

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 (Mhair 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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Stroke The Past Present And Future

John Martyn Chamberlain



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

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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

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Table of Contents Stroke The Past Present And Future

1. Understanding the eBook Stroke The Past Present And Future
 - The Rise of Digital Reading Stroke The Past Present And Future
 - Advantages of eBooks Over Traditional Books
2. Identifying Stroke The Past Present And Future
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Stroke The Past Present And Future
 - User-Friendly Interface
4. Exploring eBook Recommendations from Stroke The Past Present And Future
 - Personalized Recommendations
 - Stroke The Past Present And Future User Reviews and Ratings
 - Stroke The Past Present And Future and Bestseller Lists
5. Accessing Stroke The Past Present And Future Free and Paid eBooks
 - Stroke The Past Present And Future Public Domain eBooks
 - Stroke The Past Present And Future eBook Subscription Services
 - Stroke The Past Present And Future Budget-Friendly Options
6. Navigating Stroke The Past Present And Future eBook Formats

- ePub, PDF, MOBI, and More
- Stroke The Past Present And Future Compatibility with Devices
- Stroke The Past Present And Future Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Stroke The Past Present And Future
 - Highlighting and Note-Taking Stroke The Past Present And Future
 - Interactive Elements Stroke The Past Present And Future
- 8. Staying Engaged with Stroke The Past Present And Future
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Stroke The Past Present And Future
- 9. Balancing eBooks and Physical Books Stroke The Past Present And Future
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Stroke The Past Present And Future
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Stroke The Past Present And Future
 - Setting Reading Goals Stroke The Past Present And Future
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Stroke The Past Present And Future
 - Fact-Checking eBook Content of Stroke The Past Present And Future
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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