HOUSE OF LORDS

Select Committee on Science and Technology

Corrected oral evidence: Ageing: science, technology and healthy living

Tuesday 11 February 2020

10.20 am

Watch the meeting

Members present: Lord Patel (The Chair); Lord Browne of Ladyton; Baroness Hilton of Eggardon; Lord Hollick; Lord Kakkar; Lord Mair; Baroness Manningham-Buller; Baroness Penn; Viscount Ridley; Baroness Rock; Baroness Walmsley; Lord Winston; Baroness Young of Old Scone.

Evidence Session No. 13 Heard in Public Questions 107 - 123

Witnesses

Professor Russell Foster, Professor of Circadian Neuroscience, University of Oxford; Professor Barbara Sahakian, Professor of Clinical Neuropsychology, University of Cambridge; Dr Sana Suri, Alzheimer's Society Research Fellow, University of Birmingham; Professor Jane Raymond, Professor of Visual Cognition, University of Birmingham.

USE OF THE TRANSCRIPT

This is a corrected transcript of evidence taken in public and webcast on www.parliamentlive.tv.

Examination of witnesses

Professor Russell Foster, Professor Barbara Sahakian, Dr Sana Suri and Professor Jane Raymond.

Q107 **The Chair:** Good morning. Thank you for coming this morning to help us with this inquiry. We are live streaming on the internet. Before we start it would be very helpful if you could introduce yourselves and if you want to make a comment please feel free to do so.

Professor Barbara Sahakian: I am a professor of clinical neuropsychology at the University of Cambridge. My expertise is in cognition, the measurement of cognition and trying to enhance cognition. I mainly work with neuropsychiatric disorders and traumatic brain injury but in healthy populations as well.

I am the co-inventor of the CANTAB tests which are computerised neuropsychological tests to assess cognition. They were developed some years ago. They run on a touch sensitive computer and on iPads. They are used in the Dementia Platform UK and the Medical Research Council's deep and frequent phenotyping study. In addition, I have developed cognitive training tools that are games to improve cognition in elderly people and people with schizophrenia to try to get them to drive the neurocircuitry in the brain to improve the hippocampal function, the episodic memory and to boost their overall activity and functional activity in daily life.

Dr Sana Suri: I am an Alzheimer's Society research fellow at the University of Oxford. My research focuses on understanding the mechanisms of risk and resilience for cognitive decline and dementia. Very specifically, I am interested in the link between cardiovascular health—factors that protect the health of our heart, like blood pressure and diabetes, obesity and so on—and how that effects cognitive health and impairment as we get older.

Professor Russell Foster: I am professor of circadian neuroscience at the University of Oxford and the director of the Sleep & Circadian Neuroscience Institute. My interests span the sleep and circadian field, particularly the fundamental mechanisms that generate and regulate sleep and circadian rhythms. More recently, we have been interested in understanding the mechanisms underpinning what happens when sleep and circadian rhythms fall apart as a result of disease, societal pressures or indeed ageing. We have been targeting those systems for a range of different interventions from cognitive behavioural therapy to the development of new drugs. I am delighted to be here to flag up the importance of the relationship between sleep, mental health and ageing.

Professor Jane Raymond: I am professor of visual cognition at the University of Birmingham. My specialisation is human cognition, particularly typical human cognition, with an emphasis on what we would consider to be short-term processes that happen in the first half-second of encountering stimuli, so attention, perception and how they relate to emotional systems and even fast decision-making. In the last five years

my work has turned to looking at the effects of direct and indirect inflammation on cognition. It is a relatively new area in many ways, but we are trying to understand the role of air pollution, short-term acute inflammation and long-term sources of inflammation on attention, working memory and cognition in general.

Q108 **The Chair:** Thank you very much indeed. If I may kick off with the first question. Apart from the definition, which you might like to define, of cognitive function, how is it measured? How does it change with age? Is it age that changes it or is it some loss of function that changes it? What might be the scientific evidence of the roles of nutrition or exercise, social environment or other areas that could mitigate against cognitive function decline?

Professor Jane Raymond: Typically, what we do in experimental studies, lab studies, even home studies, is present a confined, well-described stimulus. It could be an image on a screen, or a set of words, or a simple task such as making tea. You set up a simple situation and then monitor behaviour, usually again constrained to a correct answer or an incorrect answer. You might measure the speed. You might measure the correctness. You might measure the sequence with which activities are done and whether or not the goal is completed.

Typically in these kinds of test we are looking for people to fail. We look at the mistakes. The mistakes are more informative than good behaviour. That is the general approach. The information is repeated over and over again and then you accumulate the data and measure it. You can link that to brain function because you measure brain function at the same time and can link it to physical health.

Professor Barbara Sahakian: Cognition can be measured objectively, and it can be found to be reliable and valid. We can measure different forms of cognition. We can measure attention, learning, memory planning, problem solving. We can measure what occurs in the frontal lobes primarily, which is the executive functions like the higher-level cognitive functions such as planning and problem solving. We can measure the more memory and learning functions that go on in the temporal lobe area. When people do these tests, lying in a scanner, we can see these neural activations in the brain. As you probably realise, our brains are still in development up until late adolescence, early young adulthood, so about 24 to 25 years of age—a little bit earlier in females. We are at our peak in our 20s and early 30s. In later life, cognition tends to decline somewhat. These are due to changes in the brain. We can measure these using valid tests. Some of them are non-verbal so we can avoid just measuring IQ over and over again.

Dr Sana Suri: On your question about how these cognitive functions decline or change with age, that varies depending on the type of cognitive domain that you are testing. For example, our ability to reason, solve new problems, make decisions and plan come under this general category of fluid intelligence. That gradually starts to decline as we get older, so we notice a reduction in our mental abilities which is very much a part of normal ageing. There is another category of cognition called

crystallised intelligence which refers more to our grammar, reading, vocabulary, language skills that we draw from our education and experience. That remains fairly stable or can even improve as we get older, so not all cognitive domains will change at the same rate as we get older.

Professor Russell Foster: Essentially the quality of the sleep that we get defines much of our ability to process information and much of our cognition during the day. Without sleep our cognitive abilities fall apart very rapidly. It is interesting that, as sleep changes with age, we see a correlation with declining cognitive abilities. The extent to which this is correlation or causation is a very interesting issue.

The Chair: Is it the quality of sleep or hours of sleep?

