# Manuel Casanova, M.D.

Gottfried & Gisela Kolb Endowed Chair in Psychiatry

Vice Chair of Research Department of Psychiatry School of Medicine





#### Dr. Manuel Casanova made his residency training in neurology and then spent 3 years doing a fellowship in neuropathology at The Johns Hopkins Hospital. During his stay at the Johns Hopkins Hospital, Dr. Casanova was in-charge of Pediatric Neuropathology, a fact which kindled his interest in developmental disorders of the brain. His clinical experience was enhanced by appointments as either a consultant or staff neuropathologist at Sinai Hospital (Maryland), the North Charles Hospital and the D.C. General Hospital. He spent several years as Deputy Medical Examiner for Washington, D.C., where he gained valuable experience in the post-mortem examination of Sudden Infant Death Syndrome and child abuse. His expertise in the field was recognized by honorary appointments as a Scientific Expert for the Armed Forces Institute of Pathology (AFIP) and as a Professorial Lecturer for the Department of Forensic Science at George Washington University. Dr. Casanova spent 8 years helping to establish 2 of the most successful brain banks in this country: The Johns Hopkins Brain Resource Center (3 years) and the Brain Bank Unit of the Clinical Brains Disorders Branch at the National Institutes of Mental Health (5 years). Dr. Casanova did training in psychiatry at the National Institutes of Mental Health under the tutelage of Drs. Richard Wyatt, Danny Weinberger, and Joel Kleinman. He retired as a Major in the US Army Reserves and later on as a Lt. Commander in the Public Health Service. He joined the Medical College of Georgia as a full Professor in 1991 and came to the University of Louisville in 2003 as the Gottfried and Gisela Kolb Endowed Chair in Psychiatry.

Dr. Casanova has had over twenty years of experience in the neurosciences. Although trained in the classical methods of neurology and neuropathology his interest has gradually shifted towards the study of abnormalities of cortical circuitry. His research has focused on the cell minicolumn, a vertical conglomerate of 80 to 100 neurons having a common latency of response to stimulation. Using computerized imaging analysis he has established the anatomical validity of the cell minicolumn. His earlier work has reported interhemispheric differences in the morphometry of minicolumns that could provide for the speciation of hominids. Localized in Brodmann area 22-part of Wernicke's language region-the morphometric difference may play a role both in the development of language and in its disorders. His most recent studies have looked for the presence of abnormalities of minicolumnar organization and lateralization in the brains of patients who exhibit language disturbances, including autism, Asperger's syndrome, and dyslexia. He has summarized his work on minicolumns and provided an overview of the field in recent reviews of the literature appearing in Brain and Brain, Behavior and Evolution.

# **Refereed Publications 2011-2012**

Seelan RS, Pisano MM, Greene RM, **Casanova MF**, Parthasarathy R. Differential methylation of the gene encoding Myo-Inositol 3-phosphate synthase (Isyna1) in rat tissues. Epigenomics Journal 3(1): 111-124, 2011.

**Casanova MF**, Williams EL. Prenatal Ultrasound: It's Not Just a Photograph. Autism Science Digest, 1: 58-60, 2011.

Baruth JM, Williams EL, Sokhadze E, El-Baz A, Sears L, **Casanova MF**. Beneficial effects of repetitive Transcranial Magnetic Stimulation (rTMS) on behavioral outcome measures in autism spectrum disorder. Autism Science Digest, 1: 52-57, 2011.

Mott M, Fernandez-Bortran R, **Casanova MF**. Neuroinflammation in the pathogenesis of Autism Spectrum Disorders: converging evidence for systemic and central nervous system immune interaction. Brain Research Journal, 3(2): 1-31, 2011.

**Casanova MF**, El-Baz A, Switala AE, Williams EL, Williams, D, Minshew N, Conturo T. A quantitative analysis of the shape of the corpus callosum in autism. Autism, 15(2): 223-238, 2011.

Dombroski BA, Switala AE, El-Baz A, Casanova MF. Gyral Window mapping of typical cortical folding using MRI. Translational Neuroscience, 2(2): 142-147, 2011.

