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Comment

Understanding segregated laterality phenotypes needs a comparative perspective on both genotype and envirotype Comment on "Phenotypes in hemispheric functional segregation? Perspectives and challenges" by Guy Vingerhoets

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Handedness, language lateralization and visuo-spatial lateralization represent common forms of hemispheric asymmetries in the human brain [1]. Vingerhoets's article [2] offers a new perspective on the question whether or not these and other forms of laterality represent the same or different phenotypes. Moreover, it discusses the consequences of atypical asymmetries outside of pathological phenomena.

Based on genetic and neuroscientific literature, Vingerhoets's [2] suggests that different forms of hemispheric asymmetries do not represent a common phenotype, but are constituted by at least three largely independent lateralized phenotypes. Although we generally agree, we would like to point out that also environmental influences play a key role in the ontogenetic emergence of such asymmetrical patterns. In section 2.3. ("Is there a genetic link between left handedness and atypical language dominance?"), Vingerhoets's [2] discusses the literature on the genetics of handedness and language lateralization. Citing, among other, our work on gene ontology analysis for handedness and language lateralization [3], Vingerhoets's [2] concludes:

> *"As these gene ontology sets barely overlap between phenotypes, the findings were taken to support the idea that handedness and language lateralization might be ontogenetically independent phenotypes." (p. 5)*

Here it is important to point out that genetic variation is not the most important factor in the ontogenesis of hemispheric asymmetries. For handedness, it has been shown that additive genetic effects account for only 23.64% of the variance in the behavioral data [4]. In contrast, 76.36% of the variance in behavioral data was accounted for by non-shared environmental influences [4]. Thus, we are convinced that the envirotype needs to be integrated into any ontogenetically-driven discussion about the segregation of different asymmetry phenotypes.

We have recently argued that handedness and language lateralization show a substantial amount of independent ontogenetic influences for each of them, but that there is likely to be at least some overlap in the factors that drive

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their ontogenesis, as the two phenotypes are correlated [5]. It is, of course, conceivable that this overlap is not limited to genetic factors, but that the two traits share one or more environmental factors that influence their ontogenesis. For handedness, a recent study analyzing the UK biobank data found that several early life factors influence the phenotype [6]. These factors included the year and location of birth, birthweight, being part of a multiple birth, season of birth, breastfeeding, and sex. Unfortunately, there is not much systematic research in larger cohorts on how these factors influence other asymmetry phenotypes in humans, like language lateralization or spatial lateralization. For low birthweight, there is indirect evidence from a functional connectivity neuroimaging study that it could affect language lateralization. Prematurely-born neonates showed significantly less lateralization in brain regions associated with both receptive and expressive language [7].

A key issue for future research are environmental factors that affect asymmetry phenotypes other than handedness. Here, an integration of studies in animals could properly anchor human neuropsychology within neurobiology. Studies in birds have demonstrated that a few days of ambient light before hatch affects behavioral and neuroanatomical asymmetries [8,9]. This is because avian embryos keep their right eye is close to the shell, while their body occludes their left eye, leading to stronger right eye light stimulation [10]. Incubating birds in the dark consequently has strong effects on various asymmetry phenotypes [11–13]. The tantalizing implication of these findings is that genetic factors that affect head position can kick off brain asymmetries, a finding that is possibly akin to human studies [14]. Equally, the zebrafish frequent-situs-inversus (fsi) model helps to uncover why both body and behavior show left-right reversals [15]. Neurobiological studies can also help to overcome the many pitfalls that are associated with the "crowding hypothesis" that plays a key role in the model of Vingerhoets's [2]. Single cell recording studies show that cortical neurons are far less specialized than previously assumed. Instead, they quickly learn to slightly shift their preferences, thereby creating novel inter-cellular coalitions that overtake highly specialized tasks [16]. Such a network has no major problems to incorporate functional changes that advocates of the crowding hypothesis would deem unlikely. We would also like to point out that taking a comparative perspective could be beneficial in other parts of this theoretical framework, e.g. regarding structure-function relationships.

References

[1] Ocklenburg S, Güntürkün O. The lateralized brain: the neuroscience and evolution of hemispheric asymmetries. San Diego: Academic Press Imprint Elsevier Science & Technology Books; 2018.
[2] Vingerhoets G. Phenotypes in hemispheric functional segregation? Perspectives and challenges. Phys Life Rev 2019;30:1–18. https://doi.org/10.1016/j.plrev.2019.06.002 [in this issue].
[3] Schmitz J, Lor S, Klose R, Güntürkün O, Ocklenburg S. The functional genetics of handedness and language lateralization: insights from gene ontology, pathway and disease association analyses. Front Psychol 2017;8.
[4] Medland SE, Duffy DL, Wright MJ, Geffen GM, Hay DA, Levy F, et al. Genetic influences on handedness: data from 25,732 Australian and Dutch twin families. Neuropsychologia 2009;47:330–7.
[5] Ocklenburg S, Beste C, Arning L, Peterburs J, Gunturkun O. The ontogenesis of language lateralization and its relation to handedness. Neurosci Biobehav Rev 2014;43:191–8.
[6] de Kovel CGF, Carrión-Castillo A, Francks C. A large-scale population study of early life factors influencing left-handedness. Sci Rep 2019;9:584.
[7] Kwon SH, Scheinost D, Lacadie C, Sze G, Schneider KC, Dai F, et al. Adaptive mechanisms of developing brain: cerebral lateralization in the prematurely-born. NeuroImage 2015;108:144–50.
[8] Buschmann JU, Manns M, Güntürkün O. "Let There be Light!" pigeon eggs are regularly exposed to light during breeding. Behav Process 2006;73:62–7.
[9] Manns M, Güntürkün O. Monocular deprivation alters the direction of functional and morphological asymmetries in the pigeon's (Columba livia) visual system. Behav Neurosci 1999;113:1257–66.
[10] Güntürkün O, Ocklenburg S. Ontogenesis of lateralization. Neuron 2017;94:249–63.
[11] Rogers LJ. Light experience and asymmetry of brain function in chickens. Nature 1982;297:223–5.
[12] Deng C, Rogers LJ. Prehatching visual experience and lateralization in the visual Wulst of the chick. Behav Brain Res 2002;134:375–85.
[13] Skiba M, Diekamp B, Güntürkün O. Embryonic light stimulation induces different asymmetries in visuoperceptual and visuomotor pathways of pigeons. Behav Brain Res 2002;134:149–56.
[14] Güntürkün O. Human behaviour: adult persistence of head-turning asymmetry. Nature 2003;421:711.
[15] Barth KA, Miklosi A, Watkins J, Bianco IH, Wilson SW, Andrew RJ. fsi zebrafish show concordant reversal of laterality of viscera, neuroanatomy, and a subset of behavioral responses. Curr Biol 2005;15:844–50.
[16] Rigotti M, Barak O, Warden MR, Wang XJ, Daw ND, Miller EK, et al. The importance of mixed selectivity in complex cognitive tasks. Nature 2013;497:585–90.