

CURRICULUM VITAE

Theodora Svetoslavova Handjieva-Darlenska, MD, PhD



Contact information

Name: Theodora Svetoslavova Handjieva-Darlenska, MD, PhD

Address: Medical Faculty, Medical University
Department of pharmacology and toxicology,
PO Box 1413
2, Zdrave, Str. Sofia, Bulgaria

Date of birth: 16-07-1980

Telephone: +359/ 897985410

E-mail: teodorah@abv.bg

Education

- 2007-2010 PhD project at Department of Human Nutrition, Life Sciences Faculty, University of Copenhagen, Denmark; Title: *Predictors of weight loss in dietary obesity management programs, Scientific supervisor: Prof. Arne Astrup**
- 2006-2009 Defended PhD in Medical Faculty, Medical University ó Sofia, Bulgaria; Title: *Ghrelin and obesity: mechanisms of pharmacological approach, Scientific supervisor: Prof. Nadka Boyadjieva***
- 1999-2005 Medical Faculty, Medical University ó Sofia, Bulgaria
- 1994-1999 French Language High School õAlphonse de Lamartineö - Sofia
- 1987-1994 Primary School- Sofia
- 1990-2006 English Language Course in Alliance
- 2002-2005 German Language Course in Alliance

Activities and membership

- 2010 Member of the OC of the 9th International symposium on obesity and related Diseases, Albena, Bulgaria (www.isord2011.com)
- 2009- present Assistant professor in Department of pharmacology and toxicology, Medical Faculty, Medical University ó Sofia, Bulgaria
- 05.2010 Organizer and communicator of the European Obesity Day (EOD) in Bulgaria
- 10.2009 Organizer and communicator of the International Obesity Day in Bulgaria

- 2009- present Member of the Bulgarian Pharmacological Society
- 2007- present Member of the European Academy of Nutrition Sciences (EANS)
- 2006 - present Member of the Young Investigators United, section of the European Association for the Study of Obesity (EASO)
- 2006 - present Member of the "PhD club" in Medical University of Sofia, Bulgaria
- 05.2006 Member of the OC of "Second Balkan Congress on Obesity", Albena, Bulgaria
- 2000-2004 President of the OC of "International Congress of Medical Sciences" (ICMS)
- 2000-2002 Public Relations of "Association of Medical Students in Bulgaria" (AMSB)
- 2002-2003 President of Association of Medical Students in Bulgaria
- 2001-2003 Member of Student's Council of Medical University-Sofia
- 03.02, 03.03, 08.03 Participant in General Assemblies of International Federation of Medical Student's Associations (IFMSA)
- 2001- present Member of "Bulgarian Association for the Study of Obesity and Related Diseases" (BASORD)

Scientific experience

- 05.2010 Lecturer in the 14th National nutrition symposium, Golden Sands Resort, Varna, Bulgaria
- 05.2010 Lecturer in the 5th National congress of the Bulgarian Diabetes Association with international participation, Sunny Day Resort, Varna, Bulgaria
- 09.2009 Lecturer in the 2d Central European Congress on Obesity (CECON), Budapest, Hungary
- 05.2009 Participant in the 17th European Congress on Obesity (ECO), Amsterdam, The Netherlands
- 09.2008 Participant in the 1st Central European Congress on Obesity (CECON), Karlovi Vary, Czech Republic
- 05.2008 Participant in the 16th European Congress on Obesity (ECO), Geneva, Switzerland
- 07.2007 Participant in the 10th European nutrition conference, Paris, France
- 05.2007 Participant in the 8th National Congress of Nutrition, Varna, Bulgaria
- 04.2007 Participant in the 15th European Congress on Obesity (ECO), Budapest, Hungary
- 11.2006 Participant in a round table about the "Actual problems of obesity in Bulgaria", organized by BASORD
- 10.2006 Participant in 1st International congress of Controversies in Obesity, Diabetes and Hypertension (CODHy)
- 09.2006 Participant in 10th International Congress on Obesity (ICO), Sydney, Australia
- 05.2006 Participant in "Second Balkan Congress on Obesity", Albena, Bulgaria
- 05.2005 Participant in 4th "International Congress of Medical Sciences", Sofia
- 06.2004 Participant in 7th Varna International Symposium of Obesity and Related Diseases, satellite symposium of 13th European Congress of Obesity (ECO), Prague
- 06.2005 Participant in 13th ECO, Prague
- 05.2004 Participant in 3rd "International Congress of Medical Sciences", Sofia
- 11.2003 Participant in 14th "European Student's Conference", Charite, Berlin
- 08.2003 Participant in "International Congress of Diabetology", Paris

