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Review article

Parent–offspring transaction: Mechanisms and the value of within family designs☆

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ABSTRACT

Parenting is best understood as a transactional process between parents and their offspring. Each responds to cues in the other, adapting their own behavior to that of their partner. One of the goals of parenting research in the past twenty years has been to untangle reciprocal processes between parents and children in order to specify what comes from the child (child effects) and what comes from the parent (parent effects). Child effects have been found to relate to genetic, pre and perinatal, family-wide, and child-specific environmental influences. Parent effects relate to stresses in the current context (e.g. financial strain, marital conflict), personality and ethnicity but also to adverse childhood experiences (e.g. parental mental health and substance abuse, poverty, divorce). Rodent models have allowed for the specification of biological mechanisms in parent and child effects, including neurobiological and genomic mechanisms, and of the causal role of environmental experience on outcomes for offspring through random assignment of offspring–mother groupings. One of the methods that have been developed in the human and animal models to differentiate between parent and child effects has been to study multiple offspring in the family. By holding the parent steady, and studying different offspring, we can examine the similarities and differences in how parents parent multiple offspring. Studies have distinguished between family average parenting, child-specific parenting and family-wide dispersion (the within family standard deviation). These different aspects of parenting have been differentially linked to offspring behavioral phenotypes.

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Introduction

Parenting is best understood as a transactional process between parents and their offspring. Each responds to cues in the other, adapting their own behavior to that of their partner. Biology and behavior are finely interwoven in these transactional processes. Characteristics of children, influenced by both genetic and uterine experiences have effects on the parenting that children receive. Parenting is influenced not only by such child characteristics but by the experiences and characteristics of parents. And to add further complexity to the dynamics of reciprocal interactions, there are individual differences in the extent to which one is influenced by others. These influences interact in the context of life history shaped by natural selection, which defines the degree of 'plasticity' within biological systems that underlie phenotype. Thus, one person can be highly influenced by the behavior of another, while others are less influenced, both behaviorally and biologically.

One of the goals of human parenting research in the past twenty years has been to find methods for untangling reciprocal processes between parents and children: what comes from the child, what comes from the parent, what is emergent between them, as well as which bits of these processes influence the biology and behavior of offspring? One of the methods that has been developed in human parenting research has been to study multiple children in the family environment. By holding the parent steady, and studying their different offspring, we can examine the similarities and differences in how parents parent multiple siblings and factors that explain such differential parenting. When the siblings are twins, it is also possible to determine the extent to which genetic influences explain the differences in the parenting received by children. These within family designs in human research serve to further the understanding of the mechanisms that underlie parents' and children's influence on one another.

Animal studies of parent–offspring interaction have also, in recent years, exploited within family designs (Pan et al., 2014). Rodent models have the advantage that the breeding cycle is short (2 months from birth to adulthood) and the litters are large (3–9 pups per litter for mice and 8–18 pups per litter for rats). Of course, the beauty of the animal models in parenting research is the unambiguous demonstration of causal influence when random assignment is used and the understanding of social processes at the level of biological mechanisms. To date, there is a much more extensive literature on the topic of differential parenting in humans relative to non-human model organisms. The goal of this paper is to review the findings from the human and rodent literatures that inform why offspring from the same family are differently parented as well as the impact of such differential parenting on development.

What is differential parenting?

Differential parenting refers to differences in the parenting received by different children in the same family. Differential positivity refers to one child in the family receiving more positive affect, engagement, and involvement from the parent than another child in the family. Differential negativity refers to the parent directing more affectively negative behavior towards one sibling than towards another. Depending on the methods used for assessing human parenting, less than 50% of the variance in parental negativity and positivity is the same across siblings (using parental report) and this is reduced to around 25% with observational measurement studies (Browne et al., 2012; Jenkins et al., 2003a). The similarity in parenting is higher for monozygotic twins than dizygotic twins or full siblings, an issue we return to below (Avinun and Knafo, 2014).

One way that differential parenting has been framed is as a potentially negative factor (Plomin and Daniels, 1987; Turkheimer and Waldron, 2000). This is because children who are treated more negatively than their siblings show small increases in psychopathology over time (see 'Effect of differential parenting on offspring'). However, for both conceptual and empirical reasons, parenting siblings differentially embodies both negative and positive elements (Jenkins et al., 2003a). With respect to the positive aspect, parenting can be understood as a problem solving task. Parents have socialization goals for their children in which they try to moderate their children's predispositions to enable smooth integration with the society (Grusec and Ungerer, 2003). As parents respond to individual differences in their children and make judgments about what to require of them, when to push, etc. their sensitivity (seen as the essence of good parenting (Ainsworth et al., 1978)) results in differential parenting. On the other hand, links to adjustment, sibling relationship quality and children's accounts (see section 'What is the effect of differential parenting on the offspring?') suggest a more negative component. The child who gets less praise, or elicits more negativity, feels disadvantaged. Thus, when we observe differences in the parental behavior directed to individual siblings in all likelihood both negative and positive (pathogenic and benign) elements are embodied within the same score, with the same score differentially correlated with child outcomes.

