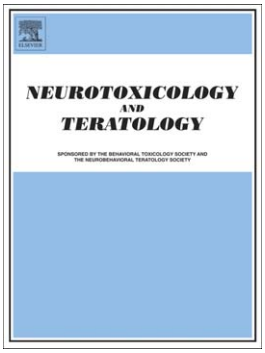

Minimally invasive biomarkers of general anesthetic-induced developmental neurotoxicity

X. Zhang, F. Liu, W. Slikker Jr., C. Wang, M.G. Paule

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Minimally invasive biomarkers of general anesthetic-induced developmental neurotoxicity

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1. Introduction

In the USA more than one million children less than 5 years old undergo general anesthesia every year, including 1.5 million infants less than 12 months of age. Although general anesthesia is often required to alleviate pain and stress, stabilize vital signs and provide consistent conditions for surgery and diagnostic procedures, questions remain regarding the long-term neurotoxic and neurodegenerative effects of anesthetic exposure on the developing brain (Aker et al., 2015; Jevtovic-Todorovic, 2010; Mann and Kahana, 2015; Sun, 2010). Recent experimental evidence indicates that early exposure to general anesthetics can have adverse effects on the developing central nervous system (CNS). While anesthetic-induced neurotoxicity has been investigated primarily using neurophysiological, neuropathological and behavioral approaches, additional non-invasive biomarkers that allow for the dynamic detection and monitoring of adverse effects are highly desired (Pogge and Slikker, 2004; Zhang et al., 2013c). Molecular imaging technologies, such as magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) allow for the noninvasive collection of imaging data providing anatomical and functional information regarding biochemical, physiological, pathological and pharmacological processes *in vivo.*

Amongst a variety of molecular imaging systems, PET is a unique modality with both high spatial resolution (typically ~2 mm for microPET scanners appropriate for use with small animals) and high sensitivity that offers relative and absolute quantitation (Chatziioannou, 2002; Luker et al., 2003; Myers, 2001; Phelps, 2000; Walker et al., 2004; Zhang et al., 2013c). With the high sensitivity of PET (nanomolar to picomolar concentrations can be detected), biological processes of interest can be studied by measuring the uptake and retention of radiotracers that target those processes (Jacobs et al., 2003; Zimmer et al., 2014c). PET imaging can, thus, provide valuable insights into brain-related biological processes, including those associated with neuronal plasticity, neuronal apoptosis, degeneration, regeneration, and neurotoxicity (Hammoud, 2016; Ory et al., 2015; Ory et al., 2016; Pagano et al., 2016; Roy et al., 2016; Wang et al., 2007; Zimmer et al., 2014a; Zimmer et al., 2014b; Zimmer et al., 2014c). MicroPET imaging using animal models of human diseases allows for