A neuronal circuit analysis platform for drug discovery

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BRIEF DESCRIPTION

Researchers at UC Irvine have characterized an electrophysiological-based drug discovery approach that offers a new modality with which to screen potential therapeutics and characterize mutations. This new level of analysis utilizes elements that are shared between rodents and humans, improving upon the uncertainties associated with rodent behavior. It also incorporates the full complexity of operations in a single assay, while rapidly specifying site(s) of action, thereby accelerating R&D for psychiatric illnesses.

SUGGESTED USES

Encompasses a circuit based system to inform how experimental compounds, known drugs, other inputs, and genetic mutations affect complex brain operations. The technique leads to localization of action, which in turn enables description of mode of action. This will focus the development of therapeutics to an unprecedented degree. Moreover, by examining a complex system, the assay dramatically reduces the chances of overlooking an unexpected mechanism of action. The system can therefore be used to improve prediction of clinical outcomes and better characterize brain disorders such as epileptic seizures and alterations that occur with aging.

FEATURES/BENEFITS

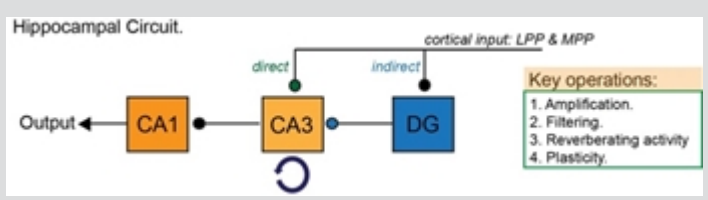
·Expedite the development of therapeutics for patients suffering from neuropsychiatric illnesses.

·Accelerate R&D of therapeutic targets for neuropsychiatric illnesses by providing a novel readout of therapeutic efficacy.

·Capture results that more accurately translate to what may happen in human illness (circuit-based results versus traditional isolated component studies and behavior-based results).

FULL DESCRIPTION

Our understanding of neuropsychiatric illnesses such as depression, addiction, and anxiety has greatly improved in recent years. These disorders are complex and characterized by cognitive dysfunction, which are defined as deficits in attention, verbal and nonverbal learning, short-term and working memory, visual and auditory processing, problem solving, processing speed, and/or motor functioning. Several assays exist for the functional testing of these behavioral deficits in preclinical rodent models of neuropsychiatric illness. Traditionally, R&D efforts have used these assays to screen for potential therapeutic compounds that may rescue these behavioral deficits but poor success has been shown when attempting to translate these findings into humans. Therefore, a functional readout that is more similar between mice and humans may accelerate R&D efforts for neuropsychiatric illnesses.



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OTHER INFORMATION

CATEGORIZED AS

» **Medical**
» Disease: Central Nervous System
» Disease: Substance Abuse
» Research Tools
» Screening
» **Research Tools**
» Screening Assays

RELATED CASES

Researchers at UC Irvine have developed and characterized methods for using a circuit-based approach for drug discovery. These methods utilize an in vitro brain slice preparation to analyze neuronal circuit operations across the entire hippocampal circuit, a brain region heavily associated with many neuropsychiatric illnesses. (1) Compared to behavior, brain circuit function is far more alike between mice and humans, suggesting this system would provide more translatable readouts of a potential therapeutic's efficacy. A schematic of the circuit and its key operations are shown in the figure. These operations are well-characterized across many neuropsychiatric disorders and in the context of aging, offering suitable readouts for how potential therapeutics may rescue deficits associated with these conditions. Because the hippocampus is a key player in mediating many of the aforementioned cognitive dysfunctions, this system provides an optimal brain region for drug discovery efforts pertaining to a variety of neuropsychiatric and age-related illnesses. (2) The assay system incorporates, or can incorporate, virtually all of the transmitter and peptide systems found in brain as well as accompanying glial supportive cells. The simple readout developed by the inventors thus is sensitive to perturbations in any of dozens of subsystems. Follow-on diagnostics developed by the inventors then localize sites of action. The system thus substitutes a very broad survey followed by precision testing for the essentially protein-by-protein assays currently in use. (3) Because the invention uses a complex system, it is more realistic than current drug testing procedures.

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STATE OF DEVELOPMENT

In vitro studies.

Applicants have demonstrated the utility of the system in detecting neurobiological substrates in a rodent model of depression and in defining the site of action for a much discussed therapeutic.

PATENT STATUS

Patent Pending

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