



**Universiteit
Leiden**
The Netherlands

Translational pharmacology of dopamine receptor agonists and antagonists : prolactin and oxytocin as biomarkers

Stevens, J.

Citation

Stevens, J. (2011, September 22). *Translational pharmacology of dopamine receptor agonists and antagonists : prolactin and oxytocin as biomarkers*.

Retrieved from <https://hdl.handle.net/1887/17851>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/17851>

Note: To cite this publication please use the final published version (if applicable).

**Translational pharmacology of
dopamine receptor agonists and antagonists**

Prolactin and oxytocin as biomarkers

Translational pharmacology of dopamine receptor agonists and antagonists

Prolactin and oxytocin as biomarkers

PROEFSCHRIFT

ter verkrijging van de graad van Doctor aan de Universiteit van Leiden,
op gezag van Rector Magnificus prof. mr. P. F. van der Heijden,
volgens besluit van het College voor Promoties,
te verdedigen op donderdag 22 september 2011, klokke 11.15 uur
door Jasper Stevens, geboren te Geldrop in 1979.

PROMOTIECOMMISSIE

Promotor

Prof. dr. M. Danhof

Co-promotoren

Dr. E. C. M. de Lange

Dr. P. H. van der Graaf

Overige leden

Dr. J. H. Proost, Rijksuniversiteit Groningen

Dr. A. Vermeulen, Johnson & Johnson

Prof. Dr. A. P. IJzerman

Prof. Dr. J. Bouwstra

Prof. Dr. M. Oitzl.

***THE RESEARCH DESCRIBED IN THIS THESIS WAS FINANCIALLY SUPPORTED BY PFIZER
AND CONDUCTED AT THE LEIDEN/AMSTERDAM CENTER FOR DRUG RESEARCH,
LEIDEN UNIVERSITY, THE NETHERLANDS.***



Translational pharmacology of dopamine receptor agonists and antagonists

Prolactin and oxytocin as biomarkers

For Nienke and my parents.

Contents

- 1 Background, objectives and outline 9**
- 2 Translational pharmacology of intranasal administration of dopamine receptor agonists and antagonists 13**
- 3 A new minimal-stress freely-moving rat model for preclinical studies on intranasal administration of CNS drugs 43**
- 4 Online solid phase extraction with liquid chromatography-tandem mass spectrometry to analyze remoxipride in small plasma-, brain homogenate-, and brain microdialysate samples 59**
- 5 Systemic- and direct nose-to-brain transport in the rat; a pharmacokinetic model for remoxipride after intravenous and intranasal administration 77**
- 6 Mechanism-based PK-PD model for the prolactin biological system response following a dopamine inhibition challenge - quantitative extrapolation to humans 97**
- 7 Conclusions and general discussion 123**

Appendices

- **Nederlandse samenvatting 135**
- **Nawoord 143**
- **List of Publications 145**
- **Abbreviations 147**