James was a long-standing member of the Physiological Society and an innovative ‘hands-on’ neurophysiologist.

I first met James in 1968 when he joined our lab in the Department of Pharmacology at St Barts Hospital Medical College as a “research technician” (in practice much more than that) while studying for a B,Sc. in Psychology at Birkbeck College. (Prior to that he had started his research career as a technician in the Poisons Reference Centre at Guy’s.) Among his contemporaries at Barts were Norman Bowery, Norman Scholfield and Paul Adams (all PhD students), and Mike Brownstein (a visiting postgraduate student from the University of Chicago undertaking an elective). With these colleagues James established a close scientific and social rapport (including, among other activities, creating an ad hoc in-house jazz band using self-assembled ‘instruments’) and thereafter maintained a lifelong friendship.

After finishing his B.Sc. at Birkbeck (and inter alia co-authoring three papers from Barts, including one in Nature, refs1–3), he went on to do a Ph.D. in the Physiology Department at University College London (UCL) under the supervision of Ivor Gartside. His thesis comprised an anatomical and electrophysiological dissection of the circuitry underlying the extracellular potentials in slices of the guinea-pig olfactory cortex that are evoked by lateral olfactory tract stimulation – at the time when James started (in 1971) still a relatively little-used preparation. Characteristically, his thesis was elegantly written and beautifully illustrated, but – also characteristically – somewhat delayed in its production.

Following a postdoc with Channi Kumar at the Institute of Psychiatry (1974–8) looking at animal models of morphine addiction (ref.4), James re-joined us, now in an MRC Group in the Department of Pharmacology at the School of Pharmacy. His contemporaries there included Reg Docherty, Trevor Smart, Andy Constanti, Neil Marrion, Charles Bourque, John and Giti Garthwaite, Malcolm Caulfield and Sasha Selyanko (now unfortunately also deceased). He migrated transiently back to UCL with some members of the same group in 1987, but very soon was appointed to a Readership in Physiology at the Royal Free Hospital School of Medicine. However, by default, James rejoined UCL (at least nominally) when UCL and RFHMS merged in 1998, and more intimately in terms of laboratory location after he retired in 2003 – an event accompanied by the translocation of a near-lifetime’s accumulation of highly-personalized equipment. Indeed, James was still doing occasional experiments
on that equipment, and also at the School of Pharmacy in a renewed collaboration with Andy Constanti on his favourite part of the brain (the olfactory tubercle), when he met his untimely death in March of this year.

During his research career, James completed many trail-blazing studies on a variety of neurophysiological topics. Perhaps his most important and influential work was that he completed during a short sabbatical with Paul Adams in Galveston, Texas, which they described in their very highly cited 1982 paper (ref.5; 894 citations). This contained two “firsts” – the first identification of the M-current in a mammalian central neuron, and the first detection of a hyperpolarization-activated cation current in any neuron. This latter current Halliwell & Adams termed the ‘queer current’, \( I_q \), by analogy with the just-described cardiac ‘funny’ current, \( I_f \) (both now designated \( I_h \)). The difficulties in doing this work at that time (before slice patch-clamping) cannot be over-estimated since, in addition to near-perfect ‘sharp’ microelectrode impalement, James and Paul had to contend with the vagaries and limitations of the temperamental Dagan switch-clamp amplifier. Indeed, a read-through of their “Methods” section (which includes the use of a nylon mesh from a Safeway tea-strainer to mount the slice) is an instructive exercise for the modern electrophysiologist, and, coupled with Paul’s deep knowledge of voltage-clamp methodology, gives an excellent indication of James’ skill and patience. James subsequently used these same skills to provide the first evidence for M-currents in human cortex (ref.6). This resulted from an introduction to David Bowen at the Institute of Neurology by Malcolm Caulfield (then at Glaxo), and involved James hopping across from the School of Pharmacy to the Institute at short notice with a bucket of iced Krebs’ solution to catch the neurosurgeon’s discards.

