Some Milestones from a Century of Brain Research in the Province of Alberta, 1910 to 2010

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Photograph from the earlier period of U of C (neuroscience) research groups: Dr. Naweed Syed (postdoc), Piotr Kruk (PhD candidate), Dr. Andrew Bulloch, Dr. Rick Ridgeway (postdoc), circa 1989 in the Health Sciences Centre, examining photomicrographs showing neuronal plasticity in molluscan neurons. Electrophysiology equipment can be seen in the left background – photograph courtesy of Dr. Andrew Bulloch.

For reasons of space-restriction and rather spurious research literature on the subject, this historical section can only give an abstract overview on some milestones from a century of brain research in Alberta. It is simply a preliminary exploration of the history of neuroscience in this province: The Western Canadian ("Prairie") Province of Alberta has seen a remarkable advancement of neuroscience as well as somewhat disparate developments of its brain research activities over the past hundred years.

After the formation of the province – on September 1, 1905, especially the creation of the University of Alberta (U of A) in Edmonton, owing to the Tory's University Act of 1910, proved to be a major step toward the establishment of a post-secondary institution of higher learning in Western Canada (Jamieson 1947). It was fortunate for the scientific and medical development of the Prairie Provinces that the creation of a university hospital would soon be envisaged upon the university's completion – following this was the handing-over of the conduct of medical examinations to the U of A by the College of Physicians and Surgeons of Alberta (CPSA) in 1912 (Lampard 2008). The founding of the U of A and the creation of a medical training program with neurological and psychiatric training segments in it proved to be a *novum* in the early 20th century history of the Canadian university system. At that time, the only two formally constituted training programs were at McGill in Montreal and the University of Toronto (U of T) where almost all of the qualified trainees in the psychiatric, neurological and neurosurgical workforce of Canada came from (Weir 2011). In Alberta's other major city – Calgary; neurological and neurosurgical training as well as active brain research commenced only after the end of the Second World War with the arrival of Dr. Charles W. Taylor (1916-1999). He settled in southern Alberta in 1954 and opened a practice in what was still called "neurological surgery". This became the cornerstone in the development of clinical neuroscience activities in the southern part of the province (Annear et al. 2004). Dr. Taylor's pioneering work preceded the creation of the University of Calgary (U of C) Faculty of Medicine in 1968/9 (ca. 60 years after the foundation of the Uof A) by one-and-a-half decades (Cochrane 1968). In looking at these distinct developments that happened in Edmonton and Calgary, the beginning of neuroscience in Alberta could hardly be more unusual. The addition of the third Albertan university in Lethbridge (U of L) – founded one year after the U of C (in 1967) – fits well into the picture. Its expanding laboratories in experimental psychology and the emerging renown of its foundational program in the behavioural neurosciences (Kolb 1999) eventually led to the festive opening of the Canadian Centre for Behavioural Neuroscience in 2001. Throughout a century-long history, the three centres at the U of A, U of C and U of L – in conjunction with a network of smaller, recent universities, university colleges and the Alberta Health Services (combination of the former health regions) – progressed to a solid and vibrant research-landscape which literally put Albertan neuroscience on the global map. Some of the landmark events which contributed to this history (including major

shapers of the field, institutional foundations, technological and political developments) will now be described in more detail.

The Early Decades

Within a few years after its foundation, the U of A attracted a number of psychiatrically and neurologically trained physicians, who came to Edmonton from Queen's Square in London or other premier brain research overseas' institutions. A significant number of U of A's clinical and laboratory staff received their postgraduate training from various universities in major North American centres; for example, McGill and the University of Toronto in Canada; Harvard, the University of Chicago, and Washington University in St. Louis in the United States (Gilchrist 2004). Of particular importance for the development of clinical and research facilities at the U of A was the structural financial support through the American Rockefeller Foundation (RF) during the 1920s and 1930s. This was made possible through the engagement of Alan Gregg (1890-1957), who headed their funding program in psychiatry, psychosomatics and neurology (Brown 1997). The RF provided major structural grants to the U of A – in line with its vital financial contributions to five other Canadian universities and medical schools; Dalhousie in Halifax, NS; McGill in Montreal, Quebec; the University of Manitoba (U of M) in Winnipeg; and the U of T, in Ontario. Furthermore, researchers such as the Edmonton neurophysiologist, Ardrey W. Downs (1913-1966) were awarded fellowships assisting them to pursue postgraduate training abroad. Some of these were major German centres such as the Kaiser Wilhelm Institutes for Psychiatry in Munich and Brain Research in Berlin (Stahnisch 2011).

