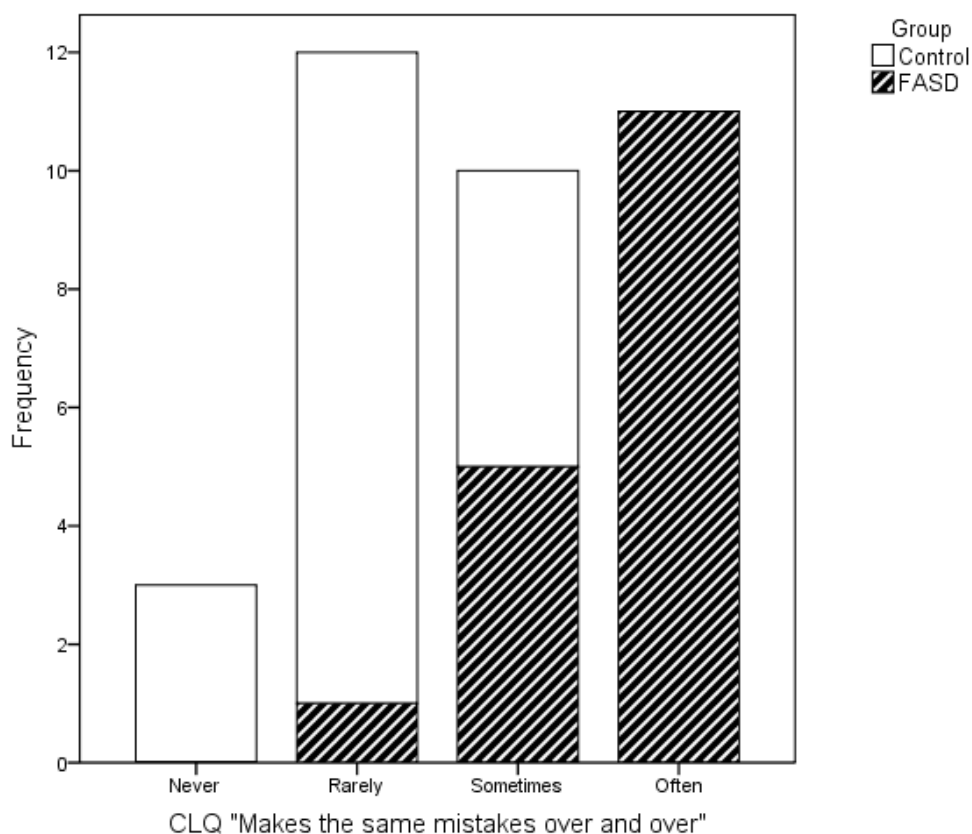
Note: CLQ: Children's Learning Questionnaire; CBCL: Child Behavior Checklist

* $p < .05$, ** $p < .01$, *** $p < .001$

One item on the CLQ was particularly relevant for this study: "Makes the same mistake over and over again." As expected, parents of children in the FASD group ranked their children significantly higher on this item than parents of children in the Control group ($t(34) = 6.946$, $p < .001$). In fact, at the most extreme ends of the spectrum, there was almost no overlap between groups (see Figure 3). There was no significant difference between discrimination and shift slow learners versus fast learners on mean CLQ item 19 scores, $t(34) = -.733$, *ns*. Neither were there significant differences between probabilistic non-learners, slow learners, and fast learners in either the Control group, $F(2, 15) = 2.718$, *ns*, or the FASD group, $F(2, 13) = .140$, *ns*.

Figure 3

Participant Ratings on Item 19 of the CLQ by Group



Parent Reports and Probabilistic Learning. When examined separately by group, neither the Control nor the FASD group showed any significant correlations between any of the a priori identified parent reported subscales of the CBCL (Aggression, Social problems, Rule Breaking) and probabilistic learning performance. Nor was response to misleading feedback significantly correlated with a priori identified parent reports in either the Control group (r range $-.035$ to $.119$, ns) or the FASD group (r range $-.399$ to $.001$, ns). However, when the remaining five subscales were examined for exploratory purposes, the FASD group showed significant correlations between task performance and Anxiety/Depression ($r = .702$, $p = .002$), and Withdrawal/Depression ($r = .745$, $p = .001$). In all cases, higher levels of problems on these scales were associated with better scores in the probabilistic learning task. The Control group did not show any significant correlations between task performance and the remaining subscales.

For exploratory purposes, in order to make sense of these unexpected findings, correlations were calculated with each of the CBCL subscales and FSIQ. In the Control group, there were no significant correlations (r range $-.040$ to $-.402$). In the FASD group, FSIQ was significantly positively correlated with three of the internalizing subscales including Anxiety/Depression ($r = .562, p = .019$), Withdrawal/Depression ($r = .702, p = .002$), and Somatic Problems ($r = .636, p = .006$). This suggests that perhaps intelligence moderates the relationship between CBCL internalizing symptoms and probabilistic learning scores. Also in the FASD (but not the Control) group, Anxiety/Depression and Withdrawal/Depression (but not the CLQ or other CBCL scales) were significantly negatively correlated with the percent of misleading trials where the participant was misled by the incorrect feedback ($r = -.517, p = .040, r = -.612, p = .012$, respectively).

One-way ANOVAs were conducted with parent-reported scores (CLQ, CBCL) as the dependent variables, and learning category (quick, slow or non-learners) as the independent variables. No parent-reported score was significantly associated with learning speed category.

Parent Reports and Discrimination Learning/Shifting Performance. With no significant group difference in discrimination and shift learning, the two groups were examined together. No parent reports were significantly correlated with discrimination learning or shift learning scores (see Tables 15). There was a trend ($r_s = -.308, p = .068$) towards a negative correlation between CLQ scores and mean discrimination scores (better transfer of learning was associated with less errors to learn the discriminations).

