

## Commentary: Violent Aggression Predicted by Multiple Pre-Adult Adverse Experiences

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### Article Info

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Sociological research and the related sociological theories have for considerable time described the fact that an early exposure to negative environmental factors lastingly shapes individual conduct and can significantly contribute to serious behavioral problems in later life<sup>1</sup>. The relatively extensive body of psychiatric, psychological and biological literature on single select risk factors also links these factors with the emergence and gravity of mental disorders, e.g.<sup>2-8</sup>.

While many of these mainly theoretical considerations and also of first observations in humans (often with small N numbers) all appear plausible, as yet concrete data are essentially lacking. Sources which systematically examine the consequences of an accumulation of well-defined early risk factors, and which are based on an adequately large number of samples are virtually non-existent. Such an accumulation, however, is not infrequent and seems to have an especially damaging effect on the persons affected.

Some years ago we already showed that an accumulated environmental risk before the age of 18 years leads to an up to 10 years earlier onset of schizophrenia in affected persons<sup>9</sup>. A hereon based, very recent follow-up study of ours on patients with none or just one risk factor versus patients with more than three risk factors resulted in the completely unexpected finding that high-risk persons have an over fivefold increased probability of a later forensic hospitalization.

In accordance with common sociological theories, we thus hypothesized that risk accumulation in childhood and adolescence may induce severe aggression and criminal behavior in grown-ups, independent of a mental disease. We subsequently identified in six independent cohorts (four schizophrenia cohorts and two cohorts from the general population as controls) pre-adult risk experience: life in a big city ("urbanicity"), migration and physical or sexual abuse as primary, and cannabis and alcohol abuse as secondary risk factors<sup>10</sup>.

All factors individually were already marginally associated with higher aggression in adulthood. The accumulation of these factors, however, led in all six cohorts to a strong prediction of violent aggression and criminal behavior in an impressively reproducible stair pattern (overall Odds Ratio: 10.5). In fact, groups of adult individuals having more than three risk factors accumulated during childhood and adolescence consist of nearly 50% of subjects convicted for bodily injury, sexual assault, murder, or forensic history

across all replication samples. The differences between men and women were insignificant; women merely show an overall somewhat weaker manifestation of the results. On the other hand, the same percentage (the other close to 50%) obviously exhibits some - as yet unexplained - resilience, e.g.<sup>11</sup>. This interesting observation certainly deserves now to be studied systematically. What are the underlying mechanisms of resilience and how can they be achieved or perhaps even activated? The results of respective experimental, preclinical and clinical studies may give rise to future targeted intervention strategies.

Surprisingly, the risk factors themselves are interchangeable; apparently the number of these influencing factors is more important than their individual character. Life in a big city plus physical maltreatment plus cannabis consumption sum up to comparable consequences for later aggressive behavior as do sexual abuse plus migration plus alcohol<sup>10</sup>. But what are the potential molecular and cellular mechanisms (general reviews e.g.<sup>12,13</sup>), that make one in two young brains vulnerable and persistently altered?

A genome wide association study (*Illumina array*) for the exploration of different methylation of DNA in blood cells of carefully selected extreme group individuals yielded, on the whole, negative results. In contrast, the determination of *histone-deacetylase1 (HDAC1)* mRNA<sup>14</sup> in peripheral mononuclear cells show a significant increase in the high-risk group, which points at persistent robust epigenetic changes<sup>10</sup>. Also here, follow-up studies are now indicated. These should include experimental approaches to pharmacological<sup>15</sup> and/or psychotherapeutic reversal.

Our data show for the first time on a solid scientific basis a disease-independent fatal relationship between accumulated, precisely defined pre-adult environmental risks and violent aggression. Some of these risks (alcohol, cannabis, and to some degree also negative effects of big cities<sup>8</sup>) are clearly avoidable. An explorative analysis shows that also polytoxicomania (use of various different legal or illegal drugs) can contribute highly significantly to the described accumulation effect<sup>16</sup>.

Alarmed by these dismaying data we decided to further pursue this line of research which is of considerable socio-political significance worldwide. We especially see young migrants, already arriving in Germany with a "risk burden", as being vulnerable to a high degree, and consider early intervention measures and respective professional offers of assistance as indispensable.

For this reason, we plan to win public financiers, hopefully supported by politics, for a follow-up study which will be dedicated to an expansion of our recently published findings as well as to the formulation and scientific *proof-of-effectiveness* of targeted interventions. Further cross-sectional and longitudinal studies including

specific assessments of different environmental risk factors, combined with genetic, epigenetic and brain imaging measures, are needed to clarify the developmental mechanisms that lead to aggression in especially vulnerable groups or that contribute to resilience in others. Understanding the detrimental mechanisms will ultimately assist in preventing or even reversing them.

To provide a solid basis for a respective funding application we are currently collecting information on risk factors experienced by a pilot sample (N=100) of young people who reached our country at an age of approximately 18 years (16-25 years of age) as war refugees, partly as unaccompanied refugee minors. First results point to a substantial accumulation of risk factors in nearly all test persons.

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