DEVELOPMENTAL ALCOHOL EXPOSURE INCREASES SOMATOSENSORY RESPONSES IN PRIMARY AUDITORY CORTEX

Dongil Keum[1], William A Foxworthy[2], M. Alex Meredith[2], Leslie P. Keniston[2,3], Brian L. Allman[3], Alexandre E. Medina[1]

1-Department of Pediatrics, University of Maryland, Baltimore; 2- Department of Anatomy and Neurobiology, Virginia Commonwealth University School of Medicine, Richmond, VA; 2- Department of Physical Therapy, University of Maryland Eastern Shore, Princess Anne, MD; 3 Department of Anatomy, School of Medicine and Dentistry, University of Western Ontario, Ontario, Canada

INTRODUCTION

There is compelling evidence suggesting that FASD subjects suffer from sensory stimulus overload and can be easily distracted by unexpected sensory stimuli while trying to focus. Subjects report being uncomfortable and distracted by sensory crowded environments and show hypersensitivity to touch, smell, sound, and light.

Our lab have developed a ferret model of FASD in which animals receive 3.5g/Kg of alcohol every other day between P10-P30. Using this model we have shown that developmental alcohol exposure can disrupt organization, plasticity and sensory integration in visual cortical areas **(Fig 1.)**

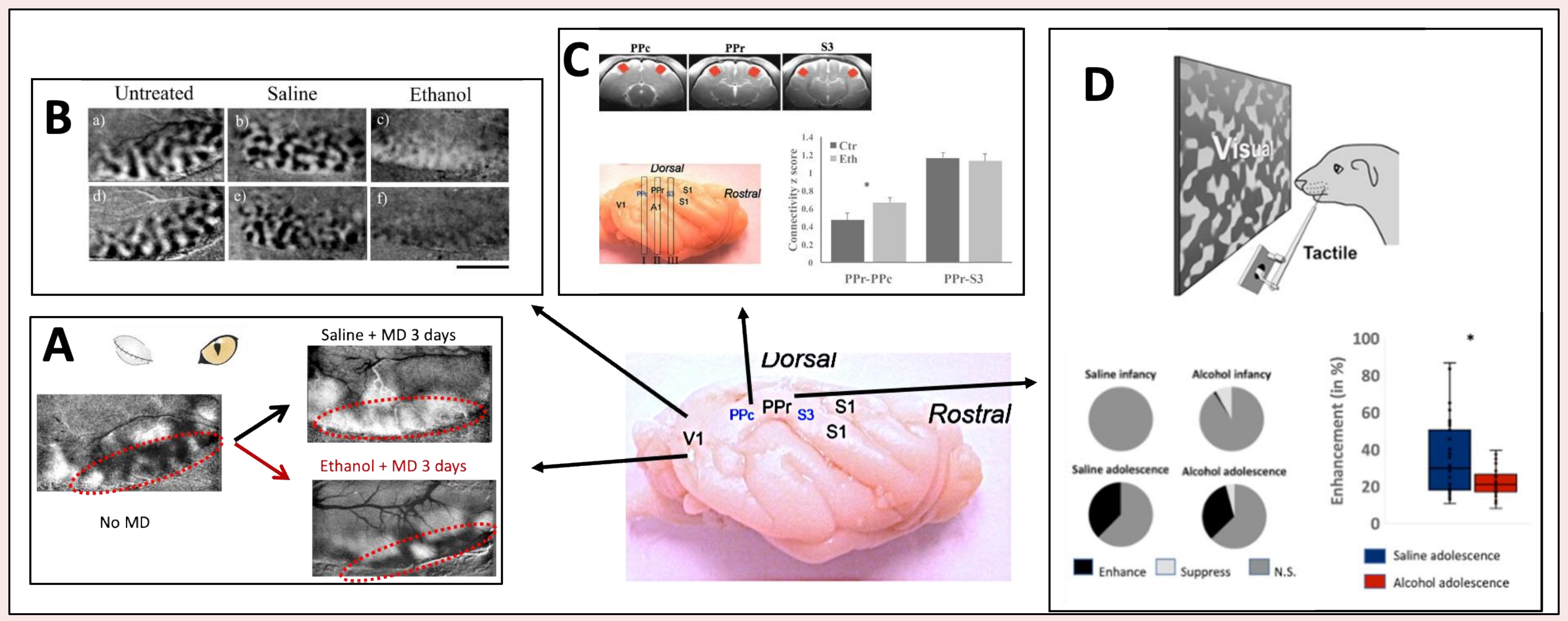


Fig 1. Visual processing alterations in the ferret model of FASD. A. *Ocular dominance plasticity deficits. In vivo optical imaging of intrinsic signals in the primary visual cortex (V1; region marked by red dashed lines) of a normal ferret (no monocular deprivation; no MD). Dark regions represent areas where most neurons are "wired" to the contralateral eye, whereas white regions are "wired" to the ipsilateral. After a contralateral monocular deprivation (MD) during a critical period of plasticity, saline controls show most of V1 dominated by neurons "wired" to the experienced ipsilateral eye (white regions). In contrast, a similar period of MD fails to show this kind of plasticity in alcohol exposed animals (dark regions still dominant) (Medina et al. 2003 J. Neurosci).