Residency

- 2010 Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark
- 2009 Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark
- 2008 Human Nutrition - Medical Research Center (MRC), Cambridge, UK
- 2007 Institute for Human Nutrition, University of Copenhagen, Denmark
- 09.2004 Department of Endocrinology in öKarolinska Institutetö, Stockholm, Sweden
- 09.2004 Department of Endocrinology in öSaghlenska University Hospitalö, Gottenberg, Sweden
- 09.2005 Institute for Human Nutrition, University of Copenhagen, Denmark
- 08.2004 Clerkship in department of Internal Medicine, öStadt Krankenhausö, Munchen
- 08.2003 Clerkship in department of Internal Medicine, Hospital öPierre Brocaö, Paris
- 08.2002 Clerkship in department of Physiology, öUniversidad Autonoma de Madridö
- 08.2001 Clerkship in Hospital öAin Shaimsö, Cairo
- 07.2001 Clerkship in department of Endocrinology, öAlexandrovska Hospitalö, Sofia

Projects

- 2009-2010 Researcher-trainer in the project öMultilingual Virtual Human Patientö (MVHP), funded by the Education and training, Lifelong Learning Programme of the European Commission
- 2005-2009 Researcher in the Bulgarian center of the project öDiOGenesö (Diet, Obesity, Genes), Contract no.FP6-513946, funded by the Sixth Framework Program of the European Commission
- 2007-2008 Principal investigator in Grant # 7-D/2007, funded by Medical University ö Sofia Title: öThe effect of glucose and insulin on the hypothalamic regulation of experimental model of obesityö
- 2006-2010 Researcher in scientific project, funded by the Ministry of Education and Science. Title: öThe role of nutrition in the balance between Ghrelin and Leptin in the mechanisms of obesityö
- 2005-2006 Principal investigator in Grant # 45, funded by Medical University ö Sofia Title: öExperimental studies on the role of Ghrelin in the regulation of hypothalamic mechanism of control of obesityö

Courses

- 04.2010 Participation in the 16th European Nutrition Leadership Programme, Luxembourg
- 02.2010 Participation in the öHealthy Aging Courseö, Medical University, Sofia
- 10.2008 PhD Course öMethodology of the PhD thesisö, Medical University, Sofia
- 03.2008 Mass-media training, organized by the EU-funded project öDiOGenesö
- 02.2008 Project management course, organized by University of Cambridge, UK
02. 2008 Communication skills course, organized by University of Cambridge, UK
- 06.2007 Scientific course öGenomics on Obesityö, organized by INSERM, Toulouse
- 04.2007 SCOPE Course, organized by EASO in ECOö2007
- 06.2006 PhD Course öEnergy balance in humansö in Department of Human Nutrition, KVL, Copenhagen, Denmark
- 05.2006 SCOPE Course, organized by EASO in öSecond Balkan Congress on Obesityö

Prizes

04. 2010 ILSI-Europe grant for participation at 16th European Nutrition Leadership Programme, Luxembourg
- 05.2008 Travel Grant for 16th European Congress on Obesity (ECO), Geneva, funded by the European Association for the Study of Obesity (EASO)
- 05.2008 Third Prize in the contest of FameLab contest, organized by the British Council, Europe
- 12.2007 Research exchange programme award, funded by the British Council
- 05.2005 Second Prize for Oral Clinical Presentation in 4th ICMS
- 05.2004 First Prize for Oral Preclinical Presentation in 3rd ICMS
- 12.2003 Mini Nobel Prize for Medicine

