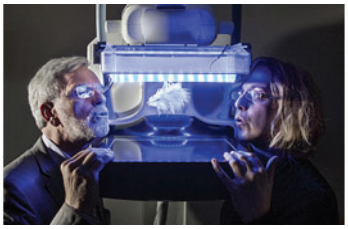
INNOVATION EXCHANGE AMSTERDAM

Collaboration Opportunity

Abuse Potential Evaluation with Pharmaco-MRI

- **Assessing abuse liability of experimental drugs in man using MRI methods**
- **Evaluate and mitigate abuse risk of novel Mechanisms-of-Action**

CNS, Drug safety measurement and abuse potential 2015

Background

Assessment of abuse potential of experimental drugs that engage with novel Mechanisms of Action is required as part of their development. The FDA strongly encourages industry to pay more attention to the risk for drug abuse in experimental drugs to avoid future non-medical use.

Today, a variety of preclinical animal models for drug dependence and abuse exist albeit with varying translational properties. Because of this, innovative drug development faces a signifi cant risk of choosing a suboptimal animal model, dosing and administration regime.

Applications

Novel drugs acting on novel Mechanisms of Action require a comprehensive approach to mitigate risks associated with the MOA and its (ant)agonists.

Pharmaco-MRI methods in humans offer such a comprehensive solution.

Compounds with an established safety and pharmacokinetic record can be evaluated in humans using MRI methods. Accordingly, activation of human brain networks can be recorded and compared with network responses to known drugs of abuse. Moreover, changes in brain responses upon repeated administration such as sensitization or tolerance can be recorded to further assess abuse potential.

Analysis of network activation patterns with reference to those of known drugs.

Dosing and repetitive administration is fl
exible and can be
combined with pharmacokinetics.

Sensitized volunteers may be considered to further establish lack of abuse potential.

MRI platform

The Spinoza Centre for Neuroimaging and the AMC share expertise and MRI infrastructure to address abuse liability issues. These are accessible to all parties engaging in innovative drug development.

Experimental drugs that show no signifi cant activation of abuse networks in the brain after single or repeated administration can be con-sidered safe with regard to illicit use. Moreover, lack of abuse potential of an experi-mental drug also establishes its Mechanism of Action as unlikely to be involved in abuse.

Researchers

L. Reneman, MD PhD, Neuroradiology, AMC
E. Ronken, PhD, Spinoza Centre for Neuroimaging

Key Publications

Schrantee A, Reneman L. Pharmacological imaging as a tool to visualise dopaminergic neurotoxicity [review]. Neuropharmacology. 2013 (in press) doi:pii: S0028-3908(13)00298-0

M.L. Schouw. Pharmacological MRI in the assessment of monoaminergic function. University of Amsterdam. PhD Thesis. 2013. Uitgeverij BoxPress.

Schouw ML, Kaag AM, Caan MW, Heijtel DF, Majoie CB, Nederveen AJ, Booij J, Reneman L. Mapping the hemodynamic response in human subjects to a dopaminergic challenge with dextroamphetamine using ASL-based pharmacological MRI. Neuroimage. 2013 15;72:1-9.

Schouw ML, De Ruiter MB, Kaag AM, van den Brink W, Lindauer RJ, Reneman L. Dopaminergic dysfunction in abstinent dexamphetamine users: results from a pharmacological fMRI study using a reward anticipation task and a methylphenidate challenge. Drug Alcohol Depend. 2013; 130:52-60.

Contact information:
Sanne Stembert
Tel: +31 20 566 8022
E-mail: s.j.stembert@amc.uva.nl