Visit 1	AHI (continuous) n=242			
	Unadjusted		Adjusted	
	Beta coefficient	P value	Beta coefficient	P value
MAP (mmHg)	0.395	*<.001	0.277	*0.004
MPI	-0.016	*0.001	-0.006	0.260
sFlt-1 (pg/mL)	39.211	0.650	109.469	0.272
PlGF (pg/mL)	0.357	0.785	0.683	0.614
sFlt-1/PlGF	-0.869	0.368	0.139	0.892
Endoglin (ng/mL)	-0.029	0.039	-0.020	0.194
Glucose (mg/dL)	0.608	*<0.001	0.375	*0.040
Mean insulin (mU/L)	-0.046	0.821	-0.115	0.621
HOMA-IR	0.010	0.870	-0.015	0.824

Visit 2	AHI (continuous) n=130			
	Unadjusted		Adjusted	
	Beta coefficient	P value	Beta coefficient	P value
MAP (mmHg)	0.243	0.270	0.083	0.711
MPI	0.010	0.072	0.009	0.126
sFlt-1 (pg/mL)	-39.082	0.875	-176.812	0.837
PlGF (pg/mL)	0.291	0.974	3.719	0.688
sFlt-1/PlGF	-0.316	0.888	-0.327	0.890
Endoglin (ng/mL)	0.004	0.929	-0.027	0.576
Glucose (mg/dL)	0.180	0.542	0.085	0.784
Mean insulin (mU/L)	-0.072	0.767	-0.029	0.907
HOMA-IR	-0.018	0.770	-0.012	0.847

Table 2: Apnea-Hypopnea Index (AHI) as a continuous variable
Abbreviations: MAP=mean arterial blood pressure, MPI=mean pulsatility index, sFlt-1=soluble FMS-like tyrosine kinase 1, PlGF=placental growth factor, HOMA-IR=homeostatic model assessment for insulin resistance

43 Adding fetal surgery to general anesthesia does not impair brain development in the rabbit model

Lennart Van der Veeken[1], Doaa Emam[2], Tom Bleeser[3], Ignacio J. Valenzuela[3], Steffen Rex[3], Jan Deprest[1]
[1]Department of Development and Regeneration, Cluster Woman and Child, Biomedical Sciences, KU Leuven, Leuven, Belgium, [2]Department Obstetrics and Gynaecology, University Hospitals Tanta, Tanta, Egypt / KU Leuven, Leuven, Belgium, [3]KU Leuven, Leuven, Belgium

OBJECTIVE: Fetal spina bifida repair is increasingly being performed. Fetuses are operated on and exposed to external, potentially harmful factors in a time window when the developing brain is extremely vulnerable. Until now, little is known if and how open fetal surgery impacts fetal brain development. We aim to assess the impact of fetal surgery on the developing fetal brain in the rabbit model, which is representative of human brain development.

STUDY DESIGN: This is a randomized, sham-controlled study in time-mated pregnant does at day 28 of gestation (term=31d). This corresponds to the end of the second trimester in humans. In 11 does, anesthesia was induced with propofol and maintained with 4 vol-% (equivalent of 1 MAC) sevoflurane for 75 minutes. Maternal vital signs were continuously monitored. A laparotomy was performed and two pups in each horn were randomized to undergo either no intervention (sham) or simulated fetal surgery: hysterotomy, intramuscular injection of atropine, fentanyl, and cisatracurium, skin incision along the fetal spine, suturing and uterine closure (fetal surgery). Fetuses from unmanipulated does were included as controls. At term, does were delivered by cesarean section under ketamine-medetomidine sedation and local anesthesia. At day 1, pups underwent motoric and sensory neurologic testing followed by euthanasia and brain harvesting for histologic assessment of neurons, synapses, proliferation and glia cells.

RESULTS: Survival was equal in the three groups and body weight, brain weight and brain-to-body weight ratio were comparable. On day 1, sham and fetal surgery pups had a similar motoric and sensory neurobehavioral outcome. Likewise, neuron and synaptic density was comparable as was proliferation and gliosis. Compared to controls both groups had similar neurobehavioral outcome despite limited histologic changes, i.e. lower neuron density in the prefrontal cortex and hippocampus.

CONCLUSION: In rabbits, maternal surgery under general anesthesia leads to confined histologic changes but no functional changes at birth, and without an additional effect of fetal surgery .

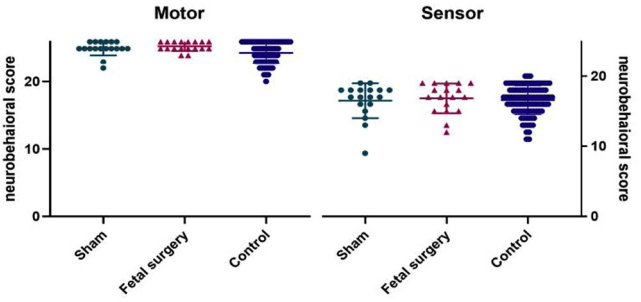

Figure 1: Motor and sensory testing on postnatal day 1

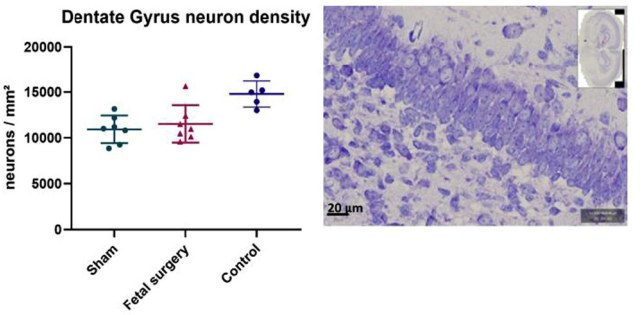

Figure 2: Neuron density in the dentate gyrus A) individual data points B) close up of the dentate gyrus stained with cresyl violet