

Table 1: Studies investigating the association between the Val158Met *COMT* polymorphism and anxiety in children and adolescents

Study	Age in years (sample size)	Study design	Genotype groups	Anxiety Measures	Statistical analysis Between groups' difference (effect size, ES)	Sex differences	Genotype by stress interaction
Arbelle et al., 2003	7-8 (n=98)	Cross-sectional	Val/Val, Val/Met, Met/Met	Schedule for Affective Disorders and Schizophrenia for School-Age Children, Martin Temperament Assessment Battery and Achenbach Behavior Checklist	Univariate ANOVA Non significant $\eta^2 = 0.20$	Not investigated	Not investigated
Olsson et al., 2005	14 and 24 (n=962)	Longitudinal 2 measures (10 years)	Val/Val, Val/Met, Met/Met	Clinical Interview Schedule-Revised (CIS-R)	Logistic regression and ANOVA Met/Met: higher persistent episodic anxiety ES: Information not available	Met allele effects only in females	Not investigated
Olsson et al., 2007	14 and 24 (n=962)	Longitudinal 2 measures (10 years)	Val/Val, Val/Met, Met/Met	Clinical Interview Schedule-Revised (CIS-R)	Logistic regression Double recessive interaction: twofold reduction of persistent generalized anxiety in <i>COMT</i> (Met/Met) and 5HTTLPR (S/S) individuals ES: Information not available	No sex interaction	Genetic protection under high stress conditions positive, not significant
Evans et al., 2009	6-7 (n=8431)	Cross-sectional	Met/Met, Met/ValA, Met/ValB, ValA/ValA, ValA/ValB,	Strengths and Difficulties Questionnaire (SDQ) and Life Event Questionnaire	Logistic regression Non-significant ES: Information not available	No sex interaction	Anxiety and depression in adults; no and <i>COMT</i> genotype by

ValB/ValB					stress interaction		
Gadow et al., 2009	4-14 (n=67)	cross-sectional	Met/-, Val/Val	Child Symptom Inventory-4 (CSI-4)	ANOVAs marginally significant for teacher ratings of social phobia (0.06) (Met/- higher levels) ES: $\eta^2 = 0.06$	Not investigated	Not investigated
Middeldorp et al., 2010	7, 10, 12, 14 and 18; (n=1240)	Longitudinal 5 measures (11 years)	Val/Val, Val/Met, Met/Met	Child Behavior Check List (CBCL) at ages 7, 10 and 12; Youth Self Report (YSR) at 14 and 18 years	Factorial association model and path analysis No effect for anxiety or depression ES: Information not available	Not investigated	Authors did not investigate
Shashi et al., 2010	7-16 (n=40)	Cross-sectional	Val/-, Met/-	Child Behavior Checklist (CBCL) and Computerized Diagnostic Interview for Children (C-DISC)	Non-parametric (Mann-Whitney) Val allele associated with higher frequency of anxiety disorders ES: Cohen's d = 1.03	No sex interaction	Not investigated
Sheikh et al., 2013 (Study 1)	~3.5 (n=476)	Cross-sectional	Val/Val, Met/-	Preschool Age Psychiatric Assessment (PAPA)	Non-parametric (Mann-Whitney) Val/Val children, higher levels of depressive symptoms ES: Cohen's d = 0.28*	Not investigated	Not investigated

Sheikh et al., 2013 (Study 2)	~3.5(n=4 09)	cross- sectional	Val/Val, Met/-	Early Childhood Inventory-4 (ECI-4)	Non-parametric (Mann- Whitney) Val/Val children, higher levels of depressive symptoms Cohen's d = 0.29*	Not investigated	Not investigated
Lehto et al., 2013	15, 18 e 25 (n= 593)	longitudinal 3 measures (10 years)	Val/Val, Val/Met, Met/Met	Mini-International Neuropsychiatric Interview (MINI 500)	Mixed linear models, ANOVA or ANCOVA Val/Val higher neuroticism scores ES: Information not available	Val/Val effects only in females over age 25	Not investigated
Sheikh et al., 2017	~3 (n=409)	cross- sectional	Val/Val, Met/-	Child Behavior Checklist	Regression-based framework Val/- higher anxiety under stress ES: Cohen's d = 0.15*	Higher depressive and anxious symptoms in girls	Stress, inferred from cortisol levels, moderated the association between COMT Val158Met polymorphism and anxiety

Note: Clinical samples were used in Gadow et al., 2009 (Autism Spectrum Disorder) and in Shashi et al., 2010 (22q11.2 deletion syndrome). Middeldorp et al., 2010 sample includes 288 monozygotyc male twins and 320 monozygotyc female twins; 382 male singletons and 392 female singletons.

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