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Celebrating the life and research of BNA Past-President Colin Blakemore

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Abstract
Professor Sir Colin Blakemore was a remarkable neuroscientist, persuasive communicator, and brave advocate for animal research who, sadly, passed away in June 2022 from amyotrophic lateral sclerosis. His work helped establish the concept of neuronal plasticity, which was fundamental to our understanding of the postnatal brain and continues to impact our outlook on neurodegenerative disorders. The BNA2023 Festival of Neuroscience dedicated its last plenary session in his honour, bringing together five prominent neuroscientists whose careers were shaped by Professor Blakemore. Here, we summarise the speakers' reflections on how Colin's support, generosity, and foresight influenced their academic paths, inspired their research, and changed their outlook on life.

Keywords
Colin Blakemore, mentorship, BNA2023

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Introduction

> The astonishing tangle within our heads makes us what we are.
>
> –From *Mechanics of the Mind*, by Colin Blakemore, 1977.

Colin Blakemore was a brilliant neuroscientist, eloquent and persuasive science communicator, and a passionate advocate for animal research. His work shaped our understanding of neural plasticity – the capacity of the brain to rewire itself and adapt to the surrounding environmental changes, which is now a dominant theme in the field. He spoke and wrote about neuroscience and society with clarity and elegance in many media outlets and his support for policy openness, animal research, and rationality influenced policymakers and scientific education. Amongst his remarkable achievements, Colin was president of the British Neuroscience Association (BNA, 1997–2000) and remained one of the BNA's patrons until his death at the age of 78 from amyotrophic lateral sclerosis (ALS). This article is a recap of the final plenary session in the BNA2023 Festival of Neuroscience, celebrating the rich life and research of Colin Blakemore. Below, I summarise the reflections of five prominent neuroscientists whose careers were shaped and influenced by him (Figure 1).

Colin's legacy of enrichment: Dr Helen Grote (Imperial College London)

At the age of 16, Helen came across Colin on a school trip when she attended an introductory lecture on neuroscience at the Methodist Central Hall, Westminster. Enchanted by Colin's talk, she visited her local public library to borrow a copy of his book *Mechanics of the Mind*. Later on, her BA studies as an undergraduate medical student at Magdalen College, Oxford, formally reintroduced Helen to Colin's laboratory and his work. Colin's lectures on the visual system introduced Helen to the concept of neuronal plasticity, specifically through his early work on how alterations to the visual environment during development can disrupt the orientation of cortical cells (Blakemore and Cooper, 1970). Colin's interest in neuronal plasticity further extended to adult conditions, such as Huntington's disease (HD) and stroke.

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Figure 1. Five neuroscientists whose careers were shaped by Colin Blakemore. From left to right: Andrew Parker, Tara Spires-Jones, Zoltán Molnár, Helen Grote, and Anthony Hannan.

His work was a clear demonstration of how the provision of a stimulating environment could impact the onset and progression of neurodegenerative disorders (Van Dellen et al., 2000).

As a postgraduate student in Colin's laboratory, Helen's research investigated the molecular mechanisms of environmental enrichment, particularly its effects on neurons and synapses, neurogenesis, and gene expression. She investigated R6/1 transgenic mice, a model expressing a human huntingtin transgene with an expanded CAG (Cytosine, Adenine, Guanine) repeat that closely recapitulates human HD. At the age of 5 months, the R6/1 mice exhibited deficits in the trafficking of brain-derived neurotrophic factor (BDNF) to the striatum and hippocampus from the cortex, which was rescued by environmental enrichment (Spires et al., 2004).

Colin's 'greater foresight and understanding of the importance of neuronal plasticity in the adult as well as the developing brain' subdued any concerns Helen had on the future implications of this work. The recent results of the longitudinal Track-HD study, which studies a cohort of HD gene expansion carriers, demonstrated a positive effect of intellectual enrichment, such as high education levels, verbal intellectual ability, and occupational function, on Met66 allele carriers of the BDNF gene (Papoutsi et al., 2022), nicely reflecting on work undertaken by Helen and Tara Spires in Colin's laboratory 18 years earlier. Now working as an NHS (National Health Service) Consultant Neurologist, Helen continues to see the impact of environmental enrichment, such as education, exercise, diet, and modulation of stress in mitigating the progression of neurological conditions. For example, in Parkinson's disease, exercise is routinely recommended as a part of treatment, given the reported benefits in delaying disease onset and progression, and controlling both motor and non-motor functions (Ramaswamy et al., 2018).

