INTRODUCTION
Intrauterine Growth Restriction (IUGR) due to placental insufficiency affects 5-10% of all pregnancies and it is associated with a wide range of short and long-term neurodevelopmental disorders [1]. Different approaches have been considered to understand IUGR effects on brain development. Recently, connectomics has been used to analyze brain reorganization in IUGR children at one and two years of age [3]. Connectomics [4] estimates the brain network and describes it by different graph measures [5]. Diffusion tensor imaging (DTI) can be used to infer the connectivity between regions, since it allows in-vivo estimation of fiber tracts inside the brain. In this study, DTI based connectomics was used to describe short- and long-term brain reorganization in IUGR. The connectome of a cohort of preterm IUGR and control children at 1, 6 and 9 years of age was estimated and analyzed to evaluate differences in the architecture of neural circuitry and its evolution during development.

SUBJECTS
Three cohorts of preterm children (gestational age (GA): 28-35 weeks) were considered, being scanned at 1, 6 and 9 years of age respectively. The 1-year-old cohort was acquired at Barcelona Clinic Hospital, and the 6- and 9-year-old cohorts were acquired at Geneva University Hospital. Subjects were scanned in a 3T TIM TRIO MR Siemens. Weighted images were acquired by MPRAGE sequence (TR=2050ms, TE=2.41ms, TI=1050ms, 0.86x0.86x0.9mm³, for the 1-year-old infants; TR=2500ms, TE=2.91ms, Ti=1100ms, 1.81x1.82x2mm³, for the 6- and 9-year-old children). Diffusion weighted images (DWI) were acquired using a diffusion-sensitized EPI sequence covering 30 diffusion directions with a b-value of 1000s/mm² and an additional image without diffusion weight (TR=9300ms, TE=94ms, 1.64x1.64x3 mm³, for 1-year-old; TR=10200ms, TE=107ms, 1.81x1.82x3 mm³, for 6- and 9-year-old). All studies were performed with informed parental consent and were approved by the ethical committee of both hospitals. Infants were classified in two groups: children born moderately preterm with normal growth (controls) and children with IUGR defined as estimated fetal weight below 10th centile confirmed after birth together with an abnormal umbilical artery pulsatility index and/or cerebroplacental ratio and/or mean uterine artery pulsatility index. Group distribution is shown in the Table.

METHODS
Connectivity matrices were estimated for each subject, and graph metrics describing the network were computed, following a methodology described earlier [2]. First, the brain was segmented in white matter (WM) and gray matter (GM) using the unified segmentation model [6], and parcelled in 93 regions based on AAL atlas [7]. Parcellation was performed using a block-matching algorithm to obtain the elastic transformation relating the AAL template and the brain was segmented in white matter (WM) and gray matter (GM) using the unified segmentation model [6], and parcelled in 93 regions based on AAL atlas [7]. Connectivity between regions was calculated using a diffusion tensor imaging (DTI) based connectomic approach [5]. Among subjects and controls, nodal degree decreased with age, which could be related to axonal retraction occurring during development [9], while FA strength (which could be related to myelination) increased, as the brain connections become stronger and more organized with age [9]. Efficiency (both local and global) was decreased in IUGR in the FA-w networks, but increased in the FA-n networks. This fact could be explained as a compensatory mechanism in IUGR, where brain would be reorganized in order to compensate diminished connectivity (decreased connection amount or strength). In summary, network measures showed a pattern of brain reorganization in IUGR that is consistent in both control and IUGR brains. In addition, a pattern of developmentally reorganized connectivity can be identified, that seems to be preserved both in IUGR and controls regardless of structural differences between them [10].

RESULTS
Results show a similar pattern of variation between IUGR and controls at every age, as can be seen in figures, where * stands for differences between cases and control with a significance level p<0.1. Average degree, FA strength and global and local efficiency of FA-w network were decreased in IUGR, while the global and local efficiency of FA-n network were increased in IUGR. Differences were more significant at younger period. At 1 year of age, differences in degree (p=0.003), FA strength (p=0.023), global (p=0.002) and local (p=0.004) FA-n efficiency were statistically significant. At 6 years of age, the differences were significant in FA strength (p=0.006), global (p=0.004) and local (p=0.025) FA-w efficiency. At 9 years of age, the differences were not significant, but they followed the same trend as in younger ages.

REFERENCES