The advantage of the within family design is that it allows us to parse the direct parenting score (that which is received by an individual offspring) into component parts: that which is in common to all children and that which is unique to one child. Most studies of differential parenting have only involved one sibling pair and use the difference score as the measurement of interest (Mullineaux et al., 2009). More subtle distinctions can be achieved by including the parenting to all children in the family and doing the analysis with multilevel modeling to distinguish between family-wide and child specific parenting. Such a design allows for the distinction of 3 parenting elements: the average parenting across children (family-wide mean), the within family standard deviation (family-wide dispersion) and each child's deviation from the mean (child-specific) (Meunier et al., 2013). Such distinctions have been found to be differentially predictive of child behavior, an issue we return to in the section 'Effect of differential parenting on offspring'. Even more important is the methodology from the Social Relations Model (Kenny et al., 2006) because it allows us to differentiate between a person effect (an aspect of a person's behavior that is evident in all their interactions) versus an effect of a relationship (the way in which a person behaves in a specific relationship). By observing a person interacting with every other person in the family (called a round-robin design) we can determine the extent to which an individual behaves in the same way across all family members (called the person's actor effect), elicits the same behavior from all family members (called the person's partner effect), the extent to which all family members behave similarly to one another and different from other families (called the family effect) and the components of interpersonal behavior that are unique to one particular dyad (the dyad effect). The component that this design offers, over the multilevel differential parenting design, is that we can isolate the behavior of the child that occurs in all relationships from the behavior that is specific to one mother–child relationship. Is the mother being specifically reactive to one child or does the child behave provocatively with everyone and elicit irritation from everyone? This enables us to understand processes in differential parenting more accurately. We return to this issue when we consider gene–environment correlation.

The animal studies have, to date, not attempted to isolate and remove the contribution of the individual pup to the parenting that the pup receives. However, it has been noted for some time that the care received by individual pups varies substantially within litters. Decades ago, it was observed that male rodent pups receive twice the ano-genital licking that female pups receive within a litter, and that these differences have sex-specific effects on offspring behavior and neuroendocrine development (Moore, 1984). Recently, a handful of animal studies have used rank order measurement within families distinguishing between pups that receive above and below average (in their litter) levels of care (Cavigelli et al., 2010; Pan et al., 2014; Ragan et al., 2012; van Hasselt et al., 2012a, 2012b). Studies that have

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used a within family design have demonstrated that the amount of care that individual animals receive shows large and stable inter-individual differences across the pre-weaning period. A few studies to date have reported that pup-initiated behaviors modify the maternal response. For example, tactile stimulation of the mother by the pup increases maternal licking in rats (Ragan et al., 2012), data supporting previous observations that maternally-directed orienting behaviors by neonates plays a critical role in nursing (Polan et al., 2002). These studies have built on evidence that the amount of parental care provided is closely associated with the expression of a number of behavioral phenotypes in the offspring (e.g. ultrasonic vocalization, exploration in the elevated plus maze), even among genetically identical individuals. These differences in care received also have long-term impacts on several aspects of neuroplasticity and neuroendocrine function. This form of parentally-mediated phenotypic plasticity has been described in terms of parental 'provisioning' of resources that maximize fitness and of developmental plasticity that enables matching the offspring phenotype to the environment it will likely encounter (Crean and Marshall, 2009). These concepts are consistent with the more general evolutionary requirement that variation (e.g. between and within litters) must exist in order for adaptation to occur.

Child effects in differential parenting

Differential parenting is, in part, a function of characteristics of offspring to which parents respond. Although we cover this issue more fully below (under rGE and genetic influence) here we consider the broad range of factors thought to explain differential parenting. Age of child plays a strong role with parents showing higher levels of engagement and reciprocal positivity towards younger children (Dunn and Plomin, 1986; Jenkins et al., 2003a). Being a boy has been found to elicit more parental negativity as well as more parental conflict patterns that may be explained by higher levels of externalizing behavior in boys (Jenkins et al., 2005a; Joussemet et al., 2008). Externalizing behavior (poor emotion regulation, negative temperament, oppositional behavior, aggression, hyperactivity and inattention) has been found to be an important child characteristic that is associated with negative parental behavior, explains within family differences in parenting (Browne et al., 2012; Lysenko et al., 2013) and is associated with parental stress (Theule et al., 2013). Positive temperament and prosociality may also be relevant (Barnett et al., 2012).

