R

References

[1] P. Kwan, S. C. Schachter, and M. J. Brodie, "Drug-Resistant Epilepsy," *N. Engl. J. Med.,* vol. 365, pp. 919-926, 2011.

[2] E. H. Reynolds and J. V. Kinnier Wilson, "Psychoses of epilepsy in Babylon: the oldest account of the disorder," *Epilepsia,* vol. 49, pp. 1488-1490, 2008.

[3] H. Cushing, "A note upon the faradic stimulation of the postcentral gyrus in conscious patients," *Brain,* vol. 32, pp. 44-53, 1909a.

[4] J. Hughlings Jackson, "Note on the comparison and contrast of regional palsy and spasm," *Lancet,* pp. 295-297, 1867.

[5] J. Hughlings Jackson, "Remarks on the disorderly movements of chorea and convulsion," *Med Times Gazette,* vol. ii, pp. 642-643, 1867.

[6] J. Hughlings Jackson, "A study of convulsions," *Trans St Andrews Med Grad Assoc,* vol. 3, pp. 162-204, 1870.

[7] J. Hughlings Jackson, "On the anatomical, physiological, and pathological investigation of epilepsies. A study of convulsions.," *West Riding Lunatic Asylum Med Reports,* vol. 3, pp. 315-319, 1873.

[8] V. Horsley, "The function of the so-called motor area of the brain," *British Medical Journal,* vol. 11, pp. 125-132, 1909.

[9] E. A. Spiegel, H. T. Wycis, M. Marks, and A. J. Lee, "Stereotaxic apparatus for operations on the human brain," *Science,* vol. 106, pp. 349-350, 1947.

[10] D. E. Sheer, *Electrical stimulation of the brain. An interdisciplinary survey of Neurobehavioral integrative systems*. Austin, Texas: University of Texas Press, 1961.

[11] I. S. Cooper, A. R. Upton, and I. Amin, "Reversibility of chronic neurologic deficits. Some effects of electrical stimulation of the thalamus and internal capsule in man," *Applied neurophysiology,* vol. 43, pp. 244-258, 1980.

[12] M. Šramka, G. Fritz, M. Galanda, and P. Nádvorník, "Some observations in treatment stimulation of epilepsy," *Acta Neurochir. (Wien),* vol. 23 (Suppl), pp. 257-262, 1976.

[13] A. R. Upton, I. S. Cooper, M. Springman, and I. Amin, "Suppression of seizures and psychosis of limbic system origin by chronic stimulation of anterior nucleus of the thalamus," *International journal of neurology,* vol. 19-20, pp. 223-230, 1986.

[14] E. B. Geller, T. L. Skarpaas, R. E. Gross, R. Goodman, G. Barkley, C. Bazil, *et al.*, "Brain-responsive neurostimulation in patients with medically intractable mesial temporal lobe epilepsy," *Epilepsia,* vol. 58, pp. 994-1004, 2017.

[15] V. Salanova, T. Witt, R. Worth, T. R. Henry, R. E. Gross, J. M. Nazzaro, *et al.*, "Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy," *Neurology,* vol. 84, pp. 1017-1025, 2015.

[16] G. Buszaki, *Rhytms of the Brain*. New York: Oxford University Press, 2006.

[17] H. Berger, "Uber das Elektrenkephalogramm des Menschen," *Archiv fur Psychiatrie und Nervenkrankheiten,* vol. 87, pp. 527-570, 1929.

[18] D. Contreras and M. Steriade, "Cellular basis of EEG slow rhythms: a study of dynamic corticothalamic relationships," *Journal of Neuroscience,* vol. 15, pp. 604-622, 1995.

[19] S. Diekelmann and J. Born, "The memory function of sleep," *Nature Reviews Neuroscience,* vol. 11, 2010.

[20] M. A. Busche, M. Kekus, H. Adelsberger, T. Noda, H. Forstl, I. Nelken, *et al.*, "Rescue of long-range circuit dysfunction in Alzheimer's disease models," *Nature Neuroscience,* vol. 18, pp. 1623-1630, 2015.

[21] L. I. Schmitt, R. D. Wimmer, R. Nakajima, M. Happ, S. Mofakham, and M. M. Halassa, "Thalamic amplification of cortical connectivity sustains attentional control," *Nature,* vol. 545, pp. 219-223, 2017.

[22] M. F. Wells, R. D. Wimmer, L. I. Schmitt, G. Feng, and M. M. Halassa, "Thalamic reticular impairment underlies attention deficit in Ptchd1(Y/-) mice," *Nature,* vol. 532, pp. 58-63, 2016.

[23] R. D. Wimmer, L. I. Schmitt, T. J. Davidson, R. Nakajima, K. Deisseroth, and M. M. Halassa, "Thalamic control of sensory selection in divided attention," *Nature,* vol. 526, pp. 705-709, 2015.

[24] D. Williams, "A study of thalamic and cortical rhythms in petit mal," *Brain,* vol. 76, pp. 50-69, 1953.

[25] P. Andersen, S. A. Andersson, and T. Lomo, "Nature of thalamo-cortical relations during spontaneous barbiturate spindle activity," *Journal of Physiology,* vol. 192, pp. 283-307, 1967.

[26] T. Bal, "Synaptic and membrane mechanisms underlying synchronized oscillkations in the ferret lateral geniculate nucleus *in vitro*," *Journal of Physiology,* vol. 483, pp. 641-663, 1995.

[27] J. Gotman, "Interhemispheric relations during bilateral spike-and-wave activity," *Epilepsia,* vol. 22, pp. 453-466, 1981.

[28] M. Steriade and R. R. Llinás, "The functional states of the thalamus and the associated neuronal interplay," *Physiological Reviews,* vol. 68, pp. 649-742, 1988.

[29] M. von Krosigk, T. Bal, and D. A. McCormick, "Cellular mechanisms of a synchronized oscillation in the thalamus," *Science,* vol. 261, pp. 361-364, 1993.

[30] J. R. Huguenard and D. A. Prince, "Intrathalamic rhytmicity studied in vitro: nominal T-current modulation causes robust antioscillatory effects," *Journal of Neuroscience,* vol. 14, pp. 5485-5502, 1994.

[31] U. Kim, M. V. Sanchez-Vives, and D. A. McCormick, "Functional dynamics of GABAergic inhibition in the thalamus," *Science,* vol. 278, pp. 130-134, 1997.

[32] M. V. Sanchez-Vives and D. A. McCormick, "Functional properties of perigeniculate inhibition of dorsal lateral geniculate nucleus thalamocortical neurons in vitro," *Journal of Neuroscience,* vol. 17, pp. 8880-8893, 1997.

[33] H. K. Meeren, J. P. Pijn, E. L. Van Luijtelaar, A. M. Coenen, and F. H. Lopes da Silva, "Cortical focus drives widespread corticothalamic networks during spontaneous absence seizures in rats," *J. Neurosci.,* vol. 22, pp. 1480-1495, 2002.

[34] P. O. Polack, I. Guillemain, E. Hu, A. Depaulis, and S. Charpier, "Deep layer somatosensory cortical neurons initiate spike-and-wave discharges in a genetic model of absence seizures," *J. Neurosci.,* vol. 27, pp. 6590-6599, 2007.

[35] P. O. Polack, S. Mahon, M. Chavez, and S. Charpier, "Inactivation of the somatosensory cortex prevents paroxysmal oscillations in cortical and related thalamic neurons in a genetic model of absence epilepsy," *Cerebral Cortex,* vol. 19, pp. 2078-2091, 2009.

[36] S. Sasaki, K. Huda, T. Inoue, M. Miyata, and K. Imoto, "Impaired feedforward inhibition of the thalamocortical projection in epileptic Ca2+ channel mutant mice, tottering," *Journal of Neuroscience,* vol. 26, pp. 3056-3065, 2006.

[37] D. W. Cope, G. Di Giovanni, S. J. Fyson, G. Orbán, A. C. Errington, M. L. Lorincz*, et al.*, "Enhanced tonic GABAA inhibition in typical absence epilepsy," *Nat. Med.,* vol. 15, pp. 1392-1398, 2009.

[38] J. H. Jackson, "Case of tumour of the middle lobe of the cerebellum," *Brain,* vol. 29, pp. 425-440, 1906.

[39] R. S. Fisher and A. L. Velasco, "Electrical brain stimulation for epilepsy," *Nat. Rev. Neurol.,* vol. 10, pp. 261-270, 2014.

[40] R. S. Fisher, C. Acevedo, A. Arzimanoglou, A. Bogacz, J. H. Cross, C. E. Elger*, et al.*, "ILAE official report: a practical clinical definition of epilepsy," *Epilepsia,* vol. 55, pp. 475-482, 2014.

[41] S. L. Moshé, E. Perucca, P. Ryvlin, and T. Tomson, "Epilepsy: new advances," *Lancet,* vol. 385, pp. 884-898, 2015.

[42] M. P. Kerr, "The impact of epilepsy on patients' lives," *Acta Neurologica Scandinavia,* vol. 194, pp. 1-9, 2012.

[43] P. Perucca and F. G. Gilliam, "Adverse effects of antiepileptic drugs," *Lancet Neurology,* vol. 11, pp. 792-802, 2012.

[44] B. C. Jobst and G. D. Cascino, "Resective epilepsy surgery for drug-resistant focal epilepsy: a review," *JAMA,* vol. 313, pp. 285-293, 2015.

[45] E. Krook-Magnuson, G. G. Szabo, C. Armstrong, M. Oijala, and I. Soltesz, "Cerebellar Directed Optogenetic Intervention Inhibits Spontaneous Hippocampal Seizures in a Mouse Model of Temporal Lobe Epilepsy," *eNeuro,* vol. 1, 2014.

[46] L. Kros, O. H. J. Eelkman Rooda, J. K. Spanke, P. Alva, M. N. Van Dongen, A. Karapatis*, et al.*, "Cerebellar output controls generalized spike-and-wave discharge occurrence," *Annals of Neurology,* vol. 77, pp. 1027-1049, 2015.

[47] I. S. Cooper, "Effect of chronic stimulation of anterior cerebellum on neurological disease," *Lancet,* vol. 1, p. 206, 1973.

[48] S. A. Chkhenkeli, M. Šramka, G. S. Lortkipanidze, T. N. Rakviashvili, E. S. Bregvadze, G. E. Magalashvili*, et al.*, "Electrophysiological effects and clinical results of direct brain stimulation for intractable epilepsy," *Clin. Neuro.l Neurosurg.,* vol. 106, pp. 318-329, 2004.

[49] M. Šramka and I. S. Chkhenkeli, "Clinical experience in intraoperational determination of brain inhibitory structures and application of implanted neurostimulators in epilepsy," *Stereotact. Funct. Neurosurg.,* vol. 54-55, pp. 56-59, 1990.

[50] D. J. Englot, E. F. Chang, and K. I. Auguste, "Vagus nerve stimulation for epilepsy: a meta-analysis of efficacy and predictors of response," *Journal of Neurosurgery,* vol. 115, pp. 1248-1255, 2011.

[51] C. Bodin, S. Aubert, G. Daquin, R. Carron, D. Scavarda, A. McGonigal*, et al.*, "Responders to vagus nerve stimulation (VNS) in refractory epilepsy have reduced interictal cortical synchronicity on scalp EEG," *Epilepsy Research,* vol. 113, pp. 98-103, 2015.

[52] C. C. de Vos, L. Melching, J. van Schoonhoven, J. J. Ardesch, A. W. de Weerd, H. C. van Lambalgen, *et al.*, "Predicting success of vagus nerve stimulation (VNS) from interictal EEG," *Seizure,* vol. 20, pp. 541-545, 2011.

[53] M. Fraschini, M. Puligheddu, M. Demuru, L. Polizzi, A. Maleci, G. Tamburini, *et al.*, "VNS induced desynchronization in gamma bands correlates with positive clinical outcome in temporal lobe pharmacoresistant epilepsy," *Neuroscience Letters,* vol. 536, pp. 14-18, 2013.

[54] R. Fisher, V. Salanova, T. Witt, R. Worth, T. Henry, R. Gross, *et al.*, "Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy," *Epilepsia,* vol. 51, pp. 899-908, 2010.

[55] M. J. Morrell, "Responsive cortical stimulation for the treatment of medically intractable partial epilepsy," *Neurology,* vol. 77, pp. 1295-1304, 2011.

[56] G. K. Bergey, M. J. Morrell, E. M. Mizrahi, A. Goldman, D. King-Stephens, D. Nair, *et al.*, "Long-term treatment with responsive brain stimulation in adults with refractory partial seizures," *Neurology,* vol. 84, pp. 810-817, 2015.

[57] U. Eckert, C. D. Metzger, J. E. Buchmann, J. Kaufmann, A. Osoba, M. Li, *et al.*, "Preferential networks of the mediodorsal nucleus and centromedian-parafascicular complex of the thalamus--a DTI tractography study," *Human brain mapping,* vol. 33, pp. 2627-2637, 2012.

[58] S. Haber and N. R. McFarland, "The place of the thalamus in frontal cortical-basal ganglia circuits," *Neuroscientist,* vol. 7, pp. 315-324, 2001.

[59] Y. D. van der Werf, M. P. Witter, and H. J. Groenewegen, "The intralaminar and midline nuclei of the thalamus. Anatomical and functional evidence for participation in processes of arousal and awareness," *Brain Research. Brain research reviews,* vol. 39, pp. 107-140, 2002.

[60] A. Valentín, E. García Navarrete, R. Chelvarajah, C. Torres, M. Navas, L. Vico, *et al.*, "Deep brain stimulation of the centromedian thalamic nucleus for the treatment of generalized and frontal epilepsies," *Epilepsia,* vol. 54, pp. 1823-1833, 2013.

[61] F. Velasco, A. L. Velasco, M. Velasco, F. Jiménez, J. D. Carrillo-Ruiz, and G. Castro, "Deep brain stimulation for treatment of the epilepsies: the centromedian thalamic target," *Acta Neurochir. (Suppl.),* vol. 97, pp. 337-342, 2007.

[62] F. Velasco, M. Velasco, C. Ogarrio, and G. Fanghanel, "Electrical stimulation of the centromedian thalamic nucleus in the treatment of convulsive seizures: a preliminary report," *Epilepsia,* vol. 28, pp. 421-430, 1987.

[63] F. Velasco, M. Velasco, A. L. Velasco, and F. Jiménez, "Effect of chronic electrical stimulation of the centromedian thalamic nuclei on various intractable seizure patterns: I. Clinical seizures and paroxysmal EEG activity," *Epilepsia,* vol. 34, pp. 1052-1064, 1993.

[64] F. Velasco, M. Velasco, A. L. Velasco, F. Jimenez, I. Marquez, and M. Rise, "Electrical stimulation of the centromedian thalamic nucleus in control of seizures: long-term studies," *Epilepsia,* vol. 36, pp. 63-71, 1995.

[65] F. Velasco, M. Velasco, A. L. Velasco, D. Menez, and L. Rocha, "Electrical stimulation for epilepsy: stimulation of hippocampal foci," *Stereotact. Funct. Neurosurg.,* vol. 77, pp. 223-227, 2001.

[66] G. Moruzzi, "Effects at different frequencies of cerebellar stimulation upon postural tonus and myotatic reflexes," *Electroencephalography and Clinical Neurophysiology,* vol. 2, pp. 463-469, 1950.

[67] K. D. Graber and R. S. Fisher, "Deep Brain Stimulation: Animal Models," in *Jasper's Basic Mechanisms of the Epilepsies*, J. L. Noebels, M. Avoli, M. A. Rogawski, R. W. Olsen, and A. V. Delgado-Escueta, Eds., ed Bethesda, US: National Center for Biotechnology Information, 2012.

[68] J. Bidziński, T. Bacia, K. Ostrowski, and L. Czarkwiani, "Effect of cerebellar cortical electrostimulation on the frequency of epileptic seizures in severe forms of epilepsy," *Neurol. Neurochir. Pol.,* vol. 15, pp. 605-609, 1981.

[69] I. S. Cooper, I. Amin, M. Riklan, J. M. Waltz, and T. P. Poon, "Chronic cerebellar stimultion in epilepsy. Clinical and anatomical studies," *Arch. Neurol.,* vol. 33, pp. 559-570, 1976.

[70] R. Davis, "Cerebellar stimulation for cerebral palsy spasticity, function and seizures," *Arch. Med. Res.,* vol. 31, pp. 290-299, 2000.

[71] R. Davis and S. E. Emmonds, "Cerebellar stimulation for seizure control: 17-year study," *Stereotactic Functional Neurosurgery,* vol. 58, pp. 200-208, 1992.

[72] R. S. Dow, W. Smith, and L. Maukonen, "Clinical experience with chronic cerebellar stimulation in epilepsy and cerebral palsy," *Electroencephalogr. Clin. Neurophysiol.,* vol. 43, p. 906, 1977.

[73] S. Gilman, G. W. Dauth, V. M. Tennyson, L. T. Kremzner, R. Defendini, and J. W. Correll, "Clinical, morphological, biochemical, and physiological effects of cerebellar stimulation," in *Functional Electrical Stimulation: Applications in Neural Prosthesis*, 5 ed New York: Marcel Dekker, 1977.

[74] G. L. Krauss and M. Z. Koubeissi, "Cerebellar and thalamic stimulation treatment for epilepsy," *Acta. Neurochir. Suppl.,* vol. 97, pp. 347-356, 2007.

[75] L. F. Levy and W. C. Auchterlonie, "Chronic cerebellar stimulation in the treatment of epilepsy," *Epilepsia,* vol. 20, pp. 235-245, 1979.

[76] J. M. Van Buren, J. H. Wood, J. Oakley, and F. Hambrecht, "Preliminary evaluation of cerebellar stimulation by double-blind stimulation and biological criteria in the treatment of epilepsy," *J. Neurosurg.,* vol. 48, 1978.

[77] F. Velasco, J. D. Carrillo-Ruiz, M. Velasco, A. L. Velasco, I. Marquez, and R. Davis, "Double-blind, randomized controlled pilot study of bilateral cerebellar stimulation for treatment of intractable motor seizures," *Epilepsia,* vol. 46, pp. 1071-1081, 2005.

[78] G. D. Wright, D. McLellan, and J. G. Brice, "A double-blind trial of chronic cerebellar stimulation in twelve patients with severe epilepsy," *J. Neurol. Neurosurg. Psych.,* vol. 47, pp. 769-774, 1984.

[79] J. Voogd, "The human cerebellum," *Journal of chemical neuroanatomy,* vol. 26, pp. 243-252, 2003.

