ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Neuroscience, Erasmus MC, Rotterdam
Project Title:	Neuronal mechanisms underlying adaptation of locomotion in health and disease
Abstract:	As we walk, we continuously adapt our movements to changes in the environment, such as a moving underground or obstacles in the way. Such adaptations involve integration of all limbs and depend critically on the cerebellum. We have developed an automated test for locomotion adaptation in mice: the Erasmus Ladder. The Erasmus Ladder provides a detailed description of the temporal and spatial aspects of locomotion performance and adaptation and we have successfully tested a range of mutant mice with this test. Using the Erasmus Ladder we can introduce obstacles at fixed time intervals to a conditioning stimulus, such as a tone, and even detect subtle changes in movement adaptation patterns that would not be noticed using more classical paradigms. To further our understanding of cerebellar control of locomotion adaptation we propose to combine the Erasmus Ladder test with real time recordings of neuronal activity of different locomotion areas in the cerebellum of specific mutant mouse lines. Based on these findings, we will rescue specific ataxic and dystonic phenotypes using optogenetic stimulation of the cerebellum and/or connected brain regions. A proper understanding of what happens in healthy and diseased mutant brains during locomotion will help us to optimize diagnosis and eventually develop treatment for patients suffering from ataxia.
Requirements of candidate:	Background: We expect you to be motivated to study cerebellar networks. You are creative and intelligent and you are not afraid to try something new. Ideally, you have experience with imaging, animal behavior and/or computer programming. Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*

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Supervisor information:	Prof. dr. C.I. De Zeeuw c.dezeeuw@erasmusmc.nl www.neuro.nl **Selection of recent publications** Badura A, Schonewille M, Voges K, Galliano E, Renier N, Gao Z, Witter L, Hoebeek FE, Chedotal A, De Zeeuw CI (2013) Climbing fiber input shapes reciprocity of Purkinje cell firing. Neuron Baudouin SJ, Gaudias J, Gerharz S, Hatstatt L, Zhou K, Punnakkal P, Tanaka KF, Spooren W, Hen R, De Zeeuw CI, Vogt K, Scheiffele P (2012) Shared synaptic pathophysiology in syndromic and nonsyndromic rodent models of autism. Science Boele HJ, Koekkoek SK, De Zeeuw CI, Ruigrok TJ (2013) Axonal sprouting and formation of terminals in the adult cerebellum during associative motor learning. J Neurosci Clopath C, Badura A, De Zeeuw CI, Brunel N (2014) A cerebellar learning model of vestibulo-ocular reflex adaptation in wild-type and mutant mice. J Neurosci De Gruijl JR, Hoogland TM, De Zeeuw CI (2014a) Behavioral correlates of complex spike synchrony in cerebellar microzones. J Neurosci De Gruijl JR, Sokol PA, Negrello M, De Zeeuw CI (2014b) Modulation of electrotonic coupling in the inferior olive by inhibitory and excitatory inputs: integration in the glomerulus. Neuron Galliano E, Potters JW, Elgersma Y, Wisden W, Kushner SA, De Zeeuw CI, Hoebeek FE (2013a) Synaptic transmission and plasticity at inputs to murine cerebellar Purkinje cells are largely dispensable for standard nonmotor tasks. J Neurosci Galliano E, Gao Z, Schonewille M, Todorov B, Simons E, Pop AS, D'Angelo E, van den Maagdenberg AM, Hoebeek FE, De Zeeuw CI (2013b) Silencing the majority of cerebellar granule cells uncovers their essential role in motor learning and consolidation. Cell Reports. Gao Z, van Beugen BJ, De Zeeuw CI (2012a) Distributed synergistic plasticity and cerebellar learning. Nature Reviews Neurosci Gao Z, Todorov B, Barrett CF, van Dorp S, Ferrari MD, van den Maagdenberg AM, De Zeeuw CI, Hoebeek FE (2012b) Cerebellar ataxia by enhanced Ca(V)2.1 currents is alleviated by Ca2+-dependent K+-channel activators in Cacna1a(S218L) mutant mice. J Neurosci Gutierrez-Castellanos N, Winkelman BH, Tolosa-Rodriguez L, Devenney B, Reeves RH, De Zeeuw CI (2013) Size does not always matter: Ts65Dn Down syndrome mice show cerebellum-dependent motor learning deficits that cannot be rescued by postnatal SAG treatment. J Neurosci Heck DH, De Zeeuw CI, Jaeger D, Khodakhah K, Person AL (2013) The neuronal code(s) of the cerebellum. J Neurosci Jaarsma D, van den Berg R, Wulf PS, van Erp S, Keijzer N, Schlager MA, de Graaff E, De Zeeuw CI, Pasterkamp RJ, Akhmanova A, Hoogenraad CC (2014) A role for Bicaudal-D2 in radial cerebellar granule cell migration. Nature Comm Ly R, Bouvier G, Schonewille M, Arabo A, Rondi-Reig L, Lena C, Casado M, De Zeeuw CI, Feltz A (2013) T-type channel blockade impairs long-term