In the rodent literature, a number of pup cues have been found to be associated with maternal care, although the extent to which these processes explain within family differential parenting is not yet known. Mothers do not respond to differential olfactory cues from young although they do respond differentially to male and female pups based on odor/taste of urine. The role of audition in differential maternal behavior has not yet been demonstrated, but is quite likely. Whereas auditory cues seem not to be necessary for the initial expression of maternal behavior, they affect such behavior later on. Ultrasonic vocalizations (USVs) emitted when individual pups are displaced from the nest help their mothers orient to them and increase the likelihood of transport to the nest, and deafening does increase the latency of maternal sniffing and retrieving and increases accidental stepping on pups (Stern, 1997). Lactating mice prefer USVs and synthesized calls with certain acoustic properties over other ultrasounds and can detect calling pups at more than 100 cm from the nest (Ehret, 2005). Moreover, dopamine receptor subtypes influence the acoustic properties of USVs differentially, with selective dopamine type 1 (D1) receptor antagonism altering acoustic parameters to a greater extent than D2 receptor antagonism, though D2 antagonists reduce USVs in pups (Curry et al., 2013; Ringel et al., 2013). Taken together, pups with different dopamine profiles may have different patterns of ultrasonic calls. In summary, it is likely that within litter differences in maternal care may be explained by vocalizations as well as male/female differences in the odor and taste of urine, although the within litter analyses have not yet been conducted. It will be important for future work to determine whether there are behavioral differences in pups, discerned at birth, that explain within litter differences in parental care and the extent to which these differences are explained by underlying biological mechanisms.

Mechanisms in child-effects

The reasons for individual differences in child behavior are a very large topic area that encompasses all of the developmental and environmental processes in child development. Our consideration of these mechanisms in the current paper is consequently highly selective. As our interest is in sibling differences, we concentrate on biological (genetic and uterine) and social processes that have been found to explain sibling differences or represent good candidates for such an explanation.

Genetic influence and the evocative gene–environment correlation

Among humans, it is clear that parents react to differences among their children that are due to within-family genetic variation. Plomin et al. (1977) proposed three types of gene–environment correlations (rGE): passive, active, and evocative. Applied to parenting, passive rGE happens when the parent not only provides the environment but also shares genes with the child, thus creating an association between the genes of the child and the parenting he or she receives. Active rGE, which is less relevant to parenting, refers to instances in which the child selects an environment (e.g. befriends peers) based on his or her genetics. Finally, evocative rGE, in which parents react to children's genetically influenced characteristics, is the kind of rGE likely to create parental differential treatment. Parents respond to the genetically influenced differences between siblings.

In a now-classic study, the negative control received by adopted children from their adoptive parents was associated with the biological mothers' antisocial behavior, suggesting that a genetic risk in children affected the parenting they received in their adoptive families (O'Connor et al., 1998). More recently, in a large adoption study, biological mothers' positive temperament related to lower harsh parenting by adoptive fathers (Hajal et al., 2015). Most evidence for evocative rGEs comes from twin studies. A meta-analysis found that parents treat their children more similarly if they are monozygotic (MZ) twins than if they are dizygotic (DZ) twins, this genetic effect accounting for 23% of the variance in parents' behavior (Avinun and Knafo, 2014). Thus, within-family differences in parental negativity and positivity, both in affect and control behavior, were attributable to genetic differences between siblings.

Of course, children's genes cannot directly affect their parents, and it is important to understand what aspects of children's genetically-influenced behavior affect the parenting they receive. It has been argued that the presence of an evocative rGE necessitates four conditions (Jaffee, in press). First, the child's behavior should be under genetic influence. Extensive research has shown that child temperament, cognitive abilities, and psychopathology are all heritable to some extent (Plomin et al., 2008). Second, the parenting variable should also show a putative genetic effect. Third, there should be a phenotypic association between the child variable and the parenting variable, preferably using a longitudinal design controlling for previous levels of parenting and child behavior. Fourth, multivariate genetic analyses should show that the phenotypic association reflects an overlap in the genetic factors (looking at the child's genes) accounting for both variables (child and parent).

Children's disruptive or antisocial behavior may be a key variable in how they affect the parenting they receive. For example, children's antisocial behavior was associated with their experiences of corporal punishment, an effect largely accounted for by a genetic factor common to these two variables (Jaffee et al., 2004). In another study, children's psychopathic personality at 9–10 years of age accounted for 14% of the

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genetic influences on parental negativity in middle adolescence (Tuvblad et al., 2013).

