The mastermind research approach for prediction of human CNS drug effects: “Right place, right time, right concentration” in health and disease

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CNS disorders remain the world’s leading cause of disability. Currently, no cures are present, which indicates a high unmet need for good CNS drugs and drug therapies.

Apart from a drug’s physicochemical properties and blood–brain barrier (BBB) transport, the rate and extent of many processes that govern brain target site kinetics and CNS effects are regulated dynamically. Therefore, heterogeneous conditions such as species, gender, genetic background, tissue, age, diet, disease, drug treatment, might result in considerable inter-individual and intra-individual variation.

Drugs should access the CNS “at the right place, at the right time, and at the right concentration”. To improve CNS therapies and drug development, details of inter-species and inter-condition variations are needed to enable target site pharmacokinetics and associated CNS effects to be translated between species and between disease states. Studies need to be designed according to the “Mastermind approach”. This strategic and systematic CNS drug research approach, using advanced preclinical experimental designs and mathematical modeling will enable us to identify the contributions and variability of individual processes on the causal path between drug dosing and CNS effect in animals that can be translated to the human situation.

On the basis of a few advanced preclinical microdialysis based investigations it will be shown that the “Mastermind approach” has a high potential for the prediction of human CNS pharmacokinetics and CNS drug effects. Examples will be shown for acetaminophen, methotrexate and remoxipride.

Biography
Elizabeth C M de Lange has completed her PhD in 1993 and was tenured in 2001 at the Leiden Academic Centre of Drug Research, Leiden University (LACDR), the Netherlands. She currently is the Acting Head of the Division of Pharmacology of the LACDR. She is also the CEO of the CNS Drug Courses and Consultancy Company “In Focus”. She has published over 65 papers in reputed journals, over 10 Book Chapters, co-edited the book “Drug Delivery to the Brain- Physiological Concepts, Methodologies and Approaches”. Furthermore she serves at editorial board member of reputed journals.

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