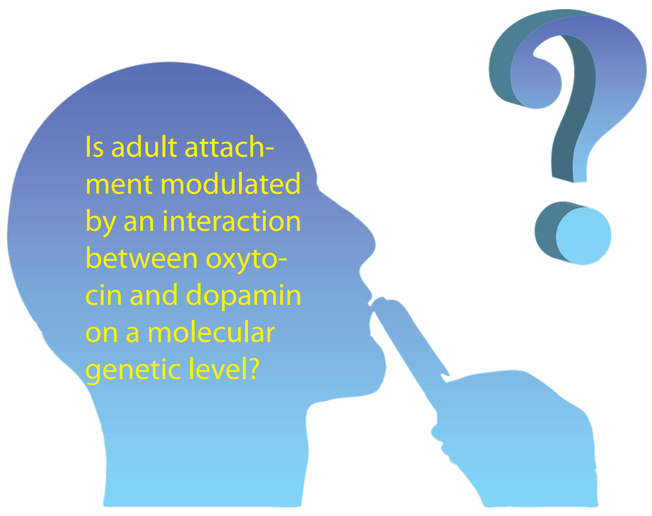
Interaction between Oxytocin and Dopamin and Attachment: A molecular genetic approach

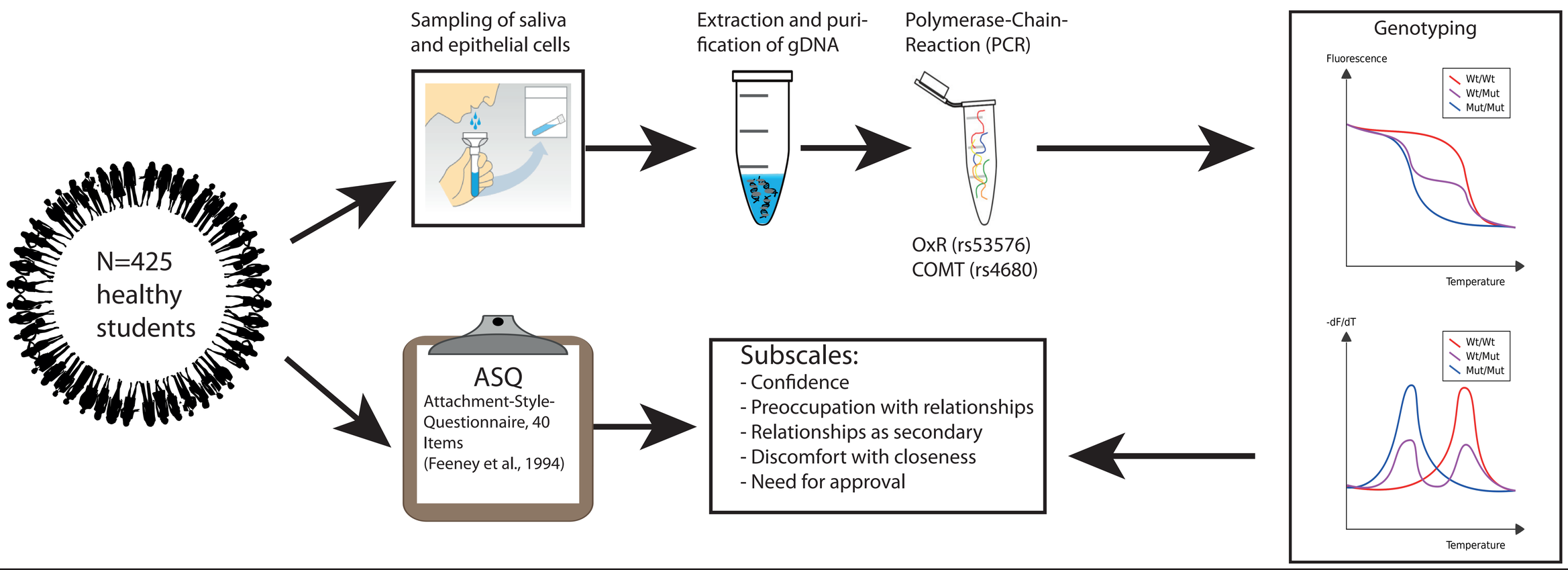
Juergen Hennig & Aisha Munk
Dept. of Psychology, University of Giessen, Germany
juergen.hennig@psychol.uni-giessen.de

Introduction

Oxytocin becomes secreted from the paraventricular nucleus of the hypothalamus into many areas of the brain including those associated with dopaminergic function. Interactions between both systems are known for some time [1]. However, studies in humans are rare compared to animal research. Moreover, investigating an interaction based on a candidate gene approach has not been untertaken so far.