Skills

Languages: English- fluent
French- fluent
German- talkative

Computer skills: Windows, MS Office, PowerPoint, SPSS program

Interests

Scientific interests: Nutrition and obesity, pharmacology, endocrinology

Personal interests: Aerobics, jogging, cinema, theatre, traveling

Publications

Handjieva-Darlenska T, Handjiev S, Larsen TM, Van Baak MA, Jebb S, Papadaki A, Pfeiffer A, Martinez JA, Kunesova M, Holst C, Astrup A, Saris WH. Initial weight loss on an 800 kcal diet as a predictor of weight loss success after 8 weeks: the Diogenes study, Eur J Clin Nutr (in press)

Aston, L.M., Jackson, D., Monsheimer, S., Whybrow, S., **Handjieva-Darlenska, T.**, Kreutzer, M., Kohl, Papadaki, A., Martinez, J.A., Kunova, V., Van Baak, M.A, Astrup, A., Saris, W.H.M, Jebb, S.A.A., Lindroos, A.K. Developing a methodology for assigning glycaemic index values to foods consumed across Europe. Obes Rev 2010, 11 (1), 92-100

Larsen TM, Dalskov S, van Baak M, Jebb S, Kafatos A, Pfeiffer A, Martinez JA, **Handjieva-Darlenska T**, Kunesová M, Holst C, Saris WHM, Astrup A. The Diet, Obesity and Genes (Diogenes) Dietary Study in eight European countries – a comprehensive design for long-term intervention. Obes Rev 2009, 11 (1), 76-79

Moore CS, Lindroos AK, Kreutzer M, Larsen TM, Astrup A, van Baak M, **Handjieva-Darlenska T**, Hlavaty P, Kafatos A, Kohl A, Martinez JA, Monsheimer S,

Jebb S. Dietary strategy to manipulate ad libitum macronutrient intake, and glycaemic index, across eight European countries in the Diogenes Study. *Obes Rev* 2009, 11 (1), 67-75

Handjieva-Darlenska T, Boyadjieva N. The effect of high-fat diet on plasma ghrelin and leptin levels in rats. *J Physiol Biochem*, 65 (2), 157-164, 2009.

Handjieva-Darlenska T, N. Boyadjieva. Changes in the metabolic parameters in experimental nutritional model of obesity in rats. *Compt Rend Acad Bulg Sci*, 60, 2007, 6, 701-704.

Handjieva-Darlenska T, N. Boyadjieva. Effect of Orlistat (Xenical) on plasma levels of ghrelin in rats with/without experimental nutritional model of obesity. *Compt Rend Acad Bulg Sci*, 60, 2007, 9, 1031-1034.

Handjieva-Darlenska T, N. Boyadjieva. Experimental study on the effect of two (low and high glycemic index) diets on the epididymal fat pad in obese rats. *Compt Rend Acad Bulg Sci*, 60, 2007, 12, 1343-1346.

Handjieva-Darlenska T, N. Boyadjieva. Obesity: pharmacotherapy and pharmacogenetics. Monographic book in Bulgarian and English languages, Ed. Simel 2007.

Author of 15 articles in Bulgarian scientific journals; Author of chapters on Pharmacotherapy of obesity in Books for medical students and general practitioners, 2009, 2010

Dissertation/ Dissertation abstract

* Title: *Predictors of weight loss in dietary obesity management programs*
Scientific supervisor: Prof. Arne Astrup

The overall aims of the PhD project

1. To analyse for biological predictors of individual total body weight loss outcome with emphasis on measures of anthropometrics from 3 large dietary intervention studies (Diogenes, Nugenob, and Tobes.).