[80] H. Zhou, Z. Lin, K. Voges, C. Ju, Z. Gao, L. W. Bosman*, et al.*, "Cerebellar modules operate at different frequencies," *Elife,* vol. 3, p. e02536, 2014.

[81] C. I. De Zeeuw, F. E. Hoebeek, L. W. J. Bosman, M. Schonewille, L. Witter, and S. K. Koekkoek, "Spatiotemporal firing patterns in the cerebellum," *Nat. Rev. Neurosci.,* vol. 12, pp. 327-344, 2011.

[82] M. Najac and I. M. Raman, "Integration of Purkinje cell inhibition by cerebellar nucleo-olivary neurons.," *Journal of Neuroscience,* vol. 35, pp. 544-549, 2015.

[83] A. L. Person and I. Raman, "Purkinje neuron synchrony elicits time-locked spiking in the cerebellar nuclei," *Nature,* vol. 481, pp. 502-505, 2012.

[84] T. D. Aumann and M. K. Horne, "Ramification and termination of single axons in the cerebellothalamic pathway of the rat," *J. Comp. Neurol.,* vol. 376, pp. 420-430, 1996.

[85] A. C. Bostan, R. P. Dum, and P. L. Strick, "Cerebellar networks with the cerebral cortex and basal ganglia," *Trends in cognitive sciences,* vol. 17, pp. 241-254, 2013.

[86] E. G. Jones, "The Thalamus 2nd Edition," 2 ed. New York: Cambridge University Press, 2007.

[87] F. Palesi, J. D. Tournier, F. Calamante, N. Muhlert, G. Castellazzi, D. Chard, *et al.*, "Contralateral cerebello-thalamo-cortical pathways wih prominent involvement of associative areas in humans in vivo," *Brain structure & function,* vol. 220, pp. 3369-3384, 2015.

[88] T. J. Ruigrok and T. M. Teune, "Collateralization of cerebellar output to functionally distinct brainstem areas. A retrograde, non-fluorescent tracing study in the rat," *Frontiers in systems neuroscience,* vol. 8, p. 23, 2014.

[89] T. M. Teune, J. van der Burg, J. van der Moer, J. Voogd, and T. J. Ruigrok, "Topography of cerebellar nuclear projections to the brain stem in the rat," *Progress in brain research,* vol. 124, pp. 141-172, 2000.

[90] R. D. Proville, M. Spolidoro, N. Guyon, G. P. Dugué, F. Selimi, P. Isope, *et al.*, "Cerebellum involvement in cortical sensorimotor circuits for the control of voluntary movements," *Nature Neuroscience,* vol. 17, pp. 1233-1239, 2014.

[91] S. F. Sawyer, S. J. Young, P. M. Groves, and J. M. Tepper, "Cerebellar-responsive neurons in the thalamic ventroanterior-ventrolateral coplex of rats: in vivo electrophysiology," *Neuroscience,* vol. 63, pp. 711-724, 1994.

[92] M. Uno, M. Yoshida, and I. Hirota, "The mode of cerebello-thalamic relay transmission investigated with intracellular recording from cells of the ventrolateral nucleus of cat's thalamus," *Exp. Brain Res.,* vol. 10, pp. 121-39, 1970.

[93] H. Arnts, M. Kleinnijenhuis, J. G. Kooloos, A. N. Schepens-Franke, and A. M. van Cappellen van Walsum, "Combining fiber dissection, plastination, and tractography for neuroanatomical education: Revealing the cerebellar nuclei and their white matter connections," *Anatomical sciences education,* vol. 7, pp. 47-55, 2014.

[94] B. J. Hunnicutt, B. R. Long, D. Kusefoglu, K. J. Gertz, H. Zhong, and T. Mao, "A comprehensive thalamocortical projection map at the mesoscopic level," *Nature Neuroscience,* vol. 17, pp. 1276-1285, 2014.

[95] I. Sugihara, H. Fujita, J. Na, P. N. Quy, B. Y. Li, and D. Ikedia, "Projection of reconstructed single Purkinje cell axons in relation to the cortical and nuclear aldolase C compartments of the rat cerebellum," *J. Comp. Neurol.,* vol. 512, pp. 282-304, 2009.

[96] A. D. Norden and H. Blumenfeld, "The role of subcortical structures in epilepsy," *Epilepsy Behav.,* vol. 3, pp. 219-231, 2002.

[97] J. T. Paz and J. R. Huguenard, "Microcircuits and their interactions in epilepsy: is the focus out of focus?," *Nature Neuroscience,* vol. 18, pp. 351-359, 2015.

[98] R. S. Fisher, C. Acevedo, A. Arzimanoglou, A. Bogacz, J. H. Cross, C. E. Elger, *et al.*, "ILAE official report: a practical clinical definition of epilepsy," *Epilepsia,* vol. 55, pp. 475-482, 2014.

[99] P. O. Polack and S. Charpier, "Intracellular activity of cortical and thalamic neurones during high-voltage rhythmic spike discharge in Long-Evans rats in vivo," *Journal of Physiology,* vol. 571, pp. 461-476, 2006.

[100] T. Bal and D. A. McCormick, "Mechanisms of oscillatory activity in guinea-pig nucleus reticularis thalami in vitro: a mammalian pacemaker," *Journal of Physiology,* vol. 468, pp. 669-691, 1993.

[101] C. C. Huang, K. Sugino, Y. Shima, C. Guo, S. Bai, B. D. Mensh, *et al.*, "Convergence of pontine and proprioceptive streams onto multimodal cerebellar granule cells," *Elife,* vol. 2, p. e00400, 2013.

[102] P. M. Cooke and R. S. Snider, "Some cerebellar influences on electrically-induced cerebral seizures," *Epilepsia,* vol. 4, 1955.

[103] A. Fernandez-Guardiola, E. Manni, J. H. Wilson, and R. S. Dow, "Microelectrode recording of cerebellar and cerebral unit activity during convulsive afterdischarge," *Exp. Neurol.,* vol. 6, pp. 48-69, 1962.

[104] A. Kandel and G. Buzsáki, "Cerebellar neuronal activity correlates with spike and wave EEG patterns in the rat," *Epilepsy Res.,* vol. 16, pp. 1-9, 1993.

[105] F. E. Hoebeek, L. Witter, T. J. Ruigrok, and C. I. De Zeeuw, "Differential olivo-cerebellar cortical control of rebound activity in the cerebellar nuclei," *Proc. Natl. Acad. Sci. U.S.A.,* vol. 107, pp. 8410-8415, 2010.

[106] Y. Shinoda, M. Kano, and T. Futami, "Synaptic organization of the cerebello-thalamo-cerebral pathway in the cat. I. Projection of individual cerebellar nuclei to single pyramidal tract neurons in areas 4 and 6," *Neuroscience Research,* vol. 2, pp. 133-156, 1985.

[107] K. Alvina, J. T. Walter, A. Kohn, G. Ellis-Davies, and K. Khodakhah, "Questioning the role of rebound firing in the cerebellum," *Nature Neuroscience,* vol. 11, pp. 1256-1258, 2008.

[108] F. Bengtsson, C. F. Ekerot, and H. Jorntell, "In vivo analysis of inhibitory synaptic inputs and rebounds in deep cerebellar nuclear neurons," *PLoS One,* vol. 6, 2011.

[109] M. L. Molineux, J. E. McRory, B. E. McKay, J. Hamid, W. H. Mehaffey, R. Rehak, *et al.*, "Specific T-type calcium channel isoforms are associated with distinct burst phenotypes in deep cerebellar nuclear neurons," *PNAS,* vol. 103, pp. 5555-5560, 2006.

[110] N. C. Rowland and D. Jaeger, "Responses to tactile stimulation in deep cerebellar nucleus neurons result from recurrent activation in multiple pathways," *Journal of Neurophysiology,* vol. 99, pp. 704-717, 2008.

[111] L. Witter, C. B. Canto, T. M. Hoogland, J. R. de Gruijl, and C. I. De Zeeuw, "Strength and timing of motor responses mediated by rebound firing in the cerebellar nuclei after Purkinje cell activation," *Frontiers in neural circuits,* vol. 7, pp. 1-14, 2013.

[112] M. Uusisaari and T. Knöpfel, "Diversity of neuronal elements and circuitry in the cerebellar nuclei," *Cerebellum,* vol. 11, pp. 420-421, 2012.

[113] R. R. Myers, K. J. Burchiel, J. J. Stockard, and R. G. Bickford, "Effects of acute and chronic paleocerebellar stimulation on experimental models of epilepsy in the cat: studies with enflurane, pentylenetetrazol, penicillin, and chloralose," *Epilepsia,* vol. 16, pp. 257-267, 1975.

[114] R. G. Heath and J. W. Harper, "Ascending projections of the cerebellar fastigial nucleus to the hippocampus, amygdala, and other temporal lobe sites: evoked potential and histological studies in monkeys and cats," *Experimental Neurology,* vol. 45, pp. 268-287, 1974.

[115] J. Chaumont, N. Guyon, A. M. Valera, G. P. Duqué, D. Popa, P. Marcaggi, *et al.*, "Clusters of cerebellar Purkinje cells control their afferent climbing fiber discharge," *PNAS,* vol. 110, pp. 16223-16228, 2013.

[116] T. L. Babb, A. G. J. Mitchell, and P. H. Crandall, "Fastigiobulbar and dentatothalamic influences on hippocampal cobalt epilepsy in the cat," *Electroencephalography and Clinical Neurophysiology,* vol. 36, pp. 141-154, 1974.

[117] R. S. Dow, A. Fernandez-Guardiola, and E. Manni, "The influence of the cerebellum on experimental epilepsy," *Electroencephalography and Clinical Neurophysiology,* vol. 14, 1962.

[118] D. C. Hemmy, S. J. Larson, A. J. Sances, and E. A. Millar, "The effect of cerebellar stimulation on focal seizure activity and spasticity in monkeys," *Journal of Neurosurgery,* vol. 46, pp. 648-653, 1977.

[119] R. A. Badawy, A. Lai, S. J. Vogrin, and M. J. Cook, "Subcortical epilepsy?," *Neurology,* vol. 80, pp. 1901-1907, 2013.

[120] J. F. Fulton, "A case of cerebellar tumor with seizures of head retraction described by Wurffbain in 1691," *J. Nerv. Ment. Dis.,* vol. 70, pp. 577-583, 1929.

[121] P. R. McCrory, P. F. Bladin, and S. F. Berkovic, "The cerebellar seizures of Hughlings Jackson," *Neurology,* vol. 52, pp. 1888-1890, 1999.

[122] S. Boop, J. Wheless, K. Van Poppel, A. McGregor, and F. A. Boop, "J. Neurosurg. Pediatr.," *12,* vol. 3, 2013.

[123] M. D. Mark, T. Maejima, D. Kuckelsberg, J. W. Yoo, R. A. Hyde, V. Shah, *et al.*, "Delayed postnatal loss of P/Q-type calcium channels recapitulates the absence epilepsy, dyskinesia, and ataxia phenotypes of genomic Cacna1a mutations," *J. Neurosci.,* vol. 31, pp. 4311-4326, 2011.

[124] T. Maejima, P. Wollenweber, L. Teusner, J. L. Noebels, S. Herlitze, and M. D. Mark, "Postnatal loos of P/Q-type channels confined to rhombic-lip-derived neurons alters synaptic transmission at the parallel fiber to Purkinje cell synapse and replicates genomic Cacna1a mutation phenotype of

ataxia and seizures in Mice," *J. Neurosci.,* vol. 33, pp. 5162-5174, 2013.

[125] E. Galliano, Z. Gao, M. Schonewille, B. Todorov, E. Simons, A. S. Pop, *et al.*, "Silencing the majority of cerebellar granule cells uncovers their essential role in motor learning and consolidation," *Cell Reports,* vol. 3, pp. 1239-1251, 2013.

[126] J. T. Paz, T. J. Davidson, E. S. Frechette, B. Delord, I. Parada, K. Peng, *et al.*, "Closed-loop optogenetic control of thalamus as a tool for interrupting seizures after cortical injury," *Nat. Neurosci.,* vol. 16, pp. 64-70, 2013.

[127] A. Hayaran, S. Wadhwa, G. Gopinath, and V. Bijlani, "Developing dentate nucleus in man: a qualitative and quantitative study," *Experimental Brain Research,* vol. 89, pp. 640-648, 1992.

[128] S. Tellmann, S. Bludau, S. Eickhoff, H. Mohlberg, M. Minnerop, and K. Amunts, "Cytoarchitectonic mapping of the human brain cerebellar nuclei in stereotaxic space and delineation of their co-activation patterns," *Frontiers in neuroanatomy,* vol. 9, 2015.

[129] M. Šramka, G. Fritz, M. Galanda, and P. Nádvorník, "Some observations in treatment stimulation of epilepsy," *Acta Neurochir. (Suppl.),* vol. 23, pp. 257-262, 1976.

[130] B. P. Hermann, K. Bayless, H. R., J. Parrish, and M. Seidenberg, "Cerebellar atrophy in temporal lobe epilepsy," *Epilepsy & Behavior,* vol. 7, pp. 279-287, 2005.

[131] R. Crooks, T. Mitchell, and M. Thom, "Patterns of cerebellar atrophy in patients with chronic epilepsy: a quantitative neuropathological study," *Epilepsy Res.,* vol. 41, pp. 63-73, 2000.

[132] M. Sévin, G. Lesca, N. Baumann, G. Millat, O. Lyon-Caen, M. T. Vanier, *et al.*, "The adult form of Niemann-Pick disease type C," *Brain,* vol. 130, pp. 120-133, 2007.

[133] A. M. J. M. van den Maagdenberg, T. K. Pizzorusso, S., N. Terpolilli, M. Shapovalova, F. E. Hoebeek, C. F. Barrett, *et al.*, "High cortical spreading depression susceptibility and migraine-associated symptoms in Ca(v)2.1 S218L mice," *Annals of Neurology,* vol. 67, pp. 85-98, 2010.

[134] T. Joensuu, S. Tegelberg, E. Reinmaa, M. Segerstråle, P. Hakala, H. Pehkonen, *et al.*, "Gene expression alterations in the cerebellum and granule neurons of Cstb(-/-) mouse are associated with early synaptic changes and inflammation," *PLoS One,* vol. 8, p. 89321, 2014.

[135] V. Villanueva, J. Alvarez-Linera, P. Gómez-Garre, J. Gutiérrez, and J. M. Serratosa, "MRI volumetry and proton MR spectroscopy of the brain in Lafora disease," *Epilepsia,* vol. 47, pp. 788-792, 2006.

[136] U. Specht, T. May, R. Schulz, M. Rohde, A. Ebner, R. C. Schmidt, *et al.*, "Cerebellar atrophy and prognosis after temporal lobe resection," *Journal of neurology, neurosurgery, and psychiatry,* vol. 62, pp. 501-506, 1997.

[137] J. W. Miller, B. C. Gray, and G. M. Turner, "Role of the fastigial nucleus in generalized seizures as demonstrated by GABA agonist microinjections," *Epilepsia,* vol. 34, pp. 973-978, 1993.

[138] N. Tsuru, H. Kawasaki, S. Genda, K. Hara, H. Hashiguchi, and Y. Ueda, "Effect of unilateral dentate nucleus lesions on amygdaloid kindling in rats," *Epilepsia,* vol. 33, pp. 213-221, 1992.

[139] N. R. Ghatak, R. A. Santoso, and W. M. McKinney, "Cerebellar degeneration following long-term phenytoin therapy," *Neurology,* vol. 26, pp. 818-820, 1976.

[140] I. Savic and J. O. Thorell, "Localized cerebellar reductions in benzodiazepine receptor density in human partial epilepsy," *Archives of neurology,* vol. 53, pp. 656-662, 1996.

[141] J. Annese, N. M. Schenker-Ahmed, H. Bartsch, P. Maechler, C. Sheh, N. Thomas, *et al.*, "Postmortem examination of patient H.M.'s brain based on histological sectioning and digital 3D reconstruction," *Nature Communications,* vol. 5, p. 3122, 2014.

[142] J. C. Augustinack, A. J. van der Kouwe, D. H. Salat, T. Benner, A. A. Stevens, J. Annese, *et al.*, "H.M.'s contributions to neuroscience: a review and autopsy studies," *Hippocampus,* vol. 24, pp. 126-1286, 2014.

[143] Y. Li, H. Du, B. Xie, N. Wu, J. Wang, G. Wu, *et al.*, "Cerebellum abnormalities in idiopathic generalized epilepsy with generalized tonic-clonic seizures revealed by diffusion tensor imaging," *PLoS One,* vol. 5, pp. 1-7, 2010.

[144] K. M. Park, Y. H. Han, T. H. Kim, C. W. Mun, K. J. Shin, S. Y. Ha, *et al.*, "Cerebellar white matter changes in patients with newly diagnosed partial epilepsy of unknown etiology," *Clinical neurology and neurosurgery,* vol. 138, pp. 25-30, 2015.

[145] K. M. Park, T. H. Kim, Y. H. Han, C. W. Mun, K. J. Shin, S. Y. Ha, *et al.*, "Brain morphology in juvenile myoclonic epilepsy and absence seizures," *Acta Neurologica Scandinavia,* 2015.

[146] E. Calabrese, P. Hickey, C. Hulette, J. Zhang, B. Parente, S. P. Lad, *et al.*, "Postmortem diffusion MRI of the human brainstem and thalamus for deep brain stimulator electrode localization," *Human brain mapping,* vol. 36, pp. 3167-3178, 2015.

[147] S. Groppa, J. Herzog, D. Falk, C. Riedel, G. Deuschl, and J. Volkmann, "Physiological and anatomical decomposition of subthalamic neurostimulation effects in essential tremor," *Brain,* vol. 137, pp. 109-121, 2014.

[148] A. M. Lozano and N. Lipsman, "Probing and regulating dysfunctional circuits using deep brain stimulation," *Neuron,* vol. 77, pp. 406-424, 2013.

[149] M. S. LeDoux, J. F. Lorden, and J. Meinzen-Derr, "Selective elimination of cerebellar output in the genetically dystonic rat," *Brain research,* vol. 697, pp. 91-103, 1995.

[150] S. M. Sherman, "The function of metabotropic glutamate receptors in thalamus and cortex," *Neuroscientist,* vol. 20, pp. 136-149, 2014.

[151] P. Mahlknecht, P. Limousin, and T. Foltynie, "Deep brain stimulation for movement disorders: update on recent discoveries and outlook on future developments," *Journal of neurology,* vol. 262, pp. 2583-2595, 2015.

