## **Functional decline**

Progressive functional decline in epilepsy is largely unexplained.

Whelan et al. formed the ENIGMA-Epilepsy consortium to understand factors that influence brain measures in epilepsy, pooling data from 24 research centres in 14 countries across Europe, USA and South America, Asia, and Australia. Structural brain measures were extracted from MRI brain scans across 2149 individuals with epilepsy, divided into four epilepsy subgroups including idiopathic generalized epilepsies (n = 367), mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE; left, n = 415; right, n = 339), and all other epilepsies in aggregate (n = 1026), and compared to 1727 matched healthy controls.

They ranked brain structures in order of greatest differences between patients and controls, by metaanalysing effect sizes across 16 subcortical and 68 cortical brain regions. They also tested effects of duration of disease, age at onset, and age-by-diagnosis interactions on structural measures. They observed widespread patterns of altered subcortical volume and reduced cortical grey matter thickness. Compared to controls, all epilepsy groups showed lower volume in the right thalamus (Cohen's d = -0.24 to -0.73; P <  $1.49 \times 10-4$ ), and lower thickness in the precentral gyrus bilaterally  $(d = -0.34 \text{ to } -0.52; P < 4.31 \times 10-6)$ . Both MTLE subgroups showed profound volume reduction in the ipsilateral hippocampus (d = -1.73 to -1.91, P <  $1.4 \times 10-19$ ), and lower thickness in extrahippocampal cortical regions, including the precentral and paracentral gyri, compared to controls (d = -0.36 to -0.52; P <  $1.49 \times 10-4$ ). Thickness differences of the ipsilateral temporopolar, parahippocampal, entorhinal, and fusiform gyri, contralateral pars triangularis, and bilateral precuneus, superior frontal and caudal middle frontal gyri were observed in left, but not right, MTLE (d = -0.29 to -0.54;  $P < 1.49 \times 10$ -4). Contrastingly, thickness differences of the ipsilateral pars opercularis, and contralateral transverse temporal gyrus, were observed in right, but not left, MTLE (d = -0.27 to -0.51;  $P < 1.49 \times 10$ -4). Lower subcortical volume and cortical thickness associated with a longer duration of epilepsy in the all-epilepsies, all-other-epilepsies, and right MTLE groups (beta, b < -0.0018;  $P < 1.49 \times 10$ -4). In the largest neuroimaging study of epilepsy to date, we provide information on the common epilepsies that could not be realistically acquired in any other way.

The study provides a robust ranking of brain measures that can be further targeted for study in genetic and neuropathological studies. This worldwide initiative identifies patterns of shared grey matter reduction across epilepsy syndromes, and distinctive abnormalities between epilepsy syndromes, which inform our understanding of epilepsy as a network disorder, and indicate that certain epilepsy syndromes involve more widespread structural compromise than previously assumed <sup>1)</sup>.

1)

Whelan CD, Altmann A, Botía JA, Jahanshad N, Hibar DP, Absil J, Alhusaini S, Alvim MKM, Auvinen P, Bartolini E, Bergo FPG, Bernardes T, Blackmon K, Braga B, Caligiuri ME, Calvo A, Carr SJ, Chen J, Chen S, Cherubini A, David P, Domin M, Foley S, França W, Haaker G, Isaev D, Keller SS, Kotikalapudi R, Kowalczyk MA, Kuzniecky R, Langner S, Lenge M, Leyden KM, Liu M, Loi RQ, Martin P, Mascalchi M, Morita ME, Pariente JC, Rodríguez-Cruces R, Rummel C, Saavalainen T, Semmelroch MK, Severino M, Thomas RH, Tondelli M, Tortora D, Vaudano AE, Vivash L, von Podewils F, Wagner J, Weber B, Yao Y, Yasuda CL, Zhang G, Bargalló N, Bender B, Bernasconi N, Bernasconi A, Bernhardt BC, Blümcke I, Carlson C, Cavalleri GL, Cendes F, Concha L, Delanty N, Depondt C, Devinsky O, Doherty CP, Focke NK, Gambardella A, Guerrini R, Hamandi K, Jackson GD, Kälviäinen R, Kochunov P, Kwan P, Labate A, McDonald CR, Meletti S, O'Brien TJ, Ourselin S, Richardson MP, Striano P, Thesen T, Wiest R, Zhang J, Vezzani A, Ryten M, Thompson PM, Sisodiya SM. Structural brain abnormalities in the common epilepsies assessed in a worldwide ENIGMA study. Brain. 2018 Jan 22. doi: 10.1093/brain/awx341. [Epub ahead of print] PubMed PMID: 29365066.

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