IN BRIEF…

Manganese, a friend or foe to dopaminergic neurons?

GD Stanwood, **DB Leitch**, V Savchenko, J Wu, VA Fitsanakis, DJ Anderson, **JN Stankowski**, M Aschner, B McLaughlin (2009). Manganese exposure is cytotoxic and alters dopaminergic and GABAergic neurons within the basal ganglia. *J Neurochem*. **110** (1): 378-89.

Manganese is a naturally occurring element essential for the proper metabolism of amino acids, protein and lipids. It is crucial for maintaining proper cellular functioning including maintenance of redox states, facilitating protein conformation, modulating ion and energy homeostasis and overall signal transduction in neurons. Over exposure to manganese can result in various irreversible neurological phenomenon such as motor symptoms similar to that of Parkinsons, dystonia and gastrointestinal tract dysfunction. In this study, the authors explored the neurotxic potential of manganese in dopaminergic neurons *in vivo* in mice, looking especially at the vulnerability of nigrostrial pathways. They found that manganese chloride exposure, even at subtoxic doses changed the neuronal cytoskeleton of dopaminergic neurons. When the manganese treatment was extended to a period of 30days, a 20% reduction in TH-posiive neurons was observed in the substantia nigra pars compacta (SNpc), quantified by a widespread reduction in SNpc cell numbers through Nissil body staining. Parts of the basal ganglia including the striatum were also affected during treatment, showing sensitivity to nigrostriatal pathways. This study provides chronicles the timely repercussions of acute and chronic manganese exposure and provides an explanation for the motor manifestations observed from manganese intoxification.

How quickly can you detect a face? Temporal dynamics within neural constructs involved in the detection of familiar and novel faces

Blackford JU, **Avery SN**, Shelton RC, Zald DH. (2009). Amygdala temporal dynamics: temperamental differences in the timing of amygdala response to familiar and novel faces. *BMC Neurosci*. 10:145.

Inhibited temperament involves a predisposition of individuals to respond to new people, places or things with wariness or avoidance behavior, a characteristic trait known to be associated with increased risk for social anxiety disorder and major depression. Within the human brain, functional magnetic resonance imaging (fMRI) has shown the magnitude of blood oxygen level dependent (BOLD) responses in the amygdala for novel stimuli to be associated with inhibited temperament. The authors in this study used an event related fMRI paradigm to investigate the temporal dynamics (latency, duration and peak) of the BOLD response to novel stimuli within the amygdala. They presented both novel and familiar faces to both inhibited and uninhibited temperament populations. Results indicated that the amygdala in inhibited participants responded faster to novel faces than familiar faces. In addition, they found that the inhibited participants showed both a longer and greater amygdala response to all faces in comparison to the uninhibited population, even though there were no differences in the peak BOLD response. Blackford and colleagues speculate that this temporal computational bias for novel stimuli within the amygdala may lead to greater neophobic responses and could allude to a plausible mechanism for the development of social anxiety.

apoptosis during embryogenesis. The rapid and controlled clearance of these dead cells is vital, as non-ingested cells can generate inflammation and detrimental immune responses.

In a recent *Nature Neuroscience* article, a team led by Bruce Carter recognizes a specialized glial cell, satellite glial cell precursors (SGC), in the clearance of dead neurons in the dorsal root ganglia of embryonic mice. Previously, it was unclear which cells were responsible for apoptotic clearance, with default responsibility handed to macrophages. However, through confocal and electron microscopy and *in vitro* assays, the group demonstrates that the vast majority of apoptotic neurons are associated or engulfed within SGC's, highlighting an unrecognized role for glial cells in phagocytosis.

In addition, the group provided a potential molecular mechanism for engulfment of dead cells. Jedi-1 and MEGF10, homologues of known *c. elegans* and *Drosophila* proteins, are expressed in the brain and specifically within SGCs in the DRG. Transient expression of the either protein in cultured HEK cells led to binding of neuronal corpses, and overexpression of the proteins in glial cells leads to increased engulfment of dead cells, suggesting a clear role for Jedi-1 and MEGF10 as engulfment receptors. Through their research, Wu et al establish satellite glial cell precursors as members of the 'clean-up' crew in the peripheral nervous system, performing a similar role as microglia in the brain, and importantly implicate two receptors as crucial sensors in the proper clearance of apoptotic cells.

Original Research Article:
HH Wu, E Bellmunt, **JL Scheib**, V Venegas, C Burkert, LF Reichardt, Z Zhou, I Fariñas, BD Carter (2009). Glial precursors clear sensory neuron corpses during development via Jedi-1, an engulfment receptor. *Nat Neurosci.* **12** (12): 1534-1541.

Bad huntingtin, protective effect

Huntington's disease (HD) is a unique neurodegenerative disorder in that it has been mapped to a single locus, the *huntingtin* gene. In the disease, huntingtin protein progressively undergoes an expansion of a polyglutamate region. Onset of symptoms correlates with a specific number of polyglutamate repeats, such that the disease progressively worsens with age. Thus far, research has been unable to explain how mutant huntingtin leads to a remarkably specific loss of medium spiny neurons in the striatum, a primary cause of the motor deficits seen in patients. One hypothesis is that striatal neurons are situated in an environment that may uniquely impact their vulnerability to mutant HTT; a