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The influence of vestibular system and fetal presentation on handedness, cognitive and motor development: A comparison between cephalic and breech presentation

Jad Hamaoui¹  | Nicolas Stefaniak²  | Hervé Segond¹

¹Laboratoire de Psychologie des Cognitions (UR 4440), Université de Strasbourg, Strasbourg, France

²Laboratoire Cognition Santé Société (UR 6291), Université de Reims Champagne-Ardenne, Reims, France

Correspondence

Jad Hamaoui, Laboratoire de Psychologie des Cognitions (UR 4440), Université de Strasbourg, France.
Email: jhamaoui@unistra.fr

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Abstract

Genetics are undoubtedly implicated in the ontogenesis of laterality. Nonetheless, environmental factors, such as the intrauterine environment, may also play a role in the development of functional and behavioral lateralization. The aim of this study was to test the Left-Otolithic Dominance Theory (LODT; Previc, 1991) by investigating a hypothetical developmental pattern where it is assumed that a breech presentation, which is putatively associated with a dysfunctional and weakly lateralized vestibular system, can lead to weak handedness and atypical development associated with language and motor difficulties. We used the ALSPAC cohort of children from 7 to 10 years of age to conduct our investigation. Our results failed to show an association between the vestibular system and fetal presentation, nor any influence of the latter on hand preference, hand performance, or language and motor development. Bayesian statistical analyses supported these findings. Contrary to our LODT-derived hypotheses, this study offers evidence that fetal presentation does not influence the vestibular system's lateralization and seems to be a poor indicator for handedness. Nonetheless, we found that another non-genetic factor, prematurity, could lead to atypical development of handedness.

KEYWORDS

ALSPAC, breech presentation, handedness, language and motor development, left otolith dominance theory, vestibular system

1 | INTRODUCTION

Although the ontogenesis of handedness remains unclear (Ocklenburg et al., 2021), the interest in studying the development of laterality increased considerably over the past decades. This has been driven by findings showing that non-right-handers are more frequently associated with neurodevelopmental and psychiatric disorders (e.g., autism, developmental dyslexia, developmental coordination disorder, schizophrenia; Berretz et al., 2020; Darvik et al., 2018; Eglinton &

Annett, 1994). Several theoretical frameworks have been proposed in order to explain this relationship (e.g., Annett, 2002; Berretz et al., 2020; Bishop, 2013; McManus, 2002).

Behavioral lateralization, which includes handedness, appears to manifest very early in life (Hepper, 2013; Reissland et al., 2015). A lateralized behavior can be identified before birth, where most fetuses suck their right thumb early in gestation and exhibit a rightward head orientation during the last weeks of gestation (Hepper et al., 1991; Ververs et al., 1994a). These lateralized patterns can predict

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early, but also later, post-natal lateralized behavior, such as handedness (Hepper et al., 2005). Genetics are undoubtedly involved in handedness (Cuellar-Partida et al., 2021; McManus, 2021; Medland et al., 2006, 2009). Recently, using the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort, Schmitz et al. (2022) conducted a large study investigating the heritability of lateral preferences (i.e., handedness, footedness, eyedness). The authors found that individuals with parental left-sidedness are more likely to present the same trait. In addition, they suggested that all these phenotypes share a common genetic factor. Nonetheless, the influence of other factors (i.e., environmental and epigenetic factors) could also be involved in its ontogenesis (Bishop, 2013; Michel, 2021; Schmitz et al., 2017). Among these factors, it has been proposed in the Left-Otolithic Dominance Theory (LODT) that the intrauterine environment could influence the development of handedness (Previc, 1991).

More specifically, according to LODT (Previc, 1991), cerebral lateralization is influenced by fetal presentation in the last trimester of gestation. Most cephalic fetuses lie head-down with their back turned to the mother's left side, and their right ear facing outward (Previc, 1991). This leftward turning preference in the cephalic presentation may be a result of the uterus torsion on the right due to the maternal bladder and rectum positioned on the same side (Ververs et al., 1994b). This uterus asymmetry will allow more space for the fetus' head and body to turn on the left side (Ververs et al., 1994b). Another explanation can be given for the predominance of the fetal left occiput positioning and it is linked to the maternal positioning during pregnancy. Pregnant women prefer the left lateral position in the third trimester of pregnancy since a supine or right lateral position leads to a compression of the right inferior vena cava by the weighted uterus, which results in a hypotension syndrome (Matsuo et al., 2007). Thus, a left occiput position will allow more stability for the fetus in mothers adopting a left lateral position, whereas a right occiput position will lead to instability since the fetus's center of gravity will be higher than that of the mother (for further details see Matsuo et al., 2007, p. 282). It is noteworthy that it is central to Previc's theory that the ratio between leftward and rightward cephalic positions is 2:1. However, a study conducted on 1250 women using transabdominal ultrasound examinations, a superior method to abdominal palpation (Webb et al., 2011), showed that the ratio is closer to 1.53:1 in favor of the leftward cephalic orientation (Ahmad et al., 2014).

According to the LODT, the left occiput presentation will contribute to the lateralization of the vestibular system. During mother's locomotion, the acceleration of the mother during locomotion would influence the asymmetric development of the otolithic pathways. Specifically, the left utricle would more benefit from stimulations of the inertial force (for more details, see Previc, 1991, p. 318). Thus, in most cases, the head position in the bony maternal pelvis at the end of gestation will lead to an over-excitation of the left otoliths. This will result in an early stimulation of the right hemisphere's vestibular cortex, leading to early specialization in information processing of body positioning in space and visuo-spatial processing. Consequently, this will allow the left hemisphere to specialize in motoric performance, increasing the ability of the right side of the body for voluntary motor movements.

RESEARCH HIGHLIGHTS

- The vestibular system is not related to the fetal presentation, and children with breech presentation were not associated with a dysfunctional vestibular system.
- Handedness and neurodevelopmental disorders were not associated with the fetal presentation in utero.
- Whilst genetics and randomness are implicated in the development of handedness, non-genetic factors such as prematurity may exhibit genuine association with handedness.
- Higher prevalence of left-handers and motor difficulties were found among premature children.

