Multi-biomarker pharmacokinetic-pharmacodynamic relationships of central nervous systems active dopaminergic drugs
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Propositions to the thesis

'Multi-Biomarker PK/PD Relationships of CNS Active Dopaminergic Drugs'

1. Even selective drugs may perturb multiple biochemical pathways, urging the need for multi-biomarker approaches over single-biomarker approaches. This thesis

2. Both affinity and signal transduction efficiency may explain differences with regard to in vivo potency among biomarkers. By integrating pharmacological knowledge into a multi-biomarker PK/PD approach it becomes possible to separate these two underlying factors. This thesis

3. CNS biomarker discovery needs a combination of serial plasma sampling, intracerebral microdialysis, PK/PD modeling and time-dependent multivariate pharmacometabolomics data analysis. This thesis

4. Neurotransmitter levels in the blood (or plasma) may not necessarily be a good biomarker of pharmacological effects in the brain. This thesis


7. Pharmacometabolomics is a straightforward approach to discover system-wide biochemical biomarkers of drug effects. It can be applied in a non-invasive manner via plasma sampling; it captures genomic, proteomic and environmental influences; and the costs are relatively low. (T. Burt & S. Nandal, Clin. Transl. Sci., 2016)

8. Rats and mice are not small humans, however, many biochemical pathways overlap. Qualitative and quantitative characterization of pharmacokinetics in relation to these pathways is essential for a proper translation of drug effects between species. (Based on E.M. Blais et al., Nat. Comm., 2017; M. Danhof et al., Tr. Pharmacol. Sci., 2008)

9. 'It is a capital mistake to theorise before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.' (Sir Arthur Conan Doyle, Sherlock Holmes – The complete illustrated short stories, Chancellor Press, 1985, p.6)

10. A sustainable way of life is too much seen as only a preference of a small group of people, while the urgency of climate change requires an effort from all of us.

11. Philosophy of Science should be a mandatory course in the academic education of Life Sciences.

12. ‘Let food be thy medicine and medicine be thy food.’ Often wrongly attributed to Hippocrates

Willem van den Brink,
Leiden, 21 november 2018