* ***B.*** *In vivo optical imaging of intrinsic signals shows orientation selectivity columns. Top row shows maps where dark and white regions represent areas that display higher responses to a visual stimulus moving in 0º orientation (horizontal) or 90º (vertical) respectively. In the bottom rows dark and white regions represent responsiveness to 45º and 135º stimulus orientation respectively. Please note that the alcohol animals show much less defined maps in all orientations (Krahe et al. 2009 PLoS ONE).* ***C.*** *Resting state functional MRI show hyperconnectivity between visual inputs into PPr (PPc➔PPr) but not in somatosensory inputs (S3➔PPr) (Tang et al. 2018 Acer)* ***D.*** *In vivo electrophysiology show altered MSI in alcohol treated animals. Recordings are made after visual only, tactile only or visual+tactile stimulation. A multisensory enhancement and suppression occur when neuronal firing after visual+tactile is significantly higher (enhancement) or lower (suppression) than when visual or tactile stimulation is done in isolation. Please note that there is more suppression in alcohol treated animals than in saline controls (pie charts). Moreover, the magnitude of enhancement is significantly smaller in alcohol treated animals (Keum et al. 2023 Eur J Neurosci).*

While our lab has demonstrated that developmental alcohol exposure has a major impact in striate and extrastriate visual cortex areas, much less is known about the effects of alcohol in auditory processing regions.

We propose that the sensory deficits caused by developmental alcohol exposure are not restricted to visual streams and that aberrant sensory responsiveness and disrupted integrative properties would also be seen in other sensory cortical areas.

Here we will present some our preliminary data based on 3 FASD and 3 control animals tested during ferret adolescence. We Investigated auditory-tactile integration in the Lateral Rostral Suprasylvian Sulcus (LRSS) and A1/AAF cortical areas.