Independent samples t-tests showed that among parent reports, only CLQ scores were significantly different between fast and slow learners on the discrimination and shift task ($t(34) = 2.238, p = .032$). Slow learners had a mean CLQ score of 32.2 (sd 15.0), while fast learners had a mean CLQ score of 44.4 (sd 14.4).

Summary of Results

Overall, the Control group showed faster probabilistic learning compared to the FASD group, but not faster categorical discrimination and shift learning. Those individuals who had difficulty with one task did not necessarily have difficulty with the other task.

Although probabilistic learning was significantly lower in the FASD group, both groups demonstrated a similar pattern of performance. Both groups evidenced improvement throughout the task. Moreover, neither group appeared to show a significant difference in performance as a result of the abstractness of the reinforcer.

In the discrimination and shift learning task, there were no between-group differences. Within-group analysis revealed that the FASD group performed significantly faster reversal shifts compared to nonreversal shifts while the Control group performed equally in the two conditions. There were no significant correlations between task performance and a priori identified parent reports.

Discussion

This dissertation investigated various aspects of reinforcement learning in children and adolescents affected by FASD in comparison to Controls matched for age and gender. This goal of this research was to empirically test the commonly held clinical wisdom that individuals with FASD do not learn from behavioral consequences. To this end, participants completed two experimental tasks of simultaneous visual discrimination reinforcement learning. In the first, a computerized probabilistic learning task was administered to each participant twice, once with tokens as the reinforcer, and once with points on the screen as the reinforcer. The second task assessed categorical discrimination and shift learning. This task was also administered twice, utilizing both a reversal and a nonreversal shift with tokens as the reinforcer. Finally, parents completed questionnaires in order to examine the relationship between reinforcement learning and everyday behavioral and social functioning. It was hypothesized that (1) the FASD group would show impaired reinforcement learning and shifting; (2) the FASD group would respond differently to the abstractness of reinforcers compared to the Control group; and (3) parent reports would predict reinforcement learning and shifting.

Overall Reinforcement Learning

Research suggests that fetal alcohol exposure may be associated with damage to or dysfunction of the mesolimbic dopamine system, a key system in reinforcement learning. Although there is a large body of animal research which has examined the impact of fetal alcohol exposure on reinforcement learning (with variable results), there is very little research in fetal-alcohol affected humans. Despite the lack of research support,

the notion that children with FASD are not able to learn from behavioral consequences is frequently repeated to parents and other caregivers. The goal of the current study was to begin to examine various aspects of reinforcement learning in children and adolescents with FASD.

The probabilistic learning task and the discrimination portion of the categorical learning task both assessed basic reinforcement learning - the ability to learn in response to rewards and consequences. As hypothesized, the FASD group showed significantly weaker probabilistic reinforcement learning compared to the Control group. The effect size for this group difference was large, suggesting a meaningful difference in probabilistic reinforcement learning between the two groups. However, there were no group differences in the discrimination component of the categorical learning task.

Why the discrepancy between the two reinforcement learning tasks? In fact, there was no significant correlation between performance on the probabilistic task and performance on the discrimination and shift learning tasks. Those participants who were slow learners on one task were not necessarily slow learners on the other task.

The results might best be interpreted using Ashby and colleagues' rule-based versus implicit learning systems (Ashby, Alfonso-Reese, Turken, & Waldron, 1998). Both the probabilistic and the categorical discrimination learning tasks primarily draw on a rule-based system as the rules are verbalizable and can be discovered using explicit hypothesis testing. However, compared to the probabilistic learning task, the categorical learning task has a more readily verbalizable solution which can be uncovered in as little as two trials. In contrast, the probabilistic learning task requires integration over many more trials, and its solution is less easily verbalizable. Therefore, the probabilistic learning task provides a greater challenge to the rule-based system. According to Ashby, young children tend to rely on the implicit system. To extend this logic, older children with developmental or acquired damage to the brain regions which support the rule-based system would also tend to rely on the less-efficient implicit system, particularly for difficult tasks. In fact, in the probabilistic learning task, participants in the FASD group more frequently changed from a correct response to an incorrect response based on misleading feedback compared to the Control group. In other words, they were more likely to be guided by recent information, rather than proceeding based on integration

over multiple trials (as would be expected if they were using an explicit hypothesis testing approach).

Another possible explanation for the difference between tasks could be that differences in the mode of task presentation may have impacted the results. The discrimination and shift learning task required the participant to wait for the examiner's response after each trial. Typically, participants would physically move their gaze from the stimulus book to look at either the examiner or the tokens after each trial. Compared to the self-paced computerized probabilistic task, the discrimination and shift learning task may have been less impacted by impulsive responding. However, this is not supported by task analysis. Across groups, faster MRT in the probabilistic task was associated with better task performance, presumably because once the participant learned the best response, they responded faster and more accurately. This suggests that poor probabilistic performance can not be explained by impulsive (quick) responding.

Finally, it is possible that there was a ceiling effect on the categorical learning task. In support of this notion, the data were highly skewed towards maximal performance (in the direction of zero errors), with violation of the assumption of normality sufficiently strong so as to preclude parametric analysis.

