**Brain imaging and genetics in patients with congenital hypogonadotropic hypogonadism (CHH): a multicenter Belgian study.**

Valdes-Socin H, Libioulle C, Harvengt J., Pintiaux A, Jonas C, Parent AS, Geenen V, Corman V, Debray FG. , Dideberg V., T’Sjoen G, De Leerner A, Beckers D, Destree A, Roland D, Lederer D, Boscolo, M, Bours V., Maiter D and Beckers A.

CHH is a genetic syndrome that combines reproductive and brain abnormalities. The brain phenotype has been incompletely characterized. We aimed to study neuroradiological and genetic features in this first Belgian cohort of 56 patients with CHH by next generation sequencing on a MiSeq® Instrument (Illumina) and by using a validated targeted approach with xGen® Lockdown® Probes (IDT)..

Until now, we found some 26 genetic variants, including FGFR1, GnRHR, CHDT, TAC3, WDR11, HS6ST1, PROKR2 and KISSR genes. A total of 21 patients presented a normal brain MRI, whereas 11 other patients presented structural abnormalities: a Chiari type 1 malformation (CM1) (n=3), an anterior pituitary hypoplasia (n=3), a Rathke’s pouch cyst (n=1), a septooptic dysplasia (n=2), an hydrocephalus (n=1) and an arachnoidal cyst (n=1).

This is the largest Belgian series of CHH. We describe for the first time five novel pathogenic variants. Moreover, we suggest a new syndromic association between CHH and CM1. Multicenter studies and systematic brain MRI are necessary to extend the phenotype and the genotype of CHH patients.