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Effects of normal and abnormal loading conditions on morphogenesis of the prenatal hip joint: application to hip dysplasia

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ABSTRACT

Joint morphogenesis is an important phase of prenatal joint development during which the opposing cartilaginous rudiments acquire their reciprocal and interlocking shapes. At an early stage of development, the prenatal hip joint is formed of a deep acetabular cavity that almost totally encloses the head. By the time of birth, the acetabulum has become shallower and the femoral head has lost substantial sphericity, reducing joint coverage and stability. In this study, we use a dynamic mechanobiological simulation to explore the effects of normal (symmetric), reduced and abnormal (asymmetric) prenatal movements on hip joint shape, to understand their importance for postnatal skeletal malformations such as developmental dysplasia of the hip (DDH). We successfully predict the physiological trends of decreasing sphericity and acetabular coverage of the femoral head during fetal development. We show that a full range of symmetric movements helps to maintain some of the acetabular depth and femoral head sphericity, while reduced or absent movements can lead to decreased sphericity and acetabular coverage of the femoral head. When an abnormal movement pattern was applied, a deformed joint shape was predicted, with an opened asymmetric acetabulum and the onset of a malformed femoral head. This study provides evidence for the importance of fetal movements in the prevention and manifestation of congenital musculoskeletal disorders such as DDH.

1. Introduction

During prenatal joint development, the two opposing cartilaginous rudiments of a joint develop their reciprocal and interlocking shapes through a process known as morphogenesis (Pacifici et al., 2005). Joint morphogenesis is a continuous process which commences prior to, and continues after, joint cavitation (Nowlan and Sharpe, 2014). Human hip joint morphogenesis has been described by Ralis and McKibbin (1973). At gestational week 11, a globular femoral head is almost completely enclosed by a deep-set acetabulum. From that time until birth, the acetabulum becomes shallower and the femoral head loses substantial sphericity, becoming more hemi-spherical. The coverage of the femoral head is at its lowest at birth (Ráliš and McKibbin, 1973), which most likely means that the hip joint is at its most unstable shape at this time. Alterations of the normal process of joint morphogenesis are highly relevant to postnatal skeletal malformations, particularly to developmental dysplasia of the hip (DDH). DDH occurs when the hip joint is malformed, unstable or dislocated, and occurs in 1.3 per 1000 births (Leck, 2000). Two types of dislocation have been defined (American Academy of Pediatrics, 2000). Teratologic dislocations occur early in utero, and are usually associated with neuromuscular abnormalities, while typical dislocations occur *in utero* or after birth in otherwise healthy infants. In the most severe cases of DDH, the femoral head is completely dislocated from the acetabulum, while in less severe manifestations, the femoral head is partially dislocated or easily dislocatable from the acetabulum (Ponseti, 1978). The risk of DDH increases with abnormal fetal movements or suboptimal intrauterine conditions. Fetal breech position, particularly extended breech where the hips are flexed and knees extended, has been shown to increase the risk of hip instability and dysplasia (Luterkort et al., 1986; Muller and Seddon, 1953). Portinaro et al. (1994) hypothesized that ligamentous laxity or malpositioning in utero can lead to abnormal joint loading, where the femoral head can displace and encourage deformity. First-born infants are twice as likely to be affected by DDH compared with the successive siblings (Record and Edwards, 1958), likely due to a narrower intra-uterine cavity in these pregnancies (Hinderaker et al., 1994). It has been

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proposed that the reason why the left hip has a higher risk of DDH than the right is due to the common position of the fetal left leg beside the mother's spine, which limits hip abduction (Aronsson et al., 1994; Ward and Pitsillides, 1998).

Despite the acknowledged influence of fetal movements on hip joint formation, the mechanism by which these movements affect joint morphogenesis is still unknown. Previous studies suggest that prenatal joint growth and shape depend on two major factors, the biological (i.e. intrinsic) growth, due to hormones, genes and nutrients, and the mechanobiological growth, due to muscle, ligament and joint forces (Giorgi et al., 2014; Heegaard et al., 1999). In this study, we develop a mechanobiological simulation of prenatal hip joint morphogenesis with which to propose and test hypotheses on how fetal movements impact upon the shape of the developing hip joint, in order to provide new insights into the normal physiology of joint morphogenesis and into the etiology of DDH. We predict growth and shape change of an idealised hip joint, correlate our predictions with human hip joint shape data, and investigate the effects of reduced, or asymmetric, movement at various stages of fetal development. We hypothesise that reduced movements due to suboptimal intrauterine conditions, or asymmetric loading on the acetabulum due to fetal breech position or increased joint laxity, may negatively influence hip joint shape at birth.

2. Methods

2.1. Model geometry and material properties

An idealised 2D geometry of a simplified hip joint was created in Abaqus (Dassault Systemes, CAE module, version 6.12). The joint consisted of two opposing cartilage rudiments: the proximal femur and the pelvis, which included a concave acetabular region (Fig. 1A). The interlocking shape was designed with the same proportions of a human hip joint at gestational week (GW) 11 of development (Ráliš and McKibbin, 1973), while the initial dimensions were arbitrary (Fig. 1A). The initial depth-to-diameter ratio of the acetabulum was approximately 75%, and the femoral head perfectly matched the acetabular shape with a height-to-diameter ratio of approximately 85% (Fig. 1A and B). The junction of the three cartilagineous ends of the ilium, ischium and pubis, known as the triradiate cartilage, is the site of radial acetabular growth during the fetal period (Portinaro et al., 1994; Scheuer and Black, 2004). The femoral head does not undergo secondary ossification until after birth (Scheuer and Black, 2004), and the models were entirely cartilaginous for the duration of the simulations. Cartilage (E=1.1 MPa, υ=0.49) (Tanck et al., 2004; Wong et al., 2000) was assumed to be linear elastic, isotropic and homogeneous (Carter and Beaupre, 1999; Shefelbine and Carter, 2004).