Helen finally reflected on her time with Colin, both inside and outside the laboratory. Colin was 'approachable, kind and friendly', and taught her the importance of mentorship. His encouragement promoted confidence in her academic abilities that set the ground for her future career as a neurologist and clinical lead of the neurogenetics service at Imperial College, London. His impact on her personal career has been formative, through continuous support and generous references for fellowships and job applications. To Helen, 'his legacy will continue to live on in the scientific work that has been done' and in her own clinical practice, because the understanding of neuronal plasticity and gene–environment interactions that Colin drove forward is now paving the way for treatments of a number of neurodegenerative diseases.

In celebration of cerebration (Blakemore, 2005): Prof Anthony Hannan (Florey Institute, University of Melbourne)

Upon completion of his PhD in Sydney, Australia, Tony arrived in Oxford in 1996. He was impressed by the adventurous and innovative culture that Colin nurtured in the University Laboratory of Physiology (which is now incorporated into the Department of Physiology, Anatomy and Genetics), Oxford, which encouraged him to take scientific risks and follow his curiosity. Tony had the opportunity to test new ideas through setting up transgenic and genetic knock-out mouse models in the department for the first time, which was actively facilitated by Colin (Nithianantharajah and Hannan, 2006). This involved establishment of a transgenic mouse model of HD, with collaborators, to test the hypothesis of environment enrichment, at a time when HD was considered as 'the epitome of genetic determinism'. Their work on HD mouse models demonstrated that, compared with standard housing, environmental enrichment delays disease onset in HD mice (Van Dellen et al., 2000), a robust finding that was independently replicated by many other studies using other preclinical models of HD, and extended many different neurological and psychiatric disorders (Nithianantharajah and Hannan, 2006).

Following this, Colin's group further explored potential molecular mechanisms, including the role of BDNF in HD and its amelioration by environmental enrichment (Spires et al., 2004). Tony described the translational relevance of their work, including how molecules like BDNF (that are changed by disease and corrected by the beneficial effects of cognitive stimulation and physical activity) can be targets for novel therapeutics, or 'enviromimetics', which could mimic or enhance the beneficial effects of environmental stimulation (Nithianantharajah and Hannan, 2006). Their work also provided evidence of *in vivo* cortical plasticity changes coupled with cognitive deficits modelling dementia, informing HD pathogenesis and therapeutic possibilities (Mazarakis et al., 2005).

Colin's flexibility and encouragement allowed Tony and his team to follow-up on the importance of the PLC-β1 signalling pathway in critical periods of postnatal plasticity by exploring the PLC-β1 knock-out mice. Indeed, their work showed that gene-editing ablation of PLC-β1 disrupted these aspects of cortical development with specific effects on experience-dependent neural plasticity and synaptogenesis (Hannan et al., 2001; Spires et al., 2005). As Tony set up his independent laboratory at the Florey Institute, University of Melbourne, Colin's generosity further extended in allowing him to carry forward and build on these projects (Figure 2).

