

Stroke: The past, present and future

I. Mhairi Macrae¹ and Stuart M. Allan²

Abstract

Since the inception of the British Neuroscience Association, there have been major advances in our knowledge of the mechanistic basis for stroke-induced brain damage. Identification of the ischaemic cascade led to the development of hundreds of new drugs, many showing efficacy in preclinical (animal-based) studies. None of these drugs has yet translated to a successful stroke treatment, current therapy being limited to thrombolysis/thrombectomy. However, this translational failure has led to significant improvements in the quality of animal-based stroke research, with the refinement of rodent models, introduction of new technologies (e.g. transgenics, in vivo brain imaging) and improvements in study design (e.g. STAIR, ARRIVE and IMPROVE guidelines). This has run in parallel with advances in clinical diagnostic imaging for detection of ischaemic versus haemorrhagic stroke, differentiating penumbra from ischaemic core, and improved clinical trial design. These preclinical and clinical advances represent the foundation for successful translation from the bench to the bedside in the near future.

Keywords

Stroke, cerebral ischaemia, preclinical, brain injury

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Clinical diagnosis of stroke: a transformational story

Significant advances in brain imaging mean that stroke patients can now expect an acute diagnostic scan to differentiate between haemorrhagic, ischaemic and stroke mimics when admitted to hospital (Heit and Wintermark, 2017). If the stroke is ischaemic, the occluded vessel can be identified and time from stroke onset used to determine whether thrombolysis, to break down an occluding embolus/thrombus, or endovascular embolus/thrombus extraction (thrombectomy) is warranted. Thrombolytic treatment with intravenous recombinant tissue plasminogen activator (IV rtPA), given up to 4.5 h from stroke onset, significantly increases the prospect of a good recovery, with the greatest benefit seen with the shortest onset-to-treatment times (Röther et al., 2013).

In patients where a large proximal occlusion is identified, endovascular thrombectomy within 6 h of stroke onset improves the chance of a good outcome (Powers et al., 2015). However, less than 10% of acute ischaemic stroke patients receive intravenous thrombolysis in most centres and only 7%–15% are expected to qualify for acute endovascular intervention (Henninger and Fisher, 2016). Therefore, there is significant scope for stroke researchers (clinical and preclinical) to develop strategies for more patients to benefit from thrombolysis/thrombectomy and test new therapies as adjunct or standalone treatments for patients where thrombolysis/thrombectomy is contraindicated.

Ischaemic stroke patients being considered for recruitment into a clinical trial may also have a computed tomography (CT)

or magnetic resonance imaging (MRI) ‘penumbra’ scan to identify how much tissue affected by the stroke is still capable of recovery (Warach et al., 2016). Since penumbral tissue has a limited lifespan of hours and available tissue for salvage varies significantly in the patient population, penumbral imaging also ensures that only patients with remaining biological target tissue are recruited into acute stroke therapeutic trials (Muir and Macrae, 2016). The lack of penumbral imaging in the early, unsuccessful clinical neuroprotection trials, some of which recruited patients at time points beyond the likely survival of penumbra, is likely to have resulted in recruitment of stroke patients with no remaining target tissue for salvage, thereby diluting the power to detect therapies with potential efficacy. MRI penumbral imaging is now available for longitudinal rodent stroke studies where loss of penumbra over time can be tracked and the consequences of therapeutic intervention determined (Figure 1), thereby providing more informative data on the

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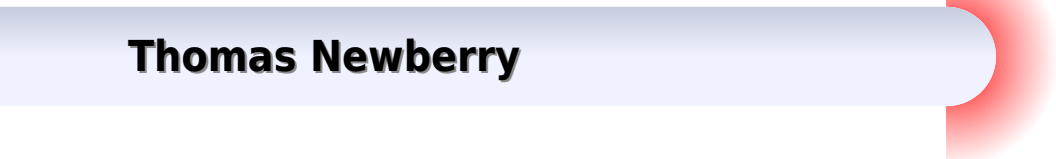
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Stroke The Past Present And Future

Thomas Newberry



Stroke The Past Present And Future:

The Timespace of Human Activity Theodore R. Schatzki, 2010-04-12 This book shows that a concept of activity timespace drawn from the work of Martin Heidegger provides new insights into the nature of activity society and history Although the book is a work of theory it has significant implications for the determination and course not just of activity but of sociohistorical change as well Drawing on empirical examples the book argues 1 that timespace is a key component of the overall space and time of social life 2 that interwoven timespaces form an essential infrastructure of important social phenomena such as power coordinated actions social organizations and social systems and 3 that history encompasses constellations of indeterminate temporalspatial events The latter conception of history in turn yields a propitious account of how the past exists in the present In addition because the concept of activity timespace highlights the teleological character of human action the book contains an extensive defense of the teleological character of such allegedly ateleological forms of activity as emotional and ceremonial actions Since finally the book's ideas about timespace and activity as an indeterminate event derive from an interpretation of Heidegger the work furthers understanding of the relevance of his thought for social and historical theory The book combines textual interpretation theoretical argumentation and empirical substantiation Many of its empirical examples are taken from the Blue Grass Horse Country around Lexington Kentucky where the author resides

