



Phenotypic outcomes in CNS serotonin and serotonin-mediated behavior are modulated by gene X environment interactions: A nonhuman primate model

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The serotonin transporter and monoamine oxidase A genes both contain functional length polymorphisms in their promoters (5-HTTLPR, MAOA-LPR, respectively) that are also present in rhesus macaques (*Macaca mulatta*), and comparative sequence analysis suggests that these loci are “ancient”, having derived from a common ancestor. Both loci influence aggressive and impulsive behavior in our rhesus that the phenotypic expression of an identical genotype is going to be different depending on the environment, demonstrating gene by environment interactions. Nonhuman primates reared in parentally deprived environments tend to have lower mean CSF 5-HIAA concentrations, a major risk factor for aggressive behavior. The risk for aggressive behavior is increased if they possess a less efficient 5HTTLPR genotype (the short allele). New data will be presented showing that rhesus of Chinese origin have a higher frequency of the short 5-HTTLPR allele, exhibit lower CSF 5-HIAA concentrations, and exhibit high rates of aggression. High- and low-activity MAOA-LPR alleles show a genotype by environment interaction effect on aggressive behavior, such that mother-reared male monkeys with the low-activity allele exhibit higher measures of normal and elicited aggression, suggesting that early parental absence interacts with genotype to produce interindividual variation in normal, non-pathologically aggressive behavior. Of particular interest is new data showing that subjects with the low activity allele may exhibit impulse control deficits. Males living in social groups were assessed for their latency to approach a stranger using an Intruder Challenge Test. Males with low MAOA activity had substantially shorter mean approach times to a potentially dangerous intruder, with a statistically significant genotype by age interaction, in that younger subjects with low MAOA activity had shorter mean approach times rivaling those of adults with either genotype. Such findings highlight the genetic, environmental and maturational interplay that occurs as the serotonin system develops, and emphasizes the importance and benefit of early parental input and how it potentially influences the phenotypic expression of different functional 5-HTT and MAOA genotypes.

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