

Part of the conference series  
**Breakthrough science and technologies**  
Transforming our future

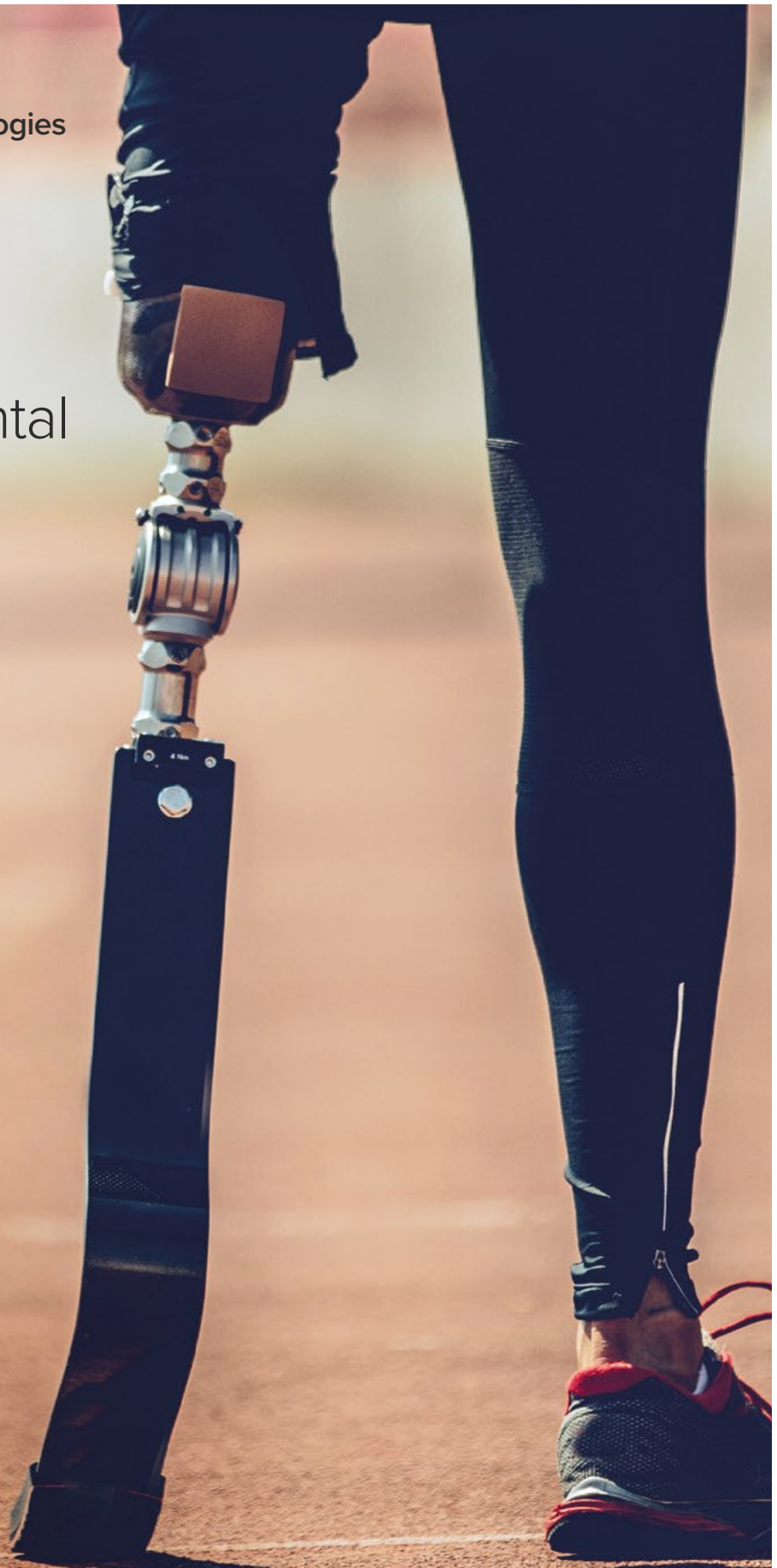
# Trauma recovery: new science and technology for mental and physical health

Held on 4 March 2020

Conference report

THE  
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FOUNDATION



# Introduction

On 4 March 2020, the Royal Society held an international conference in partnership with the Invictus Games Foundation to explore recent innovations in the field of trauma science and recovery. This is an area of vital concern in which new technologies and treatments have the real potential to improve the lives of those affected by trauma in the near future. The meeting brought together leading experts from industry, academia, the military, healthcare and the wider scientific community, as well as those who have experienced trauma.

The programme was shaped by Professor Russell Foster CBE FRS (University of Oxford), Professor Jackie Hunter CBE (BenevolentAI) and Sir Simon Wessely FMedSci (King's College London). The day focused on two broad themes: our increased understanding of the human biology of mental and physical health following trauma, and the application of innovative new technologies and interactions with industry to help individuals adapt to life-changing injuries. At a private reception following the conference, speakers gave interactive demonstrations – from virtual reality environments used to treat mental health disorders to best-in-class prosthetics – to guests including Prince Harry, Duke of Sussex and patron of the Invictus Games Foundation.

This conference is part of a series organised by the Royal Society entitled Breakthrough science and technologies: Transforming our future, which addresses the major scientific and technical challenges of the next decade. Each conference covers key issues including the current state of the UK industry sector, the future direction of research and the wider social and economic implications.

The conference series is organised through the Royal Society's Science and Industry programme which demonstrates the Society's commitment to integrate science and industry across its activities, promote science and its value, build relationships and foster translation.

This report is not a verbatim record, but a summary of the discussions that took place during the day and the key points raised. Comments and recommendations reflect the views and opinions of the speakers and not necessarily those of the Royal Society.



**Image:** Delegates networking at the conference.

# Executive summary

Conference speakers explored a range of developments, from the results of large-scale cohort studies to robotics for rehabilitation and direct neural control of prosthetics.

Key topics included:

- The effects of trauma on mental and physical health;
- Technology to rehabilitate and recover from mental and physical trauma; and
- Critical areas of scientific focus to drive forward innovations.

Key themes:

- Technological and healthcare developments for trauma recovery within the military bring significant benefit to the wider civilian population.
- Recent neural science advances are leading to greater control of prosthetics and freedom for amputees.
- Virtual Reality is an incredibly powerful tool in the treatment of mental health disorders. Greater investment in VR by technology companies has led to accelerated innovation in this space.
- Traumatic Brain Injury and Post-Traumatic Stress Disorder share symptoms and are often misdiagnosed. Greater investment and research are needed to diagnose and treat the conditions correctly and efficiently.
- Sleep is an overlooked and critical factor in the recovery of mental health disorders caused by trauma. New treatments and initiatives can help individuals with visual impairments and patients on acute trauma wards to regulate their sleep and regain emotional and physiological health.
- While there is great momentum and funding to develop new treatments during times of conflict, there is a need to maintain this in times of peace so that we are better placed to help veterans in the future.



**Image:** Dame Sue Ion FREng FRS, Chair of the Royal Society Science, Industry and Translation Committee, welcoming guests to the Royal Society.

This optimistic conference demonstrated examples of where the impact of trauma has been mitigated and blunted. Sectors must work in concert to consider what can be achieved in the short and medium term (periods of years not decades), how to drive these achievements forward and how to prioritise based on the experiences of those who have suffered traumatic injury in order to drive forward change for the better. When combined, science, engineering, motivation, courage and hope have the power to transform lives.

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“While injury and trauma are facts of life, trauma need not be a life sentence. I’m convinced that the impossible is genuinely being transformed tangibly into the possible, and individuals who have suffered mental and physical injury can achieve the almost limitless potential of the human spirit. The Royal Society is committed to promoting science for the benefit of humanity, and in collaboration with the Invictus Games Foundation has truly achieved this today.”