[152] J. Cooperrider, H. Furmaga, E. Plow, H. J. Park, Z. Chen, G. Kidd*, et al.*, "Chronic deep cerebellar stimulation promotes long-term potentiation, microstructural plasticity, and reorganization of perilesional cortical representation in a rodent model," *Journal of Neuroscience,* vol. 34, pp. 9040-9050, 2014.

[153] C. W. Hess, D. E. Vaillancourt, and M. S. Okun, "The temporal pattern of stimulation may be important to the mechanism of deep brain stimulation," *Experimental Neurology,* vol. 247, pp. 296-302, 2013.

[154] R. Apps and R. Hawkes, "Cerebellar cortical organization: a one map hypothesis," *Nat. Rev. Neurosci.,* vol. 10, pp. 670-681, 2009.

[155] D. Jaeger, "Mini-review: synaptic integration in the cerebellar nuclei--perspectives from dynamic clamp and computer simulation studies," *Cerebellum,* vol. 10, pp. 659-666, 2011.

[156] K. J. van Dijk, R. Verhagen, A. Chaturvedi, C. C. McIntyre, L. J. Bour, C. Heida*, et al.*, "A novel lead design enables selective deep brain stimulation of neural populations in the subthalamic region," *Journal of neural engineering,* vol. 12, p. 046003, 2015.

[157] K. Gadhoumi, J. M. Lina, F. Mormann, and J. Gotman, "Seizure prediction for therapeutic devices: A review," *Journal of Neuroscience Methods,* vol. 260, pp. 270-282, 2016.

[158] M. N. van Dongen, A. Karapatis, L. Kros, O. H. J. Eelkman Rooda, R. M. Seepers, C. Strydis*, et al.*, "An implementation of a wavelet-based seizure detection filter suitable for realtime closed-loop epileptic seizure suppression," in *IEEE Biomedical Circuits and Systems Conference*, ed, 2014, pp. 504-507.

[159] A. Berényi, M. Belluscio, D. Mao, and G. Buzsàki, "Closed-loop control of epilepsy by transcranial electrical stimulation.," *Science,* vol. 337, pp. 735-737, 2012.

[160] E. Krook-Magnuson, C. Armstrong, M. Oijala, and I. Soltesz, "On-demand optogenetic control of spontaneous seizures in temporal lobe epilepsy," *Nature Communications,* vol. 4, p. 1376, 2013.

[161] P. Suffczynski, S. Kalitzin, and F. H. Lopes Da Silva, "Dynamics of non-convulsive epileptic phenomena modeled by a bistable neuronal network," *Neuroscience,* vol. 126, pp. 467-484, 2004.

[162] P. N. Taylor, Y. Wang, M. Goodfellow, J. Dauwels, F. Moeller, U. Stephani*, et al.*, "A computational study of stimulus driven epileptic seizure abatement," *PLoS One,* vol. 9, p. 114316, 2014.

[163] U. Seneviratne, M. Cook, and W. D'Souza, "The electroencephalogram of idiopathic generalized epilepsy.," *Epilepsia,* vol. 53, pp. 234-248, 2012.

[164] L. Kros, O. H. J. Eelkman Rooda, C. I. De Zeeuw, and F. E. Hoebeek, "Controlling cerebellar output to treat refractory epilepsy," *Trends in Neurosciences,* vol. 38, pp. 787-799, 2015.

[165] R. Hawkes, S. Blyth, V. Chockkan, D. Tano, Z. Ji, and C. Mascher, "Structural and molecular compartmentation in the cerebellum," *The Canadian Journal of neurological sciences,* vol. 20, pp. S29-S35, 1993.

[166] A. Pijpers, J. Voogd, and T. J. Ruigrok, "Topography of olivo-cortico-nuclear modules in the intermediate cerebellum of the rat," *Journal of Comparative Neurology,* vol. 492, pp. 193-213, 2005.

[167] O. Yizhar, L. E. Fenno, T. J. Davidson, M. Mogri, and K. Deisseroth, "Optogenetics in neural systems," *Neuron,* vol. 71, pp. 9-34, 2011.

[168] A. R. Houweling and M. Brecht, "Behavioural report of single neuron stimulation in somatosensory cortex," *Nature,* vol. 451, pp. 65-68, 2008.

[169] C. Guo, L. Witter, S. Rudolph, H. L. Elliott, K. A. Ennis, and W. G. Regehr, "Purkinje cells directly inhibit granule cells in specialized regions of the cerebellar cortex," *Neuron,* vol. 91, pp. 1330-1341, 2016.

[170] A. M. Valera, F. Binda, S. A. Pawlowski, J. L. Dupont, J. F. Casella, J. D. Rothstein, *et al.*, "Stereotyped spatial patterns of functional synaptic connectivity in the cerebellar cortex," *Elife,* vol. 5, 2016.

[171] L. Witter, S. Rudolph, R. T. Pressler, S. I. Lahlaf, and W. G. Regehr, "Purkinje cell collaterals enable output signals from the cerebellar cortex to feed back to purkinje cells and interneurons," *Neuron,* vol. 91, pp. 312-319, 2016.

[172] B. Sauer and N. Henderson, "Site-specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 85, pp. 5166-5170, 1988.

[173] GENSAT. (2016). *Gensat website for Cre mice*.

[174] L. Madisen, A. R. Garner, D. Shimaoka, A. S. Chuong, N. C. Klapoetke, L. Li, *et al.*, "Transgenic mice for intersectional targeting of neural sensors and effectors with high specificity and performance," *Neuron,* vol. 85, pp. 942-958, 2015.

[175] L. Madisen, T. Mao, H. Koch, J. M. Zhuo, A. Berenyi, S. Fujisawa, *et al.*, "A toolbox of Cre-dependent optogenetic transgenic mice for light-induced activation and silencing," *Nature Neuroscience,* vol. 15, pp. 793-802, 2012.

[176] J. Oberdick, R. J. Smeyne, J. R. Mann, S. Zackson, and J. I. Morgan, "A promoter that drives transgene expression in cerebellar purkinje and retinal bipolar neurons," *Science,* vol. 248, pp. 223-226, 1990.

[177] J. J. Barski, K. Dethleffsen, and M. Meyer, "Cre recombinase expression in cerebellar Purkine cells," *Genesis,* vol. 28, pp. 93-98, 2000.

[178] T. D. Nguyen-Vu, R. R. Kimpo, J. M. Rinaldi, A. Kohli, H. Zeng, K. Deisseroth, *et al.*, "Cerebellar Purkinje cell activity drives motor learning," *Nature Neuroscience,* vol. 16, pp. 1734-1736, 2013.

[179] L. Petreanu, D. Huber, A. Sobczyk, and K. Svoboda, "Channelrhodopsin-2-assisted circuit mapping of long-range callosal projections," *Nature Neuroscience,* vol. 10, pp. 663-668, 2007.

[180] M. Yamada, Y. Seto, S. Taya, T. Owa, Y. U. Inoue, T. Inoue, *et al.*, "Specification of spatial identities of cerebellar neuron progenitors by ptf1a and atoh1 for proper production of GABAergic and glutamatergic neurons," *Journal of Neuroscience,* vol. 34, pp. 4786-4800, 2014.

[181] J. Szcurkowska, A. W. Cwetsch, M. dal Maschio, D. Ghezzi, G. M. Ratto, and L. Cancedda, "Targeted in vivo genetic manipulation of the mouse or rat brain by in utero electroporation with a triple-electrode probe," *Nature Protocols,* vol. 11, pp. 399-412, 2016.

[182] V. Lukashchuk, K. E. Lewis, I. Coldicott, A. J. Grierson, and M. Azzouz, "AAV9-mediated central nervous system-targeted gene delivery via cisterna magna route in mice," *Molecular therapy. Methods & clinical development,* vol. 3, 2016.

[183] J. R. McLean, G. A. Smith, E. M. Rocha, M. A. Hayes, J. A. Beagan, P. J. Hallett, *et al.*, "Widespread neuron-specific transgene expression in brain and spinal cord following synapsin promoter-driven AAV9 neonatal intracerebroventricular injection," *Neuroscience Letters,* vol. 576, pp. 73-78, 2014.

[184] H. Hirai, "Progress in transduction of cerebellar Purkinje cells in vivo using viral vectors," *Cerebellum,* vol. 7, pp. 273-278, 2008.

[185] T. Tsubota, Y. Ohashi, K. Tamura, and Y. Miyashita, "Optogenetic inhibition of Purkinje cell activity reveals cerebellar control of blood pressure during postural alterations in anesthetized rats," *Neuroscience,* vol. 210, pp. 137-144, 2012.

[186] T. Tsubota, Y. Ohashi, K. Tamura, A. Sato, and Y. Miyashita, "Optogenetic manipulation of cerebellar Purkinje cell activity in vivo," *PLoS One,* vol. 6, p. e22400, 2011.

[187] M. K. Bosch, J. M. Nerbonne, and D. M. Ornitz, "Dual transgene expression in murine cerebellar Purkinje neurons by viral transduction in vivo," *PLoS One,* vol. 9, p. e104062, 2014.

[188] J. C. Dodge, J. Clarke, A. Song, J. Bu, W. Yang, T. V. Taksir, *et al.*, "Gene transfer of human acid sphingomyelinase corrects neuropathology and motor deficits in a mouse model of Niemann-Pick type A disease," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 102, pp. 17822-17827, 2005.

[189] W. F. Kaemmerer, R. G. Reddy, C. A. Warlick, S. D. Hartung, R. S. McIvor, and W. C. Low, "In vivo transduction of cerebellar Purkinje cells using adeno-associated virus vectors," *Molecular therapy,* vol. 2, pp. 446-457, 2000.

[190] D. F. Aschauer, S. Kreuz, and S. Rumpel, "Analysis of transduction efficiency, tropism and axonal transport of AAV serotypes 1, 2, 5, 6, 8 and 9 in the mouse brain," *PLoS One,* vol. 8, p. e76310, 2013.

[191] B. Asrican, G. J. Augstine, K. Berglund, S. Chen, N. Chow, K. Deisseroth, *et al.*, "Next-generation transgenic mice for optogenetic analysis of neural circuits," *Frontiers in neural circuits,* vol. 7, 2013.

[192] M. R. Celio and C. W. Heizmann, "Calcium-binding protein parvalbumin as a neuronal marker," *Nature,* vol. 293, pp. 300-302, 1981.

[193] S. A. Heiney, J. Kim, G. J. Augustine, and J. F. Medina, "Precise control of movement kinematics by optogenetic inhibition of purkinje cell activity," *Journal of Neuroscience,* vol. 34, pp. 2321-2330, 2014.

[194] M. I. Aller, A. Jones, D. Merlo, M. Paterlini, A. H. Meyer, U. Amtmann, *et al.*, "Cerebellar granule cell Cre recombinase expression," *Genesis,* vol. 36, pp. 97-103, 2003.

[195] Y. Kim, T. Kim, J. K. Rhee, D. Lee, K. Tanaka-Yamamoto, and Y. Yamamoto, "Selective transgene expression in cerebellar Purkinje cells and granule cells using adeno-associated viruses together with specific promoters," *Brain research,* vol. 1620, pp. 1-16, 2015.

[196] G. Astorga, J. Bao, A. Marty, G. J. Augustine, R. Franconville, A. Jalil*, et al.*, "An excitatory GABA loop operating in vivo," *Frontiers in cellular neuroscience,* vol. 9, 2015.

[197] J. Kim, S. Lee, S. Tsuda, X. Zhang, B. Asrican, B. Gloss*, et al.*, "Optogenetic mapping of cerebellar inhibitory circuitry reveals spatially biased coordination of interneurons via electrical synapses," *Cell Reports,* vol. 7, pp. 1601-1613, 2014.

[198] L. Ankri, Z. Husson, K. Pietrajtis, R. Proville, C. Léna, Y. Yarom*, et al.*, "A novel inhibitory nucleo-cortical circuit controls cerebellar Golgi cell activity," *Elife,* vol. 4, 2015.

[199] T. Tsubota, Y. Ohashi, and K. Tamura, "Optogenetics in the cerebellum: Purkinje cell-specific approaches for understanding local cerebellar functions," *Behavioural brain research,* vol. 255, pp. 26-34, 2013.

[200] Q. Wang, A. M. Henry, J. A. Harris, S. W. Oh, K. M. Joines, J. Nyhus*, et al.*, "Systematic comparison of adeno-associated virus and biotinylated dextran amine reveals equivalent sensitivity between tracers and novel projection targets in the mouse brain," *Journal of Comparative Neurology,* vol. 522, pp. 1989-2012, 2014.

[201] E. S. Boyden, F. Zhang, E. Bamberg, G. Nagel, and K. Deisseroth, "Millisecond-timescale, genetically targeted optical control of neural activity," *Nature Neuroscience,* vol. 8, pp. 1263-1268, 2005.

[202] W. Kruse, M. Krause, J. Aarse, M. D. Mark, D. Manahan-Vaughan, and S. Herlitze, "Optogenetic modulation and multi-electrode analysis of cerebellar networks in vivo," *PLoS One,* vol. 9, p. e105589, 2014.

[203] s. u.-d. lab. (2016, 22 december 2016). *irradiance calculator tool*. Available: http://web.stanford.edu/group/dlab/cgi-bin/graph/chart.php

[204] S. I. Al-Juboori, A. Dondzillo, E. A. Stubblefield, G. Felsen, T. C. Lei, and A. Klug, "Light scattering properties vary across different regions of the adult mouse brain," *PLoS One,* vol. 8, p. e67626, 2013.

[205] Y. Liu, S. L. Jacques, M. Azimipour, J. D. Rogers, R. Pashaie, and K. W. Eliceiri, "OptogenSIM: a 3D Monte Carlo simulation platform for light delivery design in optogenetics," *Biomedical optics express,* vol. 6, pp. 4859-4870, 2015.

[206] C. Brabec, V. Dyakonov, J. Parisi, and N. S. Sariciftci, *Organic photovoltaics: Concepts and Realization*. Berlin Heidelberg: Springer-Verlag, 2003.

[207] M. Gratzel, "Photoelectrochemical cells," *Nature,* vol. 414, pp. 338-344, 2001.

[208] R. Williams, "Becquerel photovoltaic effect in binary compounds," *Journal of chemical physics,* vol. 32, pp. 1505-1514, 1960.

[209] P. Ledochowitsch, A. Yazdan-Shahmorad, K. E. Bouchard, C. Diaz-Botia, T. L. Hanson, J. W. He*, et al.*, "Strategies for optical control and simultaneous electrical readout of extended cortical circuits," *Journal of neuroscience Methods,* vol. 256, pp. 220-231, 2015.

[210] D. W. Park, A. A. Schendel, S. Mikael, S. K. Brodnick, T. J. Richner, J. P. Ness*, et al.*, "Graphene-based carbon layered electrode array technology for neural imaging and optogenetic applications," *Nature Communications,* vol. 5:5258, 2014.

[211] F. Wu, E. Stark, P. C. Ku, K. D. Wise, G. Buzsáki, and E. Yoon, "Monolithically Integrated μLEDs on Silicon Neural Probes for High-Resolution Optogenetic Studies in Behaving Animals," *Neuron,* vol. 88, pp. 1136-1148, 2015.

[212] T. C. Pappas, W. M. S. Wickramanyake, E. Jan, M. Motamedi, M. Brodwick, and N. A. Kotov, "Nanoscale engineering of a cellular interface with semiconductor nanoparticle films for photoelectric stimulation of neurons," *Nano Letters,* vol. 7, pp. 513-519, 2007.

[213] A. Berndt, S. Y. Lee, C. Ramakrishnan, and K. Deisseroth, "Structure-guided transformation of channelrhodopsin into a light-activated chloride channel," *Science,* vol. 344, pp. 420-424, 2014.

[214] X. Han, X. Qian, J. G. Bernstein, H. H. Zhou, G. T. Franzesi, P. Stern*, et al.*, "Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain," *Neuron,* vol. 62, pp. 191-198, 2009.

[215] X. Li, D. V. Gutierrez, M. G. Hanson, J. Han, M. D. Mark, H. Chiel*, et al.*, "Fast noninvasive activation and inhibition of neural and network activity by vertebrate rhodopsin and green algae channelrhodopsin," *Proceedings of the National Academy of Sciences of the United States of America,* vol. 102, pp. 17816-17821, 2005.

[216] C. Mateo, M. Avermann, L. J. Gentet, F. Zhang, K. Deisseroth, and C. C. Petersen, "In vivo optogenetic stimulation of neocortical excitatory neurons drives brain-state-dependent inhibition," *Current Biology,* vol. 21, pp. 1593-1602, 2011.

[217] G. Nagel, M. Brauner, J. F. Liewald, N. Adeishvili, E. Bamberg, and A. Gottschalk, "Light activation of channelrhodopsin-2 in excitable cells of Caenorhabditis elegans triggers rapid behavioral responses," *Current Biology,* vol. 15, pp. 2279-2284, 2005.

[218] S. Zhao, J. T. Ting, H. E. Atallah, L. Qiu, J. Tan, B. Gloss*, et al.*, "Cell type-specific channelrhodopsin-2 transgenic mice for optogenetic dissection of neural circuitry function," *Nature Methods,* vol. 8, pp. 745-752, 2011.

[219] A. M. Herman, L. Huang, D. K. Murphey, I. Garcia, and B. R. Arenkiel, "Cell type-specific and time-dependent light exposure contribute to silencing in neurons expressing Channelrhodopsin-2," *Elife,* vol. 3, 2014.

[220] M. Mahn, M. Prigge, S. Ron, R. Levy, and O. Yizhar, "Biophysical constraints of optogenetic inhibition at presynaptic terminals," *Nature Neuroscience,* vol. 19, pp. 554-556, 2016.

[221] I. N. Christie, J. A. Wells, P. Southern, N. Marina, S. Kasparov, A. V. Gourine*, et al.*, "fMRI response to blue light delivery in the naive brain: implications for combined optogenetic fMRI studies," *Neuroimage,* vol. 66, pp. 634-641, 2013.

[222] M. A. Long and M. S. Fee, "Using temperature to analyse temporal dynamics in the songbird motor pathway," *Nature,* vol. 456, pp. 189-194, 2008.

[223] E. Moser, I. Mathiesen, and P. Andersen, "Association between brain temperataure and dentate field potentials in exploring and swimming rats," *Science,* vol. 259, pp. 1324-1326, 1993.

[224] J. M. Stujenske, T. Spellman, and J. A. Gordon, "Modeling the spatiotemporal dynamics of light and heat propagation for in vivo optogenetics," *Cell Reports,* vol. 12, pp. 525-534, 2015.

