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ORIGINAL ARTICLE

Brain morphometric correlates of MAOA-uVNTR polymorphism in violent behavior

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KEYWORDS
Magnetic resonance imaging;
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Abstract
Introduction: Violent behavior is influenced by genetic factors, and the MAOA-uVNTR polymorphism has been associated with violent behavior, specifically the low activity variant. It has been suggested that this polymorphism impacts on grey matter concentration in structures associated with behavioral inhibition and emotion processing, however in previous imaging studies well defined violent subjects have not been explored.
Objective: To investigate the effect of MAOA-uVNTR polymorphism on brain structure of violent subjects.
Methods: The grey matter concentration of 47 adult male subjects from a community sample classified as violent or controls, was assessed through DARTEL-voxel-based morphometry technique.
Results: A significant genotype by behavior interaction was found in which violent-low activity allele carriers had decrease of grey matter concentration in right superior temporal pole compared to controls of the same allelic variation.
Discussion: This findings suggests that grey matter integrity in superior temporal pole could be a neurobiological correlate of the allelic association between MAOA-uVNTR polymorphism and violent behavior due to its implication in socio-emotional processing.

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PALABRAS CLAVE
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Correlación morfométricos cerebrales del polimorfismo MAOA-uVNTR en la conducta violenta

Resumen
Introducción: La conducta violenta tiene una influencia genética importante, el polimorfismo MAOA-uVNTR se ha asociado con la conducta violenta. Se ha sugerido que dicho polimorfismo impacta la concentración de materia gris en estructuras asociadas con la inhibición conductual y el procesamiento emocional, sin embargo, no se han explorado estos efectos en sujetos violentos.
Objetivo: Investigar el efecto del polimorfismo MAOA-uVNTR sobre la estructura cerebral en sujetos violentos.
Método: Se comparó la concentración de materia gris mediante la técnica de morfometría basada en voxel con el procedimiento DARTEL en 47 hombres adultos miembros de la comunidad clasificados como controles o violentos.
Resultados: Se encontró una interacción significativa entre genotipo y conducta en la cual los sujetos violentos portadores del alelo de baja actividad presentaron reducciones de materia gris en el polo temporal superior derecho, al ser comparados con los controles de la misma variación alélica.
Discusión: Estos hallazgos sugieren que la integridad de la materia gris en polo temporal superior podría subyacer a la asociación alélica entre MAOA-uVNTR y violencia, debido a la implicación de esta estructura cerebral en el procesamiento socio-emocional.

Introduction

At present, violent behavior is a public health problem due to socially negative outcomes. The study of its genetic and neurobiological basis allows to understand its etiology and to develop evidence-based intervention programs to decrease its frequency.

It has been suggested that impulsive violence is associated with alterations in emotion regulation that depends on the integrity of brain structures such as temporal pole, orbitofrontal cortex, ventromedial cortex, dorsolateral cortex, anterior cingulate and amygdala.[1]

Structural brain imaging studies have demonstrated that violent, antisocial and violent psychopathic individuals show alterations in grey matter concentration. In one study of subjects with early onset of antisocial personality disorder that committed violent crimes, reductions in grey matter concentration in post central gyrus, superior frontotemporal areas, medial frontal gyrus and orbitofrontal cortex and mainly in left posterior cingulate and right insula cortices were found. When individuals with both high psychopathy and antisocial traits were compared to a control group, reductions in grey matter concentration in medial temporal gyrus and parahippocampus were found. These brain alterations could be related with the onset and maintenance of persistent violent behavior.[2] The increase of psychopathy traits is a risk factor for violent behavior, whereas in two studies of psychopathic individuals, grey matter reductions in medial and lateral areas of orbitofrontal cortex and superior and anterior temporal areas[3,4] were found; according to these studies the reductions in these brain structures could underlie the emotional dysfunction that characterizes these violent populations. In a recent study it has been reported that youth homicide offenders, compared to non-homicide offenders and after controlling brain volumes, psychopathy scores and substance dependence, had grey matter reductions in right superior and middle temporal gyrus, left parahippocampus, fusiform gyrus and inferior temporal gyrus. A classification through supported vector machine, in which prefrontal and temporal cortices were included as predictors, showed that the structural alterations classified offenders in the two groups with 81% accuracy.[5]

The anatomical alterations found in violent individuals could be a result out of genetic influences. The findings about genetic contribution to violent behavior are consistent, it has been suggested that genetic factors explain about 50% of variance of violent, aggressive and impulsive behavior.[6–10] Seemingly male subjects are more vulnerable to the effects of genetic factors on heritability and stability of violent traits throughout life, which can be related to the high prevalence of violent behavior in men.[9,11,12]

The variable number tandem repeat (VNTR) functional polymorphism in the promoter region of monoamine oxidase A (MAOA) coding gene (Xp11.4-11.3) has been proposed as a candidate for violent behavior. MAOA is an enzyme that mainly degrades serotonin (5HT) in brain, but also degrades norepinephrine and dopamine.[13] The MAOA-uVNTR has two common alleles that impact on the enzymatic transcription, so it has been suggested that carriers of 3.5 or 4 repeats have high enzymatic expression of MAOA, whereas carriers of 2, 3 or 5 repeats have lower enzyme expression.[14] MAOA enzyme plays a fundamental role in neurodevelopment regulating the pattern of neural differentiation and maturation, but the lack or low activity of MAOA in prenatal stages leads to an abnormal neurodevelopment.[15]