Professor Russell Foster CBE FRS, University of Oxford.

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# Trauma recovery: group studies and personal perspectives

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## **The ADVANCE Study: study rational and preliminary cardiovascular results**

The ADVANCE Study (Armed SerVices Trauma Rehabilitation OutCome) is the first prospective study to investigate the long-term physical and psychosocial outcomes of battlefield casualties related to recent armed conflict in 2002-2014. Professor Christopher Boos, Poole Hospital NHS Foundation Trust, described the study's initial findings.

Historical and retrospective data suggest an association between combat-related traumatic injury and an increased risk of cardiovascular disease (CVD). While American amputees in World War Two displayed increased CVD risk if they had proximal opposed to distal limb amputations, inconsistent results were found from a literature review regarding the link between trauma-induced amputation and CVD. This could be because the study used a control group of healthy civilians, instead of veterans. The ADVANCE Study seeks to rectify this, providing a contemporary study with prospective data and a properly constructed control group.

The ADVANCE cohort study aims to recruit 1,200 adult male UK military service personnel following deployment to Afghanistan between 2002 and 2014. The cohort will be split with 600 individuals who sustained significant combat-related injuries matched to 600 non-injured adults by deployment, age, sex, service, rank and role, with outcomes measured over 20 years. The study seeks to understand the physical and psychosocial outcomes from Afghan-injured service personnel to find the best possible care going forward, including pre-emptive measures to reduce that risk and help people move into society when leaving armed services. The study is nearing the end of recruitment which should be completed within the next six months.



**Image:** Professor Christopher Boos, Poole Hospital NHS Foundation Trust.

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“We hope to use the knowledge gained to help support and plan the best possible care for our injured service personnel, so that if we do identify areas of increased vulnerability, we can take preventative measures to reduce that risk and improve society as a whole.”

Professor Christopher Boos, Poole Hospital NHS Foundation Trust.

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The general hypothesis is that combat-related traumatic injury leads to a high level of co-morbidities, poor long-term quality of life and mental health, as well as poor functional, social and employment outcomes.

A further hypothesis of the study is that combat-related traumatic injury leads to an increased Cardiovascular disease risk. This risk will be measured in the participants by assessment of their blood lipid and high sensitivity CRP (marker of chronic inflammation) levels, body mass index, blood pressure, heart rate variability and arterial stiffness.

### Arterial stiffness

Arterial stiffness is an important independent predictor of adverse cardiovascular events, cardiovascular mortality, all-cause mortality and stroke. Stiffer arteries are less able to buffer the hydrostatic effects of blood leaving the heart and lead to an increase in blood pressure and faster blood flow. Our hypothesis is that lower limb amputation leads to an increased cardiovascular risk profile and earlier reflection of the forward travelling arterial wave from the heart. This earlier wave reflection leads to augmentation and increase in central blood pressure which is a risk factor for stroke and other adverse cardiovascular events.

### Results

Preliminary cardiovascular risk data is presented on the first 845 consecutive participants. In the study, data is compared for the 453 non-injured participants and 392 with combat-related traumatic injury, which consists of 273 with traumatic injury without amputation (TIWA) and 119 with lower limb amputations. Key initial results from amputees include:

- Higher hip and waist circumferences than non-amputees.
- Lowest HDL cholesterol (good cholesterol) in individuals with proximal amputations versus distal amputations and versus TIWA and non-injured service personnel.
- Higher levels of glycated haemoglobin, a marker for diabetes.
- Higher creatinine clearance, indicating that kidneys are working overtime.
- Higher heart rate in amputees than TIWA and non-injured groups.
- Lower subendocardial viability ratio (SEVR) – an indirect marker of coronary blood flow in amputees.
- Higher HsCRP levels (a marker of chronic systemic inflammation and a known Cardiovascular risk) among amputees.

This is the first study to identify increased biomarkers of subclinical CVD risk among amputees with recent combat related traumatic injury. There are consistent early signals among amputees versus non-injured service personnel, including greater visceral fat, greater relative vascular inflammation, lower HDL cholesterol and lower SEVR. No change is observed in arterial stiffness or blood pressure at this stage, but the above changes precede potential future changes in arterial stiffness. The reason for these differences could include more sedentary lifestyle, greater occurrence of post-traumatic stress disorder (PTSD), or testosterone deficiency in amputees. The observed cardiometabolic changes feed into haemodynamic changes, which in turn lead to disease such as stroke and heart attack.

## The principles of (recovering from) war

Recovering from the realities of traumatic injury is a long, complicated and often painful process. However, just as warfare has been optimised, so should recovery. Afghanistan veteran and scientist Dave Henson MBE, Imperial College London, offered his personal perspective of recovering from war.

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“Everything is long-term: there is no recovered, it’s all recovery. We need to ensure that the resources available to those who need recovery are sustainable and long-term.”

Dave Henson MBE.

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Henson’s training in science and the military has been essential in guiding his recovery. Following an undergraduate degree in mechanical engineering with a year in the army and a dissertation in adaptive supports for disabled veterans, Henson joined a commissioning course in Sandhurst and subsequently the Royal Engineers, fulfilling his teenage dream of being in the army. As an upsurge troop in Afghanistan, Henson complemented the UK’s counter-IED taskforce: improvised explosive devices (IEDs) had been the leading cause of injury for all troops in Afghanistan. Unfortunately, while clearing a compound of IEDs Henson stood on a device disguised by recent rain, requiring a bilateral amputation of his legs.

### Recovery through sport

The recovery pathway can and should be optimised, and there is a role for new technologies and treatments within this process. Determined to leave the army with the same physical fitness with which he entered it, sport formed a critical part of Henson’s recovery. He was selected to be Captain of the British team in the inaugural Invictus Games, winning gold in the 200m sprint, and went on to win bronze in the 200m at the 2016 Paralympic Games. For Henson, this represented a transition from being an injured serviceman to being someone who also had a present and a future.

### Optimising recovery with the principles of war

The components of fighting power (figure 1) used to describe the capability of the armed forces can be applied directly to recovery. Combined with the principles of war, a planning tool for prompt and effective use of the available resources, these enabled Henson to optimise and structure his recovery within a familiar framework. The principles of war as applied to recovery are:

- **Selection and maintenance of aim** – essential in any recovery.
- **Maintenance of morale** – including family and peer support groups going through rehabilitation in a similar situation: as soon as Henson was in hospital he was visited by other amputees.
- **Offensive action** – action over reaction, taking ownership of situation and dictating what to do with it.
- **Security** – weighing up risk and reward and taking a risk to push a person forward.
- **Surprise** – seizing the initiative and taking advantage of all opportunities.
- **Concentration of force and economy of effort** – balancing and prioritising your resources to understand where your main effort lies and allocate appropriate resource to move forward.
- **Flexibility and cooperation** – work with your support providers, such as your physiotherapist, to move forward and take their advice.
- **Sustainability** – ensure that there are enough resources to last for a lifetime’s recovery.