Time, Temporality, and History in Process Organization Studies Juliane Reinecke, Roy Suddaby, Ann Langley, Haridimos Tsoukas, 2020 Time temporality and history are inherently important constructs in process organization studies yet have struggled to move beyond limited conceptualizations in management theory This volume draws together emerging strands of interest to adopt a more nuanced approach in understanding the temporal aspects of organizational processes

Medicine, Risk, Discourse and Power John Martyn Chamberlain, 2015-11-19 This book critically explores from a comparative international perspective the role medicine plays in constructing and managing natural and social risks including those belonging to modern medical technology and expertise Drawing together chapters written by professional practitioners and social scientists from the UK South America Australia and Europe the book offers readers an insightful and thought provoking analysis of how modern medicine has transformed our understanding of both ourselves and the world around us but in so doing has arguably failed to fully recognize and account for its unintended and negative effects This is an essential read for social scientists practitioners and policymakers who want to better understand how they can develop new ways of thinking about how modern medicine can promote social goods and enhance public health

Professional Practice and Learning Nick Hopwood, 2016-01-22 This book explores important questions about the relationship between professional practice and learning and implications of this for how we understand professional expertise Focusing on work accomplished through partnerships between practitioners and parents with young children the book explores how connectedness in action is a fluid evolving accomplishment with four essential dimensions times spaces bodies and things Within a broader

sociomaterial perspective the analysis draws on practice theory and philosophy bringing different schools of thought into productive contact including the work of Schatzki Gherardi and recent developments in cultural historical activity theory The book takes a bold view suggesting practices and learning are entwined but distinctive phenomena A clear and novel framework is developed based on this idea The argument goes further by demonstrating how new coproductive relationships between professionals and clients can intensify the pedagogic nature of professional work and showing how professionals can support others learning when the knowledge they are working with and sense of what is to be learned are uncertain incomplete and fragile *The Tabernacle and the Temple* Thomas Newberry,1887 , *My Back Nine* Tony Caico,2010-12-29 After riding the gravy train for more than ten years in the mortgage banking industry author Tony Caicos industry and his life met at an intersection and crashed His worth was so closely tied to what he did for a living that he no longer knew who he was After some careful soul searching his healing began and he put his life back on track Using the back nine holes of a golf course as a guide Caico uses his experiences to help others analyze what they need to do better to truly enjoy the second half of their lives Each golf hole represents one of the following nine key life components family health and wellness knowledge career spirituality leadership relationships self improvement and happiness In *My Back Nine* Caico synthesizes current thinking and research on careers evaluating strengths and formulating life plans to offer a guide to making changes for the better The essential qualities needed for success in golfpreparation focus patience discipline integrity and honestyare the same qualities necessary to be successful in life *My Back Nine* shows how both life and sports can often create real winners on and off the playing field **The Philosophy of Time** L. Nathan Oaklander,2008 *The Philosophy of Time* is a new title in the Routledge series Critical Concepts in Philosophy It meets the need for an authoritative reference work to make sense of the subject s vast literature and the continuing explosion in research output Edited by L Nathan Oaklander a leading scholar in the philosophy of time this new Major Work from Routledge brings together in four volumes the canonical and the very best cutting edge scholarship in the field to provide a synoptic view of all the key issues and current debates **History of Woman Wuffrage** Elizabeth Cady Stanton,1882 **The Americana** ,1923 **Potter's American Monthly** ,1879 **The Poetical Works of Elizabeth Margaret Chandler** Elizabeth Margaret Chandler,Benjamin Lundy,1836 **Poetical Works** Elizabeth Margaret Chandler,1836 [Essays, Philanthropic and Moral](#) Elizabeth Margaret Chandler,1836 Elizabeth Margaret Chandler was a Quaker and the first woman writer to make the abolition of slavery her principal theme **The Poetical Works of Elizabeth Margaret Chandler: with a Memoir of Her Life and Character, by Benjamin Lundy. [With a Portrait.]** Elizabeth Margaret Chandler,1836 **Essays, Philanthropic & Moral** Elizabeth Margaret Chandler,1845 *History of woman suffrage. Vol.1-3, ed. by E.C. Stanton, S.B. Anthony, and M.J. Gage; vol.4, ed. by S.B. Anthony and I.H. Harper; vol.5,6, ed. by I.H. Harper* Susan Brownell Anthony,Ida Husted Harper,Elizabeth Cady Stanton,1882 *History of Woman Suffrage: 1861-1876* Elizabeth Cady Stanton,Susan

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