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Identifying the interaction of maternal sensitivity and two serotonin-related gene polymorphisms on infant self-regulation

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ABSTRACT

During infancy, orienting and gaze aversion serve as major self-regulatory mechanisms and play an important role in the development of deliberate self-regulation and control. The present study examined the interaction of intrinsic factors (MAOA-uVNTR and 5-HTTLPR gene polymorphisms) and extrinsic factors (maternal sensitivity) on early infant self-regulatory behavior. We assessed 5-HTTLPR (ss + sl versus ll) and MAOA-uVNTR (3 and 4 among boys, and 3/3, 3/4, and 4/4 among girls) polymorphisms, determined maternal sensitivity during mother–child free play, and coded infant self-regulatory behavior (i.e., orienting shifts in a temperament test) in 281 six-month-old infants. We found that infants who experienced a lower level of maternal sensitivity and had the short allele of 5-HTTLPR variants and the 3/3 MAOA-uVNTR polymorphism displayed lower self-regulation capacity than did those infants with a higher level of maternal sensitivity. This finding suggested a modulatory role of maternal sensitivity. Moreover, these findings are consistent with the genetic vulnerability hypothesis, which states that beneficial environmental factors serve as a buffer against harmful genetic predispositions during child development.

1. Introduction

1.1. Self-regulation and maternal sensitivity

Self-regulation, a core aspect of the temperament development theory proposed by Rothbart (Strelau, 1998), is defined as a series of processes that facilitate or inhibit behavioral and attentional reactions to enable people to function properly in society (Eisenberg, Fabes, & Guthrie, 1997; Rothbart, Ellis, & Posner, 2004). The theory of self-regulation indicates that very young infants have the capacity to engage in sensorimotor activities and voluntarily make contact with others (Kopp, 1989), and this capacity is important for the formation and execution of self-control in toddlerhood through to adulthood (Rothbart et al., 2004). During childhood and adulthood, self-regulation has been found to be associated with aggressive behavior (Crockenberg, Leerkes, & Bárrig Jó, 2008), attention-deficit hyperactivity disorder (Durall, 1999), and other antisocial behavior

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(Ellis, Rothbart, & Posner, 2004), in that having sufficient self-regulation helps suppress negative dominant responses, thereby allowing more positive sub-dominant responses to be performed.

Because of its critical importance in child social development, the environmental factors related to individual differences in self-regulation have been extensively studied (Calkins & Dedmon, 2000; Eisenberg, 2005). Maternal sensitivity in infancy refers to the pattern of maternal behavior in which mothers respond promptly, appropriately, and contingently to their infants' cues. This is important for the development of a secure mother–child attachment relationship. Ainsworth et al. and Bowlby have demonstrated that the harmonization of maternal caregiving behaviors to infant cues and responses is essential for shaping sensitive parenting, which is exemplified by child-centered responses to the physical and emotional needs of the infant (Mills-Koonce et al., 2007). Repeated experiences with sensitive maternal parenting allow children to develop a strong ability to use their full repertoire of emotional communication in a well-regulated manner (Tronick, 1989). Bell et al. found an association between maternal insensitivity and infant irritability, whereby infants with insensitive parents cry much more easily than infants with responsive, sensitive mothers. Recently, a longitudinal study found that maternal sensitivity was related to positive aspects of mood in infancy. Further, infants with less sensitive parents show higher "fussy" activity levels than do those with more sensitive parents (Kivij rvi et al., 2001).

1.2. Behavioral genetic study of self-regulation

Behavioral genetics research based on twin and adoption studies has provided evidence for the genetic influences of active control (Goldsmith, Buss, & Lemery, 1997), which underlies the emergence of self-regulation in the second year of life. Thus, individual differences in self-regulation can be attributed to genetic and/or environmental factors. As referred to by Shonkoff and Phillips (2000) "developmental psychologists stand at the threshold of a new era in understanding the biological bases for human growth and continue to address fundamental questions about parenting influences. The dynamic interplay between gene action and environmental processes continues throughout life."