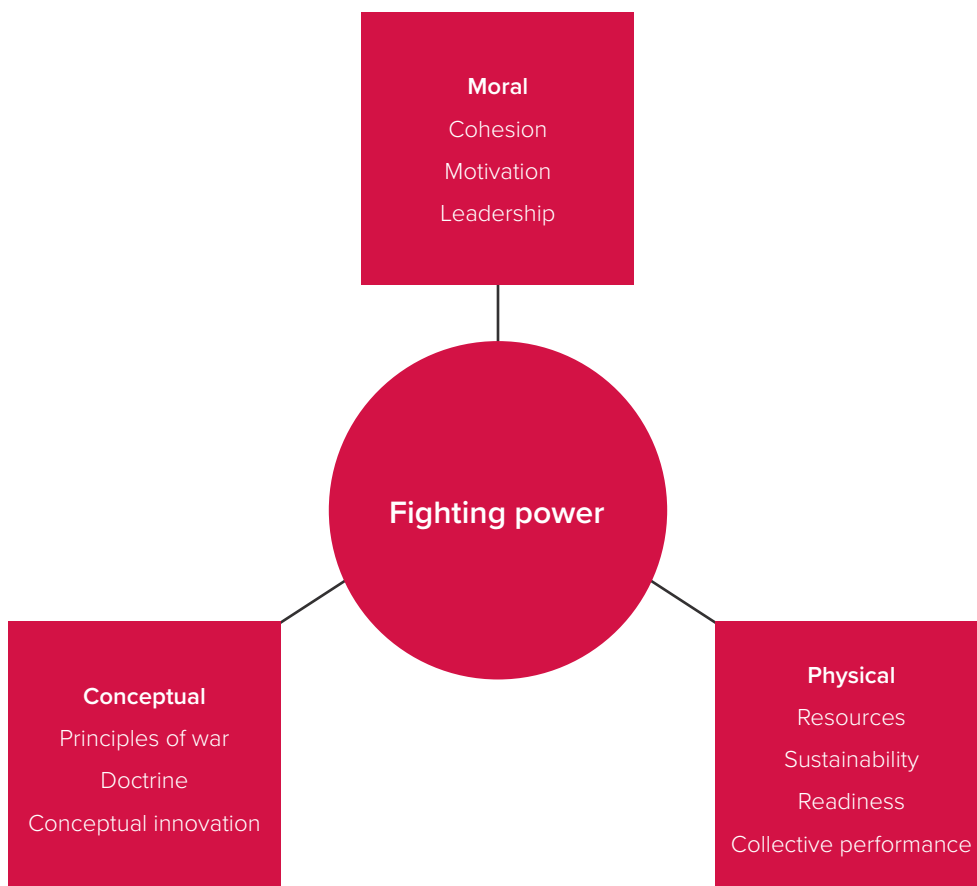
Innovation forms another key component of military capacity. Henson highlighted key innovators in the recovery space, thanking them and suggesting them as groups to turn to: Stanford Hall; Combat Stress; Help for Heroes; Blesma, The Limbless Veterans; Battle Back; The US Department of Defence Warrior Games; The Endeavour Fund; and The Invictus Games Foundation. He looks forward to future work by the University of Birmingham, JHUB, Imperial College Centre for Blast Injury Studies, The ADVANCE Study, and CASEVAC club.



**Image:** Dave Henson MBE, Imperial College London.

**FIGURE 1**

The capability of armed forces is often described using 'Fighting Power', comprising conceptual, moral and physical components. Image courtesy of Dave Henson.



# New treatments for sleep and mental health disorders

## Introduction

A circadian rhythm is a natural, internal process that regulates the sleep-wake cycle. Professor Russell Foster CBE FRS, University of Oxford, explained how traumatic injury to the eyes can profoundly affect sleep and disrupt circadian rhythm. The suprachiasmatic nucleus (SCN) is the brain's 'master clock', which dictates the timing of hormone release, emotions, behaviours and the sleep cycle. This is set to the external world by detecting the light-dark cycle – jetlag occurs due to the mismatch of external daytime with the internal world.

If an individual suffers major eye damage, this clock cannot be set to the external world and they drift away from the light/dark cycle. Circadian rhythm disruption harms a person's emotional, cognitive and physiological health as the individual becomes 'out of sync' with the day/night cycle and becomes socially isolated, which can further exacerbate trauma-related symptoms. The three domains of health that are affected are as follows:

- **Emotional:** anxiety, loss of empathy, use of stimulants and sedatives, negative salience, risk taking, impulsivity and illegal drug use.
- **Cognitive:** impaired performance, memory, attention, communication, motor performance, decision making and dissociation.
- **Physiological:** CVD, altered stress response, altered sensory thresholds, cancer, lowered immunity, type II diabetes, depression and psychosis.

Yet there is hope: sleep and circadian rhythm disruption presents a therapeutic target for new drugs. Foster's work has shown that in addition to the rods and cones that provide us with our sense of vision, there is a third group of light sensitive cells in the eye known as photosensitive retinal ganglion cells (pRGCs) which regulate our circadian rhythms and set the body clock to the outside world.

This understanding provides two treatment options:

1. Eye damage that renders an individual visually blind, due to the loss of rods and cones, may preserve the pRGCs. In such cases, appropriate light treatments (including seeking out enough natural light to regulate sleep-wake timing) can be used to restore a sense of time.
2. Based upon an understanding of how the pRGCs regulate the circadian system, drugs are being developed that can 'fool' the body clock that it has seen light. These new drugs will be used to restore sleep/wake timing in individuals who have lost their eyes and will soon be tested with Blind Veterans UK.

This offers the hopeful message that visual blindness need not result in circadian blindness in humans.



Image: Professor Russell Foster CBE FRS, University of Oxford.



## How to sleep well – understanding the causes and cures for a bad night after trauma

Normal quantity and timing of sleep is critical for normal brain function including mood, memory and metabolism. This makes sleep a key tool for recovery after a physical or mental health problem. Dr Kirstie Anderson, Newcastle-upon-Tyne Hospitals NHS Foundation Trust, explained how technology can be used to help people have better nights.

### Impact of sleep disturbance on brain function

Testing memory and cognition in a patient population with bipolar disorder showed that the patients perform as well as individuals without bipolar disorder, provided they have normal sleep. It is therefore important to protect sleep, especially in hospital wards where patients are particularly vulnerable to mental health problems, such as the acute trauma ward.

### Causes of poor sleep after trauma

“Sleep disturbance” is not a diagnosis. To be treated effectively, the distinct and treatable sleep disorders must be properly defined as one of the following:

- **Hypersomnia:** excessive sleepiness - struggling to stay awake during the day;
- **Insomnia:** inability to fall and/or stay asleep most nights for longer than three months with daytime impact;
- **Parasomnia:** abnormal behaviours while sleeping, including nightmares, sleepwalking, night terrors;
- **Circadian rhythm disorder:** desynchronisation of internal sleep-wake rhythms and the external light-dark cycle.

### Effective digital and psychological therapies

The STOPbang questionnaire can be used to screen for those at high risk of obstructive sleep apnoea – this affects 20-30% of the population with severe or enduring mental health problems compared to 5% of the general population. Digital technologies now provide an empowering solution for patients, for example remote CPAP monitoring and a phone app to treat the pauses in breathing can restart normal sleep and help people to resume normal life.

It is common practice to prescribe for daytime diseases but forget the impact of drugs on night sleep, for example neuropathic pain medication and opioids have a negative impact on sleep quality and obesity. While drugs are of value, psychological therapies have historically been undervalued. Image rehearsal therapy is a simple but highly effective therapy used to treat chronic nightmares including in those with PTSD, improving PTSD symptomatology and sleep quality.

Cognitive Behavioural Therapy for insomnia (CBTi) is now the recommended first approach for insomnia in both the UK and the US and is effective for treating insomnia. The therapy has been digitised to allow greater access to all including the NHS approved platforms Sleepstation and Sleepio.

Ensuring good sleep in hospital beds is a key part of recovery. The SleepWell pilot study within the acute in-patient psychiatry wards across Newcastle found that reducing hourly night observations by nurses significantly improved sleep quality, with a 23% decrease in use of hypnotics and a decrease in mental health issues such as deliberate self-harm.



