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Main and interaction effects of childhood trauma and the *MAOA* uVNTR polymorphism on psychopathy

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ABSTRACT

Psychopathy is characterized by callous affect, interpersonal manipulation, a deviant lifestyle, and antisocial behavior. Previous research has linked psychopathic traits to childhood trauma, but also to the upstream variable number tandem repeat (uVNTR) polymorphism of the monoamine oxidase A (*MAOA*) gene. An interaction between childhood trauma and *MAOA* genotype has been associated with antisocial behavior, but so far little is known about interaction effects of childhood trauma and the *MAOA* uVNTR on psychopathy. In order to bridge this gap, we used data of 1531 male and 1265 female twins and their siblings from a Finnish community sample to estimate structural equation models. The psychopathy and childhood trauma constructs were conceptualized as bifactor models with one general and two orthogonal group factors. Data comprised self-reports on childhood trauma and psychopathic traits as well as *MAOA* uVNTR genotype. In both genders, childhood trauma was associated with the general factor that represents the overarching psychopathy construct, and with the group factor that captures social deviance, but not with the group factor capturing psychopathic core personality traits. Women with a low activity variant of the *MAOA* uVNTR reported slightly higher levels of psychopathy than those with a high activity allele, but only with respect to the general psychopathy factor. There was no evidence for an interaction effect between *MAOA* uVNTR genotype and childhood trauma on psychopathy in either gender. Our results suggest that psychopathy in general and social deviance in particular are associated with childhood trauma in men and women, and that psychopathic traits are subject to variation in the *MAOA* uVNTR genotype in women.

1. Introduction

Antisocial behavior includes a range of behavioral aspects such as aggression, disrespect for social norms, and irresponsibility, but also legal aspects related to criminality and delinquency (Morgan and Lilienfeld, 2000). Antisocial behavior, in combination with an unstable lifestyle, represents one important component (i.e., social deviance) of the psychopathy construct described by Hare (2003). However, psychopathy is not only characterized by social deviance, but more strongly by a restricted range and depth of emotions, manipulative skills, and deceitfulness (i.e., psychopathic core personality traits; Herpertz and Sass, 2000). The distinction between psychopathic core personality traits and social deviance is the foundation for the differentiation between so called primary (or true) and secondary (or symptomatic/pseudo-) psychopathy (Arieti, 1963; Karpman, 1941). Primary psychopathy is characterized by high levels of interpersonal-affective deficits, whereas secondary psychopathy is defined by an unstable lifestyle and antisocial behavior (Mealey, 1995). Notably, psychopathy and antisocial personality disorder (ASPD) present overlapping, but distinct concepts, which is illustrated by the fact that almost all psychopathic offenders are diagnosed with ASPD, whereas roughly a third of inmates with ASPD are psychopathic (Mokros et al.,

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Regarding etiological pathways, genetic as well as environmental factors are assumed to contribute to the manifestation of psychopathy. On the environmental level there is growing evidence that psychopathic traits are linked to childhood trauma (Craparo et al., 2013; Gao et al., 2010). Importantly, psychopathy can only be diagnosed in adults (Hare, 2003). However, so-called callous-unemotional (CU) traits, such as a lack of empathy and remorse, callousness, and deficient emotionality in childhood and adolescence have been linked to the manifestation of psychopathic traits in adulthood (Frick et al., 2014). In this regard, children who have suffered abuse and/or neglect are more likely to become callous, unemotional, and remorseless (Weiler and Widom, 1996). This notion received support by Kimonis et al. (2013), who found that adolescents with CU traits present with higher rates of abuse and neglect than their non-psychopathic counterparts. There are differential theoretical pathways for the development of affective deficits in psychopathic individuals. With respect to abuse, Porter (1996) suggested a dissociative pathway for the development of CU traits, where chronic exposition to physical or sexual abuse or other types of trauma results in successive affective inhibition and detachment of emotions (Porter, 1996; Weiler & Widom, 1996). With regard to neglect, McCord (2001) described that neglectful parents are unable or unwilling to provide their children with emotional cues that are indispensable for the development of adequate emotional responses.

Moreover, there is evidence that antisocial and psychopathic features have genetic underpinnings (Ficks and Waldman, 2014; Johansson et al., 2008). One candidate gene that has gathered attention with regard to antisocial and recidivistic violent behavior is the monoamine oxidase A (*MAOA*) gene (Ficks and Waldman, 2014; Tiihonen et al., 2015). It is located on the X chromosome and encodes for the MAOA enzyme, which is involved in the depletion of several amines such as serotonin (Sabol et al., 1998). The *MAOA* gene has a functional polymorphism with a 30-base pair variable number tandem repeat in the upstream regulatory region (uVNTR). This polymorphism has several alleles, including 2-, 3-, 3.5-, 4-, 5-, and 6-repeat variants (Huang et al., 2004; Sabol et al., 1998). The alleles with 3.5 and 4 repeats (often termed *MAOA*-H) show significantly higher gene transcription than those with 2 and 3 repeats (*MAOA*-L; Deckert et al., 1999; Kim-Cohen et al., 2006; Sabol et al., 1998). Findings on transcription efficiency for the less common 5-repeat allele have so far been diverging or unclear (Deckert et al., 1999; Sabol et al., 1998).

