Pathophysiology and Consequences of Craniosynostosis
Novel approaches in genetic, neuroimaging and aesthetic studies

Propositions

1. In a university medical center in Rotterdam, the Netherlands, overall genetic diagnostic yield was 35% in a cohort of craniosynostosis patients born between 2010 and 2021. Diagnostic yield in patients with syndromic craniosynostosis (62%) was significantly higher than the yield in patients with non-syndromic craniosynostosis (6%). *(This thesis*)

2. If no genetic diagnosis is obtained through microarray and/or the whole exome sequencing craniosynostosis panel, we should consider extensive genetic diagnostics. *(This thesis)*

3. Preoperatively, microstructural properties of major frontal lobe white matter tracts in metopic synostosis patients under the age of 3 years were not significantly different from healthy controls. *(This thesis)*

4. Preoperatively, white matter volume in metopic synostosis patients under the age of 2 years, is smaller compared to controls and appears to show accelerated growth in the first two years of life. *(This thesis)*

5. Photo scores, developed for assessing phenotypical severity of sagittal and metopic synostosis preoperatively and head shape analysis postoperatively, show substantial interrater agreement on the overall phenotype but considerable interrater differences for specific phenotypical features. *(This thesis)*

6. Patient registries are potentially valuable sources of data for supporting regulatory decision-making on medicines, but they are greatly underused owing to heterogeneity in registry design, the data collected and its quality, as well as to data sharing impediments. *(McGettigan et al. 2019 Drug Safety)*

7. Artificial Intelligence and machine learning will not put health professionals out of business; rather, they will make it possible for health professionals to do their jobs better and leave time for the human–human interactions that make medicine the rewarding profession we all value. *(Haug Drazen 2023 N Engl J Med)*

8. Genomics can only be part of the solution if it is integrated with broader social, economic and political efforts aimed at addressing disparities in health outcomes. For genomics to be truly equitable, it must operate within a just health-care system and a just society. *(McGuire Nature Reviews Genetics 2020)*

9. The brain is a world consisting of a number of unexplored continents and great stretches of unknown territory. *(Santiago Ramon y Cajal 1906)*

10. Dog ownership is associated with lower risk of death over the long term, which is possibly driven by a reduction in cardiovascular mortality. *(Kramer et al. Circ Cardiovasc Qual Outcomes 2019)*

11. True education is a kind of never ending story — a matter of continual beginnings, of habitual fresh starts, of persistent newness. *(J.R.R. Tolkien)*

Linda Gaillard, 31 October 2023