**Image:** Dr Kirstie Anderson, Newcastle-upon-Tyne Hospitals NHS Foundation Trust.

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“If sleep is a tool for recovery, then one place where we should protect sleep is the acute trauma ward environment.”

Dr Kirstie Anderson, Newcastle-upon-Tyne Hospitals NHS Foundation Trust.

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## Knowledge for the benefit of Blind Veterans and wider humanity

Major General (Rtd) Nick Caplin, Blind Veterans UK, expanded on the devastating physical and mental effects of sight loss. Blind Veterans UK researches factors to maintain and improve quality of health and social inclusion, while accelerating innovation.

Loss of sight is both physically and mentally challenging and leads to a plethora of difficulties at different stages of life. Research by Blind Veterans UK seeks to enable beneficiaries to maintain and improve the quality of their health and well-being, their level of social inclusion and their satisfaction with life. As well as social wellbeing, Blind Veterans UK focuses on biomedical research and technological innovations. Focused evaluation has directed three of their main key areas for research:

- Sleep
- Traumatic brain injury (TBI); and
- Development of autonomous vehicles for disabled individuals.

### Sleep

Collaboration with Professor Russell Foster CBE FRS seeks to better understand circadian disruption experienced by blind veterans. In the area of sleep, 80% of veterans report poor sleep and shortened sleep (average ~5.7 hours) along with significant poor health and a 41% risk of mental health disorders, predominantly depression and anxiety. New treatment options to improve sleep are being developed for the veterans.

### Traumatic Brain Injury

Due to the physical proximity, any traumatic event injuring the eye is likely also to have affected the brain. The symptoms of PTSD and TBI are remarkably similar (figure 2), including confusion, memory deficits, mood changes and insomnia. However, the diagnosis given by a GP depends on whether the GP knows if that person is a veteran: if they do, they go down the mental health route, which may not be the correct avenue, if not, they are likely to follow a neurological treatment route.

Another focus of research is to understand links between brain injury and sight loss. Age-related macular degeneration is observed decades before expected due to TBI. Research seeks to uncover whether sight loss is related to a TBI event long before, or a series of brain events with cumulative impact.

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“Our work clearly is all about discovering new knowledge for the benefit of blind veterans today and tomorrow – and for a broader population as well.”

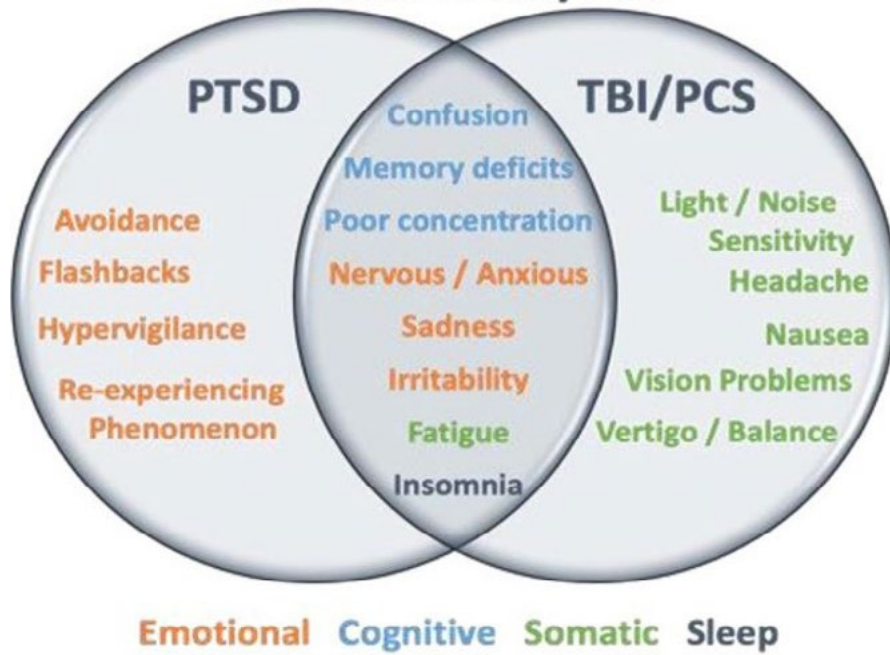
Major General (Rtd) Nick Caplin, Blind Veterans UK.

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**Image:** Major General (Rtd) Nick Caplin, Blind Veterans UK. Dr Tom Zampieri, President of the Blinded Veterans Association and Mr Bryan Naylor, a member of Blind Veterans UK, took part in the Q&A session.

## Overlapping signs and symptoms of PTSD & TBI/PCS



Credit: Hussain et al., submitted.

### Autonomous vehicles

98% of blind veterans want to drive again and regain their independence, and this is acting as a major initiative for Blind Veterans UK to accelerate development of new autonomous vehicles. An autonomous pod has been developed in conjunction with the self-driving vehicle company Aurrigo and is being trialled in Blind Veterans UK's Brighton centre with over 400 visually impaired participants.

Bind Veterans UK's research is detailed and wide-ranging, working internationally with the Blinded Veterans of America and following veterans over their lifetime. While this rich data resource focuses on the needs of ex-soldiers, the knowledge and new treatment options will not only benefit blind veterans today and tomorrow but will inform health and wellbeing in the broader visually impaired population and general society.

## Using Virtual Reality (VR) to deliver engaging, efficacious, and fast psychological intervention

Virtual Reality (VR) can help to deliver effective psychological interventions rapidly. Mental health disorders are very common, but far too few people receive the best treatments. Professor Daniel Freeman, University of Oxford, posited that delivering automated treatments in VR can help provide the best possible evidence-based psychological treatments to large numbers of individuals – within a safe virtual environment.

Using VR simulations, individuals can repeatedly experience problematic situations and be taught how to overcome difficulties via evidence-based psychological treatments. VR technologies have progressed significantly, and investment by major technology companies has helped it become accessible to the public.

Key advantages of VR include:

- The potential to automate provision of psychological therapy without a real-world therapist.
- Treatments can be made more compelling, rewarding and interactive compared to traditional therapies.
- Effective, expert, personalised psychological interventions can be digitised and automated, allowing consistent rollout to more patients such as through the gameChange<sup>1</sup> project for schizophrenia.
- Awareness of the patient that a computer environment is not real, but their minds and bodies behave as though it is. People will much more easily face difficult situations in VR than in real life and be able to try new therapeutic strategies that they can then bring into the real world.

### VR treatment of fear of heights

Psychological therapy can be hugely powerful for treating mental health problems: after 2.5 hours of VR therapy, a patient's fear of heights was treated so that he was able to stand on a balcony. The success of VR treatment requires a clear linkage between the problem, in this case fear of height, and the individual's rationale to deal with it. The VR therapy aims to build new thoughts about height, developing a curious attitude, dropping defences and overriding the old fear response.

### VR treatment of psychosis

A large-scale clinical trial seeks to use VR to treat the clinical target for psychosis, social withdrawal: 65% of psychosis patients demonstrate extreme levels of avoidance.



Image: Professor Daniel Freeman, University of Oxford.

The University of Oxford has developed a six-session automated treatment with a virtual therapist and user-centred design, including VR avatars animated and voiced by actors to maximise lifelikeness. The patient can choose which VR scenarios to enter, and with each entry the task becomes harder. The platform is halfway through a randomised controlled trial involving 432 patients with psychosis, looking at outcomes including real world performance and anxiety in certain situations.

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“All mental health problems play out in day-to-day situations – for example, being by heights for acrophobia, being around alcohol for alcohol disorders, and being around people for social anxiety. The best therapy is active: going into the troubling situations and helping people think, feel and behave differently.”

Professor Daniel Freeman, University of Oxford.