In a large twin study using parent reports, reciprocal effects were found between parental negativity and children's antisocial behavior from age 4 to age 7. Genetically influenced antisocial behavior at age 4 accounted for 3% of the variance in parental negativity at age 7, thus showing an evocative rGE (Larsson et al., 2008). In a study of older twins, parent–child conflict at age 11 independently contributed to adolescents' externalizing problems at age 14, suggesting a parent effect. In addition, externalizing problems at age 11 independently predicted change in parent–adolescent conflict towards age 14, indicating a child effect. A genetic correlation between conflict and externalizing problems indicates that the child's genetically-influenced externalizing problems evoked conflict with parents. Considering relationship patterns in the family, the authors suggested a "downward spiral" in which parent–child conflict and children's externalizing influence each other (Burt et al., 2005).

The internalizing symptoms of anxiety and depression are also implicated in evocative rGE. Eley et al. (2010) observed twins and their mother interact in a cooperative Etch-a-Sketch task. High maternal control was positively associated with eight-year old children's anxiety, and further analyses showed that children's genetic influences on anxiety overlapped with those on maternal control. In a twin/sibling study, parents' conflict-negativity towards their children and adolescents' antisocial behavior and depressive symptoms predicted changes in each other over a three-year old period, so that high conflict was associated with increase in symptoms and vice versa. The overlap in genetic influences on adolescent and parent behavior suggests that children's genetically-influenced traits evoke further negativity in parents (Neiderhiser et al., 1999). The influence of parents' behavior suggests, again, a downward spiral of mutual negative influences in some families. In another study, adolescents' depressive symptoms correlated positively with punitive discipline received from their parents. Again, genetic factors largely accounted for this association (Lau et al., 2006).

Most of the research on this topic has focused on externalizing and internalizing symptoms. Research in other domains of child functioning, such as cognitive abilities, is still needed. One twin study did find evidence for an evocative rGE between parental negativity and positivity and children's prosocial behavior (Knafo and Plomin, 2006).

The way in which internalizing and externalizing symptoms are displayed in the parent–child relationship is likely to be especially relevant to the creation of differential parenting. In one study of observed interactions between children and mothers, genetic influences were found for children's control attempts towards their mothers (but not warmth). These genetic effects on children's behaviors largely overlapped with children's genetic effects on mothers' control towards them, indicating an evocative rGE in which children's control attempts affected mothers' control (Klahr et al., 2013). Similarly, children with the 9-repeat variant of a polymorphism in the dopamine active transporter 1 (DAT1) tended to show more negative affect towards their parents in a standardized parent–child interaction. Parents, in turn, showed more hostility and lower guidance/engagement towards their children if the latter were 9-repeat allele carriers. Mediation analyses supported a gene → child negative affect → parenting evocative rGE process (Hayden et al., 2013).

Extending the construct of the evocative gene–environment correlation (which refers to a single parent–child dyad) we can look at the extent to which child behavior evokes the same response from all family members (by using the Social Relations Model design described above). In a study of 680 families, Rasbash et al. (2011) observed the interactions of all dyads in each family for expressions of negativity and positivity. They found that no partner effect was evident for positivity: individuals did not elicit the same levels of positivity from different family members. They did, however, find a significant partner effect for negativity. Nine percent of the variance in family negativity was attributable to what one individual systematically elicited from other family members. Actor effects were found to explain about 20% of the variance in negativity. This means that children do express a similar level of negativity towards the different people with whom they interact (at the level of 20%), and that individuals do elicit systematic responses from others but not quite to the same degree (10%). Thus, we see that some people are more tolerant than others of provocative child behavior. Understanding these results in the context of the evocative gene environment correlation, we can conclude that there are genetically driven child characteristics that elicit responses from those with whom the child interacts, and that individuals vary on their tolerance for such negative child behavior. Of course, it is beneficial for society that strong partner effects for challenging children do not operate! Such children's lives would be unbearable if everyone with whom they interacted always reacted to their negativity with matching negativity.

Environmental processes (child-specific and family-wide) that influence child behavior

A large number of environmental circumstances have been found to contribute to children's problem behaviors. Risk factors such as social disadvantage and the quality of an individual's experience in close relationships (parent, sibling, peer) are the strongest and most consistent of these (reviewed in Jenkins et al., In Press). For instance the influence of parenting on a range of child phenotypes has been extensively studied for 50 years (O'Connor, 2002).

As the literature on environmental risks for child development is so large, in the present paper we only consider those risks directly related to sibling differential experience. Distinctions have been made between risk factors that are shared by all siblings (called family-wide risks), while others are unique to one sibling (called child-specific risks). Even some risks that initially appear to be family-wide, such as parental conflict are really best thought about as child-specific. For instance Jenkins et al. (2005a) found that there was a family-wide process involved in parental conflict, but that there were also child-specific components: certain children elicited more parental conflict and were more often in the room, than their siblings. Thus, again, we see the role of child characteristics in the ways that children shape the environmental experiences that they have (rGE) and the way that such experiences subsequently influence them.

