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PROGRESS

Disease-predisposing or resilience-promoting? Decoding the systems biology and behavioural predictors and determinants of the tipping point of stress

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The concept of a tipping point can be easily visualized when we consider the climate crisis: through more and more detailed insights into climate change, we have learned that even the smallest events can ultimately throw a complex system out of balance when the dynamics approach a critical threshold, the so-called tipping point. A very similar scenario can be observed when it comes to the effects of stress on our body: moderate stress is positive and protects us against future stressful experiences, a phenomenon called stress inoculation. Prolonged exposure to severe stress, in turn, can have negative effects on the body. The precise mechanisms that decide whether the consequences of stress are positive or negative remain largely unclear, and we don't yet understand what happens at this tipping point. Chronic social stress is an important risk factor for depression, but while under chronic stress, only a minority of people develop clinical depression. The majority are able to maintain good mental health despite unfavorable conditions, a phenomenon called resilience. Resilience to stress is an active process, however, the exact biological mechanisms strengthening resilience are still poorly understood. This project takes a very unique approach to understanding what molecular, biochemical, and behavioral changes herald and signal this tipping point where stress switches from its positive to negative effects: our consortium will combine the expertise of leading European scientists in the fields of behavior, computational, molecular and physiological analyses, and neuroscience to identify "fingerprints" of stress resilience. We will also test whether stress inoculation training can increase resilience and shift the tipping point. Our goal is to identify markers which precede or signal the tipping. Our results will allow early prediction of the tipping point so that preventive measures can be taken in time to prevent full-blown depression from developing.

Finally, this knowledge will contribute to develop tailored prevention or treatment strategies to fight stress-associated depressive disorders more effectively in the future.