During the first half of the 20th century however, these developments led to a structural imbalance in the biomedical research landscape of Alberta. This is further exemplified through the fact that Dr. Howard Havelock Hepburn (1885-1972) – the first Chief of the Neurosurgical Division at the University of Alberta Hospital (UAH) – had to provide neurosurgical services to the entire population of the province as well as many patients from southern Saskatchewan and British Columbia. Dr. Hepburn, a McGill graduate, came to Edmonton in 1910 and was one of the inaugural professors of the U of A Medical School. Between 1920 and 1950, patients from other Albertan cities – such as Calgary, Red Deer or Lethbridge – still had to be transported to Edmonton by automobile, ambulance and occasionally by propeller airplane in order to receive diagnostic and special treatment (Annear et al. 2004). This incongruence in neurological and neurosurgical care, as well as basic brain research capacity, began to change with the arrival of other versatile clinicians to the southern part of Alberta, such as the British-born, McGill-trained neurosurgeon Dr. Reginald B. Deane (1872-1947?) who relocated to Lethbridge in the late 1920s. Dr. Charles W. Taylor – already mentioned above – received his undergraduate medical training in England and specialized in neurological surgery from the U of T. In 1954, which was a few years after the Second World War, he opened a surgical practice in Calgary and became the consulting neurosurgeon to the Calgary General Hospital (CGH). Communication between the Alberta neurosurgeons and the Edmonton neurologists was facilitated further by the annual spring meetings of the Alberta Neurosurgical Society. Ever since the 1950s, these meetings brought the clinical neuroscientific community to Banff. A rich opportunity for exchanges about the latest research developments was offered as well as the privilege of having social get-togethers on the ski slopes of the Rocky Mountains (Weir 2011). The overlapping workforce in neurology, neurosurgery and psychiatry of the 1950s and 1960s is further highlighted by the fact that these fields had not yet fully separated (Gavrus 2011). Thus, not only did the "neurological surgeons" perform oncological and traumatological operations (e.g. treating scull impression fractures or hemorrhages) –, but they also performed psychosurgical procedures (leucotomies and prefrontal lobotomies). These operations became part of the standard repertoire in the neurosurgical divisions and practices of Edmonton, Red Deer and Calgary with numerous psychosurgical operations being performed on patients with psychopathic disorders and severe states of depression. Patients with acute neurosurgical conditions, however, still had to be sent to the UHA and Edmonton General Hospital (EGH), which was headed by the London-trained neurosurgeon, Dr. Vance MacDonald (d. 1956?) (Annaer et al.2004).

The provision of medical neurological services in Alberta was also substantially disparate: Edmonton had academically trained neurologists and psychiatrists during the first years of its medical program but Calgary had none. Thus, Calgary internists, in conjunction with the neurosurgeon, Dr. Taylor had to treat many patients with medical neurological disorders which included for example, multiple sclerosis (MS), epilepsy, amyothrophic lateral sclerosis and neurodegenerative conditions. Two years after Dr. Taylor's arrival, a second neurological surgeon, Dr. Ralph Arthur Bailey (d. 1964), a McGill graduate who had moved to Calgary after the completion of his neurosurgical training at the University of Manchester arrived to assist. Soon afterwards, Dr. Allan Hepburn (1924-2010) – the son of Edmonton's Howard. H. Hepburn came to work at Calgary's oldest hospital, the Holy Cross and created much general interest in the neurosurgical and neurological field in his capacity as the President of the Calgary Medical Society. In addition, Dr. Hepburn, Jr. created the "Central EEG Laboratory" at the Academy Medical Building in downtown Calgary and another EEG laboratory at the CGH – providing diagnostic services to the entire medical community. In the following decades, the number of neurosurgeons in Calgary eventually grew to a dozen (Annaer et al. 2004).