However, there is little direct evidence for genetic contributions to self-regulation in twin studies. Recently, a twin study conducted by Soussignan et al. (2009) showed that the heritability of emotional regulation, which emerges in the first year of life and is an important subset of broader self-regulatory processes (Kopp, 1989), ranged from 19% to 31%. This study assessed infant social gaze, gaze aversion, positive expression, negative expression, motor activity level, and self-comfort in a set of 115 monozygotic and 156 dizygotic 5-month-old twins. Most behavioral responses were influenced by a non-shared environment, and only emotional regulation (categorized as gaze aversion) was found to be related to genetic factors. Thus, in the present study, genes and environmental interactions were assessed to test their unique contributions to infant self-regulatory behavior.

Serotonin has been linked to the inhibition of behavioral and emotional reactions (Soubrie, 1986). Dysfunctions in the serotonergic system results in less fearful reactions to strangers' approach and less pleasure in a structured play situation (Auerbach, Faroy, Ebstein, Kahana, & Levine, 2001). Serotonergic dysfunction has also been linked to mood problems, such as antisocial behavior (van Goozen, Fairchild, Snoek, & Harold, 2007). Serotonin has also been associated with neural areas that underlie the executive attentional network involved in self-regulation (Posner, Rothbart, & Sheese, 2007).

A serotonin functional polymorphism consists of a variable number of tandem repeats in the promoter region of the human serotonin transporter gene, which influences serotonin transporter gene transcription; this, in turn, affects serotonin re-uptake in the synapse (Lesch et al., 1996). The re-uptake of serotonin is approximately two-fold higher in cells containing the homozygous long allele variant (ll) of *SLC6A4* than those containing either the heterozygous or homozygous short allele variants (ss, sl) (Lesch & Mossner, 1998). In contrast, the short allele variants reduce transcriptional efficiency and, therefore, decrease serotonin transporter expression and increase re-uptake of synaptic serotonin (Lesch et al., 1996).

Genetic association and neuroimaging studies have suggested the important role of serotonin in emotion and emotional regulation. A study with a Caucasian population found that 5-HTTLPR was related to extraversion, an emotion-related personality trait (Gillihan, Farah, Sankoorikal, Breland, & Brodkin, 2007). Participants with the short allele of the 5-HTTLPR variants showed lower levels of self-rated extraversion than those with the long allele of the 5-HTTLPR variant, suggesting that participants with the short allele of the 5-HTTLPR variants experience more emotion. Additionally, an fMRI study performed in adults found that when they were shown fearful stimuli, individuals with the short allele variants of the 5-HTTLPR displayed greater neuronal activity in the amygdala, which suggested poorer self-regulation ability (Hariri et al., 2002).

Numerous studies have focused on the 5-HTTLPR polymorphism of the serotonergic system, which is an excitatory neurotransmitter in the central nervous system. Monoamine oxidase A (MAOA) is a mitochondrial catabolic enzyme, which is involved in regulating serotonergic signals through catabolism of vesicular serotonin in the presynaptic region. An upstream variable number of tandem repeats with the MAOA promoter region (MAOA-uVNTR) is related to the transcriptional efficiency of the gene. A few imaging studies have shown that MAOA variation is involved in emotion and its regulation (Buckholtz & Meyer-Lindenberg, 2008; Buckholtz et al., 2008). Many studies in adults have investigated the association between MAOA-uVNTR polymorphisms and human dispositional characteristics such as aggression, impulsivity, and antisocial behavior, which are known to be linked with early child self-regulation (Trentacosta & Shaw, 2009).

However, it should be noted that inconsistent results regarding the association between 5-HTTLPR or MAOA-uVNTR polymorphism and social behaviors have been reported (Cervilla et al., 2007; Garpenstrand et al., 2000, 2002; Jorm et al., 2000; Surtees et al., 2006). One factor that contributed to the inconsistent results was the different age of the participants