Phenotype-environment interactions in genetic syndromes associated with severe or profound intellectual disability.

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Abstract

Background: The research literature notes both biological and operant theories of behavior disorder in individuals with intellectual disabilities. These two theories of genetic predisposition and operant reinforcement remain quite distinct; neither theory on its own is sufficient to explain challenging behavior in genetic syndromes and an integrated approach is required.

Method: This literature review integrates the two approaches by exploring how environmental factors can influence problem behavior in genetic syndromes associated with intellectual disability. Particular attention is paid to studies that describe evidence that problem behaviors in syndromes that are considered to be phenotypic are associated with other aspects of an established behavioral phenotype.

Results: The review highlights how the study of phenotype-environment interactions within syndromes can promote understanding of the aetiology of problem behaviors both within genetic syndromes and, ultimately, the wider population of individuals with severe intellectual disabilities. The review also evaluates the current status of research and the methods typically employed.

Conclusions: Implications for intervention, future research and extending existing causal models of challenging behavior are discussed.
Introduction

Challenging behavior is a significant problem that can have an impact on the lives of those displaying such behaviors, as well as those who care for them (Hassiotis, Parkes, Jones, Fitzgerald & Romeo; 2008; Hastings, 2002; Olsson & Hwang, 2001; Schwartz & Rabinovitz; 2003). There is growing evidence that challenging behavior is more common in some genetic syndromes than would be expected, given other characteristics such as degree of intellectual disability (e.g. Anderson & Ernst, 1994; Berney, Ireland & Burn, 1999; Clake & Boer, 1998; Collins & Cornish, 2002; Dykens & Clarke, 1997; Dykens & Smith, 1998; Holland, Whittington, Webb, Boer & Clarke, 2003; Hyman, Oliver & Hall, 2002; Symons, Clarke, Hatton, Skinner & Bailey, 2003). The focus of this systematic review is the interaction between some of the established characteristics of the behavioral phenotype of genetic syndromes and environmental influences on challenging behavior.

A review of this empirical research is important in order to evaluate the current status of evidence for interactions that might inform more complete models of challenging behavior and highlight potentially productive areas for further work. There is emerging evidence in the literature to suggest that problem behaviors associated with genetic syndromes could be influenced by an interaction between an aspect of the behavioral phenotype and operant processes (e.g. O’Reilly, 1997; Oliver, Murphy, Crayton & Corbett, 1993; Taylor & Oliver, 2008). Examination of specific forms of phenotype-environment interactions within syndromes will promote understanding of the aetiology of problem behaviors both within genetic syndromes and, ultimately, the wider population of individuals with severe intellectual disabilities and extend existing causal models.
Prior to the review, the seemingly opposing biological and environmental theories are described briefly to provide context. A systematic review follows with critique of methodology used in the study of problem behavior associated with genetic syndromes. Environmental influences on behaviors within genetic syndrome research are detailed and relationships between behavioral phenotypes and features of syndromes are discussed. Finally, the review will highlight the importance of functional analytic studies that incorporate facets of behavioral phenotypes to further understand the behavior of children and adults with genetic syndromes. Future research is discussed with particular reference to effective early intervention strategies.

**Apparently opposing theories of challenging behavior**

There is robust evidence from cohort studies that challenging behavior in people with intellectual disabilities is associated with a number of characteristics or risk markers such as a greater degree of intellectual disability, communication impairments, Autism Spectrum Disorder and the presence of stereotyped, compulsive and impulsive behaviors (Bodfish et al., 1995; Brylewski & Wiggs, 1999; Deb, Thomas, & Bright, 2001; McClintock, Oliver & Hall, 2003; Powell, Bodfish, Parker, Crawford, & Lewis, 1996; Rojahn, Matson, Naglieri, & Mayville, 2004). In addition, genetic syndromes are a significant risk marker for the development of challenging behavior (Arron et al., 2006) and might thus be considered part of the behavioral phenotype for some syndromes.

A behavioral phenotype is defined by an increased probability of behavioral characteristics evident in those with a syndrome compared with individuals without the syndrome (Dykens, 1995). Evidence suggests that certain forms of self-injurious and aggressive behavior may
constitute part of the behavioral phenotype of a number of genetic syndromes. Gene-behavior associations of varying specificity have been demonstrated repeatedly across a number of syndromes, for example, Cri du Chat, Cornelia de Lange, Lesch-Nyhan, Fragile-X, Smith-Magenis and Angelman syndromes (Finucane, Simon & Dirrigl, 2001; Horsler & Oliver, 2006a; Nyhan, 1972; Symons et al., 2003).

In syndromes in which estimates of challenging behavior are consistently higher than might be expected, it has often been assumed that the behavior has strong biological determinants. One line of evidence in the literature concerns neurotransmitter systems, more specifically the dopamine, opioid and serotonin systems and how these may be abnormal. Much research over the last twenty years has focussed on the role of neurotransmitters in the expression of self-injury in some individuals. For example, in Lesch-Nyhan syndrome where self-injurious behavior (SIB) is observed in almost all individuals with the syndrome (Christie et al., 1982), the dopaminergic system has been implicated (Clarke, 1998). In brief, evidence arises from neuropathological, neuroimaging and neurochemical studies of individuals with Lesch-Nyhan syndrome (Schroeder et al., 2001). Functional loss of dopamine terminals has been found in positron-emission tomography studies of healthy individuals with Lesch-Nyhan syndrome and in post mortem studies. It has also been suggested that there is a super-sensitivity of postsynaptic dopamine receptors that results from the loss of dopamine terminals and this dopamine loss acts to mediate the self-injury (Casas-Bruge et al., 1985 cited by Ernst et al., 1996; Clarke, 1998; Ernst et al., 1996; Turner & Lewis, 2002). Van Acker (1991) also suggested that abnormalities in the dopamine system might account for the hand stereotypies and loss of purposeful hand movements that are associated with Rett syndrome.
Other studies have examined a broader range of potential biological factors and identify brain regions that may be centrally involved in the expression of SIB. Several researchers have identified abnormalities of the basal ganglia as potentially associated with self-injury. The basal ganglia are made up of several structures, including the striatum and the globus pallidus. Lesions to the basal ganglia in humans have been associated with a variety of outcomes, including movement disorders, speech disorders, obsessive-compulsive behaviors and disinhibition (Bhatia & Marsden, 1994). Dysregulation of basal ganglia structures has been implicated in a range of disorders such as Tourette’s syndrome, Parkinson’s disease, Autism, Rett syndrome and Lesch-Nyhan syndrome (Albin & Mink, 2006; Cromwell & King, 2004; Holden, Wilman, Wieler & Martin, 2006; Sears et al., 1999). What is striking is that SIB is commonly observed in the majority of these disorders.

