

Médico y Neurólogo Clínico de la U. de Antioquia. Licencia especial en Neuropediatría con énfasis en Neuropsicología de la Universidad Católica de Lovaina, Bélgica. Profesor Titular en neurología del comportamiento de la Facultad de Medicina de la Universidad de Antioquia. Coordinador del Grupo de Neurociencias de Antioquia. Ha sido autor y coautor de más 200 publicaciones en revistas científicas nacionales e internacionales sobre aspectos clínicos, neurológicos, neuropsicológicos, neurogenéticos y moleculares de trastornos neurodegenerativos como las enfermedades de Alzheimer, Parkinson, Huntington, Wilson y CADASIL y sobre trastornos del neurodesarrollo como el déficit de atención con hiperactividad. Ha presentado numerosas ponencias en congresos nacionales e internacionales y es co-autor de varios libros y capítulos de libros. Actualmente es el Investigador principal en Colombia del ensayo clínico API COLOMBIA, uno de los más ambiciosos estudios de prevención de la enfermedad de Alzheimer financiado por el NIH, Banner y Genentech-Roche.

BIOGRAPHICAL SKETCH

NAME: Lopera, Francisco Javier

POSITION TITLE: Professor of Behavioral Neurology, Chief of Neurosciences Program-University of Antioquia, Coordinator Group of Neurosciences of Antioquia

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Antioquia-Colombia	MD	1970-1979	Medicine
University of Antioquia-Colombia	Neurologist	1981-1984	Clinical Neurology
Catholic University of Lovaine (Belgium)	Training	1987-1989	Neuropsychology

A. PERSONAL STATEMENT

At the Neuroscience Group of Antioquia University, I function as the Director of the Neuroscience Group who work in basic and clinical neurosciences, in developmental and neurodegenerative disorders. As a Behavioral Neurologist in the Department of Internal Medicine, Clinical Neurology Service at Medical School of the Antioquia University, I play an active role in assisting patients with Alzheimer's Disease, CADASIL, Parkinson disease, Huntington disease, Mild cognitive impairment, Fronto-temporal dementia, and other forms of dementias. I also play a role in assisting patients with ADHD, language impairment, conduct disorders, and other neuro-developmental problems. I have been working with a large groups of families with FAD due to a common PSEN1 mutation (E280A) for over 30 years, an endeavor that has ultimately led to my position as Principal investigator in Colombia of the collaborative project with Banner Health and Genentech for Prevention therapy in FAD. I have expertise as a Behavioral Neurologist, studying both adults and children as well as performing research of various neurodegenerative and developmental disorders in these populations.

Along with my research program, I play an active role in mentoring students of the Global Brain Health Institute (GBH). I am excited to work with Dr Bruce Miller and Atlantic Fellow Dr. Agustin Ibanez to establish and characterize a first-in-class neurodegenerative disease cohort in South America. I am committed to the goals of this project and look forward to working with them on the clinical study of people with Alzheimer's disease and controls.

B. POSITIONS AND HONORS

Positions and Employment

- 1975- 1978 Instructor of Neuropsychology, University of Antioquia
 1978- 1979 Intern of Medicine University of Antioquia
 1979- 1980 Rural Medicine, Lazcario Barboza Hospital, Acandí, Chocó.
 1980- 1981 Director of Lazcario, Barboza Hospital, Acandí, Chocó.
 1982- 1984 Neurology resident, University of Antioquia.
 1984- 1986 Neurologist and Assistant Professor in Neuropsychology. U de A and ISS.
 1987- 1989 Assistant Medicine in Cliniques Universitaires Saint Luc. University of Lovaine. Belgium.
 1989- 1991 Assistant Professor in Clinical Neurology, University of Antioquia.
 1991- 2005 Chief of Neurosciences Program, University of Antioquia.
 1993- current Professor in Behavioral Neurology, University of Antioquia.
 1996- 1998 Chief of Neurology Service, University of Antioquia

