

EDITORIAL

Professor Keith Andrew Wesnes (1950 to 2020)

Keith Andrew Wesnes died at the age of 69 at his home in Goring, in April. Keith was involved in the fields of cognitive neuroscience, psychopharmacology, and drug development.

He was a prolific scientific collaborator, establishing strong working relationships with researchers across a diverse range of topics, including central nervous system drug discovery, nutraceutical and medical foods, and Alzheimer's disease (AD) and dementia.

He was ahead of many of his contemporaries by recognizing the value of automation for research into human cognition very early in his career, and this strong belief combined with his entrepreneurial spirit led to pioneering work in computerized cognitive test development.

He held academic positions at Northumbria University, Swinburne University of Technology, and the College of Medicine and Health, University of Exeter; and founded two computerized cognitive test companies: Cognitive Drug Research Ltd (CDR System); and Wesnes Cognition Ltd (CogTrack).

Driven in his working life and frequently frustrated with the status quo, Keith was an inspiring role model, as well as being a kind and generous mentor, and a gregarious friend.

During the 1970s, having originally planned to study physics, Keith completed a BSc in experimental psychology (1970 to 1973), achieving a first degree, followed by a Medical Research Council-funded PhD in human cognitive psychopharmacology (1973 to 1976) at Reading University. During his PhD, Keith's work focused on the effects of smoking and nicotine on cognition. These studies were able to demonstrate the ability of nicotine to positively impact cognitive test performance and were to have a profound impact on Keith's subsequent work in two ways. The first was in contributing to an emerging body of evidence that manipulation of the brain's cholinergic system could have both positive and deleterious effects on human cognition. The second was that in taking advantage of computerization, tests could be devised which made use of rapid stimulus presentations and which recorded both the accuracy and reaction time of responses—and in doing so provided sensitive indices of performance. These were able to characterize the effects of interventions in a temporally accurate and domain-specific manner.

Using mainframe computers at first, Keith then foresaw that the advent of commercially available personal computers in the 1970s would hugely increase the utility of computerized tests. This was to open up a field of research across dementia and nootropic drug development.

His 1984 paper with his PhD supervisor David Warburton "Effects of scopolamine and nicotine on human rapid information processing performance" was the subject of a "Landmarks in Psychopharmacology" commentary in 2002, highlighting the enduring importance of this early work.¹

During the early to mid-1980s Keith, David, and others published a series of research papers exploring the cognitive effects of nicotine, scopolamine, and temazepam. This period of his life was also spent developing and validating a standardized test battery and by the end of the 1980s, the first commercial research using the CDR Cognitive Assessment System, delivered on the BBC Master Microcomputer would begin to be published.²

The company CDR Ltd was officially founded by Keith in 1986 to provide proprietary cognitive assessment services.

The CDR System, as it became known, was specifically designed for integration into clinical research and was intended to be applied across a range of patient populations and settings, in order to give rapid, repeatable, sensitive, and highly reliable assessments of cognitive function. In addition to its use in commercial, sponsored research, a cornerstone of the company's ethos was allowing academic researchers to use the system for free, which Keith proudly termed the collaborative research program. An understanding of the value of the data generated from the tests and its ability to characterize the nature of the effects of drugs, disease, and other insults and interventions was particularly far-sighted.

Ultimately, the CDR System was to be used in more than 1300 clinical trials and included in several hundred peer-reviewed research papers, conference presentations, and review articles. A comprehensive library of nootropic, cognitive impairment, and disease state data began to be developed and published, with this data continuing to provide important insights for drug development today.³⁻⁸

CDR Ltd occupied several different locations near Reading in the southeast of England, as well as an office in Chicago. The company was latterly located in the small village of Goring, nestled in the Thames valley. The office in Goring was just a short walk from Keith's home down a very steep hill, and more often than not a short drive back, sometimes via one of the many country pubs, or the local Indian restaurant.

At work, he was surrounded in his office by dozens of conference badges (NCDEU, BAP, ASCO, AAN, BPS, ECTRIMS, etc.), business awards, and cabinets filled with packaging from various marketed products (from breakfast cereal, through energy drinks, to treatments

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for AD) that had been the subject of studies employing the CDR System.^{9–11}

From the outset, Keith looked to mentor and support his employees and provide opportunities for them to progress in both academia and business. A long-standing member of the British Association for Psychopharmacology, a trip to Harrogate for the BAP conference became a yearly event, generating research collaborations and enormous bills at the hotel bar in equal measure.