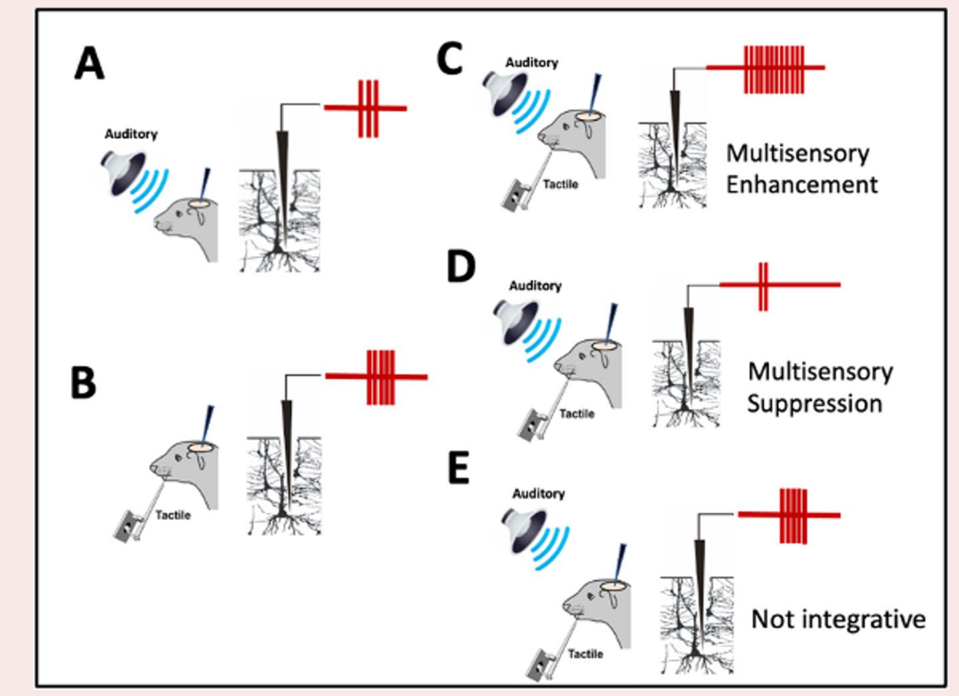
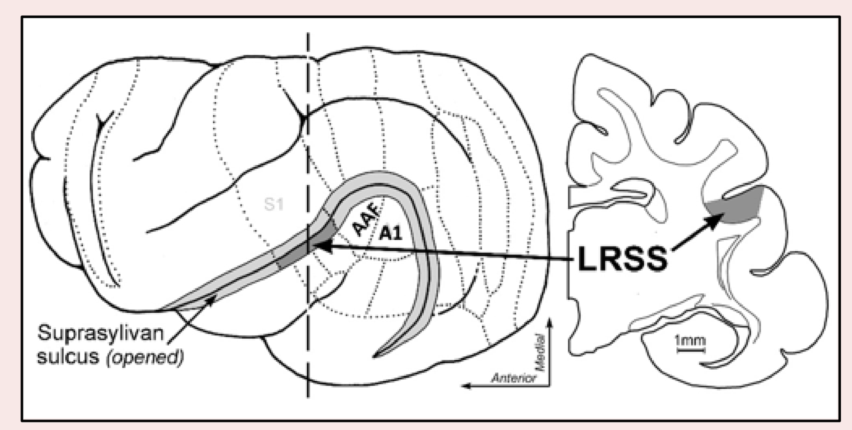


Fig. 2: Examples of multisensory integration (MSI): A. *An auditory stimulation elicited 3 spikes in one given neuron.* ***B.*** *A tactile stimulation elicited 5 spikes in the same neuron recorded in* ***A.*** *When recording from this same neuron but now combining auditory+tactile stimulation three outcomes are possible: A significant increase in number of spikes (****C.*** *Multisensory enhancement); a decrease (****D.*** *Multisensory suppression); or a number that is not distinguishable than the strongest unimodal stimuli (****E.*** *not integrative).*



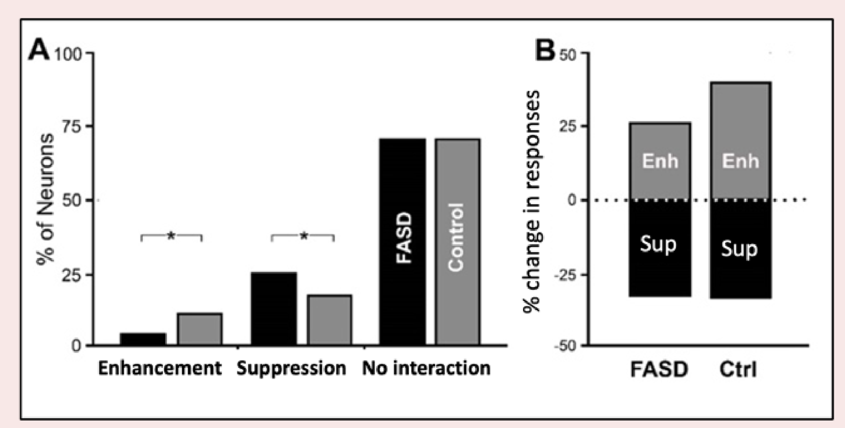


Fig. 3 A. *Proportions of neurons exhibiting MS enhancement, MS suppression and non-integrative neurons. FASD animals show less MS enhancement and more MS suppression than controls (p<0.01; chi-square). Magnitude of enhancement (positive values) and suppression (negative values). While the magnitude of suppression was not different between groups, FASD animals had a trend showing less enhancement than controls.* ***B.*** *Magnitude of enhancement and suppression in alcohol exposed and controls. Our preliminary data shown a non-significant trend for alcohol-exposed animals having a smaller increase in responses. However, decrease in responses were not changed.*