potentiation at the parallel fiber-Purkinje cell synapse and cerebellar learning. PNAS

Rahmati N, Owens CB, Bosman LW, Spanke JK, Lindeman S, Gong W, Potters JW, Romano V, Voges K, Moscato L, Koekkoek SK, Negrello M, De Zeeuw CI (2014) Cerebellar potentiation and learning a whisker-based object localization task with a time response window. J Neurosci

Raike RS, Weisz C, Hoebeek FE, Terzi MC, De Zeeuw CI, van den Maagdenberg AM, Jinnah HA, Hess EJ (2013) Stress, caffeine and ethanol trigger transient neurological dysfunction through shared mechanisms in a mouse calcium channelopathy. Neurobiol of Disease

Saab AS, Neumeyer A, Jahn HM, Cupido A, Simek AA, Boele HJ, Scheller A, Le Meur K, Gotz M, Monyer H, Sprengel R, Rubio ME, Deitmer JW, De Zeeuw CI, Kirchhoff F (2012) Bergmann glial AMPA receptors are required for fine motor coordination. Science

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Schonewille M, Gao Z, Boele HJ, Veloz MF, Amerika WE, Simek AA, De Jeu MT, Steinberg JP, Takamiya K, Hoebeek FE, Linden DJ, Huganir RL, De Zeeuw CI (2011) Reevaluating the role of LTD in cerebellar motor learning. Neuron

Seja P, Schonewille M, Spitzmaul G, Badura A, Klein I, Rudhard Y, Wisden W, Hubner CA, De Zeeuw CI, Jentsch TJ (2012) Raising cytosolic Cl- in cerebellar granule cells affects their excitability and vestibulo-ocular learning. EMBO J

Sepulveda-Falla D, Barrera-Ocampo A, Hagel C, Korwitz A, Vinueza-Veloz MF, Zhou K, Schonewille M, Zhou H, Velazquez-Perez L, Rodriguez-Labrada R, Villegas A, Ferrer I, Lopera F, Langer T, De Zeeuw CI, Glatzel M (2014) Familial Alzheimer's disease-associated presenilin-1 alters cerebellar activity and calcium homeostasis. J Clin Invest

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van Dorp S, De Zeeuw CI (2014) Variable timing of synaptic transmission in cerebellar unipolar brush cells. PNAS

van Versendaal D, Rajendran R, Saiepour MH, Klooster J, Smit-Rigter L, Sommeijer JP, De Zeeuw CI, Hofer SB, Heimel JA, Levelt CN (2012) Elimination of inhibitory synapses is a major component of adult ocular dominance plasticity. Neuron

Zariwala HA, Borghuis BG, Hoogland TM, Madisen L, Tian L, De Zeeuw CI, Zeng H, Looger LL, Svoboda K, Chen TW (2012) A Cre-dependent GCaMP3 reporter mouse for neuronal imaging in vivo. J Neurosci

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