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Impact of Maternal Prenatal Risk Factors On Oxytocin Methylation, and On Occurrence of Conduct Disorders During Adolescence

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Youth with high callous-unemotional traits (CU) are at risk for early-onset and persistent conduct problems. Research suggests that
there may be different developmental pathways to CU (genetic/constitutional vs environmental), and that the absence or presence
of co-occurring internalizing problems is a key marker. However, it is unclear whether such a distinction is valid. Intermediate
phenotypes such as DNA methylation, an epigenetic modification regulating gene expression, may help to clarify etiological
pathways. This is the first study to examine prospective inter-relationships between environmental risk (prenatal/postnatal) and
DNA methylation (birth, age 7 and 9) in the prediction of CU (age 13), for youth low vs high in internalizing problems. We focused
on DNA methylation in the vicinity of the oxytocin receptor (OXTR) gene as it has been previously implicated in CU. Participants
were 84 youth with early-onset and persistent conduct problems drawn from the Avon Longitudinal Study of Parents and Children.
For youth with low internalizing problems (46%), we found that (i) OXTR methylation at birth associated with higher CU (age 13) as
well as decreased experience of victimization during childhood (birth–age 9), (ii) higher prenatal parental risks (maternal
psychopathology, criminal behaviors, substance use) associated with higher OXTR methylation at birth and (iii) OXTR methylation
levels were more stable across time (birth–age 9). In contrast, for youth with high internalizing problems, CU were associated with
prenatal risks of an interpersonal nature (that is, intimate partner violence, family conflict) but not OXTR methylation. Findings
support the existence of distinct developmental pathways to CU.

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