

Seminario: **Plasticidad en el centro de la excitabilidad neuronal -el segmento inicial axonal- en isquemia cerebral.**

Resumen: En ocasiones, la degeneración de algunas neuronas puede causar daño al tejido nervioso que las rodea. Un ejemplo de este problema son los eventos subsiguientes a una isquemia cerebral. La sobreexcitación de un circuito por una entrada excesiva de Ca^{2+} en los terminales sinápticos puede causar muerte neuronal y alteraciones en los alrededores del circuito. Las neuronas que pierden el control sobre su excitabilidad son, por tanto, potencialmente peligrosas para un tejido. El segmento inicial del axón es una de las regiones críticas en el control de la excitabilidad neuronal porque es el lugar donde se limita el umbral de disparo de las señales eléctricas de las neuronas.

En células granulares del hipocampo, la excesiva actividad produce daños en el hipocampo en isquemia y en epilepsia. Hemos encontrado que el segmento inicial axonal de estas células, ante situaciones de anoxia, puede dismantelar algunas de sus proteínas básicas para volver a insertarlas tras un periodo de recuperación. Al hacer esto, las neuronas reducen su excitabilidad y evitan el daño a su alrededor.

El mecanismo subyacente a este fenómeno incluye una entrada de Ca^{2+} específica del segmento inicial, a través de un intercambiador $\text{Na}^+/\text{Ca}^{2+}$ (NCX). Cuando el intercambiador se bloquea específicamente, el segmento inicial de las células granulares no se dismantela, la excitabilidad no se reduce, y ocurre más muerte celular en las células diana.

Nuestros datos proponen por tanto un mecanismo drástico de plasticidad axonal orientado a proteger el tejido nervioso de su propia actividad en condiciones de shock metabólico.

PERSONAL INFORMATION

NAME: Ricardo
SURNAME: Scott
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DATE OF BIRTH: December 15th, 1970
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- **CURRENT POSITIONS:**

- Lecturer on Master of Neuropsychology at UNIR University (PART TIME)
- International Baccalaureate Examiner (PART TIME)
- Biology Teacher at El Valle School in Alicante. LOMCE and International Baccalaureate (PART TIME)

- **KEY WORDS:**

Research, Neuroscience, Education, Biochemistry, Neuropsychology, Creativity

ACADEMIC TRAINNING

- PhD in Medicine and Surgery (Neurociences) Universidad Autónoma de Madrid, Abril 2001.
- Master Thesis in Brain Metabolism. Instituto de Investigaciones Biomédicas de Madrid, Dec 1996
- Degree in Biological Sciences (Molecular Biology and Biochemistry). Universidad Autónoma de Madrid, 1995
- Psychology subjects (1st and 4th course) at UNED (2003-2016)

RESEARCH EXPERIENCE

<i>DATE</i>	<i>WORK</i>	<i>INSTITUTION</i>
Dec 09-May 2015	Ramón y Cajal Researcher I3 Program Excellence	Instituto de Neurociencias UMH-CSIC, Alicante
Jan 03 Oct 08	Senior Research Fellow Wellcome Trust. UK	Institute of Neurology University College London (Dmitri Rusakov's Lab)
Jul 01-Dec 03	Postdoctoral Research Fellow. Marie Curie Research Training Network	Institute of Neurology University College London (Dimitri Kullmann's Lab)
Mar 97-Jul 01	PhD in Medicine and Surgery (April 23 rd , 2001)	School of Medicine Universidad Autonoma de Madrid

TEACHING EXPERIENCE

- Contratado Doctor Certificate for Teaching (ANECA)
- Biology Teacher at El Valle School (International Baccalaurate and Bachillerato LOMCE) (October 2016-Present)
- International Baccalaurate Examiner (Jan 2016-present)
- Associate Professor at UNIR University (Master of Neuropsychology in Education, Scientific advisor for student's Final Research Work) (June 2016-present)
- Expert in Educational Technology Innovation, Universidad Miguel Hernández, Alicante, Spain (2015, one year)
- Lecturer at the Master "Neurociencias: de la investigación a la clínica" (PhD program) at the Instituto de Neurociencias in Alicante (2012-2015)
- Teacher for National Biology Olympics winners, one-day visits at the Instituto de Neurociencias (2012-2014)

- Street Science event Teacher in Alicante, 2012
- Teacher for one-day visits at the Instituto de Neurociencias for several primary Schools (2010-2015)
- Invited lecturer at School of Medicine, Universidad Castilla-La Mancha, Albacete, Spain. "Signaling and cell death". 1st course of Medicine degree (1 intensive month, 2006)
- Invited lecturer at School of Medicine, Universidad Castilla-La Mancha, Albacete, Spain. "Clinical aspects of Epilepsy". Lecture for Medicine students (1st-5th courses) (2006)
- Doctorate Courses in Neuroscience Program at the Instituto de Investigaciones Biomédicas, Madrid. Practical course in Nuclear Magnetic Resonance. (1995)
- Secondary School Teacher in Science. Colegio Monfort, Madrid (1994-95)