The 1960s marked further turning points in the province of Alberta: The population of its two major cities – Edmonton and Calgary – doubled with about half of the population now living in urban centres rather than rural settlements. In 1961, a well-trained psychiatrist and neurologist from Vancouver, Dr. David Blair (b. 1921?) arrived in Calgary. As a specialist in the early rehabilitation of paraplegics and quadriplegics, he inaugurated an innovative rehabilitation centre at the CGH which soon gained important provincial significance. In 1967, with the introduction of Medicare in Canada (Lampard 2009), an effective healthcare system made for further diversification in neurological care facilities and basic brain research programs. In 1966, after decades of intensive political discussions –the University of Calgary (U of C) had already become an independent post-secondary institution and a second Medical School was also created in Southern Alberta. With its inception in 1969/1970, the Faculty of Medicine comprised a Department of Psychiatry and included a specialized Division of Neurology. Many local Calgary neurosurgeons, psychiatrists and neurologists were to engage in the undergraduate and continuing medical education programs at the U of C Faculty of Medicine (Boschma 2005). Around 1970, the clinical neuroscience group at the CGH had expanded further and Dr. Hepburn found another neurosurgical colleague in Dr. K. Michael Hunter. The medical neurological service now witnessed the arrival of three more trained neurologists: Roger West, T. Peter Seland and Thomas G. Braun. The latter, however, relocated to Chapel Hill, NC after eight years of neurological practice at the Foothills Medical Centre. With regard to the available diagnostic and research technologies, Dr. Braun stated: "Technological advances in neuroradiology were limited to nuclear brain scans, direct stick arteriography, and pneumencephalograms. Electroencephalograms were used for the diagnosis of epileptic conditions as well as an aid to identify brain tumours" (Brown qtd. by Annear et al. 2004). An autonomous service in Neuroradiology only came into existence in 1967 with the arrival of Calgary's first neuroradiologists, Dr. B.V. Evans – a neuroradiological fellow from Boston and Toronto – and Dr. Harold Swanson, who introduced cerebral catheter angiography to Western Canada. For a five-year term another neuroradiologist, Dr. D'Arcy Lawrence was enticed to join the Foothills' team after he completed his postgraduate training in neuroradiology at the Montreal Neurological Institute (MNI).

In 1973, efforts were made to purchase a Computer Tomography (CT) scanner for Calgary with the intention to "allow [the] departments of Radiology and Neurosurgery to compete with the leaders of [the] country" (Robert G. Lee, qtd. after Annear et al. 2004). In 1974, the Foothills Hospital received political priority over the CGH for the installation of the CT, an achievement that was largely due to the engagement of radiologist, Dr. Hector Ewart Duggan (1916-1989) and neurosurgeon, Dr. Francis E. Leblanc. This first scanner in Western Canada began its service in March of 1975. During this time, one of the neurosurgeons from the Faculty of Medicine, Dr. Douglas Cochrane, reminisced about the practicability of the new EMI-scanners (developed by Electric and Musical Industries, Ltd.): "The scanner, while revolutionary in its time, required patience […] many hours were spent holding restless patients in the scanner as each slice took over a minute" (Cochrane qtd. by Annear et al. 2004). The

arrival of this innovative research technology became a major boosting factor for many following neuroscientific activities in Alberta.