There is also a robust literature focusing on the role of the environment in the development of challenging behavior. More specifically there is substantial empirical evidence in support of the application of operant theory that considers challenging behavior as a learned behavior, shaped and maintained by reinforcing consequences (Carr & Durand, 1985; Iwata, Dorsey, Slifer, Bauman & Richman, 1982/1994; Oliver, 1995). In this way, challenging behavior is viewed as being functional and, perhaps most importantly, changeable via effective environmental intervention.

**Models that integrate biological and operant explanations**

Accounts of the biological and operant studies of challenging behavior remain quite distinct and, arguably, compete. The emerging literature exploring environmental factors influencing
challenging behavior in genetic syndromes offers an opportunity to integrate the two models. Biological theories alone are insufficient to account for challenging behavior within genetic syndromes, as they would predict no within-syndrome variability and no effect on behavior of operant processes. Operant theory alone is also insufficient to account for challenging behavior across syndromes, as it would predict that prevalence rates would be equal as environmental influences are, presumably, randomly distributed across groups. Within and between syndrome variability of the prevalence of broad classes and specific forms of behavior indicates that whilst associations between genetic disorders and behavior are robust, within syndrome variability alludes to other aetiological factors. At present, in most behavioral phenotype research, investigators have yet to go beyond the demonstration of simple gene–behavior associations (Hodapp & Dykens, 2001) to elucidate pathways from gene to behavior. This systematic review will examine studies in which the influence of environmental factors on problem behaviors in genetic syndromes has been explored. There is particular attention paid to studies that link problem behaviors that are considered to be phenotypic of a given syndrome with some other aspect of the behavioral phenotype of that syndrome.

Studies that link phenotypic problem behaviors to other aspects of the behavioral phenotype allude to phenotype-environment interactions. The term phenotype-environment has been adopted throughout this review as it implies that a facet of the behavioral phenotype might interact with operant reinforcement of challenging behavior. Phenotype-environment-interactions suggest plausible causal routes to problem behaviors in genetic syndromes. A recent study examining aggression in Angelman syndrome by Strachan et al. (2009) is an example of such an interaction. The results of their study, which utilised experimental functional analysis, suggested
that a genetic predisposition to find social contact rewarding (see Horsler and Oliver, 2006b) may account for the high levels of aggressive behavior observed in the syndrome (see Arron et al., 2006); if social contact from adults is presented contingent on the occurrence of aggressive behavior. This association may then account for the comparatively high levels of aggression observed in Angelman syndrome. Examination of operant influences on behaviors of social importance within genetic syndromes, in which there is a high prevalence of these behaviors would provide a useful starting point for building comprehensive aetiological models of challenging behavior.

**Aims of the review**

This literature review has two aims:

1. A systematic review of the literature will be conducted and studies describing an environmental influence on problem behaviors associated with genetic syndromes will be identified. An initial hand search will identify syndromes of interest, which will then be searched for electronically. Studies will then be divided into three categories. The first category will highlight studies in which the influence of the environment on a problem behavior in a genetic syndrome has been appraised. However, the behavior will not be widely documented as part of the behavioral phenotype for that syndrome. The decision about whether or not behavior is phenotypic will be made after key papers studying the syndrome identified are reviewed. If no evidence is found to suggest that the behavior is part of the phenotype the paper will be included in this category. The second category will highlight studies in which the influence of the environment on a problem behavior in a genetic syndrome has been appraised and the behavior is documented as part of the behavioral phenotype for that syndrome. The third category will
highlight studies in which the influence of the environment on a problem behavior in a genetic syndrome has been appraised and the behavior is documented as part of the behavioral phenotype for that syndrome. In addition, the target behavior is associated with another aspect of the behavioral phenotype or feature of the syndrome.

2. To appraise the status of current research and the methodologies used and identify future directions for research.

Methods

The first stage of identifying potential studies involved hand searching all issues of the following journals from January 1993 to December 2008:

- American Journal on Mental Retardation (AJMR)
- Behavioral Interventions (BI)
- Behavior Modification (BM)
- Journal of Applied Behavior Analysis (JABA)
- Journal of Applied Research in Intellectual Disabilities (JARID)
- Journal of Autism and Developmental Disorders (JADD)
- Journal of Intellectual Disability Research (JIDR)
- Research in Developmental Disabilities (RIDD)

These journals were selected as they are typically the journals that would report on problem behaviors in people with severe intellectual disability. Inclusion and exclusion criteria for published studies can be found in Table 1. A limit of the previous fifteen years was set on the initial search as this is the period in which the importance of genetic aetiology has been increasingly recognised and growth in the research area is evident (Hodapp & Dykens, 2001).
As Table 1 shows, papers in which at least one participant with a genetic syndrome associated with moderate to severe intellectual disability were identified. Of these, only those papers that reported on challenging or problem behaviors were taken forward. Finally, the influence of the environment on the problem behavior must be appraised, through at least two phases of observational data collection, in which there was objective measurement of the dependent variable.

From the initial hand search, 23 papers were identified which reported on ten different syndromes (Cornelia de Lange, Angelman, Rubinstein-Taybi, William’s, Soto’s, Prader-Willi, Lesch-Nyhan, Fragile-X, Smith-Magenis and Rett syndromes). The ten syndrome names identified were the then entered into Psycinfo and Web of Science electronic databases in order to identify further papers on these syndromes published after 1970. Alternative names for the syndromes were derived from the Online Mendelian Inheritance in Man database (OMIM) (all search terms are outlined in Table 2). The electronic database search found a further seventeen papers.

Results and discussion

Tabulated papers

Tables 3, 4 and 5 describe all of the studies identified from the hand and electronic search and divides these studies into the categories that were outlined in the aims. Table 3 outlines seven
studies that show an appraisal of environmental influences on behaviors that are not typically classified as part of the behavioral phenotype for the syndromes reported.