2.2. Movements and boundary conditions

The pelvis was fixed for all translations and rotations at its proximal end and at its sides. In the case of normal (symmetric) movement, the shaft of the femur was initially aligned with the vertical axis of the pelvis in order to obtain a perfect match between the femoral head and the acetabulum (Fig. 1A). The explicit module of Abaqus (Dassault Systemes, CAE module, version 6.12) was used to simulate dynamic joint movements by applying a rotation to the centre of the femoral head. A complete cycle of motion included four different phases, a pre-load phase followed by three rotations of the femoral head around its centre. During the pre-load phase, an axial displacement of 1 μm was applied on the distal rudiment towards the proximal rudiment, and this displacement was maintained through the entire motion to generate contact between the two rudiments. The three rotations were as follows: (1) anticlockwise rotation of the femoral head, from the midline position to the extreme left; (2) clockwise rotation, from left to right; (3) anticlockwise rotation of the femoral head to the initial midline position. Frictionless, impenetrable contact was modelled between the two components of the model.

Growth and morphogenesis of the hip joint from GW 11 to term were modeled with 28 cycles, where one cycle was equivalent to approximately one week. Two variables were identified as decreasing over the course of development, namely the rate of fetal growth (and therefore the rate of *rudiment expansion*) and the *range of hip motion* (Fig. 1C). By plotting the fetal weight change (Doubilet et al., 1997) on a logarithmic scale, we identified three stages during which the fetus grows at different rates (Fig. 1C), namely: 1) early stage, from GW 11 to 18; 2) middle stage, from GW 19 to 34; 3) late stage, from GW 35 to term. The rate of *rudiment expansion* in the model was adapted according to the rate of fetal growth (Fig. 1C) and was implemented by varying the orthonormal thermal expansion capabilities of the finite element solver.

There is very little information on the range of motion of the prenatal hip joint. However, fetal cine-MRI can now be used for viewing and assessing fetal movements (Hayat et al., 2011). Using fetal cine-MRI data obtained from our collaborators (Profs Hajnal and Rutherford, King's College London, UK), we were able to make a realistic estimate of the range of motion at the hip over gestation. Five MR images sequences, corresponding to 5 subjects, were analysed and the maximum range of hip motion over the 1.5 min average time frame of the scan was calculated. Scans were taken with a slice thickness of 30–40 mm (Hayat et al., 2011). The angle generated by the intersection of the line of the spine and the longitudinal axis of the femur was used to quantify the hip motion as shown in Fig. 2A and B. All the image sequences belonged to the middle stage of development: three in the early-middle (GW: 21, 22) and two in the late-middle (GW: 29, 34) stages. The first set showed a maximum range of motion of 90° with an average value over the three sequences of 52°. The second set showed a maximum range of motion of 15° with an average value of 12.5°. Because all the scans belonged to the middle stage, we assumed higher and lower range of motion for the early and late stages, with an intermediate value for the middle stage. Therefore, symmetrical movements from $+/-40^\circ$ in the early stage, $+/-30^\circ$ in the middle stage, and $+/-5^\circ$ in the late stage were used to simulate the physiological range of hip motion over the course of development. In addition to physiological loading conditions, we explored the effects of altering movement patterns. Reduced movements were simulated by decreasing joint motion by approximately 80% at each of the three stages of development, as described in Table 1. Absent movements were simulated by retaining the femoral head in its initial position for the entire simulation without any rotation applied (but still maintaining the pre-load compression). The effects of asymmetric movements were also simulated. Asymmetric movements differed from symmetric movements only for the initial configuration, where the longitudinal axis of the femoral head was rotated by 20° to the right of the vertical axis of the acetabulum (Fig. 1D). Rotations occurred about this new offset axis instead of the vertical axis. This new setup was also used to explore the effect of reduced asymmetric movements at each of the three stages of development as described in Table 1. Finally, simulations with a constant rate of rudiment expansion were run in order to separate out the influences of growth rate and range of movements on the resulting joint shape.