Also of substantial long-term significance were the experiments James did with Reg Docherty on transmission in the interpeduncular nucleus (IPN; ref.7). They were looking for a convenient cholinergic tract in the c.n.s. to do the sort of experiments on cholinergic transmission one could do in the peripheral nervous system when Mike Brownstein (on a lab visit from NIH) pointed out that the habenulo-interpeduncular tract (HIT) – or fasciculus retroflexus of Meynert (FRM) – was the richest choline acetyltransferase-containing tract in the brain. However, to our collective surprise it turned out that direct transmission was glutamatergic, not cholinergic, even though the IPN neurons themselves could be readily excited by nicotinic agonists; instead, the principal effect of acetylcholine was on the presynaptic fibres in the HIT/FRM (ref.8). Both of these conclusions have been amply confirmed in other labs (e.g., McGehee et al., 1995: Science, 269, 1692-1696) and only very recently has a slow postsynaptic nicotinic current been detected after repetitive HIT stimulation (Ren et al., 2011: Neuron, 69, 449-452). The habenular-interpeduncular system is now known to play a crucial role in regulating nicotine intake during nicotine addiction (Fowler et al., 2011: Nature, 471, 597-601) – in a curious way recapturing James’ earlier interest in drug addiction.

There are many other instances of James’ pioneering activities. Thus, in collaboration with Oliver Dolly at Imperial College, James identified the transient potassium ‘A-current’ as a target for the neurotoxin \( \alpha \)-dendrotoxin (ref.9). This provided the crucial information necessary for Oliver’s subsequent use of \( \alpha \)-dendrotoxin to purify Kv channel proteins and to show that the mature channel is an oligomer of \( \alpha \) and \( \beta \)-subunits (see, e.g., Dolly et al., 1994: Biochem Soc Trans. 22, 473-8). Another example was his fine work with Asun Colino (then visiting from Salamanca) in which they dissected the multiple actions of 5-hydroxytryptamine on hippocampal neurons (ref.10). This paper greatly clarified the different excitatory and inhibitory effects of 5-HT, and has been much-cited in consequence.

James continued to maintain this ‘Spanish connection’, both through subsequent publications with Professor Colino (e.g., refs.11, 12) and through his work with Laura Chavez-Noriega (then a Ph.D. student from Mexico with Tim Bliss at the National Institute for Medical Research), in which they uncovered the postsynaptic excitability changes accompanying LTP (ref.13). A spiritual connection with Spain might also be discerned in James’ interesting work with Tony Horne on the tiny granule cells in the islets of Calleja, a transmitter-rich structure in the olfactory tubercle which had been largely ignored by electrophysiologists. In their first paper (ref. 14) they showed that the neurons exhibited spontaneous action potential activity \textit{in vitro} and got some
good voltage-clamp recordings of some of their membrane currents. In the second paper (ref.15) they reported the occurrence of unusual stepwise increments in membrane conductance of 100 pS or more, which were amplified to cataclysmic proportions by dopamine through an action on D₃ receptors; this they attributed to the presence of gap junctions (connexins) between the neurons whose activity was enhanced by dopamine – the converse of the dopamine D₁ uncoupling of amacrine cell gap junctions in the retina.

This is very much a personal selection of James’ achievements: for example, it omits work on β-bungarotoxin with Oliver Dolly, on 4-AP with Catherine Stansfeld, on the piriform cortex with Andy Constanti, and on THA with Elizabeth Grove; and also his well-cited reviews on hippocampal neuron currents in *Progr. Brain Res* in 1990. James’ last published paper was as recent as 2010 (ref.16), and there is still much material awaiting publication.

James was the epitome of the well-rounded scientist. He was a delightful person to have around in a lab or Department, totally unselfish, always willing to help and advise his colleagues (both junior and not-so-junior) - indeed, he was as much interested in their research as in his own (a somewhat rare attribute nowadays). He also had wide interests outside the lab, with a refined taste for food and its preparation, for wine and for coffee, a love of things French and Spanish, and special passions for old motorcycles and for jazz. His untimely death not only robbed us all of an innovative experimentalist, but also deprived him and his wife Sheila of the opportunity for fully enjoying these fruits of a good life.