Williams EL, Casanova MF. Above genetics: lessons from cerebral development in autism. Translational Neuroscience, 2(2): 106-120, 2011.

**Casanova MF**, Starkstein S, Jellinger K. Clinicopathological correlates of behavioral and psychological symptoms of dementia. Acta Neuropathologica, 122(2): 117-135, 2011.

Vladimir B, Jaroslav B, and **Casanova MF**. Plausible mechanisms for brain structural and size changes in human evolution. Collegium Anhropologicum 25(3):949-955, 2011.

El-Baz A, Elnakib A, **Casanova MF**, Gimel'farb G, Switala AE, Jordan D, Rainey S. Accurate automated detection of autism related corpus callosum abnormalities. Journal of Medical Systems, 35(5):929-939, 2011.

A. Elnakib, **M. Casanova**, G. Gimel'farb, A. Switala, and A. El-Baz, "Autism Diagnostics by Centerline-Based Shape Analysis of the Corpus Callosum," Proc. of IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'11), Chicago Illinois, USA, March 30–April 2, 2011, pp. 1843-1846.

M. Nitzken, **M. Casanova**, G. Gimel'farb, F. Khalifa, A. Elnakib, A. Switala, and A. El-Baz, "3D Shape Analysis of the Brain Cortex with Application to Autism," Proc. of IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'11), Chicago Illinois, USA, March 30–April 2, 2011, pp. 1847-1850.

M. Nitzken, **M. Casanova**, G. Gimel'farb, A. Elnakib, F. Khalifa, A. Switala, and A. El-Baz, "3D Shape Analysis of the Brain Cortex with Application to Dyslexia," Proc. of IEEE International Conference on Image Processing (ICIP'11), Brussels, Belgium, September 11-14, 2011, pp. 2713-2716.

Sokhadze G, Kaplan M, Edelson SM, Sokhadze EM, Baruth J, El-Baz A, Hensley MK, **Casanova MF**. Modulatory effects of ambient prism lenses on spatial attention in autism: an event related potential study. Journal of Neurotherapy 15(4):413-415, 2011.

Baruth J, **Casanova M**, Sears L, Sokhadze E. Transcranial magnetic stimulation (rTMS) modulates selective attention and executive functioning in autism. Journal of Neurotherapy 15(4): 431-432, 2011.

Sokhadze E, Baruth J, Sears L, Sokhadze GE, El-Baz A, Hensley M, Tasman A, **Casanova MF**. Event-related potential study of attention regulation in ADHD, Autism Spectrum Disorder, and Typical Children. Journal of Neurotherapy 15(4): 443-445, 2011.

Sokhadze E, Baruth J, Sears L, Sokhadze GE, El-Baz AS, Hensley M, Gross E, Tasman A, **Casanova MF**. Neuromodulation using rTMS improves error monitoring and correction function in autism spectrum disorders. Journal of Neurotherapy 15(4):445-447, 2011.

**Casanova MF**, El-Baz A, Switala A. Laws of conservation as related to brain growth, aging, and evolution: symmetry of the minicolumn. Frontiers in Neuroanatomy, 5:66, 2011.

**Casanova MF**, Mott M, Sokhadze EM. The neuropathology of autism: a review of the current literature. The Siberian Journal of Special Education, 2, 2012. http://sibsedu.kspu.ru/english/upl/6/The\_Neuropathology\_of\_Autism.pdf

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Gross E, El-Baz AS, Sokhadze GE, Sears L, **Casanova MF**. Sokhadze EM. Induced EEG gamma oscillation alignment improves differentiation between autism and ADHD group responses in a facial categorization task. J Neurotherapy, 16(2): 78-91, 2012.

**Casanova MF**, Baruth JM, El-Baz AS, Tasman A, Sears L, Sokhadze EM. Repetitive TMS (rTMS) modulates ERP indices of attention in autism. Translational Neuroscience, 3(2): 1-11, 2012.

Sokhadze E, Sokhadze G, **Casanova M.** Neuromodulation using transcranial DC stimulation (TDCS) and repetitive transcranial magnetic stimulation (rTMS) as a translational neuroscience approach to treat autism. Neuroconnections, pp. 16-18, Summer 2012.