2.3. Growth and morphogenesis

Growth and morphogenesis of the rudiments were controlled by biological and mechanobiological growth rates (Giorgi et al., 2014). The biological contribution was considered to be proportional to the chondrocyte density (Heegaard et al., 1999). For the femoral head, the chondrocyte density was greatest at the proximal epiphysis of the rudiment (Heegaard et al., 1999), while for the pelvic rudiment, the chondrocyte density was greatest at the acetabulum, as shown in Fig. 3A. We are unaware of any study quantifying the rate of expansion at the triradiate cartilage. However, by comparing the rates of growth of the murine long bones (Hansson et al., 1972) and the pelvis (Harrison, 1958), we calculated that during very early postnatal development, the pelvis grows at a rate which is close to the half that of the femur in the mouse. Therefore, we implemented our model so that the maximum value for the biological contribution at the acetabulum was half that of the femur. For sensitivity analysis purposes, simulations were also run with the same biological contribution between the pelvis and femur. The mechanobiological growth rate was proportional to the dynamic compressive hydrostatic stress generated by the movements (Giorgi et al., 2014). The overall

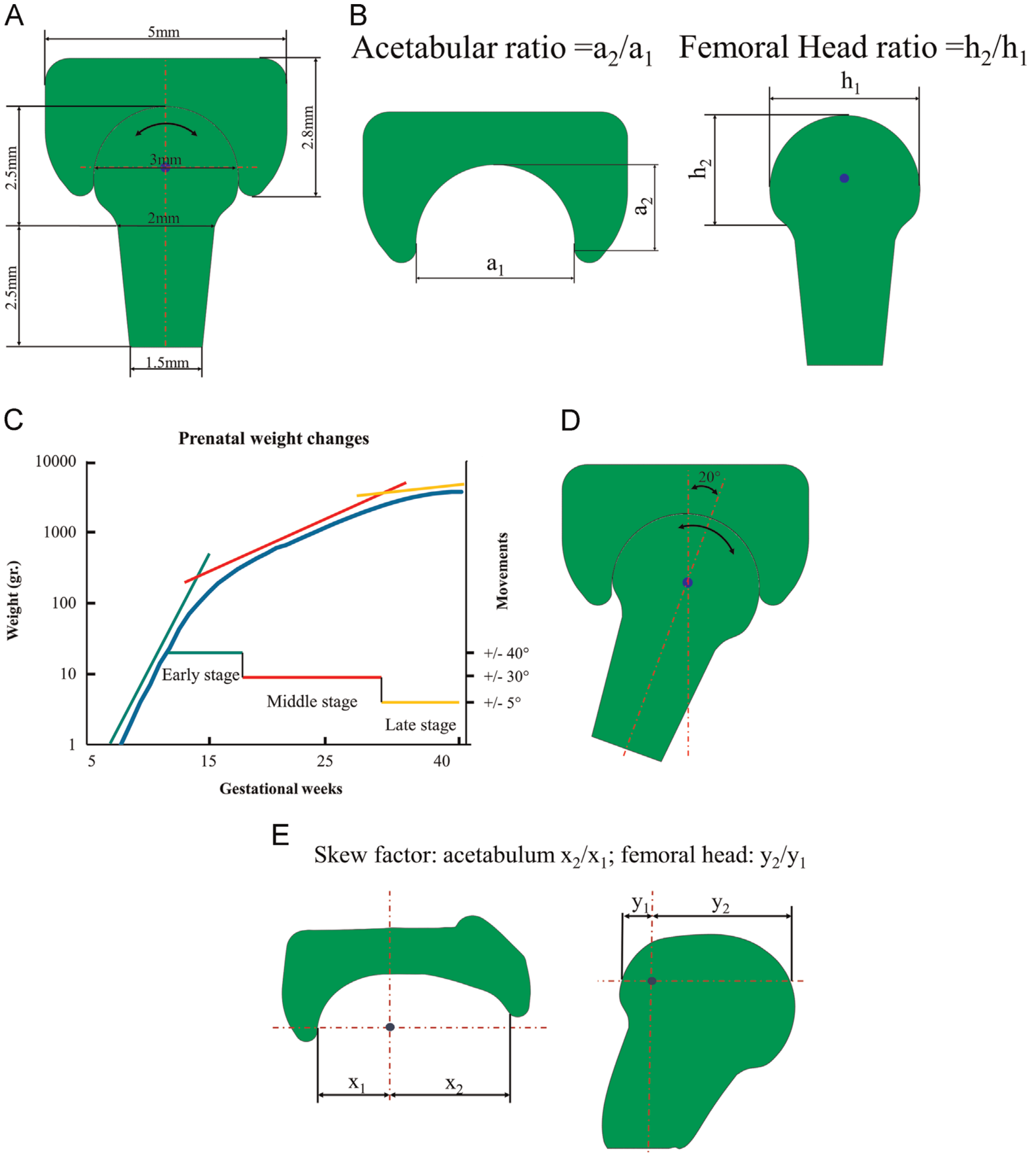

Fig. 1. (A) Dimensions of initial model of concave pelvis and spherical femoral head region. (B) Changes in shape were assessed by the measurements proposed by Ralis and McKibbin (1973), where the acetabular shape was assessed by the ratio between the deepest height (a_2) to the greatest width (a_1) of the acetabular cavity, and the femoral head shape was assessed as the ratio between the greatest height (h_2) as measured perpendicularly to the greatest diameter, and the greatest diameter (h_1) of the femoral head. (C) Changes in fetal weight on a logarithmic scale (extracted from data from (Doubilet et al., 1997) taken as a measure of the rate of fetal growth. Three stages of fetal growth were identified by fitting lines to regions of the growth curve; the movements applied for each stage are superimposed. (D) Initial configuration used for the abnormal (asymmetric) movement; the femoral head is rotated 20° to the right of the vertical axis of the acetabulum. (E) Method used to calculate the acetabular and femoral head skew factors; the former measured as the ratio of the distances between a reference point, calculated as the center of the initial acetabular cavity, and the left (x_1) and right (x_2) extremities of the acetabular space, the latter as the ratio of the distances between a reference point, calculated as the centre of the initial femoral head, and the left (y_1) and right (y_2) extremities which lie on the horizontal line passing through the reference point of the femoral head.