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1. [www.gameChangeVR.com](http://www.gameChangeVR.com)

## Innovations in the treatment of post-traumatic stress disorder

Professor Barbara Rothbaum, Emory Healthcare Veterans Program, is exploring how to increase the efficacy of Cognitive Behavioural Therapy (CBT) for trauma. This utilises virtual reality exposure therapy, intensive outpatient therapy, exposure therapy combined with pharmacological cognitive enhancers, and early treatment immediately after exposure to trauma.

### Virtual Reality Exposure Therapy

Symptoms of PTSD are part of the normal response to trauma, and treatments have traditionally included:

- **CBT:** the patient is reminded of trauma in a therapeutic manner so that the relationship to trauma changes, including physical changes in the brain and body.
- **Prolonged Exposure (PE) Therapy:** a kind of CBT in which patients repeatedly recount their traumatic experience aloud and listen to it, thereby confronting safe reminders of the trauma. This has more evidence of efficacy than any other approved PTSD treatment.

Virtual Reality Exposure Therapy (VRE) is a new method to deliver exposure therapy. This combines imaginal exposure with a VR environment mimicking a patient's description to create a sense of presence for the user, such as in a war zone, on a plane to treat fear of flying, or around drug users to treat addiction. VRE was found to be effective for PTSD following initial use with Vietnam veterans, and is now being used worldwide to treat trauma survivors. With increased computing power, graphics are more lifelike and offer the flexibility to adjust parameters such as the time of day, room configuration and sounds within a scene.

### Enhancing Exposure Therapy with pharmacological agents

In a novel application, the efficacy of VRE can be enhanced by combining it with cognitive enhancers such as the old antibiotic D-Cycloserine (DCS). In this treatment, VRE is underdosed but preceded by a pill which enhances the learning. A decrease in PTSD symptoms (such as acoustic startle and salivary cortisol reactivity) is observed in patients for up to 12 months using DCS versus controls (alprazolam, placebo).



Image: Professor Barbara Rothbaum, Emory Healthcare Veterans Program.

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“I really think the intensive outpatient model is the way to go for treatment of PTSD. These patients have more sessions in two weeks than most people have in a year, and PTSD and depression symptoms are significantly reduced during that time.”

Professor Barbara Rothbaum, Emory Healthcare Veterans Program.

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2 A response in which skin momentarily becomes a better conductor of electricity after a stimulus.

Research is now evaluating the use of the psychedelic 3,4-methylenedioxymethamphetamine (MDMA) on the extinction of fear learning. MDMA in rodent studies was found to enhance the extinction of fear and is now being tested in humans, with the aim to test this treatment on treatment-resistant PTSD patients later in 2020.

### **Enhancing retention in treatment with intensive treatment formats**

The Emory Healthcare Veterans Programme is an innovative intensive outpatient programme offering daily therapy over two weeks. The initial results of this massed PE treatment show that it is successful in treating PTSD, mild TBI and military sexual trauma, with a significant decrease in trauma-potentiated acoustic startle and heart rate reactivity.

### **Early interventions**

Around 70% of people will be exposed to a traumatic event during their lifetime, but not all develop PTSD. It is possible to predict which individuals will get PTSD by their increased skin conductance response<sup>2</sup> hours after trauma. This creates an opportunity to predict PTSD incidence and act immediately: providing Exposure Therapy within hours of trauma exposure could halve the rate of PTSD.

# Recovery from physical injuries

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## Improving lives for people following traumatic brain injury

TBI arises as a result of a physical injury to the brain and dramatically affects the lives of the patient and those around them, as well as the economy. Professor Melinda Fitzgerald, Curtin University and the Perron Institute for Neurological and Translational Science in Western Australia, explored the work of the Australian Mission for TBI.

TBI arises from a range of circumstances such as concussion from playing sport, falling or severe injury arising from a road accident. There is a real clinical need in this field: outcomes for patients with TBI have not improved over last decade, including 30-40% mortality for severe TBI and a high rate of long-term disability. This is partly due to variability in TBI presentation and its treatment.

Injury severity ranges from mild (eg concussion) to moderate to severe brain trauma. There are 20,000 moderate to severe cases annually in Australia. Concussion makes up 80-90% of TBI cases and repeated injury worsens outcomes. Most people recover well from concussion but 20% have persisting post-concussion symptoms (PPCS). PPCS cannot be predicted, and therefore these individuals slip through the net in healthcare treatment. TBI also spans a spectrum of severity from deficits in cognition to vegetative states, varying degrees of lack of emotional control, poor mental health, disrupted balance and sleep disturbances. Refining treatment is critical to improve the lives of patients and those around them.

### The Australian Mission for TBI

The Australian Mission for TBI presents a unified approach across Australia and has received \$50 million AUD of federal funding over 10 years. The aims of the Mission are currently being developed and will include identification of predictors of poor outcome and recovery following TBI and development of feasible interventions to improve lives.

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“There is a clear clinical need in this area as outcomes for patients with traumatic brain injury have not improved over the last decade.”

Professor Melinda Fitzgerald, Curtin University and the Perron Institute for Neurological and Translational Science.

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**Image:** Professor Melinda Fitzgerald, Curtin University and the Perron Institute for Neurological and Translational Science in Western Australia.

The first call for funding focused on personalising care following TBI, and projects under review include looking at preinjury factors (eg family), injury related factors (eg distance from primary care) and markers of early damage (eg innovative blood biomarkers). Founded alongside the Mission for TBI, Vision TBI is a company that will work to alleviate the distress of people who experience TBI through a range of activities that include the filling of funding gaps for TBI related research that federal money cannot support, such as tracking cohorts over long periods of time.

Establishing a suite of biomarkers to accurately predict outcomes will help to reduce redundant imaging, indicate any need for more intensive monitoring, enable individualised patient prognosis, focus on neurorehabilitation, and identify cohorts for clinical trials of interventions. The approach will include a large data platform to enable the prediction of outcomes following injury. The new CREST Concussion Recovery Study aims to identify a suite of pre-, peri- and post-injury factors that present soon after mild TBI and could be used to predict PPCS. The research of the Australian Mission for TBI has the potential to be transformative and lead to substantially improved outcomes for people who have experienced TBI.



## RoboTrainer: Making effective rehab training available to everyone

Physical rehabilitation following neurological damage can be challenging when patients are weakened and motivation runs dry. Dr Anders Sørensen, University of Southern Denmark, introduced RoboTrainer, a simple, low cost training robot that allows trauma victims to complete rehabilitative training in clinics or even in their own homes.

Many trauma victims suffer neurological damage to motor function that severely inhibits rehabilitative training. This risks atrophy, circulatory disease and other physical complications, while depression may further undermine their quality of life. In the past, underwater training, exoskeletons and advanced training machines could break this vicious circle, but these have high operational costs and require a high volume of training to make a difference.

### RoboTrainer

RoboTrainer is a wire training robot that provides physical rehabilitation for individuals who have experienced trauma, stroke, muscle/skeletal illness or neurological illness, amongst other things. The devices are optimised for simplicity and low operational cost (~£100/session), while rapid prototyping enabled creation of an advanced robot controller of force, velocity and position. RoboTrainer can provide extreme resistance or reduce gravity if there is not enough muscle strength remaining for an individual to raise their arm. Initial studies show that the devices can easily be operated by physical therapists in simple clinics, and potentially by patients and their helpers at home.

This tool could offer a new paradigm to replace other existing robotised training machines, such as linked robots and exoskeletons (eg HAL-Exoskeleton) which are expensive, cumbersome, and exclusive to centralised facilities. Unlike these existing solutions, RoboTrainer also enables treatment of low severity patients, increasing training quality and quantity.

