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Themed Section: Imaging – the Interface with Pharmacology

EDITORIAL

Imaging – the interface with pharmacology: looking to the future

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Linked Articles
This article is part of a themed section on Imaging. To view the other articles in this section visit http://dx.doi.org/10.1111/bph.2011.163.issue-8 *BJP* has previously published an *Imaging in Pharmacology* themed section, edited by A Davenport and C Daly. To view this section visit http://dx.doi.org/10.1111/bph.2010.159.issue-4

Basic research is constantly adopting novel, innovative and powerful approaches to enable a deeper interrogation of the specific subject matter. A clear example of this strategy is the development of multiple imaging modalities, both *in vitro* and *in vivo* based, that have revolutionized medical research, drug discovery, diagnosis and clinical monitoring. In this themed section of the *British Journal of Pharmacology*, we highlight a number of imaging platforms which are discussed in relation to their applicability for pharmacological experiments, including longitudinal studies. As such, the authors endeavour to describe the technology, its limitations and how these approaches can complement pharmacological research. In addition, there is discussion of the role of pharmacological imaging from a clinical perspective.

Since the development of the light microscope in the 17th century, imaging has become an increasingly important tool in both medical research and clinical practice. This strategy took a leap forward around the turn of the 20th century, following Roentgen's discovery of X-rays (1895) and their applicability to diagnostic imaging. Since then, a wide array of approaches to image at the macroscopic, cellular and subcellular level have effectively revolutionized both medical practice and basic research. Examples include the advent of nuclear medicine, ultrasound and tomography through to 2-photon imaging and optogenetic approaches of the modern era.

Our intention is not to provide a history of medical imaging, we will focus more squarely upon some recent advances in imaging approaches from a pharmacological perspective. This is not, and not intended to be, an exhaustive review of all forms of imaging, but rather a collection of divergent examples of how imaging and pharmacology can synergize and facilitate both basic research and clinical monitoring/drug development. From a clinical perspective, Rohini Sharma and Eric Aboagye discuss 'Development of Radiotracers for Oncology – the interface with Pharmacology'. In this article, they concentrate on positron emission tomography (PET) ligands used in cancer, including their use in clinical trials and pharmacokinetics/dynamics. In addition, they also discuss some of the issues surrounding the development and synthesis of new radiotracers (Sharma and Aboagye, 2011). Another article that concentrates on PET imaging is that by Paul Cumming and colleagues which details the use of micro-PET for longitudinal imaging studies in rodents. This powerful approach enables correlation of alterations in brain chemistry with complex behaviour patterns. In this context, the authors have used micro-PET imaging to provide insights enabling further elucidation of neuropharmacological mechanisms underlying drug addiction (Cumming *et al.*, 2011).

In the context of synaptic plasticity, a pair of reviews shed light on *in vivo* calcium imaging (Russell, 2011) and signal transduction in dendritic spines undergoing structural plasticity (Patterson and Yasuda, 2011). The former article describes the development and use of a range of calcium sensors in conjunction with high-resolution imaging modalities, such as 2-photon microscopy. In addition, this review also looks ahead to the prospects of imaging in awake behaving animals, an area of research that while established, will no doubt push the boundaries further in due course. The article by Patterson and Yasuda includes a description of the elegant approach, whereby fluorescence lifetime imaging microscopy has allowed imaging of signal transduction in single dendritic spines to be realized. Clearly, such knowledge is of fundamental importance to our understanding of brain function.

In summary, this themed section should provide a useful resource to those who already do, or wish to, utilize imaging modalities to complement and enhance pharmacological research. Admittedly, given the nature of technological advancement, new approaches will continue to appear and evolve. It is up to the research community to engage these techniques in the pursuit of knowledge.

Another recent themed section on Imaging in Pharmacology covered a further broad spectrum of pharmacological studies, from whole animal imaging to gene expression, emphasizing the importance of imaging techniques in pharmacology (http://onlinelibrary.wiley.com/doi/10.1111/bph.2010.159.issue-4/issuetoc; Davenport & Daly, 2010).

Rose (2010) reviews the emerging technique of bimolecular fluorescence complementation to GPCR signalling particularly measuring interactions with G-proteins and β-arrestin. Finch *et al*. (2010) review the application of semi-automated imaging to interrogate compartmentalization and trafficking of 7TM receptors.

The use of fluorescent labelled ligands in receptor pharmacology to allow visualization and quantification of receptors in a single cell is covered in relation to the adenosine A_1 as a GPCR target by Baker *et al*. (2010), while Daly *et al*. (2010) have exploited the increase in spatial precision that can be achieved by using confocal imaging with fluorescent labelled ligands to visualize receptors binding four dissimilar fluorescent ligands (α_1-adrenoceptors, β-adrenoceptors, angiotensin II and cannabinoid receptors) in arteries (see also Methven *et al*., 2009a,b). Fluorescence imaging is not limited to visualizing receptors but has the potential to quantify the uptake of transmitters: Parker *et al*. (2010) demonstrate the use confocal microscopy to visualize the accumulation of substrates of the norepinephrine transporter NET.

A major challenge in imaging is to translate results from florescent probes *in vitro* to *in vivo*. Ortolano *et al*. (2010) image fluorescent labelled lymphocytes in an animal model of stroke and Johnström *et al*. (2010) report the use of PET to dynamically image receptors *in vivo* within target organs, utilising the conversion of the inactive precursor of endothelin-1 to the active form. Finally, anticipating the new era of regenerative medicine, Baril *et al*. (2010) review strategies for non-invasive imaging of gene therapy, to allow the precise spatiotemporal measurement of gene expression particularly in longitudinal studies involving gene transfer vectors.

British Journal of Pharmacology welcomes manuscripts employing imaging technologies to study pharmacological processes and is developing ways to support authors, such as online supplementary data that can be in movie or 3D display formats. Note that colour in figures is completely free of cost to the author.

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