To help put the reinforcement learning findings from this study in a broader perspective, the results can be compared to expected patterns for general (non-reinforced) learning in individuals with FASD. There is strong evidence that FASD is associated with a general slow speed of learning. That is, children with FASD are able to learn from repetition, although they take longer (more repetition), and overall learn less. If FASD were associated with a true dysfunction of the reinforcement learning system, reinforcement learning would be expected to take a different pattern (e.g., very slow learning curve, flat learning curve). Taking a closer look at probabilistic learning in the current study, the groups showed similar rates of improvement from the first to the second halves of the probabilistic tasks (speed of learning), while neither group showed significant improvement between the first and second probabilistic condition (learning savings). In addition, both groups demonstrated a significant correlation between intelligence and performance in the first (but not the second) probabilistic task suggesting that how quick one "catches on" to learn a novel reinforcement task is associated strongly

with intelligence. Together, these findings suggest that probabilistic learning in children with FASD proceeds in a manner similar to general learning – it is slower, but not abnormal in process – and it is strongly influenced by the most recent information. Slower but not dysfunctional reinforcement learning is consistent with Kodituwakku’s suggestion that impaired reversal learning was due to slow (not deficient) skills.

Shift Learning

Successful navigation of life’s challenges involves not only the efficient formation of response-reinforcement associations, but also the ability to modify behavior in response to changes in emotionally salient contingencies. Although there is a large body of animal and human research to support the notion that fetal alcohol exposure is associated with impairments in cognitive set shifting (i.e., cool executive functioning), the current study is only the second study to evaluate shifting in response to reinforcement (i.e., hot executive function) in children with FASD. It is also the first designed to directly compare two types of shifts (reversals and nonreversals) in this population. Specific predictions for the pattern of group differences in shifting performance were based on the premise that children with FASD would demonstrate a pattern of performance typical of younger children (equivalent reversal and nonreversal shift learning), while the Control group would demonstrate an age-appropriate pattern (reversal faster than nonreversal). Contrary to hypotheses, there were no group differences in shift learning. Surprisingly, the current study found that FASD group showed the “typical” pattern of faster reversal shifts compared to nonreversal shifts, while the Control group demonstrated equal performance in the two types of shifts. The lack of expected group differences in shifting, and the finding that the Control group showed equivalent performance in the two shift conditions may be explained by a ceiling effect, most readily apparent in the Control group.

There is evidence of reversal learning impairments in a number of patient populations including individuals with damage to the temporal and frontal lobes (Rolls, Hornak, Wade, & McGrath, 1994; Swainson et al., 2000), adults with Parkinson’s Disease (Swainson et al., 2000), and individuals with psychopathy (D. G. V. Mitchell, Colledge, Leonard, & Blair, 2002). Furthermore, Kodituwakku and colleagues (2001) found that children and adolescents with FASD had more difficulty with visual

discrimination and reversal learning while the current study did not. This could be accounted for by the types of stimuli utilized in the tasks. Stimuli in the Kodituwakku study were abstract fractal images, requiring attention to visual detail, similar to the probabilistic learning stimuli in the current study. In contrast, stimuli in the current study were composed of common shapes and solid colors. The highly abstract nature of the stimuli in Kodituwakku's study may have made the rule difficult to verbalize, therefore providing a stronger challenge to the rule-based system. This would fit with the finding in Kodituwakku's study that children in that FASD group were slower than their peers to learn to discriminate the correct response, and also showed fewer reversals in the allotted number of trials.

Concreteness of Reinforcers

The token economy is a behavioral management system frequently employed with individuals with special needs such as intellectual disability, ADHD, autism, and behavioral disorders. In this system, individuals earn and may also lose tokens based on a formal set of rules. Tokens are typically traded for rewards including tangible goods or privileges. Furthermore, systems of rewards and punishments are frequently advocated for typically-developing children to promote prosocial behavior and reduce unwanted behavioral problems (e.g., Phelan, 2004; Webster-Stratton, 2006). In addition to formal contingency management systems, successful navigation of everyday life requires learning from one's own mistakes and successes based on both tangible/concrete (e.g., being given a cookie for doing a chore, burning your hand after touching a hot stove) and intangible/abstract (e.g., praise, disapproving looks) reinforcement.

One goal of the present study was to test whether speed of reinforcement learning differed based on the concreteness of the reinforcers when both were worth the same amount toward a final reward. It was hypothesized that the FASD group would respond differently to the two conditions, while the Control group would not. The direction of the hypothesis was not specified, as a dysfunctional reinforcement learning system could cause impairment in either direction.

The type of reinforcers used in this study were chosen for ease of comparison with typical reinforcers used in the daily lives of children, as well as in research settings. A more direct method of addressing the importance of concreteness in reinforcement

might utilize first order reinforcers such as candy or coins rather than points and tokens. While this would be an interesting research question, its value in terms of external validity is questionable (a typical behavioral intervention is not likely to use candy or money as a reinforcer). Therefore, points and tokens were chosen both for their functional equivalency (they were “worth” the same amount towards a prize) and their applicability to everyday settings.

As expected, the Control group showed equivalent performance regardless of the abstractness of the reinforcers. Unexpectedly, the FASD group also showed no difference between the two conditions. Due to the fact that the Control group demonstrated a slightly higher mean score in the Points condition compared to the Tokens condition, while the FASD group showed the opposite pattern, the group difference in performance was no longer significant in the Tokens condition. This does raise the possibility that with a larger sample size, significant findings may emerge. However, lack of within-group differences in both groups means that the current study must conclude that neither type of reinforcement is more effective than the other. Although individuals with FASD are frequently noted to have difficulty with abstract concepts, this difficulty does not appear to extend to abstractness of reinforcers. The findings here further support the notion that reinforcement learning mechanisms in individuals with FASD are not fundamentally different from those of matched Controls.

