



For the **Stepwise Functional Connectivity** method see *J Neurosci* 2012; **32**: 10649–61

For more about the **Stepwise Functional Connectivity analysis** see [http://gordon.mgh.harvard.edu/sepulcre\\_lab/research.html](http://gordon.mgh.harvard.edu/sepulcre_lab/research.html)

## Lifeline

**Jorge Sepulcre** is an Associate Professor and Lab Director at the Gordon Center for Medical Imaging, Massachusetts General Hospital, and Harvard Medical School (Boston, MA, USA). Currently, he studies the vulnerability of brain networks to Alzheimer's disease pathology through nuclear and molecular neuroimaging, graph-theory, and other analytical methods.

### What has been the greatest achievement of your career?

My work, in close collaboration with my team, is truly a privilege. Our achievements come from an environment of creativity and enjoyment, which, in my opinion, is what is needed to develop innovative methods and investigate properties of the brain networks. I am particularly pleased with the Stepwise Functional Connectivity analysis I developed that allowed us to uncover how the multisensory and sensory-motor systems integrate in the human brain, and also helped us to understand how amyloid and tau interact in large-scale brain circuits in patients with neurodegenerative diseases.

### What inspires you?

My inspiration comes from my desire to observe a new phenomenon and promote its discovery, and to contemplate its beauty. Then, if that finding can help improve other people's lives, that's priceless.

### If you had not entered your current profession, what would you have liked to do?

I have always loved nature, so probably it would have been something related to biology, ethology, or wildlife preservation.

### What do you think is the most neglected field of science or medicine at the moment?

We neuroscientists tend to frequently forget the big questions that brought us to science. We end up devoting our time trying to solve small problems that do not lead to big advances. This is not exactly a neglected field but a common practice that we all do—this, in my opinion, diminishes our abilities to solve real problems.

### What is your favorite book or film, and why?

I do not have a favorite book, but I enjoy reading essays from philosophers such as Martin Buber or Miguel de Unamuno, or the drama work of Federico García Lorca.

### How do you relax?

My perfect relaxing day includes playing basketball with my son, or spending time outdoors with my family.

### How would you improve the public's understanding of research?

I think we have to build strong and scientifically involved communities that actively ask about what we do. Disease-related associations are a good example, but ideally, other groups that are not necessarily associated with medicine should interrogate our science in the public domain.

## Focal Point

### Tuberculous meningitis and hydrocephalus in Filippino de' Medici

Filippino was the son of Francesco I de' Medici and Giovanna d'Austria, Grand Duke and Grand Duchess of Tuscany. He was born on May 20, 1577, and died aged 5 years on March 29, 1582.<sup>1</sup> He had several low-grade feverish episodes on Feb 6, 1582 and on March 13, before his condition worsened abruptly on March 27.<sup>1</sup> Court physicians withdrew 5 ounces of blood to cure the shaking fever and lethargy but, after 17 days of alternating fever, drowsiness, and convulsions, he lost consciousness. Death occurred about 10 hours later.<sup>1</sup>

At the original autopsy in 1582, the fluid equivalent of "a glass of water" was found between the meninges and the brain. Hardening (fibrosis) of the lungs in several different areas, a discoloured and "cork-like" liver, and diffuse anaemia were also noted.<sup>1</sup> Filippino's remains were exhumed by researchers in 2004, and diagnosis of rickets, including hydrocephalus, was formulated at that time.<sup>2</sup>

Based on the 16th century autopsy report<sup>1</sup> and on the presence of a hyper-vascularisation and new bone formation on the inner cranial table (near to the superior sagittal sinus),<sup>2</sup> which are consistent with abnormal inflammation, we propose that chronic meningitis due to miliary tuberculosis<sup>3,4</sup> was the most likely cause of the hydrocephalus and Filippino's death.

Children under 5 years of age who have miliary tuberculosis are more likely to develop life-threatening meningeal tuberculosis.<sup>4</sup> Filippino had a vitamin D deficit as a toddler because he was breastfed even after the age of two years,<sup>2</sup> and medical accounts from March 27, 1582 further report that he was affected by a parasitic intestinal worm infestation.<sup>1</sup> Together, the vitamin deficiency and parasite infection might have led to an impaired immune response, and possibly increased the risk for miliary tuberculosis in this child.

*Raffaella Bianucci, Philippe Charlier, Antonio Perciaccante, Otto Appenzeller, Donatella Lippi*

- 1 Pieraccini G. La stirpe dei Medici di Cafaggiolo. Firenze: Nardini Editore, 1986, pp 258–61.
- 2 Castagna M, Giuffra V, Fattori S, et al. (2015). Rickets at the Medici Court of Florence: The Case of Don Filippino (1577–1582). *Medicina Secoli* 2014; **26**: 779–92.
- 3 Principi N, Esposito S. Diagnosis and therapy of tuberculous meningitis in children. *Tuberculosis (Edinb)* 2012; **92**: 377–83.
- 4 Sharma Sk, Mohan A, Sharma A, Mitra DK. Miliary tuberculosis: new insights into an old disease. *Lancet Infect Dis* 2005; **5**: 415–30.