PUBLICATIONS

- **Scott RS**, Sánchez-Aguilera A, van Elst K, Lim L, Dehorter N, Eun Bae Sung, Bartolini G, Peles E, Kas M, Bruining H, and Marín O. Loss of Cntnap2 causes generalized axonal excitability deficits, developmental delay in cortical myelination, and abnormal stereotyped motor behavior. *Cerebral Cortex*, Dec. 28th, (2017)
- **Scott RS***, Henneberger CH, Padmashri R, Anders S, Rusakov DA. Neurons adapt to excitatory input by rapidly altering the preferred site of axonal spike initiation. *Nat Commun*. May 23;5:3817 (2014)
* *Corresponding author*
- Chacón MR, Navarro AI, Cuesto G, del Pino I, **Scott RS**, Morales M, Rico B Focal Adhesion Kinase regulates actin nucleation during neuronal filopodia formation. *Development*. Sep;139(17):3200-10. (2012)
- **Scott RS**, Bustillo D, Olivos-Oré LA, Cuchillo-Ibañez I, Barahona MV, Carbone E, Artalejo AR. Contribution of BK channels to action potential repolarisation at minimal cytosolic Ca²⁺ concentration in chromaffin cells. *Pflugers Arch*. Oct;462(4):545-57 (2011)

- Karayannis T, Elfant D, Huerta-Ocampo I, Teki, S, **Scott RS**, Rusakov DA, Jones MV and Capogna M. Slow GABA Transient and Receptor Desensitization Shape Synaptic Responses Evoked by Hippocampal Neurogliaform Cells. *The Journal of Neuroscience*, 30(29):9898-909 (2010)
- Ruiz A, *Campanac E, ***Scott RS**, Rusakov DA, Kullmann DM. GABAA receptors enhance glutamatergic transmission and facilitate LTP induction at hippocampal mossy fiber synapses. *Nature Neuroscience*, 13(4):431-8. (2010)
 - * *Equal contribution.*
 - ** *Article recommended in Faculty of 1000 Biology Reports, 18th August 2010*
- **Scott R***. Lalic T, Kullmann DM, Capogna M, Rusakov DA. Synapse-specific coupling of kainate autoreceptors and Ca²⁺ stores in hippocampal mossy fibers. *The Journal of Neurosci* 28(49), (2008)
 - * *Corresponding author*
- **Scott R**, Rusakov DA. Ca²⁺-stores and use-dependent facilitation of presynaptic Ca²⁺ signaling *PNAS* 105(45), (2008) ([Comment](#))
- **Scott R***. Ruiz A, Kullmann DM, Rusakov DA. Analog modulation of mossy fiber transmission on hippocampal CA3 cells is uncoupled from presynaptic Ca²⁺. *The Journal of Neuroscience* 28(30), (2008)
 - **Corresponding author*
- Price CJ*, **Scott R***, Rusakov DA, Capogna M. GABAB receptor modulation of feed-forward inhibition through hippocampal neurogliaform cells. *The Journal of Neuroscience*, 28(27):6974–6982. (2008)
 - **Equal contribution.*
 - ** *Editor's choice in Science 18th July vol. 321 (2008)*
- **Scott R**. "Use dependent control of presynaptic Ca²⁺ signalling at individual central synapses" *J Anat.* 210(6):642-50. (2007) (Review)
- **Scott R**, Dmitri Rusakov. Principal determinants of activity-dependent presynaptic Ca²⁺ dynamics at individual mossy fiber – CA3 pyramidal cell synapses. *The Journal of Neuroscience* 26(26):7071-81. (2006)
- Kullmann DM, Ruiz, A. Rusakov, DA, **Scott R**, Semyanov A., and Walker M. Presynaptic, extrasynaptic and axonal GABA_A receptors in the CNS: where and

why? *Progress in biophysics and molecular biology* 87(1): 33-46 (2005)
(Review)

- Ruiz A, Fabian-Fine A., **Scott R**, Walker M, Rusakov DA, Kullmann DM. Presynaptic GABA_A receptors modulate axonal excitability and synaptic transmission in the brain. *Neuron* 39(6): 961-73. (2003)
- Ulate G, **Scott R.**, Gilabert JA, Artalejo AR. Purinergic modulation of Ca²⁺ channels and exocytosis in bovine chromaffin cells. *Drug Development Research* 52: 89-94 (2001) (Review)
- Ulate G, **Scott R**, González J, Gilabert JA, Artalejo AR. Extracellular ATP regulates exocytosis by inhibiting multiple Ca²⁺ channel types in bovine chromaffin cells. *Pflügers Arch* 439: 304-314 (2000)
- **Scott R**, Kiessling K, Parekh AB. An examination for the role of intracellular ATP in the activation of store operated calcium influx and Ca²⁺-dependent-capacitance increase in rat basophilic leukemia cells. *Pflügers Arch.* 436: 928-933 (1998)
- Cruz F, **Scott R**, Barroso I, Santisteban P, Cerdán S. Ontogeny and cellular localization of the pyruvate recycling system in rat brain. *J. Neurochem.* 70: 2613-19 (1998)

NEAR SUBMISSION

- Serra C, Ayuso I, Henneberger C, Rangunathan P, Rusakov DA, Alcázar A, **Scott RS**. Fast, reversible and neuroprotective axon initial segment disassembly after brief ischemia.