Professor Russell Foster: You can measure sleep in lots of different ways. For example: the duration of sleep, the time it takes to fall asleep, and sleep efficiency which is the time spent in bed awake vs the time spent in bed asleep. All of those decrease with age. Some of the other parameters that you can measure, for example, are non-REM and REM sleep. Non-REM sleep is divided into a number of stages. Deep sleep is slow-wave non-REM sleep. We get very little of that in the later years. In fact, it has been estimated that when we are in our 90s there may be no slow-wave sleep at all.

Precisely what that means is unclear but slow-wave sleep has been correlated with the ability to consolidate memories and also to process information. Again, part of the cognitive decline could be associated with changes in the pattern of sleep. Essentially, most of the parameters of sleep change with age.

Q109 **The Chair:** What is the scientific basis of suggesting that nutrition, social interaction, reducing stress, et cetera, play any part in mitigating against loss of cognition?

Dr Sana Suri: There was a recent review in the *Lancet* that brought together all of the evidence on these very risk factors and pointed towards about seven to nine modifiable lifestyle factors that can be associated with cognitive decline: social isolation, stress, depression, anxiety and the ones that you have mentioned fall within those factors as well. A lot of that evidence comes from observational studies where we followed up longitudinal cohorts of people and observed their behaviour and then relate that to cognitive performance in older age.

The evidence from those observational studies is quite strong for this link. Interventional studies are a bit more mixed. The evidence, for example for exercise, is not as strong from interventions as it is from observations. Interventions show some evidence that exercise improves cognition. Some studies find no evidence of beneficial effects. Some find beneficial effects in very specific domains such as attention or executive function. The causal link is under investigation still.

Professor Jane Raymond: One possibility, although it is somewhat speculative, is there could be inflammation as an underlying mechanism.

Stress, loneliness, sadness, these kinds of thing—bereavement, for example—can cause activation of the immune mechanisms. As the immune system gets older, it does not work as well. This can cause neural inflammation, which has been associated with cognitive problems.

Professor Barbara Sahakian: There are factors to do with stress. One is that when we are under stress we resort to habitual behaviour as opposed to goal-oriented behaviour, where we are trying to solve complex problems, so our performance is less good under stress. Chronic stress is known to damage the hippocampus. The hippocampus is the first area to be affected in Alzheimer's disease. You can see the hippocampus volume gets smaller in depressed people who have been chronically depressed for a long time. Obviously, it reduces in Alzheimer's disease. These can be multiple, repeated effects of stress.

Professor Russell Foster: The relationship between sleep deprivation and stress, again, is quite interesting. If you are sleep deprived, you will be stressed. Short-term stress is a good thing. Long-term stress, as Barbara was saying, is the problem. An analogy would be running an engine in first gear which gives you that immediate acceleration, which can be useful, but if you keep the engine in first gear you are going to destroy the engine. That is what is going on with chronic stress. Many of the things associated with long-term sleep disruption could be attributed to sustained activation of the stress axis.

The Chair: Baroness Walmsley, you had a supplementary.

Baroness Walmsley: I was wondering if you could say anything about positive links with nutrition issues?

Professor Barbara Sahakian: Obviously obesity and diabetes are very strong risk factors for cognitive problems, including dementia. I think the best evidence for better cognition is keeping a healthy diet and exercising, because exercise has been shown to increase neurogenesis in the brain, particularly in areas like the hippocampus. Also lifelong learning is a great way to boost cognition.

Q110 **Baroness Penn:** I should declare an interest as vice-chair of the Specialised Health Care Alliance. You mentioned a couple of factors that are at least correlated, possibly causational, in respect of the change in cognitive function with age. I think I have heard obesity and nutrition mentioned, inflammation and stress and then maybe a less strong association with exercise. Is there anything that is not on that list that I have just mentioned? To go to the end where more causation is known, are there factors or interventions where we know enough about them to recommend them as things we should do to protect against cognitive decline in older age?

Professor Barbara Sahakian: Education and lifelong learning are very important. I was involved in the UK Government Foresight project on mental capital and well-being where the terms "well-being", "resilience" and "cognitive reserve" were of key focus and subsequently widely adopted. When that was launched in 2008, the use of those terms went way up. The project takes a lifetime approach and shows the detracting

factors for mental capital and well-being or cognition and wellbeing and the promoting factors, which are pointed out in blue, across the whole lifespan.[1] Preparing and keeping good brain health is highly important throughout the whole lifespan.

Professor Jane Raymond: Another factor which is perhaps not in people's control so much is exposure to air pollution. High levels of air pollution are associated with high levels of Alzheimer's disease in many cities. Many studies have shown this relationship; whether it is causal is another question but it is related to inflammation, which affects the hippocampus, which affects memory, which affects cognitive health.

Dr Sana Suri: One of the most convincing pieces of evidence from clinical trials of interventions has come from the use of anti-hypertensive drugs to manage high blood pressure, particularly in midlife from the 40 to 65 year age range. In that middle age range, obesity, type 2 diabetes, smoking and high blood pressure stand out as very important risk factors where we can potentially intervene.

Baroness Penn: On that final point, can you help me understand what the link is, or what our understanding of the link is, between high blood pressure or air pollution and decline in cognitive function? What does it do to the brain? What is the link as far as we understand it?

Dr Sana Suri: One of the hypothesised pathways from things that affect the health of the heart and how that eventually starts affecting the health of the brain is via the blood flow, so affecting the quantity and the quality of the blood flowing to the brain and eventually causing damage to the smallest blood vessels that are within the brain. That can have knock-on effects on the health of the brain cells, how they form connections with other cells and the build-up of some of the toxic pathology that we see characteristic of Alzheimer's disease in the form of these two proteins called amyloid and tau, which build up inside the brain cells and around. So there is a cascade of events that are set into motion by some of these lifestyle risk factors that we have just mentioned.

The Chair: Professor Foster, you wanted to come in.

Professor Russell Foster: Yes. I am here as a sleep bore. Essentially, sleep disruption in the mid-years has turned out to be an interesting predictor of dementia in the later years. What is going on is not absolutely clear but, to follow up on Sana's point, beta-amyloid, this misfolded protein associated with dementia is cleared from the brain while we sleep. Sleep-deprived individuals have higher levels of beta-amyloid and, indeed, deposition of beta-amyloid within the brain. I think that is one important association.

Q111 **Viscount Ridley:** Can I press you all a little further on cause and effect here? We all know it is very easy to fall into motivated reasoning and to think that you have found the cause when in fact you might have found the consequence of something. In the case of the correlation between depression and cognitive decline, or sleep and cognitive decline, or

[1] Beddington et al., Nature, 2008

obesity and cognitive decline, how do we know it is the obesity causing the cognitive decline rather than vice versa? Is it possible that the cognitive decline is causing the bad sleep rather than the other way around?