Srivasta DP, Jones KA, Woolfrey KM, Burgdorf J, Russell TA, Kalmbach A, Lee H, Yang C, Bradberry MM, Wokosin D, **Casanova MF**, Seino S, Moskal JR, Waters J, Penzes P. Social, communication, and cortical structural impairments in Epac2deficient mice. J Neuroscience 32(34):11864-11878, 2012.

Abdelrahman M, Ali AM, Farag A, **Casanova MF**, Farag AA. New approach for classification of autistic vs. typically developing brain using white matter volumes. Computer and Robot Vision, 284-9, 2012.

Elnakib A, Nitzken M, HeYeon P, El-Baz A, **Casanova MF**, Gimel'farb G. Agerelated brain cortex change using 3D shape analysis. Proceeding so the 21st International Conference on Pattern Recognition (ICPE), Tsukuba Science City, Japan, November 2012, in press.

Sokhadze E, El-Baz A, **Casanova MF**. Event related potential study of attention regulation during illusory figure categorization task in ADHD, Autism Spectrum Disorder, and typical children. Journal of Neurotherapy, in press.

Williams EL, Casanova MF. Hyperlexia and dyslexia in autism: hitting a moving target. J Spec Ed Rehab, 13(3-4): 39-54, 2012.

### **Book Chapters:**

**Casanova MF**, Trippe J. Radial cytoarchitecture and patterns of connectivity in autism. F. Happe and U Frith (eds) Autism and Talent. Oxford University Press: Oxford, ch. 11, pp. 135-140, 2010.

**Casanova MF**, Sokhadze E, El-Baz A, Baruth J, Mathai G, Sears L. Research at the University of Louisville Autism Center. Siri K and Lyons T (eds). Cutting Edge Therapies for Autism, Skyhorse Publishing: New York, ch. 68, pp. 410-413, 2010.

Baruth J, Sokhadze E. El-Baz A, Mathai G, Sears L, **Casanova MF**. Transcaranial Magentic Stimulation as a Treatment for Autism. Siri K and Lyons T (eds). Cutting Edge Therapies for Autism, Skyhorse Publishing: New York, ch. 63, pp. 388-397, 2010.

Farag A, Elhabian S, Abdelrahman M, Graham J, Farag A, Chen D, **Casanova MF**. Surface Modeling of the Corpus Callosum from MRI Scans. In George Bebis, Richard Boyle, Bahram Parvin, Darko Koracin, Ronald Chung, Taid Hammoud, Muhammad Hussain, Tan KarHan, Roger Crawfis, Daniel Thalmann, David Kao, Lisa Avila (ed.s) Advances in Visual Computing: 6th International Symposium, ISVC 2010, Las Vegas, NV, USA, November 29-December 1, 2010, proceedings part III. Lectures Notes in Computer Science 2010 December 13:6455: 9-18.

**Casanova MF**, Sokhadze E, El-Baz A, Baruth J, Mathai G, Sears L. Research at the University of Louisville Autism Center. Cutting Edge Therapies for Autism 2. Skyhorse Publishing, 425-429, 2011.

Baruth J, Sokhadze E. El-Baz A, Mathai G, Sears L, **Casanova MF**. Transcranial Magnetic Stimulation as a Treatment for Autism. Cutting Edge Therapies for Autism 2, 402-411, 2011.

M. Nitzken, **M. Casanova**, F. Khalifa, G. Sokhadze, and A. El-Baz, "Shape-Based Detection of Cortex Variability for More Accurate Discrimination Between Autistic

and Normal Brains," In Handbook of Multi Modality State-of-the-Art Medical Image Segmentation and Registration Methodologies: Volume 2, Chapter 7, (A. El-Baz, R. Acharya, A. Laine, and J. Suri, Editors), Springer-Verlag, New York, March 2011, pp. 161-185. (ISBN: 978-1-4419-8203-2).

Mott M, Fernandez-Bortran R, **Casanova MF**. Neuroinflammation in the pathogenesis of Autism Spectrum Disorders: converging evidence for systemic and central nervous system immune interaction. In Owen B Williams and Garet I Wilson (eds.) Advances in Brain Research. NOVA Science Publishers, Inc., New York, ch. 11, 2012.