Limitations and Directions for Future Research

Although their exact mechanism is unknown, psychostimulant medications which facilitate release and block re-uptake of the neurotransmitters norepinephrine and dopamine have been found to be effective in treating ADHD, which is frequently comorbid with FASD (Conners, 2002; Pliszka, 2006). It has been suggested that psychomotor stimulants alter the neurochemistry of the striatum causing behavior to come under increasing control by reinforcement contingencies (Taylor, Jentsch, Solanto, Arnsten, & Castellanos, 2001). Also, psychostimulants may improve response to reinforcement indirectly through increased attention and concentration. In contrast, Risperidone, the atypical antipsychotic prescribed to four participants in the FASD group (in combination with psychostimulants in every case, although one had abstained for 24 hours), is a dopamine antagonist with high affinity for D2 dopaminergic receptors

(Gelenberg & Bassuk, 1997). Medication status of participants in the FASD group could have impacted performance on the reinforcement tasks in this study. Unfortunately, previous research does not provide sufficient guidance to predict how these medications might or might not impact reinforcement learning. Ideally, medication status would have been consistent across participants. Alternatively, with a larger sample size, medication status could be examined as a variable of interest.

The reinforcement learning tasks in this study included both reward and response cost. Research from patients with Parkinson's disease has shown that increasing levels of dopamine facilitated learning from rewards, while the natural decreased levels of dopamine associated with the disease may actually facilitate learning from response costs (Frank, Seeberger, & O'Reilly, 2004). As the current study was not designed to compare methods of reinforcement, there is no way to know whether using both types of reinforcement might obscure deficits in learning from one or the other. As the introduction to this dissertation revealed, there is insufficient information regarding the impact of fetal alcohol on the dopamine system. With insufficient information to make an informed hypothesis, this line of inquiry was not followed.

This study was designed to investigate various aspects of reinforcement learning, both within and between groups. As such there was no condition without reinforcement. A no-reinforcement baseline condition would be very useful in separating learning in general from reinforcement learning. However, given that a no-reinforcement condition could be seen as withdrawal of reward (i.e. punishment), this type of study may be best examined using subgroups, each assigned to separate conditions. With the small sample size in the current study, this type of design was not feasible.

An unfortunate limitation to this study was the ceiling effect in discrimination and shift learning. Both groups performed near ceiling suggesting that the discrimination task was too simple, perhaps limiting ability to see differences. Shifting was somewhat more variable in the FASD group, such that they demonstrated the age-expected pattern of reversals faster than nonreversals. The Control group, on the other hand, performed near ceiling in both shift tasks making it difficult to interpret the results. Future studies which utilize a more challenging task would be useful in order to provide more information on shift learning. Another aspect of the discrimination and shift learning task which had the

possibility of being problematic was that the assignment of particular sets of stimuli to the categorical discrimination tasks were fixed. In other words, the same pairs of stimuli (and rules for correct choices) were always utilized in the reversal condition, while another set was always utilized in the nonreversal condition. Therefore, dimensional preferences could have had an impact on the results. Learning may be facilitated as a result of a preference for the relevant dimension (reviewed in Esposito, 1975). However, Schmittman and colleagues (Schmittmann, Visser, & Raijmakers, 2006) demonstrated that while younger children showed clear dimension preference, children 11 and older showed no significant learning differences between dimensions. Moreover, in the current study, there was no difference between discrimination learning in condition A and condition B, which suggests that there was also likely no strong dimensional preference affecting the shift condition.

An important limitation to the generalizability of this study is the representativeness of the groups. For instance, all participants in the FASD group lived in stable home situations at the time of testing (with only 1 child in the same home less than 4 years). In order to minimize self selection of only children from the most stable families, and to make participation open to the broadest range of children, testing was frequently conducted in the family's home, or in a location close to their home. Nonetheless, the practicalities of participating in research meant children in stable homes were more likely to participate.

Individuals with FASD are a diverse group with varying levels of cognitive ability. The current study included participants with all diagnoses on the fetal alcohol spectrum, but without significant intellectual deficits. This increased generalizability across the fetal alcohol spectrum and helped assure that any differences were not due to a lack of understanding the task directions. However, the current findings do not necessarily generalize to individuals with FASD who have intellectual disabilities. Due to the small sample size and the fact that the groups were not matched for IQ, this study was unable to determine if the findings were due to prenatal alcohol exposure or merely lower IQ in the FASD group. Significant group differences in IQ, and the high correlation between IQ and task performance meant that statistically controlling for IQ would have removed the variation associated with task performance. In addition, it has been argued

that IQ should not be used as a covariate in neurodevelopmental disabilities (Dennis et al., 2009). Intellectual disability is characteristic of FASD, and therefore partialling out the effects of intelligence would remove some of the true effects of prenatal alcohol exposure. Future studies should examine reinforcement learning in children with FASD and IQ-matched Controls without alcohol exposure to determine if the learning difference is alcohol related or is simply a function of lower IQ. Another important limitation to this sample was that the groups were not matched for ethnicity. Future studies would benefit from matching for ethnicity in order to ensure that group differences are not influenced by ethnic differences.

The current study was designed to tap into basic reinforcement learning mechanisms in a laboratory setting. While the benefit of this type of research is the ability to isolate aspects of reinforcement learning, there are also drawbacks. This type of research takes place in a highly controlled environment, with specific task instructions, one-on-one interactions, and generally a lack of distractions, all of which are far from the daily reality of a typical child. Given that the current study found slow but not fundamentally altered reinforcement learning systems in individuals with FASD, it would be interesting to examine responses to behavioral consequences in a natural environment. Given the large amount of inter-individual variation in children with FASD, an A-B-A design, where the target behavior is measured for each individual before, during and after an intervention, would be an appropriate research design. Having children with FASD serve as their own control group would also be useful due to the difficulty of matching children with FASD to peers with similar family, ethnic, and SES backgrounds.