---INSERT TABLE 3 ABOUT HERE---

Table 3 shows that all studies report on single cases and the syndromes identified in these studies are: Cornelia de Lange (n=3), Rubinstein-Taybi (n=1) and Fragile-X (n=3) syndromes. Problem behaviors studied include self-injury, aggression, pica, destruction and thumb sucking, and all of the studies use experimental designs with robust internal validity to appraise environmental effects on these behaviors. Six out of the seven studies identified used experimental functional analysis as a baseline assessment (Iwata et al., 1982/1994a), widely regarded as one of the best assessment techniques for determining operant modes of reinforcement for behavior. The seventh study used natural observations at baseline followed by ABABA reversal and follow-up. Six out of seven of the studies employed interventions and of these, five used a reversal design. Interventions included mand training, functional communication training (FCT) and extinction, and all interventions produced significant decreases in target behaviors. Iwata et al. (1994a) is the only study not employing an intervention, and assessment results following analogue experimental functional analysis revealed an undifferentiated response pattern in a thirteen-year-old male with Rubinstein-Taybi syndrome. The remaining six studies did identify social function to the behaviors reported and these generally fell into the categories of attention maintenance, automatic or sensory reinforcement and escape from demands.
These studies demonstrate that problem behaviors in syndromes can be effectively subjected to standard applied behavior analytic methods to show an influence of the environment. Although worthy of note, these studies are unable to contribute to causal models of problem behaviors in genetic syndromes because the studies describe behaviors which are not syndrome specific. In addition, no known facet of the behavioral phenotype of the syndromes was deemed to be influential.

Table 4 reports on 23 papers in which the influence of the environment on a problem behavior associated with the behavioral phenotype of a given syndrome has been evaluated.

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Table 4 shows that nine of the 23 papers report on SIB in Lesch-Nyhan syndrome (documented as phenotypic by Christie et al., 1982), seven papers report on Rett syndrome; three of these describing SIB and four describing stereotyped or repetitive hand movements, both of which are deemed phenotypic (Hagberg, Aicardi, Dias & Ramos, 1983; Mount, Hastings, Reilly, Cass & Charman, 2001). Five papers report on SIB in Cornelia de Lange syndrome (documented as phenotypic by Hyman et al., 2002), one paper reports on food stealing in Prader-Willi syndrome (documented as phenotypic by Holland, Treasure, Coskeran & Dallow, 1995) and one paper reports on aggression, destruction and temper tantrums in Soto’s syndrome, which are commonly regarded as phenotypic problem behaviors (Finnegan et al., 1994).
Seventeen of the papers employed intervention, two papers utilised a descriptive analysis (Duker, 1975; Hall et al., 2001) and all others use robust experimental techniques such as reversal, alternating treatment and multiple baseline designs. Assessment outcome found behaviors to be maintained by attention, escape from demands, access to tangibles, automatic reinforcement and more idiosyncratic situations such as being in the car and having restraints removed. All interventions produced a favourable outcome (reductions in target behaviors).

These studies demonstrate that the environment can influence problem behaviors that are phenotypic. Although the majority of studies show changes in behavior with changes in the environment, some of the studies utilising experimental functional analysis show undifferentiated patterns of behavioral responding across conditions. This is evident for behaviors that are extremely high rate such as SIB in Lesch-Nyhan syndrome (e.g. Anderson et al., 1978; Grace et al., 1988; McGreevy et al., 1987) and stereotyped hand movements in Rett syndrome (Berg et al., 2000; Evans & Meyer, 1999; Iwata et al., 1986; Roane et al., 2001; Wales et al., 2004; Wehmeyer et al., 1993). In these studies, the assumption is that behavior is maintained by automatic reinforcement. It is therefore, more accurate to refer to these studies as showing no influence of social variables. The studies in Table 4 reveal that there is some support for the view that problem behaviors associated with the behavioral phenotype of genetic syndromes are operantly reinforced. For example, in Rett syndrome where the majority of studies have assumed automatic reinforcement of repetitive hand movements, Wehmeyer et al. (1993) found evidence for behavior maintained by escape from demands in a 19-year-old woman. In addition, interventions such as differential reinforcement of other behavior (DRO), differential reinforcement of incompatible behavior (DRI) and FCT have been successful at reducing
stereotyped behavior in Rett syndrome (Evans & Meyer, 1999; Iwata et al., 1986; Roane et al., 2001). Although the studies in Table 4 show how the environment may influence phenotypic behaviors, they do not provide evidence for phenotype-environment interactions, as the target behaviors are not associated with any other aspects of the behavioral phenotype.

Table 5 reports on ten papers that outline an environmental influence on problem behaviors in genetic syndromes. The behaviors are known to be associated with the behavioral phenotype of that syndrome and the behavior can also be linked to another characteristic of the syndrome, therefore providing support for phenotype-environment interactions.

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Table 5 shows that two papers report on SIB in Cornelia de Lange syndrome (documented as phenotypic by Hyman et al., 2002), two report on phenotypic SIB in Smith-Magenis syndrome (Allanson, Greenberg & Smith, 1999; Colley, Leversha, Voullaire & Rogers, 1990) and two papers report on SIB, aggression and destruction in Williams syndrome (documented as phenotypic by Semel & Rosner, 2003). Single papers were found describing SIB in Rett syndrome, aggression in Soto’s syndrome, social avoidance and SIB in Fragile-X syndrome and aggression in Angelman syndrome; all of which are behaviors deemed to be phenotypic (Finnegan et al., 1994; Hagberg et al., 1983; Horsler & Oliver, 2006b; Mount et al., 2001; Symons et al., 2003).

Three papers employed interventions which all produced reductions in target behaviors. Five papers utilised experimental functional analysis (Iwata et al., 1982/1994) which successfully
identified the functions of problem behaviors. One study used an A-B design and three used descriptive analysis, methods that are less experimentally robust when appraising environmental influences on behavior. Assessment outcomes included attention maintenance, social escape, noisy environments, tangible reinforcement and the presence of health conditions.