Furthermore, during maternal walking, the left otolith stimulation will result in more impulses of the brain stem terminating on the vestibulospinal tract that innervates the ipsilateral control of the extensor muscles. This left-sided bias in activating the sternocleidomastoid muscle will lead to a rightward turning of the head (Ververs et al., 1994b), which was found to be associated with later right-handedness (Ferre et al., 2020; Goodwin & Michel, 1981; Ocklenburg et al., 2010). Therefore, a reversed lateralization should be observed among the cephalic fetuses with a rightward orientation and the left-ear facing outward. Thus, one can directly test the LODT by comparing leftward and rightward cephalic presentations. Some evidence supports this hypothesis showing that newborn infants with a leftward intrauterine orientation exhibit a rightward head orientation preference in supine position after birth and a later right-handedness, whereas newborns with a rightward intrauterine orientation were more prone to a leftward head orientation preference and a later left-handedness (Churchill et al., 1962; Goodwin & Michel, 1981; Michel & Goodwin, 1979). In addition, prenatal vestibular asymmetries resulting from a lateralized fetal presentation can be related to behaviors other than handedness, such as postural biases and lateralized reflexes (e.g., Asymmetric Tonic Neck Reflex, grasping reflex), which are generally greater on the right side of the body (Previc, 1991, p. 317).

Importantly, given that children with neurodevelopmental disorders such as Developmental Dyslexia (DD) are generally poorly lateralized, the LODT provides an explanation for the link between lateralization and neurodevelopmental disorders. Previc (1991) has suggested that a vestibular hypoactivity and an otolithic impairment, which may alter the otolithic asymmetry (Previc, 1996, p. 453), could explain higher incidence of neurodevelopmental disorders (Previc, 1991, 1996). Thus, minor vestibulo-cerebellar symptoms (e.g., postural control deficit), that presumably reflect otolithic impairments, could represent a risk factor for neurodevelopmental disorders. In line with this assumption, it has been reported that children with DD and Developmental Coordination Disorder (DCD) exhibit atypical lateralization (Berretz et al., 2020; Biotteau et al., 2016; Darvik et al., 2018; Eglinton & Annett, 1994), and spatial, postural and proprioceptive impairments,



which are clinical symptoms observed when the vestibular system is dysfunctional (Blythe, 2017, p. 14 to 18).

Although the LODT provides an explanation for the link between fetal presentation, handedness, and neurodevelopmental disorders, studies that tested this theoretical framework are surprisingly scarce. To the best of our knowledge, Fong et al.'s (2005) is the most recent study that empirically tested this model. The authors investigated the head orientation of cephalic and breech presentations after 36 weeks of gestation. They found that cephalic fetuses exhibited a lateralized head position, mostly to the right, whereas breech fetuses showed no preference to either side. These results were interpreted using the LODT, where it was postulated that breech fetuses have a less asymmetrical stimulation of their otoliths since their position allows for more freedom in head movements. This would lead to lesser vestibular lateralization, which, consequently, would result in a weaker manifestation of lateralized head orientation. Also, this lesser vestibular lateralization among breech children can be explained by intrinsic factors to the development of the vestibular system (Fong et al., 2005). It is postulated that a mature vestibular system in the last trimester is required for adopting a typical position (head down), whereas fetuses in a breech presentation are presumed to have a dysfunctional vestibular system (Eliot, 2000, p. 143; Blythe, 2017, p. 184, 185). Thus, since the vestibular dysfunction may alter the otolithic asymmetry (Previc, 1996, p. 453), it may explain why breech children are lesser lateralized. To our knowledge, only one empirical study tested the relationship between fetal presentation and the vestibular system, and found that school age children born in breech ($n = 42$) showed significantly weaker vestibular reactions after thermic and rotational balance tests than those born in cephalic presentation ($n = 30$; Tymnik et al., 1981; cited by Fong et al., 2005). Nonetheless, due to the lack of other empirical support for this view, replications are required to test this hypothesis.

Our first aim was to test whether breech fetal presentation is associated to vestibular dysfunctions. If so, we should observe that children born in breech presentation present more difficulties in performing tasks involving the vestibular system. More specifically, the saccule and the utricle, which constitute the otolith organs, respond to gravity, which suggest that they contribute to maintaining postural stability (McCaslin et al., 2011). Thus, to test the hypothesis that breech children present an atypical vestibular functioning, one can assess the link between breech presentation and children's scores on clinical balance tests. Basta et al. (2005) found that patients diagnosed with otolith disorder demonstrate poor postural performance on the Standard-Balance-Deficit-Test (SBDT) which evaluates the ability to use somatosensory, visual, and vestibular information to maintain postural control. Specifically, two subtests from the SBDT obtained the greatest diagnostic power to indicate a utricular or sacculo-utricular disorder (i.e., "standing on two legs with eyes closed", which reduces the visual input, and "standing with two legs on a foam with eyes closed", which reduces visual and somatosensory inputs).

The second aim of this study was to test indirectly the LODT by investigating, through handedness, the influence of fetal presentation on postnatal lateralized behaviors. Since breech fetuses showed weaker lateralization than cephalic fetuses (Fong et al., 2005) and

fetal presentation has been associated with handedness (Churchill et al., 1962; Ehrlichman et al., 1982; Ferre et al., 2020; Michel, 2021; Michel & Goodwin, 1979), we expected an association between breech presentation and weaker handedness. Among the few studies that investigated the association between breech presentation and handedness, some authors found that breech presentation tends to be associated with non-right handedness (Smart et al., 1980), whereas others failed to find any association (Levander et al., 1989; McManus, 1981; Tan & Nettleton, 1980).

There are several reasons that could account for this lack of association. Since the prevalence of breech presentation is only around 4.51% (Fruscalzo et al., 2014) a lack of statistical power may be responsible. Large samples are required to examine this link which has often not been the case (e.g., eight breech presentations in Levander et al., 1989; 51 breech and other abnormal presentations in Tan & Nettleton, 1980; 32 breech presentations in Smart et al., 1980). McManus (1981) was the only study to analyze a large sample of 203 breech births derived from the National Child Development Study (NCDS). However, the author only examined the prevalence of right- and left-handedness, whilst breech presentation may not be associated with right- or left-handedness per se, but rather with weak handedness. Furthermore, handedness can be understood in several complementary ways that should be taken into account. Indeed, handedness is a multidimensional trait that encompass both hand preference and hand performance (Buenaventura Castillo et al., 2020). McManus (1981) only tested the hand preference, even though the NCDS includes both hand preference and hand performance measures.