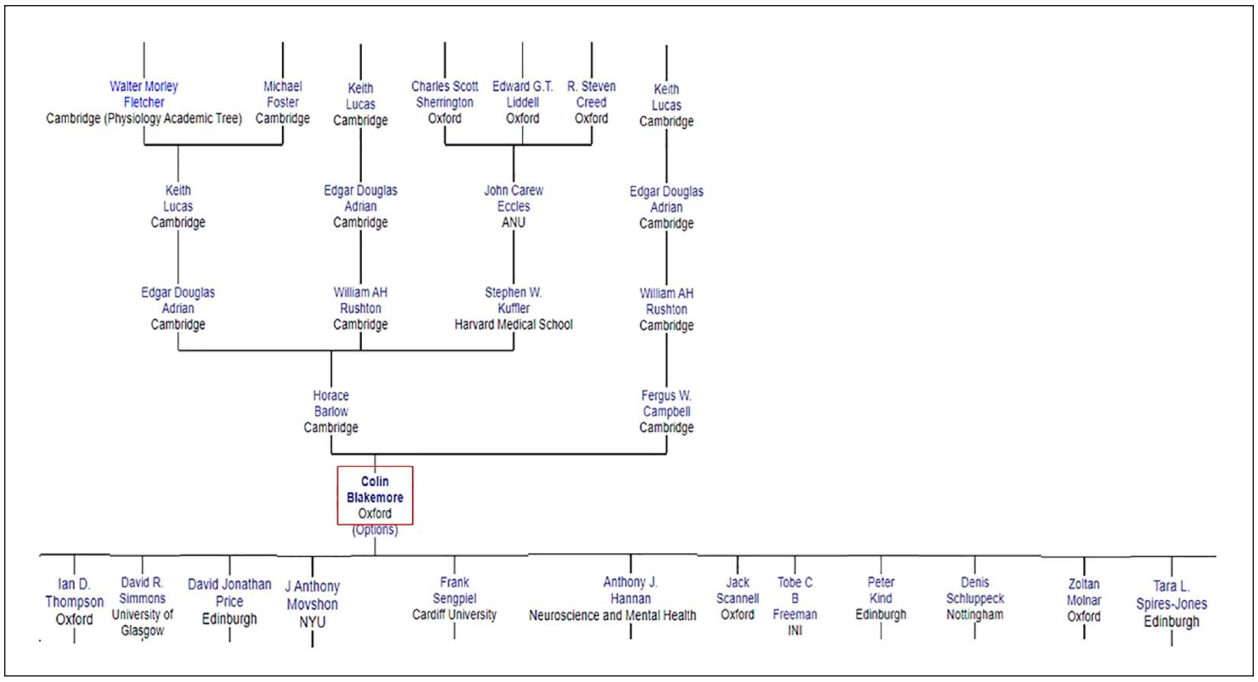

Figure 2. Snapshot of Neurotree as presented by Anthony Hannan showing Colin's academic children (Neurotree.org).

Colin taught Tony that 'science is fun – you work hard, and you play hard and that's part of what keeps a lot of people in this wonderful career, together with the importance and impact of biomedical research'. His courage in standing up for medical research resonated both locally and internationally. With Colin, there was always 'courage, generosity and extraordinary intellect'.

The spirit of guidance: Prof Zoltán Molnár (University of Oxford)

Zoltán started as a PhD student in Colin's laboratory after graduating from the Albert Szent-Györgyi Medical University in Hungary, became a Senior Scholar at Hertford College, Oxford, then a Medical Research Council (MRC) career development fellow, and then a junior research fellow at Merton College, Oxford. Spending a lot of time in Colin's laboratory, Zoltán's interest in the field of cerebral cortical development and evolution was nurtured, thereby shaping his research career. Colin encouraged him to think about big, fundamental questions. Together, they investigated how the differentiation of the cerebral cortex into distinct regions with 'minute variations in cytoarchitecture' reflects different circuitry and computational functions.

Zoltán was the first in Colin's laboratory who introduced *in vivo* and *in vitro* mouse models to study cortical development and plasticity. The tactile-somatosensory activation upon whisker stimulation, mediated by thalamo-cortical input, offered a huge advantage when investigating interactions between the sensory experience and the developing brain. As such, Zoltán began investigating thalamo-cortical development to understand how thalamic fibres interact with the developing cerebral cortex and how they impose different cytoarchitectural patterns on the cortex. Their work, using tracing studies and *in vitro* co-cultures, revealed a lack of preference of thalamic connections towards cortical areas and helped elucidate patterns of thalamic innervation (Molnár and Blakemore, 1991, 1995). Working on this project for several years, Zoltán recalls how Colin always encouraged and supported him. Together, they formulated the 'Handshake hypothesis', which described how reciprocal descending cortical axons interact and guide the ascending thalamic axons to navigate to their appropriate cortical targets at the pallial–subpallial boundary (Molnár and Blakemore, 1995). Moreover, Colin encouraged Zoltán to explore activity patterns in the developing brain as well as ways to 'silence the brain' using a Snap25 null mutant mouse model to address the effects of synaptic activity on prenatal development (Molnár et al., 2002, 2003), which he still investigates to this day (Molnár et al., 2020).