Professor Russell Foster: The model that we use links neurodegenerative disease and, indeed, psychiatric illness, with sleep disruption. Because sleep draws from all the key brain neurotransmitter systems and multiple brain structures, there will be an overlap in those pathways. If there is an abnormality that predisposes you to a neurodegenerative disease, let us say a change in dopamine, or indeed a psychiatric condition, it is going to have an effect upon sleep at some level, so there will be a genetic and mechanistic overlap between the neurodegenerative disease and sleep generation. However, it is more complicated because the disrupted sleep, will distort physiology, both brain function and broader physiology, which will then exacerbate the pathology, whether it be neuropsychiatric or dementia. Of course, those conditions will feed back and further destabilise sleep. So the relationships involves a mechanistic overlap of brain pathways, and positive feedback loops that act to worsen both the pathology and sleep

How do we test that? In the context of psychiatric illness, where we have more data, it is very interesting. Some of the genes associated with sleep and circadian rhythms have also been linked to psychiatric illness and vice versa. We have taken genes that have been linked to psychiatric illness, mutated them in a mouse and found that the sleep/wake is similarly changed.

What does all that mean? We have tried to stabilise sleep in individuals with mild psychiatric illness using cognitive behavioural therapy. When you do that, you reduce the severity of the levels of hallucinatory experiences and delusions. I think there is a very nice bit of evidence to show that distorted sleep is actually exacerbating the condition, but it is not that simple because you have got that overlap in the middle.

Professor Barbara Sahakian: Two of the main ways that we measure relationships between different factors are associative and longitudinal studies where we look, for example whether the depression starts before the dementia and we make the association that that is leading into the dementia in some cases. In these large-scale epidemiological studies we look at what reduces the risk for dementia, such as exercise and similar beneficial benefactors, and also what increases the risk. We are studying associations. In animals you can do more direct studies where you can see new brain cells in the hippocampus due to a rat running in a wheel or a similar type of study, and there speak more to causation.

Q112 **Baroness Rock:** If I may, I would like to direct this question primarily at Dr Suri and Professor Sahakian. What are the distinctions between general cognitive decline and dementias? Are the processes the same but there are different levels of severity, or are the processes very distinct? Can general decline turn into dementia? Why has there been seemingly slow process in developing treatment for dementias? What are the main barriers?

Professor Barbara Sahakian: What happens first in Alzheimer's dementia, which is the most common form, is that you will get changes in the hippocampus. We heard about the tangles and plaques. There are problems in episodic memory. Basically that is trying to remember where you left your mobile phone in the house or where you parked your car in a multi-storey carpark. It is that type of problem. Those are the first ones to appear.

Slowly, it spreads out to all sorts of other types of cognitive problems. But the CANTAB PAL test, which I have developed for early detection in memory clinics, looks specifically at that type of memory because it is the first one to change. Later you get a more global pattern. In some of the other dementias the changes may start in more frontal-striatal areas so there might be changes in executive function. In Parkinson's disease, for instance, you might not see the changes in the episodic memory test but you will see them in cognitive flexibility and that type of cognitive domain. That will be the first change, but slowly the brain gets affected and there are problems more generally. Slowly, as the whole brain gets affected, the dementias blend much more but they start in different areas of the brain and so you can see different cognitive patterns early on which are more specific to that type of dementia. You can also see that using imaging studies.

I actually did one of the first published studies in the *Lancet* with Raymond Levy and others. We had one of the first memory clinics. We looked at the cholinesterase inhibitor drugs. Those are drugs like Aricept, which is now approved by NICE for the treatment of Alzheimer's disease. We published that in the *Lancet* many years ago. When I did that study, I was hoping it was going to lead to a great improvement in episodic memory. All we saw was improvement in attentional function and that was what we more or less reported. Those drugs have not turned out to be as exciting as they might have been. They are still very useful and keep people out of institutionalised care for longer. Even people in institutionalised care who have the drugs, if they have been on them since the start, tend to perform better and have better cognitive function. We need more effective treatments. We need ones that are actually improving this episodic memory problem.

The trouble is that the FDA and the EMA wanted everyone to work on severe and moderate Alzheimer's disease to start with, so the clinical trials were in these more advanced patient groups. By that time there is such severe damage to the brain that a drug is not going to be able to work through a system with that much damage. Therefore, the trails were never very successful with any of those treatments.

There is a drug called Modafinil, which I think should be tried in clinical trials in Mild Cognitive Impairment. It is reasonably safe. Healthy people are using it all the time to boost their cognition. I have reported on Modafinil as an add-on to antipsychotic drugs in schizophrenia. A lot of my colleagues who are neurologists use it as an add-on in Parkinson's disease. We have also looked at it in depression. We were trying to help people get back into work. People recovering from depression still sometimes have residual cognitive problems. There are potential drugs

out there but I think, unfortunately, most of the pharmaceutical companies have left the field of psychiatry. Some of them have left the field of Alzheimer's disease as well. At present there are not many new possibilities, due to reduced novel drug development.

The Chair: Dr Suri, you wanted to come back to the original question.

Dr Sana Suri: On your question about the distinction from normal cognitive decline in ageing, dementia is a very distinct process from normal ageing. It is not a consequence of just getting older. There is a very distinct biological pathway that differentiates dementia-related cognitive decline with the normal cognitive decline that we will experience when we get older.

As we get older, we experience a reduction in our mental abilities and our neural resources. Our memory can be affected, reaction times, processing speed, but not to the extent that they will interfere with our activities of daily living or our ability to carry out those activities independently. For example, we will still be able to wash ourselves, to dress, feed and get from A to B.

In dementia, these cognitive declines become progressively worse with time such that eventually they begin to interfere with our ability to perform functions independently. That is because of this very distinct biological cascade that is taking place within the brain cells and around them. They are distinct processes.

Professor Barbara Sahakian: The first cognitive domain that declines in normal ageing is psychomotor slowing. The first cognitive domain that declines in Alzheimer's disease is episodic memory.

Baroness Rock: That is very helpful. Thank you.

Q113 **Viscount Ridley:** I have been reading some very strongly worded articles in the medical literature and in popular literature criticising Alzheimer's research for focusing on possibly the wrong issue for a long time. The amyloid hypothesis has become such a paradigm that people who think that it is a symptom not a cause of the problem are being ignored and are not being funded et cetera, and if we had been more open to other hypotheses over the last 20 to 30 years we might have made more progress in drugs on Alzheimer's. Do any of you share that criticism? Do you feel it is valid, or do you think it is too strong? I am looking particularly at Dr Suri because of the Alzheimer's Society link, but all of you are welcome to answer.