Hand preference is the preferred hand for completing common manual tasks (Scharoun & Bryden, 2014), and it can be generally assessed by questionnaires, such as the Edinburgh Handedness Inventory (Oldfield, 1971). This kind of tool provides two pieces of information: directionality and consistency. The directionality indicates if a person prefers the use of the left, right, or both hands, while consistency refers to how strongly a person prefers to use the same hand for doing different kind of tasks. When the non-preferred hand is used for at least one task, the person is considered as having inconsistent handedness. A highly inconsistent handedness is the most common definition of weak handedness, and is also called "mixed handedness" (Fagard et al., 2015). Thus, mixed handedness is the use of the right hand for some activities and the left for others. Nonetheless, knowing the preferred hand is insufficient to obtain a global overview on handedness since the preference for one hand for manual tasks does not necessarily reflect its ability to perform these tasks efficiently. This performance on manual tasks is referred to as the hand performance, and it differentiates the abilities of both hands to conduct tasks requiring speed and dexterity (Scharoun & Bryden, 2014). Thus, when one is interested in assessing handedness, the performance on manual tasks must be taken into account, and an asymmetry in the hand performance reflects a lateralized handedness. In summary, it is necessary to investigate directionality, consistency, and degree of handedness. It should be noted that the LODT does not state which dimension of handedness the fetal presentation should influence. Thus, this study included both hand preference and hand performance in order to determine



how fetal presentation impact handedness. We can predict from the LODT that children born in breech presentation should exhibit weaker handedness than children born in cephalic presentation.

The LODT suggests that vestibular impairment is expected to alter the otolithic asymmetry, leading to a lesser lateralization, and increasing the probability of atypical development associated with neurodevelopmental disorders. Thus, the third aim of this study is to test the prediction that, if breech presentation reflects vestibular dysfunctions and lesser lateralization as has been suggested, children born in breech presentation should be more often associated with neurodevelopmental disorders (i.e., language and motor impairments). To our knowledge, no studies investigated the developmental pattern that include breech presentation, atypical lateralization, and an atypical development that may be associated with neurodevelopmental disorders.

Beyond the hypotheses related to fetal presentation, several predictions need to be also tested. First, since vestibular impairments should alter the otolithic asymmetry, which may lead to weak lateralization (Previc, 1996), we can expect that mixed handers will be more associated with balance difficulties than right- and left-handers. Second, children with neurodevelopmental disorders should present non-right handedness at a higher rate (see Darvik et al., 2018 and Eglinton & Annett, 1994 for meta-analyses). Third, children with neurodevelopmental disorders should present with more difficulties in performing tasks involving the vestibular system (see Rochelle & Talcott, 2006 and Verbecque et al., 2021 for meta-analyses).

2 | METHODS

2.1 | Participants

The data analyzed for the current study come from the Avon Longitudinal Study of Parents and Children (ALSPAC). The objective of this large cohort is to understand the influence and the interaction between physical and social environmental factors and genetic inheritance on mental and physical health from infancy to adulthood. Pregnant women in south-west England with an expected delivery date between April 1, 1991 and December 31, 1992 were recruited. The total sample size for analyses is 15,454 pregnancies, resulting in 15,589 fetuses (Boyd et al., 2013; Fraser et al., 2013). The exclusion criteria were non-singleton birth, premature birth (before 37 weeks of gestation), and low birthweight (below 2500 g). According to the LODT, the differential stimulation of the otolith organs due to the fetal presentation will occur in the 3rd trimester of pregnancy (i.e., after the 28th week of gestation). Therefore, the fetal presentation data used in this study were collected at onset of labor. The total sample size after exclusion and missing data is 7047. Figure 1 summarizes the flowchart of the sample size according to the exclusion criteria. Among the 7047 births, 95.53% of the participants were born in a cephalic presentation ($n = 6732$ including 3279 females) and 4.47% were born in breech presentation ($n = 315$ including 175 females) during the 3rd trimester (see Figure 1).

Ethical approval for the study was obtained from the Research Ethics Committee of the University of Strasbourg (see <https://cil.unistra.fr/registre.html#proc-374>), from the ALSPAC Ethics and Law Committee, and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time.

2.2 | Measures

The data collected in this study are from obstetric medical records, psychological and clinical examinations undertaken by the participants until they reached the age of 10. The details of all the data are available through a fully searchable data dictionary with a variable search tool on the following webpage: <http://www.bristol.ac.uk/alspac/researchers/our-data/>. See Appendix 1 for the ALSPAC variable codes for all the measures used.

2.2.1 | Assessment of the vestibular system

Following Basta et al.'s (2005) results, the closest measure of the static balance in ALSPAC database is the "heel-to-toe balance on a beam, eyes closed" subtest, which is a part of clinical tests assessing balance and administered at the age of 10. This test should be the most sensitive to vestibular dysfunctions. In the "heel-to-toe balance on a beam, eyes closed" subtest, the tester gave a demonstration followed by a short practice session. In this test, the duration of balance was recorded based on two trials, one for the right foot forwards and the other for the left foot forwards, and the test was stopped after 20 s. For every child, a second attempt was given if the maximum score of 20 on the first attempt was not achieved. Children who reached the maximum score on the first attempt were considered to have reach 20 s on the second attempt without being asked to perform it. It meant that they were given a final score of 40(20 from the first and 20 from the second attempt). For the other children, the sum of the scores (i.e., number of seconds) from both attempts was calculated (see Humphriss et al., 2011 for more details about this variable).

2.2.2 | Assessment of handedness

Hand preference

Participants' hand preference was assessed at 9 years of age with a six-item questionnaire consisting of whether the child uses the "left", "right" or "either" hand for drawing, throwing a ball, coloring, holding a toothbrush, cutting, and hitting things.

This questionnaire allows us to assess both mixed handedness (i.e., inconsistent hand preference between different tasks) and ambidexterity (i.e., consistent use of either hand for the same tasks).