There are environmental exposures that relate specifically to the presence of siblings in the home. Larger family size is associated with higher levels of problem behavior (Doan et al., 2012), as is being laterborn (Rostila et al., 2014). It has also been suggested that older siblings train their younger siblings in difficult behavior (Slomkowski et al., 2001) although studies that control for genetic influence have not confirmed this training effect (Steele et al., 2013). Siblings influence learning outcomes (such as language and theory of mind) which are important contributors to child behavior (Jenkins et al., 2003b; Prime et al., 2014).

In the experimental rodent literature (which allows for stronger causal inference about the role of parenting in offspring development) variations in maternal care have been shown to influence a range of physiological and health-related offspring outcomes, from fearfulness and the response to stress, to growth and reproductive behavior (Meaney, 2001). Consequently, environmental factors that alter the levels of maternal care provided are associated with these outcomes in offspring. Chronic psychosocial stress in the mother during pregnancy is associated with lower levels of maternal care, increased behavioral and endocrine responses to stress in adult offspring, and long-term changes in the function of stress-related genes in the brain and in placenta (Champagne and Meaney, 2006; Mueller and Bale, 2008). Dietary factors are also increasingly recognized to have long-term impacts on these same cognitive domains in offspring. For example, similar to the effects of chronic psychosocial stress, maternal overnutrition appears to alter anxiety-like behavior in offspring in part by programming the

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neural systems that underlie the response to stress, and potentially via alterations in maternal care (Sasaki et al., 2013; Sasaki et al., 2014; Purcell et al., 2011). In rodents, these factors have been studied at the level of family-wide effects, and their impacts on within-family variation are presently unknown. However, given the interaction of these factors with maternal care, their influence on within-family variation should be explored.

Person by environment interaction

Not only are siblings differentially exposed to risky environments, but siblings vary markedly in their susceptibility to environmental influences (Rutter, 2013). Although on average, there is a raised risk to all children through exposure to risky environments, the effects come about because a subsample of children show marked vulnerability to adversity, while others remain relatively unaffected. One source of differential vulnerability relates to endogenous processes in the individual: genetic vulnerability, temperament, pre and perinatal risks, gender (boys are typically more vulnerable to environmental risks than girls), IQ, prior levels of adjustment and many others (Jenkins, 2009). Many studies have shown that variability on certain genetic markers is associated with stronger environmental effects (Kim-Cohen et al., 2006). Although there is little direct evidence from within-family comparisons, one study showed that within the same family, parenting–child behavior associations were found among siblings carrying the 7-repeat allele of the DRD4-III polymorphism but not among the non-carrying sibling (Knafo et al., 2011). To the extent that such differences in child behavior elicit parental behavior, these person x environment interactions should further increase parental differential treatment of their children.

Another source of differential vulnerability is the relational environment. Individual vulnerability to environmental adversity is buffered by the presence of close relationships in the person's life. Such effects have been shown for parents, siblings, friendships, and non-parental adults (Gass et al., 2007; Jenkins, 2009). Thus, differential reactivity to family stressors results in greater variation on sibling behavior. In turn, such behavioral effects of children influence the parenting that they receive.

Pre and perinatal events that contribute to child effects

A range of events during pregnancy have been found to predict children's problem behavior: maternal smoking (Abbott and Winzer-Serhan, 2012), blood pressure (Wade and Jenkins, 2014), placental dysfunction (Roza et al., 2008), infection (Depino, 2006) and depression and anxiety (O'Donnell et al., 2013) have all been found to be associated with increased behavioral and physiological difficulty in children. The mechanisms of these exposures and the way in which early brain development is compromised are not yet well documented. Child birthweight and gestational age are well established markers for later pathology (Aarnoudse-Moens et al., 2009; Colman et al., 2007; Johnson et al., 2010) that predict problem behavior across the life course. Birthweight is one of the few perinatal markers that has been investigated in siblings. It has been shown to explain differences between MZ twins in problem behavior (Asbury et al., 2006; van Os et al., 2001). As this design controls for genetic influence, as well as shared environmental effects, these findings underscore the role of birthweight as a causal risk factor in child problem behavior. Furthermore, differential parenting has been found to be explained by sibling differences in birthweight (Asbury et al., 2006).

