Impact in psychiatry research through experimentation, translation to industry, policy development and public engagement

Barbara J. Sahakian * 

Department of Psychiatry, University of Cambridge, Cambridge, UK

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ABSTRACT

In this article, I discuss areas where scientists can have impact and that I feel are important for the future of innovative research and societal impacts. Initially, I summarise my research career. I then move on to problem solving, using techniques such as functional neuroimaging and psychopharmacology, and new developments, such as the application of the computerised neuropsychological tests CANTAB, which I co-invented. CANTAB was inspired by the need for early detection, pharmacological treatment and neuropsychological understanding of cognitive deficits in neurodegenerative and neuropsychiatric disorders. Finally, I address neuroethical and societal concerns through books, articles and the media and affected UK government policy through the Foresight Project. In future, young scientists hopefully will contribute more time to these important areas of policy development and public engagement.

1. Introduction

I am delighted to be invited by Professors Lynn DeLisi, Brita Elvevaag, Diane Gooding, Sohee Park and Sibylle Schwab to contribute to the Special Issue of Psychiatry Research, which celebrates the careers and innovative science of women who have contributed to the advancement of our knowledge of psychiatric disorders. I very much hope that by describing the impact of my research and contributions to psychiatry more generally, that this will inspire young scientists to develop a career in this area and to discover new treatments to improve the outcomes of people with mental health disorders. I have purposely discussed a range of areas where I feel scientists can have impact rather than focus solely on my research contributions, as I feel it is important for the future of innovative research and societal impacts.

2. Research career

I am Professor of Clinical Neuropsychology in the Department of Psychiatry at the University of Cambridge. In my career I have led the early detection, pharmacological treatment and neuropsychological understanding of cognitive deficits in neurodegenerative diseases and psychiatric disorders, combining my innovative invention and application of novel computerised neuropsychological tests (CANTAB) with functional neuroimaging and psychopharmacology. I was among the first to test cholinergic therapy in dementia and to evaluate cognitive enhancing effects of stimulant drugs in attention deficit hyperactivity disorder and in healthy humans, work that has advanced theoretical understanding of the neurochemical modulation of cognitive control mechanisms. I have addressed societal concerns through books, many articles and media communications and by helping to found the newly developing field of neuroethics. I have importantly influenced U.K. Government mental health policy through the 2008 Foresight Project on Mental Capital and Wellbeing. I am a past President of the British Association for Psychopharmacology.

My work lies at the intersection of psychopharmacology, neuropsychology and psychiatry. In terms of citation impact, according to one survey, I have the highest h-index among women psychologists or neuroscientists in the U.K. (4th in the world for women in neuroscience and 67th overall) (https://research.com/scientists-rankings/neuroscience;https://research.com/scientists-rankings/psychology).

Underpinning my research, I am a co-inventor of the CANTAB (Cambridge Neuropsychological Test Automated Battery), one of the first to be implemented via a computer and with touch-screen methodology and now used in over 800 universities, institutes and hospitals in over 80 countries worldwide (www.camcog.com). The development of CANTAB was especially important due to the necessity for neuropsychological tests of frontal lobe function and to the lack of tests of early detection of Alzheimer’s disease. In addition, these CANTAB tests were

* Corresponding author.
E-mail address: bjs1001@cam.ac.uk.

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particularly needed to assess the efficacy of novel pharmacological treatments. Adapting these tests for neuroimaging allowed for a better understanding of the neural mechanisms that underlie the cognitive processes in both healthy people and patient groups.

3. Pharmacological treatment of dementia and other neuropsychiatric disorders

I was one of the first researchers to suggest that attentional dysfunction in Alzheimer’s disease (AD) could be ameliorated using pharmacotherapy, such as cholinesterase inhibitors. My earlier observations indicated that these drugs would enhance signal-to-noise ratio in the forebrain cholinergic system which modulates attention (Sahakian et al., 1993). Our randomised, double-blind, placebo-controlled trial for cholinesterase inhibitors as a treatment for cognitive problems in mild to moderate Alzheimer’s disease was published in The Lancet (Eagger et al., 1991). Cholinesterase inhibitors (eg. Aricept, Donepezil) are now widely used and approved by National Institute for Health and Care Excellence (NICE) as a treatment for AD and their use is on the increase. I have also led with proof-of-concept studies for enhancing attention and information processing in patients with AD through stimulation of cortical nicotinic receptors (Sahakian et al., 1989). These studies have led to novel drug development programmes within the pharmaceutical industry, which used this study as a basis for new treatment for cognitive and behavioural symptoms in AD.

