Gene expression in the fastigial nucleus:

Piecing together the story behind eye movement abnormalities in autism

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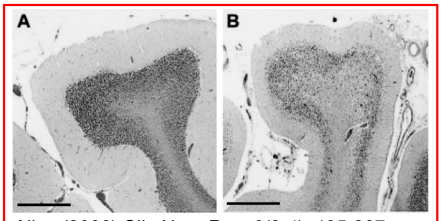
The problem:

Humans rely heavily on accurate visual information to interpret the world around us and guide our motor actions. However accurate visual perception is underpinned by accurate eye movemnets. The network that refines the accuracy of eye movements is a simple loop between the superior colliculus, cerebellar vermis lobules VI-VII, the caudal fastigial nucleus and brainstem pre-motor nuclei.



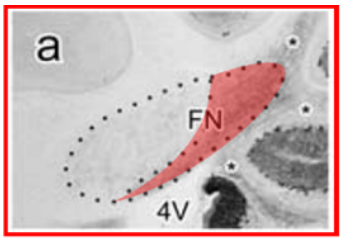
Allen (2006) Clin Neur Res, 6(3-4), 195-207

Autism is a neurodevelopmental disorder typically associated with social and language impairments. However it is increasingly recognised that motor dysfunction is also a characteristic feature. In particular, eye movements are inaccurate (undershoot or overshoot the target), and are slower to adapt (refine motor error) over time.

Neuroanatomical abnormalities have also been found in this ocular motor loop, such as smaller vermis lobules VI-VII (Work of Eric Courchesne) and reduced Purkinje cell density (Bauman and Kemper). Neurodevelopmental abnormalities within the fastigial nucleus have als been found, with nuclei are abnormally large in younger brains (<12 years), but are abnormally small and and decreased in number in older brains (>21 years) (Kemper & Bauman, 2002).

Rationale:

Given that the caudal fastigial nucleus is the primary output structure for cerebellar ocular motor signals, and that during development, Purkinje cells migrating to vermis lobules VI-VII migrate through the fastigial nucleus, the aim of this project was to identify genes tha are specifically or highly expressed in the caudal, but not rostral portion of the fastigial nucleus. This might help to identify genes that underpin atypical cerebellar development and ocular motor dysfunction in autism.

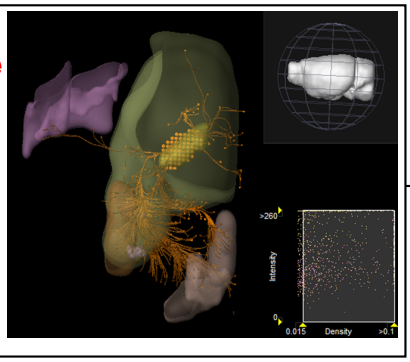


Sugihara & Shinoda (2007) J Neurosci, 27(36):9696-710

Methods & findings:

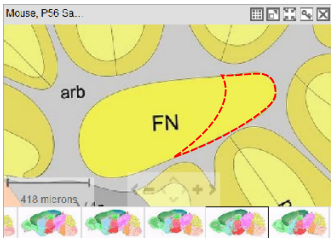
1. Determine whether ocular motor networks in the mouse are comparable to primates

Tools used: Mouse connectivity atlas
Outcome: OM networks are comparable across mouse and humans



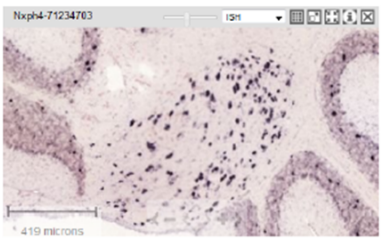
2. Identify genes highly expressed in the fastigial nucleus.

Tools used: Mouse AGEA search
Outcome: Identified 8 genes highly expressed within FN



3. Determined whether the 2 identified mouse genes were also highly expressed in the human caudal FN

Tools used: Human brain microarray data
Outcome: NXPH4 is highly expressed within caudal FN of both human and mouse



4. Manually examine saggital sections for regional specificity to the caudal FN

Tools used: Mouse ISH data
Outcome: Identified 2 genes highly expressed within caudal FN