Epigenetic influences

In addition to genetic mechanisms, biological mechanisms that alter gene function without changing the inherited genetic sequence, called 'epigenetic', also contribute to inter-individual variation. Within a given individual, virtually all cells have an identical genotype. Epigenetic mechanisms are required to regulate patterns of gene transcription (i.e. RNA expression) that are needed to produce each of the more than 200 cell types from a common genome. These mechanisms fall into three primary categories: histone modifications, non-coding RNAs, and DNA modifications. Histone modifications affect the binding of DNA to the histone proteins around which it is wrapped, altering the accessibility of the DNA to other factors that regulate transcription. Non-coding RNAs, expressed genetic elements that do not code for proteins, are highly abundant in the genome (more than 80% of the genome produces RNA) and regulate the expression of other genes. DNA modifications alter the structure of the DNA itself through, for example, the addition of methyl groups that affect the binding of transcription factors to specific nucleotide sequences. This category of epigenetic mechanism is often called 'DNA methylation'. Although several different forms of DNA modifications exist, DNA methylation remains the best understood epigenetic mechanism and is the most widely studied, particularly in human subjects, due to technical considerations and evidence that it is among the most stable forms of epigenetic mechanism. During development, much of the DNA is demethylated and re-methylated at specific time-points in egg, sperm and embryo, with the exception of imprinted genes that escape this 'reprogramming'. For imprinted genes, gene expression depends upon which parent it was inherited from, so called 'parent-of-origin' effects. One example is the insulin-like growth factor 1 gene, which regulates offspring growth in a parent-of-origin manner. Many other non-imprinted genes also show epigenetic 'plasticity' that may have origins in evolutionary adaptation (Weber et al., 2007). As we will discuss, epigenetic 'plasticity' is affected to some degree by variations in environmental factors during development.

The degree of susceptibility of genes to epigenetic variation by environmental factors is still rather poorly understood. In MZ twins, variation in DNA methylation between co-twins is present at birth (Gordon et al., 2012), and cross-sectional studies indicate it increases with age (Fraga et al., 2005). Other factors are also associated with altered DNA methylation, including parental age, and artificial reproductive technology (ART), though it is unclear whether infertility leading to ART or interactions with the age of parent are responsible for these alterations (Melamed et al., 2015). A number of fundamental questions remain unresolved, including the degree of individual variation in specific tissues that influences developmental trajectories, such as placenta. Parental maltreatment has also been implicated in epigenetic modifications in offspring. For example, we found that childhood sexual and physical abuse or severe neglect is associated with alterations in DNA methylation in a number of genes that regulate neuroplasticity within the hippocampus of adult suicide victims (McGowan et al., 2008; Suderman et al., 2012). Methylation of the promoter of the glucocorticoid receptor gene, a major regulator of the endocrine response to stress, is associated with impaired binding of the EGR1 transcription factor and down-regulation in the expression of the stress-related Glucocorticoid Receptor (GR) gene in the hippocampus of suicide victims with a history of abuse, but not of non-abused suicide victims or controls who died of other causes (McGowan et al., 2009). It was once thought that epigenetic mechanisms such as DNA methylation remain static after development particularly in non-dividing cells such as neurons, but recent evidence suggests some genes are epigenetically responsive to environmental signals throughout life (Sweatt, 2013). Finally, in addition to environmental factors, the epigenetic profile is influenced by the underlying genetic sequence as well as stochastic factors, particularly during cellular replication when the epigenetic pattern must be faithfully maintained. These influences are a subject of current investigations (Petronis, 2010; Teh et al., 2014). Rodent offspring show levels of DNA methylation in the GR gene promoter that vary as a function of both between-family and within-family levels of maternal care received (Pan et al., 2014). To date, the role of inter-individual differences in epigenetic profiles as a mechanism of differences in the parenting that siblings receive is unexplored in humans. However, given the degree of inter-individual variation in epigenetic mechanisms at birth and early in life in biological systems subserving social behavior and stress, their

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involvement as a causal factor in differences in parenting received or in the effects of differential parenting seems likely.

Birth order influences

As we described above, there are birth order and family size influences on the problem behavior and personalities of children, but these two factors also influence the parenting that children receive. Larger family size has been found to be associated with fewer parenting resources to individual children and this parenting process has been referred to as resource dilution (Downey, 1995, 2001). This effect has been shown for basic caregiving, cognitive stimulation, and interpersonal relations. Furthermore, laterborn children receive less language input directly from their parents, the quality of input is less supportive of language development and they receive less engagement and positivity from parents (Jenkins et al., 2003a; Oshima-Takane et al., 1996). Negative parenting has not been found to differ by birth order. Interestingly, there is evidence that older siblings provide some compensation for being laterborn in a large family. When laterborn children in large families have older siblings who are sensitive to their thoughts and competencies during challenging cognitive tasks (referred to as cognitive sensitivity), their language skills are much better than children who do not have cognitively sensitive older siblings (Prime et al., 2014).