Two of the papers in Table 5 are studies demonstrating that behaviors that are in the behavioral repertoire of a syndrome may become operantly reinforced. For example, Oliver et al. (1993) showed that phenotypic stereotyped hand to mouth movements in Rett syndrome were maintained by automatic or sensory reinforcement. Interestingly, harder hits to the mouth were found to be associated with continuous adult attention, suggesting a social escape function to the behavior. The authors proposed that the period of social withdrawal documented in early life in Rett syndrome produces an increased susceptibility to operant reinforcement by escape, such that the phenotypic behavior of rapid hand movements was differentially negatively reinforced by escape from social interaction and eventually become injurious. Similarly, in Cornelia de Lange syndrome, SIB may appear in an individual’s repertoire in response to painful health conditions. An association between challenging behavior and gastroesophageal reflux in Cornelia de Lange syndrome has been noted in previous research (Luzzani, Macchini, Valade, Milani & Selicorni, 2003) suggesting that, pain and discomfort may be a contributing factor to the development and maintenance of challenging behavior in some individuals. Once in the behavioral repertoire, SIB may then become operantly reinforced and associate with particular environmental events (Arron et al., 2006; Moss et al., 2005). In addition, reduced sensitivity to pain in Cornelia de Lange syndrome may prevent the establishment of a contingency between injurious behavior and painful consequences (Johnson, Ekman, Freisen, Nyhan & Shear, 1976).
Table 5 also outlines papers that describe challenging behavior in syndromes resulting from a predisposition to find particular stimuli aversive. Hyperacusis or hypersensitivity to sound is reported to be present in approximately 95% of individuals with Williams syndrome (Van Borsel, Curfs & Fryns, 1997). O’Reilly et al. (2000a) showed the potential for hyperacusis to alter the reinforcing effectiveness of particular environmental events. More specifically, using experimental functional analysis, O’Reilly et al. found that background noise was associated with an increase in escape maintained aggressive behavior in a five year old girl with Williams syndrome, thus showing the ability of a genetic predisposition to alter the reinforcing properties of environmental events. In addition, O’Reilly (1997) found that otitis media (a commonly observed health condition in Williams syndrome) could act as an establishing operation that lowered the threshold at which sound is experienced as aversive. O’Reilly found that SIB in a 26 month old girl with Williams syndrome was highest when there was noise in the environment in the presence of otitis media.

There is some evidence to suggest that the Hypothalamo- Pituitary- Adrenal (HPA) axis might be dysfunctional in individuals with Fragile-X syndrome and this may explain why behavioral anxiety is present during social situations (Hessl et al., 2002). Hall et al. (2006) found evidence to suggest that this biological predisposition may interact with environmental events such that, certain social situations evoke more social escape behaviors. Using a series of experimental conditions, Hall et al. found that interview and singing conditions produced more social escape behaviors which included gaze aversion, physical dissent, face hiding, fidgeting and SIB than did a silent or oral reading condition. In Soto’s syndrome, behavioral phenomena of Attention Deficit Hyperactivity Disorder (ADHD), such as impulsivity and overactivity (Finnegan et al., 1994;
Sarimiski, 2003) may result in more immediate, smaller reinforcers being preferred to larger, more delayed reinforcers and this may be linked to difficulties with self-control and inhibition. Vollmer et al. (1999) showed that impulsivity might be directly linked to aggressive behavior maintained by access to tangible items in Soto’s syndrome. For two young boys, aggressive behavior was more likely to occur if it produced immediate and small reinforcers. Lastly, the social escape function of SIB in Rett syndrome provides further evidence for challenging behavior in syndromes resulting from a predisposition to find particular stimuli aversive. In this example, the degenerative nature of Rett syndrome often leads to an increase in autistic characteristics and social withdrawal, leading to social interactions becoming aversive for individuals (Oliver et al., 1993).

Finally, Table 5 presents papers that describe challenging behavior in syndromes resulting from a predisposition to find particular stimuli rewarding. For example, in Angelman syndrome high levels of laughing and smiling and pro-social behaviors that are considered to be part of the behavioral phenotype (Horsler & Oliver, 2006b) have been described as one behavioral outcome of genomic imprinting (Brown & Consedine, 2003; Oliver et al., 2007). Individuals with Angelman syndrome typically have a genetic propensity to find social contact very rewarding and thus, studies examining the functions of self-injurious and aggressive behavior have found these behaviors to be maintained by access to social attention (Kahng et al., 2000). Individuals with Smith-Magenis syndrome have also been found to engage in more self-injurious, aggressive and disruptive behavior at times of low social attention (Bass & Speak, 2005; Taylor & Oliver, 2008). In both Angelman and Smith-Magenis syndromes, the genetic predisposition to find social contact rewarding may act as an accelerator for the mutual social reinforcement of challenging
behavior. In Smith-Magenis syndrome, the reduced pain perception may result in increased response efficiency for engaging in the behavior as the cost (injury to self) is reduced (Greenberg et al., 1991).

Summary of the results

In summary, the literature shows that behavior in syndromes can be influenced by environmental factors (see Table 3) and often these behaviors are phenotypic problem behaviors (see Table 4). This research supports the potential role of an operant conceptualisation of challenging behavior in genetic syndromes and supports the view that phenotypic behaviors can be subject to change through environmental interventions. There is also growing evidence to suggest that phenotype-environment interactions may govern the presentation of these behaviors through a number of different pathways (see Table 5). Namely, behaviors may enter the repertoire and then become operantly reinforced or there may be particular aspects of the syndrome that drive operant reinforcement and influence the likelihood of problem behaviors being shown.

Implications for a comprehensive model of challenging behavior

Through the identification of single case experimental designs, the results of the literature review have shown that there are a number of phenotype-environment interactions that can be identified in syndromes. These are clearly extremely important for building syndrome sensitive models of challenging behavior in which different weight is given to different child characteristics.

In addition to syndrome specific models, more broadly, each phenotype-environment interaction that has been identified delineates a potential causal route to problem behavior. These routes
could inform a comprehensive aetiological model of challenging behavior for the total population of people with intellectual disabilities. This integration of behavioral phenotype and operant theories in order to inform causal models has started to emerge in the literature and to date Oliver (1993; 1995) and Langthorne and McGill (2008) have proposed conceptual models to explain the development of SIB. In each model individual characteristics of genetic origin interacts with environmental characteristics to drive the development of self-injury.