[225] J. M. Sorokin, T. J. Davidson, E. Frechette, A. M. Abramian, K. Deisseroth, J. R. Huguenard*, et al.*, "Bidirectional Control of Generalized Epilepsy Networks via Rapid Real-Time Switching of Firing Mode," *Neuron,* Dec 14 2017.

[226] L. M. Palmer, B. A. Clark, J. Grundemann, A. Roth, G. J. Stuart, and M. Hausser, "Initiation of simple and complex spikes in cerebellar Purkinje cells," *J Physiol,* vol. 588, pp. 1709-17, May 15 2010.

[227] P. Vetter, A. Roth, and M. Hausser, "Propagation of action potentials in dendrites depends on dendritic morphology," *J Neurophysiol,* vol. 85, pp. 926-37, Feb 2001.

[228] K. H. Lee, P. J. Mathews, A. M. Reeves, K. Y. Choe, S. A. Jami, R. E. Serrano*, et al.*, "Circuit mechanisms underlying motor memory formation in the cerebellum," *Neuron,* vol. 86, pp. 529-40, Apr 22 2015.

[229] I. M. Raman and B. P. Bean, "Ionic currents underlying spontaneous action potentials in isolated cerebellar Purkinje neurons," *J Neurosci,* vol. 19, pp. 1663-74, Mar 01 1999.

[230] Z. Gao, B. Todorov, C. F. Barrett, S. van Dorp, M. D. Ferrari, A. M. van den Maagdenberg*, et al.*, "Cerebellar ataxia by enhanced Ca(V)2.1 currents is alleviated by Ca2+-dependent K+-channel activators in Cacna1a(S218L) mutant mice," *J Neurosci,* vol. 32, pp. 15533-46, Oct 31 2012.

[231] J. T. Walter, K. Alvina, M. D. Womack, C. Chevez, and K. Khodakhah, "Decreases in the precision of Purkinje cell pacemaking cause cerebellar dysfunction and ataxia," *Nat Neurosci,* vol. 9, pp. 389-97, Mar 2006.

[232] S. L. Jackman, B. M. Beneduce, I. R. Drew, and W. G. Regehr, "Achieving high-frequency optical control of synaptic transmission," *Journal of Neuroscience,* vol. 34, pp. 7704-7714, 2014.

[233] B. Y. Chow, X. Han, A. S. Dobry, X. Qian, A. S. Chuong, M. Li*, et al.*, "High-performance genetically targetable optical neural silencing by light-driven proton pumps," *Nature,* vol. 463, pp. 98-102, 2010.

[234] E. G. Govorunova, O. A. Sineshchekov, R. Janz, X. Liu, and J. L. Spudich, "Natural light-gated anion channels: A family of microbial rhodopsins for advanced optogenetics," *Science,* vol. 349, pp. 647-650, 2015.

[235] J. Wietek, J. S. Wiegert, N. Adeishvili, F. Schneider, H. Watanabe, S. P. Tsunoda*, et al.*, "Conversion of channelrhodopsin into a light-gated chloride channel," *Science,* vol. 344, pp. 409-412, 2014.

[236] A. S. Chuong, M. L. Miri, V. Busskamp, G. A. Matthews, L. C. Acker, A. T. Sorensen*, et al.*, "Noninvasive optical inhibition with a red-shifted microbial rhodopsin," *Nature Neuroscience,* vol. 17, pp. 1123-1129, 2014.

[237] F. Zhang, L. P. Wang, M. Brauner, J. F. Liewald, K. Kay, N. Watzke*, et al.*, "Multimodal fast optical interrogation of neural circuitry," *Nature,* vol. 446, pp. 633-639, 2007.

[238] G. M. Alexander, S. C. Rogan, A. I. Abbas, B. N. Armbruster, Y. Pei, J. A. Allen*, et al.*, "Remote control of neuronal activity in transgenic mice expressing evolved G protein-coupled receptors," *Neuron,* vol. 63, pp. 27-39, Jul 16 2009.

[239] T. J. Stachniak, A. Ghosh, and S. M. Sternson, "Chemogenetic synaptic silencing of neural circuits localizes a hypothalamus-->midbrain pathway for feeding behavior," *Neuron,* vol. 82, pp. 797-808, May 21 2014.

[240] J. Levitz, C. Pantoja, B. Gaub, H. Janovjak, A. Reiner, A. Hoagland*, et al.*, "Optical control of metabotropic glutamate receptors," *Nature Neuroscience,* vol. 16, pp. 507-516, 2013.

[241] D. V. Gutierrez, M. D. Mark, O. Masseck, T. Maejima, D. Kuckelsberg, R. A. Hyde*, et al.*, "Optogenetic control of motor coordination by Gi/o protein-coupled vertebrate rhodopsin in cerebellar Purkinje cells," *J Biol Chem,* vol. 286, pp. 25848-58, Jul 22 2011.

[242] M. Uusisaari and E. De Schutter, "The mysterious microcircuitry of the cerebellar nuclei," *J Physiol,* vol. 589, pp. 3441-57, Jul 15 2011.

[243] M. Uusisaari and T. Knöpfel, "Functional classification of neurons in the mouse lateral cerebellar nuclei," *Cerebellum,* vol. 10, pp. 637-646, 2011.

[244] L. Borgius, C. E. Restrepo, R. N. Leao, N. Saleh, and O. Kiehn, "A transgenic mouse line for molecular genetic analysis of excitatory glutamatergic neurons," *Mol Cell Neurosci,* vol. 45, pp. 245-57, Nov 2010.

[245] B. D. Houck and A. L. Person, "Cerebellar premotor output neurons collateralize to innervate the cerebellar cortex," *The Journal of Comparative Neurology,* vol. 523, pp. 2254-2271, 2015.

[246] Z. Husson, C. V. Rousseau, I. Broll, H. U. Zeilhofer, and Dieudonné, "Differential GABAergic and glycinergic inputs of inhibitory interneurons and purkinje cells to principal cells of the cerebellar nuclei," *J. Neurosci.,* vol. 34, pp. 9418-9431, 2014.

[247] Y. Lefler, Y. Yarom, and M. Y. Uusisaari, "Cerebellar inhibitory input to the inferior olive decreases electrical coupling and blocks subthreshold oscillations," *Neuron,* vol. 81, pp. 1389-1400, 2014.

[248] M. W. Bagnall, B. Zingg, A. Sakatos, S. H. Moghadam, H. U. Zeilhofer, and S. du Lac, "Glycinergic projection neurons of the cerebellum," *Journal of Neuroscience,* vol. 29, pp. 10104-10110, 2009.

[249] T. A. Blenkinsop and E. J. Lang, "Synaptic action of the olivocerebellar system on cerebellar nuclear spike activity," *J Neurosci,* vol. 31, pp. 14708-20, Oct 12 2011.

[250] S. T. Kitai, R. A. McCrea, R. J. Preston, and G. A. Bishop, "Electrophysiological and horseradish peroxidase studies of precerebellar afferents to the nucleus interpositus anterior. I. Climbing fiber system," *Brain Res,* vol. 122, pp. 197-214, Feb 18 1977.

[251] H. Lu, B. Yang, and D. Jaeger, "Cerebellar Nuclei Neurons Show only small excitatory responses to optogenetic olivary stimulation in transgenic mice: In vivo and in vitro studies," *Frontiers in neural circuits,* vol. 10, 2016.

[252] N. Zheng and I. M. Raman, "Synaptic inhibition, excitation, and plasticity in neurons of the cerebellar nuclei," *Cerebellum,* vol. 9, pp. 56-66, Mar 2010.

[253] V. Gauck and D. Jaeger, "The control of rate and timing of spikes in the deep cerebellar nuclei by inhibition," *J Neurosci,* vol. 20, pp. 3006-16, Apr 15 2000.

[254] S. Dykstra, J. D. Engbers, T. M. Bartoletti, and R. W. Turner, "Determinants of rebound burst responses in rat cerebellar nuclear neurons to physiological stimuli," *J Physiol,* vol. 594, pp. 985-1003, Feb 15 2016.

[255] A. R. Best and W. G. Regehr, "Inhibitory regulation of electrically coupled neurons in the inferior olive is mediated by asynchronous release of GABA," *Neuron,* vol. 62, pp. 555-65, May 28 2009.

[256] C. H. Chen, R. Fremont, E. E. Arteaga-Bracho, and K. Khodakhah, "Short latency cerebellar modulation of the basal ganglia," *Nature Neuroscience,* vol. 17, pp. 1767-1775, 2014.

[257] D. G. Tervo, B. Y. Hwang, S. Viswanathan, T. Gaj, M. Lavzin, K. D. Ritola, *et al.*, "A Designer AAV Variant Permits Efficient Retrograde Access to Projection Neurons," *Neuron,* vol. 92, pp. 372-382, Oct 19 2016.

[258] B. D. Houck and A. L. Person, "Cerebellar loops: a review of the nucleocortical pathway," *Cerebellum,* vol. 13, pp. 378-85, Jun 2014.

[259] Z. Gao, M. Proietti-Onori, Z. Lin, M. M. Ten Brinke, H. J. Boele, J. W. Potters, *et al.*, "Excitatory Cerebellar Nucleocortical Circuit Provides Internal Amplification during Associative Conditioning," *Neuron,* vol. 89, pp. 645-657, 2016.

[260] J. Y. Lin, "A user's guide to channelrhodopsin variants: features, limitations and future developments," *Exp Physiol,* vol. 96, pp. 19-25, Jan 2011.

[261] A. I. Chen, C. N. Nguyen, D. R. Copenhagen, S. Badurek, L. Minichiello, B. Ranscht, *et al.*, "TrkB (tropomyosin-related kinase B) controls the assembly and maintenance of GABAergic synapses in the cerebellar cortex," *J Neurosci,* vol. 31, pp. 2769-80, Feb 23 2011.

[262] F. Andermann and S. F. Berkovic, "Idiopathic generalized epilepsy with generalized and other seizures in adolescence," *Epilepsia,* vol. 43, pp. 317-320, 2001.

[263] O. C. Snead, 3rd, "Basic mechanisms of generalized absence seizures," *Ann. Neurol.,* vol. 37, pp. 146-57, 1995.

[264] A. Clemente-Perez, S. R. Makinson, B. Higashikubo, S. Brovarney, F. S. Cho, A. Urry, *et al.*, "Distinct thalamic reticular cell types differentially modulate normal and pathological cortical rhythms," *Cell Reports,* vol. 19, pp. 2130-2142, 2017.

[265] R. Apps and M. Garwicz, "Anatomic and physiological foundations of cerebellar processing," *Nat. Rev. Neurosci.,* vol. 6, pp. 297-311, 2005.

[266] J. C. Eccles, "The development of the cerebellum of vertebrates in relation to the control of movement," *Naturwissenschaften,* vol. 56, pp. 525-534, 1969.

[267] V. Gauck and D. Jaeger, "The contribution of NMDA and AMPA conductances to the control of spiking in neurons of the deep cerebellar nuclei," *J. Neurosci.,* vol. 23, pp. 8109-8118, 2003.

[268] H. J. Groenewegen, J. Voogd, and S. L. Freedman, "The parasagittal zonation within the olivocerebellar projection. II. Climbing fiber distribution in the intermediate and hemispheric parts of cat cerebellum," *J. Comp. Neurol.,* vol. 183, pp. 551-601, 1979.

[269] J. J. Van der Want, L. Wiklund, M. Guegan, T. J. Ruigrok, and J. Voogd, "Anterograde tracing of the rat olivocerebellar system with Phaseolus vulgaris leucoagglutinin (PHA-L). Demonstration of climbing fiber collateral innervation of the cerebellar nuclei," *J. Comp. Neurol.,* vol. 288, pp. 1-18, 1989.

[270] V. Chan-Palay, "Fine structure of labelled axons in the cerebellar cortex and nuclei of rodents and primates after intraventricular infusions with tritiated serotonin," *Anat. Embryol. (Berl.),* vol. 148, pp. 235-265, 1975.

[271] V. Chan-Palay, "Fine structure of labelled axons in the cerebellar cortex and nuclei of rodents and primates after intraventricular infusions with tritiated serotonin," *Anatomy and Embryology,* vol. 148, pp. 235-265, 1975.

[272] H. J. Groenewegen, J. Voogd, and S. L. Freedman, "The parasagittal zonation within the olivocerebellar projection. II. Climbing fiber distribution in the intermediate and hemispheric parts of cat cerebellum," *Journal of Comparative Neurology,* vol. 183, pp. 551-601, 1979.

[273] J. J. Van der Want, L. Wiklund, M. Guegan, T. J. Ruigrok, and J. Voogd, "Anterograde tracing of the rat olivocerebellar system with Phaseolus vulgaris leucoagglutinin (PHA-L). Demonstration of climbing fiber collateral innervation of the cerebellar nuclei," *Journal of Comparative Neurology,* vol. 288, pp. 1-18, 1989.

[274] H. Jahnsen, "Electrophysiological characteristics of neurones in the guinea-pig deep cerebellar nuclei in vitro," *Journal of Physiology,* vol. 372, pp. 129-147, 1986.

[275] D. Mouginot and B. H. Gahwiler, "Characterization of synaptic connections between cortex and deep nuclei of the rat cerebellum in vitro," *Neuroscience,* vol. 64, pp. 699-712, 1995.

[276] C. I. de Zeeuw, F. E. Hoebeek, and M. Schonewille, "Causes and consequences of oscillations in the cerebellar cortex," *Neuron,* vol. 58, pp. 655-658, 2008.

[277] M. M. Ten Brinke, H. J. Boele, J. K. Spanke, J. W. Potters, K. Kornysheva, P. Wulff*, et al.*, "Evolving Models of Pavlovian Conditioning: Cerebellar Cortical Dynamics in Awake Behaving Mice," *Cell Reports,* vol. 13, pp. 1977-1988, 2015.

[278] A. Devor and Y. Yarom, "Electrotonic coupling in the inferior olivary nucleus revealed by simultaneous double patch recordings," *Journal of Neurophysiology,* vol. 87, pp. 3048-3058, 2002.

[279] J. P. Welsh, B. Chang, M. E. Menaker, and S. A. Aicher, "Removal of the inferior olive abolishes myoclonic seizures associated with a loss of olivary serotonin," *Neuroscience,* vol. 82, pp. 879-897, 1998.

[280] B. N. Harding and S. G. Boyd, "Intractable seizures from infancy can be associated with dentato-olivary dysplasia," *Journal of neurological sciences,* vol. 104, pp. 157-165, 1991.

[281] Y. Saito, M. Hayashi, Y. Miyazono, T. Shimogama, and K. Ohno, "Arthrogryposis multiplex congenita with callosal agenesis and dentato-olivary dysplasia.," *Brain & Development,* vol. 28, pp. 261-264, 2006.

[282] C. F. Fletcher, C. M. Lutz, T. N. O'Sullivan, J. D. Shaughnessy, R. Hawkes, W. N. Frankel*, et al.*, "Absence epilepsy in tottering mutant mice is associated with calcium channel defects," *Cell,* vol. 87, pp. 607-617, 1996.

[283] J. L. Noebels and R. L. Sidman, "Spike-Wave and focal motor seizures in the mutant mouse tottering," *Science,* vol. 204, pp. 1334-1336, 1979.

[284] C. Stosiek, O. Garaschuk, K. Holthoff, and A. Konnerth, "In vivo two-photon calcium imaging of neuronal networks.," *Proc Natl Acad Sci U S A,* vol. 100, pp. 7319-7324, 2003.

[285] S. Tsutsumi, M. Yamazaki, T. Miyazaki, M. Watanabe, K. Sakimura, M. Kano*, et al.*, "Structure-function relationships between aldolase C/zebrin II expression and complex spike synchrony in the cerebellum.," *J. Neurosci.,* vol. 35, pp. 843-852, 2015.

[286] J. R. de Gruijl, T. M. Hoogland, and C. I. de Zeeuw, "Behavioral correlates of complex spike synchrony in cerebellar microzones," *Journal of Neuroscience,* vol. 34, pp. 8937-8947, 2014.

[287] G. R. Holt, W. R. Softky, C. Koch, and R. J. Douglas, "Comparison of discharge variability in vitro and in vivo in cat visual cortex neurons," *J. Neurophys.,* vol. 75, pp. 1806-1814, 1996.

[288] C. I. de Zeeuw, J. I. Simpson, C. C. Hoogenraad, N. Galjart, S. K. Koekkoek, and T. J. Ruigrok, "Microcircuitry and function of the inferior olive," *Trends in Neurosciences,* vol. 21, pp. 391-400, 1998.

[289] J. Voogd and T. J. Ruigrok, "The organization of the corticonuclear and olivocerebellar climbing fiber projections to the rat cerebellar vermis: the congruence of projection zones and the zebrin pattern," *Journal of neurocytology,* vol. 33, pp. 5-21, 2004.

[290] C. I. de Zeeuw and M. M. Ten Brinke, "Motor Learning and the Cerebellum," *Cold Spring Harbor perspectives in biology,* vol. 7, 2015.

[291] S. Choi, E. Yu, D. Kim, F. J. Urbano, V. Makarenko, H. S. Shin*, et al.*, "Subthreshold membrane potential oscillations in inferior olive neurons are dynamically regulated by P/Q- and T-type calcium channels: a study in mutant mice," *Journal of Physiology,* vol. 588, pp. 3031-3043, 2010.

[292] J. J. White and R. V. Sillitoe, "Genetic silencing of olivocerebellar synapses causes dystonia-like behaviour in mice," *Nature Communications,* vol. 8, 2017.

[293] S. Khosrovani, R. S. van der Giessen, C. I. de Zeeuw, and M. T. De Jeu, "In vivo mouse inferior olive neurons exhibit heterogeneous subthreshold oscillations and spiking patterns," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 104, pp. 15911-15916, 2007.

[294] R. llinás, "Inferior olive oscillation as the temporal basis for motricity and oscillatory reset as the basis for motor error correction," *Neuroscience,* vol. 162, pp. 797-804, 2009.

[295] R. llinás and Y. Yarom, "Properties and distribution of ionic conductances generating electroresponsiveness of mammalian inferior olivary neurones in vitro," *Journal of Physiology,* vol. 315, 1981.

[296] P. Bazzigaluppi, T. J. Ruigrok, P. Saisan, C. I. de Zeeuw, and M. T. de Jeu, "Properties of the nucleo-olivary pathway: an in vivo whole-cell patch clamp study," *PLoS One,* vol. 7, p. e46360, 2012.