Dr Sana Suri: I think it is a failing. When you have been looking at clinical trials from 2002 to 2012, 99.6% of clinical trials have failed and there have been no new drugs on the market. A lot of these clinical trials have focused on amyloid. It is time for us to broaden our scope of the clinical trials, to diversify the targets to make sure that we are looking not only at this one protein but a lot of the other pathways that precede the accumulation of that protein, such as inflammation, sleep stress and, importantly, vascular risk and blood flow to the brain as well. I think that is a concern that we need to be addressing in future clinical trials.

Professor Barbara Sahakian: We need to focus on mild cognitive impairment, the very earliest stages of Alzheimer's disease where people have these more specific problems and where you might be able to delay the onset for a long time. Whether the treatment is symptomatic or even halts the underlying disease process it is important to treat early when there is still intact functioning of the brain. It is important to detect early and treat early and not wait until the damage is done in the brain and is going to be hard to repair.

Dr Sana Suri: I want to point out that dementia is not something that just happens overnight. It is a disease that takes 20 to 30 years to start having effects. We start seeing clinical symptoms only at the very terminal end of the disease. There is a very valuable window of opportunity in our 40s, 50s and 60s where we can intervene—yes, as early as our 40s, 50s and 60s—to try to slow down, as Barbara was talking about, the progression of this protein deposition.

Professor Russell Foster: To touch on the vascular issues, I think the estimates are about 80% of people with dementia will also have some sort of sleep-related respiratory problem, such as obstructive sleep apnoea. Obstructive sleep apnoea is when the musculature of the throat essentially collapses while you are asleep and you deprive the brain of oxygen. The brain realises this and then wakes you up. You gasp for air and you have these great snoring and gasping sounds. There is a huge surge in blood pressure and that may well be associated with damage to the small blood vessels. There is an interesting correlation there.

The Chair: How strong is that correlation?

Professor Russell Foster: From my reading of the literature, about 80% of individuals with dementia will have some form of sleep related respiratory problem. It is not finely classified in terms of obstructive sleep apnoea versus other breathing problems.

Lord Winston: Is there histological evidence of damage to red blood vessels at that stage?

Professor Russell Foster: My knowledge is from the eye where you can actually see the breakdown of the small vasculature in the eye with sleep apnoea.

The Chair: You have caused a lot of excitement. Lord Kakkar, Baroness Young, Baroness Walmsley.

Q114 **Lord Kakkar:** If I might just return to the question on the distinction between the physiological decline of old age and the cognitive decline of Alzheimer's pathology or dementia pathology, is there still an important research effort associated with understanding better the so-called physiological decline that is age related? How much are we able to characterise that and predict that for the individual and therefore help potentially to intervene and to limit that physiological process?

Professor Barbara Sahakian: That is a great question. We do not have a lot of data on an individual level. We mostly have group data showing that it is psychomotor slowing which is the first hallmark of the ageing

process. I suppose it would be relatively easy, as we do with the CANTAB test, to measure psychomotor speed and refer back to the normative data, so there is a big normative database. After conducting the test you would be able to establish whether an individual is performing within or below the norm relative to people of the same age, education and IQ level. This method could indicate whether someone is a fast decliner. You could easily do that using the measures that we have.

Usually part of the problem is that we are keen to measure our physical health with Fitbits and all sorts of wearable devices but people do not usually think about their well-being and cognitive health. We need to think more about monitoring our cognitive health. Usually people do not come to clinics until, as we have heard, they have declined quite a lot and we can see that they are already in a state that is beyond the normal ageing process.

Lord Kakkar: Has that psychomotor decline that we might term physiological been related to quality of life in any way?

Professor Jane Raymond: We have been doing some studies on younger people who are obese and also show high levels of inflammation. Their psychomotor slowing is about the same as an old person. A young 35 year-old who is obese looks like a 65 year-old in terms of psychomotor slowing. It is possible that they also are at risk, so in terms of future generations—we know we have a high problem with obesity both in childhood and young people nowadays—what they are going to be like when they are old is quite worrying because of that. If it is progressive and their psychomotor slowing is distinct now it can progress.

Also people are aware that in their daily life their cognitive function fluctuates: "I'm really tired today" or "I'm a bit worried" or "I'm a bit distracted". We are accustomed to some fluctuation but it is the notion that the fluctuations are following a mean change that we do not measure and it would be good if we did, I think.

Q115 **Baroness Young of Old Scone:** Can I go back to one of the points that Baroness Penn raised? We have not had any new drugs. There are some treatments that you have described. Are we not spending enough on this area? Are we not focusing on the right issues? What are the barriers to more successful research in the area of ageing and dementia?

Dr Sana Suri: One of the barriers is funding. There is one dementia researcher for every four cancer researchers. We do face a shortage of brain power that is invested towards dementia. We face a shortage of funding as well. The annual cost to society for dementia is £10 billion more per year than cancer, yet we do not receive as much in funding. One of the ways in which we are able to target these barriers or challenges that researchers face currently is with more investment into funding.

The Chair: Professor Foster?

Professor Russell Foster: Again, within the context of sleep we know that there is a correlation between disrupted sleep and the development

of dementia. Poor sleep in the middle years can predispose you to dementia- it's a clear risk factor. The trouble is that across society in general we have marginalised sleep. Around 36% of our biology is sleep biology and in five years of medical training a medic may get one or two lectures in that area. The importance of sleep in underpinning many of the issues that we have talked about is largely disregarded. I think we must embed sleep research in medical training.

Professor Jane Raymond: Another answer to this question is that the understanding of cognition remains fuzzy. There is a tendency among the medical professions to use off-the-shelf tests which are rather crude and may be good for diagnosing stroke and simple things, but for some disorders like Alzheimer's and understanding the progression of age-related decline, we need very sensitive tests to measure people's responses to situations.

Professor Barbara Sahakian: I have to challenge that. We have sensitive tests and there is nothing fuzzy about measuring cognition.

Q116 **Baroness Walmsley:** If there are people walking around at 40, 50, 60 with early onset Alzheimer's or other kinds of dementia, how on earth are we going to know which 40, 50 and 60 year-olds? Is there a case for some kind of screening? Can I also ask about cognitive reserve, and do you all agree what it is? Is it just education? Perhaps you could say something about that as well.