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“The training algorithms and a very high dose make RoboTrainer a very effective mode of rehabilitation.”

Dr Anders Sørensen, University of Southern Denmark.

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### Results

Some chronic (abandoned) patients have significant potential to recover even after two to three years, the conventional area of no return after which a patient is considered unsuitable for further rehabilitation. RoboTrainer appears to enable patients' potential.

The trainer's success is thought to be due to:

- Personalised training algorithms;
- High training frequency (50 sessions over 15 weeks); and
- Patients' motivation to work with a robot partner being equivalent to that of training with a human.

By using the RoboTrainer, chronic patients with neurological damage experienced very significant functional and strength improvements. In one case, a wheelchair-bound stroke patient recovered the ability to walk after 15 weeks of treatment; after 14 additional months the patient could get out of bed, go to the bathroom unassisted and climb stairs.



Image: Dr Anders Sørensen, University of Southern Denmark.

## Driving neural recovery following Spinal Cord Injury

Professor Jane Burridge, University of Southampton, presented work that combines Functional Electrical Stimulation (FES) with a cycling ergometer. This novel application uses the patient's voluntary effort as feedback in a virtual cycle race. The aim is to restore function through neuroplasticity – the ability of a brain to form and reorganise synaptic connections.

Three key areas driving growth in the neural interface field are:

- Increased understanding of the brain and spinal cord;
- Miniaturisation of sensors and interfaces; and
- Increases in computer power for signal processing, managing large data and decision-making algorithms (AI).

Recent research has shown potential for neural recovery in both animals and people with incomplete Spinal Cord Injury (SCI). While some studies have used implanted systems for recovery, the 'iCycle' is an inexpensive non-implanted novel cycling ergometer built on an understanding of neuroplasticity and motivation, that has recently been tested on a small number of patients.

The 'iCycle' uses FES to stimulate leg muscles on alternate revolutions only, meaning that patients drive the pedals voluntarily on alternate pushes. The amount of voluntary effort the person exerts is monitored and used as feedback in a virtual cycle race, motivating the patient to see their bike go faster on-screen. Using voluntary effort with synchronised FES – opposed to FES alone – helps to achieve greater neuroplasticity. This is thought to be through a mechanism known as Hebbian<sup>3</sup> learning, creating better neurological connections and leading to recovery.



Image: Professor Jane Burridge, University of Southampton.

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“We need to test whether the iCycle is effective – marginal walkers with an incomplete injury are most likely benefit. By training on the iCycle they could become independently mobile.”

Professor Jane Burridge, University of Southampton.

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3. Hebbian learning theory is a neuroscientific theory claiming that an increase in synaptic efficacy arises from a presynaptic cell's repeated and persistent stimulation of a postsynaptic cell. It attempts to explain synaptic plasticity, the adaptation of brain neurons during the learning process (Wikipedia, accessed 6 July 2020). This theory was put forward by Donald Hebb in the mid 20th century to explain learning associated with successful practice and has since been demonstrated experimentally. It can be summed up by the catchphrase “neurons that fire together, wire together”.

## iCycle

A study was conducted of spinal injury patients using a wheelchair for a minimum of two hours a day. After four weeks of iCycle treatment, patients exhibited improved clinical outcomes including spinal cord independence, muscle strength, independence of mobility and spasticity.

A similar study (Yasar) using FES alone without voluntary efforts by patients saw similar improvements after six rather than two months of treatment. A second study (Wagner) using implanted phasic spinal cord stimulation saw a similar rate of improvement but extended over five months. This highlights the importance of a patient's voluntary effort.



**Image:** The iCycle being used in a clinical setting.  
Courtesy of Professor Jane Burridge.

## Key results

- The iCycle treatment is safe, well accepted, and patients stayed for all sessions.
- Recovery rate is improved when voluntary effort is combined with FES cycling.
- The duration of intervention may need to be longer, while feedback on recovery over time may increase patient motivation.
- Findings need to be verified via randomised controlled trials, supported by an increased understanding of the mechanisms of effect.
- Future production of wearables for FES would allow such treatments to be used at home.



**Image:** The graphics used to motivate the patient.  
Courtesy of Professor Jane Burridge.

## Making direct neural interface therapies a clinical reality

Oliver Armitage, BIOS, presented pioneering work that uses AI to turn direct neural interface therapies – using electronic devices that interact with the nervous system – into a clinical reality.

Direct neural interfaces for limb control have been used in a range of research and pilot studies for decades, and clinical practice regularly uses neuromodulation for pain or other conditions. However, direct neural interface therapies have so far not been translated into the clinic, largely due to the technology required for real-time decoding and encoding being too costly and large to put into implantable medical devices.

Neural interfaces balance performance and clinical practicality with goal treatments including:

- Spinal cord injury;
- Direct neural control and feedback for prosthetics, hypertension, diabetes and rheumatoid arthritis; and
- Tetraplegia.

Neural interfaces transfer data from software to biology. However, they must also interpret the information coming back from the nervous system in a bi-directional connection to understand the device's clinical effect, such as stimulation to achieve neuroplasticity or to feel a motor stimulation. Information transfer happens in the same way throughout the body, meaning that the device can be placed in different locations depending on the application – such as organ homeostasis for diabetes, or stimulating the somatic nervous system to treat motor sensory conditions.

Turning direct neural interfaces into a widespread clinical reality requires the following key developments:

- Standardising interfaces using machine learning and AI: open source methods from large companies like Facebook can help accelerate this.
- Creating technology that can be scaled across thousands of people: clinical applications can learn from consumer technologies, such as Apple's Siri, which does not have to be trained from scratch in every device.
- Development of additional wearables, physiological understanding, and a clinical interface to remotely monitor the patient's progress and the device's health.

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“Neural interfaces are starting to get a lot more attention, both internationally and in the UK, and so it's a very exciting time for these technologies.”

Oliver Armitage, BIOS.

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**Image:** Oliver Armitage, BIOS.

New technology by BIOS uses AI to continuously decode and encode neural information in real-time on small-scale devices. This is bringing neural recording and stimulation to the clinic and will facilitate long-term direct neural interfaces for lifelong health, delivering the promise of decades of research.

BIOS is developing a full-stack neural interface platform that uses AI to decode and encode the signals from the brain to the body to treat chronic health conditions. This neural approach can be used for chronic conditions including hypertension, diabetes, and rheumatoid arthritis, and for the control and monitoring of prosthetic limbs. They aim to build a platform technology that enables third party partners to create their own neural treatment applications, building on top of their technology or integrating aspects of it into their existing work. Machine learning allows continuous monitoring of outcomes and updating of software without removing the implant.

Clinical trials seek to gather the full patient picture. In these, 24 patients have been monitored for more than two years, measuring clinically relevant outcomes (eg six-minute walk distance) while observing how the device is performing at a technical level.

## Amputee Biomechanics: it is not just about getting active

The expectation is that very many amputees will be able to maintain high levels of activity through to old age, yet this seems to be out of reach for many. Professor Anthony Bull, Imperial College London, presented research into biomechanics that seeks to understand why amputation is associated with an increased likelihood of osteoarthritis and what can be done to mitigate against damage.

### Long-term effect of amputation

Compared to other amputee populations, military veterans are young, very well rehabilitated, highly motivated and very healthy before injury. The British Military Afghanistan lower limb amputee cohort has an average of 1.6 amputations per person – that is, most individuals have an above and through knee bilateral amputation. However, no matter the degree of motivation and quality of surgery and prosthetics, bilateral transfemoral (above knee) amputees require almost double the energy to walk.

