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IMMUNE ACTIVATION IN PSYCHIATRIC AND PRE-PSYCHIATRIC DISEASE H.A. Drexhage¹, R.C. Drexhage¹, E. Mesman², N. van Beveren³, M. Hillegers², W.A. Nolen⁴

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Accumulating evidence indicates an activated immune system as a vulnerability factor for the development of schizophrenia (SCZ) and bipolar disorder (BD). In support we detected:

- 1. Monocytosis and monocyte activation (e.g. a specific gene expression signature of inflammation related genes in a coherent pattern) in naturalistically treated SCZ and BD patients, and
- 2. T cell activation in the same patients, be it that it were Treg cells that were more numerous in BD, while in SCZ Treg and Th17 cells numbers were raised.

We also tested 70-80 children at ages of 16 and 21 yrs, having1-2 parent(s) with BD. This offspring has a higher chance of developing a mood disorder and over 25% had developed a mood disorder at 21 yrs. Not only the offspring with a lifetime diagnosis of mood disorder had activated monocytes and more Treg cells (similar as BD patients), but also around 40-50% of euthymic offspring had this immune activation profile. Importantly children who were psychiatrically healthy at 16yrs, and had developed a mood disorder at 21 yrs of age, all had activated monocytes at 16yrs.

Our data show that both the monocyte and T cell arm of the immune system are activated in SCZ and BD, this activation preceding the onset of first episodes in individuals at risk. Our approach opens new avenues for early detection of psychiatric disease based on the immune state of individuals at risk, enabling possible selection of those individuals who might benefit from an immune modulation treatment to prevent disease.