A score of 1 was attributed each time the child answers "left" or "right", and a score of 0 for the "either" response. We calculated a

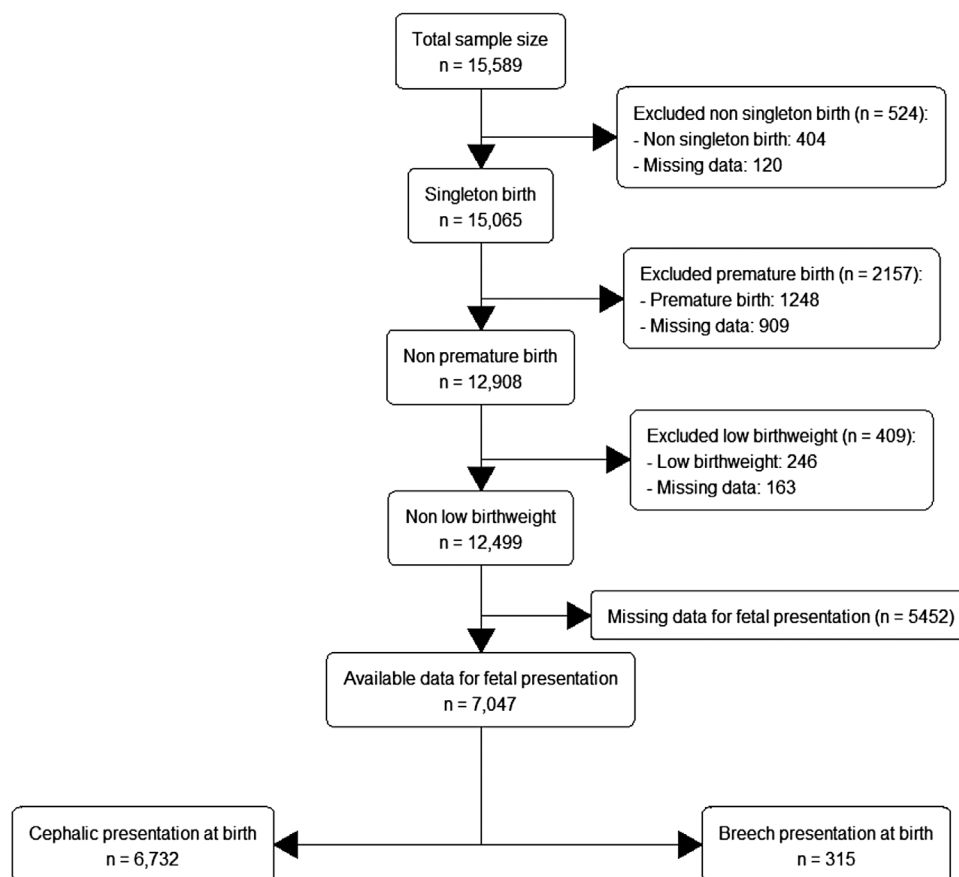


FIGURE 1 Flowchart of the sample size according to the exclusion criteria

Laterality Index (LI) with the formula:

$$LI = \frac{(nR - nL)}{\text{Total number of responses}} \times 100$$

where nR and nL correspond to the number of right- and left-hand use, respectively. Then, we used the cut-offs proposed by Fagard et al. (2015) to distinguish weak from lateralized children. In their study, Fagard and colleagues (2015) searched for the best criterion to evaluate weak handedness (i.e., both mixed handedness and ambidexterity). They suggested that a cut-off of -30 to $+30$ of the LI is able to efficiently distinguish between mixed and ambidextrous children from right- and left-handers. Based on this criterion, we created a nominal variable with three categories: children with a LI between -100 and -30 were considered left-handers, -30 to $+30$ were considered mixed-handers, from $+30$ to $+100$ were considered right-handers. In the present paper, mixed handedness will be used to refer to both mixed handed and ambidextrous children. The proportion of mixed handed individuals identified in Fagard et al. (2015) was 3.3%, whereas in the present study it was 4.7%.

Hand performance

It has been suggested that fine differences of motor lateralization tend to be hidden when using motor tasks, such as dot-filling, that share similarities with daily activities like writing (Peters, 1998). Since the use of

a pen is needed, the preferred hand's strong specialization due to experience may influence the performances on such tasks (Buenaventura Castillo et al., 2020; Peters, 1998). In contrast, other hand performance tasks may appear more sensitive in identifying lateral specialization in motor control (Peters, 1998). Motor tasks such as pegboard task do not require the use of a writing utensil, resulting in the reduced influence of experience. Thus, such tasks are more relevant for the assessment of hand performance.

The pegboard test was conducted at 7 years of age as a subtest of the Movement Assessment Battery for Children (M-ABC; Henderson & Sugden, 1992). It consisted of placing, one at a time and as quickly as possible, 12 pegs into a pegboard. The board was held with one hand and the pegs inserted with the other. The task was carried out with both hands, after it had been described and demonstrated by the tester, and after a practice session with each hand. The time needed for each hand to complete this task was recorded. We computed the PegQ index using the formula:

$$\text{PegQ} = \frac{(L - R)}{(L + R)} \times 100$$

with L referring to the time in seconds to perform the task with the left hand and R referring to the time in seconds to perform the task with the right hand. A negative index refers to a better performance of the left hand, a positive index is interpreted as a better performance of



the right hand, and an index of 0 reflect an equal performance of both hands.

2.2.3 | Neurodevelopmental disorders

Language impairment

Literacy was assessed at the age of 9. The difference between reading age based on the Neale Analysis of Reading Ability (NARA-II, Neale, 1997) and the chronological age was calculated. When the assessed reading age is more than 30 months behind the chronological age, and the child's IQ is greater than or equal to 85, the child is diagnosed with Developmental Dyslexia (DD). The ALSPAC dataset provides one binary variable consisting of children without DD and children with DD.

Motor impairments

Motor coordination was assessed at the age of 7 using the M-ABC (Henderson & Sugden, 1992). The subtests administered to the children were the pegboard task and threading lace task (for manual dexterity), bean bags task (for ball skills), and heel-to-toe walking task (for balance). The ALSPAC dataset provides a binary variable consisting of children without motor impairments, and children with motor impairments (i.e., scores below the 5th percentile on the M-ABC), reflecting a Developmental Coordination Disorder (DCD).

