

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.  
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NAME <b>Eero Castrén</b>	POSITION TITLE <b>Sigrid Juselius Professor of Neuroscience</b>		
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Kuopio, Kuopio, Finland	MD	08/1983	Medicine
University of Kuopio, Kuopio, Finland	PhD	10/1989	Neuropharmacology
National Institute of Health, Bethesda,, MD, USA	Postdoc	1986-89	Neuroscience
Max Planck Institute of Psychiatry, Germany	Postdoc	1990-94	Neurotrophic factors

**NOTE: The Biographical Sketch may not exceed four pages. Follow the formats and instructions below.**

### A. Personal Statement

My research has focused on the effects of neuronal plasticity and neurotrophic factors, particularly the brain-derived neurotrophic factor BDNF, on the adult brain and their role in the mechanism of action of drugs acting on the central nervous system. We have been working in border area between neuropharmacology and developmental neuroscience, which has turned out to be very useful. Our recent findings has revealed a critical role of experience-dependent neuronal plasticity in the mechanism of antidepressant drug action and a possibility to use pharmacology to reactivate a developmental-like plastic state in adult brain.

### B. Positions and Honors

#### Positions and Employment

1986-1989: Postdoctoral Fellow, Laboratory of Clinical Science, NIMH, NIH, Bethesda, MD.  
 1990-1992: Postdoctoral Fellow, Max Planck Institute for Psychiatry, Martinsried, Germany.  
 1992-1994: Staff Scientist, Max Planck Institute for Psychiatry, Martinsried, Germany.  
 1995-1998: Research Director, A.I. Virtanen Institute, University of Kuopio.  
 1998-2003: Professor of Molecular Pharmacology, A.I. Virtanen Institute, University of Kuopio.  
 2003-2012: Sigrid Juselius Professor of Neuroscience, Neuroscience Center, University of Helsinki.  
 2011 : Visiting Professor, Columbia University, New York, US (on leave from the University of Helsinki)  
 2013- : Director, Neuroscience Center, University of Helsinki.

#### Other Experience

1996: Organizer and Chairman: International symposium on "Neurotrophins in Neuronal Development and Plasticity", August 4-5, 1996, Finland.  
 1989-2003: Vice-Dean, A.I. Virtanen Institute, University of Kuopio.  
 2002: Organizer and Chairman: International Summer School on Schizophrenia, Kuopio, Finland.  
 2002-2003: Chairman, Department of Neuroscience, A.I. Virtanen Institute, University of Kuopio.  
 2000-2003: Director, Kuopio University Neuroscience Center  
 2003-2006: President, Finnish Brain Research Society

- 2005- : Member, Scientific Advisory Panel, European College of Neuropsychopharmacology  
2007-2009: Member, Scientific Council, University of Helsinki.  
2007- : Member, Scientific advisory board, ERA-Net NEURON programme, European Union  
2010 : Chairman, 10<sup>th</sup> International Conference on Neurotrophic factors (NGF2010)  
June 10-13, Helsinki Finland  
2011- Member, Programme Committee, ERA-Net NEURON programme, European Union

### **Honors**

- 1986-1989: Visiting Fellowship, Fogarty International Center.  
1989-1990: Scientific Assistant Fellowship, Academy of Finland.  
1990: Best thesis award, the Finnish Society of Pharmacology  
1990-1992: Fellowship, Alexander von Humboldt Foundation, Germany.  
1993 : Fellowship, Max Planck Society, Germany.  
2003- : Sigrid Juselius Professorship in Neuroscience, Neuroscience Center, University of Helsinki.  
2004- : Member, Finnish Academy of Science and Letters  
2011: Schaefer Scholar award, Columbia University (for a sabbatical at the lab of Dr. René Hen, Dept. of Psychiatry, Columbia University, New York.  
2012: Fellow, European College of Neuropsychopharmacology

### **C. Selected Peer-reviewed Publications**

Castrén E., Zafra F., Thoenen H. and Lindholm D. Light regulates the expression of brain-derived neurotrophic factor mRNA in rat visual cortex. *Proc. Natl. Acad. Sci. USA* 89: 9444-9446, 1992.

Saarelainen T., Hendolin P., Koponen E., Lucas G., MacDonald E., Agerman K., Haapasalo A., Nawa H., Erfors P., Aloyz R. and Castrén E. Activation of the trkB neurotrophin receptor is induced by antidepressant drugs and is required for antidepressant-induced behavioral effects. *J. Neurosci.* 23 :349-357, 2003.