Honors

- 1997 Premio de Ciencias Exactas, Físicas y Naturales, 1997., Fundación Alejandro Ángel Escobar.
 1997 Medalla Francisco José de Caldas, en la categoría Oro, Universidad de Antioquia.
 2001 Premio AFIDRO A LA INVESTIGACION MÉDICA, Academia Nacional de Medicina.
 2002 Premio AVENTIS en la categoría Investigación Clínica, Academia Nacional de Medicina.
 2002 DISTINCIÓN PAUL HARRIS, Rotary International.
 2004 Premio a la Investigación profesoral. U de A.
 2007 SCOPUS AWARD. (Elsevier and Colciencias)
 2008 Award: Máxima distinción U de A. Medalla al mérito científico Francisco Antonio Zea, categoría Oro.
 2014 Premio de Ciencias Exactas, Físicas y Naturales, 2013. Fundación Alejandro Ángel Escobar
 2015 Award Alcaldía de Medellín categoría: Una Vida dedicada a la Investigación.

Other Experience

2010 - present PI of API COLOMBIA (with Dr. Eric Reiman and Pierre Tariot), Alzheimer's Prevention Initiative (API- Colombia)

2017- 2022: Longitudinal Pet –TAU in ADAD population (With Yakeel Qurios)

C. Contribution to Science

1. Identification and description of the World's largest Autosomal Dominant Alzheimer's disease Population.

With my team "The Neuroscience Group of the University of Antioquia", in Medellin, Colombia, South América, we have identified in the last 30 years, the largest population with familial alzheimer's disease (FAD) caused by the PSEN1 E280A mutation (mutación "paisa") and investigated the clinical and pathological characteristics of this form of FAD. We have had the opportunity to develop and study cognitive, imagenological, and biochemical biomarkers. We defined also the preclinical states of AD in this special population.

This exceptional population has provided the basis for the API clinical trial that will test a monoclonal anti-amyloid "crenezumab" (AC Immune/Genentech/Hoffman La-Roche) therapy aimed at controlling A β production or timely removal of excessive toxic A β peptide deposits.

- a. **Lopera F**, Ardilla A, Martinez A et al. Clinical features of early-onset Alzheimer disease in a large kindred with an E280A presenilin-1 mutation. JAMA. 1997;277(10):793-799.
- b. Acosta-Baena N, Sepulveda-Falla D, Lopera-Gómez CM, Jaramillo-Elorza MC, Moreno S, Aguirre-Acevedo DC, Saldarriaga A, **Lopera F**. Pre-dementia clinical stages in presenilin 1 E280A familial early-onset Alzheimer's disease: a retrospective cohort study. Lancet Neurol. 2011 Mar;10 (3):213-20. PMID: 21296022.
- c. Rosselli MC, Ardila AC, Moreno SC et al. And Lopera F. Cognitive decline in patients with familial Alzheimer's disease associated with E280a presenilin-1 mutation: a longitudinal study. J Clin Exp Neuropsychol. 2000;22(4):483-495.
- d. Lendon CL, Martinez A, Behrens IM et al. And Lopera F. E280A PS-1 mutation causes Alzheimer's disease but age of onset is not modified by ApoE alleles. Hum Mutat. 1997;10(3):186-195.

- e. Sepulveda-Falla D, Glatzel M, Lopera F. Phenotypic profile of early-onset familial Alzheimer's disease caused by presenilin-1 E280A mutation. *J Alzheimers Dis.* 2012;32(1):1-12. Review

2. Preclinical Biomarkers AD prevention therapies. In collaboration with Banner Alzheimer Institute in Phoenix, Arizona, we started our Colombia Alzheimer's Prevention Initiative (API- Colombia) including biomarker development and prevention trials in cognitively unimpaired persons who, based on their genetic background and age, are at the highest imminent risk of progression to the clinical stages of AD. In this collaboration we are evaluating biomarkers, anti-amyloid agents and amyloid hypothesis in unimpaired PSEN1 E280A mutation carriers launching a new era in AD prevention research.

a. **Association Between Amyloid and Tau Accumulation in Young Adults With Autosomal Dominant Alzheimer Disease.**

Quiroz YT, Sperling RA, Norton DJ, Baena A, Arboleda-Velasquez JF, Cosio D, Schultz A, Lapoint M, Guzman-Velez E, Miller JB, Kim LA, Chen K, Tariot PN, Lopera F, Reiman EM, Johnson KA.
JAMA Neurol. 2018 May 1;75(5):548-556. doi: 10.1001/jamaneurol.2017.4907.

