Gene-Environment Interactions and the Functional Analysis of Challenging Behavior in Children with Intellectual and Developmental Disabilities

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Abstract

It is argued that an approach characterised by either genetic or environmental determinism fails to adequately describe the contingencies involved in the evocation and maintenance of challenging behaviors in children with intellectual and developmental disabilities. Instead, challenging behavior should be considered as a result of the interaction of genetic and environmental variables. This argument is illustrated through a conceptual model for the development of challenging behaviour and recently gathered data on differences in the functions of challenging behavior in children with different genetic syndromes. The findings are further discussed in the context of a developmental systems model, in which neither the influence of genetic nor environmental contributions can be fully understood without taking account of the other. This expanded model may hold important implications for the understanding of challenging behavior.

Keywords

Intellectual and developmental disability, challenging behavior, functional analysis, gene-environment interaction, developmental systems

Challenging behavior in certain cases is clearly influenced by genetic sources of variability. Evidence suggests that certain forms of challenging behavior may constitute part of the behavioral phenotype of a number of genetic syndromes. Gene to behavior associations of varying specificity have been repeatedly demonstrated across a number of syndromes, including fragile X syndrome (Symons, Clark, Hatton, Skinner, & Bailey, 2003), and Smith-Magenis syndrome (Finucane, Dirrigl, & Simon, 2001).

Few would subscribe to the view that genes 'cause' such behaviors. There is considerable within-syndrome variability in the extent to which individuals with a given syndrome go on to develop behaviors considered 'phenotypic' (Hodapp & Dykens, 2001). Environmental factors have been shown to contribute to such variability (Hessl et al., 2001). Even in cases where strong gene-behavior associations do exist it does not necessarily follow that these occur independent of environmental influence. For example, even at the molecular level, the environment has been shown to alter gene expression (Restivo et al., 2005). Gene-behavior associations reflect not only the direct effect of genes but also the effects of environment and, where present, the effects of gene-environment interactions (GxE). It is not necessarily the case, therefore, that a strong gene-behavior association indicates the absence of environmental influence. Despite the apparent ubiquity of GxE, however, most behavioral phenotype research has failed to go beyond the demonstration of simple gene-behavior associations (Hodapp & Dykens, 2001).

The continued neglect of environmental influences in behavioral phenotype research may limit our understanding of the development of challenging behavior and paradoxically the role that genes play in this process. As Moffitt, Caspi and Rutter (2005) state:

> *Ignoring nurture may have handicapped the field's ability to understand nature (p.478).*

The functional effects of genes upon behavioral development remain poorly understood. There is a need for behavioral phenotype researchers to go beyond gene-behavior association and to begin to incorporate GxE relations into the study of challenging behavior.

Others have focused exclusively on the environmental determinants of challenging behavior. Functional analysis is the hallmark of the applied behavior analytic approach to the assessment and treatment of challenging behavior (Hanley, Iwata, & McCord, 2003). Over the past decade, investigators have begun to incorporate an individual's biological functioning into the

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analysis of such behaviors (e.g., Langthorne, McGill, & O'Reilly, 2007). This has had a profound impact on the assessment and treatment of challenging behavior displayed by people with intellectual and developmental disabilities.

However, the influence of genetic and other biological variables has not yet been integrated with models of the early development of challenging behavior. For example, despite the status of genetic syndromes as significant 'risk markers' for the later development of self-injurious behavior (McClintock, Hall, & Oliver, 2003), a conceptual model that accounts for their influence on early behavior-environment relations is lacking. Secondly, the focus of behavior analysis on behavioral function has led to a neglect of form. As has been repeatedly demonstrated there are highly specific relationships between certain genetic syndromes and particular topographies of challenging behavior which current 'operant' models say little about.