With regard to delineating causal pathways from genetic characteristics to behavior in order to inform a comprehensive model, the results of this review have revealed that one plausible pathway to challenging behavior might be through an attenuated or accentuated specific motivation. For example, a heightened motivation to seek out social attention in Angelman and Smith-Magenis syndrome may result in challenging behavior that is maintained by access to attention (Kahng et al., 2000; Taylor & Oliver, 2008). In addition, for self-injury in Smith-Magenis syndrome, the pathway from genetics to central and peripheral nervous system development may be influenced by reduced pain perception. In this way, there may be a reduced cost for the individual when engaging in the behavior (Greenberg et al., 1991). Conversely, the review has highlighted syndromes where there may be attenuated motivation and predispositions to find particular stimuli aversive. Evidence for this pathway is provided by the finding that social performance situations result in more social anxiety and thus motivation for challenging behavior in Fragile-X syndrome (Hall et al., 2006), and the finding that the period of social withdrawal documented in early life in Rett syndrome produces an increased vulnerability and susceptibility to operant reinforcement by escape (Oliver et al., 1993).
A comprehensive model might also consider the pathway from genes to accentuated or attenuated sensory input given the findings related to hyperacusis in Williams syndrome. The review has highlighted the potential of hyperacusis to alter the reinforcing effectiveness of particular environmental events in Williams syndrome leading to challenging behavior (O’Reilly et al., 2000a). In addition, the review has drawn attention to the importance of health conditions and how these may offer a plausible route to challenging behavior. For example, SIB in a young girl with Williams syndrome was only found to occur during periods of otitis media. Otitis media may have acted as an establishing operation related to escape from ambient noise (O’Reilly, 1997), whilst pain and discomfort in Cornelia de Lange syndrome may result in SIB entering an individual’s behavioral repertoire. Once in the repertoire there is then the potential for the behavior to become operantly reinforced and associate with particular environmental events (Arron et al., 2006; Moss et al., 2005).

Finally evidence from Soto’s syndrome has drawn attention to specific cognitive impairments that may drive the development of challenging behavior. Impulsivity and overactivity, which are common in Soto’s syndrome, may be associated with difficulties with self-control and inhibition such that challenging behavior may become operantly reinforced by access to immediate rewards (Vollmer et al., 1999). Woodcock, Oliver and Humphreys (2009) also proposed a phenotype-environment interaction in Prader-Willi syndrome in which deficits in task switching (proposed as part of the cognitive endophenotype of Prader-Willi syndrome) result in temper tantrums when there is a decrease in predictability in the environment and thus, there is high demand placed upon cognitive resources needed for attention switching. There is then the potential for temper tantrums to be subject to operant reinforcement via social contingencies. Although evidence in
support of specific causal pathways to challenging behavior has been identified through a number of single cases, a comprehensive model still needs to be developed.

**Future research directions**

Now that the potential for causal pathways has been identified, future research might usefully examine these syndrome specific models via empirical study. In particular, specific predictions regarding challenging behavior that is regarded as phenotypic within a given syndrome can be tested. For example, given the results of the single case studies in this literature review, predictions about challenging behavior in Williams syndrome might be made. Specifically, it might be predicted that hyperacusis and the presence of otitis media might alter the reinforcing properties of environmental events, to drive the expression of self-injury and aggression or functionally similar escape maintained behaviors. For Angelman and Smith-Magenis syndromes, it might be predicted that given the genetic predisposition to find social contact rewarding, challenging behavior would evidence stronger maintenance by positive social reinforcement. Such predictions need to be assessed in large scale, cross-syndrome comparison studies and the utilisation of experimental functional analysis would offer a robust assessment of environmental influences on behaviors.

It is also notable that the pathways proposed have been described as single points in time and the way that these pathways *develop* has not been discussed. Advantages have been highlighted with respect to the study of the developmental trajectories of language and cognitive capacities within neurodevelopmental disorders such as Williams and Down syndrome (Thomas *et al.*, 2009). It is important to emphasise investigation of hypotheses from a developmental perspective given that,
in some syndromes there are known changes in aspects of the behavioral phenotype. For example, behavioral characteristics demonstrated in individuals with Williams syndrome include hypersociability characterised by social disinhibition and increased empathy (Bellugi et al., 2007; Martens, Wilson & Reutens, 2008). However, over time there appears to be a change in the profile of sociability within Williams syndrome with some decrease in sociability and increase in behavioral and emotional problems, communication disturbance and anxiety as individuals get older (Einfield, Tonge & Rees, 2001; Gosch & Pankau, 1997). In addition, SIB in Rett syndrome has been shown to have different social functions (functions to escape and to obtain social attention) depending on the stage of a child’s development. Specifically, the profile of Rett syndrome causes social interaction to be reinforcing and punishing at different developmental stages (Oliver et al., 1993). An important avenue for future research is the consideration that over time certain motivations and facets of the syndrome may change, and this may have implications for variability in challenging behavior at different stages of development.

Future research also needs to examine whether the potential causal pathways are applicable to intellectual disability that is not genetically determined, for example, in foetal alcohol syndrome or in ASD and ADHD, which are behaviorally defined conditions. In addition, there are other risk markers for the development of challenging behavior such as ASD and impulsivity (McClintock et al., 2003) that have not been outlined in the review that may be implicated in the development of challenging behavior for some individuals. Such factors need to be explored within a larger group design and incorporated into a comprehensive model.

Implications for intervention
The findings of the systematic review provide important implications for early intervention of challenging behavior at a syndrome level. Early intervention in children with intellectual disabilities may be more effective at reducing challenging behavior and enhancing other adaptive skills and abilities than a reactive approach (See Richman, 2008 for overview). Preparing families and professionals with knowledge and information enhances intervention opportunities, allows behavior to be anticipated and responses to challenging behavior to be monitored. As challenging behavior develops and dyadic reinforcement takes place, the behavior will become more established in an individual’s behavioral repertoire (Oliver, 1995; Oliver, Hall & Murphy, 2005). Although prevention of the behavior entering a behavioral repertoire is perhaps only realistic or possible for a subset of individuals, pre-emptive and early intervention strategies may be beneficial. In Cornelia de Lange syndrome for example, SIB may appear in an individual’s repertoire in response to painful health conditions. Ensuring that health conditions commonly seen in Cornelia de Lange syndrome (e.g. gastroesophageal reflux, otitis media) are immediately and effectively treated may help to prevent potentially injurious responses.

