

## Stellingen J de Jong

1. Psychiatric disorders are categorized continuous traits that are influenced by a complex mix of biological and environmental risk factors that exert their effect on disease outcome during varying neurodevelopmental periods (this thesis).
2. Nearly all current day psychiatric medications were discovered serendipitously during the previous century (this thesis).
3. Disease mechanism-informed treatments have yet to be introduced into psychiatry (this thesis).
4. Genetic variants that are rare on a population-wide level typically have a large effect size on phenotypic outcome and can be leveraged to inform us regarding psychiatric disease mechanisms (this thesis).
5. Studying the functional consequences of rare, large-effect genetic variations causal of brain disorders using patients' stem cell-derived neuronal systems is a promising approach to overcome some of the obstacles encountered in the translational process from preclinical animal model findings to human patients (this thesis).
6. Environmental stressors that increase risk for mental illness possibly exert their effects by interfering with biological processes that may also be disrupted by the effects of genetic variation.
7. Overemphasizing the role and importance of biological risk factors, while at the same time overlooking the role of environmental risk factors or societal conditions that predispose to mental illness, can leave large groups of patients without the care they urgently need.
8. "Diagnosis needed to rest in order to let research catch up. It made no sense to keep rearranging the furniture of descriptive psychiatry, creating new diagnoses or altering the thresholds of existing ones, based only on the whims of the experts who happened to be in the room. [...] Changes in diagnoses should be few and far between until we gained much deeper understanding of what causes the mental disorders and how best to define and treat them." — Allen Frances, *Saving Normal: An Insider's Revolt Against Out-Of-Control Psychiatric Diagnosis, DSM-5, Big Pharma, and the Medicalization of Ordinary Life*

9. “Mental disorders should be diagnosed only when the presentation is clear-cut, severe, and clearly not going away on its own. The best way to deal with the everyday problems of living is to solve them directly or to wait them out, not to medicalize them with a psychiatric diagnosis or treat them with a pill.”  
— Allen Frances, *Saving Normal: An Insider's Revolt Against Out-Of-Control Psychiatric Diagnosis, DSM-5, Big Pharma, and the Medicalization of Ordinary Life*
10. “Every genetic “illness” is a mismatch between an organism’s genome and its environment. In some cases, the appropriate medical intervention to mitigate a disease might be to alter the environment to make it “fit” an organismal form (building alternative architectural realms for those with dwarfism; imagining alternative educational landscapes for children with autism). In other cases, conversely, it might mean changing genes to fit environments. In yet other cases, the match may be impossible to achieve: the severest forms of genetic illnesses, such as those caused by nonfunction of essential genes, are incompatible with all environments. It is a peculiar modern fallacy to imagine that the definitive solution to illness is to change nature—i.e., genes—when the environment is often more malleable” — Siddhartha Mukherjee, *The Gene: An Intimate History*
11. “Every person must choose how much truth he can stand.” — Irvin D. Yalom, *When Nietzsche Wept*