Taking Science to the Xtremes: a unique PhD experience

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Obtaining a PhD is a long and often rocky road. Now in my final year of doctoral study, I am taking a moment to look back at the successes and (far more frequent) failures of PhD life, particularly my first year experience. This was, quite literally, full of ups and downs as I found myself undertaking research as part of the Xtreme Everest 2 (XE2) expedition team.

Background

XE2 was a research expedition undertaken in 2013 by the Centre of Altitude Space and Extreme Environment Medicine, University College London (http://www.xtreme-everest.co.uk/), to follow up Caudwell Xtreme Everest conducted in 2007. The premise of both expeditions was to investigate human physiological responses to low oxygen (O_2) conditions (hypoxia) through high altitude exposure, where the inspired partial pressure of O_2 is decreased. This research goal aligns with those of my own PhD, which broadly involves investigation into metabolic responses to hypoxic conditions.

View of the Khumbu glacier and Everest (furthest peak) from Kala Patthar (5,643m)

Kathmandu Laboratory team members: (from left) Dr Ronan Astin, Dr Will Jenner, Bradley Jarvis, Dr Grace Gilbert-Kawai, Dr Chris Tomlinson, Dr Andrew Wight, Dr Jo Court, Professor Mike Grocott, Katie O'Brien and Dr Denny Grocott.

O_2 is the stuff of life. Mammals are reliant upon a sufficient supply of O_2 to maintain energetic and redox homeostasis. Conditions where O_2 supply is limited, termed hypoxia, present a significant physiological challenge and in severe cases may be fatal. Hypoxia is also a state prevalent in a range of disease conditions where O_2 delivery to the tissues is impaired, making our understanding of hypoxic adaptation highly clinically relevant.

Despite its importance in human physiology, the pathways involved in acclimatisation to hypoxia remain unclear and are particularly difficult to study in pathological states given the plethora of confounding factors and complications present in patients. The Xtreme Everest studies offer an alternative model for exploring hypoxic adaptation through assessment of a large cohort of healthy humans exposed to progressive environmental hypobaric hypoxia during strictly controlled ascent to high altitude. In addition to testing native lowlanders, a fundamental aspect of XE2 was to investigate the responses of the renowned 'Kings of the Mountains', the native ancestral high altitude dwellers (Sherpas). Baseline testing of lowland subjects was undertaken in London prior to the start of the expedition and for Sherpa participants at Kathmandu (1,300m). Data were subsequently collected at Namche Bazaar (3,500m) and Everest base camp (5,300m) on the ascent and Kathmandu on the descent. My role was to work as a scientific investigator in the Kathmandu Laboratory.

Subject testing: a perspective from the Kathmandu Laboratory

'Logistics', a term I was to become all too familiar with during our 3-month testing period. From the outset, XE2 was an incredibly ambitious undertaking: establishing functioning laboratories at each of the test locations was no easy task and required rigorous preparation. At each test centre, a large number of experiments were conducted to gain a detailed characterisation of phenotype. These included: cardiopulmonary exercise testing (CPET), assessment of nitric oxide metabolism, skeletal muscle mitochondrial respirometry and analysis of microvascular blood flow to name a few. To say that each laboratory was

Kathmandu Laboratory team members Katie O'Brien and Dr Ronan Astin processing blood samples

required to be multi-disciplinary is an understatement.

For the Kathmandu lab team, set up began immediately upon arrival to enable testing to commence as soon as possible. This began with testing of Sherpa subjects, which was reliant upon the assistance of Nepali translators, and concluded with the testing of native lowlanders. Each member of the laboratory team had multiple roles in the daily routine. My own included processing of blood, saliva, breath condensate and urine samples, followed by assessment of subjects' forearm microvascular blood flow.