Early intervention strategies may also shift the focus from behavior and move more towards managing motivation and increasing awareness of syndrome specific vulnerability and susceptibility to operant reinforcement. In Angelman syndrome for example, awareness of aspects of the behavioral phenotype such as the excessive motivation to gain social attention and its possible link with aggressive behavior, offers significant implications for early intervention. Knowledge of this underlying motivation may have wider reaching implications for individuals with Angelman syndrome and their families. It is probable that this drive for social attention is likely to affect a host of other behaviors in addition to challenging behavior, particularly those
behaviors which are linked to increased allocation of social resources (Brown & Consedine, 2004). Sleep disturbances are commonly reported in the syndrome (Chertkoff-Waltz, Beebe & Byars, 2005; Didden, Korzilius, Smits & Curfs, 2004; Miano et al., 2004; Pelc, Cheron, Boyd & Dan, 2008) and the drive for social attention may result in children waking other people at night. Anecdotally there are also reports of stranger approach and sibling relationship difficulties as an individual competes for social resources. The findings may also provide an opportunity to minimise conditions known to mediate operant conditioning. For example in Rett and Fragile-X syndromes, knowledge of the predisposition to find high levels of social interaction aversive at certain points in development and particular situations may help to minimise the reinforcement of challenging behavior. Functional Communication Training (FCT; Carr & Durand, 1985) has proven to be particularly effective for challenging behavior maintained by social consequences. The main target of FCT is to replace an aberrant behavior with an alternative communicative response that is functionally equivalent (Carr and Durand, 1985). In syndromes, knowledge of operant vulnerability and susceptibility could inform FCT so that alternative functionally equivalent responses could be reinforced before the development of challenging behavior. The findings also provide potential implications for assessment, and emphasise the importance of assessment to intervention designs that determine the functions of challenging behavior and manipulate operant determinants in intervention. The results of the review provide some evidence for syndrome specific models in which there may be causal pathways from genetic cause to behavior. Within any given syndrome, many pathways may be operational, however, syndrome specific phenotype-environment interactions provide us with information on which pathway might be most significant. In turn, this provides information on which particular assessments should be prioritised in which syndromes. For example in Cornelia de Lange syndrome, a pain
assessment may be prioritised given the link between health conditions and SIB (Luzzani et al., 2003). In Soto’s syndrome levels of impulsivity may be assessed first, or in Smith-Magenis syndrome a motivational assessment for challenging behavior may be foremost.

Demonstrations that behavior in genetic syndromes can be influenced by environmental factors are important as they counter determinist positions which suggest that behaviors are wholly accounted for by an underlying biological aetiology (see for example Deb, 1997; Harris, 1987) and thus are unchangeable. An operant conceptualisation of challenging behavior that is part of the behavioral phenotype of a syndrome negates therapeutic nihilism. This review has shown the role of the environment may be instrumental in shaping and maintaining behaviors in genetic syndromes and thus, it is not inevitable that challenging behavior will develop. In this way, responsive intervention for already established challenging behavior is very important. The review has identified high risk and vulnerable groups for the development of challenging behavior that need to be targeted with intervention.

The findings presented also highlight the need for dissemination of information. As Oliver (1993) indicates, important questions around the process of dissemination include: What will be disseminated, by whom and how? Academics and researchers most commonly undertake active dissemination; however, the role of syndrome support groups in the research process has been evolving in recent years. Support groups have been successful in developing working partnerships with researchers from many disciplines. The groups have now become more proactive in determining the research agenda, and have taken advantage of new technologies for dissemination that gives a role for support groups to commission and disseminate research. A
collaborative approach between parent groups and researchers is likely to prove important to ensuring that research focuses on the most pressing problems of those who have syndromes and their families. Furthermore, such collaborations promote rapid dissemination of robust findings to shortcut the typical delays of research moving to influence practice.
REFERENCES


Cortisol and behavior in Fragile-X syndrome. *Psychoneuroendocrinology, 27,* 855-872,


Interventions. Routledge.