**Professor David Brown,**

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References

*Authors in alphabetical order (journal format)*


Comments by some of his associates and friends

A personal reflection by Trevor Smart, James' last Head of Department:

I shared part of a lab with James' during my PhD at the School of Pharmacy and there are several happy memories of those days. James was a great repository of endless, useful and sometimes useless information. He was exceedingly generous with his time in helping others, and was the first port of call concerning questions relating to brain anatomy and mechanical engineering. Indeed, scattered around the lab in a manner resembling a breaker's yard, James would fashion something very useful out of parts most of us would have long since consigned to the bin. His engineering ingenuity knew no bounds and his productions were always manufactured to the highest standards of craftsmanship. He took this precision and dedication into his research and always had invaluable advice to offer. His projects were always interesting and one thing I noted was his complete disregard for time and deadlines, and his strong sense of loyalty to others. This manifest in many ways: the one I remember most was his desire to bring in a portable cooker to make pancakes for all in the lab on Shrove Tuesday, whilst attired with a French Berry hat and hooped jumper and red scarf. My last discussion with him was about his motorcycles and he had just hand painted his front mudguard (one of many Ariel bikes) using acrylic paint and a paintbrush. No mean feat, and of course, there were no brush marks – I still don't know how he achieved that – but that was James! He is of course sorely missed: not many can mix culinary and engineering skills - it is unusual, and as such he represented a diminishing breed in present-day science, that of the multi-talented 'character'.

Professor T.G.Smart,
Department of Neuroscience, Physiology and Pharmacology,
University College London,
London, WC1E 6BT

From Norman Scholfield, a lab colleague of James' at St. Barts Hospital Medical School, and afterwards at the School of Pharmacy:

James Vincent Halliwell (Vince to many)

I worked with James in David Brown's laboratory at St Bartholomew's, at the School of Pharmacy, London, in my lab in Belfast, and got to know him as a close friend. James had a deep scientific intellect which has been eloquently detailed by David Brown. To describe James as a 'hands on scientist' very much under-describes his skills in these days of out-of-box equipment and kits for everything. Physiology, more than any other discipline, has been founded upon developing contrivances in pursuit of fundamental knowledge. Unfortunately, such people are a dying breed and replaced by the office bound scientist. James had perseverance – one project on intracellular recording from two neurones simultaneously in the same brain slice yielded a success about once a month. This requires real dedication and in the age of RAE and REFs, would never keep the paymasters happy. His attention to detail is also reflected in his dedication, deep understanding and the appreciation of the beauty in machines, including motorbikes produced in the heyday of the British engineering industry. Sadly, there remain some of his fine machines still awaiting restoration. James was very much from the 'Monty Python' era and this was very much reflected in his humour such as the Sow's Ear Laboratory of Pharmacology. He will be sorely missed by us all, especially Sheila and members of his extended 'family' (the Team).

C. Norman Scholfield,
Naresuan University, Thailand (late of Queens University Belfast).
From Ivor Gartside, his Ph.D. supervisor at UCL:

James was the kind of PhD student that you probably do not see anymore. He came with his own problem, built his own (beautiful) baths etc, and virtually supervised himself. He was a delight to have in the Lab, although I was a morning person and James was most certainly not. He was fun to have around and I probably learned as much from him as he did from me.

From Jeffrey Noebels, a fellow student at University College in the 70s (currently in the Department of Neurology at Baylor):

James friendship meant a great deal to me – one of his other “firsts” was to take a naïve psychologist under his wing as a lab partner in the UCL physiology class in 1971 and allow me to assist him with some early brain slices ...a front row seat that changed my life! (I am attaching the evidence – though we have since both cleaned up our act!). It began with the prepyriform cortex, shifted later to the hippocampus, and although the last time I visited his lab he was surrounded by wonderful imagery of seahorses, he had moved on .... to the “Isles of Calleja”! That was James. If one adjective could best describe James it would be “joyful” - be it the wonder of discovery, the joy of teaching, or of the life that he shared with those around him.