2.3 | Statistical analysis

Our statistical analyses were computed in R 4.1.0 (R Core Team, 2021). Tests of assumptions are presented in Appendix 2 and Appendix 3. When non-parametrical tests were used, it is recommended to use more robust measures of central tendency and dispersion such as median (med) and median absolute deviation (mad), respectively (Wilcox, 2011).

Although the database is large enough to maintain high statistical power even when missing data are handled using listwise deletion, this procedure can bias estimates (Little & Rubin, 2019), especially when the percentage of missing data is large. Thus, we performed our analyses using both listwise deletion and Multiple Imputation (MI). Using the *nanian* package (Tierny & Cook, 2018), Little's test suggests that the missing values of the total sample are Missing Completely At Random ($\chi^2(100) = 92.9, p = 0.679$). For the MI, we used the *mice* and *miceadds* packages (van Buuren & Groothuis-Oudshoorn, 2011; Robitzsch et al., 2021). To find the minimal number of imputed datasets required, we used the *howManyImputations* package (von Hippel, 2020). For a coefficient of variation of 0.01, that is, coefficient that summarizes the imputation variation in the standard error estimate, and for an alpha of 0.01, we needed 4946 imputed datasets. Therefore, we chose to input 5000 datasets in total to pool the results and conduct the statistical analyses.

Concerning the dataset after a listwise deletion procedure, we computed a sensitivity power analysis for each hypothesis (Perugini et al., 2018) in order to determine the minimal statistically detectable effect

given the sample size of the ALSPAC database. These sensitivity analyses were computed in G*Power 3.1 (Faul et al., 2007) with an α -level of 0.05, and a power of 0.80. In addition, Bayesian analyses were conducted to determine if non-significant results could be interpreted as evidence in favor of the null. A Bayes Factor (BF) below 0.33 indicates evidence in favor of the null model, whereas BF greater than 3 is interpreted as evidence in favour of the alternative model (Wetzels et al., 2011). The BF was calculated with the BayesFactor package (Morey & Rouder, 2015). If non-parametric analyses were required, a rank transformation was applied on the variables before conducting the analyses.

3 | RESULTS

3.1 | Preliminary analysis: Testing the hand preference's cut-offs ($n = 2771$)

Data for hand preference were available for 2393 right-handers, 133 mixed handers, and 245 left-handers. In order to determine whether the cut-offs chosen for the hand preference appropriately distinguished weak from strong lateralized children, we performed an ANOVA with Welch's correction on the hand performance task's scores (i.e., PegQ) as dependent variable and the hand preference categories (i.e., right, left, and mixed handers) as independent variable.

There was a significant effect of hand preference on the PegQ scores, $F(2, 253.22) = 263.81, p < 0.001, est.\omega^2 = 0.160$. Pairwise Games-Howell post-hoc comparisons (for unequal variances) showed that all the hand preference categories are well distinguished from each other. Right-handed children scored higher values on the PegQ than mixed-handed children ($t = 9.68, p = < 0.001$; right-handers' mean = 8.27 and mixed handers' mean = -0.31), and mixed handed children scored higher values on the PegQ than left-handers ($t = 4.45, p = < 0.001$; left-handers' mean = -4.99). Interestingly, mixed handed children had a mean of -0.31 on the PegQ, showing that these children present nearly an equal performance of both hands, which support the choice of the cut-off chosen to classify children with weak handedness (see Figure 2).

3.2 | Testing the hypotheses

To examine the hypothesis that breech children present more difficulties in their balance control, reflecting an otolith impairment, we compared breech and cephalic children's scores on the static balance task using Mann-Whitney U test. This analysis showed no significant differences between breech (med = 18.5, mad = 11.49) and cephalic (med = 17.5, mad = 11.12) children (see Table 1 for a summary of the results).

We conducted a chi-square test to examine if breech children are more associated with a weak hand preference than cephalic children. No difference was found between breech and cephalic children

**TABLE 1** Summary of the statistical analyses and results

| Statistical test | <i>n</i> after listwise deletion | Sensitivity analysis | Results | Bayes factor ₁₀ |
|---|----------------------------------|----------------------|--|----------------------------|
| H1: Association between the vestibular system and fetal presentation | | | | |
| Mann-Whitney U test | 3669 | 0.221 | U = 281738, <i>p</i> = 0.357, RBC = 0.042 | 0.07 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.484 | |
| H2a: Association between fetal presentation and hand preference | | | | |
| Chi-squared | 3852 | 0.050 | $\chi^2(2) = 1.44$, <i>p</i> = 0.931, Cramer's V = 0.0006 | 0.001 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.851 | |
| H2b: Association between fetal presentation and hand performance | | | | |
| <i>t</i> -test | 3639 | 0.224 | <i>t</i> (3637) = −0.04, <i>p</i> = 0.970, Cohen's <i>d</i> = −0.003 | 0.09 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.827 | |
| H3a: Association between fetal presentation and language impairments | | | | |
| Fisher's exact test | 3875 | 0.045 | <i>p</i> = 0.268 | 0.07 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.207 | |
| H3b: Association between fetal presentation and motor impairments | | | | |
| Fisher's exact test | 3511 | 0.047 | <i>p</i> > 0.99 | 0.02 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.917 | |
| H4a: Association between hand preference and static balance | | | | |
| Kruskal-Wallis test | 2975 | 0.057 | $\chi^2(2) = 0.77$, <i>p</i> = 0.681, $\epsilon^2 = < 0.001$ | 0.02 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.455 | |
| H4b: Association between hand performance and static balance | | | | |
| Spearman's correlation | 2915 | 0.073 | <i>r</i> = 0.02, <i>p</i> = 0.174 | 0.11 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.599 | |
| H5a: Association between language impairments and hand preference | | | | |
| Fisher's exact test | 3129 | 0.055 | <i>p</i> = 0.401 | 0.003 |
| MI's <i>p</i> -value from the pooled data | | | LH <i>p</i> = 0.636; RH <i>p</i> = 0.284* | |
| H5b: Association between language impairments and hand performance | | | | |
| <i>t</i> -test | 3062 | 0.349 | <i>t</i> (3060) = −0.84, <i>p</i> = 0.402, Cohen's <i>d</i> = −0.104 | 0.19 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.520 | |
| H5c: Association between motor impairments and hand preference | | | | |
| Fisher's exact test | 2681 | 0.060 | <i>p</i> = 0.500, | 0.001 |
| MI's <i>p</i> -value from the pooled data | | | LH <i>p</i> = 0.289; RH <i>p</i> = 0.760* | |
| H5d: Association between motor impairments and hand performance | | | | |
| Welch's <i>t</i> -test | 3478 | 0.403 | Welch's <i>t</i> (48.8) = −0.19, <i>p</i> = 0.848, Cohen's <i>d</i> = −0.031 | 0.16 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.780 | |
| H6a: Association between the vestibular system and language impairments | | | | |
| Mann-Whitney U test | 3407 | 0.334 | U = 111288, <i>p</i> = 0.288, RBC = 0.073 | 0.22 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.303 | |
| H6b: Association between the vestibular system and motor impairments | | | | |
| Mann-Whitney U test | 2834 | 0.470 | U = 30825, <i>p</i> < 0.001, RBC = 0.388 | 317.54 |
| MI's <i>p</i> -value from the pooled data | | | <i>p</i> = 0.0004 | |