[297] P. Svensson, F. Bengtsson, and G. Hesslow, "Cerebellar inhibition of inferior olivary transmission in the decerebrate ferret," *Experimental Brain Research,* vol. 168, pp. 241-253, 2006.

[298] M. C. Anderson, E. Y. Chung, and M. H. Van Woert, "Effect of inferior olive lesion on seizure threshold in the rat," *Life Sciences,* vol. 40, pp. 2367-2375, 1987.

[299] M. C. Anderson, E. Y. Chung, and M. H. Van Woert, "Strychnine seizure potentiation by azaspirodecanedione anxiolytics in rats," *European Journal of Pharmacology,* vol. 155, pp. 279-283, 1988.

[300] M. C. Anderson, E. Y. Chung, and M. H. Van Woert, "The effects of inferior olive lesion on strychnine seizure," *Brain research bulletin,* vol. 25, pp. 599-603, 1990.

[301] A. Badura, M. Schonewille, K. Voges, E. Galliano, N. Renier, Z. Gao*, et al.*, "Climbing fiber input shapes reciprocity of Purkinje cell firing," *Neuron,* vol. 78, pp. 700-713, 2013.

[302] C. I. De Zeeuw and A. S. Berrebi, "Postsynaptic targets of Purkinje cell terminals in the cerebellar and vestibular nuclei of the rat," *Eur. J. Neurosci.,* vol. 7, pp. 2322-2333, 1995.

[303] W. Graf, J. I. Simpson, and C. S. Leonard, "Spatial organization of visual messages of the rabbit's cerebellar flocculus. II. Complex and simple spike responses of Purkinje cells.," *Journal of Neurophysiology,* vol. 60, pp. 2091-2121, 1988.

[304] V. Yakhnitsa and N. H. Barmack, "Antiphasic Purkinje cell responses in mouse uvula-nodulus are sensitive to static roll-tilt and topographically organized," *Neuroscience,* vol. 143, pp. 615-626, 2006.

[305] F. E. Hoebeek, J. S. Stahl, A. M. Van Alphen, M. Schonewille, C. Luo, M. Rutteman, *et al.*, "Increased noise level of purkinje cell activities minimizes impact of their modulation during sensorimotor control," *Neuron,* vol. 45, pp. 953-965, 2005.

[306] M. Ito, M. Yoshida, and K. Obata, "Monosynaptic inhibition of the intracerebellar nuclei induced from the cerebellar cortex," *Experientia,* vol. 20, pp. 575-576, 1964.

[307] M. Ito, M. Yoshida, K. Obata, N. Kawai, and M. Udo, "Inhibitory control of intracerebellar nuclei by the purkinje cell axons," *Experimental Brain Research,* vol. 10, pp. 64-80, 1970.

[308] C. D. Aizenman and D. J. Linden, "Rapid, synaptically driven increases in the intrinsic excitability of cerebellar deep nuclear neurons," *Nature Neuroscience,* vol. 3, pp. 109-111, 2000.

[309] K. Alvina, G. Ellis-Davies, and K. Khodakhah, "T-type calcium channels mediate rebound firing in intact deep cerebellar neurons," *Neuroscience,* vol. 158, pp. 635-641, 2009.

[310] J. D. Engbers, D. Anderson, R. Tadayonnejad, W. H. Mehaffey, M. L. Molineux, and R. W. Turner, "Distinct roles for I(T) and I(H) in controlling the frequency and timing of rebound spike responses," *Journal of Physiology,* vol. 589, pp. 5391-5413, 2011.

[311] S. S. Feng and D. Jaeger, "The role of SK calcium-dependent potassium currents in regulating the activity of deep cerebellar nucleus neurons: a dynamic clamp study," *Cerebellum,* vol. 7, pp. 542-546, 2008.

[312] S. S. Feng, R. Lin, V. Gauck, and D. Jaeger, "Gain control of synaptic response function in cerebellar nuclear neurons by a calcium-activated potassium conductance," *Cerebellum,* vol. 12, pp. 692-706, 2013.

[313] V. Gauck, M. Thomann, D. Jaeger, and A. Borst, "Spatial distribution of low- and high-voltage-activated calcium currents in neurons of the deep cerebellar nuclei," *Journal of Neuroscience,* vol. 21, 2001.

[314] J. R. Pugh and I. M. Raman, "Potentiation of mossy fiber EPSCs in the cerebellar nuclei by NMDA receptor activation followed by postinhibitory rebound current," *Neuron,* vol. 51, pp. 113-123, 2006.

[315] T. Sangrey and D. Jaeger, "Analysis of distinct short and prolonged components in rebound spiking of deep cerebellar nucleus neurons," *European Journal of Neuroscience,* vol. 32, pp. 1646-1657, 2010. [316] N. Zheng and I. Raman, "Ca currents activated by spontaneous firing and synaptic disinhibition in neurons of the cerebellar nuclei," *Journal of Neuroscience,* vol. 29, pp. 9826-9838, 2009.

[317] D. Aksenov, N. Serdyukova, K. Irwin, and V. Bracha, "GABA neurotransmission in the cerebellar interposed nuclei: involvement in classically conditioned eyeblinks and neuronal activity," *Journal of Neurophysiology,* vol. 91, pp. 719-727, 2004.

[318] D. H. Heck, C. I. de Zeeuw, D. Jaeger, K. Khodakhah, and A. L. Person, "The neuronal code(s) of the cerebellum," *Journal of Neuroscience,* vol. 33, pp. 17603-17609, 2013.

[319] F. E. Hoebeek, S. Khosrovani, L. Witter, and C. I. De Zeeuw, "Purkinje cell input to cerebellar nuclei in tottering: ultrastructure and physiology," *Cerebellum,* vol. 7, pp. 547-558, 2008.

[320] R. N. Holdefer, J. C. Houk, and L. E. Miller, "Movement-related discharge in the cerebellar nuclei persists after local injections of GABA(A) antagonists," *Journal of Neurophysiology,* vol. 93, pp. 35-43, 2005.

[321] M. Najac and I. Raman, "Synaptic excitation by climbing fibre collaterals in the cerebellar nuclei of juvenile and adult mice," *Journal of Physiology,* vol. 595, pp. 6703-6718, 2017.

[322] Y. Wu and I. Raman, "Facilitation of mossy fibre-driven spiking in the cerebellar nuclei by the synchrony of inhibition," *Journal of Physiology,* vol. 595, pp. 5245-5264, 2017.

[323] A. T. Berg, S. F. Berkovic, M. J. Brodie, J. Buchhalter, J. H. Cross, W. van Emde Boas*, et al.*, "Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009," *Epilepsia,* vol. 51, pp. 676-685, 2010 2010.

[324] P. Jallon, P. Loiseau, and J. Loiseau, "Newly diagnosed unprovoked epileptic seizures: presentation at diagnosis in CAROLE study. Coordination Active du Réseau Observatoire Longitudinal de l' Epilepsie," *Epilepsia,* vol. 42, pp. 464-475, 2001.

[325] J. T. Paz, A. S. Bryant, K. Peng, L. Fenno, O. Yizhar, W. N. Frankel*, et al.*, "A new mode of corticothalamic transmission revealed in the Gria4(-/-) model of absence epilepsy," *Nat. Neurosci.,* vol. 14, pp. 1167-1173, 2011.

[326] H. Blumenfeld and D. A. McCormick, "Corticothalamic inputs control the pattern of activity generated in thalamocortical networks," *J. Neurosci.,* vol. 20, pp. 5153-5162, 2000.

[327] H. Blumenfeld and D. A. McCormick, "Corticothalamic inputs control the pattern of activity generated in thalamocortical networks," *Journal of Neuroscience,* vol. 20, pp. 5153-5162, 2000.

[328] J. R. Huguenard and D. A. McCormick, "Thalamic synchrony and dynamic regulation of global forebrain oscillations," *Trends Neurosci.,* vol. 30, pp. 350-356, 2007.

[329] I. S. Cooper, M. Riklan, S. Watkins, and D. McLellan, "Safety and efficacy of chronic stimulation," *Neurosurgery,* vol. 1, pp. 203-205, 1977.

[330] A. Bava, T. Manzoni, and A. Urbano, "Effects of fastiginal stimulation on thalamic neurones belonging to the diffuse projection system," *Brain research,* vol. 4, pp. 378-380, 1967.

[331] S. F. Sawyer, J. M. Tepper, and P. M. Groves, "Cerebellar-responsive neurons in the thalamic ventroanterior-ventrolateral complex of rats: light and electron microscopy," *Neuroscience,* vol. 63, pp. 725-745, 1994.

[332] S. Tokuda, B. J. Beyer, and W. N. Frankel, "Genetic complexity of absence seizures in substrains of C3H mice," *Genes Brain Behav.,* vol. 8, pp. 283-289, 2009.

[333] C. Marescaux, M. Vergnes, and A. Depaulis, "Genetic absence epilepsy in rats from Strasbourg - a review," *J. Neural Transm. Suppl.,* vol. 35, pp. 37-69, 1992.

[334] B. J. Kaplan, T. N. Seyfried, and G. H. Glaser, "Spontaneous polyspike discharges in an epileptic mutant mouse (tottering)," *Experimental Neurology,* vol. 66, pp. 577-586, 1979.

[335] M. Loureiro, T. Cholvin, J. Lopez, N. Merienne, A. Latreche, B. Cosquer*, et al.*, "The ventral midline thalamus (reuniens and rhomboid nuclei) contributes to the persistence of spatial memory in rats," *J. Neurosci.,* vol. 32, pp. 9947-9959, 2012.

[336] C. E. Rasmussen and C. K. I. Williams, "Gaussian processes for machine learning," ed. Cambridge, MA, U.S.A.: The MIT Press, 2006.

[337] C. Bandt and B. Pompe, "Permutation entropy: a natural complexity measure for time series," *Phys. Rev. Lett.,* vol. 88, p. 174102, 2002.

[338] I. Osorio, M. G. Frei, and S. B. Wilkinson, "Real-time automated detection and quantitative analysis of seizures and short-term prediction of clinical onset," *Epilepsia,* vol. 39, pp. 615-627, 1998.

[339] J. M. H. Karel, S. A. P. Haddad, S. Hiseni, R. L. Westra, W. A. Serdijn, and R. L. M. Peeters, "Implementing wavelets in continuous-time analog circuits with dynamic range optimization," *IEEE Transactions on Circuits and Systems - I,* vol. 59, pp. 229-242, 2012.

[340] G. van Luijtelaar, F. Y. Onat, and M. J. Gallagher, "Animal models of absence epilepsies: what do they model and do sex and sex hormones matter?," *Neurobiology of Disease,* vol. 72, pp. 167-179, 2014.

[341] G. van Luijtelaar and M. Zobeiri, "Progress and outlooks in a genetic absence epilepsy model (WAG/Rij)," *Current medicinal chemistry,* vol. 21, pp. 704-721, 2014.

[342] O. Akman, S. L. Moshé, and A. S. Galanopoulou, "Sex-specific consequences of early life seizures," *Neurobiology of Disease,* vol. 72, pp. 153-166, 2014.

[343] J. L. Nathanson, Y. Yanagawa, K. Obata, and E. M. Callaway, "Preferential labeling of inhibitory and excitatory cortical neurons by endogenous tropism of adeno-associated virus and lentivirus vectors," *Neuroscience,* vol. 161, pp. 441-450, 2009.

[344] J. A. Heckroth, "Quantitative morphological analysis of the cerebellar nuclei in normal and lurcher mutant mice. I. Morphology and cell number," *Journal of Comparative Neurology,* vol. 343, pp. 173-182, 1994.

[345] P. Alva, L. Kros, O. H. J. Eelkman Rooda, C. I. De Zeeuw, R. Adams, N. Davey, *et al.*, "Combining machine learning and simulations of a morphologically realistic model to study modulation of neuronal activity in cerebellar nuclei during absence epilepsy," *BMC Neuroscience,* vol. 15, p. 39, 2014.

[346] P. Alva, L. Kros, R. Maex, C. I. De Zeeuw, R. Adams, N. Davey, *et al.*, "A potential role for the cerebellar nuclei in absence seizures " *BMC Neuroscience,* vol. 14, p. 170, 2013.

[347] N. C. Rowland and D. Jaeger, "Coding of tactile response properties in the rat deep cerebellar nuclei," *Journal of Neurophysiology,* vol. 94, pp. 1236-1251, 2005.

[348] T. D. Aumann, J. A. Rawson, D. I. Finkelstein, and M. K. Horne, "Projections from the lateral and interposed cerebellar nuclei to the thalamus of the rat: a light and electron microscopic study using single and double anterograde labelling," *Journal of Comparative Neurology,* vol. 349, pp. 165-181, 1994.

[349] M. Steriade, "Two channels in the cerebellothalamocortical system," *Journal of Comparative Neurology,* vol. 354, pp. 57-70, 1995.

[350] P. Andersen, J. C. Eccles, and T. A. Sears, "The ventro-basal complex of the thalamus: types of cells, their responses and their functional organization," *J. Physiol.,* vol. 174, pp. 370-399, 1964.

[351] A. Destexhe, D. Contreras, and M. Steriade, "Mechanisms underlying the synchronizing action of corticothalamic feedback through inhibition of thalamic relay cells," *Journal of Neurophysiology,* vol. 79, pp. 999-1016, 1998.

[352] Y. Zhang, M. Mori, D. L. Burgess, and J. L. Noebels, "Mutations in high-voltage-activated calcium channel genes stimulate low-voltage-activated currents in mouse thalamic relay neurons," *Journal of Neuroscience,* vol. 22, pp. 6362-6371, 2002.

[353] V. Chan-Palay, *Cerebellar Dentate Nucleus: Organization, Cytology and Transmitters*. Heidelberg: Springer-Verlag, 1977.

[354] B. Y. Chow and E. S. Boyden, "Optogenetics and translational medicine," *Science Translational Medicine,* vol. 5, p. 177ps5, 2013.

[355] M. Creed, V. J. Pascoli, and C. Luscher, "Addiction therapy. Refining deep brain stimulation to emulate optogenetic treatment of synaptic pathology," *Science,* vol. 347, pp. 659-664, 2015.

[356] J. J. Engel, *Outcome with respect to epileptic seizures*. New York: Raven Press, 1987.

[357] R. S. Fisher, "Therapeutic devices for epilepsy," *Annals of Neurology,* vol. 71, pp. 157-168, 2012.

[358] K. M. Hartikainen, L. Sun, M. Polvivaara, M. Brause, K. Lehtimaki, J. Haapasalo*, et al.*, "Immediate effects of deep brain stimulation of anterior thalamic nuclei on executive functions and emotion-attention interaction in humans," *Journal of Clinical and experimental neuropsychology,* vol. 36, pp. 540-550, 2014.

[359] J. X. Brooks, J. Carriot, and K. E. Cullen, "Learning to expect the unexpected: rapid updating in primate cerebellum during voluntary self-motion," *Nature Neuroscience,* vol. 18, pp. 1310-1317, 2015.

[360] M. Manto, J. M. Bower, A. B. Conforto, J. M. Delgado-Garcia, S. N. da Guarda, M. Gerwig, *et al.*, "Consensus paper: roles of the cerebellum in motor control--the diversity of ideas on cerebellar involvement in movement," *Cerebellum,* vol. 11, pp. 457-487, 2012.

[361] P. Angaut, F. Cicirata, and M. R. Pantó, "An autoradiographic study of the cerebellopontine projections from the interposed and lateral cerebellar nuclei in the rat," *Journal fur Hirnforschung,* vol. 26, pp. 463-470, 1985.

[362] P. Angaut, F. Cicirata, and F. Serapide, "Topographic organization of the cerebellothalamic projections in the rat. An autoradiographic study," *Neuroscience,* vol. 15, pp. 389-401, 1985.

[363] M. Bentivoglio and H. G. Kuypers, "Divergent axon collaterals from rat cerebellar nuclei to diencephalon, mesencephalon, medulla oblongata and cervical cord. A fluorescent double retrograde labeling study," *Experimental Brain Research,* vol. 46, pp. 339-356, 1982.

[364] D. Cohen, W. W. Chambers, and J. M. Sprague, "Experimental study of the efferent projections from the cerebellar nuclei to the brainstem of the cat," *Journal of Comparative Neurology,* vol. 109, pp. 233-259, 1958.

[365] H. Daniel, J. M. Billard, P. Angaut, and C. Batini, "The interposito-rubrospinal system. Anatomical tracing of a motor control pathway in the rat," *Neuroscience Research,* vol. 5, pp. 87-112, 1987.

[366] A. J. Haroian, L. C. Massopust, and P. A. Young, "Cerebellothalamic projections in the rat: an autoradiographic and degeneration study," *Journal of Comparative Neurology,* vol. 197, pp. 217-236, 1981.

[367] E. Kuramoto, T. Furuta, K. C. Nakamura, T. Unzai, H. Hioki, and T. Kaneko, "Two types of thalamocortical projections from the motor thalamic nuclei of the rat: a single neuron-tracing study using viral vectors," *Cerebral Cortex,* vol. 19, pp. 2065-2077, 2009.

[368] E. Kuramoto, S. Ohno, T. Furuta, T. Unzai, Y. R. Tanaka, H. Hioki*, et al.*, "Ventral medial nucleus neurons send thalamocortical afferents more widely and more preferentially to layer 1 than neurons of the ventral anterior-ventral lateral nuclear complex in the rat," *Cerebral Cortex,* vol. 25, pp. 221-235, 2015.

[369] M. Deschenes, J. Bourassa, V. D. Douan, and A. Parent, "A single-cell study of the axonal projections arising from the posterior intralaminar thalamic nuclei in the rat," *European Journal of Neuroscience,* vol. 8, pp. 329-343, 1996.

[370] M. Deschenes, J. Bourassa, and A. Parent, "Striatal and cortical projections of single neurons from the central lateral thalamic nucleus in the rat," *Neuroscience,* vol. 72, pp. 679-687, 1996.

[371] M. Parent and A. Parent, "Single-axon tracing and three-dimensional reconstruction of centre median-parafascicular thalamic neurons in primates," *Journal of Comparative Neurology,* vol. 481, pp. 127-144, 2005.

[372] Y. B. Saalmann, " Intralaminar and medial thalamic influence on cortical synchrony, information transmission and cognition," *Frontiers in systems neuroscience,* vol. 8, 2014.

[373] F. Clascá, P. Rubio-Garrido, and D. Jabaudon, "Unveiling the diversity of thalamocortical neuron subtypes," *European Journal of Neuroscience,* vol. 35, pp. 1524-1532, 2012.