Professor Barbara Sahakian: Cognitive reserve is a combination of your genetics and your education. IQ comes into effect here and that is blending with genetics but education is very important. It has been demonstrated in many ways. It is preventative. If you have a high IQ or good education, if you develop Alzheimer's disease or schizophrenia, if you get a traumatic brain injury, you are protected from the worst outcomes of that. For instance, in schizophrenia, your cognitive performance is better. In traumatic brain injury, you are less likely to get depression. In Alzheimer's disease you will be able to find strategies to overcome the damage in the brain for much longer.

The Chair: So there is such a thing as a cognitive reserve that individuals have?

Professor Barbara Sahakian: That is correct.

Q117 **Lord Hollick:** Professor Raymond, I would like to come back to your comment about Fitbits. To what extent does wearable technology give us the opportunity to get any early clues as to cognitive decline?

The Chair: You might include in that also motoneuron or psychomotor movement.

Professor Jane Raymond: I think wearable technology has helped people to monitor their sleep, for example, helped them monitor their nutritional state, even their heart rate, that sort of thing. We do not use those things now to measure how quickly you can add to numbers or how

quickly you can come up with the names of three countries or something like this. That might be a measure of speed.

Professor Russell Foster: Most of the commercially available devices to measure sleep are very, very poor. What they are good for is telling you roughly when you went to sleep and when you got up. Their analysis of slow-wave sleep or REM sleep is bordering on the nonsense and can actually be very misleading. I had somebody come up to me after a public talk recently to say, "I'm not getting any slow-wave sleep so what I've decided to do is wake myself up at 4 am and check how much slow-wave sleep I'm getting". It is causing huge anxiety. Whilst the devices we are using in the lab are very effective, most of the commercially available devices are not and my recommendation is not to take them too seriously beyond providing information of when you sleep and wake.

Professor Jane Raymond: But that is useful to people because it helps them behave well.

Professor Russell Foster: Yes, but they are not told that the other metrics are nonsense.

The Chair: Presumably there are no apps for psychomotor slowing either.

Professor Barbara Sahakian: There is a company called Peak in London which is a games based company has and we have technology-transferred some of our games for cognitive training to them. Both Peak and our group are measuring psychomotor reaction times as people learn these tasks. We are looking across the adult lifespan up to 80 years of age.

Lord Browne of Ladyton: There has been an explosion of available technology in relation to wearable devices, apps, whatever. Whatever we think of them as to how to monitor your physical health, lots of people seem to find them helpful, including people in this room. Apart from that one example you gave us, is anybody looking to see if this technology can be developed in some way—an app to see if we can make people monitor their cognitive ability and health?

Professor Russell Foster: Potentially they could be very useful. In the same way if you want to lose weight you change your eating behaviour, you measure your weight in the morning, you see that there has been a change of weight and that reinforces your new behaviour. They could be very useful. Those of us who have engaged with that sector have had our fingers burnt.

One group we worked with was Jawbone. We had a signed agreement between the University of Oxford and the organisation to provide the raw data so that we could do objective analysis on those devices, and they reneged on the deal and never supplied us with those data. If the device companies would engage properly with the scientific community, they could become useful devices but at the moment the commercial drive is such that they will not because they are terrified of us turning around and publishing something saying the device is nonsense.

Professor Jane Raymond: There are cognitive training games that people play that are apps. The evidence that they work is pretty fuzzy and not very clear and is questionable. Those are both good and dangerous at the same time. The one thing that we have not talked about at all is brain stimulation, which is adding electricity to the brain as another method for improving function. There is some evidence that that might work, especially if it was in conjunction with certain kinds of mental activities.

Q118 **Baroness Manningham-Buller:** I want to come back to sleep because I have always been fascinated by your research, Professor Foster. We have covered quite a lot of this issue already in answer to other questions. You talked about the parameters of sleep as we grow older. Is it understood why quality of sleep does decline? None of us, I think, on this Committee is yet at the 90s stage where we will have no deep sleep, according to you, but why will we have no deep sleep in our 90s? Is it understood why quality of sleep does decline at this stage? Some of us on this Committee, not all of us, are young.

Professor Russell Foster: Not in great detail, no. There is quite a bit of handwaving. For example, it is thought that the circadian system becomes less robust. What does that mean? The amplitude, the power of the clock driving the timing of sleep wave may be diminished. There is some reasonable evidence for that. One area where there is good data is the input of light into the circadian clock systems. What you need is light to set the internal clock which can instruct the timing of sleep. There is evidence that the light input to the circadian system diminishes with age.

For example, a colleague of mine in the Netherlands went into the nursing home environment, increased the amount of light in the day areas and provided darkness in the bedrooms, and improved the robustness of the sleep/wake cycle and with that got a 10% increase in levels of cognition.

Baroness Manningham-Buller: Is that at any age?

Professor Russell Foster: This study was in the aged.

Baroness Manningham-Buller: It would also apply younger presumably?

Professor Russell Foster: Absolutely. In fact, some of the instructions that we give to our young adolescents, is to get exposure to light in the morning and again around dusk, and this will help stabilize the sleep/wake cycle. Returning to the topic of why sleep changes and why the aged experience less or no slow-wave sleep is not clear. The only thing I would say is because sleep is the integrated product of all the neurotransmitter systems and multiple brain structures, sleep is a very good metric of overall brain health. As these systems start to fall apart as we age, it is perhaps no surprise that sleep changes and that the structure of the sleep/wake cycle and, indeed, the stages of sleep become disrupted.

Baroness Manningham-Buller: You have been a leader in this area for

some time. Where do you think the gaps in the research for the effect of sleep on ageing are most acute or indeed any aspect of that?

Professor Russell Foster: I think low-hanging fruit would be education and education right from the beginning, starting in adolescence and then reinforcing the importance of sleep education through the middle years and into old age. Many feel they have no control over their sleep. For example but cognitive behavioural therapy for insomnia (CBTi) can be very effective in allowing us to take some ownership of our sleep and to stabilise it. In terms of healthy aging, a key bit of data for me is that poor sleep in the middle years leads to a greater risk of dementia in the later years, so sleep education before we get old is critical in my view

In terms of fundamental research, like all of us, I suspect, it is high-resolution, longitudinal studies correlating ageing, dementia, cognition and sleep using a battery of high-resolution assays. We have databases, such as the 100,000 genomes project, for example, at UK Biobank, but, as Barbara and I were discussing outside, the assays for sleep are very poor as are the assays for cognition. Actigraphy, and objective measures are being introduced on a limited scale, and this will be very helpful. Also we should not forget that to understand fundamental cellular and molecular mechanisms, we still need to use animal models.