mechanobiological contribution to growth was calculated at each node of the model as the average stresses throughout a full joint motion and was also weighted by the chondrocyte density, based on the assumption that the greater the number of cells, the greater the potential to respond to mechanical loading (Giorgi et al., 2014). The total growth was the sum of the biological and mechanobiological contributions as shown by the equations below (Giorgi et al., 2014):

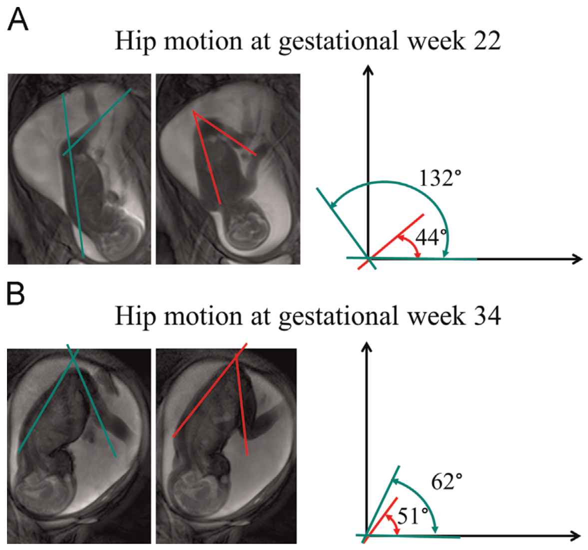

Fig. 2. (A) Two timeframes from a fetal cine-MRI at 22 gestational weeks showing a hip flexion-extension range of 88°. (B) Timeframes from a fetal cine-MRI at 34 gestational weeks showing a hip flexion-extension of 11°. These data were used to estimate the range of motion at the hip over gestation. Fetal cine-MR images courtesy of Professors Hajnal and Rutherford, King's College London, UK.

Table 1
Ranges of motion, in degrees, applied about an axis during each stage of development for simulations involving symmetric and asymmetric movements. When symmetric movements were applied, the centre of the axis of rotation was through the midline of the femoral head, with the initial position of the femoral head being perpendicular to the acetabulum. Equivalent reductions in the early, middle, late stages, and absent movements, were also simulated for the abnormal initial position of the femur which was rotated 20° to the right.

Type of movements	**Early** Week 11–18	**Middle** Week 19–34	**Late** Week 35-term
Symmetric movements [°]			
Physiological	+/−40	+/−30	+/−5
Early reduction	+/−10	+/−30	+/−5
Middle reduction	+/−40	+/−8	+/−5
Late reduction	+/−40	+/−30	+/−1
No movements	0	0	0

$$\frac{d\varepsilon}{dt} = \frac{d(\varepsilon_b)}{dt} \dot{+} \frac{d(\varepsilon_m)}{dt}$$

where

$$\frac{d(\varepsilon_b)}{dt} = \dot{\varepsilon}_b = C_d = (0.14 - 0.87\xi^2 - 2.66\xi^3)$$

$$\frac{d(\varepsilon_m)}{dt} = \dot{\varepsilon}_m = -C_d * \left(\frac{\sum_{i=1}^{N} \sigma_{hi}}{N} \right)$$

where $\dot{\varepsilon}_b$ and $\dot{\varepsilon}_m$ are the biological and mechanobiological contribution to growth respectively (Shefelbine and Carter, 2004), C_d the chondrocyte density, which is a function of ξ, the distance from the end of the rudiment. σ_h the compressive hydrostatic stress, and N the number of movements per step.

Morphological changes due to growth or adaptation were analysed relative to the initial shape of the joint. The changes in shape were assessed over time by looking at two parameters, the "acetabular ratio" and the "femoral head ratio". These parameters are derived from the measurements proposed by Rališ and McKibbin (1973) and as shown in Fig. 1B. The congruence of the joint over the developmental period was assessed as the degree of joint coverage, which was measured as the length of the edges in common between the acetabulum and the femoral head. As a measure of asymmetry, we calculated the acetabular and femoral head skew factors (Fig. 1E). A reference point was identified using the centre of the initial acetabular cavity, the crossing point between its vertical and horizontal axes (Fig. 1A and E). This reference point was then kept constant over development, and the skew factor was calculated as the distance between this point and its most left and right extremities (Fig. 1E). The same technique was used for the femoral head, where the skew factor was calculated as the distance between the rotational center, and the left and right extremes on the horizontal line through the reference point.