*: LH: Left-handedness category; RH: Right-handedness category; Logistic regressions were conducted on the pooled data.

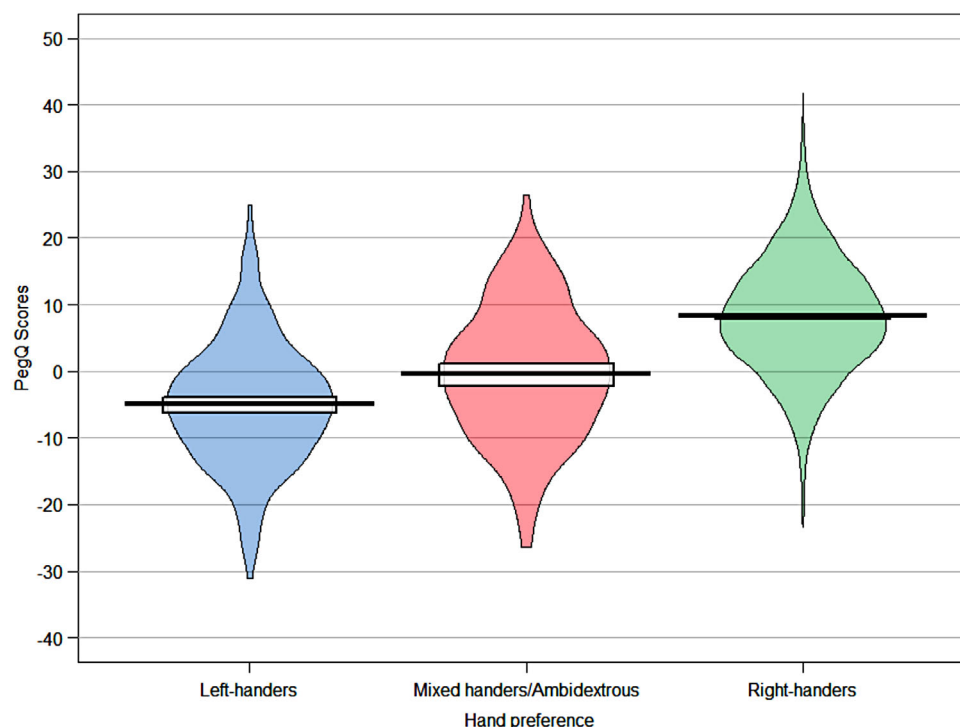


FIGURE 2 Hand performance scores according to children's hand preference

(see Table 1, see Table A in Appendix 4 for descriptive statistics). Similarly, a t-test showed no significant differences in PegQ between breech presentation ($M = 6.56$, $SD = 9.72$) and cephalic presentation ($M = 6.59$, $SD = 9.88$).

Fisher's exact tests were performed due to small cell counts to examine whether breech presentation shows a greater association with neurodevelopmental disorders. These analyses were not significant for either for DD or for DCD (see Table 1, see Table B and Table C in Appendix 4 for descriptive statistics).

To examine whether mixed hands exhibited more difficulties on balance tasks than right- or left-handers, we conducted a Kruskal-Wallis test with the static balance scores as dependent variable and the hand preference categories (i.e., right, left, and mixed hands) as the independent variable. Results suggest that hand preference is unrelated to static balance scores (see Table 1). Spearman's correlation showed an absence of an association between hand performance and static balance (see Table 1).

Fisher's exact test was conducted to examine the association between hand preference and neurodevelopmental disorders. No association was found, either between hand preference and DD or between hand preference and DCD (see Table 1, see Table D and Table E in Appendix 4 for descriptive statistics). A t-test analyzing hand performance showed that there is no significant difference between children with DD ($M = 7.58$, $SD = 9.67$) and children without DD ($M = 6.56$, $SD = 9.83$). Similarly, a Welch's t-test showed no significant difference between children with DCD ($M = 6.23$, $SD = 13.0$) and children without DCD ($M = 6.59$, $SD = 9.80$). See Table 1 for the summary of the results.

To examine the hypothesis of an association between neurodevelopmental disorders and balance difficulties, we conducted Mann-Whitney tests to compare children's scores on the static balance task. As shown in Table 1, no significant difference was found between children with DD (med = 15.8, mad = 10.01) and without DD (med = 18.0, mad = 11.86). In contrast, significant difference was found between children with DCD (med = 11.8, mad = 6.67) and without DCD (med = 18.0, mad = 11.86).