Jeffrey L. Noebels, M.D.,Ph.D.
Professor of Neurology, Neuroscience, and Molecular and Human Genetics
Department of Neurology, Baylor College of Medicine
Houston, Texas 77030.
From Reg Docherty, a collaborator with James at the School of Pharmacy, and currently at Kings College London:

James’ direct contributions to science are impressive enough. But his indirect contributions were also impressive. Personally, I learned more from him than from any other person before or since, and many scientists more accomplished than I will continue to spread his influence far and wide. He was not a scientist in the entrepreneurial mould - he simply found pleasure in knowledge and discovery and that was enough for him. Shortly before he died, discussing the ills of society more generally (with no beer involved on this particular occasion), he said to me, "...people have forgotten the meaning of 'enough' ". His own material generosity, his generosity of spirit, and his complete lack of guile were amongst his most admirable traits. He was a gifted scientist and an outstanding human being.

Dr. R.J.Docherty,
Wolfson CARD, School of Biomedical Sciences,
King’s College London,
London, SE1 9RT.
From Asun Colino, a visiting research collaborator with James at the School of Pharmacy:

James was my mentor, my scientific master, but most important, he was my friend during the last 25 years. My most special memories come from 1986. At that time, he introduced me to many electrophysiological techniques, such as how to record intracellular neurons, to get good recordable slices, to do current- and voltage-clamp techniques. That learning in his lab was really enjoyable for both of us through all the different steps: recording cells, at lunch time, checking our results. I will never in my life forget my stay at the School of Pharmacy. His lab was somehow magical, and he was the wizard who ruled it.

From Charles Bourque, a colleague of James’ at the School of Pharmacy and currently at McGill University:

I was very fortunate to work with James Halliwell while I was a Postdoc in Prof. David Brown's Laboratory at the School of Pharmacy (December 1984 to July 1987). James and I each occupied one of two small electrophysiology rooms that opened onto a shared alcove that served as James' office and coffee station. This was a hub for animated discussions that took place around a well-worn chalk board. Countless hours were spent there discussing biophysics, food, travel, beer, languages, philosophy and the Hitchhiker's Guide to the Galaxy. Many other formidable colleagues and friends were associated with David's MRC group at that time (some in the photo below) and I learned a great deal about science from all of them. But it was the close interactions I held with James that had the strongest influence on how I now do science and live my life. Unfortunately our paths rarely crossed after my departure in the summer of 1987. But we remained spiritual friends, as noted below.

One incident illustrates. After receiving what I felt were harsh reviews from The Journal of Physiology on a paper I submitted in 1986, I drew a sketch showing a dartboard labelled "Editorial Decisions at The Journal of Physiology". The drawing indicated that missing the board resulted in immediate rejection and that hitting a particularly tiny central bull's-eye was the only way to receive acceptance. The sketch showed also that hitting any of the board's non-bulls-eye area rendered a decision to "reject but allow re-consideration after extensive revisions with many new additional experiments". This sketch was immediately pinned to the wall next to the chalkboard. Shortly after becoming an Editor for The Journal in 2000, I received a letter from James. The
envelope contained my original 14 year-old drawing, along with a note saying "I'm sure you now need this more than I do"! James was my friend and he is sorely missed.

James, Reg Docherty, Charles Bourque and Neil Marrion

Charles W. Bourque, Ph.D., James McGill Professor
Centre for Research in Neuroscience,
L7-216, Division of Neurology,
McGill University and Montreal General Hospital,
Montreal, QC
Canada H3G 1A4.
From Brian Robertson, an old scientific friend and sometime Professor of Neuroscience at Leeds University:

