

NAME OF PRESENTING AUTHOR: Mikael O Ekblad

EMAIL ADDRESS OF PRESENTING AUTHOR: moekbl@utu.fi

LOCATION OF PRESENTING AUTHOR: Europe

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TITLE: The Effect of Smoking During Pregnancy on Severity and Directionality of Externalizing and Internalizing Symptoms: A Genetically-Informed Approach

FULL AUTHOR LIST: Mikael O Ekblad<sup>1,2</sup>, MD, PhD, Kristine Marceau<sup>1</sup>, PhD, Emily Rolan<sup>1</sup>, MS, Rohan HC Palmer<sup>3</sup>, PhD, Alexandre Todorov<sup>4</sup>, PhD, Andrew C Heath<sup>4</sup>, D.Phil., Valerie S Knopik<sup>1</sup>, PhD

AFFILIATIONS:

<sup>1</sup>Department of Human Development and Family Studies, Purdue University, West Lafayette, Indiana, USA

<sup>2</sup>Department of General Practice, Turku University and Turku University Hospital, Turku, Finland

<sup>3</sup>Behavioral Genetics of Addiction Laboratory, Department of Psychology, Emory University

<sup>4</sup>Department of Psychiatry, Midwest Alcoholism Research Center, Washington University School of Medicine, St Louis

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ABSTRACT:

Objective. To examine the association between maternal smoking during pregnancy (SDP) and (i) severity and (ii) directionality of externalizing and internalizing symptoms in a sample of sibling pairs while rigorously controlling for familial confounds.

Study design. The Missouri Mothers and Their Children Study includes families (N=173) selected for sibling pairs (aged 7 to 16 years) discordant for SDP. This sibling comparison study is designed to disentangle the effects of SDP from familial confounds.

An SDP severity score was created for each child using a combination of SDP indicators (timing, duration, and amount). Principal component analysis of externalizing and internalizing behavior, assessed with the Child Behavior Checklist and Teacher Report Form, was used to create symptom severity and directionality scores.

Results. The variance in severity and directionality scores was primarily a function of differences between siblings (71% and 85%, respectively) rather than differences across families (29% and 15%, respectively). The severity score that combines externalizing and internalizing symptom severity was not associated with SDP. However, a significant within-family effect of SDP on symptom directionality ( $b = 0.07$ ,  $p = 0.04$ ) was observed in the sibling comparison model.

Conclusion. The positive directionality score indicates that SDP is associated with differentiation of symptoms towards externalizing rather than internalizing symptoms after controlling for familial confounds with a sibling comparison model. This supports a potentially causal relationship between SDP and externalizing behavior.

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