Parent effects in differential parenting

As well as the child factors that drive parenting, parental experiences and contexts explain differential parenting. When the social context for parenting is more negative, parents show greater differences in the ways that they treat different children in the family. Low socioeconomic status is one of the most persistent correlates of differential parenting, with lower parental income and education being associated with higher degrees of differential positivity and negativity across the sibship (Atzaba-Poria and Pike, 2008; Crouter et al., 1999; Jenkins et al., 2003a). Marital conflict has also been found to be associated with differential negativity. When there is more conflict and argument between parents, the degree of differential parental negativity with respect to the sibship is greater (Deal, 1996). Marital conflict and socioeconomic status have been found to interact in the prediction of differential parenting showing that when these risks combine they potentiate one another in their impact on differential parenting (Jenkins et al., 2003a).

Individual differences in parents' personality have been found to explain differential parenting. High levels of agreeableness in mothers and fathers are associated with lower levels of reported differential parenting. Parental personality may have an effect on their reactivity to child behavior. Oppenheimer et al. (2013) were interested in examining the extent to which the gene–environment correlation was influenced by parental personality. They found that the relationship between child catechol-O-methyltransferase genotype (COMT) and positive parental behavior varied as a function of parental personality. Parents with low levels of neuroticism and high levels of extraversion exhibited greater sensitive responding to youth with the valine/valine genotype. Thus, parental personality contributes to parents being more or less reactive to genetically driven aspects of child behavior, which in turn contributes to differential parenting. Of course, such parental differences in reactivity may themselves also be genetically driven (Fortuna et al., 2011; Kaitz et al., 2010).

The same pattern is seen for adversities in the parents' own childhoods, particularly when we look at the number of adverse events that parents have experienced in their childhoods. When parents have had more stressful and riskier childhoods, the likelihood of differential parenting is greater (Meunier et al., 2013). As yet, there has been little consideration of the role of ethnicity in differential treatment research. Given the strong differences in parenting across ethnicities (Bornstein and Lansford, 2014), we would also expect ethnicity to be related to differential parenting.

We can conclude from these findings that when human parenting resources are taxed, through stresses such as low socioeconomic status, marital conflict and exposure to adverse experiences in childhood, children are treated more differentially by parents. It has been suggested that when parents struggle with fewer basic resources, they respond by concentrating available resources on one child (Henderson et al., 1996). The stress created by resource limitations may result in two reactions that increase differential parenting: an increased need for support and comfort (drawing the parent to one child more than another) and decreased tolerance (and thus increased reactivity) to the irritating behavior of an individual child.

Animal models have helped identify biological mechanisms associated with the effects of parenting behavior on offspring phenotypes, and there is a large amount of evidence showing that experiences during early life affect later parenting behavior in rodents (Barrett and Fleming, 2011). As yet, all of this work relates to parenting towards an individual offspring rather than differential parenting. Thus, female offspring that receive low levels of licking and grooming (LG) show impaired maternal behavior in adulthood compared to offspring of relatively high LG mothers (Champagne and Meaney, 2007). Similar effects on maternal behavior have been noted with complete maternal deprivation or prolonged periods of neonatal separation (Lovic et al., 2001). Cross-fostered female offspring exhibit maternal LG similar to that of their adoptive mothers, suggesting the intergenerational transmission of maternal care via a behavioral mechanism (Champagne et al., 2003; Francis et al., 1999). These phenotypic outcomes are associated with stable changes in gene expression that persist throughout the lifespan, and appear to involve epigenetic mechanisms. Individual differences in maternal LG are associated with differences in mRNA expression of endocrine-related genes in areas of the brain that regulate maternal behavior. For example, differences in estrogen receptor alpha expression in the medial preoptic area of offspring were found to vary with levels of maternal care received, and these differences were shown to be associated with differences in DNA methylation of a STAT5 transcription factor binding site within this brain region (Champagne et al., 2006). Indeed, epigenetic changes associated with maternal care were subsequently shown to be widespread, influencing many other genes implicated in neuroplasticity and stress-related processes (McGowan et al., 2011; Murgatroyd et al., 2009; Roth et al., 2009). Recent evidence by Szyf and colleagues has extended these observations to non-human primates (Provencal et al., 2012; for a review of the biology of maternal care in non-human primates see Saltzman and Maestripieri, 2011). Thus, postnatal programming effects can derive from environmentally induced alterations of mother–offspring interactions, involving systems that determine methylation patterns in specific gene loci related to maternal behavior. Though untested at present, it is possible that inter-individual epigenetic signatures that arise early in life and appear to be stably maintained throughout the pre-weaning period, such as those in the estrogen receptor alpha gene, constitute a biological mechanism of plasticity that interacts with differential parenting initially in response to parental signals and subsequently as a feedback mechanism that elicits differential treatment from parents.

Thus, there is clear evidence from rodent models that experiences in childhood profoundly affect a parents' ability to parent but the extent to which these early experiences affect the way that multiple offspring are parented has not yet been examined.

What is the effect of differential parenting on the offspring?