Table 1: Inclusion and exclusion criteria for papers in the initial hand search of the systematic review.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>The paper reports at least one participant that has a genetic syndrome</td>
<td>Review paper</td>
</tr>
<tr>
<td>The genetic syndrome reported is associated with moderate to severe intellectual disability</td>
<td>Paper reports prevalence data only</td>
</tr>
<tr>
<td>Environmental influences on a problem behavior displayed by a participant (s) are appraised</td>
<td>If the paper concerns Autism or Down syndrome(^1)</td>
</tr>
<tr>
<td>At least two phases of observational data collection with measurement of the dependent variable</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Autism is not considered to be a genetic syndrome as no known genetic basis has been identified. Down syndrome is not typically related to challenging or problem behaviors.
<table>
<thead>
<tr>
<th>Search Term</th>
<th>Variation from OMIM database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angelman, Angelman Syndrome</td>
<td>Happy puppet, Happy puppet syndrome</td>
</tr>
<tr>
<td>Cri du Chat, Cri du Chat Syndrome</td>
<td>Crying cat syndrome, 5-p, 5-p syndrome, 5-p deletion syndrome</td>
</tr>
<tr>
<td>Cornelia de Lange, Cornelia de Lange Syndrome</td>
<td>CdLS, CdL, Typus degenerativus amstelodamensis, de lange syndrome, Brachmann-de Lange, Brachmann-de Lange Syndrome, BdLS</td>
</tr>
<tr>
<td>Fragile- X, Fragile-X syndrome</td>
<td>Martin-Bell Syndrome, FXS, Marker X syndrome</td>
</tr>
<tr>
<td>Lesch-Nyhan, Lesch-Nyhan Syndrome</td>
<td>LNS</td>
</tr>
<tr>
<td>Prader-Willi, Prader-Willi Syndrome</td>
<td>PWS, Prader-Labhart-Willi syndrome</td>
</tr>
<tr>
<td>Rett, Rett Syndrome</td>
<td>RTS, RTT</td>
</tr>
<tr>
<td>Rubinstein-Taybi syndrome</td>
<td>Rubinstein syndrome, Broad-thumb halux syndrome</td>
</tr>
<tr>
<td>Smith-Magenis, Smith-Magenis Syndrome</td>
<td>SMS</td>
</tr>
<tr>
<td>Sotos, Sotos syndrome</td>
<td>-</td>
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<tr>
<td>Williams, Williams syndrome</td>
<td>WS, Williams Beuren syndrome, WB</td>
</tr>
</tbody>
</table>
Table 3: Studies in which the influence of the environment on a problem behavior in a genetic syndrome has been appraised, however, the behavior is not documented as part of the behavioral phenotype for that syndrome.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Syndrome</th>
<th>Age</th>
<th>Gender</th>
<th>Behavior</th>
<th>Study Design</th>
<th>Experimental method</th>
<th>Assessment outcome</th>
<th>Treatment outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iwata et al. (1994a)</td>
<td>Rubinstein-Taybi</td>
<td>13yrs</td>
<td>Male</td>
<td>Self-injury</td>
<td>Alternating treatment design</td>
<td>4 analogue conditions: social disapproval, demand, play and alone</td>
<td>Undifferentiated response pattern</td>
<td>-</td>
</tr>
<tr>
<td>Kern, Mauk, Marder &amp; Mace</td>
<td>Cornelia de Lange</td>
<td>7yrs</td>
<td>Female</td>
<td>Breath holding</td>
<td>Multi-element baseline A-B-A-B reversal</td>
<td>Baseline: EFA; (Iwata et al., 1984/1992). Treatment: extinction, scheduled attention and mand training</td>
<td>Breath holding maintained by attention</td>
<td>Breath holding reduced from 15.7% to 3.6% of time in attention condition</td>
</tr>
<tr>
<td>Piazza et al. (1998)</td>
<td>Cornelia de Lange</td>
<td>7yrs</td>
<td>Female</td>
<td>Pica</td>
<td>Multi-element baseline A-B-A-B reversal</td>
<td>Baseline: EFA; (Iwata et al., 1984/1992). Treatment: Alone condition plus matched stimuli</td>
<td>Pica maintained by automatic reinforcement</td>
<td>Mean rate of pica reduced from 1.2 to 0.1 following treatment</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Age</td>
<td>Gender</td>
<td>Target Behavior</td>
<td>Baseline &amp; Follow-up</td>
<td>Treatment &amp; Intervention</td>
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<tr>
<td>O’ Connor, Sorensen-Burnworth, Rush &amp; Eidman (2003)</td>
<td>Fragile-X syndrome</td>
<td>14yrs</td>
<td>Male</td>
<td>Destruction (included aggression, self-injury and destruction)</td>
<td>Multi-element baseline A-B-A-B reversal and follow-up</td>
<td>Baseline: EFA: (Iwata et al., 1984/ 1992) and mand analysis Treatment: Individual system intervention (Hagopian et al., 2002) Behavior maintained by adult compliance with his mands 98.1% reduction in behavior from baseline. Successful transference to home and school and 6 &amp; 9 month follow-up</td>
<td></td>
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</tr>
<tr>
<td>Saloviita &amp; Pennanen (2003)</td>
<td>Fragile-X</td>
<td>11yrs</td>
<td>Male</td>
<td>Thumb sucking</td>
<td>ABABA reversal and follow-up</td>
<td>Baseline: Nat obs Treatment: Verbal prompts, praise and chewing gum Behavior maintained by automatic reinforcement Reduction from baseline to treatment of 53% to 1% (mean time engaging). Follow up at 22% time</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Authors</th>
<th>Syndrome</th>
<th>Participants</th>
<th>Study Design</th>
<th>Experimental method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duker (1975)</td>
<td>Lesch-Nyhan</td>
<td>13 Male</td>
<td>Self-injury</td>
<td>Descriptive analysis and treatment</td>
<td>Behavior occurring in car when stationary</td>
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<tr>
<td></td>
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<td></td>
<td>Baseline: Recreation of high-risk situations (e.g. car)</td>
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<td></td>
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<td></td>
<td>Treatment: Extinction</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Baseline: No restraint, response prevention</td>
<td>Consistently high levels of self-injury in baseline</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Treatment: Punishment, positive reinforcement of self-injury or non self-injury and timeout</td>
<td>Positive reinforcement of non self-injury and timeout rapidly reduced behavior. Maintenance at 24months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Baseline: No restraint, response prevention</td>
<td>Treatment: Systematic desensitisation with extinction (15 trials)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Treatment: Punishment, positive reinforcement of self-injury or non self-injury and timeout</td>
<td>Anecdotal reports from parents that self-injury maintained by attention and phobic reaction in response to</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Baseline: Physical attention</td>
<td>Self-injury extinguished and all physical restraints removed. Maintained at 18 month follow-up</td>
</tr>
<tr>
<td>Bull &amp; LaVecchio (1978)</td>
<td>Lesch-Nyhan syndrome</td>
<td>10yrs Male</td>
<td>Self-injury and physical restraint</td>
<td>Baseline followed by repeated treatment design and follow-up</td>
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</tr>
<tr>
<td>Study</td>
<td>Population</td>
<td>Age</td>
<td>Gender</td>
<td>Intervention</td>
<td>Baseline Design</td>
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<tr>
<td>Menolascino, McGee &amp; Swanson (1982)</td>
<td>Cornelia de Lange syndrome</td>
<td>14yrs</td>
<td>Male</td>
<td>Self-injury</td>
<td>Baseline: Extinction of non-compliance with task demands and positive reinforcement</td>
</tr>
<tr>
<td>Study</td>
<td>Syndrome</td>
<td>Age</td>
<td>Gender</td>
<td>Behavior</td>
<td>Baseline Intervention</td>
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<tr>
<td>Dossetter, Couryer and Nicol (1991)</td>
<td>Cornelia de Lange syndrome</td>
<td>14yrs</td>
<td>Female</td>
<td>Self-injury</td>
<td>Treatment only</td>
</tr>
<tr>
<td>Bay, Mauk, Radcliffe &amp; Kaplan (1993)</td>
<td>Cornelia de Lange syndrome</td>
<td>6yrs</td>
<td>Male</td>
<td>Self-injury, aggression, destruction</td>
<td>Multi-element baseline and treatment</td>
</tr>
<tr>
<td>Paisey, Whitney &amp; Wainczak (1993)</td>
<td>Rett syndrome</td>
<td>3yrs</td>
<td>Female</td>
<td>Self-injury</td>
<td>Multiple baseline</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Syndrome</td>
<td>Age (yrs)</td>
<td>Gender</td>
<td>Primary Behavior</td>
<td>Treatment Design</td>
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<tr>
<td>Wehmeyer, Bourland &amp; Ingram (1993)</td>
<td>Rett Syndrome</td>
<td>19-23</td>
<td>Female</td>
<td>Stereotyped hand movements</td>
<td>Alternating treatment design</td>
</tr>
<tr>
<td>Evans and Meyer (1999)</td>
<td>Rett Syndrome</td>
<td>5</td>
<td>Female</td>
<td>Stereotyped hand movements</td>
<td>Multiple baseline longitudinal study</td>
</tr>
<tr>
<td>Study</td>
<td>Diagnosis</td>
<td>Age</td>
<td>Sex</td>
<td>Behavior</td>
<td>Treatment &amp; Assessment</td>
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</tr>
<tr>
<td>Hall, Oliver &amp; Murphy (2001)</td>
<td>3 ppts with Lesch-Nyhan syndrome</td>
<td>17, 25 and 30 months</td>
<td>Male</td>
<td>Self-injury</td>
<td>Descriptive analysis Nat obs at 3 monthly intervals for 18 months</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Syndrome</td>
<td>Age</td>
<td>Gender</td>
<td>Behavior</td>
<td>Intervention Design</td>
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<tr>
<td>Roane, Piazza, Sgro, Volkert &amp; Anderson (2001)</td>
<td>Rett syndrome</td>
<td>14 and 23 yrs</td>
<td>Female</td>
<td>Hand wringing and hand mouthing</td>
<td>Multi-element baseline Intervention: Combined alternating treatment and reversal</td>
</tr>
<tr>
<td>Bergen, Holborn &amp; Scott-Huyghebaert (2002)</td>
<td>Lesch-Nyhan syndrome</td>
<td>28 yrs</td>
<td>Male</td>
<td>Self-injury</td>
<td>Alternating treatment</td>
</tr>
<tr>
<td>Wales, Charman &amp; Mount (2004)</td>
<td>Rett syndrome</td>
<td>13-17 yrs</td>
<td>Female</td>
<td>Repetitive and movements</td>
<td>Alternating treatment design (A-B-C-D)</td>
</tr>
</tbody>
</table>