Clinical Implications

The ultimate goals of identifying and understanding the sequelae of fetal alcohol exposure are to increase diagnostic accuracy and inform interventions. Accurate diagnosis and targeted interventions may in turn contribute to the prevention of secondary disabilities, improve quality of life for affected individuals and their families, and reduce the tremendous cost of health care, social services, and other expenses associated with the disorder.

Reinforcement learning was chosen as a focus for this study because it is a function often cited as deficient in individuals with FASD, but which has received

minimal research attention in the human population. Outside of reinforcement learning, there is strong evidence from research into learning in general (reviewed in this dissertation) that although individuals with FASD are typically slow to learn, learning with repetition does occur, and retention of learned information is generally intact. The current study suggests that reinforcement learning may work in the same way: reinforcement learning may be slow, but learning does occur, with learning typically guided by the most recent information. There is no evidence that reinforcement learning mechanisms are fundamentally altered in individuals with FASD.

This conclusion leads to two main clinical implications. First, it supports the notion that individuals with fetal alcohol exposure *can* learn from the consequences of their behavior. As such, behavioral interventions should not be automatically ruled out as an option for intervention. However, the second and equally important conclusion is that *learning from reinforcement will take individuals with FASD more repetition*. Without this knowledge, frustration and hopelessness (and giving up) may set in before learning takes place.

There is much variability under the fetal alcohol spectrum, and therefore these findings must not be over-generalized to apply to all individuals with FASD. For example, given the within-group positive correlation between probabilistic reinforcement learning and intellectual function, the findings of this study may not necessarily apply to individuals with FASD who have intellectual impairments. Even within the current sample population of individuals with IQs above the cutoff for intellectual impairment, there was a subgroup of non-learners, the majority of them in the FASD group. It may be that these children would have learned if given even more repetition than was available in this study, or it may be that they would not have learned at all. This highlights the variability in the population, and means that there is no one solution that will fit for all children.

Another important caveat is that reinforcement learning is only one piece of what is required for successful behavioral interventions. Behavioral interventions could fail for a number of reasons, even in the context of intact reinforcement learning. For example, there could be problems with the application of the intervention. Children with FASD often experience chaotic environments, multiple home placements, or other challenging

situations which could be associated with inconsistent reinforcement, unclear expectations, unrealistic expectations, etc. In addition, children with FASD are frequently cited as having difficulty with transfer of learning, as can be seen from parent reports in the current study and in McInerney (2007). Therefore, learning consequences in one particular environment (the classroom), may not generalize to another environment (a different classroom or the playground). Furthermore, problems with impulsivity, or acting without thinking, mean that learned consequences do not always successfully guide behavior. Finally, children may have difficulty applying learned consequences to complex situations with multiple demands. Clearly, the findings from this study are but one piece of the puzzle in understanding reinforcement learning mechanisms in children with FASD.

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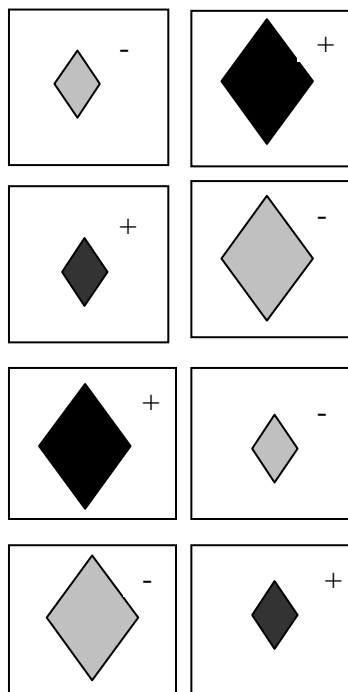
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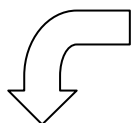
Appendix A

DISCRIMINATION

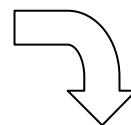
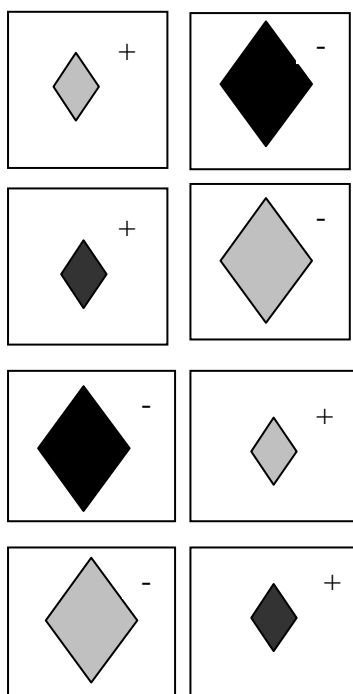


+ Rewarded

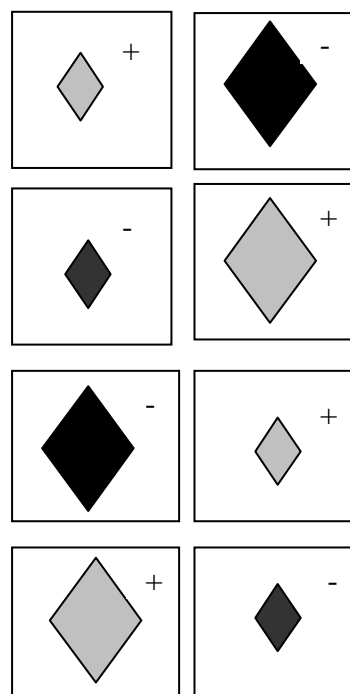
- Non-rewarded



NONREVERSAL SHIFT



REVERSAL SHIFT



Appendix B

University of Victoria
Department of Psychology

Parent Consent Form

Reinforcement Learning in Children and Adolescents with Fetal Alcohol Spectrum Disorder

Your child is being invited to participate in a study entitled Reinforcement Learning in Children and Adolescents with Fetal Alcohol Spectrum Disorder (FASD). This study is being conducted by Jen Michel, a graduate student in clinical psychology and will be used as part of her doctoral dissertation.