4 | DISCUSSION

Whilst genetic factors clearly play an important role in the ontogenesis of laterality (Cuellar-Partida et al., 2021; McManus, 2021; Medland et al., 2006, 2009), non-genetic prenatal factors may also influence the development of behavioral and functional lateralization (Bishop, 2013; Michel, 2021). Previc (1991) proposed a theoretical framework to explain the link between the intrauterine environment, and children's laterality, language and motor development. However, although this model could at least partly explain the etiology of developmental disorders, few studies had tested it. Thus, our objective was to test Previc's Left Otolithic Dominance Theory (1991) by exploring the associations between early vestibular lateralization, fetal presentation, and handedness. Moreover, we wanted to know how these factors could be involved in the etiology of neurodevelopmental disorders. Our hypothesis inferred from the LODT is that a higher prevalence of neurodevelopmental disorders should be observed among children with breech presentation since they supposedly present



a dysfunctional vestibular system and atypical lateralization (Fong et al., 2005). Both these characteristics are found among individuals with DCD and DD (Berretz et al., 2020; Darvik et al., 2018; Eglinton & Annett, 1994; Blythe, 2017).

To our knowledge, Tymnik et al.'s (1981; cited by Fong et al., 2005) study is the sole study to empirically support the view that a breech presentation is a consequence of a vestibular dysfunction. Thus, we first aimed to bring new empirical evidence of Tymnik et al.'s (1981) findings, and we hypothesized that breech born children should present more difficulties than cephalic children on a static balance task, reflecting otolith dysfunctions. We did not find any difference between breech and cephalic children. Our results suggest that a failure to adopt a cephalic presentation is not explained by a vestibular system dysfunction. Other factors, such as genetics, birth stress and pregnancy complications (e.g., uterine malformations, low volume of amniotic fluid) may explain why fetuses stay in breech presentation during gestation (Nordtveit et al., 2008).

According to our second hypothesis, breech position should allow the head to move more freely, leading to a lesser asymmetrical stimulation of the otoliths, and thus to a weak cerebral lateralization. Based on this theoretical framework, we predicted that children born in breech presentation should be less lateralized (i.e., more mixed handedness) than children with cephalic presentation. This prediction was refuted by our results. Fetal presentation failed to predict children's handedness, regardless of hand preference or hand performance (for similar results, see Rönnqvist & Hopkins, 2000). It is possible that the absence of significant results between handedness and fetal presentation can be attributed to the measures used in this study. For hand preference, the 6-items questionnaire may presents some limitations (e.g., Edlin et al., 2015). Nonetheless, this assessment appeared to provide useful information about handedness. For instance, Schmitz et al. (2022) successfully identified a heritability estimate of handedness using the same 6-item questionnaire of ALSPAC, finding a similar heritability estimate to what was previously reported in twin studies (Medland et al., 2006, 2009). Thus, we believe that the questionnaire has scientific validity and can inform the relationship between hand preference and fetal presentation. For hand performance, the PegQ of the peg-board task was based only on the scores of one trial. This is suboptimal since intra-individual variability is important, and one should ideally calculate an average time for each hand derived from several trials (e.g., Annett, 1970). Nonetheless, there is some indication in the present study that our measure is valid even if the reliability could have been improved with greater control of intra-variability. The trial of the peg-board task used in this study was preceded by a demonstration of the experimenter, a practice session with each hand, and the PegQ do match the categories derived from the hand preference questionnaire.

Therefore, the role of the fetal presentation on newborns' lateralization may have been overstated in the LODT due to the fact that, contrary to the LODT which supposes a fixed head position in the last weeks of gestation (Previc, 1991), fetus' heads can move freely even in the cephalic presentation (Rönnqvist & Hopkins, 1998), and some fetuses continue to switch their positions from cephalic to breech presentations and vice-versa until the end of the pregnancy (Ververs et al., 1994a).

If our results challenge the link suggested by the LODT between fetal presentation and handedness, it remains possible that fetal presentation may only have an influence on early-lateralized behavior, whereas later lateralization will be affected by other factors, such as social (e.g., caregiver's handedness) and cultural factors (Michel, 2021; Previc, 1991). In addition, postnatal visual stimulation can possibly lead to a readjustment of the asymmetrical vestibular system, which may reduce the effect of the early fetal presentation on later behaviors. In line with this assumption, an association was found between fetal presentation and early behavioral asymmetries (Fong et al., 2005; Goodwin & Michel, 1981; Michel & Goodwin, 1979), and handedness at the age of 2 (Churchill et al., 1962), but disappeared when handedness was assessed at the age of 7 (Vles et al., 1989). To determine the likelihood of this assumption, and to directly test the LODT, one could conduct a longitudinal study starting from gestation, where it would be possible to assess only the fetuses who adopted the same presentation during the last trimester while comparing fetuses with a rightward and leftward orientation. Afterward, one can measure early and later handedness, that is, before and after the potential influence of social and cultural factors.

We predicted that the prevalence of neurodevelopmental disorders would be higher among children born in breech presentation, but our results did not corroborate our hypothesis, neither for DD nor for DCD (for similar results see Bartlett et al., 2000; Eide et al., 2005). These results support our previous findings where we failed to show a significant relation between breech presentation, dysfunctional vestibular system, and weak handedness, which were supposed to be related to neurodevelopmental disorders (Darvik et al., 2018; Eglinton & Annett, 1994; Blythe, 2017).

Based on our results, fetal presentation seems to be a poor indicator of vestibular dysfunction. Nonetheless, it is possible that handedness is directly related to early vestibular asymmetries, as suggested by Previc (1991). According to Previc (1991, 1996), a dysfunctional vestibular system may lead to a reduced otolithic asymmetry, resulting in a lesser cerebral lateralization. Thus, we tested this relation by predicting that mixed handed children would present more difficulties on a static balance task, which is supposed to reflect otoliths impairments. However, our results did not support this prediction. This is in line with Previc and Saucedo's (1992) study, which did not find a correlation between handedness and a task that measured vestibular asymmetry in high school students. It is possible that the absence of association reflects sociocultural influence and/or weak reliability of the vestibular asymmetry measures, as suggested by Previc and Saucedo (1992). However, another explanation is that handedness is not associated with the vestibular lateralization, and a weak handedness does not reflect a vestibular dysfunction. Nevertheless, these results neither exclude the relationships between neurodevelopmental disorders and handedness, nor refute the role of the vestibular system on neurodevelopmental disorders.