The omission of genetic influences from functional analysis stems from a 'misunderstanding' of the relations between biological and behavioral events and an assumption that such factors are private, inaccessible and in some cases hypothetical (Thompson, 2007). Such an omission is particularly striking given that central to the operant model, from which functional analysis has itself evolved, is the phylogenic and ontogenic selection of behavior (Skinner, 1966). Behavior analysis as a philosophy and a science is contextual (Morris, 1988), and the occurrence of any response can only be understood in regard to the historical and current context (both genetic and environmental) in which that act is embedded. Paradoxically, despite the prominence Skinner gave to genetic influences, their analysis has remained largely outside the realm of applied behavior analysis.

■ GXE AND THE EARLY DEVELOPMENT OF CHALLENGING BEHAVIOR

A GxE approach is based on the assertion that environmental 'pathogens' cause behavioral disorders and genes influence susceptibility to these 'pathogens' (Caspi & Moffitt, 2006). Several studies have recently demonstrated that the effects of exposure to an environmental 'pathogen' may be conditional on a person's genotype. For example, Caspi et al. (2002) demonstrated that a functional polymorphism in the gene encoding the neurotransmitter-metabolizing enzyme monoamineoxidase A (MAOA) served to moderate the effects of child maltreatment on the later development of anti-social behavior. Similar GxE have been shown to influence the development of psychosis in adolescent cannabis users (Caspi et al., 2005), and the development of ADHD symptoms (Brookes et al., 2006).

Genes do not code for specific behaviors, rather the effects of genes upon behavior-environment relations are by virtue of their effects on the organism as a whole developmental system (Johnston & Edwards, 2002). This system comprises of bidirectional relations between environmental, behavioral, physiological, neural and genetic sources of variability (Gottlieb, 2003). The role of DNA is to specify the production of mRNA, which