b. **Dynamic Causal Modeling of Preclinical Autosomal-Dominant Alzheimer's Disease.**

Penny W, Iglesias-Fuster J, Quiroz YT, Lopera FJ, Bobes MA.
J Alzheimers Dis. 2018 Mar 16. doi: 10.3233/JAD-170405.

c. **Subjective memory complaints in preclinical autosomal dominant Alzheimer disease.**

Norton DJ, Amariglio R, Protas H, Chen K, Aguirre-Acevedo DC, Pulsifer B, Castrillon G, Tirado V, Munoz C, Tariot P, Langbaum JB, Reiman EM, Lopera F, Sperling RA, Quiroz YT.
Neurology. 2017 Oct 3;89(14):1464-1470. doi: 10.1212/WNL.0000000000004533. Epub 2017 Sep 6

d. **Brain Information Sharing During Visual Short-Term Memory Binding Yields a Memory Biomarker for Familial Alzheimer's Disease.**

Parra MA, Mikulan E, Trujillo N, Sala SD, Lopera F, Manes F, Starr J, Ibanez A.

- e. **Precuneus Failures in Subjects of the PSEN1 E280A Family at Risk of Developing Alzheimer's Disease Detected Using Quantitative Electroencephalography.**
Ochoa JF, Alonso JF, Duque JE, Tobón CA, Baena A, Lopera F, Mañanas MA, Hernández AM.
J Alzheimers Dis. 2017;58(4):1229-1244. doi: 10.3233/JAD-161291.
- f. Reiman EM, Quiroz YT, Fleisher AS, Chen K, Velez-Pardo C, Jimenez-Del-Rio M, Fagan AM, Shah AR, Alvarez S, Arbelaez A, Stern CE, Tirado V, Munoz C, Reiman RA, Huentelman MJ, Alexander GE, Langbaum JB, Kosik KS, Tariot PN, **Lopera F**. Brain imaging and fluid biomarker analysis in young adults at genetic risk for autosomal dominant Alzheimer's disease in the presenilin 1 E280A kindred: a case-control study. Lancet Neurol. 2012;11(12):1048-56.
- g. Fleisher AS, Chen K, Quiroz YT, Jakimovich LJ, Gutierrez Gomez M, Langois CM, Langbaum JB⁷, Roontiva A, Thiyyagura P, Lee W, Ayutyanont N, Lopez L, Moreno S, Munoz C, Tirado V, Acosta-Baena N, Fagan AM, Giraldo M, Garcia G, Huentelman MJ, Tariot PN, **Lopera F**, Reiman EM, Alzheimer's Prevention Initiative (2015). Relationships between biomarkers and age in the presenilin 1 E280A autosomal dominant Alzheimer's disease kindred: a cross-sectional study JAMA Neurol 72, 316-324 PMID: PMC4355261
- h. Langbaum JB, Fleisher AS, Chen K, Ayutyanont N, **Lopera F**, Quiroz YT, Caselli RJ, Tariot PN, Reiman EM (2013). Ushering in the study and treatment of preclinical Alzheimer's disease. Nat Rev Neurol. 9, 371-381. PMID: PMC4084675
- i. Cuetos F, Arango-Lasprilla JC, Uribe C, Valencia Claudia and Lopera Francisco. Linguistic changes in verbal expression: a preclinical marker of Alzheimer's disease. J Int Neuropsychol Soc. 2007;13(3):433-439.

3. Clinics and Genetics of Alzheimer's Disease and related Neurodegenerative diseases

We have studied clinics and genetics factors in neurodegenerative diseases and modifying factor of Onset of Alzheimer's disease in population with Autosomal dominant EOAD.

a. Genetic Ancestry and Susceptibility to Late-Onset Alzheimer Disease (LOAD) in the Admixed Colombian Population.