We predicted that a higher prevalence of language and motor impairments would be found among children with an atypical handedness, which was not corroborated by our results. These results differ from previous studies which showed that non-right handedness was associated with DD (Peters et al., 2006; for a meta-analysis see

Eglinton & Annett, 1994), and with DCD (Cairney et al., 2008; see for a meta-analysis Darvik et al., 2018). It has also been shown that children with these disorders exhibit atypical functional lateralization (see for reviews Berretz et al., 2020 and Biotteau et al., 2016). One explanation for our results could be that our analysis is underpowered. Indeed, several studies highlighted that the influence of atypical lateralization is small and large sample size is required to detect this weak but genuine association between language impairments and atypical lateralization (Eglinton & Annett, 1994; Porac, 2016; for a power analysis see Bishop, 2013). Nonetheless, in the present study, the sensitivity power analyses showed that we should be able to detect very small effect sizes, which makes this explanation less likely. Alternatively, it may be that atypical lateralization is not one of the factors causing neurodevelopmental disorders (Berretz et al., 2020). More specifically, it has been proposed that the association between atypical lateralization and neurodevelopmental disorders is due to a common mechanism underlying their ontogenesis, which is stress. Indeed, through an alteration in the hypothalamic-pituitary-adrenal axis, early life or chronic stress may lead to atypical cerebral lateralization and to neurodevelopmental or psychiatric disorders (Berretz et al., 2020). Following this view, Davis et al. (2022) showed that prematurity, which is related to early life stress (Field & Diego, 2008), exhibits atypical functional lateralization. As a non-planned complementary analysis (see Appendix 5), we tested the relation between prematurity, handedness, and neurodevelopmental disorders. Among preterm (< 37 weeks gestation), very preterm (< 32 weeks gestation), and extremely preterm children (< 28 weeks gestation), we found a higher prevalence of left-hand preference and DCD compared to children born at term (> 37 weeks gestation), and this all the more so when the prematurity is great (see Appendix 5, also see Table F, Table G, and Table H in Appendix 5 for descriptive statistics). These results replicate previous studies that have found a link between prematurity and atypical handedness (e.g., de Kovel et al., 2019; see Domellöf et al., 2011 for a meta-analysis). This analysis suggests that the higher prevalence of neurodevelopmental disorders in non-right handedness is not a direct relationship but could be mediated by intrauterine stress. In other words, these results support that the development of laterality is not entirely due to genetic factors, and intrauterine factors such as early stress, could play a role in the ontogenesis of laterality, but also neurodevelopmental disorders (Berretz et al., 2020).

Finally, we expected that individuals with neurodevelopmental disorders such as DD and DCD will present more difficulties on static balance performance, which reflect otolith impairments. In line with previous studies (Fong et al., 2012; Verbecque et al., 2021), we showed that children with DCD exhibited significantly lower scores on the static balance task, supported by the Bayesian statistics. Contrary to our hypothesis, no difference on static balance was found between children with and without DD. Previous studies led to mixed results with some showing a postural instability in dyslexia (e.g., Pozzo et al., 2006), whilst others suggested that balance impairments are not related to reading skills (Rochelle & Talcott, 2006). Indeed, the association between vestibular impairments and dyslexia seems to be moderated by other factors and may be found only among children with

dyslexia exhibiting visuospatial difficulties (Bemporad & Kinsbourne, 1983; Previc, 1991), or among children with dyslexia who present comorbidities, such as DCD (Rochelle & Talcott, 2006) and Attention-Deficit/Hyperactivity Disorder (Rochelle & Talcott, 2006; Wimmer et al., 1999). This may explain the absence of difference between the children with and without DD.

Because our study relied on a large-scale archival database, we were limited to the variables present in ALSPAC which were not made to specifically answer our hypotheses and for which errors and inaccuracies are possible due to the influence of multiple experimenters in the acquisition of the data. Nonetheless, using such data from a large-scale study allows for the analysis of a large sample of rare populations (i.e., breech fetal presentation). This is essential to deal with the lack of statistical power inherent in rare phenomena and therefore represents an important tool in tackling the replicability crisis. Furthermore, although the sample size is large, most of our results are statistically non-significant. Thus, whilst the data has some limitations, it was still able to probe the theoretical model that we are testing and tends to refute it. Therefore, our results can be considered valid and raise the important question of the relevance of designing a longitudinal study (which would be expensive in time, human resources, and participants) to specifically test this model if there is nothing in an existing large-scale database to support it.

5 | CONCLUSION

Our study aimed to test the LODT. We found no evidence to support the hypothesis that breech presentation at birth is linked to children's vestibular system functioning, handedness, language and motor abilities. Our findings are in line with the perspective that handedness is mainly dependent on genetic factors and randomness (McManus, 2021), but also support previous findings in which nongenetic factors, such as stress, may exhibit a genuine but weak influence on handedness (de Kovel et al., 2019). Thus, if handedness is influenced at least partially by environmental factors as well as through epigenetics regulation (Berretz et al., 2020; Schmitz et al., 2017), the influence of stress and, as yet unidentified additional non-genetic factors deserves further investigation.

AUTHOR CONTRIBUTIONS

Jad Hamaoui and Hervé Segond conceived the paper. Jad Hamaoui and Nicolas Stefaniak wrote the paper with inputs from Hervé Segond. All authors contributed to the review and approval of the final version of the article.

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CONFLICT OF INTEREST

No potential conflict of interest was reported by the author(s).

ETHICS STATEMENT

Ethical approval for the study was obtained from the Research Ethics Committee of the University of Strasbourg (see <https://cil.unistra.fr/registre.html#proc-374>), from the ALSPAC Ethics and Law Committee, and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time.

DATA AVAILABILITY STATEMENT

The informed consent obtained from ALSPAC participants does not allow the data to be made freely available through any third party maintained public repository. However, data used for this submission can be made available on request to the ALSPAC Executive. The ALSPAC data management plan describes in detail the policy regarding data sharing, which is through a system of managed open access. Full instructions for applying for data access can be found here: <http://www.bristol.ac.uk/alspac/researchers/access/>. The ALSPAC study website contains details of all the data that are available (<http://www.bristol.ac.uk/alspac/researchers/our-data/>).

ORCID

Jad Hamaoui  <https://orcid.org/0000-0003-2935-813X>

Nicolas Stefaniak  <https://orcid.org/0000-0001-8947-7849>

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