2. To assess predictors of abdominal and visceral fat reduction and *risk factors*.

Data-management, statistical analyses, results presentation, literature review, and writing a minimum of 3 scientific publications for international peer-reviewed journals.

Materials and methods. Data from three large intervention studies are in use. The PhD study was designed to examine if initial weight loss (i.e. the weight loss achieved the first or second week) after controlling for anthropometrical baseline variables can predict the outcome of the 8(10)-week dietary intervention (body weight loss), drop-out rate and success in achieving the weight loss outcome. Possible baseline anthropometrical variables and the diet group will be included in the analysis as covariables. Any identified predictor will be assessed for clinical use by calculation of sensitivity, specificity and therapeutic index. Statistical modelling testing initial weight loss as a potential predictor individually in a basic model including diet group, gender, age group and partner number in a linear regression model. Related to DiOGenes and Nugenob projects 3 synopses were written. **Results.** The weight loss at week 8 was positively correlated with initial body weight, height, BMI, waist and hip circumference, sagittal diameter, fat mass (kg) and fat free mass (kg), and gender, (all $P < 0.01$). In the multivariate regression model, adjusted for partner, only initial body weight, early weight loss (week 1), and weight loss at week 3 were significant predictors of weight loss outcome at week 8: weight loss (kg) at week 8 = $0.09 + 0.046 \cdot \text{baseline body weight (kg)} + 0.311 \cdot \text{weight}$

loss (kg) at week 1 + 1.284*weight loss (kg) at week 3 ($R^2 = 68\%$, $P < 0.0001$). A weight loss of $\times 2.6$ kg at week 1 during the LCD period was identified as the optimal cut-off predictor for at least 10 kg weight loss at week 8. This study suggests that initial body weight, early weight loss (week 1), and weight loss at week 3 are predictors of final weight loss during an 8 week LCD, and may be used as early biomarkers of subsequent responses to a LCD diet.

** Title: *Ghrelin and obesity: mechanisms of pharmacological approach*
Scientific supervisor: Prof. Nadka Boyadjieva

Introduction: Obesity is increasing world-wide and has strong social impact. Hypothalamus plays an important role in the regulation of appetite and metabolism through hormonal balance between ghrelin and leptin. Ghrelin increases appetite, whereas leptin decreases it. The **aim** of our studies is to investigate the role of ghrelin in the mechanisms of obesity and the impact of certain medications and the glycemic index of food. Therefore, we have used both experimental and clinical approaches.

Materials and methods: 350 male Wistar rats were used in our studies. Two experimental models of obesity were developed based on either a high-fat diet (HFD) or a high fructose diet. The HFD model of obesity was applied in the experiments with Orlistat, the glycemic index (GI) and the intracerebroventricular (ICV) administration of insulin and glucose. The rat body weight was measured during the experiments. At the end of the nutritional periods the weight of different organs was measured. Blood was collected for further analyses of lipids and blood glucose, as well as for plasma levels of ghrelin and leptin estimation. 30 subjects with overweight and obesity participated in the clinical trial. They were randomized into two dietary regimens, differing by the GI of the carbohydrate foods. Anthropometric measurements, fat tissue analyses, examinations for biochemical parameters, and plasma levels of ghrelin and leptin were performed. The **results** demonstrated a decrease in the plasma levels of ghrelin and an increase of the plasma leptin levels following HFD in rats. Chronic intake of fructose solution (10%) stimulated ghrelin secretion. No effect on plasma leptin concentrations was detected. The long-term intake of Orlistat decreased plasma levels of ghrelin and body weight in rats with or without obesity. ICV administration of insulin and glucose inhibited the hypothalamic leptin expression in both obese and control animals. GI modulated the balance between ghrelin and leptin in rats and humans. The low GI diet increased plasma ghrelin levels and thus, ameliorated the disturbed balance between ghrelin and leptin. Our results contribute to the understanding of the mechanisms of obesity and the role of different therapeutic strategies, i.e. diet and drug therapy, in the balance of the hormonal control of appetite and metabolism.