Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–8, 2017

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2017.06.017

● *Original Contribution*

EFFECT OF PRETERM BIRTH ON ECHOGENICITY IN BASAL GANGLIA

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(*Received* 13 *February* 2017; *revised* 6 *June* 2017; *in final form* 16 *June* 2017)

Abstract—In this study, the influence of prematurity on echogenicity of deep gray matter at 30-wk corrected age was assessed using ultrasound measurements. In an observational cohort study, ultrasound scans of 224 extremely preterm infants were prospectively collected. Gray values were assessed in putamen and globus pallidus. Intra- and inter-observer reliability was analyzed and showed excellent agreement. The globus pallidus to putamen ratio was significantly related to gestational age at birth, adjusted regression coefficient in points per wk: 1.28 (95% confidence interval [CI]: 0.38–2.19) for left and 2.12 (95% CI: 1.23–3.02) for right-side images. At 30-wk corrected age this was still the case, adjusted regression coefficient: 0.45 (95% CI: −0.57 to 1.47) for left and 1.29 (95% CI: 0.10–2.48) for right. The putamen is more hyperechoic with lower gestational age. Measuring ultrasound gray values in deep gray matter seems highly reproducible. Prematurity shows a negative correlation with echogenicity of the putamen, this persists at 30-wk corrected age, suggesting altered maturation. (E-mail: j.dudink@umcutrecht.nl) © **2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Prematurity, Preterm birth, Cerebral ultrasound, Echogenicity, Putamen, Globus pallidus.**

INTRODUCTION

Advances in prenatal and neonatal care have led to increased survival of infants born preterm, but preterm birth can still seriously compromise the normal development of the newborn brain (Doyle et al. 2010; Draper et al. 2009; Schlapbach et al. 2012). Transfontanellar cerebral ultrasound (CUS) is traditionally used to detect major brain abnormalities during neonatal intensive care treatment (de Kieviet et al. 2012). CUS has several advantages: the technique is relatively inexpensive, it allows for serial bedside scanning with limited disturbance of the vulnerable infants and major lesions (such as venous infarctions) can be clearly diagnosed (Ecury-Goossen et al. 2015). However, subtler alterations of brain microstructure, often seen as hyperechogenicity, are notoriously difficult to quantify (Volpe 2009). Advanced magnetic resonance imaging techniques, such as diffusion tensor imaging, do provide quantitative measurements of brain tissue microstructure (Dudink et al. 2008; Ment et al. 2009; Smyser et al. 2013; Tusor et al. 2014), but lack the advantages of bedside ultrasound (Ecury-Goossen et al. 2015). In preterm infants, most types of brain injury, including white-matter injury, are linked to impaired development of basal ganglia and thalamus *via* direct effects or secondary network injury (Inder et al. 2005; Kersbergen et al. 2015; Lin et al. 2001; Volpe 2009). In very preterm infants the putamina have been described as more hyperechoic on ultrasound than in term or near-term infants (Leijser et al. 2004; Soghier et al. 2006; van Wezel-Meijler et al. 2011). It is unclear whether this finding partly reflects altered maturation (pathology) because both prospective cohort studies and quantification are lacking.

To be able to *objectively* measure echogenicity using standard ultrasound machines, variables such as probe physics, post processing and time gain compensation (TGC) have to be taken into account before gray values

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can be reliably measured and compared among images (Vansteenkiste et al. 2009). Calculating ratios of gray values such as the globus pallidus to putamen (GPP) ratio (with both structures measured at the same depth and TGC segment), solves most of these challenges.

The objective of this study was to find a *reliable* method to measure relative gray values in basal ganglia of preterm infants born <29 wk gestation, to study the influence of prematurity on echogenicity of deep gray matter at birth and at 30-wk corrected age. We hypothesized that basal ganglia echogenicity would not only be associated with wk gestation at birth, but would actually show prematurity related persistent changes at 30 wk gestation, suggesting altered maturation.

METHODS

This longitudinal prospective observational cohort study was conducted in the neonatal intensive care unit of the Erasmus MC–Sophia Children's Hospital Rotterdam, The Netherlands, May 2010–January 2013. All infants born before 30 wk' gestational age (GA) was eligible. Exclusion criteria were uncertain GA and congenital brain abnormalities. Informed consent was received from both parent(s) or guardian(s) for all patients. The local medical ethics review board reviewed and approved this study.