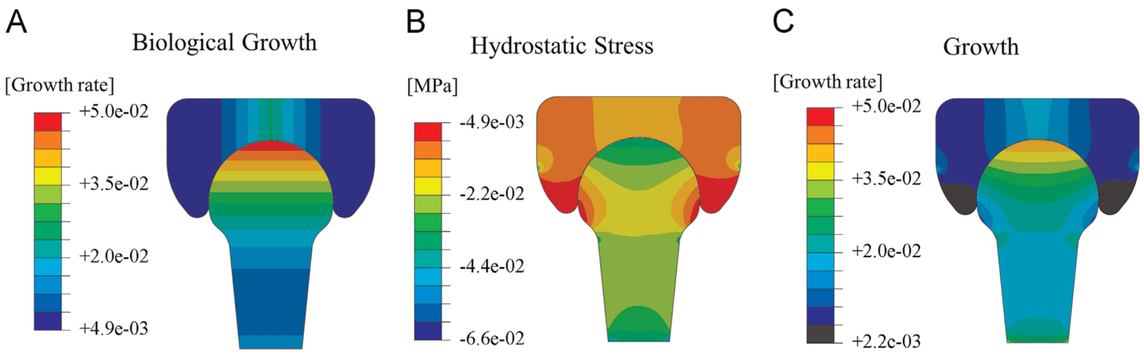

Fig. 3. (A) Biological contribution to growth; for the femoral head the chondrocyte density was greatest at the proximal end of the epiphysis, while for the pelvis the density was highest at the centre of the acetabulum. (B) Resulting hydrostatic stresses, averaged over the first full cycle of physiological motion. Stresses were higher along the acetabular rim and at the regions of curvature of the distal femoral head. (C) The stresses generated by the combination of biological and hydrostatic stresses lead to higher values of growth at the proximal end of the femoral head and at the center of the acetabulum.

3. Results

3.1. Hydrostatic stress distribution

The resulting hydrostatic stresses of an entire cycle of motion were always compressive, as shown by Fig. 3B, due to the two rudiments being always in contact. Stresses due to symmetric movements, when applied to the initial geometry, were higher in the acetabulum (especially in its rim) and along the distal curvature of the femoral head. When combined with the biological growth rates, the stresses generated by one full cycle of physiological motion showed higher values of growth at the most proximal part of the femoral head and at the middle of the acetabulum (as shown in Fig. 3C).

3.2. Morphogenesis

When growth due to physiological symmetric movements was simulated, the model predicted a progressive opening of the acetabulum, making it increasingly shallow up to birth, and a gradual decrease in roundness of the femoral head with the onset of a flatter surface at its most proximal region (Fig. 4A and B). The predicted joint at birth had roughly half the acetabular coverage of the initial shape, but maintained a clear interlocking shape (Fig. 4A). The predicted trends showed a striking similarity with the experimental data (Ráliš and McKibbin, 1973), as shown in Fig. 4B and C. The predicted decrease in the acetabular ratio over the course of the simulation is almost identical (although slightly shifted) as compared to the experimental curve, while our model predicts a faster decrease in femoral head roundness in the early phase of gestation than for the experimental data. When reduced movements at the early stage were simulated, the femoral head roundness decreased further and the acetabulum became shallower compared to the physiological predictions (Fig. 5A and B), resulting in a 60% decrease in acetabular coverage of the femoral head (as compared with the initial shape), and therefore potentially a less stable joint at birth. Reduced movements at the middle or late stage of development resulted in minimal joint shape changes from the physiological joint prediction (Fig. 5A). When absent movements were simulated the acetabulum became even shallower and the femoral head ratio decreased even further

