Uncovering the Effects of Hypoxia in CNS Disorders Using Whitley Workstations

Abstract:

Neurological disorders, including Parkinson's, Alzheimer's, and motor neuron disease, pose significant challenges to patients and researchers alike. Dr Scott Allen, lecturer at the Shepherd Institute for Translational Neuroscience, focuses on unravelling the intricate relationship between hypoxia and metabolism in these disorders. Hypoxia, characterized by low oxygen levels, has emerged as a potential contributor to reduced energy production abilities observed in individuals with motor neuron disease and Parkinson's. Astrocytes, vital supportive cells in the brain, are susceptible to hypoxia-induced metabolic alterations, which can impact neuronal function.

To investigate these phenomena, Dr Allen's team acquired an H35 Hypoxystation for culturing cells at precise oxygen levels to study hypoxia's effects on astrocytes coupled with the Whitley i2 Instrument Workstation for precise oxygen control with an integrated Seahorse Bioanalyzer for advanced real-time metabolic analysis under hypoxic conditions.

Introduction:

The Shepherd Institute for Translational Neuroscience focuses on neurological diseases such as Parkinson's, Alzheimer's, and motor neuron disease (MND), aiming to translate bench research into clinical benefits. Dr Scott Allen's research investigates how hypoxia affects the metabolism of individuals with Alzheimer's and MND, recognizing the potential role of hypoxia in reducing energy production abilities.

Culturing cells continuously under hypoxia to replicate in vivo pathological conditions in vitro has historically been challenging. Conventional cell culture methods often fail to adequately mimic the dynamic oxygen gradients experienced in diseased tissues. As a result, researchers have struggled to maintain cells under sustained hypoxic conditions representative of neurological disorders, hindering the accuracy of their studies.

Furthermore, traditional metabolic assays typically require cells to be removed from their hypoxic environment, disrupting the physiological conditions preventing the assessment of dynamic metabolic changes under low oxygen. Consequently, researchers have struggled to gain comprehensive insights into the metabolic adaptations occurring in response to hypoxia, limiting the understanding of disease mechanisms.

The specialised Don Whitley Scientific Whitley i2 Instrument Workstation provides researchers with precise control of oxygen levels within a closed environment faithfully replicating pathological in vivo conditions facilitating long-term experiments to study disease mechanisms. The integration of a Seahorse Bioanalyzer has empowered researchers to perform real-time measurements of cellular metabolomics under hypoxia for enhanced accuracy.
This holistic approach bridges the gap between gene expression studies and functional outcomes, offering a comprehensive understanding of the metabolic adaptations driving neurological disorders.

Experimental:

Dr Scott Allen's research investigates how hypoxia affects the metabolism of individuals with Alzheimer's and MND, recognizing the potential role of hypoxia in reducing energy production abilities. His lab uses the H35 Hypoxystation to reprogramme skin cells into astrocytes and subject them to varying oxygen levels using the H35's O2, CO2, temperature, and humidity controls.

Once the astrocytes have been cultured under pathological hypoxic conditions, cells are passed through a 96-well plate transfer tunnel from the H35 Hypoxystation into the Whitley i2 Instrument Workstation with precise O2 control only – ensuring hypoxic conditions are maintained.

Using the integrated Seahorse Bioanalyzer inside the Whitley i2, Dr Allen assesses in real-time the energy production pathways, mitochondria, and glycolysis under the varying low oxygen concentrations found in neurological diseases. Allowing Dr Allen to investigate how diseases like MND affect these metabolic pathways.

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By combining continuous hypoxia culturing with real-time metabolic analysis, Dr Scott's team are gaining comprehensive insights into the metabolic adaptations occurring in response to hypoxia to target pathways for drug screening and gene editing to improve patients' quality and length of life.

Conclusion:

The combination of the H35 Hypoxystation and Whitley i2 Instrument Workstation ensures there's no need to remove cells from the hypoxic conditions during an experiment; cells are cultured consistently under the desired oxygen levels. With the integration of the Seahorse Bioanalyzer, researchers can measure hypoxia's impact on cellular metabolism in real-time without the need to remove cells from their low oxygen environment. This increases the reliability of data obtained from experiments performed within these workstations.