As a candidate for dopaminergic function we used a polymorphism for the catechol-o-methyltransferase coding gene (rs4680) with carriers of the Met-allel expected to have higher (prefrontal) dopamine levels [2].
For measuring individual differences in the oxytocin-system we used the oxytocin-receptor-gene polymorphism (rs53576) with carriers of the A-allel expected to carry a „risk-allel“ for social functioning [3].



Results

Table 1:
Distribution of genotypes for Oxytocin-receptor-gene SNP (rs53576) and Catechol-O-Methyltransferase SNP (rs4680)

OXR (rs53576) \ COMT (rs4680)	Met/Met	Val/Met	Val/Val	
AA	12	22	8	42
AG	55	81	38	174
GG	61	101	47	209
	128	204	93	425

HWE: X^2= 0.42 p: n.s.

HWE: X^2= 0.46; p: n.s.

Note: All genotyp-distributions follow the Hardy-Weinberg-Equillibirum as indicated by non-significant Chi-square values.

Most important result:

A multivariate analysis of variance with all attachment subscale values included and the two factors (COMT-/OXR-genotypes) yielded a highly significant interaction effect indicating that attachment depends on both systems in general (F=2.09; df=20,1660; p<.01). However, this results primarily from „need for approval“ (see fig. 1-5)

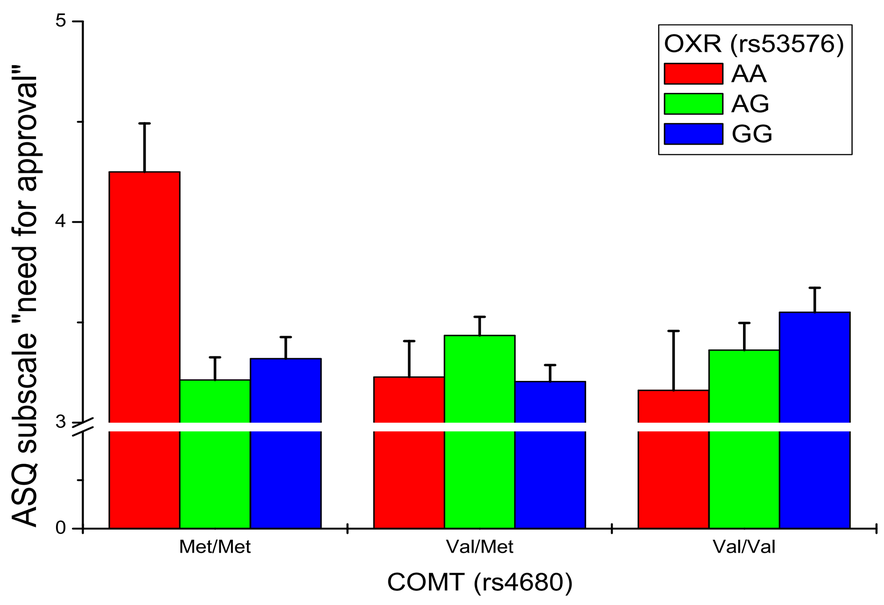


Figure 1: Means and SEM for ASQ-subscale „need for approval“. Subjects carrying the combination of AA + Met/Met have the highest levels compared to all other genotype combinations.
F(OXR x COMT)=4.8; df=4,416;p<.01)