Moreno DJ, Pino S, Ríos Á, Lopera F, Ostos H, Via M, Bedoya G.
Alzheimer Dis Assoc Disord. 2017 Jul-Sep;31(3):225-231. doi:
10.1097/WAD.000000000000195

b. Kosik K, Muñoz C, Lopez L, Arcila M, García G, Madrigal L, Moreno S, Rios S, Lopez H, Gutierrez M, Langbaum J, Cho W, Suliman Sh, Tariot P, Ho C, Reiman E and **Lopera F**. Homozygosity of the Autosomal Dominant Alzheimer Disease Presenilin 1 E280A Mutation. *Neurology* 84, 2015

c. Vélez JI, Chandrasekharappa SC, Henao E, Martinez AF, Harper U, Jones M, Solomon BD, Lopez L, Garcia G, Aguirre-Acevedo DC, Acosta-Baena N, Correa JC, Lopera-Gómez CM, Jaramillo-Elorza MC, Rivera D, Kosik KS, Schork NJ, Swanson JM, **Lopera F**, Arcos-Burgos M. Pooling/bootstrap-based GWAS (pbGWAS) identifies new loci modifying the age of onset in PSEN1 p.Glu280Ala Alzheimer's disease. *Mol Psychiatry*. 2013;18(5):568-75.

d. Lalli MA, Garcia G, Madrigal L, Arcos-Burgos M, Arcila ML, Kosik KS, **Lopera F**. Exploratory data from complete genomes of familial alzheimer disease age-at-onset outliers. *Human mutation*. 07/2012. PMID: 22829467.

e. Parkinson's disease compromises the appraisal of action meanings evoked by naturalistic texts.

García AM, Bocanegra Y, Herrera E, Moreno L, Carmona J, Baena A, Lopera F, Pineda D, Melloni M, Legaz A, Muñoz E, Sedeño L, Baez S, Ibáñez A.
Cortex. 2018 Mar;100:111-126. doi: 10.1016/j.cortex.2017.07.003. Epub 2017 Jul 17.

f. **Variable frequency of LRRK2 variants in the Latin American research consortium on the genetics of Parkinson's disease (LARGE-PD), a case of ancestry.**

Cornejo-Olivas M, Torres L, Velit-Salazar MR, Inca-Martinez M, Mazzetti P, Cosentino C, Micheli F, Perandonos C, Dieguez E, Raggio V, Tumas V, Borges V, Ferraz HB, Rieder CRM, Shumacher-Schuh A, Velez-Pardo C, Jimenez-Del-Rio M, Lopera F, Chang-Castello J, Andreé-Munoz B, Waldherr S, Yearout D, Zabetian CP, Mata IF.
NPJ Parkinsons Dis. 2018 Jan 19;4:3. doi: 10.1038/s41531-017-0025-1. eCollection 2018.

4. Clinical and Genetics studies about Attention Deficit Hiperactivity Disorder (ADHD)

We have identified and studied several families with familial ADHD and we reported genetics factors giving succceptibility for this neurodevelopmental disorder.

- g. Arcos-Burgos M, Londoño AC, Pineda DA, Lopera F, Palacio JD, Arbelaez A, Acosta MT, Vélez JI, Castellanos FX, Maximilian Muenke. Analysis of brain metabolism by proton magnetic resonance spectroscopy ((1)H-MRS) in attention-deficit/hyperactivity disorder suggests a generalized differential ontogenic pattern from controls. Attention deficit and hyperactivity disorders. 07/2012. PMCID: 23012086.
- h. Arcos-Burgos M, Jain M, Acosta MT, Shively S, Stanescu H, Wallis D, Domené S, Vélez JI, Karkera JD, Balog J, Berg K, Kleta R, Gahl WA, Roessler E, Long R, Lie J, Pineda D, Londoño AC, Palacio JD, Arbelaez A, **Lopera F**, Elia J, Hakonarson H, Johansson S, Knappskog PM, Haavik J, Ribases M, Cormand B, Bayes M, Casas M, Ramos-Quiroga JA, Hervas A, Maher BS, Faraone SV, Seitz C, Freitag CM, Palmason H, Meyer J, Romanos M, Walitza S, Hemminger U, Warnke A, Romanos J, Renner T, Jacob C, Lesch KP, Swanson J, Vortmeyer A, Bailey-Wilson JE, Castellanos FX, Muenke M. A common variant of the latrophilin 3 gene, LPHN3, confers susceptibility to ADHD and predicts effectiveness of stimulant medication. Mol Psychiatry. 2010 Nov;15(11):1053-66. PMCID: 20157310.

Complete List of Published Work in MyBibliography:

https://www.researchgate.net/profile/Francisco_Lopera/contributions