Image acquisition

All included infants were prospectively studied with CUS according to a standard protocol (on days 1, 3 and 7 after birth and then 1 × wk), using an Esaote MyLab 70 (Esaote, Genoa, Italy) with a convex probe (8.5 MHz). Standard settings included a depth of 76 mm, persistence of 11, gain of 70% and frequency of 8.5 MHz. All images were obtained by one observer (M.R.) and digitally stored in an Esaote MyLab (Esaote) environment. Lesions were reviewed by two of us (M.R., P.G.). For this study, the first good-quality CUS after birth was included and parasagittal images of both sides had to be present. Also, the first CUS of good quality performed 29–31 wk corrected age, with parasagittal images of both sides, was included. Parasagittal images through the basal ganglia were used to be able to reliably measure and compare echogenicity between nuclei in 1 image. The first region of interest (ROI) was placed in the putamen, just below the anterior limb of the internal capsule. The second ROI was placed in the same TGC segment in the globus pallidus, recognizable as a hypoechoic region between putamen and thalamus (Fig. 1) (Govaert and de Vries, 2010). Round ROIs of identical size were used (Fig. 2). Images were evaluated on 2 criteria: (i) good visibility of the entire ganglio-thalamic ovoid with anterior horn of the lateral ventricle up to and including the choroid plexus; and (ii) good visibility of the putamen, globus pallidus and thalamus in the ganglio-thalamic ovoid. Several precautions were taken to compensate for attenuation differences. ROIs were placed at the same depth and TGC segment. Only ratios between nuclei in the same image were used to compare results among images and patients.

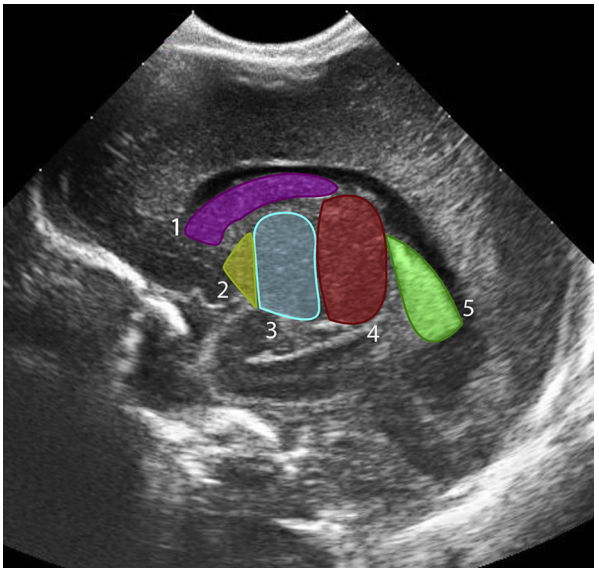

Fig. 1. Parasagittal ultrasound image through the anterior fontanel. This image gives a good overview of the structures of interest and the various nuclei are easily recognized. Structures: 1. Caudate nucleus; 2. Putamen; 3. Globus pallidus; 4. Thalamus; 5. Choroid plexus.

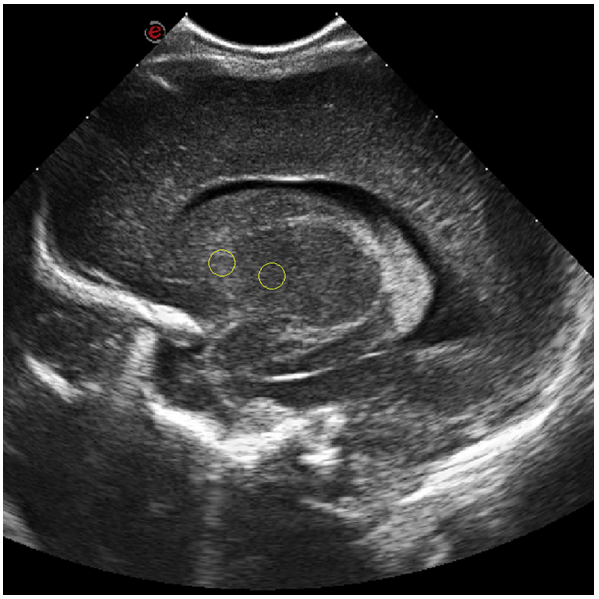

Fig. 2. Parasagittal ultrasound image through the anterior fontanel, containing two ROIs in the same time gain compensation segment. From the left to the right: putamen and globus pallidus. ROIs = regions of interest.