



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

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

License: <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