Several different aspects of differential parenting have been described in the literature. One aspect relates to the extent of a child's 'advantage' or 'disadvantage' in relation to his or her sibling/s (child-specific differential parenting) which can explain differences between children within families. Another aspect assesses the extent of differential parenting across the whole sibship (the standard deviation across the sibship) which can explain between family differences in child

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behavior. There is much evidence for the relationship between child-specific differential parenting and child outcomes in the expected direction. More child-specific parental negativity and less parental positivity in comparison to siblings is associated with an increase over time in both mental and physical health problems (Browne and Jenkins, 2012; Burt et al., 2006; Deater-Deckard et al., 2001; Mullineaux et al., 2009). Interestingly, this effect is curvilinear. Low and moderate levels of child specific differential parenting are not strongly associated with child outcomes (Burt et al., 2006; Meunier et al., 2012), but when differential parenting is marked, the effect is evident. It has also been shown that the more similar the children are with respect to age, the greater the association of differential parenting with child outcomes. This suggests that children that are similar in age experience themselves as competing for parental resources more than children with greater age gaps (Meunier et al., 2012). Differential parenting of both mothers and fathers has been shown to be associated with negative child outcomes (Meunier et al., 2012). Some studies have asked children about reasons for differential parenting. When children see differential parenting as justified (by children's age, disability, etc.) differential treatment is no longer predictive of problematic child outcomes (Kowal and Kramer, 1997).

Differential treatment has also been found to be associated with the quality of the sibling relationship. Those who experience themselves as disfavored report more negativity in sibling relationship quality (Jenkins et al., 2005b; Jenkins et al., 2012). Interestingly, this association is maintained into adulthood, as differential treatment in childhood continues to be associated with the quality of the sibling relationship as reported by 60 and 70 year olds (Suitor et al., 2008).

Animal studies confirm the role of differential parenting within litters on offspring outcomes. In rodents, differential care occurs over a relatively short time period that is closely associated with brain development. The variation in maternal care seen within litters is approximately the same as that observed across litters, where a 2–3 fold difference in the frequency of maternal licking is observed during the first postnatal week (Cavigelli et al., 2010; Ragan et al., 2012). Male but not female offspring show positive linear relationships between several measures of adolescent play behavior and the frequency of maternal care received (van Hasselt et al., 2012b) as well as sex-specific effects on several measures of neuroplasticity that support learning and memory (van Hasselt et al., 2012a). All female litters show that some behavioral differences relate to between-litter effects, while others relate to within-litter differences in the amount of maternal care received (Pan et al., 2014). Adult rats from mothers that provided higher overall levels of maternal care show increased locomotor activity in an open field relative to rats from mothers who provide less maternal care. In contrast, more time spent in the center of the open field, used as a measure of lower levels of anxiety behavior, is observed among adult rats that had received higher levels of care relative to their to their siblings regardless of the overall amount of care provided by their mothers (although see Ragan et al., 2012). As mentioned above, these differences in behavior were associated with both between-litter and within-litter difference in the methylation of specific sites within a GR gene promoter. These effects suggest that there may be specific epigenetic mechanisms that respond to maternal cues and others that respond to cues provided by the context of the litter or arise as a function of individual differences that relate to pup solicitation of maternal care, including genetic differences (Pan et al., 2014).

In humans, the other aspect of differential parenting shown to relate to child outcomes is the extent of differential treatment across the whole family (Boyle et al., 2004; Meunier et al., 2013). This is most effectively measured in studies that include sibships that are greater than two (most studies just include one sibling pair which in large families misrepresent the sibship). These studies have shown that the more differential the treatment across all children, the higher the levels of mental health problems among all children in the family (after accounting for covariates including family size, age gap etc.). This finding has been likened to the negative effect of differential income across the society on the mean level of health in the society. The higher the differential between the top and bottom 20% of the society on income, the worse the health problems in the society (Wilkinson and Pickett., 2009). This has been explained as the unequal distribution of resources within societies as having a negative impact on the health of individuals. The same argument has been made for the family: unequal allocation of parental resources across siblings is associated with more problematic development of children.

Conclusions

Most children grow up in the context of having siblings, yet most of what we know about the parent–child dyad and the effects of this dyadic exchange on development, come from designs that only examine a single parent–child dyad. The goal of this paper has been to show, through a review of human and animal findings, that using a within family design helps to uncover the unique individual characteristics (of both parents and children) that influence the dyadic relationship. For both humans and rodents, absolute levels of parenting are important in explaining offspring outcomes, but so too are differences within the family or litter. The occurrence of such differences is, to some extent, driven by the offspring but it would also appear that receiving more or less positive care than a sibling may also affect adaptation. Within family designs have been used more extensively in human than rodent research to date. As animal models allow for better investigation of causal process and mechanism, the use of within litter designs within the animal model could prove very valuable.

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