[374] L. Monconduit and L. Villanueva, "The lateral ventromedial thalamic nucleus spreads nociceptive signals from the whole body surface to layer I of the frontal cortex," *European Journal of Neuroscience,* vol. 21, pp. 3395-3402, 2005.

[375] Y. Yamamoto, T. Noda, A. Samejima, and H. Oka, "A morphological investigation of thalamic neurons by intracellular HRP staining in cats," *Journal of Comparative Neurology,* vol. 236, pp. 331-347, 1985.

[376] R. Arai, D. M. Jacobowitz, and S. Deura, "Distribution of calretinin, calbindin-D28k, and parvalbumin in the rat thalamus. Brain research bulletin," *Brain research bulletin,* vol. 33, pp. 595-614, 1994.

[377] A. L. Bodor, K. Giber, Z. Rovó, I. Ulbert, and L. Acsady, "Structural correlates of efficient GABAergic transmission in the basal ganglia-thalamus pathway," *Journal of Neuroscience,* vol. 28, pp. 3090-3102, 2008.

[378] E. G. Jones and S. H. Hendry, "Differential Calcium Binding Protein Immunoreactivity Distinguishes Classes of Relay Neurons in Monkey Thalamic Nuclei," *European Journal of Neuroscience,* vol. 1, pp. 222-246, 1989.

[379] E. Kuramoto, F. Fujiyama, K. C. Nakamura, Y. Tanaka, H. Hioki, and T. Kaneko, "Complementary distribution of glutamatergic cerebellar and GABAergic basal ganglia afferents to the rat motor thalamic nuclei," *European Journal of Neuroscience,* vol. 33, pp. 95-109, 2011.

[380] L. Rispal-Padel and A. Grangetto, "The cerebello-thalamo-cortical pathway. Topographical investigation at the unitary level in the cat," *Experimental Brain Research,* vol. 28, pp. 101-123, 1977.

[381] P. Rubio-Garrido, F. Perez-de-Manzo, C. Porrero, M. J. Galazo, and F. Clascá, "Thalamic input to distal apical dendrites in neocortical layer 1 is massive and highly convergent," *Cerebral Cortex,* vol. 19, pp. 2380-2395, 2009.

[382] J. D. Schmahmann and J. C. Sherman, "The cerebellar cognitive affective syndrome," *Brain,* vol. 121, pp. 561-579, 1998.

[383] C. J. Stoodley and C. Limperopoulos, "Structure-function relationships in the developing cerebellum: Evidence from early-life cerebellar injury and neurodevelopmental disorders," *Seminars in fetal & neonatal medicine,* vol. 21, pp. 356-364, 2016.

[384] S. S. Wang, A. D. Kloth, and A. Badura, "The cerebellum, sensitive periods, and autism," *Neuron,* vol. 83, pp. 518-532, 2014.

[385] S. Peter, M. M. Ten Brinke, J. Stedehouder, C. M. Reinelt, B. Wu, H. Zhou, *et al.*, "Dysfunctional cerebellar Purkinje cells contribute to autism-like behaviour in Shank2-deficient mice," *Nature Communications,* vol. 7, 2016.

[386] P. T. Tsai, C. Hull, Y. Chu, E. Greene-Colozzi, A. R. Sadowski, J. M. Leech, *et al.*, "Autistic-like behaviour and cerebellar dysfunction in Purkinje cell Tsc1 mutant mice," *Nature,* vol. 488, pp. 647-651, 2012.

[387] D. Popa, M. Spolidoro, R. D. Proville, N. Guyon, L. Belliveau, and C. Léna, "Functional role of the cerebellum in gamma-band synchronization of the sensory and motor cortices," *J. Neurosci.,* vol. 33, pp. 6552-6556, 2013.

[388] Z. V. Guo, H. K. Inagaki, K. Daie, S. Druckmann, C. R. Gerfen, and K. Svoboda, "Maintenance of persistent activity in a frontal thalamocortical loop," *Nature,* vol. 545, pp. 181-186, 2017.

[389] A. Bava, F. Cicirata, R. Giuffrida, S. Licciardello, and M. R. Pantó, "Electrophysiologic properties and nature of ventrolateral thalamic nucleus neurons reactive to converging inputs of paleo- and neocerebellar origin," *Experimental Neurology,* vol. 91, pp. 1-12, 1986.

[390] T. A. Ferreira, A. V. Blackman, J. Oyrer, S. Jayabal, A. J. Chung, A. J. Watt, *et al.*, "Neuronal morphometry directly from bitmap images," *Nature Methods,* vol. 11, pp. 982-984, 2014.

[391] P. Lavallée, N. Urbain, C. Dufresne, H. Bokor, L. Acsády, and M. Deschenes, "Feedforward inhibitory control of sensory information in higher-order thalamic nuclei," *Journal of Neuroscience,* vol. 25, pp. 7489-7498, 2005.

[392] Z. Rovó, I. Ulbert, and L. Acsády, "Drivers of the primate thalamus," *Journal of Neuroscience,* vol. 32, pp. 17894-17908, 2012.

[393] S. M. Sherman and R. W. Guillery, "On the actions that one nerve cell can have on another: distinguishing "drivers" from "modulators"," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 95, pp. 7121-7126, 1998.

[394] A. Groh, C. P. de Kock, V. C. Wimmer, B. Sakmann, and T. Kuner, "Driver or coincidence detector: modal switch of a corticothalamic giant synapse controlled by spontaneous activity and short-term depression," *Journal of Neuroscience,* vol. 28, pp. 9652-9663, 2008.

[395] I. Reichova and S. M. Sherman, "Somatosensory corticothalamic projections: distinguishing drivers from modulators," *Journal of Neurophysiology,* vol. 92, pp. 2185-2197, 2004.

[396] M. Seol and T. Kuner, "Ionotropic glutamate receptor GluA4 and T-type calcium channel Cav 3.1 subunits control key aspects of synaptic transmission at the mouse L5B-POm giant synapse," *European Journal of Neuroscience,* vol. 42, pp. 3033-3044, 2015.

[397] X. B. Liu, A. Munoz, and E. G. Jones, "Changes in subcellular localization of metabotropic glutamate receptor subtypes during postnatal development of mouse thalamus," *Journal of Comparative Neurology,* vol. 395, pp. 450-465, 1998.

[398] S. Ohno, E. Kuramoto, T. Furuta, H. Hioki, Y. R. Tanaka, F. Fujiyama, *et al.*, "A morphological analysis of thalamocortical axon fibers of rat posterior thalamic nuclei: a single neuron tracing study with viral vectors," *Cerebral Cortex,* vol. 22, pp. 2840-2857, 2012.

[399] C. Asanuma, W. T. Thach, and E. G. Jones, "Distribution of cerebellar terminations and their relation to other afferent terminations in the ventral lateral thalamic region of the monkey," *Brain research,* vol. 286, pp. 237-265, 1983.

[400] T. D. Aumann and M. K. Horne, "A comparison of the ultrastructure of synapses in the cerebello-rubral and cerebello-thalamic pathways in the rat," *Neuroscience Letters,* vol. 211, pp. 175-178, 1996.

[401] M. Steriade, V. Apostol, and G. Oakson, "Control of Unitary Activities in Cerebellothalamic Pathway During Wakefulness and Synchronized Sleep," *Journal of Neurophysiology,* vol. 34, pp. 389-413, 1971.

[402] M. E. Bickford, N. Zhou, T. E. Krahe, G. Govindaiah, and W. Guido, "Retinal and Tectal "Driver-Like" Inputs Converge in the Shell of the Mouse Dorsal Lateral Geniculate Nucleus," *Journal of Neuroscience,* vol. 35, pp. 10523-10534, 2015.

[403] L. R. Kelly, J. Li, W. B. Carden, and M. E. Bickford, "Ultrastructure and synaptic targets of tectothalamic terminals in the cat lateral posterior nucleus," *Journal of Comparative Neurology,* vol. 464, pp. 472-486, 2003.

[404] S. P. Masterson, J. Li, and M. E. Bickford, "Synaptic organization of the tectorecipient zone of the rat lateral posterior nucleus," *Journal of Comparative Neurology,* vol. 515, pp. 647-663, 2009.

[405] A. Rollenhagen and J. H. Lubke, "The morphology of excitatory central synapses: from structure to function," *Cell and tissue research,* vol. 326, pp. 221-237, 2006.

[406] B. Zikopoulos and H. Barbas, "Parallel driving and modulatory pathways link the prefrontal cortex and thalamus," *PLoS One,* vol. 2, 2007.

[407] B. Zikopoulos and H. Barbas, "Pathways for emotions and attention converge on the thalamic reticular nucleus in primates," *Journal of Neuroscience,* vol. 32, pp. 5338-5350, 2012.

[408] Y. Geinisman, "Perforated axospinous synapses with multiple, completely partitioned transmission zones: probable structural intermediates in synaptic plasticity," *Hippocampus,* vol. 3, pp. 417-433, 1993.

[409] S. Chung, X. Li, and S. B. Nelson, "Short-term depression at thalamocortical synapses contributes to rapid adaptation of cortical sensory responses in vivo," *Neuron,* vol. 34, pp. 437-446, 2002.

[410] R. A. Mease, P. Krieger, and A. Groh, "Cortical control of adaptation and sensory relay mode in the thalamus," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 111, pp. 6798-6803, 2014.

[411] A. N. Viaene, I. Petrof, and S. M. Sherman, "Activation requirements for metabotropic glutamate receptors," *Neuroscience Letters,* vol. 541, pp. 67-72, 2013.

[412] M. Herkenham, "Laminar organization of thalamic projections to the rat neocortex," *Science,* vol. 207, pp. 532-535, 1980.

[413] N. Yamawaki and G. M. Shepherd, "Synaptic circuit organization of motor corticothalamic neurons," *Journal of Neuroscience,* vol. 35, pp. 2293-2307, 2015.

[414] J. H. Goldberg, M. A. Farries, and M. S. Fee, "Basal ganglia output to the thalamus: still a paradox," *Trends in Neurosciences,* vol. 36, pp. 695-705, 2013.

[415] L. L. Glenn, J. Hada, J. P. Roy, M. Deschenes, and M. Steriade, "Anterograde tracer and field potential analysis of the neocortical layer I projection from nucleus ventralis medialis of the thalamus in cat," *Neuroscience,* vol. 7, pp. 1861-1877, 1982.

[416] H. W. Berendse and H. J. Groenewegen, "Restricted cortical termination fields of the midline and intralaminar thalamic nuclei in the rat," *Neuroscience,* vol. 42, pp. 73-102, 1991.

[417] A. Gummadavelli, J. E. Motelow, N. Smith, Q. Zhan, N. D. Schiff, and H. Blumenfeld, "Thalamic stimulation to improve level of consciousness after seizures: evaluation of electrophysiology and behavior," *Epilepsia,* vol. 56, pp. 114-124, 2015.

[418] D. A. McCormick and T. Bal, "Sleep and arousal: thalamocortical mechanisms," *Annual review of neuroscience,* vol. 20, pp. 185-215, 1997.

[419] K. Giber, M. A. Diana, V. Plattner, G. P. Dugué, H. Bokor, C. V. Rousseau, *et al.*, " A subcortical inhibitory signal for behavioral arrest in the thalamus," *Nature Neuroscience,* vol. 18, pp. 562-568, 2015.

[420] J. W. Miller, B. C. Gray, and M. E. Bardgett, " Characterization of cholinergic regulation of seizures by the midline thalamus," *Neuropharmacology,* vol. 31, pp. 349-356, 1992.

[421] J. Buee, J. M. Deniau, and G. Chevalier, "Nigral modulation of cerebello-thalamo-cortical transmission in the ventral medial thalamic nucleus," *Experimental Brain Research,* vol. 65, pp. 241-244, 1986.

[422] K. Franklin and G. Paxinos, *The mouse brain in stereotactic coordinates, Compact*, 2nd ed.: Academic Press, 2001.

[423] A. Aarabi, F. Wallois, and R. Grebe, "Does spatiotemporal synchronization of EEG change prior to absence seizures?," *Brain research,* vol. 1188, pp. 207-221, 2008.

[424] M. P. Beenhakker and J. R. Huguenard, "Neurons that fire together also conspire together: is normal sleep circuitry hijacked to generate epilepsy?," *Neuron,* vol. 62, pp. 612-632, 2009.

[425] J. R. Cressman, G. Ullah, J. Ziburkus, S. J. Schiff, and E. Barreto, "The influence of sodium and potassium dynamics on excitability, seizures, and the stability of persistent states," *Journal of Computational Neuroscience,* vol. 26, pp. 159-170, 2009.

[426] L. Danober, C. Deransart, A. Depaulis, M. Vergnes, and C. Marescaux, "Pathophsyiological mechanisms of genetic absence epilepsy in the rat," *Progress in neurobiology,* vol. 55, pp. 27-57, 1998.

[427] C. J. Stam, "Modern network science of neurological disorders," *Nature Reviews Neuroscience,* vol. 15, pp. 683-695, 2014.

[428] A. Adebimpe, A. Aarabi, E. Bourel-Ponchel, M. Mahmoudzadeh, and F. Wallois, "Functional Brain Dysfunction in Patients with Benign Childhood Epilepsy as Revealed by Graph Theory," *PLoS One,* vol. 10, 2015.

[429] E. Krook-Magnuson and I. Soltesz, "Beyond the hammer and the scalpel: selective circuit control for the epilepsies," *Nature Neuroscience,* vol. 18, pp. 331-338, 2015.

[430] C. B. Schafer and F. E. Hoebeek, "Convergence of primary sensory cortex and cerebellar nuclei pathways in the whisker system," *Neuroscience,* vol. 368, pp. 229-239, 2018.

[431] J. Mattis, K. M. Tye, E. A. Ferenczi, C. Ramakrishnan, D. J. O'Shea, R. Prakash, *et al.*, "Principles for applying optogenetic tools derived from direct comparative analysis of microbial opsins," *Nature Methods,* vol. 9, pp. 159-172, 2011.

[432] T. Houben, I. C. Loonen, S. M. Baca, M. Schenke, J. H. Meijer, M. D. Ferrari, *et al.*, "Optogenetic induction of cortical spreading depression in anesthetized and freely behaving mice. Journal of cerebral blood flow and metabolism," *Journal of Cerebral Blood Flow and metabolism,* vol. 37, pp. 1641-1655, 2017.

[433] A. J. Kundishora, A. Gummadavelli, C. Ma, M. Liu, C. McCafferty, N. D. Schiff, *et al.*, "Restoring conscious arousal during focal limbic seizures with deep brain stimulation," *Cerebral Cortex,* vol. 27, pp. 1964-1975, 2017.

[434] K. Franklin and G. Paxinos, *The mouse brain in stereotactic coordinates*, 2nd edition ed.: Academic Press, 2001.

[435] T. M. Teune, J. Van der Burg, J. Van der Moer, and T. J. Ruigrok, "Topography of cerebellar nuclear projections to the brain stem in the rat," *Prog. Brain Res.,* vol. 124, pp. 141-172, 2000.

[436] J. Chen and A. R. Kriegstein, "A GABAergic projection from the zona incerta to cortex promotes cortical neuron development," *Science,* vol. 350, pp. 554-558, 2015.

[437] I. Song, D. Kim, S. Choi, M. Sun, Y. Kim, and H. S. Shin, "Role of the A1G T-type calcium channel in spontaneous absence seizures in mutant mice," *Journal of Neuroscience,* vol. 24, pp. 5249-5257, 2004.

[438] A. Depaulis and S. Charpier, "Pathophysiology of absence epilepsy: Insights from genetic models," *Neuroscience Letters,* vol. 17, pp. 30141-30146, 2017.

[439] L. Kros, S. L. Lindeman, O. H. J. Eelkman Rooda, C. I. de Zeeuw, and F. E. Hoebeek, "Synchronicity and rhythmicity of Purkinje cell firing during generalized spike-and-wave discharges in a natural mouse model of absence epilepsy," *Frontiers in cellular neuroscience,* in press.

[440] L. Rispal-Padel and J. Latreille, "The organization of projections from the cerebellar nuclei to the contralateral motor cortex in the cat," *Experimental Brain Research,* vol. 19, pp. 36-60, 1974.

[441] M. Yoshida, K. Yajima, and M. Uno, "Different activation of the 2 types of the pyramidal tract neurones through the cerebello-thalamocortical pathway," *Experientia,* vol. 22, pp. 331-332, 1966.

[442] M. M. Halassa and L. Acsády, "Thalamic Inhibition: Diverse Sources, Diverse Scales," *Trends in Neurosciences,* vol. 39, pp. 680-693, 2016.

[443] J. T. Paz, M. Chavez, S. Saillet, J. M. Deniau, and S. Charpier, "Activity of ventral medial thalamic neurons during absence seizures and modulation of cortical paroxysms by the nigrothalamic pathway," *Journal of Neuroscience,* vol. 27, pp. 929-941, 2007.

[444] V. C. Bomben, I. Aiba, J. Qian, M. D. Mark, S. Herlitze, and J. L. Noebels, "Isolated P/Q Calcium Channel Deletion in Layer VI Corticothalamic Neurons Generates Absence Epilepsy," *Journal of Neuroscience,* vol. 36, pp. 405-418, 2016.

[445] C. Yu, D. Derdikman, S. Haidarliu, and E. Ahissar, "Parallel thalamic pathways for whisking and touch signals in the rat," *PLoS Biology,* vol. 4, p. e124, 2006.

[446] P. Marien, H. Ackermann, M. Adamaszek, C. H. Barwood, A. Beaton, J. Desmond*, et al.*, "Consensus paper: Language and the cerebellum: an ongoing enigma," *Cerebellum,* vol. 13, pp. 386-410, 2014.

[447] J. F. Poulet, L. M. Fernandez, S. Crochet, and C. C. Petersen, "Thalamic control of cortical states," *Nature Neuroscience,* vol. 15, pp. 370-372, 2012.

[448] E. van Diessen, S. J. Diederen, K. P. Braun, F. E. Jansen, and C. J. Stam, "Functional and structural brain networks in epilepsy:What have we learned?," *Epilepsia,* vol. 54, pp. 1855-1865, 2013.

[449] L. Claes, J. Del-Favero, B. Ceulemans, L. Lagae, C. Van Broeckhoven, and P. De Jonghe, "De Novo Mutations in the Sodium-Channel Gene SCN1A Cause Severe Myoclonic Epilepsy of Infancy," *American journal of human genetics,* vol. 68, pp. 1327-1332, 2001.

[450] L. R. Claes, L. Deprez, A. Suls, J. Baets, K. Smets, T. Van Dyck, *et al.*, "The SCN1A variant database: a novel research and diagnostic tool," *Human mutation,* vol. 30, pp. 904-920, 2009.