I have also investigated the neurochemical modulation of impulsive and compulsive behaviour in neuropsychiatric disorders, including attention deficit hyperactivity disorder (ADHD) (Piroatti et al., 2014; Shen et al., 2020) and obsessive-compulsive disorder (OCD) (Chamberlain et al., 2008). My recent articles on ADHD (del Campo et al., 2013; Pironti et al., 2014; Shen et al., 2020) have implications for determining the underlying neural mechanisms involved, and also clarifying the action of the drug methylphenidate (Ritalin) on cognition. In a series of papers, my PhD students and I were able to discover that a neural circuit including the right inferior frontal gyrus was responsible for response inhibition (Aron et al., 2003). My recent studies have questioned the previously accepted view that major abnormalities in dopamine function are the major cause of ADHD (del Campo et al., 2013; Pironti et al., 2015; Shen et al., 2020). These findings indicated that the main cause of the disorder may instead be associated with structural differences in grey matter in the brain.

In the course of conducting my research on ‘cognitive enhancing’ drugs, my students and I found that they not only improved cognition in people with neuropsychiatric disorders, but also in healthy volunteers (Turner et al., 2003; Chamberlain et al., 2006), relevant to the use of such drugs as methylphenidate and modafinil by healthy people (Sahakian et al., 2015).

4. Early detection of Alzheimer’s disease with neuropsychological measures

Based on theoretical and experimental neuroscience and neuropsychological findings, including the site of early neupathological changes and the functional role of the hippocampal formation, I was one of the first to show that new learning and memory for the location of objects in space is affected at the earliest stages of AD. I published a seminal first-authored paper in Brain in 1988, demonstrating the sensitivity of a paired associates learning test (CANTAB PAL) to AD (Sahakian et al., 1988). This paper contrasted the marked deficits seen in visuospatial learning and memory in patients with mild AD, with the relative sparing of these processes in patients with Parkinson’s disease. CANTAB PAL is now used in what the MRC-UKRI have termed ‘the world’s most in depth study to detect early signs of Alzheimer’s Disease’ (Koychev et al., 2019). CANTAB PAL is now also used on the Eisai and Biogen website to aid with screening of patients with mild cognitive impairment (MCI). In terms of translation from the laboratory into the clinic, CANTAB PAL now also runs on iPads as CANTAB mobile for use in the clinic for the early detection of amnestic MCI in the elderly. In a 2011 study (de Rover et al., 2011), my colleagues and I demonstrated that during the PAL task, the hippocampi of MCI patients were activated significantly more than controls at lower levels of difficulty during the test, and significantly less at higher levels of difficulty, thus providing neural validation for the CANTAB PAL test in the early detection of AD. I was an early proponent of the importance of early detection of AD in order to improve functional outcome and quality of life by pharmacological symptomatic treatments through training/compensatory techniques and through advanced planning of life goals and financial and clinical management. I also suggested that early detection of amnestic MCI was important because of the ongoing development of neuroprotective agents that will halt the disease process, such as the FDA approved aducanumab.

