## 2018 Seed Funding Competition Awardees

**Title:** A Study of Amiloride Intranasal Spray for Panic Attack. **PI: Marco Battaglia**

**Abstract:** Background Panic disorder (PD) affects 6% of the population and has huge social costs. It is characterized by recurrent panic attacks (PAs) that encompass dyspnoea, choking sensations and fear. Patients with PD show respiratory instability and changes in systemic CO2 concentration that acidify brain fluids: these dynamics together can evoke full-blown PAs. The PI has studied this physiology in humans and preclinical models simultaneously. In both, marked behavioural and respiratory reactions to heightened CO2 concentrations in air can be adopted as a proxy to study clinical PAs. The PI's epigenome-wide investigations showed that the Asic1 (acid-sensing-ion-channel-1) and Asic2 genes are enriched in preclinical models and humans with CO2 hypersensitivity. More recently, the PI also showed that ASIC channels blocker Amiloride (nebulised to circumvent the blood-brain barrier and enter the brain) re-establishes normal responses among CO2 hypersensitive preclinical models. Based on this innovative preclinical evidence, and available clinical evidence that inhaled Amiloride is safe for humans, this project targets the prodromal phases of PAs that are characterised by respiratory instability and rising anxiety. We will study whether PAs can be safely and efficiently blocked with Amiloride nasal spray in people with PD. Hypothesis: Amiloride nasal spray will prove superior to placebo (saline) in blocking upcoming PAs in people with PD who are being treated with antidepressants (the treatment of choice for PD) but are still presenting with PAs. Methods: double-blind randomised cross-over study of 4 weeks with Amiloride nasal spray preceded/followed by 4 weeks of saline nasal spray as placebo, adjunctive to current antidepressant (TCA/SSRIs/SNRI) treatment. Patients will rate their symptoms by ecological momentary assessment (EMA), both at baseline and in the imminence of panic attacks. They will be instructed to inhale Amiloride whenever they feel an upcoming attack, and rate their symptoms in real-time EMA immediately before inhalation of Amiloride (or placebo), and in the following minutes. This efficacy study will be preceded by a development study, via a Phase 0 Investigational New Drug Submission to the US Food and Drug Administration -an approach that cannot be taken in the current Canadian regulatory framework- conducted at the University of Utah Hospital Clinics by Collaborator Dr V Yellepeddi, an expert in therapeutic development and clinical study of new drug delivery systems, including nasal spray formulations. Significance: Through their capacity to prevent the long-term recurrence of PAs, antidepressants constitute an efficient first-line treatment for PD; however, many PD patients who take antidepressants still experience frequent PAs. Here, we propose Amiloride as an agent to block upcoming attacks that are not controlled by antidepressants. Having a safe, effective, portable and non-addictive treatment to head-off attacks - given that existing treatments are either slow to produce change (antidepressants) or fast but associated with tolerance and addiction (benzodiazepines)- may become a game changer for many people who are struggling with panic.