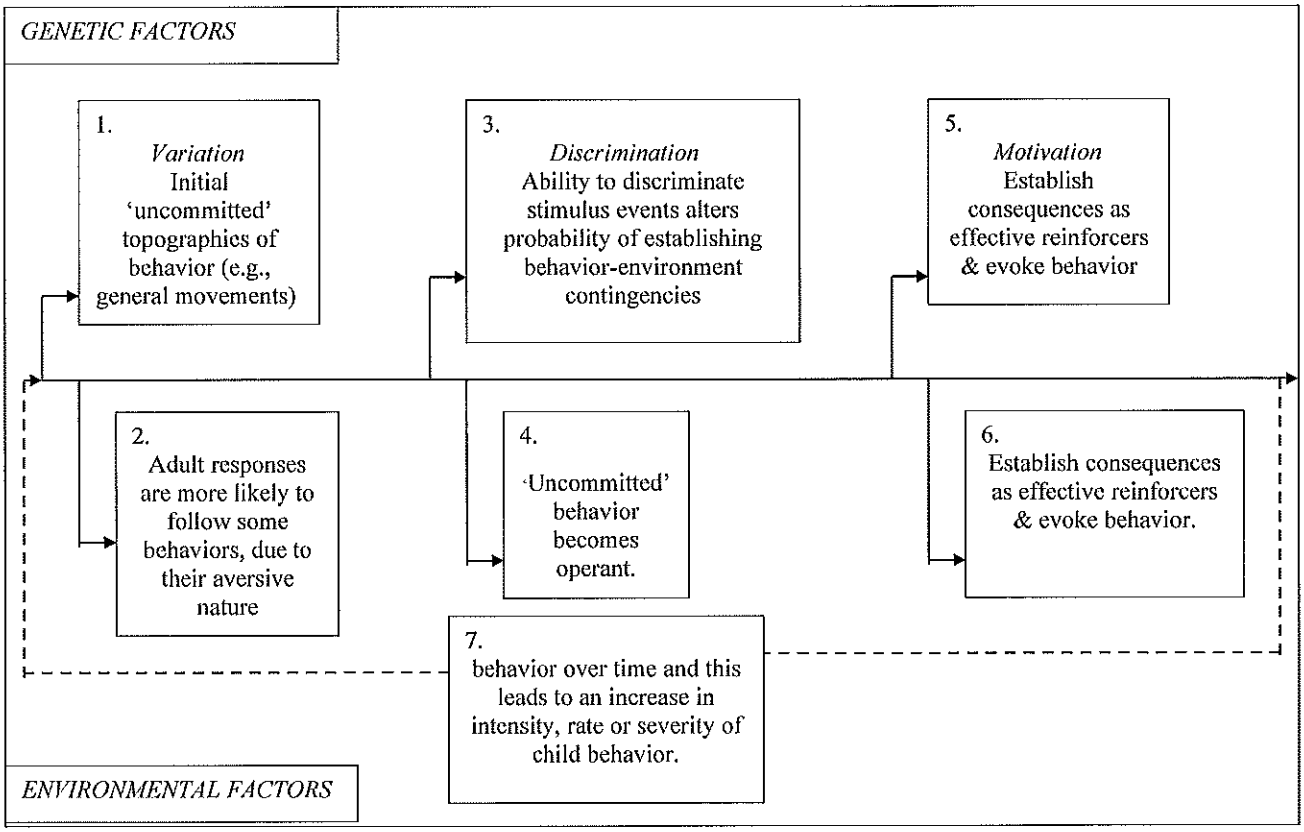

Figure 1. Model of the early development of challenging behavior

then in turn determines the production of the polypeptides that form proteins. It is these proteins that act upon the development of the individual. This process is epigenetic and is itself influenced by environmental factors. The role of genes, therefore, is to influence the development of the organism as a whole (across neural, physiological, and behavioral pathways); it is this whole organism which then interacts with the environment.

Extending the GxE model to the study of challenging behavior leads to the thesis that in some cases genes may influence susceptibility to known environmental 'pathogens' for the development of such behavior. We investigate this thesis in two ways below. First, we provide an operant analysis of GxE in the development of challenging behavior suggesting that genes may alter basic behavior-environment relations by virtue of their effect on the developmental system. Second, we investigate differences between the functions of challenging behavior in children with fragile X syndrome and Smith-Magenis syndrome.

■ A FUNCTIONAL ANALYSIS OF THE EARLY DEVELOPMENT OF CHALLENGING BEHAVIOR

Genes may influence behavior-environment relations in a number of ways (cf., Moore, 2002). Conceptually, such factors may alter the developmental system in a way that influences: (1) the stream of 'uncommitted' behavior from which an operant response evolves, that is they may contribute to initial behavioral variation; (2) the sensitivity of the individual to changes in environmental stimulation, that is they may either facilitate or inhibit the discrimination of stimulus events; and (3) the value of certain environmental consequences that serve to reinforce or punish behavior, that is they may establish or abolish the 'motivation' for the consequences that maintain challenging behavior. These effects are likely to be achieved by the influence of genes on neurobiological and physiological pathways.

Figure 1 provides a schematic representation of a model of the early development of challenging behavior based on the relations discussed above. Many of the environmental elements to this model have been comprehensively addressed in previous accounts (especially of the development of self-injurious behavior e.g., Guess & Carr, 1991). The influence of genetic factors and the role of certain other biological factors (such as health conditions), however, have to date escaped systematic appraisal. The model consists of seven stages, which for schematic purposes are presented in a linear fashion; this is not to imply that the model necessarily follows a linear path of causation or that all stages are necessary for the development of challenging behavior.

In stage 1, genetic events alter the development of the individual in a way that influences the emission of 'uncommitted' topographies of behavior from which an operant response evolves. For example, the analysis of general movements may hold particular clues for our understanding of the later development of self-injurious behavior (Symons, Sperry et al., 2003). Thus, genes contribute to initial behavioral variation, albeit pre and post-natal environmental factors may also influence this. In stage 2 it is recognized that some forms of uncommitted behavior are more likely to elicit a social response than are others and this waxes and wanes over time as the environment itself adapts to the behavior of the child. This stage is critical in the evolution from uncommitted behavior to challenging behavior. In stage 3 genetic events (in addition to pre- and post-natal environmental factors) alter individual development in such a way that determines the discrimination of stimuli. Thus genetic factors may in part determine the discrimination of certain stimulus events and thereby alter the likelihood with which certain contingencies are formed. In stage 4 challenging behavior contacts socially and non-socially mediated contingencies of reinforcement to become operant. Both genetic (stage 5) and environmental (stage 6) events establish these contingencies as effective forms of reinforcement and evoke challenging behavior by functioning as motivating operations. Finally in stage 7, the process of habituation shapes increasingly severe topographies of child behavior. Langthorne and McGill (2008) provide an extended discussion of this model, with particular reference to self-injurious behavior.

