NON-CONFIDENTIAL SUMMARY

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CAMH TECHNOLOGY ID: 014-2016

BUSINESS OPPORTUNITY

The Centre for Addiction and Mental Health is seeking partners to either license or co-develop this technology. CAMH is open to various forms of collaboration.

Novel Cell-Based Assay for Serum Assessing Anticholinergic Toxicity in Cognitive Impairment

Market Need

Drugs that block cholinergic receptor function in the brain are known to be associated with cognitive impairment, including confusion, decreased attention and memory deficits. A number of prescription medications, as well as common over-the-counter medications can increase anticholinergic load in the blood, and thus contribute to cognitive deficits. The elderly, who often take multiple medications for various different types of health issues, are particularly vulnerable in this respect. The effect of these medications on cholinergic receptors in the brain makes it difficult to differentiate cognitive deficits induced by aggregate anticholinergic burden from similar deficits resulting from pathological conditions, including mild cognitive impairment and dementia-type conditions. In combination, high anticholinergic burden and underlying dementia increases the risk of delirium and behavioral consequences. Due to the prevalence of various degrees of cognitive decline in the elderly, some 35.6 million people worldwide, at present and projected to be in excess of 115 million in 2050, it is imperative that a test be devised which accurately and objectively differentiates cognitive impairment due to anticholinergic loading and would permit rapid clinical intervention.

Technology Description

We have created two different methods to quantify the anticholinergic burden in human serum: 1) using a radiolabeled muscarinic acetylcholine receptor subtype-1 ligand; and 2) through quantification of the intracellular effects of membrane receptor activity, namely intracellular calcium mobilization (see publications included below for method details). Receptor-driven calcium mobilization can be quantified as dynamic fluorescence changes in cells stably expressing muscarinic receptors in the presence of a fluorogenic calcium binding dye. We have tested our novel serum anticholinergic activity (SAA) radioligand protocol in an open trial and have shown that a single administration of scopolamine, a known anticholinergic drug, induced significant increases in the anticholinergic burden of all subjects. Furthermore, scopolamine was shown to induce cognitive deficits after a single administration in older, cognitively intact subjects.

Stage of Development

- Proof of concept studies are complete
- In a validation study, using the SAA radioligand protocol to measure the level of anticholinergic burden in 311 older patients with mild cognitive impairment or major depressive disorder, it was shown that the SAA assay results are significantly associated with the most commonly used scales: the Anticholinergic Burden (ACB) scale and the Anticholinergic Drug Scale (ADS). The SAA assay results were also significantly associated with measures of executive function. Experiments are underway to validate the SAA calcium fluorescense assay in this same subject sample.

Advantages

- The SAA calcium fluorescence assay identifies anticholinergic as well as agonist cholinergic receptor activity.
- Validity is greatly increased by removing the confounding effect of large serum proteins and decreasing binding to internalized receptors.
- Specificity and sensitivity are significantly improved by using cell lines expressing only M1 receptors.

Notable Publications

José Nobrega, Roger Raymond, and Bruce Pollock; Journal of Pharmacological and Toxicological Methods, 2017

Susmita Chandramouleeshwaran, et al; American Journal of Geriatric Psychiatry, 2021

José Nobrega, Roger Raymond, Tarek Rajji, and Bruce Pollock: Journal of Pharmacological and Toxicological Methods, 2021

Intellectual Property

These inventions are protected by patent applications filed in CA and US

FOR MORE INFORMATION CONTACT

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