It is interesting to note that besides having a direct relationship with the Montreal "Neuro", – Dr. Leblanc was a former graduate of the Université de Montréal and neurosurgeon at the MNI – the Clinical Neuroscience Department in Calgary also had an indirect connection to a key figure in the Montreal institution. The world-renowned pioneer of epilepsy-surgery, Theodore Rasmussen (1910-2002) – succeeding Wilder Penfield (1891-1976) as the second Director of the "Neuro" since its establishment (Andermann 1991) – moved to Calgary after his McGill retirement. While his contacts to U of C neurological and neurosurgical faculty members had been rather loose before, now he was frequently asked for his opinion on the development of a neurological centre in Southern Alberta and eventually became an external consultant to the U of C Department of Pathology. Dr. Rasmussen subsequently advised on neurohistological methods and gave second opinions on complicated brain biopsies. Following his death (2002), Dr. Rasmussen was buried at a cemetery in Calgary.

Clinical Neuroscience in Calgary since 1970 and the Development of the Hotchkiss Brain Institute

After the arrival of about two dozen neurosurgeons, neurologists and psychiatrists during the 1960s and their concentration being in the CGH Bow Valley Centre, the idea surfaced of integrating the services of Neurology, Neurosurgery and Psychiatry into one institution. Although, in the early 1970s, the CGH already had an interdisciplinary clinical neuroscience group, the services in neurosurgery and neurology at the Foothills Provincial General Hospital were still marginal with respect to clinical organization. Neurology was only a division of the Department of Medicine and Neurosurgery a division of the Department of Surgery. These neurological and neurosurgical services however, soon experienced additional growth in staff numbers as well as research space allocation, moving them closer to the centre of the organizational hierarchies. Even though the Foothills Hospital had just opened in 1966, in six years there were five medical neurologists among its clinical Faculty: Drs. Robert G. Lee, C.T. Man-Son-Hing, Sanat Mukherjee, Terry Hing and Frank Ramsay, a 1957 U of A graduate who received his postgraduate training at the Minnesota University Hospital. In clinical neuroscience, there were two neurosurgeons who came to supplement the services of Dr. Charles W. Taylor and Dr. Francis Leblanc. These neurosurgeons were Terry Myles – from the Montreal MNI – and Jack L. Barlass (d. 1999) – trained at the neurosurgical service at the U of A – joined the Foothill's group also in 1966. Seven years after the creation of the Medical School, the Calgary Health Sciences Centre was completed, and there was now more laboratory space available, and the Medical Faculty saw the first class of medical students graduate from the lecture theatres of this building. Even though most neurology patients were still being distributed to a number of medical units, neurosurgery at the Foothills had now been allocated Unit 92. Furthermore, at this time, the clinical neurologists and neurosurgeons also needed to care for the pediatric patients because the Alberta Children's Hospital had not been completed.

Even though Dr. Swanson, a trained neuoradiologist, had commenced his work in the CGH in the early 1960s, the emergence of a neuroimaging group had to await the arrival of Dr. B. V. ("Bruce") Evans at the Foothills Hospital. With the recent oil boom, the acquisition of a CT scanner was now within reach, nevertheless, the Alberta government was not convinced that the financial resources would allow for an even distribution of these new technologies throughout the province. After the decision was made to install a first CT "full body" scanner at the Foothills Hospital in 1975, further concentration of neuroscience researchers at the U of C resulted. The installation of such essential research technology being only at one centre, however, raised additional concerns about the future of brain research in Calgary. The chiefs of neurology and neurosurgery from the two hospitals – the neurosurgeon Dr. Leblanc and Dr. Lee, the first academic neurologist from the U of C, as well as Drs. Peter Seland and Mike Hunter from the CGH met regularly in what were rather clandestine gatherings at the Corkscrew restaurant near the Foothills Hospital. This group later became known as the "Corkscrew Club" and produced "A Proposal for a Regional Program in Neurology and Neurosurgery for Southern Alberta". The planning document foresaw that all acute neurosurgical and neurological services were to be integrated into one main hospital