Lucas G., Hendolin P., Harkany T., Agerman K., Paratcha G., Holmgren C., Zilberter Y., Sairanen M., Minichiello L., Castrén E., and Erfors P. A reinforcement of morphine-induced analgesia by neurotrophin-4 mediated trkB activation. *Nature Neuroscience* 6: 221-222, 2003.

Koponen E., Vöikar V., Riekkari R., Saarelainen T., Rauramaa T., Rauvala H., Taira T., Castrén E. Transgenic mice overexpressing the full-length neurotrophin receptor trkB exhibit increased activation of trkB/PLC $\gamma$  pathway, reduced anxiety, and facilitated learning. *Mol. Cell. Neurosci.* 26: 166-181, 2004.

Castrén E. Neurotrophic effects of antidepressant drugs. *Curr. Opin. Pharmacol.* 4, 58-64, 2004.

Sairanen M., Lucas G., Erfors P., Castrén M, and Castrén E. BDNF and antidepressant drugs have different but coordinated effects on neuronal turnover, proliferation and survival in the adult dentate gyrus. *J. Neurosci.* 25: 1089-1094, 2005.

Castrén E. Is mood chemistry? *Nature Rev. Neurosci.* 6: 241-246, 2005.

Castrén M, Tervonen T, Kärkkäinen V., Heinonen S, Castrén E, Larsson K, Bakker CE, Oostra BA, and Åkerman KEO. Altered Differentiation of Neural Stem Cells in Fragile X Syndrome. *Proc. Natl. Acad. Sci. USA* 102, 17834-17839, 2005.

Rantamäki T., Hendolin P., Kankaanpää A., Mijatovic J., Piepponen P., Domenici E., Chao M.V., Männistö P.T. and Castrén E. Pharmacologically diverse antidepressants rapidly activate Brain-derived neurotrophic factor (BDNF) receptor trkB and induce phospholipase-C $\gamma$  signaling pathways in mouse brain. *Neuropsychopharmacology*, 32: 2152–2162, 2007.

Maya Vetencourt JF, Sale A, Viegi A, Baroncelli L., De Pasquale R, O’Leary OF, Castrén E. and Maffei L. The antidepressant fluoxetine restores plasticity in the adult visual cortex. *Science*, 320, 385-388, 2008.