With regard to antisocial behavior, examinations of potential main effects of the *MAOA* uVNTR on antisocial behavior have been inconsistent. Ficks and Waldman (2014) analyzed 31 studies and found a modest association between the 3-repeat allele and antisocial behavior, even though some of the included individual studies did not find such an association. More recent findings are similarly inconsistent with some study outcomes indicating an association between low-activity alleles and proneness to delinquent and violent behavior (Roettger et al., 2016; Tiihonen et al., 2015), whereas other studies did not find a genetic main effects of the *MAOA* uVNTR on antisocial behavior in adults (Haberstick et al., 2014) or conduct problems in adolescents (Kieling et al., 2013). A substantially smaller number of studies have been conducted on the main effect of the *MAOA* uVNTR genotype on psychopathic traits. The high-activity 4-repeat *MAOA* uVNTR genotype has been associated with violent recidivism in psychopathic offenders (Tikkanen et al., 2011), whereas the 3-repeat variant has been linked to affective deficits in adolescents with attention deficit hyperactivity disorder (Fowler et al., 2009) but also to an erratic lifestyle in adult offenders (Sadeh et al., 2013). In addition, Beaver et al. (2013) investigated the association between the 2-repeat allele and psychopathic traits in a community sample, but found no main effect on psychopathy.

Notably, not all children with a history of traumatic experiences develop psychopathic or antisocial traits as adults, and *MAOA* uVNTR genotypes have not consistently been associated with psychopathy or antisocial behavior. According to Caspi and Moffitt (2006), individuals differ from each other with regard to multiple behavioral and cognitive features that have a genetic foundation. This genetic disposition, in turn, influences the way an individual responds to environmental conditions. For example, carriers of a low-activity allele of the *MAOA* uVNTR, in comparison to a high-activity allele, show differential activation of several brain areas like the amygdala and hippocampus in reaction to emotional stimuli (Lee and Ham, 2008). It is conceivable that experiences of childhood trauma aggravate already existing neurobehavioral impairments in terms of a gene x environment (GxE) interaction (Byrd and Manuck, 2014). With regard to antisocial behavior, Caspi et al. (2002) reported that a combination of *MAOA*-L and childhood trauma acted as a precursor to antisocial behavior. This notion of an interaction effect between *MAOA* uVNTR genotype and childhood trauma was corroborated by a substantial number of studies (see meta-analyses by Byrd & Manuck, 2014, and Kim-Cohen et al., 2006). In most cases, adolescent or adult men with a *MAOA*-L polymorphism who had been maltreated as children were at higher risk of showing aggressive and antisocial behavior as adults. In contrast, women with a *MAOA*-H genotype who had suffered childhood trauma presented more antisocial behavior (Byrd and Manuck, 2014). This interaction effect between childhood trauma and *MAOA* uVNTR genotype, however, was unstable and turned non-significant after individual studies were deleted (Byrd and Manuck, 2014). Some of the included studies found main effects of trauma and/or *MAOA* uVNTR genotype, but were not able to confirm the moderating effect of *MAOA* uVNTR genotype on the association between childhood trauma and antisocial behavior (Haberstick et al., 2005; Huizinga et al., 2006).

In summary, a range of studies have examined the relationship between MAOA uVNTR genotype, childhood trauma, and antisocial behavior. The *MAOA* uVNTR, however, has not only been associated with antisocial behavior, but also with emotional dysfunction, which is at the core of psychopathy (Fowler et al., 2009). Against this backdrop, and given the inconsistent findings on direct effects of childhood trauma and *MAOA* uVNTR genotype, the question rises whether psychopathic traits might also be influenced by a GxE interaction of childhood trauma and *MAOA* uVNTR genotype. To our knowledge, only one study has investigated moderating effects of the *MAOA* uVNTR on the relation between childhood trauma and psychopathy so far, but did not find a GxE interaction (Sadeh et al., 2013).

Based on previous research, we expected a direct positive association of childhood trauma and psychopathy. Predictions about the impact of low- vs. high-activity variants of the *MAOA* genotype on psychopathic traits were hampered by the heterogeneity of previous findings. In addition, we aimed to extend the sparse literature on the interaction effect of the *MAOA* uVNTR and childhood trauma in an exploratory fashion. In contrast to most previous studies, we chose a latent variable modeling approach and controlled for effects of the covariate age at the time of data collection on main and interaction terms according to the criticism raised by Keller (2014) on common pitfalls in GxE analyses. He argued that researchers usually controlled for the effect of confounding variables on main effects of genes and environment, whereas the effect of the confounders on the interaction terms was often neglected.

2. Methods and materials

2.1. Sample

Participants were twins and their siblings drawn from the second data collection of the large-scale, population-based Genetics of Sex and Aggression project (for a detailed description of the project and data collections see Johansson et al., 2013). The second data collection was conducted in 2006 and targeted all Finnish twins at the age of 18–33 years, and their siblings aged 18 years or older. Gene data were collected for a subsample of the respondents (n = 4278). Research plans for the data collection were approved by the Ethics Committee of the