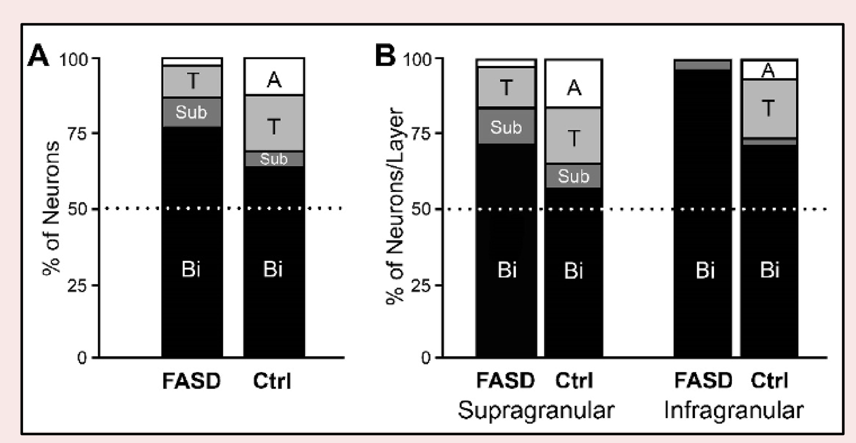


Fig. 4. *Proportions of different types of neurons in FASD and Control (Ctrl) animals. (A) In the LRSS region, multisensory bimodal (black) and subthreshold (dark grey) neurons predominated in both FASD and control conditions, but many fewer unisensory (A=auditory; T=tactile) neurons occurred in FASD cases. (B) Multisensory neurons predominated in the supragranular (L1-3) and infragranular (L5-6) layers of the LRSS, since unisensory neurons were reduced in FASD supragranular and absent in infragranular layers. Please notice that despite auditory only neurons being virtually absent in FASD animals, bimodal neurons respond to both auditory and tactile stimulation.*

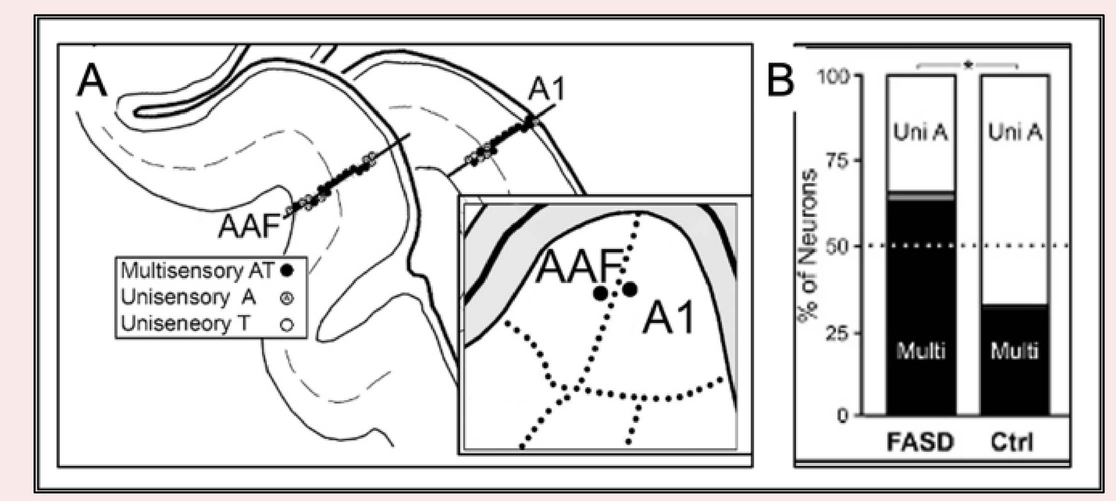


Fig. 5. *We recorded neurons using in vivo electrophysiology in A1 and AAF of alcohol treated animals (n=3) and naïve controls (n=3).* ***A.*** *Representative case of the reconstruction of an electrode track of an alcohol-treated animal. Circles represent the neuron's category based on their sensory response. Please note that the majority of neurons in both A1 and AAF were responsive to both auditory and tactile stimulation.* ***B.*** *Quantification of the proportion of neurons in a given category. Please note that multisensory neurons (responsive to both auditory and tactile stimulation) are the majority group in FASD animals (p<0.001; chi-square). A1=Primary auditory cortex; AAF=Anterior auditory field; A= auditory only; T=Tactile only; AT=Auditory+Tactile.*