As a graduate student, I am required to conduct research as part of the requirements for a Ph.D. in clinical neuropsychology. This research is being conducted under the supervision of my supervisor, Dr. Kimberly Kerns.

As children with FASD are noted to have difficulty with trial and error learning, the purpose of this research project is to evaluate reinforcement learning in children and adolescents with FASD (in comparison to typically-developing children and adolescents). The types of tasks used in this study are laboratory models for behavioral interventions which utilize rewards and response costs (consequences). Therefore, they will be useful in examining responsiveness to such interventions.

If you voluntarily agree to allow your child to participate in this research, your child will complete a series of tasks, which in total will take about 1 ½ hours and will take place at the University of Victoria unless other arrangements have been made with you. Parents are responsible for transportation to and from the site of testing. The tasks involve responding to visual stimuli presented in a booklet and on the computer. Another task (a test of verbal and visual reasoning) involves answering some questions. Participants will have the opportunity to earn a prize, which will be given directly to the participant at the end of the testing session. You will be asked to complete a series of questionnaires WHICH INCLUDE PARENT INFORMATION AND your child's history and behavior. THESE QUESTIONNAIRES TYPICALLY TAKE ABOUT 20-35 MINUTES TO COMPLETE. YOU MAY CHOOSE TO WITHDRAW YOUR PARTICIPATION BY CHOOSING TO NOT ANSWER QUESTIONS, OR BY CHOOSING NOT TO COMPLETE ANY OR ALL OF THE QUESTIONNAIRES.

It is important for you to know that it is unethical to provide undue compensation or inducements to research participants and, if you agree to allow your child to participate in this study, the form of compensation discussed above must not be coercive to you or your child. If you or your child would participate solely for the compensation offered, then you should decline.

Your child will be asked to sign a similar consent form indicating their willingness to participate in this study, and you will receive a copy of that form. Participation is entirely voluntary. Participants will be allowed to withdraw from the study at any time without explanation, with the

option of having all relevant data destroyed. If they withdraw, they will still earn a prize. There are no known or anticipated risks or adverse consequences to participation or nonparticipation in this research.

Participant's anonymity will be guaranteed by using code numbers, rather than names, to identify the results obtained from individual participants. Raw data will be kept in a locked filing cabinet. Only the primary investigator and her supervisor will have access to raw data. The key linking code numbers with individual participants will be stored in a password-protected data file, and will be deleted one year following completion of data analysis. Original paperwork will be shredded by the principal investigator at the same time. Anonymous data will be stored in a password-protected computer file indefinitely. If the information gathered from this research study is used for publication (such as in a journal or at a scholarly meeting) individual names or identifying information will not be included.

You may contact the researcher, Jen Michel, at 250-472-4195, or her supervisor, Dr. Kerns, at 250-721-7553 if you have any questions. In addition, you may verify the ethical approval of this study, or raise any concerns you might have, by contacting the Human Research Ethics Office at the University of Victoria (250-472-4545).

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Name of Child Participant

Parent Signature

Date

Name of Parent

A copy of this consent will be left with you, and a copy will be taken by the researcher.

CHILDREN'S CONSENT FORM FOR PARTICIPATION IN THE STUDY

Your name: _____.

You met with Jen Michel today. She is a student in psychology at the University of Victoria who works with Dr. Kerns. By signing this sheet, you agree to do some activities with Jen which will take about 1 $\frac{1}{2}$ hours. Some of the activities will be on the computer, and some you will do with Jen at a table. They involve things like answering questions, and learning to choose one kind of picture over another. Doing these activities will help researchers to understand more about how young people learn.

If you decide at any time that you no longer want to do these activities, just tell Jen and she will let you leave with whatever reward you have already earned. If you choose to stop, you don't have to explain yourself.

Nothing you do here today will affect your grades in school or your health.

All of your "data" (scores, numbers, and any other information) collected from you today will remain confidential - that means no one (except Jen and Dr. Kerns) will be able to know your name, or know what kind of scores you received. In fact, instead of using your name, they will use a "secret code." After one year, anything with your name on it, and the original paperwork, will all be destroyed.

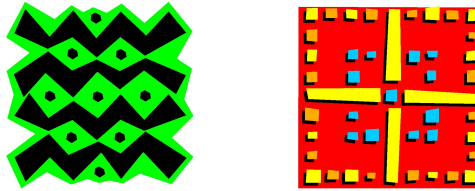
If you have any questions, you or your parents can call Jen at 250-472-4195 or her supervisor, Dr. Kimberly Kerns at 250- 721-7553.

Date: _____

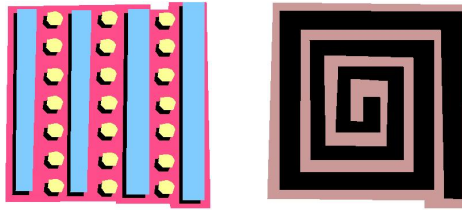
My Name: _____

Appendix C

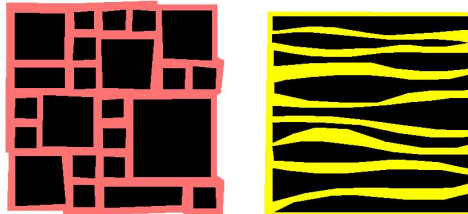
Probabilistic Learning: Practice Stimuli



