recent paper from the Bowman lab investigates this gene-environment hypothesis in the context of HD, with specific focus on the impact of metal neurotoxicology.

Williams *et al*. performed a disease-toxicant interaction screen in order to test a correlation between physiological properties shared between metal exposure and Huntington's disease. These include oxidative stress, cell stress, protein aggregation, and alterations in calcium signaling and energy metabolism. To test the correlations, they utilized several HD models in metal exposure paradigms. They first demonstrated that a mouse striatal cell line model of HD demonstrates variable cell survival responses to given metals. They note that mutant Huntingtin cells survive at similar rates over a range of concentrations in the vast majority of metals tested. However, mutant cells were less viable when exposed to cadmium and actually displayed a neuroprotective effect in the presence of manganese, without affecting the level of huntingtin protein.

The lab next capitalized on previous research to investigate the impact of manganese on established physiological processes. First, they demonstrated that HD mutant striatal cells have diminished phosphorylation of Akt, a cell stress signaling pathway associated with previous HD studies. They further show that these mutant cells have impaired accumulation of manganese, which may prevent its toxic intracellular effects. Finally they note that in an *in vivo* mouse model of HD, YAC128Q mice have a striatum-specific reduction of manganese uptake as compared to wild type mice. The neuroprotective effect of mutant HD on manganese exposure is quite surprising, and future experiments will target manganese uptake, export, and storage under the broad hypothesis that HD pathology is regulated in the context of both genetics and environment.

Original Research Article:
BB Williams, D Li, M Wegrzynowicz, BK Vadodaria, JG Anderson, **GF Kwakye**, M Aschner, KM Erikson, AB Bowman(2010). Disease-toxicant screen reveals a neuroprotective interaction between Huntington's disease and manganese exposure. *J. Neurochem*. **112** (1): 227-237.

Worth the 'EEfRT'? Role of motivation in rewarding tasks

Anhedonia is a subtype of the putative psychopathological enophenotypes in major depressive disorder (MDD), which characteristically represents an individual's aberrant motivation and reward responsivity. In order to objectively tap into the measures of reward motivation and test trait anhedonia, the authors in this study developed the Effort-Expenditure for Rewards Task (EEfRT or "effort"), a novel behavioral paradigm to explore effort based decision making in humans. The EEfRT task is a multi-trial game in which participants are given the opportunity on each trial to choose between two different task difficulty levels (hard or easy). They are required to complete the task with a specific number of button responses within a constrained period of time in order to obtain a monetary reward. Along with the EEfRT task, study participants self-reported measures of mood and trait anhedonia. Across multiple analyses, Treadway and colleagues found a significant inverse relationship between the anhedonia trait and a willingness to expend effort for rewards. From these results, the authors postulate that anhedonia is specifically associated with decreased motivation for reward. Additionally, the findings in this study enabled the authors to provide initial validation for the EEfRT behavioral paradigm as a laboratory based measure of reward motivation and effort based decision making in humans.

Original Research Article:
Treadway MT, **Buckholtz JW**, Schwartzman AN, Lambert WE, Zald DH (2009). Worth the 'EEfRT'? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PLoS One*. 4(8):e6598.

IN BRIEF…

Exploring CAMKII associations with calcium L-type channels to regulate physiological changes in tissues

SA Abiria, RJ Colbran (2010). CaMKII associates with CaV1.2 L-type calcium channels via selected beta subunits to enhance regulatory phosphorylation. *J Neurochem*. **112** (1): 150-61.

Voltage activated L-type calcium channels (LTCCs) are known to generate Ca^{2+} signals important for numerous physiological process such as muscle contraction, neurotransmitters, neuronal plasticity and others. In particular the calcium/calmodulin dependant kinase II (CaMKII) protein has been shown to augment the Ca^{2+} signals in response to growth factors or hormones. Excessive $Ca_v1.2$LTCC activity can produce a variety of pathological symptoms including cardiac arrhythmias, multi-organ human genetic disorder and cases of parkinsons disease in animal models. While CAMKII facilitates LTCC activity physiologically, the molecular basis of CAMKII interactions and its modulation of LTCCs is yet to be understood. The authors of this paper transfected HEK293 cells from the forebrain of 7-8week old rats to explore the role of β subunits in targeting CAMKII to LTCC α1 subunits. They found that CAMKII co-immunoprecipitates with forebrain LTCCs that contain $Ca_v1.2$α1 and β1 or β2 subunits, but not LTCC complexes containing b4 subunits. These targeted mechanistic interactions between CAMKII and LTCCs will be crucial in providing insights into our understanding of physiological and pathological process in different tissues.