Zoltán explained how Colin took mentoring very seriously: his relationship with Colin was a lifelong friendship. Colin's attitude to life and family was exemplary. His constant advice helped guide and direct many aspects of Zoltán's research. As Zoltán continues to follow-up many of the questions he started investigating with Colin, he feels 'his spirit is still here today' (Molnár and Hannan, 2022; Molnár and Parker, 2022).

Seeing in-depth from Colin's perspective: Prof Andrew Parker (University of Oxford and Otto-von-Guericke University, Magdeburg)

In his talk, Andrew sought to highlight how his career has been supported by Colin. He reflected on how generosity was at the heart of all of Colin's activity; 'not only was he intellectually generous in allowing people to carry on things that he started, but he was also generous in terms of helping others to get their research done'.

Andrew began by describing how Colin's interaction with the perceptual psychologist, Professor Richard Gregory, early on in his academic life helped influenced Colin's proactive, hands-on, and risk-taking approach to science. Similarly, Colin's early work with Horace Barlow and Jack Pettigrew, on how the physiology of visual perception can explain psychological phenomena, shaped Colin's view of the world (Barlow et al., 1967). Andrew was interested in the computational modelling of vision as a bridge between physiology and psychology. He recalls that upon expressing this interest to Colin, Colin was able to arrange and secure a generous funding through collaborating with Charles Smith from the System Development Foundation, which allowed Andrew to travel around the United States and learn about computational vision. Colin was able to further fund a lectureship in biological computation at the University of Oxford's Department of Physiology for Andrew at a time when universities encountered a drop in the number of available positions.

Upon his return to Oxford, Colin further supported Andrew to set up laboratory recordings from awake-behaving monkeys, owing to the similarity between Macaque and human vision regarding binocular depth. This work utilising offsets between retinal projections and the actual target position in the world demonstrated that the relative disparity signals used in primate depth perception are constructed outside area V1 (Cumming and Parker, 1999). Andrew went on to explore visual areas beyond the primary visual cortex in the macaque. His work on the dorsal visual area V5 revealed that neurons are not only selective for absolute disparity, but also code for relative disparity between moving visual features, a selectivity that is critical for self-motion through the visual environment (Krug and Parker, 2011). Andrew concluded that not only had Colin been generous with his support and ideas, but 'he'd actually left me enough space to work in, to do interesting things', many of which Andrew still pursues in his current work.

Lessons in life and science: Prof Tara Spires-Jones (University of Edinburgh)

Tara recalled her path to Oxford, starting at her local university, the University of Texas at Austin, then studying abroad in her third year at Université Paul Sabatier, Toulouse, followed by a summer internship in the laboratory of the developmental biologist, Nicole LeDouarin. Tara then stumbled upon Colin's work in the library, which prompted her to get in touch with him. Their first encounter taught her the first lesson about scientific funding. Determined to work in Colin's laboratory, Tara successfully secured a Marshall Scholarship and a National Science Foundation Fellowship to fund her PhD.

Tara inherited from Colin a love of synapses and plasticity. Her initial work allowed her to perform electron microscopy (EM) on brains. Moving on from neurodevelopment to neurodegeneration, Tara continues to investigate synapses: their synaptic structure, biochemistry, and plasticity. To Tara, Colin taught her how to adapt: 'You can change and learn and grow, you don't have to be stuck on what you do'. One of the lessons Colin taught Tara was that 'curiosity is a beautiful thing'. He constantly supported and encouraged her to chase this curiosity and find answers. Through Colin, she learnt that politics matter in science and that it is important to 'stand up for what is right'. She described how he stood up for fundamental neuroscience, how his work influenced our understanding of the individual cellular function in the visual cortex as well as our therapeutic approaches in clinical practice. She learnt from Colin about the BNA, through which she could engage with the political side of science. Colin also taught her about the importance of public engagement to make science more meaningful to both scientists and the public. Tara explained how Colin instilled a sense of community and an urge to champion trainees and colleagues. Finally, she described how she learnt the importance of having fun and enjoying the process.