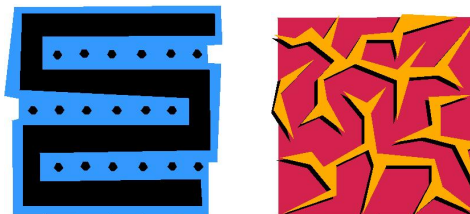
Probabilistic Learning: Set 1



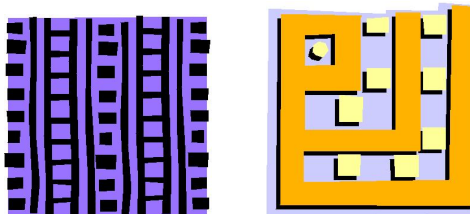
Probabilistic Learning: Set 2



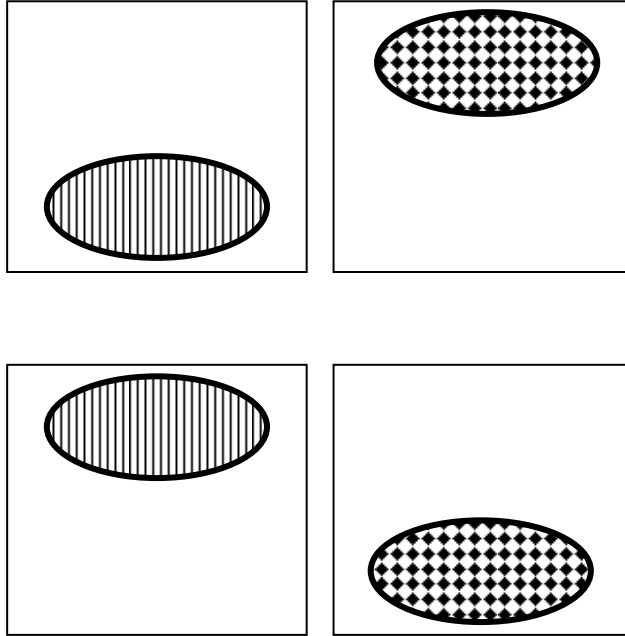
Probabilistic Learning: Set 3



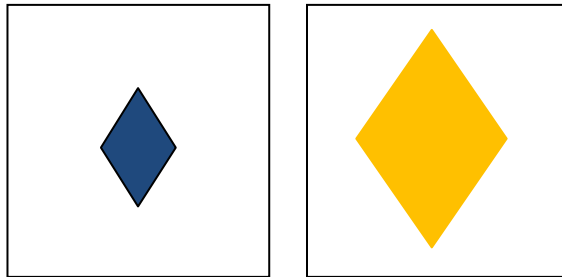
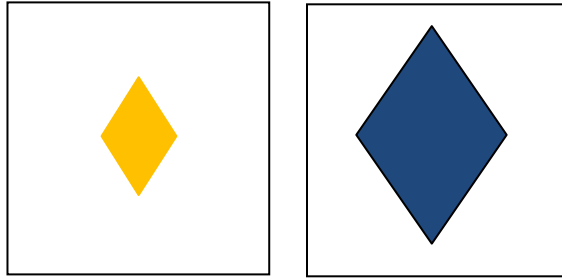
Probabilistic Learning: Set 4



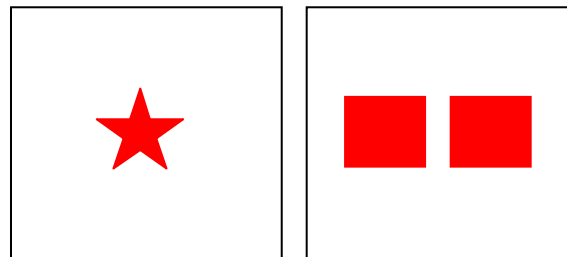
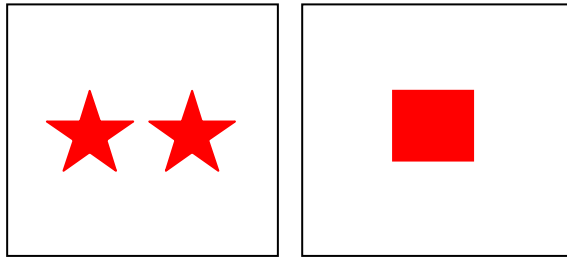
Appendix D
Practice Stimuli



Appendix E
Nonreversal (Attentional) Shifting Stimuli



Reversal (Affective) Shifting Stimuli



Appendix F
Developmental Questionnaire

Subject ID: _____
Today's Date: _____

1. Child's gender

- Male
 Female

2. Child's date of birth

Current age: _____

Month: _____

Day: _____

Year: _____

3. Child's race/ethnicity (check all that apply)

- Aboriginal/First Nation/Native American
 Asian/Pacific Islander
 Black
 Hispanic
 White
 Other _____

4. Your relationship to the child

- Biological or step-parent
 Adoptive parent. How long since the adoption? _____
 Foster parent. How long have you fostered this child? _____
 Other, please describe: _____

5. Were any prescription or nonprescription medications used by the child's biological mother during pregnancy?

- Yes
 No
 Don't know

If yes, please describe the medications and the reasons for use: _____

6. Please indicate the alcohol consumption by the child's biological mother in the month prior to pregnancy. Please complete the following table:

	Beer	Wine	Hard Liquor
None	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Less than 1 drink per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
1 - 2 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 - 7 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
More than 7 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Don't Know	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

At any point during the month prior to pregnancy was the alcohol intake 3 drinks per week or greater?

___ Yes

___ No

7. Please indicate the alcohol consumption by the child's biological mother during pregnancy.

Please complete the following table:

	Beer	Wine	Hard Liquor
None	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Less than 1 drink per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
1 - 2 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 - 7 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
More than 7 drinks per week	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Don't Know	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

At any point during pregnancy was the alcohol intake 3 drinks per week or greater?