5. Understanding core cognitive changes in depression

Depression is frequently a chronic, relapsing condition which is responsible for an enormous personal cost to patients and their families, but also a financial cost to the government due to the fact that depression is very common and many days of work are lost. Innovative research by me has demonstrated that there are cognitive impairments in depression which may in a proportion of people still remain following treatment and symptom improvement. Some of these impairments are ‘cold’ or non-emotional such as planning and problem solving, and others are ‘hot’ and involve risky decision-making or tasks in which there is a conflict between reward or gain and punishment or loss (Elliot et al., 1996; Elliot et al., 1997; Roiser et al., 2012). My research has focused on what I regard as the essence of the neurocognitive problem in depression: an attentional bias to negative stimuli in the environment and an abnormal response to negative feedback (Murphy et al., 1999). Using fMRI, colleagues and I demonstrated the neural correlates of these psychological processes. Significantly, for emotional regulation under stressful circumstances, such as negative feedback, healthy, never depressed individuals exert top down control by prefrontal cortex over the amygdala, which is deactivated (Taylor Tavares et al., 2008). Crucially, depressed individuals are unable to do so. This work on cognition, depression and implications for treatment has been highlighted in invited reviews (Clark et al., 2009; Roiser et al., 2012).

6. Policy and public engagement

I have been involved in a number of policy publications, which have influenced Government policy on public health. I have also been very active in engaging the public in neuroscience its importance for mental health. I was a lead on the UK Government Foresight Project on Mental Capital and Wellbeing (Beddington et al., 2008), which has had an enormous impact in government policy including ‘Research Changes Lives’: Medical Research Council Strategic Plan 2009-2014. Furthermore, in terms of national and global impact, the concepts advanced, including wellbeing and resilience, have been incorporated into many aspects of Government policy and public health. In addition, I was a co-author and member of the Scientific Advisory Board on the Grand Challenges in Global Mental Health (Collins et al., 2011). I was a speaker on cognitive enhancement and mental wellbeing at the World Economic Forum (WEF) 2014 in Davos, and was later appointed on two committees for the WEF (Global Agenda Council on Brain Research and Future of Neurotechnologies and Brain Science). I was on the Planning Committee for enabling discovery, development, and translation of treatments for cognitive dysfunction in depression for The National Academies of Sciences, Engineering, and Medicine Forum on Neuroscience and Nervous System Disorders (USA). Recently, I have been an expert witness for the Science and Technology Committee at the House of Lords on the topic of Ageing: Science, Technology and Healthy Living (2020) and the academic representative on the NICE Committee for
guidelines on harmful gambling (2022-).

My scientific work has been pioneering in the development of the field of neuroethics and highlighted the importance of the engagement of the public in science. In 2006 I became a founder member in the Executive Committee of the International Neuroethics Society (INS) (http://www.neuroethicsociety.org) funded by the Dana Foundation and was President from 2014 to 2016. I am committed to teaching neuroethics and engagement of the public in science to young neuro-scientists, and have advocated this through my publications, including the Oxford Handbook of Neuroethics (Illes and Sahakian, 2011), the popular science books Bad Moves: How decision making goes wrong and the ethics of smart drugs (Sahakian and LaBuzetta, 2013) and Sex, Lies, & Brain Scans. How fMRI reveals what really goes on in our minds (Sahakian and Gottwald, 2016). Both popular books were reviewed positively in Nature and Sex, Lies & Brain Scans received the British Psychological Society Popular Science Book Award. I contributed to the Royal Society 'Brain Waves' project. I have also participated in many public science festivals, radio, TV, newspapers and magazine interviews, including a BBC 1 documentary (2021), BBC Two Newnight and regular interviews on the BBC Radio 4 Today Programme. According to Meltwater (the University of Cambridge’s media monitoring service), ‘Barbara Sahakian’ was mentioned in 4053 media articles and blogs between January - July 2022. I have also published several articles in The Conversation, a media outlet for the public with evidenced-based articles, reaching over 4 million readers.

My scientific and related achievements have been recognised thus far by my Fellowship of the Academy of Medical Sciences (2004), The British Academy (2017) and the Lifetime Achievement Award of the British Association for Psychopharmacology (2021). Finally, I am very grateful to my many outstanding collaborators, postdoctoral researchers and PhD students, who have contributed to this research. I hope that this article will encourage many young scientists to pursue careers on these research topics and in these different areas of endeavour. Hopefully, this will lead to answering some of the challenging questions in neuroscience and to a better quality of life and improved wellbeing for those with mental health disorders.

Declaration of Competing Interest

I have consulted for Cambridge Cognition.

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