Baroness Manningham-Buller: Lord Kakkar will be thinking about Biobank and your answer on that and obviously the 100,000 genomes. Apart from education on light and things and education generally, particularly in the ages of the middle years, are there other pieces of advice for an ageing society to help people improve the quality of their life? You mentioned education but are there other things, apart from education and light, that you would add as a priority?

Professor Russell Foster: Other approaches for stabilising the sleep/wake cycle include, trying to go to bed and get up at the same time every day. Eat at the same time every day. Eating at the same time is a very good consolidator of the circadian system. We talked a little bit previously about diet. One of the things about diet and sleep loss that has turned out to be very interesting is that disrupted sleep can actually influence the sorts of things we eat, not least make us more likely to eat sugar

Baroness Manningham-Buller: And lead to obesity?

Professor Russell Foster: Absolutely - And lead to obesity. It is also worth pointing out that sleeping tablets are frequently given for insomnia in the elderly. Many of the sleeping tablets, Z-drugs for example, can cause some daytime sleepiness. Falls represent the greatest risk in the aged for both death and harm. It may well be one of the unanticipated actions of taking sleeping tablets at night is to cause daytime sleepiness and increase falls. It is all about connecting these bits of information together and making a coherent educational programme for our medics about sleep, allowing them to recommend more appropriate actions.

Professor Barbara Sahakian: Cognition at work is affected by poor sleep. Lord Ara Darzi and I conducted a double-blind placebo-controlled trial on surgeons where they were sleep deprived overnight.

Baroness Manningham-Buller: I do not think we want necessarily, Professor, to hear the answer to this question. Certainly none of us who is thinking of going near a surgeon in the near future.

Professor Barbara Sahakian: The doctors were not practising on people. We studied them after Modafinil because Lord Darzi was concerned that the doctors were taking excessive amounts of caffeine and might have hand tremor which is bad for surgery. We found that Modafinil improved cognitive flexibility and reduced impulsivity and in addition, their problem-solving was better. Therefore, there are some drugs that can be used to improve performance when people are sleep deprived.

Professor Russell Foster: Short-term use, Barbara, would be fine. I think the worry would be if it becomes sustained. Do you want to comment on that?

Professor Barbara Sahakian: I would not recommend it for everybody. There are occasions when people are operating on people at night and it might be better to have the best and safest method of keeping yourself awake. We know that Modafinil is used in the military as well, for keeping them awake and alert in war zones.

Professor Russell Foster: Just to give you some sense of cognitive impairment after the night shift, 57% of junior doctors in a recent study admitted to either having had a crash or near miss on the drive home after the night shift. We provide no help for those individuals at all.

The Chair: Professor, there are lots of jobs—you mentioned junior doctors—who for many, many years are sleep deprived based upon what their specialty is. Is there any evidence that there is a higher linkage in those jobs?

Professor Russell Foster: Huge.

The Chair: Be careful because Lord Winston and I fall into that category.

Baroness Manningham-Buller: I do not think you should take it personally, Chair.

Professor Russell Foster: Short and disrupted sleep as experienced by night shift workers is associated with a range of problems: cognitive impairment, increased impulsivity, cognitive decline, obesity.

Professor Barbara Sahakian: Shorter lifespan.

Professor Russell Foster: Shorter lifespan. It goes on and on.

The Chair: Thank you.

Viscount Ridley: Can I just say that I think there is nothing wrong with the cognition of our Lord Chairman?

Baroness Manningham-Buller: Or indeed Lord Winston.

Q119 **Viscount Ridley:** Or indeed, Lord Winston. Sorry, I did not mean to leave him out. If somebody is a junior doctor and goes through a period of sleeping very badly or, indeed, for other reasons has a period in early middle age when they are chronically insomniac and cannot solve the problem, and then they get over it and get better, are they going to be all right or is the damage set? You have slightly talked as if this problem always gets monotonically worse as you get older. I know from personal experience that is not true. I want to know that if one has been through a bad experience in early middle age and then one has solved it by various means, is that okay? I am asking for a friend.

Professor Russell Foster: That is a key question. From the sorts of studies that I am aware of, it is completely variable. Some individuals report never recovering from a sustained period of nightshift work; others are fine. The worry about these sorts of self-reported problems is that the tired brain is so tired it cannot detect how tired it is. So one's ability to assess one's level of tiredness or incapacity is very poor.

The classic study is on taxi drivers: "Do you find working on the nightshift is any problem?" "No". Fine. But bring them into the lab and test this assertion by doing cognitive tests including reaction times and the drop in performance is very marked. There are small subsets of individuals who are late types because they have gene polymorphisms that make their clock late. Indeed, these individuals would be very well suited to the demands of the late shift – but not the early shift! However they represent a rather small percentage of the population. So not everybody will be equally affected by night shift work.

Professor Barbara Sahakian: I would just say that fortunately our brains are still plastic. We have the best plasticity in the brain when we are younger, but you can overcome these problems and be fine again. Some of them.

The Chair: I excluded Lord Kakkar from my comment because of his extreme youth. Can I move on to Baroness Young?

Baroness Young of Old Scone: What we should be asking is: is the fact that we work late, until 10 pm, in this House a bad or good idea?

Professor Russell Foster: I would love to do a study on you, and other members of the Upper House, if that is at all possible.

Baroness Young of Old Scone: The question I wanted to raise is are we at risk of exacerbating this issue of sleep with the introduction of screen time, with so much blue related light from artificial screens?

Professor Russell Foster: There is confusion here. The data recently from Glasgow has shown that extended screen use, whether it be from apps or e-books or whatever, can certainly shorten sleep and therefore increase daytime sleepiness, but it is probably the use rather than the light. We are the group that discovered the fact that there is a third receptor system in the eye sensitive to blue light. Our findings have been used for apps, which shift our screens from blue in the daytime to red at night so that we do not shift the circadian clock.

First of all, these devices give out so little light they are probably not shifting the clock at all. In fact, a study from Harvard showed that four hours of continuous use of an e-book on its brightest intensity over five days, so four hours, five consecutive days, delayed sleep onset by 10 minutes. That is statistically significant but biologically meaningless. There is a lot of misinformation out there. It is the use rather than the light from those screens that is almost certainly the problem. We need more data, but that would be my view. We know that ebooks or tablets give out something like 30 lux or so. To get a robust entrainment of the clock you need 1,000 or 2,000 lux. So I think it is their extended use, rather than light, that is the problem.

It is very interesting that the Glasgow study showed that teenagers who were using these devices into the early hours were terribly anxious about missing out on what was going on within their social cohort.