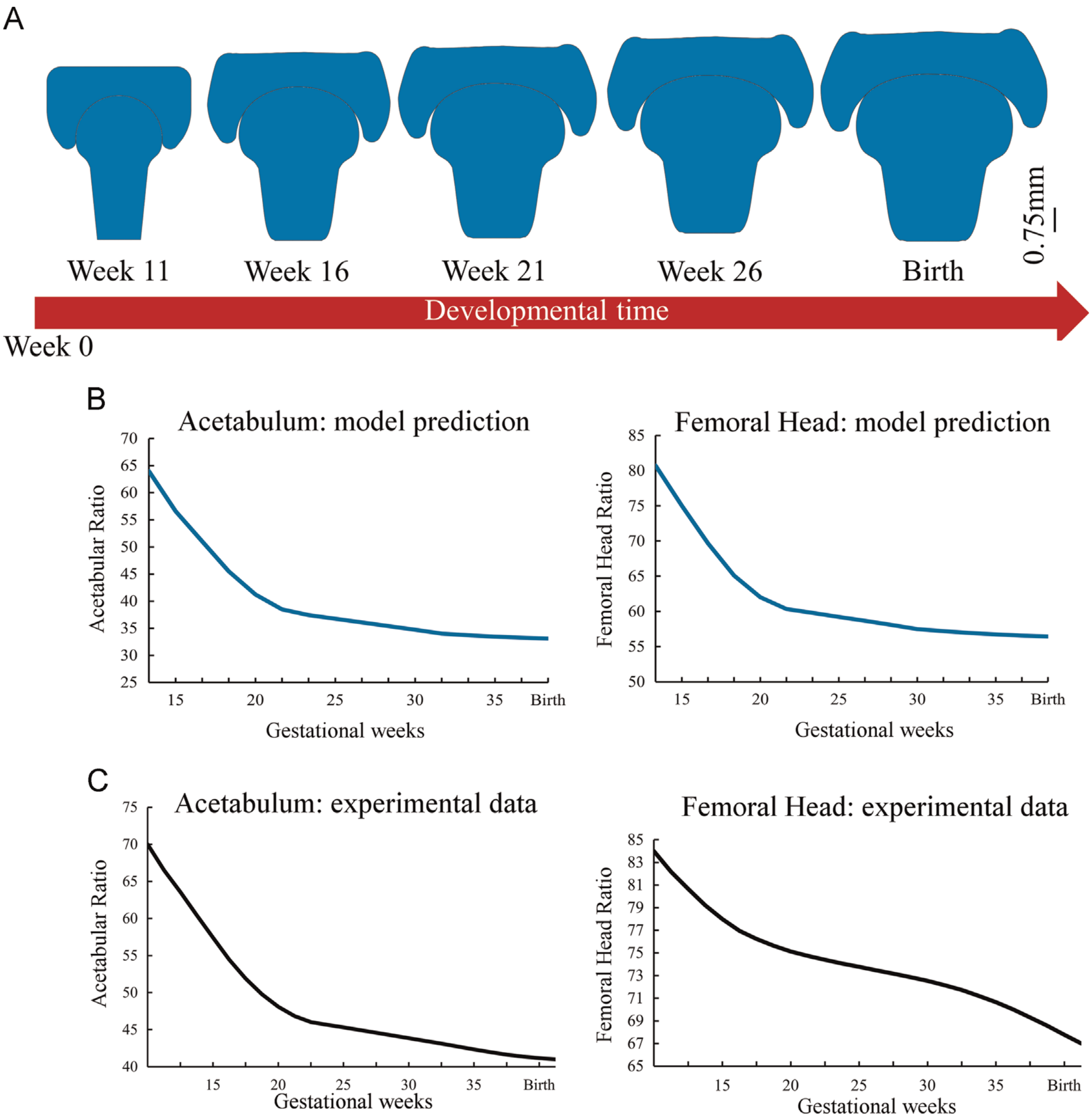

Fig. 4. (A) Predicted hip joint morphogenesis under physiological symmetric movements; a progressive opening of the acetabulum and a gradual decrease in roundness of the femoral head were predicted. (B) Quantification of the changes in shape based on the acetabular shape and femoral head roundness parameters. (C) Changes in human hip joint shape over development measured experimentally by Ráliš and McKibbin (1973).

compared with the predicted shape for early reduced movements (Fig. 5A). Therefore, the presence of movements at the early stage were most critical in maintaining acetabular coverage of the femoral head, with reduced or absent movements in the early stage contributing to decreased coverage of the femoral head, and a likely reduction in joint stability. When simulations were run with the same biological contribution between the pelvis and femur, the results showed the onset of a non-interlocking joint shape (Supplementary Fig. 1). When a constant rate of rudiment expansion was implemented, the results showed that the rates at which the acetabular ratio and the femoral head ratio decreased were inversely proportional to the ranges of movement (Supplementary Fig. 2). Therefore, the reason why movement is most critical at the early stage of development is due to the higher rate of fetal growth (rudiment expansion) used during this stage.

When an asymmetric movement pattern was applied, the acetabulum became increasingly open in the direction of the applied loads (Fig. 6A), leading to development of an asymmetric shape. The shape of the femoral head was also affected, showing a loss of head roundness and the onset of a malformed overall shape (Fig. 6A). The predicted shape is similar to the deformed shape typical of a dysplastic hip joint as shown in Fig. 6B. When asymmetric movements were reduced, or absent completely, a deeper acetabulum was predicted for simulations with reduced early, or absent movements, than for simulations with a full range of asymmetric movements, or reduced movements in the middle or late stages (Fig. 7A). By measuring the acetabular skew factor (Fig. 1E), we observed that the simulations with a full range of asymmetric movement throughout, or full asymmetric movement at the early stage, resulted in a more asymmetric acetabular shape compared with other asymmetric simulations (Fig. 7B). This suggests that, in case of asymmetric loading, the higher the range of movement at an early stage, the higher the likelihood of a skewed, shallower acetabulum. Therefore, asymmetric movements have the opposite effect on acetabular shape than symmetric movements. No influence of reduced or absent asymmetric movements, as compared to a full range of asymmetric movements, was found for the femoral head roundness or skew factor (data not shown), which always exhibited the asymmetric profile shown in Fig. 6.