Of bilateral transfemoral amputees among Vietnam veterans, only 22-35% use prostheses and 10% outside the home (compared to 70% for Iraq and Afghanistan). It is therefore the norm for Vietnam that almost all veterans after 22 years are not working and use wheelchairs. The long-term effects of anatomical deficit include:

- Phantom sensation, back pain and phantom pain for almost all individuals in the Afghan cohort.
- In general, 65% of uni-lateral amputees have arthritis in their sound limb.
- In general, a 20% higher chance of osteoarthritis in unilateral transtibial (below knee) amputee than a non-amputee, and a 300% higher chance in a unilateral transfemoral amputee.
- Pain across all studies.

It is therefore essential to develop prosthetics and rehabilitation to minimise damage to the bone and pain suffered by an individual.



Image: Professor Anthony Bull, Imperial College London.

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“I’d like to frame this talk as an anatomical deficit rather than a medical problem. My background is as a mechanical engineer and this is one of the gears having gone wrong, not a problem with the circuitry.”

Professor Anthony Bull, Imperial College London.

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## Background to biomechanics

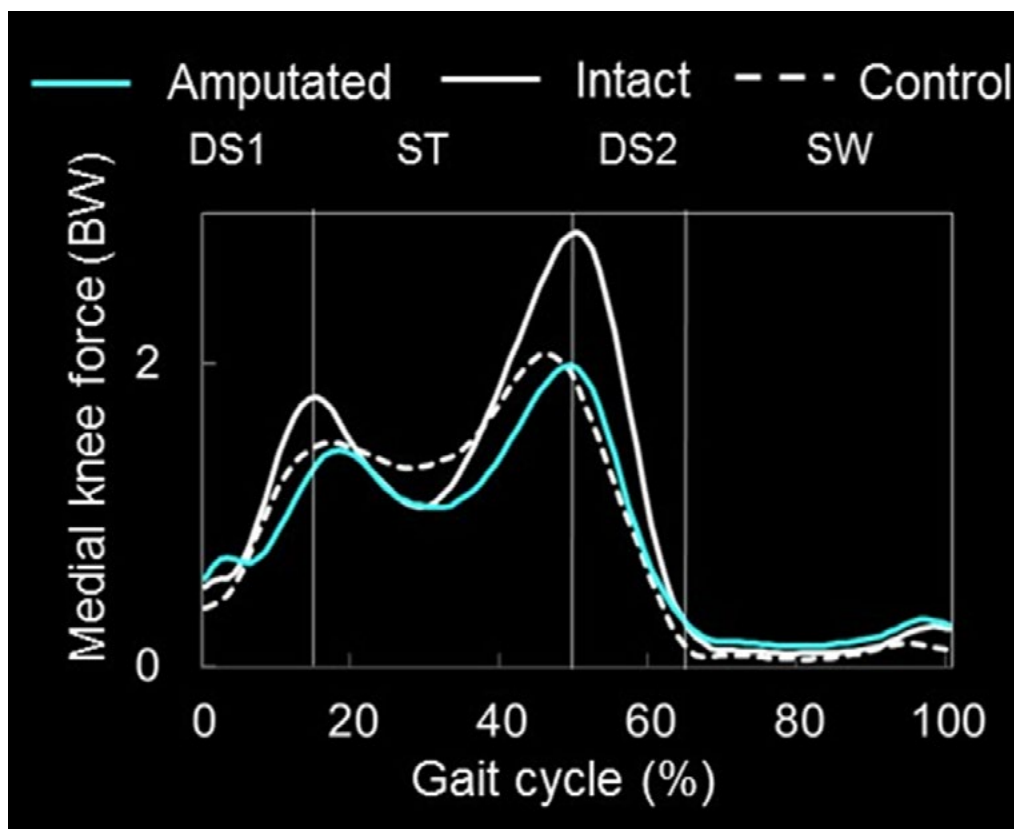
Biomechanics is the study of the interaction between forces, motion and deformation and is the underlying science that can shed light on the reasons why such high levels of performance are unsustainable for most amputees, unattainable for many and detrimental for others. Understanding amputee biomechanics can aid in devising novel rehabilitation programmes, surgery and prosthetics.

Implants facilitate quantification of forces within the knee joint in order to compare and analyse amputee biomechanics across amputee groups. This allows questions to be addressed, such as:

- Why does osteoarthritis (OA) occur in the sound knee? Greater medial knee contact force is observed in the intact limb than amputated, increasing loading (figure 3).
- What is the musculoskeletal burden of amputees in day-to-day activity? The size of the gluteus maximus increases in amputees while the quadriceps significantly decrease in volume, meanwhile the peak contact force and the hip joint increases. These are likely due to subtle changes in movement that can bring detrimental mechanical effects, potentially causing OA.
- What is the stress distribution within bones? Compared to a healthy control, an above-knee amputee has a thinner cortex of bone, while internal struts (trabecular structures) are significantly reduced in density. This is because above-knee amputees change the way they walk, causing weak bone. Bone loss is centred at the site of amputation and can therefore be treated mechanically.
- How can these problems be solved? Solutions include countering the high metabolic cost of walking with a prosthetic using powered prostheses, as well as tackling increased (and reduced) loading and higher incidence of osteoarthritis via activity limits that signal when bone needs time to repair.

FIGURE 3

Amputees exhibit greater medial and lateral knee contact force in the intact limb than controls. Increased loading supports the mechanical hypothesis explaining the higher prevalence of knee OA in this group.



Credit: Ding... Bull J Orthop Res 2020.

## The future of human wearable bionics from the industry's point of view

Dr Andreas Goppelt, Ottobock, presented advanced devices for human mobility that use artificial intelligence in their controls. For the first time, this allows patients to intuitively move their artificial limbs and lead a more active and independent lifestyle.

Ottobock creates prosthetics, orthotics and exoskeletons for human mobility. These are classed as:

- Prosthetics: an artificial body part, such as to replace a lost limb.
- Orthotics: devices such as braces that support rehabilitation and/or compensate for lost function.
- Exoskeletons: external structures that support people in physically demanding tasks, including for non-medical industrial applications.

### Prosthetics

The C-leg® is the world's first real-time microprocessor-controlled knee (MPK) and set a new standard for safety and functionality for people with transfemoral knee amputations and hip disarticulation when it was made available in 1997. The microprocessor improves balance and stability, significantly reducing the risk of falling. Today's most advanced MPK is Genium X3 for highly active users.

MPKs are effective in all five dimensions of the EQ5D score used to measure health-related quality of life in cost-utility analysis: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Clinical evidence demonstrates that patients with lower mobility grades benefit most from MPKs as evidenced by gains in EQ5D. Patients with the 'vascular' aetiology for cause of amputation benefit the most, meaning there is additional value for diabetic or elderly patients as prosthetics are both cost effective and affordable.

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“From an industry perspective we are living in very exciting times in terms of frontiers of what technology can do today with truly practical applications – not necessarily only in the research environment but products that can be brought to the market.”

Dr Andreas Goppelt, Ottobock.

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Image: Dr Andreas Goppelt, Ottobock.



## Orthotics and exoskeletons

These advances in prosthetics have now been translated into intelligent orthotics. The C-Brace® is the first knee-ankle foot orthosis with stance and swing phase control, helping patients suffering from neurological indications such as incomplete spinal cord injury, stroke, multiple sclerosis and post-polio syndrome to regain a natural gait.

Exoskeletons like the personal assistive device Paexo® help prevent work-related disorders of the musculoskeletal system, such as those caused by repeated over the shoulder industrial work. Soon to be followed by Paexo back which relieves the lower back while lifting heavy objects.