Professor Barbara Sahakian: There is an excellent book called *The Distracted Mind* by Adam Gazzaley and Larry Rosen. It gives the evidence for the fact that the use of technology, that we have so much of, is making us have problems with focusing our attention for long periods of time, getting big jobs done and staying in the flow. We get distracted too easily by messages coming in from different places and wanting to check our phones, as teenagers do, that we are having trouble focusing attention. I have actually devised an app for helping to focus attention. I hope to try to use it with ADHD children.

Lord Kakkar: Just on that point, is there evidence that maintaining that capacity to focus for a long period of time has an impact on long-term cognition and cognitive decline or physiological decline?

Professor Barbara Sahakian: The main importance in regard to focusing attention is it is hard to be creative and come up with new ideas and actually trying to generate solutions if you are constantly shifting your attention from one thing to the next. The idea is that, if you want to obtain a large goal, if there is a big project, if you have to think of a novel way of solving a problem, something creative, this short attention span is not helpful.

Lord Kakkar: Over the long term does it have an impact? Has anyone ever studied that?

Professor Barbara Sahakian: I do not think that people have looked at it over the long term yet, but there is potential to investigate this in with these new studies.

Professor Jane Raymond: It is a general barometer of good cognitive health that you can focus and maintain focus in the face of distraction. Often we measure distraction or distractibility as a metric for how good a person's cognitive ability is. Certainly as people get older they are more susceptible to distraction. This is another metric. People who have the ability to stay focused generally do well on educational measures because they can consolidate information well and can manipulate it in their mind.

Professor Russell Foster: Again, sleep will diminish your ability to focus and will affect those conditions.

Q120 **Lord Browne of Ladyton:** If I may, I want to direct this question to you, Professor Raymond, and I think the reason will become obvious. Apart from what we have already touched on today, we have had quite a lot of evidence about the role of inflammation in several age-related diseases. How can you help us better understand the impact of inflammation in cognitive function and mental health?

Professor Jane Raymond: Inflammation as it affects the brain seems to affect the hippocampus which may be related to problems in memory but it also can affect the basal ganglia. The basal ganglia are a set of neural structures that help to co-ordinate our mechanisms for learning and our motivation. There are many people who view age-related cognition problems as problems of motivation. People think, "Oh, it's too hard to learn a language" or "It's going to be too difficult to play that game of solitaire" or "It's too complicated". They assess the cost of engaging in this activity and think it is too high and do not put the effort into it. Motivation may be a fundamental problem here. If people can get over that somehow and do it anyway, they can get through some of these things.

Reward learning and dopaminergic systems are probably upset by inflammation. This may be a key mechanism that affects a wide range of cognitive functions. We know that lifestyle behaviours—excessive food intake, obesity leading to diabetes, smoking, alcohol and exposure to air pollution—cause increases in inflammation over the lifespan.

Certainly people who have disorders like arthritis or who have an organ transplant also suffer from high levels of inflammation, which they often refer to as "fuzzy brain". Fuzzy brain is a hard thing to describe and cognitively it is very difficult to measure. Our work suggests that it may have to do with the business of effort. If you give a person a task and they are suffering from a fuzzy brain syndrome, they can do the task but they cannot do it over and over and over again; they just cannot sustain it. They can rise to the challenge for the short run, but they have to put so much more mental work into doing the task that after a while they cannot sustain it.

Inflammation may produce this sort of mental fatigue. I think as people get older they recognise how much budget they have for mental effort. They can spend it now or they can spend it slowly or at once, but they know they are going to be tired at the end of it. This understanding of your mental budget is part of ageing and inflammation may make that more difficult.

Q121 **Lord Kakkar:** I should declare my interest as chairman of UK Biobank. Coming to this question of inflammation, we often hear talk of the description of the inflammasome and the capacity to potentially more objectively characterise systemic inflammation. Has that been done? Do you think we are at a place now where we can do that and have an objective measure that we can relate, for instance, to cognitive function? Indeed, is it possible or has it been done that we look at that in a large cohort at baseline, a group that had been followed over a period of time, to start to develop predictive correlates of early systemic inflammation

and cognitive function?

Professor Jane Raymond: I think that would be a great thing. I am not an immunologist so I cannot really speak to these kinds of questions, but it is getting cognitive psychologists and neurologists/neuroscientists working with the immunologists where we would make great strides. We are trying to do that now. It is all about team science really.

Lord Kakkar: Are there the mechanisms to bring those groups together?

Professor Jane Raymond: Yes, I think so. Those exist.

Lord Kakkar: Good.

Q122 **Baroness Young of Old Scone:** The Government's industrial strategy, under the Ageing Society Grand Challenge, has got as its objective ensuring five more years of healthy life by 2035. Have you seen great new opportunities open up to your areas of expertise and research as a result of the grand challenge? Or is the grand challenge missing the point on cognitive health?

Dr Sana Suri: I think that the target of five more years of healthy life by 2035, as it relates to cognitive health, is quite ambitious, but we need that kind of ambition to make strides in this field. We know that as it relates to dementia, if we can delay dementia onset by those five years it means that it is going to have an enormous impact on quality of life because more people will reach end of life without developing dementia.

It is a very ambitious target but one that is definitely needed. In order to accomplish that target, I think what we need are larger clinical trials that have very long follow-up periods so that we can actively measure cognitive outcomes over a sensible period of time and trials that are more diverse in their targets, so looking beyond amyloid and looking into some of these inflammatory and genetic pathways that we have talked about today.

Professor Barbara Sahakian: I would like to see more technology being used in mental health and also in ageing in dementia. There are some companies that are developing monitors where you can test yourself using a watch, such as Cambridge Cognition in Bottisham, and a company in Oxford. There are ways to monitor yourself online. We should get the idea into people's minds that they should be trying to track their good mental health and well-being. It has been shown that good cognition is coupled with good well-being. Both of these are coupled with GDP. I think it would be a very good way to stimulate both the economic situation but also to reach the goal you are talking about of better brain health over five more years by using some of this technology and integrating it into daily life.

Professor Jane Raymond: One thing we have not discussed much is the effect of loneliness and social isolation which is possibly related to inflammation. We did studies where we gave people a typhoid vaccine. If they were lonely, they showed much more inflammatory response than if they were not lonely. Loneliness is a very important issue and is something that people can do something about and Government can do

something about by assisting and providing funding for social programmes so that people, as they get older, are not so isolated. This could be a big advantage. It is very doable.

Dr Sana Suri: There was a point raised earlier about screening populations to try and predict who's likely to develop Alzheimer's disease when they are very young, even in their 40s and 50s. I think that would help with a strategy that is aimed at improving quality of life. Currently, there are some efforts in this area.