■ DIFFERENCES IN THE FUNCTIONS OF CHALLENGING BEHAVIOR IN FRAGILE X (FXS) AND SMITH-MAGENIS (SMS) SYNDROMES

FXS is the most common inherited cause of IDD, occurring in 1:3,600 males and 1:8,000 females in the general population (Turner, Webb, Wake, & Robinson, 1996). The genetic locus of FXS lies in a mutation on a single gene on the X chromosome known as the FMR1 gene (Verkerk et al., 1991). FXS is associated with a heightened prevalence of both aggression (Einfeld, Hall, & Levy, 1991) and self-injurious behavior (SIB) (Symons, Clark, Hatton, Skinner, & Bailey, 2003).

SMS occurs sporadically and has an estimated prevalence of 1/25,000, with an equal distribution between the genders (Greenberg et al., 1991). SMS is associated with an interstitial deletion of chromosome 17p11.2, although Slager et al (2003) suggest that haploinsufficiency of the RAI1 gene is the primary genetic cause of the syndrome. In comparison to other groups, SMS is associated with relatively high levels of aggression, as well as a range of stereotypical behaviors (Dykens & Smith, 1998) and a high prevalence of SIB (Martin, Wolters, & Smith, 2006).

Research on FXS and SMS to date has predominantly examined the form of problem behavior rather than its function. There is, however, some preliminary evidence to indicate that people with FXS and SMS may differ in the probability of displaying problem behaviors that serve certain functions. It appears that individuals with FXS may be less likely to display problem behavior that is maintained by the provision of social attention than would typically be expected and more likely to be maintained by the removal of aversive stimuli, and/or the provision of tangibles (e.g., Hall, DeBernadis, & Reiss, 2006; Symons, Clark, Hatton, Skinner, & Bailey, 2003). Symons et al., for example, using a modified version of the *Functional Assessment Interview* (FAI; O'Neil, Horner, Albin, Storey, & Sprague, 1990) reported that only 3% of children with FXS displayed attention-maintained SIB. In comparison, 65-87% were reported to display SIB in response to task demands and changes in routine.

In contrast several studies (e.g., Dykens & Smith, 1998; Smith, Dykens, & Greenberg, 1998) have noted the apparently

high level of 'attention seeking' behaviors in SMS. Taylor and Oliver (2008) reported that, for four out of the five children with SMS in their study, problem behavior was more likely to occur following periods of low adult attention or following reduced levels of demands and was likely to lead to an increase in attention or demands for those same children. Such evidence indicates that attention may hold different reinforcing properties for children with SMS than for other groups, such as children with FXS.

These groups, therefore, provided potentially fertile ground for the investigation of GxE. We conducted two studies. In the first (Langthorne & McGill, in press) we examined both between- and within-syndrome differences in the function served by problem behavior in FXS and SMS, in comparison to one another and to a control group of children with non-specific IDD. The *Questions About Behavioral Function* scale (QABF; Matson & Vollmer, 1995) was used to provide an indirect measure of behavioral function.

We found notable within-group differences for children with FXS. Children with FXS were significantly less likely to display attention-maintained than either escape- or tangible-maintained aggression or self-injurious behavior, with a non-significant trend in the same direction for destructive behaviors. Children with FXS were also less likely to display discomfort-related behaviors than escape or tangible-maintained behaviors across all topographies. In contrast, the within-group pattern of results for children with SMS showed minimal differentiation. Indeed, contrary to what had been predicted, children with SMS were no more likely to display attention-maintained challenging behavior than any other function.