- Karpova N., Jesse Lindholm J., Pruunsild P., Timmusk, T. and Castrén E., Long-lasting behavioural and molecular alterations induced by early postnatal fluoxetine exposure are restored by chronic fluoxetine treatment in adult mice. *Eur. Neuropsychopharmacology* 19: 97-108, 2009.
- Wu, X, Castrén, E. Co-treatment with diazepam prevents the effects of fluoxetine on hippocampal neurogenesis. *Biol. Psychiatry* 66: 5-8, 2009.
- Sallert M., Rantamäki T., Vesikansa A., Anthoni H., Harju K., Yli-Kauhaluoma J., Taira T., Castrén E., Lauri S.E. BDNF controls activity-dependent maturation of CA1 synapses by down regulating tonic activation of presynaptic kainate receptors. *J. Neurosci.* 29:11294 –11303, 2009.
- Rantamäki T., Vesa L., Antila H., Di Lieto A., Tammela P., Schmitt A., Lesch K.-P., Rios M. and Castrén E. Antidepressant drugs transactivate TrkB neurotrophin receptors in the adult rodent brain independently of BDNF and monoamine transporter blockade. *PLoS One* 6 (6): e20567, 2011.
- Kas M.J.H., Krishnan V, Gould T.D., Collier D.A., Olivier B., Klaus-Peter Lesch K.-P., Domenici E., Fuchs E., Gross C. and Castrén E. *Advances in Multidisciplinary and Cross-species Approaches to Examine the Neurobiology of Psychiatric Disorders.* *Eur Neuropsychopharmacol* 21: 532-544, 2011.
- Karpova N.N., Pickenhagen A., Lindholm J., Tiraboschi E., Kuleskaya N., Ágústsdóttir A., Antila H., Popova D., Akamine Y., Bahi A., Sullivan R., Hen R., Drew L.J. and Castrén E. Fear Erasure in Mouse Requires Synergy Between Antidepressant Drug Treatment and Exposure Therapy. *Science* 334:1731-1734, 2011.
- Shulga A, Magalhaes A., Autio H., Plantman S., Di Lieto A., Nykjaer A., Carlstedt T., Risling M., Arumäe U., Castrén E. and Rivera C. The loop diuretic bumetanide blocks post-traumatic p75NTR upregulation and rescues injured neurons. *J. Neurosci.* 32: 1757-70, 2012.
- Di Lieto A., Rantamäki T., Vesa L., Yanpallewar S., Antila H., Lindholm J., Rios M., Tessarollo L., Castrén E. The responsiveness of TrkB to BDNF and antidepressant drugs is differentially regulated during mouse development. *PloS One* 7(3):e32869, 2012.
- Kemppainen S., Rantamäki T., Jerónimo-Santos A., Lavoisier G., Autio H., Karpova N., Kärkkäinen E., Stavén S., Miranda H.V., Outeiro T.F., Diógenes, M.J., Laroche S., Davis S., Sebastião A.M., **Castrén E.**, Tanila H. Impaired TrkB receptor signaling contributes to memory impairment in APP/PS1 mice. *Neurobiology of Aging*, 33:1122.e23-39, 2012.
- Uutela M., Lindholm J., Louhivuori V., Wei H., Louhivuori L.M., Pertovaara A., Åkerman K., **Castrén E.**, and Castrén M.L. Diverse effects of reduced BDNF expression on the behavioral phenotype of Fmr1 knockout mouse. *Genes Brain Behavior* 11: 513-23, 2012.
- Maya-Vetencourt J.F., Tiraboschi E., Greco D., Laura Restani L., Cerri C., Auvinen P., Maffei L., and **Castrén E.** Experience-dependent NPAS4 expression mediates plasticity in adult visual cortex. *J. Physiol* 590: 4777-87, 2012.
- Savelyev S.A., Rantamäki T., Rytönen K.-M., **Castrén E.**, Porkka-Heiskanen T. Sleep homeostasis and depression: studies with the rat clomipramine model of depression. *Neuroscience* 212:149-58, 2012.
- Castrén E.**, Elgersma Y., Maffei L. and Hagerman R. Treatment of neurodevelopmental disorders in adulthood. *J. Neurosci.* 32:14074 –14079, 2012.
- Skeldal S., Sykes A.M., Glerup S., Matusica D., Palstra N., Autio H., Madsen P., **Castrén E.**, Nykjaer A. and Coulson E.J. Mapping of the interaction site between sortilin and the p75 neurotrophin receptor reveals a regulatory role for the sortilin intracellular domain in p75 neurotrophin receptor shedding and apoptosis. *J. Biol. Chem*, [Epub ahead of print], Oct 26, 2012.
- Castrén E.** Trophic factors: Neurotrophic factors. In: *Neuroscience in the 21st Century.* Ed: Pfaff D.W., Springer, Berlin, pp. 1555-1589, 2012.
- Castrén E.**, and Hen, R.: Neuronal Plasticity and Antidepressant Effects. *Trends Neurosci.* <http://dx.doi.org/10.1016/j.tins.2012.12.010>, E-published February 1, 2013.

Total number of publications: 179

Total number of citations: 7746

h-index: 45

#### **D. Research Support**

##### Ongoing Research Support

European Research Council, Advanced Investigator Grant. "Induction of juvenile-like plasticity in adult brain". 2013-2018, € 2,500,000

Academy of Finland, Center of Excellence program, the mechanism of action of CNS drugs, in particular antidepressant drugs, 2008-2013, € 663.000.

Academy of Finland, Research Grant: "Pharmacologically Induced Plasticity in Adult Brain: Role of Interneurons and Activation in the Limbic Cortex". 2012-2016, € 450,000.

Sigrid Juselius Foundation: Molecular pathways activated by antidepressant drugs in adult brain, 2012-2013 € 48 000.

##### Research Support Completed in the last three years

Sigrid Juselius Professorship in Neuroscience: The physiological, pathophysiological and pharmacological roles of BDNF signaling in adult brain. 2003 – 2012, € 250,000 annually.

Academy of Finland, Addiction program: The role of BDNF signaling in the development of addiction. 2007-2010, € 306.000.

European Union STREP Network, Memories: The role of BDNF signaling in animal models of Alzheimer's disease, 2007-2010 € 302.000

Sigrid Juselius Foundation, 2007-2011, € 200 000