[451] C. S. Cheah, F. H. Yu, R. E. Westenbroek, F. K. Kalume, J. C. Oakley, G. B. Potter, *et al.*, "Specific deletion of NaV1.1 sodium channels in inhibitory interneurons causes seizures and premature death in a mouse model of Dravet syndrome," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 109, pp. 14646-14651, 2012.

[452] I. Ogiwara, H. Miyamoto, N. Morita, N. Atapour, E. Mazaki, I. Inoue, *et al.*, "Nav1.1 localizes to axons of parvalbumin-positive inhibitory interneurons: a circuit basis for epileptic seizures in mice carrying an Scn1a gene mutation," *Journal of Neuroscience,* vol. 27, pp. 5903-5914, 2007.

[453] C. Tai, Y. Abe, R. E. Westenbroek, T. Scheuer, and W. A. Catterall, "Impaired excitability of somatostatin- and parvalbumin-expressing cortical interneurons in a mouse model of Dravet syndrome," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 111, pp. 3139-3148, 2014.

[454] F. H. Yu, M. Mantegazza, R. E. Westenbroek, C. A. Robbins, F. K. Kalume, K. A. Burton, *et al.*, "Reduced sodium current in GABAergic interneurons in a mouse model of severe myoclonic epilepsy in infancy," *Nature Neuroscience,* vol. 9, pp. 1142-1149, 2006.

[455] M. Rubinstein, S. Han, C. Tai, R. E. Westenbroek, A. Hunker, T. Scheuer, *et al.*, "Dissecting the phenotypes of Dravet syndrome by gene deletion," *Brain,* vol. 138, pp. 2219-2233, 2015.

[456] L. A. Papale, C. D. Makinson, J. Christopher Ehlen, S. Tufik, M. J. Decker, K. N. Paul, *et al.*, "Altered sleep regulation in a mouse model of SCN1A-derived genetic epilepsy with febrile seizures plus (GEFS+)," *Epilepsia,* vol. 54, pp. 625-634, 2013.

[457] F. Crick, "Function of the thalamic reticular complex: the searchlight hypothesis," *Proc. Natl. Acad. Sci. U. S. A.,* vol. 81, pp. 4586-4590, 1984.

[458] L. J. Gentet and D. Ulrich, "Strong, reliable and precise synaptic connections between thalamic relay cells and neurones of the nucleus reticularis in juvenile rats," *Journal of Physiology,* vol. 546, pp. 801-811, 2003.

[459] C. R. Houser, J. E. Vaughn, R. P. Barber, and E. Roberts, "GABA neurons are the major cell type of the nucleus reticularis thalami," *Brain Research,* vol. 200, pp. 341-354, 1980.

[460] J. T. Paz, C. A. Christian, I. Parada, D. A. Prince, and J. R. Huguenard, "Focal Cortical Infarcts Alter Intrinsic Excitability and Synaptic Excitation in the Reticular Thalamic Nucleus," *Journal of Neuroscience,* vol. 30, pp. 5465-5479, 2010.

[461] S. J. Slaght, N. Leresche, J. M. Deniau, V. Crunelli, and S. Charpier, "Activity of Thalamic Reticular Neurons during Spontaneous Genetically Determined Spike and Wave Discharges," *Journal of Neuroscience,* vol. 22, pp. 2323-2334, 2002.

[462] F. Ferrarelli and G. Tononi, "The Thalamic Reticular Nucleus and Schizophrenia," *Schizophrenia Bulletin,* vol. 37, pp. 306-315, 2011.

[463] Z. W. Zhang, J. D. Zak, and H. Liu, "MeCP2 Is Required for Normal Development of GABAergic Circuits in the Thalamus," *Journal of Neurophysiology,* vol. 103, pp. 2470-2481, 2010.

[464] M. M. Huntsman, D. M. Porcello, G. E. Homanics, T. M. DeLorey, and J. R. Huguenard, "Reciprocal Inhibitory Connections and Network Synchrony in the Mammalian Thalamus," *Science,* vol. 283, 1999.

[465] P. Barthó, A. Slézia, F. Mátyás, L. Faradzs-Zade, I. Ulbert, K. D. Harris, *et al.*, "Ongoing Network State Controls the Length of Sleep Spindles via Inhibitory Activity," *Neuron,* vol. 82, pp. 1367-1379, 2014.

[466] F. K. Kalume, J. Oakley, R. E. Westenbroek, J. Gile, H. O. de la Iglesia, T. Scheuer, *et al.*, "Sleep impairment and reduced interneuron excitability in a mouse model of Dravet Syndrome," *Neurobiology of Disease,* vol. 77, pp. 141-154, 2015.

[467] H. Jahnsen and R. Llinás, "Electrophysiological properties of guinea-pig thalamic neurones: an in vitro study," *Journal of Physiology,* vol. 349, pp. 205-226, 1984.

[468] M. Bazhenov, I. Timofeev, M. Steriade, and T. Sejnowski, "Spiking-Bursting Activity in the Thalamic Reticular Nucleus Initiates Sequences of Spindle Oscillations in Thalamic Networks," *Journal of Neurophysiology,* vol. 84, pp. 1076-1087, 2000.

[469] M. Deschenes, M. Paradis, J. P. Roy, and M. Steriade, "Electrophysiology of neurons of lateral thalamic nuclei in cat: resting properties and burst discharges," *Journal of Neurophysiology,* vol. 51, pp. 1196-1219, 1984.

[470] M. Steriade, L. Domich, G. Oakson, and M. Deschenes, "The deafferented reticular thalamic nucleus generates spindle rhythmicity," *Journal of Neurophysiology,* vol. 57, pp. 260-273, 1987.

[471] S. M. Sherman, "A wake-up call from the thalamus," *Nature Neuroscience,* vol. 4, pp. 344-346, 2001.

[472] S. M. Sherman, "Tonic and burst firing: dual modes of thalamocortical relay," *Trends in Neurosciences,* vol. 24, pp. 122-126, 2001.

[473] L. Cueni, M. Canepari, R. Luján, Y. Emmenegger, H. Watanabe, C. T. Bond, *et al.*, "T-type Ca2+ channels, SK2 channels and SERCAs gate sleep-related oscillations in thalamic dendrites," *Nature Neuroscience,* vol. 11, pp. 683-692, 2008.

[474] R. D. Wimmer, S. Astori, C. T. Bond, Z. Rovó, J. Y. Chatton, J. P. Adelman, *et al.*, "Sustaining Sleep Spindles through Enhanced SK2-Channel Activity Consolidates Sleep and Elevates Arousal Threshold," *Journal of Neuroscience,* vol. 32, pp. 13917-13928, 2012.

[475] M. I. Botez, E. Attig, and J. L. Vezina, "Cerebellar atrophy in epileptic patients," *The Canadian Journal of neurological sciences,* vol. 15, pp. 299-303, 1988.

[476] J. Milton and P. Jung, in *Epilepsy as a dynamic disease*, ed Berlin-Heidelberg: Springer-Verlag, 2003, pp. 69-82.

[477] R. M. Kelly and P. L. Strick, "Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate," *Journal of Neuroscience,* vol. 23, pp. 8432-8444, 2003.

[478] C. J. Stoodley, J. P. MacMore, N. Makris, J. C. Sherman, and J. D. Schmahmann, "Location of lesion determines motor vs. cognitive consequences in patients with cerebellar stroke," *NeuroImage. Clinical.,* vol. 12, pp. 765-775, 2016.

[479] G. Avanzini, F. Panzica, and M. de Curtis, "The role of the thalamus in vigilance and epileptogenic mechanisms," *Clinical Neurophysiology,* vol. 111, pp. S19-S26, 2000.

[480] G. K. Kostopoulos, "Spike-and-wave discharges of absence seizures as a transformation of sleep spindles: the continuing development of a hypothesis," *Clinical Neurophysiology,* vol. 111, pp. S27-S38, 2000.

[481] F. Picard, P. Mégevand, L. Minotti, P. Kahane, P. Ryvlin, M. Seeck, *et al.*, "Intracerebral recordings of nocturnal hyperkinetic seizures: demonstration of a longer duration of the pre-seizure sleep spindle," *Clinical Neurophysiology,* vol. 118, pp. 928-939, 2007.

[482] T. Futami, M. Kano, S. Sento, and Y. Shinoda, "Synaptic organization of the cerebello-thalamo-cerebral pathway in the cat. III. Cerebellar input to corticofugal neurons destined for different subcortical nuclei in areas 4 and 6," *Neuroscience Research,* vol. 3, pp. 321-344, 1986.

[483] H. Jorntell and C. F. Ekerot, "Topographical organization of projections to cat motor cortex from nucleus interpositus anterior and forelimb skin," *Journal of Physiology,* vol. 514, pp. 551-566, 1999.

[484] J. Na, S. Kakei, and Y. Shinoda, "Cerebellar input to corticothalamic neurons in layers V and VI in the motor cortex," *Neuroscience Research,* vol. 28, pp. 77-91, 1997.

[485] K. Sasaki, Y. Kawaguchi, H. Oka, M. Sakai, and N. Mizuno, "Electrophysiological studies on the cerebellocerebral projections in monkeys," *Experimental Brain Research,* vol. 24, pp. 495-507, 1976.

[486] L. F. Koziol, D. Budding, N. Andreasen, S. D'Arrigo, S. Bulgheroni, H. Imamizu, *et al.*, "Consensus paper: the cerebellum's role in movement and cognition.," *Cerebellum,* vol. 13, pp. 151-177, 2014.

[487] R. P. Dum, C. Li, and P. L. Strick, "Motor and nonmotor domains in the monkey dentate," *Annals of the New York Academy of Sciences,* vol. 978, pp. 289-301, 2002.

[488] R. P. Dum and P. L. Strick, "An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex," *Journal of Neurophysiology,* vol. 89, pp. 634-639, 2003.

[489] H. J. Park, H. Furmaga, J. Cooperrider, J. T. Gale, K. B. Baker, and A. G. Machado, "Modulation of Cortical Motor Evoked Potential After Stroke During Electrical Stimulation of the Lateral Cerebellar Nucleus," *Brain stimulation,* vol. 8, pp. 1043-1048, 2015.

[490] R. A. Badawy, J. M. Curatolo, M. Newton, S. F. Berkovic, and R. A. Macdonell, "Changes in cortical excitability differentiate generalized and focal epilepsy," *Annals of Neurology,* vol. 61, pp. 324-331, 2007.

[491] P. Manganotti, L. G. Bongiovanni, G. Fuggetta, G. Zanette, and A. Fiaschi, "Effects of sleep deprivation on cortical excitability in patients affected by juvenile myoclonic epilepsy: a combined transcranial magnetic stimulation and EEG study," *Journal of neurology, neurosurgery, and psychiatry,* vol. 77, pp. 56-60, 2006.

[492] D. Kraus, G. Naros, R. Bauer, F. Khademi, M. T. Leao, U. Ziemann, *et al.*, "Brain State-Dependent Transcranial Magnetic Closed-Loop Stimulation Controlled by Sensorimotor Desynchronization Induces Robust Increase of Corticospinal Excitability," *Brain stimulation,* vol. 9, pp. 415-424, 2016.

[493] H. Schulz, T. Ubelackter, J. Keil, N. Muller, and N. Weisz, "Now I am ready-now i am not: The influence of pre-TMS oscillations and corticomuscular coherence on motor-evoked potentials," *Cerebral Cortex,* vol. 24, pp. 1708-1719, 2014.

[494] M. Takemi, Y. Masakado, M. Liu, and J. Ushiba, "Event-related desynchronization reflects downregulation of intracortical inhibition in human primary motor cortex," *Journal of Neurophysiology,* vol. 110, pp. 1158-1166, 2013.

[495] D. Weiss, R. Klotz, R. B. Govindan, M. Scholten, G. Naros, A. Ramos-Murguialday, *et al.*, "Subthalamic stimulation modulates cortical motor network activity and synchronization in Parkinson's disease," *Brain,* vol. 138, pp. 679-693, 2015.

[496] C. S. Lin, M. A. Nicolelis, J. S. Schneider, and J. K. Chapin, "A Major Direct GABAergic Pathway from Zona Incerta to Neocortex," *Science,* vol. 248, pp. 1553-1556, 1990.

[497] N. Urbain and M. Deschenes, "Motor cortex gates vibrissal responses in a thalamocortical projection pathway," *Neuron,* vol. 56, pp. 714-725, 2007.

[498] P. Barthó, T. F. Freund, and L. Acsády, "Selective GABAergic innervation of thalamic nuclei from zona incerta," *European Journal of Neuroscience,* vol. 16, pp. 999-1014, 2002.

[499] P. L. Strick, R. P. Dum, and J. A. Fiez, "Cerebellum and nonmotor function," *Annual review of neuroscience,* vol. 32, pp. 413-434, 2009.

[500] A. T. Berg, J. T. Langfitt, F. M. Testa, S. R. Levy, F. DiMario, M. Westerveld, *et al.*, "Global cognitive function in children with epilepsy: A community-based study," *Epilepsia,* vol. 49, pp. 608-614, 2008.

[501] A. Austin, J. P. Lin, R. Selway, K. Ashkan, and T. Owen, "What parents think and feel about deep brain stimulation in paediatric secondary dystonia including cerebral palsy: A qualitative study of parental decision-making," *European Journal of Pediatric Neurology,* vol. 21, pp. 185-192, 2017.

[502] K. M. Fiest, T. T. Sajobi, and S. Wiebe, " Epilepsy surgery and meaningful improvements in quality of life: results from a randomized controlled trial," *Epilepsia,* vol. 55, pp. 886-892, 2014.

[503] L. Frings, A. Schulze-Bonhage, J. Spreer, and K. Wagner, "Remote effects of hippocampal damage on default network connectivity in the human brain," *Journal of neurology,* vol. 256, pp. 2021-2029, 2009.

[504] A. B. Waites, R. S. Briellmann, M. M. Saling, D. F. Abbott, and G. D. Jackson, " Functional connectivity networks are disrupted in left temporal lobe epilepsy," *Annals of Neurology,* vol. 59, pp. 335-343, 2006.

[505] S. Jiang, C. Luo, J. Gong, R. Peng, S. Ma, S. Tan, *et al.*, "Aberrant Thalamocortical Connectivity in Juvenile Myoclonic Epilepsy," *International journal of neural systems,* vol. epub ahead of print, 2017.

[506] K. B. Baker, D. Schuster, J. Cooperrider, and A. G. Machado, "Deep brain stimulation of the lateral cerebellar nucleus produces frequency-specific alterations in motor evoked potentials in the rat in vivo," *Experimental Neurology,* vol. 226, pp. 259-264, 2010.

[507] A. G. Machado, K. B. Baker, D. Schuster, R. S. Butler, and A. Rezai, "Chronic electrical stimulation of the contralesional lateral cerebellar nucleus enhances recovery of motor function after cerebral ischemia in rats," *Brain research,* vol. 1280, pp. 107-116, 2009.

[508] A. G. Machado, J. Cooperrider, H. Furmaga, K. B. Baker, H. J. Park, Z. Chen, *et al.*, "Chronic 30-Hz deep cerebellar stimulation coupled with training enhances post-ischemia motor recovery and peri-infarct synaptophysin expression in rodents," *Neurosurgery,* vol. 73, pp. 344-353, 2013.

[509] G. F. Molnar, A. Sailer, C. A. Gunraj, D. I. Cunic, R. A. Wennberg, A. M. Lozano, *et al.*, "Changes in motor cortex excitability with stimulation of anterior thalamus in epilepsy," *Neurology,* vol. 66, pp. 566-571, 2006.

[510] G. F. Molnar, A. Sailer, C. A. Gunraj, A. E. Lang, A. M. Lozano, and R. Chen, "Thalamic deep brain stimulation activates the cerebellothalamocortical pathway," *Neurology,* vol. 63, pp. 907-909, 2004.

[511] I. A. Prescott, J. O. Dostrovsky, E. Moro, M. Hodaie, A. M. Lozano, and W. D. Hutchison, "Levodopa enhances synaptic plasticity in the substantia nigra pars reticulata of Parkinson's disease patients," *Brain,* vol. 132, pp. 309-318, 2009.

[512] T. D. Aumann, S. J. Redman, and M. K. Horne, "Long-term potentiation across rat cerebello-thalamic synapses in vitro," *Neuroscience Letters,* vol. 287, pp. 151-155, 2000.

[513] P. Arcelli, C. Frassoni, M. C. Regondi, S. De Biasi, and R. Spreafico, "GABAergic neurons in mammalian thalamus: a marker of thalamic complexity?," *Brain research bulletin,* vol. 42, pp. 27-37, 1997.

[514] R. Spreafico, C. Frassoni, P. Arcelli, G. Battaglia, R. J. Wenthold, and S. De Biasi, "Distribution of AMPA selective glutamate receptors in the thalamus of adult rats and during postnatal development. A light and ultrastructural immunocytochemical study," *Brain research. Developmental brain research,* vol. 82, pp. 231-244, 1994.

[515] M. Steriade, E. G. Jones, and D. A. McCormick, *Thalamus*. Oxford: Elsevier, 1997.

[516] I. S. Cooper and A. R. Upton, "Use of chronic cerebellar stimulation for disorders of disinhibition," *Lancet,* vol. 1, pp. 595-600, 1978.

[517] I. S. Cooper, A. R. Upton, and I. Amin, "Chronic cerebellar stimulation (CCS) and deep brain stimulation (DBS) in involuntary movement disorders," *Applied neurophysiology,* vol. 45, pp. 209-217, 1982.

[518] A. R. Upton, I. S. Cooper, M. Springman, and I. Amin, "Suppression of seizures and psychosis of limbic system origin by chronic stimulation of anterior nucleus of the thalamus," *International journal of neurology,* vol. 19-20, pp. 223-230, 1985-1986.

[519] M. Lowenthal and V. Horsley, "On the relations between the cerebellar and other centers," *Proceedings of the Royal Society of London,* vol. 61, pp. 20-25, 1897.

[520] C. S. Sherrington, "Double (antidrome) conduction in the central nervous system," *Proceedings of the Royal Society of London,* vol. 61, pp. 243-246, 1897.

[521] J. C. Eccles, R. Llinás, and K. Sasaki, "The excitatory synaptic action of climbing fibres on the Purkinje cells of the cerebellum," *J. Physiol.,* vol. 182, pp. 268-296, 1966.

[522] R. Llinás, "The cortex of the cerebellum," *Scientific American,* vol. 232, pp. 56-71, 1975.