Conclusion

Enrichment, plasticity, and perception are not only aspects of Colin's work but appear to be some of the ways he himself influenced the people he encountered. He enriched the lives of those around him with guidance and humour. His flexibility allowed them to grow, flourish, and adapt, and his outlook on life forever changed their perspectives. His legacy lives on.

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References

Barlow HB, Blakemore C and Pettigrew JD (1967) The neural mechanism of binocular depth discrimination. *The Journal of Physiology* 193(2): 327–342.

Blakemore C (2005) In celebration of cerebration. *Clinical Medicine, Journal of the Royal College of Physicians of London* 5(6): 589–613.

Blakemore C and Cooper GF (1970) Development of the brain depends on the visual environment. *Nature* 228(5270): 477–478.

Cumming BG and Parker AJ (1999) Binocular neurons in V1 of awake monkeys are selective for absolute, not relative, disparity. *Journal of Neuroscience* 19(13): 5602–5618.

Hannan AJ, Blakemore C, Katsnelson A, et al. (2001) PLC-β1, activated via mGluRs, mediates activity-dependent differentiation in cerebral cortex. *Nature Neuroscience* 4(3): 282–288.

Krug K and Parker AJ (2011) Neurons in dorsal visual area V5/MT signal relative disparity. *Journal of Neuroscience* 31(49): 17892–17904.

Mazarakis NK, Cybulska-Klosowicz A, Grote H, et al. (2005) Deficits in experience-dependent cortical plasticity and sensory-discrimination learning in presymptomatic Huntington's disease mice. *Journal of Neuroscience* 25(12): 3059–3066.

Molnár Z and Blakemore C (1991) Lack of regional specificity for connections formed between thalamus and cortex in coculture. *Nature* 351(6326): 475–477.

Molnár Z and Blakemore C (1995) How do thalamic axons find their way to the cortex? *Trends in Neurosciences* 18(9): 389–397.

Molnár Z and Hannan AJ (2022) Professor Sir Colin Blakemore FRS, a brilliant force for good within neuroscience and beyond (1944–2022). *Nature Neuroscience* 25(10): 1249–1250.

Molnár Z, Higashi S and López-Bendito G (2003) Choreography of early thalamocortical development. *Cerebral Cortex* 13(6): 661–669.

Molnár Z, López-Bendito G, Small J, et al. (2002) Normal development of embryonic thalamocortical connectivity in the absence of evoked synaptic activity. *Journal of Neuroscience* 22(23): 10313–10323.

Molnár Z, Luhmann HJ and Kanold PO (2020) Transient cortical circuits match spontaneous and sensory-driven activity during development. *Science* 370(6514): eabb2153.

Molnár Z and Parker A (2022) Colin Blakemore (1944–2022). *Current Biology* 32(16): R858–R861.

Nithianantharajah J and Hannan AJ (2006) Enriched environments, experience-dependent plasticity and disorders of the nervous system. *Nature Reviews Neuroscience* 7(9): 697–709.

Papoutsi M, Flower M, HensmanMoss DJ, et al. (2022) Intellectual enrichment and genetic modifiers of cognition and brain volume in Huntington's disease. *Brain Communications* 4(6): fcac279.

Ramaswamy B, Jones J and Carroll C (2018) Exercise for people with Parkinson's: A practical approach. *Practical Neurology* 18(5): 399–406.

Spires TL, Grote HE, Varshney NK, et al. (2004) Environmental enrichment rescues protein deficits in a mouse model of Huntington's Disease, indicating a possible disease mechanism. *Journal of Neuroscience* 24(9): 2270–2276.

Spires TL, Molnár Z, Kind PC, et al. (2005) Activity-dependent regulation of synapse and dendritic spine morphology in developing barrel cortex requires phospholipase C-β1 signalling. *Cerebral Cortex* 15(4): 385–393.

Van Dellen A, Blakemore C, Deacon R, et al. (2000) Delaying the onset of Huntington's in mice. *Nature* 404(6779): 721–722.