



RACP Foundation Research Awards

PROGRESS REPORT

Project / Program Title	Novel early intervention therapies for fetal growth restriction related brain injury	
Name	Dr Atul Malhotra	
Award Received	2015 RACP Fellows Research Entry Scholarship	
Report Date	25 May 2016	
Chief Investigator / Supervisor	A/Prof Suzie Miller	
Administering Institution	Monash University	
Funding Period	Start Date:	1 February 2015
	Finish Date:	1 February 2018

PROJECT SUMMARY

Fetal growth restriction (FGR) is a common pregnancy complication that leads to adverse outcomes in the unborn baby, the newborn infant and later in childhood. These include developmental problems of childhood, origins of which have their origins in the fetal and neonatal period of these infants. Many growth restricted infants are delivered preterm, which requires admission to neonatal intensive care units, assisted ventilation and other life saving, but invasive, procedures. My research aims to study the effects of neonatal ventilation and intensive care on the brains of growth restricted fetuses. We are using a fetal lamb growth restriction model for this study, which results in similar characteristics to the human growth restricted baby. By using standard and sophisticated laboratory methods, we first characterised the injury that occurs in the brain. This year, we are evaluating the effects of umbilical cord blood stem cell therapy on the brains of these preterm ventilated growth restricted lambs. Alongside, these experiments, we have commenced work on novel advanced brain imaging techniques to further, non invasively, characterise brain injury as a potential early clinical diagnostic tool, and to correlate this with laboratory findings in the brains of these animals. My hope is that through this research, which has been generously funded by the RACP, we will be able to uncover mechanisms responsible for the brain injury that occurs in these vulnerable babies and to develop novel strategies to treat this relatively common problem.

PROJECT AIMS / OBJECTIVES

1. To study effects of prematurity and neonatal ventilation on brain injury in an early onset ovine model of Fetal Growth Restriction (FGR)

2. To improve detection of brain injury in an early onset ovine model of FGR using advanced imaging techniques
3. To evaluate the effects of umbilical cord blood cells on brain injury associated with prematurity and neonatal ventilation in an early onset ovine model of FGR

SIGNIFICANCE AND OUTCOMES

The completed first aim confirms our hypothesis that the growth restricted preterm brain is vulnerable to the adverse effects of neonatal ventilation. This is very significant as a significant number of growth restricted infants who are born preterm are ventilated in Australian nurseries. Currently, their brain injury is not easily diagnosed at birth and no particular protective or therapeutic measures are currently available to mitigate the risk of long term adverse neurodevelopment in this group of babies. With the rest of my aims, which will be completed in the next 2-3 years, I hope to be able to produce work in this area to address this problem and to provide insights into possible therapeutic strategies.

PUBLICATIONS / PRESENTATIONS

Presentations:

1. Malhotra A, Jenkin G, Polglase G, Allison B, Castillo-Melendez M, Wallace E, Miller S. Cell therapy and fetal growth restriction. 11th Annual Ritchie Centre Colloquium, Melbourne.
2. Malhotra A, Allison B, Castillo-Melendez M, Polglase G, Wallace E, Jenkin G, Miller S. Neonatal ventilation exacerbates brain injury in prematurely delivered fetal growth restricted lambs. PSANZ 2015, Melbourne. J Paediatr Child Health 2015; 51(S1): 29.
3. Malhotra A, Allison B, Castillo-Melendez M, Polglase G, Wallace E, Jenkin G, Miller S. Effects of neonatal care on preterm brain development in an ovine fetal growth restriction model. 12th Annual Ritchie Centre Colloquium, Melbourne.
4. Malhotra A, Castillo-Melendez M, Allison BJ, Jenkin G, Miller SL. Effects of neonatal ventilation on preterm brain development in an ovine fetal growth restriction model. Student of Brain research Symposium, Melbourne..
5. Malhotra A, Castillo-Melendez M, Allison BJ, Polglase GR, Jenkin G, Miller SL. Impact of neonatal ventilation on white matter development in an early onset ovine model of fetal growth restriction. PAS 2016, Baltimore.

Manuscript being prepared for publication:

1. Malhotra A, Ditchfield M, Fahey MC, Castillo-Melendez M, Polglase GR, Jenkin G, Miller SL. Detection and assessment of brain injury in the growth restricted fetus and neonate.