I count myself fortunate indeed to have known James for a number of years, but first got a glimpse of this lovely man through his classic 1982 *Brain Research* paper with Paul Adams. I started my PhD in 1983 doing single electrode voltage clamp on GABAergic synaptic events in hippocampal neurones, so Halliwell and Adams was a key methods paper - about the only paper really. In those days students had to pay for photocopying so you had to make tough decisions on what to read and make notes on and what to keep handy; this was a keeper. By today's standards it was both massive and comprehensive. (You try finding a Safeway tea strainer in Sydney and explaining why.) The story I'd heard was that James and Paul Adams had first submitted the Ms. to the *Journal of Physiology*, but one referee didn't like whole idea of single electrode voltage clamp, so it came out instead in *Brain Research* (note to JP Editors: around nine hundred citations). One of the many things I loved about this great paper was at the very beginning of the *Discussion*.

"Possible criticisms. It must frankly be acknowledged that voltage clamping an extended neurone with a single high resistance microelectrode is, at best, an unsanitary arrangement."

*Unsanitary* - how wonderful. Not many papers these days have such honesty; this is right up there with Hodgkin & Huxley's 'decrepit axons' and Katz & Miledi's admission that they came across the results in this present paper whilst looking for something completely different. Most publications today are too sanitised and enervated, and their methods sections have no room for crucial top tips or pointing out pitfalls. But, as David Brown points out, James was a consummate experimentalist. He was always more than happy to share his considerable knowledge and experience.

After my PhD (summer '86) I got to know James, then at the School of Pharmacy, whilst visiting a close friend from undergraduate days for lunch or a pint. The School struck me as such a fun and exciting place to work - such wonderful characters, such great work. Illicit lunch on the roof there, enjoying the numerous summertime views over the park at Brunswick Square; the fantastic Lamb pub in Lambs Conduit Street. James was always incredibly warm, friendly and generous; one couldn't help smiling involuntarily when you met him. I'd be greeted with a rolling 'r' Dr Cameron-ish burr (see Dr. Finlay's Casebook) 'Doctorrrrr Rrrroberrrtson..........!' Despite several pints of Young's beer James could offer very wise advice on so many subjects, work, life - he seemed to know so much and about so many different things. Others have commented on James' absolute unselfishness and generosity. He didn't see science as a competition with jealously guarded secrets. He saw research as it should be, as a shared endeavour for the common good but also, and perhaps most importantly, fun too. The pure fun of finding things out. He readily shared his cleverness, his enthusiasms. Incidentally, Brunswick Square seemed to make several people like that, some of them sadly no longer with us. I sometimes think the mould was broken after that time.

I've got James to thank too for getting me my first job in Academia. Oliver Dolly at Imperial College was looking for a tame electrophysiologist to continue the potassium channel/snake toxin work that he'd begun with James. Behind the scenes James must have very kindly mentioned me, for I got a cold call one day whilst in Industry. (No committees or interview panels or sample lectures then, it was a quick chat with the Head of Department and you were in. Nowadays university HR would have a screaming fit.) Thanks to James' good offices I got the lectureship and I subsequently also got a great deal of good advice from James. He was wise to the ways of the world. Here was a man who always seemed to have time for you - nothing was ever any bother. Happily James could also tell you where the best pubs were *anywhere*; he pointed out to me a nice
wee one down the road from where I then lived - I had no idea it was even there. Truly encyclopaedic knowledge....

At James' very moving funeral service several of us had exactly the same thought. We'd never heard anyone, ever, say a single nasty, or even mildly critical thing about James. This is rare indeed in a game that arouses so many petty jealousies and rivalries. I've used the term 'Nature's gentleman' before to describe one of James' former colleagues - he was the same - a very *gentle* gentleman.

Almost five hundred years ago Montaigne, after taking early retirement himself, wrote 'The value of life lies not in the length of days but in the use you make of them'. By any measure, James did a hell of a lot and gave back to us all more than his share. The sad thing is that like Montaigne, he should have had that long and active retirement, not in a tower filled with old books but in a garage, pottering about with ancient motorbikes and pursuing his diverse interests and enjoying himself: unfortunately, he didn't. He made our lives better and richer though, that's for sure.

Sheila and James Halliwell in sunnier times (2006)