GRANTS

Simons Foundation for Autism (SFARI Annual RFA)

TITLE: Role of Caspr2 (CNTNAP2) in brain circuits (exon 22 mice)
REFERENCE: 260225
FUNDING: 240.000€

PI: Elior Peles (RScott, participant)

PARTICIPANTS: 6

DATES: 3 years. Ending in Aug 2015

Spanish Ministerio de Ciencia e Innovación (MICINN)

TITLE: Plasticity of intrinsic excitability mediated by local Ca²⁺ signalling at the axonal initial segment of excitatory neurons.

REFERENCE: SAF2010-20604

FUNDING: 140.000€

PI: R. Scott

PARTICIPANTS: 6

DATES: 3 years. Ending in Jan 2014. Extended 1 year.

Spanish Ministerio de Ciencia e Innovación (MICINN)

TITLE: Analog neurotransmitter release in mammal brain

REFERENCE: RYC-2009-03979

FUNDING: 15.000€

PI: R. Scott

PARTICIPANTS: 1

DATES: 2 years. Ending in Jan 2012

Medical Research Council

TITLE: Probing presynaptic receptors with two-photon uncaging, two-photon Ca²⁺ imaging and two-photon photobleaching

REFERENCE: G0500871

FUNDING: £440.000

PI: Dmitri Rusakov (R.Scott grant co-holder)

PARTICIPANTS: 4 (including Peter Somogyi and Marco Capogna)

DATES: 3 years. Ended in Oct 2009

SELECTED MEETINGS

- Carol Serra, , Christian Henneberger, Ragunathan Padmashri Dmitri Rusakov, Alberto Alcázar **R. Scott**,. Fast and reversible axon initial segment disassembly triggered by Na⁺/Ca²⁺ exchanger after brief ischemia. *9th FENS Forum Neuroscience, Milan, Italy, 2014*
- **R. Scott**, G- Bartolini, J. Brotons, K. van Elst, E. Peles, E. Poliak, M. Kas, H. Bruining, O Marin. Long range communication defects in caspr2 (cntnap2) Mutant mice. *9th FENS Forum Neuroscience, Milan, Italy, 2014*
- **R. Scott**. Contribution of BK channels to action potential repolarization at minimal cytosolic Ca²⁺ concentration in chromaffin cells. *8th IBRO World Congress of Neuroscience, Florence, Italy, 2011*
- **R. Scott** & D. Rusakov. Cell target specific presynaptic actions of kainate receptors at individual mossy fibre synapses
European Neuroscience Institute, Seville, 2006
- **R. Scott**, T. Lalic, M. Capogna, D.M. Kullmann, D. Rusakov. Cell target specific presynaptic actions of kainate receptors at individual mossy fibre synapses.
Physiological society, London, 2006
- **R. Scott**, D. Rusakov. Presynaptic Ca²⁺ signalling at individual mossy fibre synapses. *35th Society for Neuroscience. Washington DC, 2005*

INVITED TALKS

- Axonal conduction defects in autistic-like caspr2 KO mice. Utrecht Braincenter. Holland. 2014.
- Firing control by Na⁺/Ca²⁺ exchange at the spike initiation site. Institute of Cellular Neurosciences. University of Bonn, Germany, 2012
- Axonal information processing. Pharmacology Department, *St Georges University, London, UK, 2009*
- Axonal information processing. *Institut d'Investigacions Biomèdiques de Barcelona, 2009*

- Axonal information processing. *Instituto de Neurociencias UMH-CSIC, St Joan d'Alacant, Spain, 2009*
- Use-dependent control of presynaptic calcium signalling at individual central synapses The role of Calcium in analogue coding, *Universidad de Cádiz, Spain, 2007*
- “Use dependent control of presynaptic Ca²⁺ signalling at individual central synapses” Living cell imaging of Neuronal and glial signalling. *University of Portsmouth, England, 2006*
- “Presynaptic Ca²⁺ signalling at individual mossy fibre synapses” *RIKEN Brain Science Institute, Japan. 2005*
- “Combining multiphoton microscopy with electrophysiology in slice preparations” Calcium channels and disease. *European Research Training Network. Lund, 2004*

AWARDS

- Third best poster XXII congress of the Spanish Society for Physiological Sciences. Joint meeting with the Physiological Society. Tenerife, 2003. R. Scott, DA. Rusakov, DM. Kullmann. Modulation of action potential-dependent Ca²⁺ transients in hippocampal mossy fibres by granule cell membrane potential and ionotropic GABA receptors.
- Third Price Biological Cell Imaging International Competition 2014 (Scientifica Ltd)
- Second Price for the Educational project “Teatro Creativo en Inglés”. Award Matías Terol 2015.