## Future developments: bionic reconstruction surgery and AI

Agonist and antagonist muscles are normally coupled, which is very important for proprioception, but this is lost in amputees. Advances in the fields of bionic reconstructive surgery connects agonist and antagonist muscles, allowing patients to feel movement in their prosthetic. This enables greater control for the prosthetic user and the introduction of somatosensory feedback from the device to the brain, allowing patients to lead a more active and independent life and helping to foster embodiment – making users feel like the device belongs to them.

AI learning systems promise a significant increase in quality of life from future generations of products, such as obstacle avoidance by pattern recognition. Meanwhile, training an algorithm has already generated intelligent hand prostheses where movement responds to thought.



**Image:** Professor Jackie Hunter CBE, BenevolentAI (left), chaired the session on new technology to advance the recovery of physical health. Speakers from left to right: Professor Jane Burridge, Professor Anthony Bull, Dr Andreas Goppelt, Dr Anders Sørensen, Oliver Armitage.

# Panel discussion: Where should scientists focus efforts?

Closing the conference, a panel discussion led by Sir Simon Wessely FMedSci, King's College London, comprised experts from across the military, healthcare and academia: Air Commodore Rich Withnall QHS, UK Defence Medical Services; Professor Barbara Rothbaum, Emory Healthcare Veterans Program; Wing Commander Marcus Stow, JHubMed; Professor Jane Burridge, University of Southampton; Alexandra Crick, Salisbury NHS Trust.

## Conflict as a source of medical innovation

- Many major innovations arise out of warfare: the main progress in plastic surgery came out of World War I, new modes of delivery to treat PTSD are often borne out of military psychiatry, and learnings about blood transfusion protocols from Camp Bastion in the Afghan cohort have been transferred to the NHS.
- Opportunities to repurpose existing technologies into other areas are often identified by service personnel on the ground rather than those in the office.
- Changing styles of warfare have also led to innovation in treatments. For example, the rise of asymmetric warfare (in which opponents have differing resources and knowledge) has led to increased use of improvised explosive devices, with the need to consider the new injury pattern, shapes of body armour, and ways to seat people in vehicles to protect against new types of threat. A change in adverse mental health outcomes is also being observed, linked to these kinetic injuries.
- There has, however, been a failure to translate military rehabilitation experience into the NHS, partly due to the financial cost. Due to progress in surgery we now see unexpected survivors who are short-changed in terms of rehabilitation.
- Innovation in the international medical community is rapid during conflict, but innovation slows when war stops, to the loss of service personnel's lives at the start of the next conflict. There is a need to maintain a consistent rate of innovation, while moving away from the paradigm of substantial investment for incremental gain.
- Long-term outcomes can be underreported in medicine, particularly in surgery where it takes 20 to 30 years to understand outcomes. Cohort studies such as ADVANCE provide invaluable data in understanding patterns and successes.

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“Often, it’s Service personnel on the ground who spot opportunities to better use existing technologies, rather than those in an office.”

Wing Commander Marcus Stow, JHubMed.

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“With biomarkers with nanotechnologies, we are in a position to create wearables or implantables that can measure pretty much whatever we want. The challenge is knowing what we want to measure.”

Air Commodore Rich Withnall QHS, UK Defence Medical Services.

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**Image:** (left to right) panellists, Air Commodore Rich Withnall QHS, UK Defence Medical Services; Professor Jane Burridge, University of Southampton; Professor Barbara Rothbaum, Emory Healthcare Veterans Program; Wing Commander Marcus Stow, JHubMed; Alexandra Crick, Salisbury NHS Trust and Sir Simon Wessely FMedSci, King's College London (Chair).

### Innovation at pace: barriers and drivers

- The inertia of large organisations, including universities and the NHS, means that the pace of innovation can be slow. A recent review of how to do agile commercial processes has allowed the MOD to improve in this area.
- Public services often struggle to take the risk of a failed large investment. One solution is to establish an organisation as a corporate entity attached to relevant NHS hospital or university, providing a pot of flexible funds.
- One weakness of the UK is in moving from proof of concept to the exploitation phase. Organisations such as JHubMed help to exploit and scale technologies rapidly.
- The speed of licencing new medical technologies can be perceived as slow, particularly following Brexit and the need for CE marking for sale within the European Economic Area. There is concern that the UK may lag behind the EU and that people will seek FDA approval for use in the USA rather than pursue CE marking for use in Europe.
- There are ways to fast-track healthcare technologies specifically for military use. Once this is done for the military, it can provide a general proof of concept that a technology works and may bring wider benefit.

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“We see unexpected survivors of civilian trauma now due to the lessons learnt from the military experience that have been transferred to the NHS, but these survivors are short-changed in terms of rehabilitation.”

Alexandra Crick, Salisbury NHS Trust.

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“We have got much better at saving lives but must ask whether we have got better at recovering lives when people feel threatened everywhere when they are not independent.”

Professor Jane Burridge, University of Southampton.

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### Role of the Invictus Games

- After war, competition is a potent driver of innovation, motivating athletes, engineers and medical professionals.
- Organisations such as the Invictus Games Foundation have catalysed a new conversation between clinicians, employers and the military on the effect of injury on a person's life and how that can be rehabilitated.
- The interface of athletes and clinicians provided by Invictus is unique, as each patient sets their own priorities and determines where innovation is needed in order to change their life.



**Image:** Michelle Partington, Mentis Training and Consultancy and Invictus Games competitor.

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“Many of the warriors’ lives have become so narrow by the time they come to us due to their visible or invisible injuries. Invictus broadens the scope out again.”

Professor Barbara Rothbaum, Emory Healthcare Veterans Program.

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“I was lost before being offered the opportunity to join the Invictus Games. The training, routine and camaraderie was something I had been lacking for a couple of years. It brought me out of the dark place and gave me the fire back in my belly. I no longer want to take my life, I want to take it as far as it can go.”

Michelle Partington, Mentis Training and Consultancy and Invictus Games competitor.

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# Acknowledgements

## Organisers

**Professor Jackie Hunter CBE**

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University of Oxford

**Sir Simon Wessely FMedSci**

King's College London

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**Dame Sue Ion FREng FRS**

Chair of the Royal Society Science, Industry and Translation Committee

**Professor Christopher Boos**

Poole Hospital NHS Foundation Trust

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Imperial College London

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust

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Emory Healthcare Veterans Program

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Blind Veterans UK

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## Panel members

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UK Defence Medical Services

**Wing Commander Marcus Stow**

JHubMed

**Professor Barbara Rothbaum**

Emory Healthcare Veterans Program

**Professor Jane Burridge**

University of Southampton

**Alexandra Crick**

Salisbury NHS Foundation Trust



The Royal Society is a self-governing Fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. The Society's fundamental purpose, as it has been since its foundation in 1660, is to recognise, promote, and support excellence in science and to encourage the development and use of science for the benefit of humanity.

The Society's strategic priorities emphasise its commitment to the highest quality science, to curiosity-driven research, and to the development and use of science for the benefit of society.

These priorities are:

- Promoting excellence in science
- Supporting international collaboration
- Demonstrating the importance of science to everyone

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The Invictus Games Foundation uses the power of sport and the Invictus Spirit to inspire recovery, and support the rehabilitation of wounded, injured and sick Servicemen and women and veterans (WIS) to improve their life beyond injury or illness.

The Foundation manages the process of selecting the hosts of the Invictus Games and oversees the delivery of this international sporting event involving competitors and their friends and family from 20 nations.

The Invictus Games Foundation also seeks to provide international wounded, injured or sick Service personnel with opportunities in all areas of life to help regain a sense of purpose, and to help re-engage and contribute to their communities.

The Foundation also seeks out and supports the sharing of best practice in order to foster greater international collaboration for recovery and rehabilitation.

#### **For further information**

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