From Hypothermia to Cephalosomatic Anastomoses: The Legacy of Robert White (1926–2010) at Case Western Reserve University of Cleveland

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Key words
- Brain injury
- Brain perfusion
- Cephalosomatic anastomoses
- Head transplantation
- Hypothermia
- Robert White

Abbreviations and Acronyms
BRL: Brain Research Laboratory
CNS: Central nervous system
EEG: Electroencephalography

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Citation: World Neurosurg. (2018) 113:14-25. https://doi.org/10.1016/j.wneu.2018.01.175

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Dr. Robert J. White (1926–2010) was an eminent neurosurgeon and bioethicist, renowned for his classic work in hypothermia and pioneering mammalian head transplant experiments. He founded the Division of Neurosurgery at the Cleveland Metropolitan General Hospital (currently MetroHealth Medical Center, a level 1 trauma county hospital) and became the youngest full professor at the Case Western Reserve University in Cleveland, Ohio. With over 500 research articles to his credit, he founded the Brain Research Laboratory at what was then the Cleveland Metropolitan General Hospital, which was also home to future leaders in neurosurgery, neurosciences, and allied specialties. He transferred a healthy monkey head onto a surgically beheaded monkey body under deep hypothermic conditions drawing both laurels and criticisms alike. Despite a largely controversial neurosurgical research career, his original contributions to deep hypothermia have found profound clinical applications in modern trauma and vascular neurosurgery. The new fusogens and myelorrhaphy methods being tried in Europe hold promise for a future of reanastomosing 2 homologous or heterologous tracts in the neuraxis.

INTRODUCTION

A unique research profile revolving around deep hypothermia in neuraxial injury as well as cephalosomatic anastomoses in mammalian bodies shaped the life and career of Robert White, a neurosurgeon clinician scientist (Figure 1). It is difficult to ignore the parallels between the eminence of White and the postwar emergence of Case Western Reserve University in Cleveland, Ohio, USA. He was a curious academician and clinician who pushed the envelope of basic neuroscience research with far-sighted clinical applications. In his revolutionary primate research, White found a new niche that helped him grow to a special iconic stature, advising both physicians and religious leaders in the United States and abroad. Hypothermia and cephalosomatic anastomoses experiments catapulted him into the higher echelons of neuroscience.

A HUMBLE BEGINNING

Robert J. White, also known as Bob White, was born in 1926 in Duluth, Minnesota. He was raised by his mother and aunt after his father died in World War II. Despite enormous financial struggles, he negotiated his way to a higher education, by taking up a job as an army laboratory technician. White began his undergraduate studies at the University of St. Thomas in Minnesota. He then joined the University of Minnesota Medical School in 1949 and graduated cum laude from Harvard Medical School in 1953 (Figure 1). His keen interest in the human brain began when his biology teacher admired his dissection of the frog cranium. This interest was honed into a flair for neurosurgery by the famed Francis Moore, Frank Ingraham, and Donald Matson, at Peter Bent Brigham and Children's hospitals in Boston, where White was an intern.[1]

Most of White's neurosurgical training experience came at the Mayo Clinic, where he studied brain metabolism and circulation. It was here that he surgically designed nonhuman mammalian models of brain and spinal cord for study, based on previous studies at the Mayo Clinic. Consequently, special state-of-the-art techniques were formulated to use hypothermia for cerebral protection during stages of circulatory arrest in intracranial surgery and to restrict the extent of traumatic spinal cord injury. Furthermore, sui generis complete isolation of transplanted brain preparations allowed new frontiers in the examination of neurophysiologic, immunologic, rheologic, and metabolic attributes of an isolated brain during normothermic and graded hypothermic states.[2]

In the late 1950s, White worked with David Donald, a veterinarian/physiologist at the Mayo Clinic, to develop a method of extracorporeal cooling and rewarming of the brain after complete cessation of cerebral circulation. To achieve this end, they created a surgical technique for complete isolation of the canine brain vasculature, which required an open chest.[3]

White also conducted his Ph.D. research involving total hemispherectomy in dogs. His focus of interest was to create a completely isolated yet viable brain model maintained by a donor (dog) or mechanized extracorporeal system. This strategy provided him the substantial anatomic familiarity required to translate into a