___ Yes

___ No

If alcohol was consumed, at what time during pregnancy was alcohol consumed? (check all that apply)

- 1st trimester
- 2nd trimester
- 3rd trimester
- Don't know

8. Were any street drugs (e.g., marijuana, cocaine, other) used at any time during pregnancy?

- Yes
- No
- Don't know

If yes, at what time during pregnancy were drugs consumed? (check all that apply)

- 1st trimester
- 2nd trimester
- 3rd trimester
- Don't know

Which drug(s) were used? _____

How often? _____

9. Does your child have a diagnosis of attention deficit hyperactivity disorder (ADHD) or attention deficit disorder (ADD)?

- Yes. Please indicate the subtype if known:
 - ADHD combined subtype
 - ADHD inattentive subtype (or ADD)
 - ADHD hyperactive subtype
- No
- Don't know

If yes, who made the diagnosis?

- Physician
- Psychiatrist
- Psychologist
- Other: _____

If yes, what age was your child at diagnosis? _____

If no, or don't know, do you think (suspect) your child might have ADHD or ADD?

- Yes
 No

10. Does your child have a diagnosis of a Fetal Alcohol Spectrum Disorder (FASD)?

- Yes. Age at diagnosis: _____
 No
 Don't know

If yes, what specific diagnosis was your child given?

- Fetal Alcohol Syndrome (FAS)
 Partial Fetal Alcohol Syndrome (pFAS)
 Alcohol Related Neurodevelopmental Disorder (ARND)
 Alcohol Related Birth Defects (ARBD)
 Fetal Alcohol Effects (FAE)
 Other, please describe: _____
 Don't know

If yes, who made the FASD diagnosis?

- Pediatrician
 Multi-disciplinary team (typically includes a medical doctor, a psychologist, and other professionals such as an occupational therapist, and a speech therapist)
 Other: _____

If your child was given a "4 digit code," please write it here: _____

11. Does your child have any neurological or psychiatric conditions other than ADHD or FASD? (e.g., Tourette's Disorder, seizures or epilepsy, Obsessive Compulsive Disorder, Depression, Anxiety Disorder, Conduct Disorder, or anything else)

- Yes
 No
 Don't know

If yes, please describe: _____

12. Does your child have any medical conditions (other than those already described) that may impact his or her learning or behaviour?

- Yes
 No
 Don't know

If yes, please describe: _____

13. Has your child ever lost consciousness because of a head injury?

- Yes
 No
 Don't know

If yes, please describe: _____

Does your child have a learning disability?

- Yes
 No
 Don't know

If yes, please describe: _____

14. Does your child receive special assistance in school?

- Yes
 No
 Don't know

If yes, do they have/receive (check all that apply):

- An Individual Education Plan (IEP)
 A modified program (learning outcomes are substantially different from the prescribed curriculum)
 An adapted program (retains the learning outcomes of the curriculum, but adaptations are provided so the student can participate in the program)
 Behavioral support
 Other, please describe: _____

15. Does your child currently take any prescription medications?

- Yes
 No

If yes, please list the name(s) of the medication(s) and the reason for taking them:

Name of medication	Dosage	Reason for taking medication	On medication for how long

16. Please indicate your highest level of education:

- Grade 8 or below
- Some high school
- High school diploma
- High school equivalency certificate
- Some college/university (without degree)
- Trade school degree
- College (2 year) degree
- University (4 year) degree
- Some post-graduate training
- Post-graduate degree

17. If another parent is involved in your child's life, please indicate their highest level of education:

- Grade 8 or below
- Some high school
- High school diploma
- High school equivalency certificate
- Some college/university (without degree)
- Trade school degree
- College (2 year) degree
- University (4 year) degree
- Some post-graduate training
- Post-graduate degree

18. Is there anything else you would like us to know?

Thank you very much for participating in this research project!

Appendix G

Children's Learning Questionnaire

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ID Code: _____

Please answer the following questions about your child by circling the appropriate number. Please answer all questions as honestly and thoroughly as possible, and do not skip items. *Thank you for your time and effort!*

My Child...

	Never	Rarely	Sometimes	Often
1. Is able to learn from the experience of other people (e.g., siblings, family, friends).	0	1	2	3
2. Can adapt knowledge or specific skills to handle new situations.	0	1	2	3
3. Is able to "learn by example."	0	1	2	3
4. Recognizes that some situation is one that he or she has seen before, and is able to behave now as he or she did then.	0	1	2	3
5. Gets confused or "thrown off" by small changes in details (e.g., character details in math problems).	0	1	2	3
6. Has difficulty understanding the deeper or more abstract similarities among similar situations.	0	1	2	3
7. Has trouble applying learned skills to current situations.	0	1	2	3
8. Can apply information learned at school in the "real world."	0	1	2	3
9. Can apply information learned in one situation to new, similar situations.	0	1	2	3
10. Is able to draw upon experience and knowledge to solve a problem.	0	1	2	3
11. Is able to generate unique ideas during "brainstorming" sessions with friends, family, or at school.	0	1	2	3
12. Is able to change a plan or develop alternatives if required.	0	1	2	3
13. Has trouble getting used to new situations (e.g., classes, groups, friends).	0	1	2	3
14. Has a broad knowledge base of general information.	0	1	2	3
15. Is able to learn by watching others ("modelling").	0	1	2	3
16. Can problem solve.	0	1	2	3
17. Is creative.	0	1	2	3
18. Resists changes in routine, food, places, etc.	0	1	2	3
19. Makes the same mistakes over and over.	0	1	2	3
20. Can think abstractly.	0	1	2	3
21. Learns from his or her own experiences.	0	1	2	3
22. Has trouble coming up with ideas for what to do in play or free time.	0	1	2	3