Table 5: Studies in which the influence of the environment on a problem behavior in a genetic syndrome has been appraised and the behavior is documented as part of the behavioral phenotype for that syndrome. In addition, the target behavior is associated with another aspect of the behavioral phenotype or feature of the syndrome.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Syndrome</th>
<th>Age</th>
<th>Gender</th>
<th>Behavior</th>
<th>Study Design</th>
<th>Experimental method</th>
<th>Assessment outcome</th>
<th>Treatment outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oliver et al.</td>
<td>Rett syndrome</td>
<td>3 yrs</td>
<td>Female</td>
<td>Stereotyped behavior and Self-injury</td>
<td>Alternating treatment</td>
<td>EFA: Continuous attention, non-stimulation, stimulation and demand.</td>
<td>Stereotyped behavior maintained by automatic reinforcement and self-injury maintained by escape from social interactions.</td>
<td>-</td>
</tr>
<tr>
<td>O'Reilly (1997)</td>
<td>Williams syndrome</td>
<td>26 months</td>
<td>Female</td>
<td>Self-injury</td>
<td>Alternating treatment</td>
<td>EFA: 6 conditions conducted in presence and absence of otitis media</td>
<td>Self-injury only occurring when otitis media present.</td>
<td>-</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Syndrome</td>
<td>Age</td>
<td>Gender</td>
<td>Behavior</td>
<td>Baseline</td>
<td>Treatment</td>
<td>Behaviors Maintained by Attention</td>
<td>Comments</td>
</tr>
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</tr>
<tr>
<td>Kahng, Iwata, Thompson &amp; Hanley</td>
<td>Angelman syndrome</td>
<td>31yrs</td>
<td>Female</td>
<td>Self-injury and aggression</td>
<td>Multi-element baseline</td>
<td>EFA: (Iwata et al., 1984/1992. Treatment: NCR and extinction</td>
<td>Little or no target behavior following extinction</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Multiple baseline</td>
<td>between ppts treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O’Reilly, Lacey &amp; Lancioni</td>
<td>Williams syndrome</td>
<td>5yrs</td>
<td>Female</td>
<td>Aggression and destruction</td>
<td>Alternating treatment in reversal design</td>
<td>EFA: Attention, demand and play conditions evaluated under different contexts: no noise, noise, noise with earplugs</td>
<td>Escape maintained behavior in noise condition.</td>
<td></td>
</tr>
<tr>
<td>Bass &amp; Speak</td>
<td>Smith-Magenis syndrome</td>
<td>26yrs</td>
<td>Female</td>
<td>Self-injury</td>
<td>A-B</td>
<td>Assessment. ABC charts, MAS, semi-structured interviews Treatment: DRO, self-monitoring and extinction</td>
<td>Behavior maintained by attention</td>
<td>Marked reduction in behavior post intervention</td>
</tr>
<tr>
<td>Moss et al.</td>
<td>8 ppts with Cornelia</td>
<td>4-14yrs</td>
<td>5 male, 3 female</td>
<td>Self-injury</td>
<td>Descriptive analysis</td>
<td>4 hrs nat obs per ppt</td>
<td>7/8 ppts showed self-injury associated with a larger delayed). Linked to impulsivity</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Setting</td>
<td>Behaviors</td>
<td>Analysis</td>
<td>Conditions</td>
<td>Findings</td>
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<tr>
<td>Hall, DeBernardis &amp; Reiss (2006)</td>
<td>114 pts with Fragile-X syndrome</td>
<td>6-17 yrs</td>
<td>Social escape behaviors including self-injury</td>
<td>A-B-C-D descriptive analysis</td>
<td>4 conditions: Interview, silent reading, oral reading and singing</td>
<td>Behavior higher in singing and interview conditions. Higher cortisol levels predictive of lower levels of eye contact</td>
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</tr>
<tr>
<td>Arron et al. (2006)</td>
<td>16 pts with Cornelia de Lange syndrome</td>
<td>1-16 yrs</td>
<td>Self-injury</td>
<td>A-B-A-B reversal</td>
<td>No attention and attention conditions</td>
<td>9 ppt’s behavior was related to level of attention. No association for other 7 pts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taylor &amp; Oliver (2008)</td>
<td>5 pts with Smith-Magenis syndrome</td>
<td>3-13 yrs</td>
<td>Self-injury, aggression and destruction</td>
<td>Descriptive analysis</td>
<td>9-12 hrs of nat obs per pts</td>
<td>Behaviors evoked in response to low levels of adult contact</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>