The between group comparison was generally supportive of these results. Children with FXS appeared to be less likely than either group to display attention-maintained challenging behaviors. Significant differences were found with the SMS group across all topographies of challenging behavior and against the mixed etiology group for self-injurious behaviors and aggression. In contrast, children with SMS appeared to be more likely than either comparison group to display discomfort-related challenging behaviors. Significant differences were found against the FXS group for all three topographies on this subscale and against the mixed etiology group for self-injurious behaviors and aggression. No between group differences were found for the tangible, automatic or demand subscales of the QABF.

In the second study (Langthorne, McGill, O'Reilly, Lang, Machalicek, Chan, & Rispoli, 2011; Langthorne & McGill, in preparation) we sought to overcome some of the problems associated with indirect functional assessment methods by using experimental functional analysis methods with a group of eight children with FXS and six children with SMS. Each group was representative of those who took part in the previous study.

There was notable individual variation in the occurrence of challenging behavior. The pattern of results was, however, broadly consistent with those reported in the indirect study. Specifically, no child with FXS displayed any response class of challenging behavior that appeared to be attention-maintained. In contrast, four children with SMS displayed a response class of challenging behavior that was, at least in part, attention-maintained. Four of the six participants with SMS displayed challenging behaviors that were maintained by escape from demands and/or access to tangibles. This seems to support the findings of the previous study that children with SMS may not necessarily be any more likely to display attention-maintained behaviors than behavior that serves other functions.

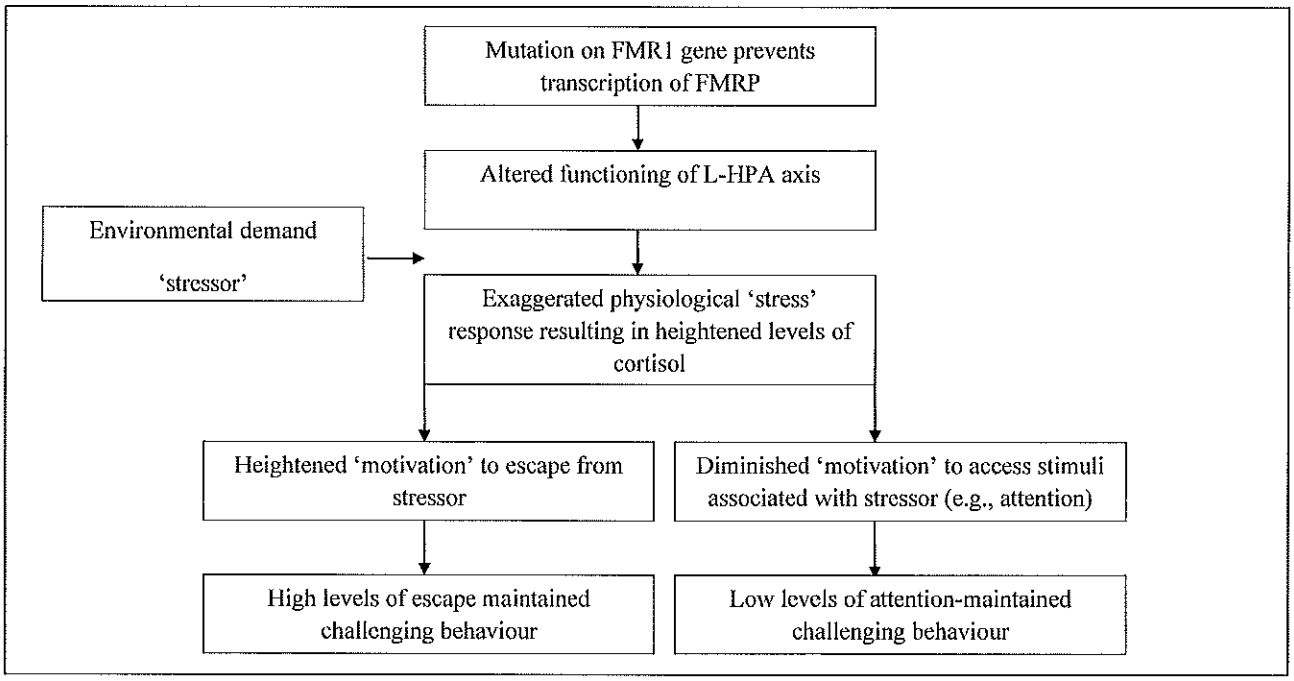

Figure 2. Hypothetical pathway between gene and behavioral function in FXS

■ GXE AND A DEVELOPMENTAL SYSTEMS MODEL.