centre so that synergies would be possible at all levels of administration, research and clinical care. It came to be an agreement paper on which committees at the CGH and the Foothills Hospital as well as the U of C Faculty of Medicine gave their feedback over many months. The medical establishment at both Calgary hospitals however criticized the planning document. The existing departments of the Foothills Hospital, for example, were threatened by the prospect that neurosurgery and neurology would be receiving more hospital beds thus creating an organizational structure of their own, and even though administrators at the CGH raised concerns regarding the externalization of two clinical and research programs – a number of recommendations by the "Corkscrew Club" were eventually accepted. Complete centralization of the clinical neuroscientific services in the Foothills complex, nevertheless, had to await the closure and demolition of the CGH in 1998, following the decision of Alberta's Premier Ralph Klein (b. 1942). In the meantime, another recommendation became a reality, namely the establishment of a more pronounced administrative link among Calgary services in neurology and neuroscience at the university and Calgary hospital levels. In the following areas this led to specialized outpatient clinics: Epilepsy, Neuro-oncology, Movement and Pain etc. at the Foothills and MS, Headaches and Spinal Cord Injuries etc. at the CGH (Annaer et al. 2004).

In the fall of 1980, a Department of Clinical Neurosciences was approved by the Faculty Council at the U of C becoming a major milestone in the local history of brain research. The new clinical department opened its services on the 1st of January, 1981 and witnessed a fairly rapid growth throughout the 1980s and 1990s – during the period of the American "Decade of the Brain". Following this was an increase of researchers and clinicians, a growth in educational programs as well as a diversification of methodological and technological changes. Another example of this development was the first Magnetic Resonance Imaging (MRI) scanner which arrived in Calgary in 1990. The functional fMRI technique came into use in 1993 and interestingly enough, significant contributions to the method of intra-operative scanning were made at the U of C. A first combined PET/CT scanner was installed in 2005 at the Seaman Family MR Research Centre at the Foothills Hospital, opening new venues for functional *in-vivo* brain research activities (Annaer et al. 2004). Many of these changes were made possible through the creation of the Alberta Heritage Foundation for Medical Research (AHFMR) through an Act of Legislature in 1980. Created with an endowment of $300 million and overseen by a board of trustees, it started its funding for students and fellows in its year of its creation. In 1987, a special fund was taken out of the endowment to finance two "Heritage Medical Research Buildings" at the U of A and the U of C, taking into account that the number of medical researchers had dramatically increased (Lampard 2008). Over the course of twenty-five years, 130 researchers and 1,000 students were supported by the foundation at all four research intensive universities in the province (and later included Lethbridge and Athabasca). Since its foundation, the AHFMR in Alberta attracted major brain researchers such as Dr. Bruce Tranmer, a Toronto- and Munich-trained clinical stroke researcher and Dr. Quentin Pittmann, who became a Fellow of the Royal Society of Canada in 2010. Other renowned neuroscientists such as the world leader in neuroplasticity research, Dr. Fred H. Gage (now: Salk Institute for Biological Studies) had received offers to come to Calgary.

The most recent history of neuroscience in Calgary takes its origin from the creation of the Department of Clinical Neuroscience, (currently headed by Dr. J. Gregory Cairncross). This former organization of research groups at the U of C Faculty of Medicine during the 1980s and 1990s, eventually led to the creation of the The Hotchkiss Brain Institute (HBI) in 2004. Under the leadership of Dr. Samuel Weiss – Gairdner Award Winner (2008) for his discovery of neuronal stem cells – and with the support of the U of C and the Calgary Health Region (now: Alberta Health Service – AHS), the Institute was established through a foundational gift from Calgary's Hotchkiss family. The Mental Health Centre for Research and Education as well as five Departments (Clinical Neuroscience; Cell Biology & Anatomy; Physiology & Pharmacology; Psychiatry; and Radiology) form part of its organizational structure. Following an international review process, the research activities at the HBI were now centered into three thematic areas (Axon Biology & Regeneration; Cerebral Circulation; and Neural Systems and Behaviour), conforming to the mission statement of the HBI which focuses on being a centre of excellence in neuroscience and mental health research.