The very nature of field expeditions requires that experiments are undertaken outside of the comfort of a scrupulously controlled environment. Whilst this was taken to the extremes for our Base Camp team (where certain items were placed in the fridge to keep warm in the face of plummeting night time temperatures!), for us, this included negotiating the temperamental Nepali national grid, hot weather and a general limit in available facilities and consumables. The limited 'laboratory' space meant the majority of protocols were performed in the same room. This made for a somewhat unique laboratory environment that was consistently sociable but required highly efficient organisation to avoid falling into chaos. The ability of each team member to adapt and work in a less than optimal environment was tested on a daily basis.

Trekking the Himalayas

Having the greatest mountain range on your doorstep is a way of life for most Nepalis. Thankfully, we were able to take advantage of this in between busy testing periods, squeezing in a jaunt up the Khumbu valley to Everest Base Camp, which gave us the chance to visit the other testing laboratories and gain first-hand experience of the trek our subjects were undertaking.

Having survived the runway landing at Lukla airport (527m in length, positioned precariously at a cliff-edge), the trek ascended through luscious greenery and across suspended bridges onto the XE2 laboratory positioned at Namche. This gradually progressed to the barren landscape surrounding the mountain medical centre at Pheriche and eventually into terrain arguably reminiscent of the moon at Everest Base Camp. It was here that I truly began to feel the strain of the drop in atmospheric pressure. With O_2 saturation readings in the high 70's, tasks that would require a low level of cardiovascular strain at sea level became heavily arduous. For instance, ascending 100m to the summit of Kala Patthar (5,643m) to bask in the glorious and quite literally breath-taking views of the Khumbu icefall left me feeling as though I was winded and suffering from a hangover. Although walking at a snail's pace, my breathing rate was equivalent to an all-out sprint and I was left with a migraine-like headache. Whilst I am no Mo Farah, I do not consider myself unfit, so this response did leave me unnerved and highly envious of our Sherpa guides whom managed the ascent unruffled, with the extra weight of my backpack. It was at this point I gained a full appreciation of the advantages genetic heritage can provide, in particular the superiority of the Sherpa population and their ability to withstand such low O2 conditions with apparent ease and minimal acclimatisation time.

The aftermath

The significance of both Xtreme Everest expeditions in the wider context of hypoxia research is yet to be fully determined as the analysis of the collected data continues. Compared to previous high altitude field studies, they undoubtedly lead the way in their rigorous study design and impressive subject cohort recruited. The ultimate test will be whether findings from this will translate into the significant advancement in our understanding of the pathophysiological effects of hypoxaemia in patients at sea level.

From the viewpoint of a young scientist about to make a leap into the research world, this expedition was an exceptional experience. As I approach the end of my PhD, I can begin to appreciate the incalculable impact it has had. The success of our laboratory work was entirely dependent upon proficient teamwork, which is something that the solo quest for a PhD does not always entail. Along with projects I have been involved with since, it has confirmed my belief that working as a member of a team trumps laboratory solitude. There are clearly instances when the latter cannot be avoided, but science should not be a lonesome struggle. Beyond the laboratory, the sheer scale of the expedition has inspired me to pursue my research interests and ultimately dream big. If you are intrigued by the extremes of physiology, why not take your experiment to that extreme environment?

At a personal level, gaining first-hand experience of being hypoxic allowed me to put the greater picture of my PhD in context. At later stages, when I have been guilty of becoming lost in the intricacies of research, 'unable to see the wood for the trees' as my supervisor so eloquently puts it, this experience has helped put it all into context. O_2 is indeed the stuff of life. ■

I obtained a degree in Physiology from King's College London in 2012 and began my PhD at the Centre of Human and Aerospace Physiological Sciences (CHAPS) the same year under the supervision of Professor Stephen Harridge (CHAPS) and Dr Lindsay Edwards (GlaxoSmithKline). My research aims to identify the metabolic responses to oxygen insufficiency (hypoxia), which is experienced upon ascent to high altitude and in a number of disease states, and the potential for dietary nitrate supplementation to alleviate hypoxic stress. I am funded by King's College London on a Graduate Teaching Assistant scheme.

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