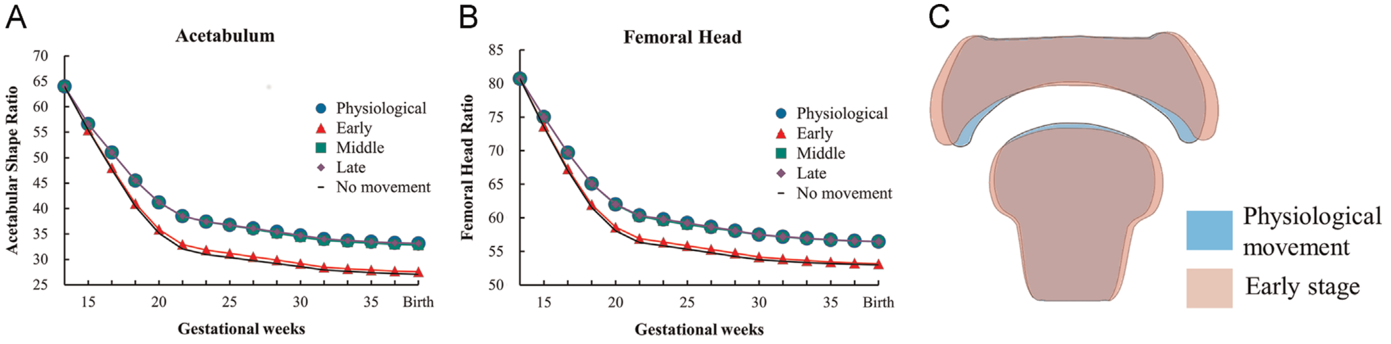

Fig. 5. (A) The effects on acetabular and femoral head shape of reduced movements at each stage of development (early, middle and late) and of a complete absence of movements. When movements were reduced at the early stage, the acetabulum became shallower and the femoral head roundness decreased compared to the predictions for physiological movements. Reduced movements in the middle and late stages of development resulted in minimal joint shape changes. When absent movements were simulated, the shape changes were similar to those of the early reduction simulation, with the predicted joint shape for absent movement having a slightly shallower acetabulum than that of the early reduction. (B) Predicted shapes under physiological movements (blue) and early reduction of movements (red). When movements were reduced in the early stage, a less rounded femoral head and a shallower acetabulum were predicted. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

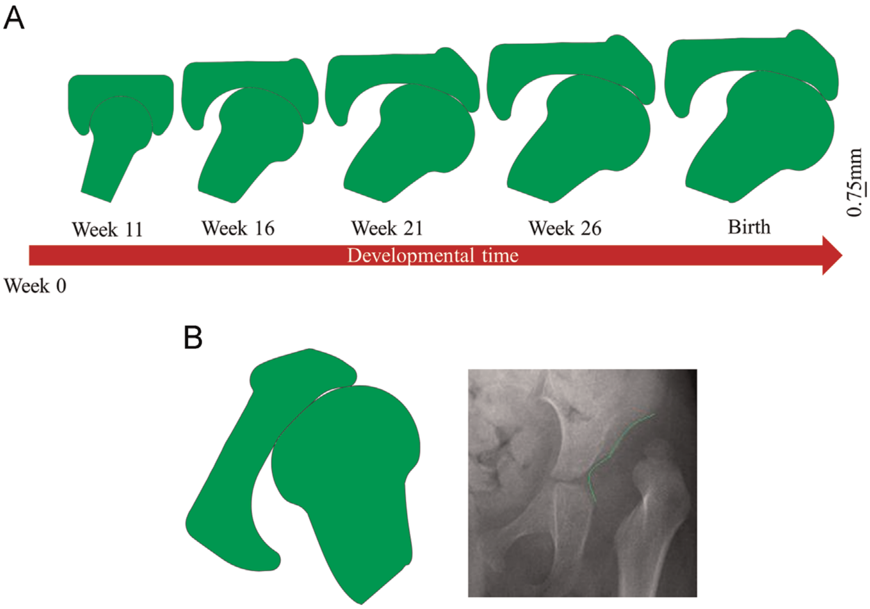

Fig. 6. (A) Predicted joint morphogenesis under asymmetric movements; a progressive opening of the acetabulum in the direction of the applied loads was predicted, while the femoral head showed a loss of head sphericity and malformation on the medial side. (B) The predicted hip joint shape at birth when asymmetric loading occurs is similar to the hip joint of a 30 month old infant affected by DDH. Image adapted with permission from Dr Frank Gaillard from website www.radiopaedia.org.

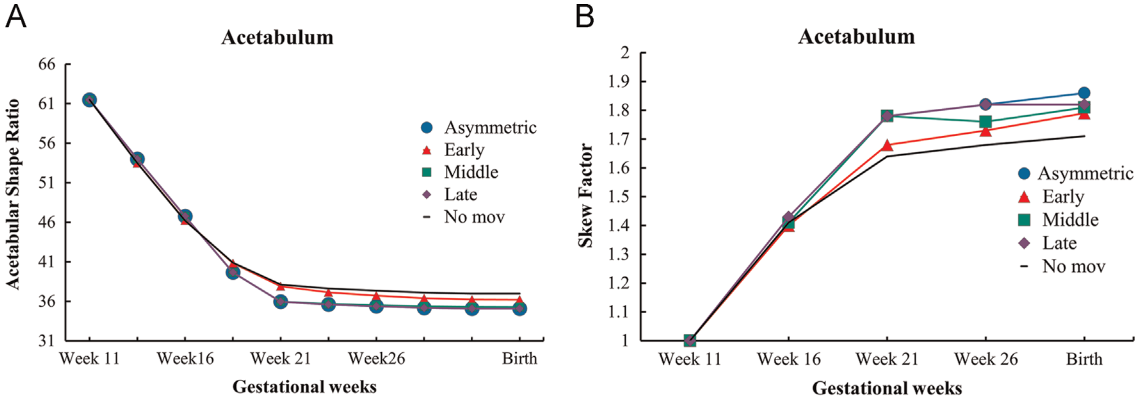

Fig. 7. (A) The effects of reduced asymmetric movements on acetabular shape and (B) skew factor at each stage of development (early, middle and late) and under a complete absence of movements. With a full range of asymmetric movement, or reduced movement at the middle or late stages, the predicted acetabular shape was shallower than for simulations with no movement or with reduced movement in the early stage.