The effects of genes on the developmental process involved in the emergence and subsequent maintenance of challenging behavior must be via neurobiological pathways (Moffitt, Caspi, & Rutter, 2005). For example, FXS has been associated with the impaired functioning of the limbic-hypothalamic-pituitary-adrenal (L-HPA) axis, which plays an important role in the mediation of the human stress response. It has been suggested that the L-HPA axis may influence the occurrence of challenging behavior in FXS, indeed positive correlations have been reported between levels of cortisol (an indicator of the functioning of the L-HPA axis) and parental report of behavioral problems (Hessl et al., 2002). Hypothetically, changes in brain circuitry that result from the mutation on the FMR1 gene that causes FXS, may lead to the altered functioning of the L-HPA axis. The onset of an environmental 'stressor', such as a demand, may lead to an exaggerated physiological stress response in children with FXS. This would be expected to enduringly heighten the child's 'motivation' to escape from such aversive stimuli and may explain the relatively high levels of negatively reinforced challenging behavior observed in this group. One would also expect children with FXS to show a diminished 'motivation' for stimuli correlated with the onset of demands, such as attention, perhaps accounting for the low levels of attention-maintained challenging behavior observed for this group. Figure 2 provides a depiction of this hypothetical pathway between gene and behavioral function in FXS.

Evidence of the complex interplay between the biology of the individual and their environment suggests that the environmental and genetic determinism that have to date characterised the investigation of challenging behavior may ultimately hamper the field and our ability to identify the determinants of such behavior. The findings above suggest that an expanded model is required to account for relations between variables at different levels of analysis, such as genes and environment, on the development of a response such as challenging behavior.

It has been argued for some time that the nature-nurture debate is 'dead in the water' (Schneider, 2003). Rather than being caused by genes or environment, development is better understood as being driven by the 'coaction' of elements that form a single integrated system (Gottlieb, 2003). Both genes and environment must work together as part of this system to produce any aspect of any living thing (Schneider, 2007).

Historically the application of behavior analysis has been concerned with addressing only part of this developmental system (i.e., the influence of behavior-environment relations). However, the radical behavioral philosophy that underpins applied behavior analysis is consistent with a developmental systems model, stressing the importance of interactions between the individual and the context in which they are embedded (Morris, 1988). Schneider (2007) notes that behavior analysis is entirely consistent with the developmental systems model, although its emphasis is on making the role of environmental factors and the behavioral principles therein explicit (p. 101). Within this approach, the question of whether a particular response is genetically or environmentally determined becomes redundant; rather the salient issue becomes what function each variable serves in relation to observable behavior (Thompson, 2007).

One contribution behavior analysis can make to the developmental systems model is to explicitly relate the influence of variables (whether endogenous or exogenous to the organism) at varying levels of analysis to underlying principles of behavior. As Thompson (2007) notes, endogenous variables, such as genetic, hormonal and neurochemical influences, can alter the reinforcing value of certain behavioral consequences (e.g., Kennedy, 2002), can function as discriminative stimuli that set the occasion for a given response (e.g., Schuster & Brady, 1971), and can function as a reinforcing consequence for certain responses (e.g., Sandman, Spence, & Smith, 1999). Relating genetic or neurobiological variables to operant principles of behavior will aid the delineation and understanding of the processes involved in GxE. Such an enterprise may hold important implications for our understanding of challenging behaviors, such as self-injury.

In sum, it is suggested that neither genetic nor environmental determinism provides an adequate model to account for challenging behavior displayed by individuals with intellectual and developmental disability. GxE may play an important role in the development and subsequent maintenance of such behaviors. The developmental systems model, which is consistent with the tenets of radical behaviorism, provides a means with which both endogenous and exogenous variables can be brought to bear on the functional analysis of challenging behavior.

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