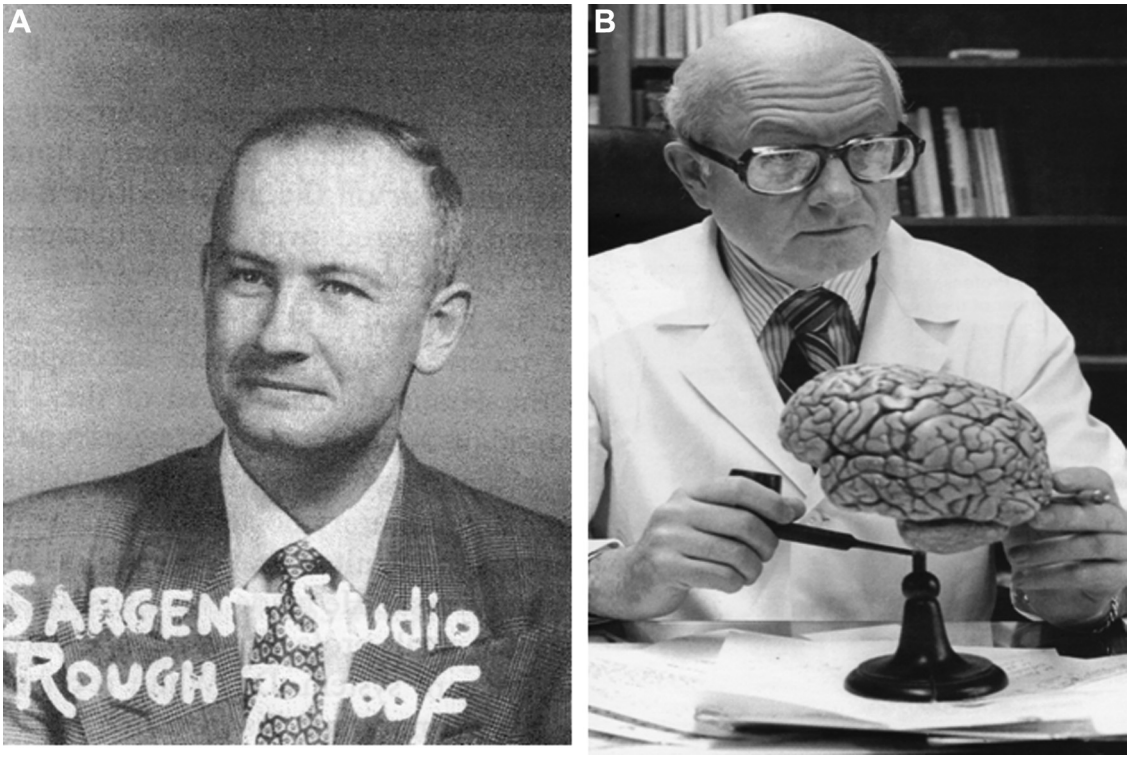

Figure 1. (**A**) White during his Harvard days in 1951. (**B**) Robert Joseph White, M.D. Ph.D., in the 1970s: an office photograph.

primate's cranial and cervical vasculature. These personal observations convinced White to select the monkey as his experimental animal for further research, with emphasis on cerebral hypothermia.[2,4]

The everlasting influence of the Mayo Clinic shaped White's future experiments, in which he analyzed the effects of subarachnoid cooling on experimental canine spinal cord injury. Initially, William Hetzelberger (a neurosurgical resident), James Kernohan (a neuropathologist), and Maurice Albin (a neuroanesthesiologist), all had contributory roles in the pathologic investigation of the spinal cord after cooling, injury, and the combination of injury with cooling. Their early studies[5] registered that the controlled cooling technique itself was not injurious to the cord tissue. This inquiry into the potential therapeutic advantages of hypothermia in spinal cord trauma even became the kernel of Albin's Master's degree in anesthesiology. White had secured his doctoral research degree (Ph.D. in experimental hemispherectomy) in 1962.[2]

THE BRAIN RESEARCH LABORATORY

White joined Cleveland Metropolitan General Hospital (Figure 2) with the charge of establishing a brain research laboratory. The Brain Research Laboratory (BRL) was established in September 1961 under the auspices of the Western Reserve University in Cleveland. A pioneer of cerebral blood flow, Byrin Bloor, donated a few pieces of equipment, as basic laboratory apparatus. From the onset, a thriving intellectual collaboration was established at the BRL between clinicians and basic scientists. Investigative collaborations blossomed among neurosurgeons, neurophysiologists, engineers, biochemists, endocrinologists, and experimental psychologists.[2] Around the same time (1967), the Case School of Applied Sciences (later named Case Institute of Technology) entered into a federation with the Western Reserve University. The product of this union was the prestigious Case Western Reserve University, a national recognized center of scientific progress and academic pursuit. White went on to become the Metropolitan General hospital's first Chief of Neurosurgery and Case Western Reserve University's youngest full professor.

During their prolific first 15 years, White and his colleagues expanded the existing body of literature on the biological behavior of the central nervous system (CNS) in deep hypothermic conditions, through the protective effects of cerebral and spinal cord cooling in patients with injuries. Thereafter, they also performed extended experiments studying the ability of the brain to survive extended periods of total circulatory arrest at extremely low temperatures.[2] Subsequent studies showed that mild hypothermia[6,7] decreases metabolic activity, thus extending the tolerance of the brain to ischemia and hypoxia.

Not only did they develop a method to steadily measure the cerebrospinal fluid pressure[8] but they also fashioned a technique to collect the fluid with an implanted plastic module.[9] In addition, they performed a series of ingenious sterile operations via a skull base (extracranial) approach, to remove the pituitary gland