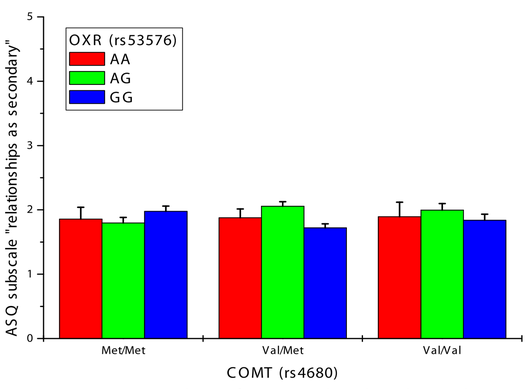


Figure 2: Means and SEM for ASQ-subscale „relationship as secondary“.
F(OXR) =1.19; df=4,416; p=n.s.
F(COMT) =0.43; df=4,416; p=n.s.
F(OXR x COMT) =2.98; df=4,416; p<.05

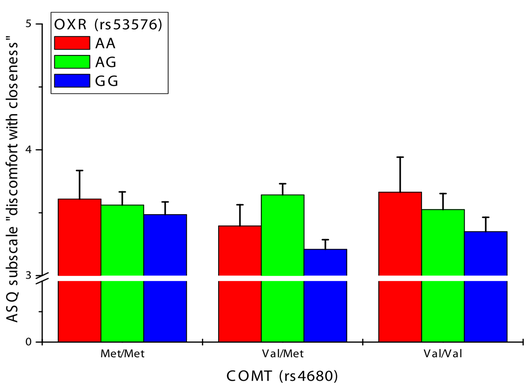


Figure 4: Means and SEM for ASQ-subscale „discomfort with closeness“.
F(OXR) =3.89; df=4,416; p<.05.
F(COMT) =0.79; df=4,416; p=n.s.
F(OXR x COMT) =1.13; df=4,416; p=n.s.

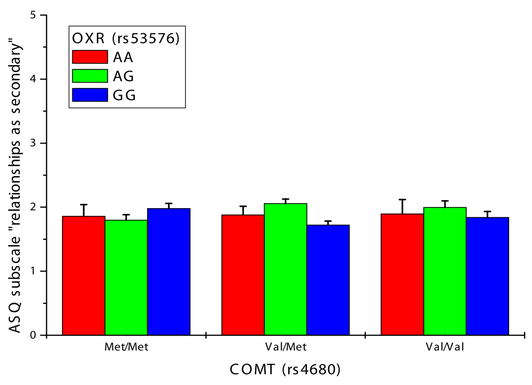


Figure 4: Means and SEM for ASQ-subscale „relationship as secondary“.
F(OXR) =1.19; df=4,416; p=n.s.
F(COMT) =0.43; df=4,416; p=n.s.
F(OXR x COMT) =2.91; df=4,416; p<.05

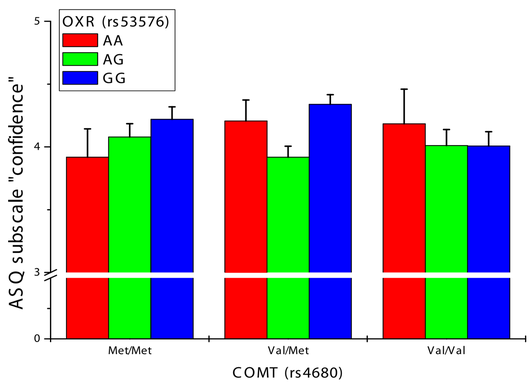


Figure 5: Means and SEM for ASQ-subscale „confidence“.
F(OXR) =2.43; df=4,416; p=n.s.
F(COMT) =0.32; df=4,416; p=n.s.
F(OXR x COMT) =1.59; df=4,416; p<.05

Oxytocin neurons from the paraventricular nucleus (PVN) project into the ventral tegmental area (VTA) and the nucleus accumbens (NAcc). Both structures are known to play a key role in reward and motivation. Dysfunctionality of VTA-OxR results in reduced social preference with no effects on other aspects of reward (e.g. drugs) in mice [5].

High/intermediate oxytocin receptor sensitivity (GG/AG) and all genotypes for COMT (rs4680):

high stimulation of VTA/NAcc → social reward & low motivation to increase social contact → low „need for approval“

Working model

(modified after Preston, 2017 [4])

Low oxytocin receptor sensitivity (AA) and low DA-degradation (COMT; Met/Met)

low stimulation of VTA/NAcc → lack of social reward and high social motivation → high „need for approval“

mismatch with high dispositional motivation and reward seeking behavior (COMT, Met/Met)[6]

References:
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