Glances at the Neuroscience Programs at the U of L (Lethbridge) and U of A (Edmonton)

Neuroscience at the U of L: Traditionally, there have been strong ties between the U of C departments and institutes and those of the U of L ever since the latter's foundation in 1967 and the creation of the Canadian Centre for Behavioural Neuroscience through the U of L's core Faculty in experimental psychology, Dr. Bryan Kolb and Dr. Ian Whishaw. Due to space constraints, readers are referred to the historical section on the "History of Academic Psychology in Alberta" (pp. 20-23).

Neuroscience at the U of A: The historical foundations of brain research at the U of A developed from within the Royal Alexandra Hospital in Edmonton and the UAH, supplied by their strength in neurosurgical and neurological care as well as clinical brain research (Macbeth 2009). Havelock Hepburn who originally created the Division of Neurosurgery at the U of A in 1934 was followed by succeeding heads, Dr. Guy Morton (1951) and Dr. Thomas Speakman (1964). Dr. Peter Allen, who returned from the Mayo Clinic in Rochester, MN in 1969, even assumed the role of UAH Vice President and Dr. Bryce Weir, being the Division Head after 1982, became the President of the Alberta Medical Association (AMA). Their official roles in the medical community reflected an increasing clinical and research importance of neurosurgery (Weir 2011). Between 1920 and 1957, patients with medical neurological conditions were treated primarily by internists and general surgeons. Dr. Ken Thompson, long-time Head of the Department of Medicine in Edmonton, personally encouraged specialized care for neurological patients, and when Dr. George Monckton from Queen Square joined the U of A – in 1957 – also a basic science-oriented brain research program came into existence. At the time when sophisticated neuroanatomical studies became available, Dr. Monckton's interest was in the area of muscle disease and accordingly, he proved to be a major figure in bringing the first electron microscope to the province of Alberta. That same year, Brain research activities in Edmonton were further augmented by the return of Dr. Henri M. Toupin (1907-1971) when assuming the position of Chief of Neurology at the Royal Alexandra Hospital (Gilchrist 2004).

The U of A Division of Neurology – a partial unit of the Department of Medicine – was formally established in 1965 by Dr. Henry Jacobs, who had received his medical training at the University of Cape Town in South Africa and his neurological specialization in Oxford, UK. In the following five years, the academic service – now comprising of two educational programs – integrated further practicing Edmonton neurologists, for example Dr. Ian Sanderson from Scotland, Dr. George Prestwick from Australia and Dr. Gilles Blaines who returned to the U of A from postgraduate training at the U of M. Research activities were largely clinical with the exception of the neurohistology program of Dr. Monckton. A major boost in basic brain research occurred later with the hiring of Donald McLean in 1970 who received his postgraduate training at three major interdisciplinary centres (McGill, Harvard and the Mayo Clinic). While he led a laboratory of electrophysiology himself, research activities were now diversified with the hiring of Kenneth Warren from London, as a MS researcher, Jack Jhamandas from Calgary and McGill, as a clinical neuropathologist, and George Ellecker from the MNI, who joined forces with McLean as another neurophysiologist. At the beginning of the 1980s, high-end clinical services in neurology were surrounded with important basic research groups (Gilchrist 2004). Today, the UAH has a dedicated neurosciences intensive care environment which focuses on the treatment of complex clinical conditions such as strokes, brain tumours, brain and spinal cord injuries. Since the 1990s, the U of A has become particularly strong in cognitive neuroscience with researchers exploring the neural correlations of human cognition and behaviour. A wide variety of methods and technologies is now applied to understand brain-behaviour relationships in animal models and humans. The spectrum of approaches includes cognitive and neuropsychological, brain imaging, electrophysiological and genetic analyses. Partly coordinated by the Centre for Neuroscience (Director, Dr. Kathryn Todd, a research psychiatrist), investigations in cognitive neuroscience occur in multiple units on campus, primarily in the Department of Psychology (for its history, see for example: Smith 1975), the Division of Neurology, the Department of Psychiatry and the interdisciplinary Centre for Neuroscience which also

relate to other neuroscience facilities in Edmonton, such as the Glenrose Rehabilitation Hospital and the Alberta In Vivo NMR Centre.

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