Mott M, Fernandez-Bortran R, **Casanova MF**. Neuroinflammation in the pathogenesis of Autism Spectrum Disorders: converging evidence for systemic and central nervous system immune interaction. In Carmelina Gemma (ed) Neuroinflammation: Pathogenesis, Mechanisms and Management. NOVA Science Publishers, Inc., New York, ch. 8, 2012.

Elnakib A, **Casanova MF**, Gimel'farb G, El-Baz A. Autism diagnostics by 3D shape analysis of the cropus callosum. In Kenji Suzuki (ed) Machine Learning in Computer-Aided Diagnosis: Medical Imaging Intelligence and Analysis. Medical Information Science Reference (an imprint of IGI Global) Hershey: Pennsylvania, ch. 15, pp. 315-335, 2012.

Baruth JM, Sokhadze E, El-Baz A, Mathai G, Sears L, **Casanova MF**. Transcranial megnetic stimulation. In Ken Siri and Tony Lyons (eds) Cutting Edge Therapies for Autism. Skyhorse Publishing, New York, ch. 23, pp. 143-152, 2012.

Pennington R, Welch KC, Sokhadze E, El-Baz A, Farag A, Williams PG, **Casanova MF**. The Louisville Model: Crossing the Divide: Collaborative Efforts towards Innovative Treatments at the University of Louisville's Autism Center. In Ken Siri and Tony Lyons (eds) Cutting Edge Therapies for Autism. Skyhorse Publishing, New York, ch. 25, pp. 161-164, 2012.

**Casanova MF**. Neural mechanisms in autism. In Fred Volkmar (ed.) Encyclopedia of Autism Spectrum Disorders, Springer, in press.

**Casanova MF**. The minicolumnopathy of autism. In J Buxbaum and P Hof (editors): The Neuroscience of Autism Spectrum Disorders, Academic Press: Oxford, chapter 3.7, pp. 327-333, 2013.

Williams EL, **Casanova MF**. Ultrasound and oxidative stress in autism. In Dietrich-Maszalska D, Gagnon S, Chauhan V (editors) Oxidative Stress in Basic Research and Clinical Practice: Studies on Psychiatric Disorders., 2012. In press.

Dombroski B, **Casanova MF**. Imaging and the corpus callosum in patients with autism. In The Comprehensive Guide to Autism, Springer, 2012, in press.

# Grant Funding

**2009-2011 Principal Investigator:** Gross morphological correlates to the minicolumnopathy of autism. RO11MH088893 \$607,859.

**2013 Principal Investigator:** Building a selective inhibitory tone in autism: an rTMS study. RO1MH086784 \$888,000.

**2003 Co-Investigator:** Behavioral and psychophysiological study of attentional, perceptual, and emotional processing after treatment with ambient prism lenses and visuo-motor exercises in children with autism spectrum disorder. Autism Research Institute \$7,500. (E Sokhadze, PI)

**2012 Casanova MF (Co-Principal Investigator):** A novel image-based diagnostic system for the accurate diagnosis of autism. Coulter Translational Research Partnership, Wallace H. Coulter Foundation Award. \$100,000

2013 Casanova MF (Principal Investigator) Effetcs of Repetitive Transcranial Magnetic on Gamma Activity and Redox State. Autism Research Institute, \$50,000.

# **External Professional Activities:**

Advisory Board: On Mental Health (OMH) stichting, Netherlands. Registration number: KvK # 24474513 Web site: www.onmentalhealth.org.

Scientific Advisory Board Lifeboat Foundation

Board of Directors Families for Effective Autism treatment (FEAT)

Editorial Board: Autism Research Associate Editor: Translational Neuroscience Editor: Autism Insights Editor: Autism Research and Treatment Editor: Autism Research and Treatment Editor: Journal of Special Education and Rehabilitation Review Editor: Frontiers in Neurodegeneration Editor: World Journal of Translational Medicine Associate Editor: Open Journal of Psychiatry Editor: The Scientific World Journal (Psychiatry and Pathology Domains) Editorial Board: Neuroscience (IBRO) Editorial Board: Acta Neuropathologica