[523] C. G. Begley and L. M. Ellis, "Drug development: Raise standards for preclinical cancer research," *Nature,* vol. 483, pp. 531-533, 2012.

[524] O. S. Collaboration, "Estimating the reproducibility of psychological science," *Science,* vol. 349, 2015.

[525] J. P. Ioannidis, D. B. Allison, C. A. Ball, I. Coulibaly, X. Cui, A. C. Culhane*, et al.*, "Repeatability of published microarray gene expression analyses " *Nature Genetics,* vol. 41, pp. 149-155, 2009.

[526] D. M. Andrade, C. Hamani, A. M. Lozano, and R. A. Wennberg, "Dravet syndrome and deep brain stimulation: seizure control after 10 years of treatment," *Epilepsia,* vol. 51, pp. 1314-1316, 2010.

[527] S. Chabardés, P. Kahane, L. Minotti, A. Koudsie, E. Hirsch, and A. L. Benabid, "Deep brain stimulation in epilepsy with particular reference to the subthalamic nucleus," *Epileptic Disorders,* vol. 4, pp. S83-S93, 2002.

[528] J. Rosenow, K. Das, R. L. Rovit, and W. T. Couldwell, "Irving S. Cooper and His Role in Intracranial Stimulation for Movement Disorders and Epilepsy," *Stereotact. Funct. Neurosurg.,* vol. 78, pp. 95-112, 2002.

A

Appendix

Summary

Nederlandse Samenvatting

Curriculum Vitae

List of Publications

Terugblik

Summary

The primary goal of this dissertation was to further elucidate questions regarding the neural mechanism of cerebellar impact on thalamic nuclei and thalamus' primary output structure the cerebral cortex. To do so key experiments were performed using amongst others optogenetics in mice having an epileptic phenotype.

In **Chapter 2** we provide an overview of cell-specific markers usable for optogenetics in both cerebellar cortex and nuclei. This high-detail description of technical issues and solutions makes it an efficient guideline for starting and experienced researchers regarding cerebellar research.

Where chapter 2 ends, **Chapter 3** continues with a re-evaluation of the therapeutic potential of cerebellar stimulation in epilepsy. This chapter gives an introduction of the impact of cerebellum and its main output structure cerebellar nuclei on thalamocortical networks. Further we give directions on how to optimize the potential impact by adjusting stimulation parameters such as frequency, regularity and synchronicity.

In **Chapter 4** we show that a substantial portion of Purkinje cells show increase simple and complex spike activity combined with increased synchronicity for adjacent and remote Purkinje cells during GSWDs. Furthermore the activation of complex spike activity indirectly implicates widespread changes in olivary firing during seizures.

Chapter 5 embodies crucial evidence for this dissertation in which we show that CN neurons are potent modulators of GSWDs in thalamocortical networks. This is an evolution of the old idea that manipulation of cerebellar cortex activity intervenes with epileptic seizures into the fact that not cerebellar cortex but cerebellar nuclei seem easier to target and stronger in their manipulation of thalamocortical activity. An obvious next question is: How are CN neurons capable of suppressing seizures? In **Chapter 6 and 7** we test the hypothesis that CN neurons can cause desynchronization in the thalamus by first showing *in vitro* differences between post synaptic responses upon cerebellar terminal stimulation in different thalamic nuclei. Second we confirm this evidence *in vivo* where we find different response types in different thalamic cells recorded in different thalamic nuclei.

Finally we test in **Chapter 8** if CN manipulation can also dampen seizures in a much more severe mouse model of generalized epilepsy; i.e. the Dravet mouse. It turns out that either electrical CN stimulation or different thalamic nuclei stimulation sites are not capable of seriously controlling the generalized convulsive seizures. In the end our colleagues show that manipulation using a SK blocker is more capable.

Samenvatting

Deze dissertatie richt zich op het verder uitwerken van de vraag wat de achterliggende mechanisms zijn waarmee het cerebellum haar invloed uitoefent op thalamocorticale netwerken. Om dit te bereiken hebben we gebruik gemaakt van verschillende technieken, waaronder optogenetica, in muizen met en zonder epilepsie.

In **Hoofdstuk 2** wordt beschreven hoe verschillende cel-specifieke markers gebruikt kunnen worden in combinatie met optogenetica voor de manipulatie van cerebellaire schors en kernen. We bespreken technische moeilijkheden en oplossingen wat maakt dat het een mooi uitgangswerk is voor de beginnende en meer ervaren onderzoeker.

Hierop voortbordurend is **Hoofdstuk 3** ontstaan waarin de therapeutische (on) mogelijkheden van cerebellaire stimulatie bij epilepsie besproken worden. Een introductie als voorbereiding op het volgende hoofdstuk wordt gegeven over de impact van het cerebellum op thalamocorticale netwerken en we geven suggesties hoe deze impact gemaximaliseerd kan worden door middel van verschillende stimulatie parameters aan te passen.

In Hoofdstuk 4 laten we zien da teen substandieel deel van de Purkinje cellen een verhoogde simplex en complex spike activiteit heeft gedurende GSWDs. Dit gaat dan ook nog eens gepaard met een verhoogde synchroniciteit tussen aanliggende en op afstand zijnde collega Purkinje cellen. Indirect geeft dit aan dat de verhoogde complex spike activiteit gezien kan worden als veranderingen in het vuurgedrag van een andere belangrijke hersenstructuur; de inferieure olijf.

Hoofdstuk 5 gaat over de kern van deze dissertatie waarin we bewijs leveren dat CN neuronen krachtige modulatoren van pathologische thalamocorticale oscillaties kunnen zijn. Een verandering in denken tov het oude idee dat juist de cerebellaire schors hier goed in zou zijn. seem easier to target and stronger in their manipulation of thalamocortical activity. Een logische vervolgvraag op hoofdstuk 5 is: Wat is het achterliggende mechanisme waarmee CN neuronen de epilepsie kunnen stoppen? Met andere woorden, wat is het effect van hun vuurgedrag op de thalamus en via de thalamus op de cerebrale schors. In **Hoofdstuk 6 en 7** testen we de hypothese dat CN neuronen thalamische neuronen kunnen desynchroniseren in hun vuurgedrag. Dit laten we eerst *in vitro* zien waarbij we in verschillende thalamische kernen verschillende sterkte in post-synaptische respons zien. Vervolgens blijkt dit ook *in vivo* waarbij er verschillende respons types lijken te zijn tussen verschillende cellen maar dat binnen dezelfde cel de respons wel hetzelfde blijft.

Als laatste testen we in **Hoofdstuk 8** of CN manipulatie ook seizures kan stoppen in een muis model met een ernstiger epileptisch phenotype; de Dravet muis. Het blijkt dat

zowel CN stimulatie als stimulatie van verschillende thalamische kernen niet in staat is de convulsieve aanvallen te stoppen.

Curriculum Vitae

Personal information

Name:	Oscar Hubert Jan Eelkman Rooda
Date of birth:	03 October 1988
Place of birth:	Rotterdam
Nationality:	Dutch

Education

01/2017 – today	**Resident Neurosurgery, ErasmusMC, Rotterdam**
08/2013 – 12/2016	PhD Student, Department of Neuroscience, Erasmus MC, Rotterdam
09/2006 – 07/2013	Medicine, Erasmus University Rotterdam Passed 'Cum Laude' for the 'Artsexamen'
08/2009 – 08/2011	Master of Science in Neuroscience, Erasmus University Rotterdam
9/2000 – 9/2006	Gymnasium, Johan van Oldenbarnevelt Amersfoort, the Netherlands Profile: Physics & Health

Teaching experience

2014 – 2016:	Supervision of medicine students (1), Master of Science students (2)
2013 – 2015:	Practical anatomy courses 1st and 3 rd year medical students (Brain, Heart and vasculature (24 hr per year)

Additional achievements

- Line Honours Round Texel 2015
- Best Poster Award ILAE Istanbul 2015

List of journal publications

M.L. van Veelen, **O.H.J. Eelkman Rooda**, T. De Jong, R. Dammers, L.N. van Adrichem, I.M. Mathijssen (2013) Results of early surgery for sagittal suture synostosis: long-term follow-up and the occurrence of raised intracranial pressure. *Child's Nervous System 29(6): 997-1005*

L. Kros, **O.H.J. Eelkman Rooda**, J.K. Spanke, P. Alva, M.N. van Dongen, A. Karapatis, E.A. Tolner, C. Strydis, N. Davey, B.H. Winkelman, M. Negrello, W.A. Serdijn, V. Steuber, A.M. van den Maagdenberg, C.I. de Zeeuw, F.E. Hoebeek (2015) Cerebellar output controls generalized spike-and-wave discharge occurrence. *Annals of Neurology 77(6): 1027-1049*

L. Kros, **O.H.J Eelkman Rooda**, C.I. de Zeeuw, F.E. Hoebeek (2015) Controlling cerebellar output to treat refractory epilepsy. *Trends in Neurosciences 38(12): 787-799*

L. Kros*, S. Lindeman*, **O.H.J. Eelkman Rooda***, P. Murugesan, L. Bina, L.W.J. Bosman, C.I. De Zeeuw* and F.E. Hoebeek* (*in press, Frontiers in Cellular Neuroscience*) Synchronicity and rhythmicity of Purkinje cell complex spike firing during GSWDs

S.V. Gornati*, C.B. Schäfer*, **O.H.J. Eelkman Rooda**, A. Nigg, C.I. De Zeeuw and F.E. Hoebeek (submitted for publication) Diversifying the cerebellar impact on thalamic nuclei

O.H.J. Eelkman Rooda*, L. Kros*, S.J. Faneyte, P.J. Holland, S.V. Gornati, T.B. Houben, H.J. Poelman, N.A. Jansen, E.A. Tolner, A.M.J.M. van den Maagdenberg, C.I. De Zeeuw and F.E. Hoebeek (Submitted) Single-pulse stimulation of cerebellar nuclei desynchronizes epileptic thalamus and cerebral cortex

S. Ritter-Makinson, A. Clemente-Perez, B. Higashikubo, A. Chkaidze, **O.H.J. Eelkman Rooda**, M.-C. Cornet, F.E. Hoebeek, M. Roberta Cilio, B. Delord, J.T. Paz (submitted for publication) Potassium current deficit in reticular thalamic cells causes epilepsy in SCN1A-deficient Dravet Syndrome

List of poster presentations

O.H.J Eelkman Rooda, L. Kros, C.I. de Zeeuw, F.E. Hoebeek (2013). Epileptic signatures in cerebello-thalamic activity of the Cacna1a^{tottering} mutant mouse. Federation of European Neurosciences (FENS) Winter School, Obergurgl, Austria.

O.H.J Eelkman Rooda, L. Kros, C.M.F. Dirven, C.I. de Zeeuw, F.E. Hoebeek (2014). Epileptic signatures in cerebello-thalamic activity of the Cacna1a^{tottering} mutant mouse. International Congress of Clinical Neurophysiology (ICCN), Berlin, Deutschland.

O.H.J Eelkman Rooda, L. Kros, C.I. de Zeeuw, F.E. Hoebeek (2014). Cerebellar output potently increases thalamic activity, disrupts oscillatory thalamo-cortical activity and stops epileptic absence seizures. FENS, Milan, Italy.

O.H.J Eelkman Rooda, L. Kros, N.A. Jansen, C.I. de Zeeuw, F.E. Hoebeek (2015). Cerebellar nuclei stimulation stops epileptic absence seizures in Cacna1a^{tottering} mouse mutants by overruling oscillatory activity in thalamic nuclei. 31st International Epilepsy Congress, Istanbul, Turkey.

O.H.J Eelkman Rooda, L. Kros, N.A. Jansen, C.I. de Zeeuw, F.E. Hoebeek (2016). Pharmacologic and optogenetic increase of cerebellar output prevents and overrules corticothalamic oscillations in epileptic mice. Gordon Research conference (GRC) 'Thalamocortical Interactions'. Ventura, California, USA.

Terugblik

Af!! Klaar! Dat was het dan. Nog een paar woorden en het is definitief af. Een raar moment? Ja zeker, maar daarom niet minder waardevol om deze terugblik op papier te zetten. Het geploeter in het lab, muizen die wel of niet meewerken, de trots van het eerste optogenetica experiment, het vinden van cerebellaire en thalamische kerncellen en de directe confrontaties met Matlab gecombineerd met het geroddel en de gezelligheid van koffie om 8u 's morgens met de bekende vroege vogels was in 1 woord geweldig. Maar of ik het weer zou doen? Het afmaken en de bijbehorende mentale pijn, al helemaal als je vervolgens in de kliniek werkt, staat ook vrij helder op m'n netvlies. En zoals elke promovendus to be weet, dit boek (behalve inleiding en discussie) was er echt nooit gekomen zonder de volgende mensen.

Met stipt op 1 en schier oneindig onoverbrugbare afstand tot de rest:

Prof. Dr. Freek Hoebeek, ik weet nog goed hoe ik in september 2009 jouw kamer binnenkwam en jij me vertelde over de toevalsbevinding die je had gedaan betreffende de vuurpatronen van cerebellaire kernen bij 'epilepsie-muizen'. Een en ander was snel beklonken en nu zijn we jaren verder waarin jij professor (verdiend!) bent geworden en ik deze promotie tot een eind heb gebracht. Trots en met veel plezier denk ik terug aan de afgelopen jaren. De werkbesprekingen, die met grote regelmaat diep in de nacht plaatsvonden, de congressen en het bier drinken om ook eens niet over werk te praten heeft de afgelopen jaren niet alleen maar een mentor-student karakter gegeven. **Veel dank**.

Prof. Dr. Clemens Dirven, als afdeling neurochirurgie zijn we aan een spannend traject (Deep Brain Stimulation) begonnen. Dat komt niet in de laatste plaats door jouw inzet tijdens mijn promotie traject. Veel dank dat ik binnen de neurochirurgie een kans heb gekregen.

Prof. Dr. Chris de Zeeuw, we hebben elkaar niet veel gesproken over het onderzoek zelf. Het vertrouwen wat daar vanuit ging en de wetenschap dat je er altijd staat op de momenten dat het nodig is, is heel veel waard voor een promovendus. Hopelijk gaan we ooit nog eens samen naar een wedstrijd van Ajax!

Erika & Mandy, jullie staan achterop, zoals afgesproken. Jullie grote mond en nog groter hart (altijd op de tong, man wat moet dat zwaar zijn) is zeldzaam. Mijn dank is oneindig.

Vanuit het lab is er nog een aantal mensen belangrijk geweest. In particular I would like to mention Elisa Galliano, Boeke van Beugen, Zhenyu Gao and Petra Plak. All of you are intelligent, meticulous and persistent which have had a profound impact on my academic rookie years. Thanks for hosting me in the warm Freek cake lab. Lieke Kros, de gemiddelde angry bird verbleekt bij de discussies die wij kunnen hebben. Desalniettemin heb ik bewondering voor de passie voor het onderzoek die je hebt en was dit boek zonder jou zeker een paar pagina's dunner of 1-2 jaar later pas uitgekomen. Dear Simo, ciao S, we started together in 2013 (Obergurugllg, still don't know how to pronounce this) not knowing the ~~pain~~ fun ahead of us. We shared many up's and down's these years but one thing is for sure; it would have been a lot more boring without you. Sade (nu jij nog!), Bibi (be ready voor het einde), Negah, Dick (namen blijven lastig), Tom, Gerard, Carmen, Nico, Hanna, Bas, Sverrir, Daniel, Huub, Henk Jan, Ilya, Sasa, Leonoor, Bastiaan, Sander, Elize (je hulp met EM is cruciaal geweest); dank voor het taart eten, tafelvoetballen en de (soms lastige) vragen over het onderzoek. Elise Buitenhuis en Loes Nijs; zonder jullie dondert de hele boel in elkaar. Het georganiseer voor al die Phd's en masterstudenten op de afdeling neurowetenschappen is een geruisloze maar absolute prestatie.

Dear Jeanne Paz, Stefanie Makinson and all lab members at the Gladstone Neurological Institute (San Francisco). Thanks for hosting me at your wonderful lab. Somewhere I hope we can collaborate again in the future, although I realize this will be a challenge ☺

Staf en assistenten van de afdeling neurochirurgie; met jullie samenwerken maakt dat ik elke dag met veel plezier kom.

Alex, Frans en Xavier. Jullie karakter eigenschappen vormen een waar kleurenpalet. Verschillend in alle opzichten en daardoor zulke goede vrienden. We hebben schitterende dingen (Texel 2015, WK 2010, En een reus als paranymf which says it all) meegemaakt en wat mij betreft nog veel meer. Voor jullie de wereld en nog een stuk!

Mannen van Huize Zeezicht, oneindige potjes fifa spelen, controllers tegen het plafond en naakt door de straat (10-0!); Samen in een pand wonen was schitterend. Ik had er een apart boek over kunnen schrijven.

Koen en Quirine, we go way back. Als basisschool rookies elke dag naar school gefietst. De wereld bleek zo veel groter te zijn dan het toen leek, maar wisten wij veel. Van school naar huis was al een avontuur op zich (5min). Een vriendschap die zo groen als gras begonnen is, maar door de jaren alleen maar groeit.

Mannen van JC Hoef, met Rotterdam als onze bakermat is het allemaal begonnen. Ondertussen kennen we elkaar al jaren en zitten we verspreid over de wereld. Dank voor alle avonden waardoor ik de boel de boel kon laten.

Lieve Em, Over en uit, Roger. Dat geldt nooit voor ons.

Lieve opa's en oma's, altijd zijn jullie geinteresseerd hoe het gaat. Dat het bijna onmogelijk was om uit te leggen weerhield jullie daar niet van. Het dreigement, dat als de verdediging niet voor kerst 2017 zou plaatsvinden mogelijk niet iedereen erbij zou zijn, leek mij bluf. Ik vind het schitterend dat jullie erbij zijn op deze dag.

Lieve Merlyn, René, Mees en Berber. Familie kan je niet kiezen zeggen ze. Wat als dat wel zo was? Ik zou jullie hebben gekozen.

Lieve Sebo Jan en Anky, dank voor jullie onvoorwaardelijke en jarenlange steun, liefde en interesse voor alles wat ik doe. Geen woorden voor de mazzel die ik met jullie heb... Lieve Steven, waar we jarenlang het kleine water 'de Potten' onveilig maakten in ons zeilbootje, waarvan we overigens dachten dat dat een heus Skutsje was, blijken kleine jongens echt groot te worden. Al jarenlang woon je in het buitenland, maar m'n kleine broertje zul je altijd blijven.

Vaak heb ik me afgevraagd of het er zou komen.

Het is er gekomen.