The Deep and Frequent Phenotyping study and the Prevent Alzheimer's study are currently running in the UK that are aimed at trying to identify ways to predict who is going to develop cognitive decline and who is going to age healthily, so we can carefully select people into clinical trials that are targeted at specific interventions that they might need. That is another area we would need to focus on to have this improved quality of life.

Professor Barbara Sahakian: Even that study could use better resources.

Dr Sana Suri: Absolutely.

Professor Barbara Sahakian: It is stretched to the limit.

Professor Barbara Sahakian: Absolutely.

Baroness Young of Old Scone: You are saying the things that could happen and should happen, but I would like to ask: is the grand challenge on healthy ageing making them happen?

Dr Sana Suri: It has brought a lot of national focus on dementia. We can see there has been a tremendous improvement in dementia resources, funding and research on ageing. I think what we need to focus on going forward is to keep this momentum going. It has been valuable to have dementia brought up to the policy focus like this. I want to be cautiously optimistic that this level of interest and enthusiasm in ageing will continue.

The Chair: Dr Suri, is your association involved with the Government's challenge?

Dr Sana Suri: The Alzheimer's Society and Alzheimer's Research UK are involved in making policy.

The Chair: In what way?

Dr Sana Suri: I am not entirely clear about the specifics of that because I do not work within those organisations, but I am happy to feed back with a written response after I consult with them.

Professor Russell Foster: On the basis of what we know in terms of the impact of sleep on ageing and dementia, we could institute some things now that would change life course history. I think that is doable within a relatively short period of time on the basis of existing evidence.

There are three key questions that I think we need to fundamentally address going forward. One is the impact of the type of sleep problem

and the risk of the type of dementia that you will develop, so cause and effect associations. The second is: how does the co-occurrence of a sleep problem and dementia affect the trajectory of the conditions? Does poor sleep of a particular type increase the trajectory of dementia, for example? The third is: if we treat sleep, and think of sleep as a therapeutic target, will we reduce levels of dementia in later life – but we need to know when, what age, and how to treat sleep.

Those are the three areas where we need more resolution in terms of sleep and aging.

Lord Hollick: Which countries, in your view, are tackling this multifaceted issue most effectively and why?

Professor Barbara Sahakian: The United States has the ABCD study. It is a large cohort, as you know, that they are following up. The study started with a cohort at nine to 10 years of age and they are following them up for 10 years. It is a huge sample (~10,000) and the resulting data are open source. Lots of researchers are already accessing that data. The study has a lot of rich data, but unfortunately, is missing data on their educational and school performance.

China is doing extremely well. Singapore is engaged in a large-scale project where they are trying to develop a better form of education within the country. Both China and Singapore are putting a lot of money into research including in the area of education and life-long learning. In China, in particular, there are large cohort studies of the elderly to investigate dementia. They are very interested in cognitive function in both those two countries and I think the studies are going to be extremely useful and informative.

Dr Sana Suri: There is a very promising trial that has come out of Finland called the FINGER trial. That is a two-year, long-term randomised control trial that has looked at these multiple interventions of diet, vascular risk, exercise and social isolation as well. They found that people who received these interventions had beneficial effects on their cognition compared to those who did not. That is one of the most promising recent clinical trials that we have seen that has approached this from multifaceted targets.

The Chair: We have heard in evidence before that what will drive more around the issues related to age, including research that some of you have brought out, would be a suggestion that there ought to be a Minister for the ageing population. The second is an institute that co-ordinates all the issues of development, research, technological development, et cetera. Would you have a comment about that, each one of you?

Professor Barbara Sahakian: I think it would be great to have a Minister for the ageing population. What I would say about an institute is that it is always good to have an institute, but researchers have different expertise in different city in the country. We have experts in sleep research in Oxford and experts in cognition in Cambridge. Unless there is some other way of dealing with how you pool all these resources into one

place, it is better to almost have a virtual institute where different research centres have the money but are investigating different aspects on the same population.

Professor Russell Foster: Ways in which virtual institutes work, and I would support a virtual institute for ageing, would be joint post-doctoral scientists, PhD scientists and, indeed, educational programmes whereby the PIs would work together as a result of their collaborative interactions. That does work, I think.

The Chair: Who will co-ordinate this virtual institute, apart from you?

Professor Russell Foster: I guess after consultation with the community - I am sure we would come up with a suitable Director.

Q123 **Lord Winston:** I have a couple of supplementary questions I would quite like to ask Professor Foster. One is: have there been any randomised control trials of what is called chromotherapy, i.e., changing the light? We tend to keep older people in quite dim lighting quite a lot of the time. The other question I want to ask you is about anticholinesterase drugs? Would you like to comment on that?

Professor Russell Foster: If we kick off with the anticholinesterases, that is really interesting. Barbara touched on these. What they do is drive up brain acetylcholine. Brain acetylcholine is one of those neurotransmitters that keeps us awake. It is also very interesting because it is one of the neurotransmitters that is turned on at high levels during REM sleep. If you take your cholinesterase inhibitors in the morning, it is fine and you improve cognition, but there has been a tendency to say, "Well, they may cause you some nausea so take them before you go to bed".

We worked with Gordon Wilcock, for example, and we saw that when the cholinesterase inhibitors were taken before bed, the structure of sleep, and REM sleep in particular, was completely disrupted. One of the primary reasons for people taking themselves off these drugs is vivid and unpleasant dreams, so presumably they are interfering with REM sleep which is when we have our most vivid dreams. This highlights the point that taking drugs at the right time is critical. Again, that message is somewhat blurred.

Professor Barbara Sahakian: As they are supposed to improve your attention and cognition, I think using them during the day is better.

Professor Russell Foster: And the other question, Lord Winston?

Lord Winston: Chromotherapy.

Professor Russell Foster: And randomised control trials. For light, no not really. Where we do have a randomised control trial, which was led by Dan Freeman in Oxford, was on the use of cognitive behavioural therapy to reduce insomnia and looking at the impact of that in almost 4,000 university students. The results showed digital CBT was very effective at reducing levels of insomnia and that correlated with a reduction in hallucinatory experiences and delusion. Randomised

controlled trials are relatively rare, and you are right, this is clearly the gold standard, but they are difficult, particularly in getting large numbers of participants.

The Chair: On that note, thank you very much. We have slightly overshot our time, but we are very grateful to you for coming today. We will send you the transcript of this session and if you have any corrections, please do so. If, on second thought you have some important information that you failed to give to us, please send it to us. We welcome that. Thank you again.