4. Discussion

In this study we describe a dynamic mechanobiological simulation of the prenatal hip joint with which we explore the effects of normal, reduced and asymmetric fetal movements on hip joint growth and morphogenesis, providing insight into the normal physiology of the hip joint and the etiology of DDH. The predicted joint shapes when physiological, symmetric movements were applied well approximated the anatomical changes in shape reported in the literature for fetal human hip joint development (Ráliš and McKibbin, 1973). In our predictions, the acetabulum progressively opened and the femoral head showed the onset of a flatter surface at its proximal end over development (Fig. 4A and B). The overall joint shape changes replicated the trends of human hip joint development, where its natural growth and development leads to a decrease in coverage of the femoral head while maintaining its interlocking shape (Fig. 4A–C).

When reduced symmetric movements at the early stage of development were simulated, the joint maintained its interlocking shape at birth but the femoral head roundness decreased and the acetabulum became shallower (Fig. 5A and B). Our results suggest that fetal movements tend to minimise the natural trend of decreasing stability (Fig. 5A). When, for sensitivity analysis, symmetric movements with a constant growth rate (rudiment expansion) were simulated, the rates at which the acetabular ratio and the femoral head ratio decreased were inversely proportional to the ranges of movement. This indicates that, with a constant growth rate, the larger the range of movement, the greater the acetabular depth and femoral head roundness. The shape predicted under early reduced movements would likely be less stable at birth than under normal physiological conditions due to the loss of joint coverage, which would increase the risk of subluxation or dislocation of the hip. When reduced movements at the middle or late stage of development were simulated, minimal changes in joint shape compared to growth under physiological movement were observed (Fig. 5A), suggesting that movement in the early stage of development is the most critical for joint shape. This may explain why the hip joint is so severely affected in cases of paralytic dislocations, where movement may have been reduced or absent from an early stage of development. When an asymmetric movement pattern was simulated, the predicted joint shape was abnormal: the acetabulum opened in the same direction as the applied loads and the femoral head lost its roundness, showing an overall deformed shape of the joint typical of hip dysplasia as shown in Fig. 6B. Acetabular depth and skew were exacerbated with greater asymmetric movement ranges (Fig. 7B), suggesting that increased movements in the case of mal-positioning or joint laxity in utero may actually increase the risk of DDH.

Although the shape of the joint and movement patterns have been simplified in this model, our simulations predicted similar anatomical changes in shape to the experimental measurements presented by Ráliš and McKibbin (1973) (Fig. 4C) allowing us to explore the effects of normal, reduced and abnormal prenatal movements on hip joint shape. While the predicted decrease in the acetabular ratio was almost identical (although slightly shifted), the decrease in femoral head ratio was faster, especially in the early phase of gestation, compared to the experimental curve (Fig. 4B and C). The difference in the predictions may be due to the shapes used, as while the simple profile used for the acetabulum is likely to represent the structure fairly well, the symmetric shape used for the femoral head is much simpler than the reality. Accurate 3D shapes of prenatal joints are currently not available, but we expect that if a more realistic femoral head shape were to be included in our model, more accurate results would be obtained from our simulations. We are unaware of any previous studies showing the physiological range of motion of the prenatal hip. For this study, the maximum range of hip motion at different stages was gathered by analysing different MR imaging sequences of the developing fetus. Even if the actual range of motion used may not perfectly match with the real physiological motion, the reduced trend of physiological symmetric movements over time reflect the finding of Hayat et al. (2011). In this study, we assumed that during normal development the movement at the fetal hip joint is symmetric, based on previous observations that at the very early prenatal age the femoral head is almost fully covered by the acetabular cavity (Ráliš and McKibbin, 1973) minimising all translations. Conditions such as fetal breech position or joint laxity which are risk factors for DDH (Luterkort et al., 1986; Muller and Seddon, 1953; Portinaro et al., 1994), were assumed to lead to asymmetric movements at the hip, due to the loss of the distributed pressure patterns that these conditions may generate. All the simulations were run using 2D dynamic models, due to the lack of access to fetal realistic hip joint shapes. However, as stated in our previous study (Giorgi et al., 2014), minimal additional insights on the effects of joint motion on shape could have be gained by using 3D simulations in the absence of realistic joint shape.

In conclusion, this study demonstrates that normal fetal movements are important for the emergence of hip joint shape and coverage. The natural tendency of the developing hip joint is to decrease in sphericity and acetabular coverage of the femoral head between 11 gestational weeks and birth (Ráliš and McKibbin, 1973) and our model predicted these physiological trends. We show that physiological, symmetric movements help to maintain some of the acetabular depth and femoral head sphericity while reduced movements at an early stage of development or completely absent movements, such as could occur from a neuromuscular disorder, lead to decreased sphericity and acetabular coverage of the femoral head, increasing the risk of subluxation or dislocation of the hip. We also show that asymmetric movements, which we hypothesise to result from fetal breech position or increased joint laxity, lead to an abnormal hip joint shape with characteristics of DDH such as a malformed femoral head and an asymmetric shallower acetabulum, which increase the likelihood of dislocation of the femoral head (Larsson et al., 1991; Ziegler et al., 2008). Therefore, this research provides evidence for the importance of fetal movements in promoting normal hip joint morphogenesis, particularly joint coverage, and an explanation of how abnormal movements could lead to joint instability and DDH in the infantile hip.

Conflict of interest

The authors have no conflicts of interest relating to this research.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jbiomech.2015.06.002.

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