Keith grew CDR Ltd to be a leading provider of computerized cognitive assessments to the pharmaceutical industry. The company won several Queen's Awards for Enterprise in the UK, something that Keith was extremely proud of. CDR Ltd was acquired by United BioSource Corporation in 2009 and the CDR System continues to be used in clinical research.

During the period 1986 to 2009, Keith established numerous research collaborations. These included a series of studies with scientists at Northumbria University exploring the effects of nutraceuticals and traditional herbal remedies, which was to open up subsequent collaborations with Swinburne University of Technology supporting a large body of work in this area.^{12–14}

As an adjunct professor at Swinburne, working with Con Stough, Luke Downey, and Andrew Scholey, he was instrumental in establishing a cognitive clinical trials capability, as well as training dozens of next-generation researchers in cognition and psychopharmacology. He is listed as the 14th most published author from Swinburne, a remarkable contribution from an adjunct. He also made significant contributions to Swinburne's research rankings and was critically involved in numerous key projects at the Centre for Human Psychopharmacology there.^{15,16}

Importantly, too, there was extensive research into cognition and treatment for dementia with Lewy bodies and Parkinson's disease dementia.^{17–21}

This work was to demonstrate the presence and relevance of attentional impairment in these disorders including attentional fluctuation, which was measurable at the level of within-test performance on the CDR System.

Several studies demonstrated the ability of the anticholinesterases to positively impact these impairments. Keith was to leverage the large CDR System normative database in understanding the clinical relevance of such effects and firmly believed that the size of a treatment effect could be best characterized by the degree to which treatment could return individuals to performance that was normal for their age.²²

Landmark longitudinal cohort studies were also established in collaboration with Newcastle University's Institute for Ageing & Health. These included studies in Dementia with Lewy Bodies with Ian McKeith;^{23,24} stroke and vascular dementia with Clive Ballard;²⁵ autonomic sensitivity with Rose Anne Kenny;²⁶ successful aging in the North East 85+ Study with Joanna Collerton;²⁷ the cognitive substudy of the Study on Cognition and Prognosis in the Elderly;²⁸ and the cognitive substudy of the Prevention Regimen For Effectively Avoiding Second Strokes,²⁹ both with Gary Ford.

From 2014 onward, Keith decided to slow down after 30 years of international travel and put his energy and entrepreneurial spirit into his own company, Wesnes Cognition Ltd, and the development of his new online CogTrack tests. Keith saw online test platforms as a vital next phase of cognitive assessment and was determined to support big data collection, and related research into normal cognitive aging and pathological decline.

This led to projects with Exeter University and the inclusion of Keith's cognitive tests in a large online registry study in the UK. Keith had already begun to develop internet-based tests in the early 2000s with CDR Ltd and as with many innovations, recognized the importance of remote, decentralized trial conduct before a substantial number of his peers.³⁰

That knowledge and experience was to be applied to the CogTrack system, which was launched within the PROTECT study (Platform for Research Online to Investigate Genetics and Cognition in Ageing) in 2015.^{31–33}

The ability of this approach to increase the scale, practicality, and efficiency of assessment was able to generate repeated test data on more than 16,000 older individuals at an early stage in the trial and will continue to provide important insights over the longer term.

CogTrack came to be used in varied studies around the world and thanks to Keith's continued commitment to inspiring and supporting research and students, many universities were using the platform through his collaborative research program.^{34–37}

Keith continued to be a prolific research collaborator and author right up to his untimely death, with published papers covering cognition associated with depression, aging, brain training, mild behavioral impairment, D-cycloserine treatment in AD, ubiquinol treatment in the elderly, and inflammation—all published in the past 2 years.

A careful record keeper, Keith has documented more than 550 research seminars around the world, 1300 oral and poster presentations at scientific meetings, 650 published abstracts, and more than 300 peer-reviewed papers and publications.

This work is a testament to his tireless energy, boundless enthusiasm, and seemingly limitless breadth of interest.

Keith Andrew Wesnes, self-styled "head honcho," far sighted, generous, and pioneering, was a scientist with a far-reaching impact on cognitive psychopharmacology. The field will continue to benefit from his work for many years to come.

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