A video interview with Professor Norman Rosenthal held on 21 July 2014, Queen Mary University of London.

Professor Norman Rosenthal MD (b. 1950) was born in Johannesburg, South Africa. He graduated as a medical doctor with high honours from the University of Witwatersrand in 1973. He immigrated to the United States, where he did his psychiatry residency and became Chief Resident. In 1979, he joined the National Institute of Mental Health in Bethesda, Maryland, where he became first a research fellow and later a tenured researcher. It was there in 1984 that he led the team that first named and described Seasonal Affective Disorder (SAD), and pioneered the use of light therapy for its treatment. The paper subsequently became a citation classic and has been cited well over 100 times. He has authored or co-authored hundreds of subsequent papers on SAD, light therapy, and related topics. Along with colleague Thomas Wehr, in 1991 he was awarded the Anna-Monika Prize for depression research for his work in this area. He is also a best-selling author, whose book Winter Blues, now in its fourth edition, has been described as 'a classic work' by the New York Times. He has also written seven other books for the general public. He is currently Clinical Professor of Psychiatry at Georgetown University. He maintains a private practice in Bethesda, Maryland and continues to research innovative treatments for depression and other psychiatric disorders.

Interview conducted by Professor Tilli Tansey, for the History of Modern Biomedicine Research Group, 21 July 2014, and transcribed by Ms Debra Gee. The unedited transcripts will be available to study in the Wellcome Library. The video recording and a link to a podcast can be found http://www.histmodbiomed.org/article/sad-30. A related interview with Professor Josephine Arendt can be fund http://www.histmodbiomed.org/article/sad-30. A related interview with

<u>http://www.histmodbiomed.org/article/josephine-arendt</u>. Funded by a Strategic Award to Professor Tilli Tansey from the Wellcome Trust.

01. MOVING FROM JOHANNESBURG TO NEW YORK CITY. NATIONAL INSTITUTE OF MENTAL HEALTH. PERSONAL EXPERIENCE INFLUENCING CHOICE OF RESEARCH.

When I moved to United States from South Africa, I arrived in New York City in 1976, I expected a lot of things to be different. But the one thing I didn't really count on, which turned out to be one of the biggest differences, was the light. In Johannesburg, which is much closer to the equator than New York City is, the days in winter were not that much shorter than the days in summer, because it's closer to the equator. And when I arrived in New York City the days were long, it was in the middle of the summer, and I seemed to have boundless energy and it seemed like just the place to be. But after the daylight saving time change suddenly a sort of fear hit me, that first day when the afternoon was dark so early. And then winter came and suddenly I had a sluggishness and a lethargy and a difficulty creating, producing, that I had not experienced before. And I thought, "What on earth is this?" And then spring came and things improved unaccountably and I thought, "Well, what was that fuss you were making about? It's not so bad." And that was an experience I had three years in a row through my residency. And then I got to the National Institute for Mental Health where I was interested in looking into research into mood disorders and biological cycles, circadian rhythms and so probably because of my own experience I gravitated to a group that was studying these questions as well as the possible role of light.

02. MEETING AL LEWY. POSTGRADUATE RESEARCH: COULD LIGHT AFFECT SEASONAL RHYTHMS IN HUMANS?

I wanted to become a psychiatric researcher from quite a young age. I was 16 years old and I wanted to try and figure out something about the brain, something new and interesting and different. And I was at the residency in New York City and I'd come there because it was a strong programme at Columbia in the research department. I'd come to study not only psychiatry but also psychiatric research and by happenstance I was at a party where I met Al Lewy who was dating one of my fellow residents. And Al and I started talking and it emerged that he and another colleague of ours, Tom Wehr, had recently found that human melatonin could be suppressed by bright environmental light. Until that time there was no real understanding that human melatonin could be suppressed by light, which is something that happens throughout the rest of the animal kingdom, but he and Tom and others had found that indeed it could be. And this opened up a whole vista because the fact that melatonin could be suppressed by light meant that light could do things other than enable people to see. And one of these things that emerged was that light is important in regulating seasonal rhythms throughout the animal kingdom. So in time the question arose: could it be possible that light could also affect seasonal rhythms in humans? That question hadn't occurred yet because the presence of such rhythms had not come to my attention at that time. It was a fortuitous meeting however.

03. MEETING HERB KERN. WAS THERE EVER A "EUREKA!" MOMENT?

One of my strongest interests was the classification of different subgroups of depressive disorders because it was clear that when you dealt with depression you were dealing with a very heterogeneous, a very mixed group of disorders. And if you ever wanted to try and understand the biology or the origins of this disorder you had to try and distil down the phenotype, or you had to distil down the specific type so that you got a pure group, and that was on my mind from early on. And then when I arrived at the National Institute for Mental Health and started working with Tom Wehr and Al Lewy, Herb Kern, a scientist, came to our attention. A gentleman who had recognised in himself a seasonal rhythm such that when the days got shorter he became depressed, and when they got longer he became hypomanic, and he had hypothesized that the seasonal variations in light were driving those rhythms. So we gave him more light in the winter time, we expanded his day creating a summer day length, or summer photoperiod, in the winter time and sure enough he came out of his depression. But what was clear to me was that one swallow did not make a summer and that we would need to get a group of people in order to try and figure out: is this a generalizable issue and is there a generalizable treatment? So I called around some colleagues who dealt with depression quite a bit and nobody had ever heard of such a thing or recognised such a thing, so at that time I did something which was akin to ambulance chasing in those days, and that is I spoke to a journalist at the Washington Post, our newspaper, about this unusual case and one or two others that had come to our attention and said, "Is there anybody in this vast metropolitan area, anybody else, who had seen a seasonal change in mood?" And she ran the article which was syndicated and to my astonishment thousands of responses came my way. So I created a systematic questionnaire and had people fill out these questionnaires and when I read their responses that's when I thought, "Eureka!" This was so exciting because there was something about the monotony of these responses, something about the replicative way in which these people answered the questions: "I slow down when October comes; I sleep too much; I can't wake up in the morning; I eat more than usual especially sweets and starches; I gain weight; I can't concentrate; I become depressed because

I fail at various things; I withdraw from friends and family." Again and again and again I heard this and I thought, "Wow, we've got a syndrome over here because it would be too much coincidence for everybody to be answering these questions in the same way."

04. CLINICAL RESEARCH & FIRST MAJOR STUDIES. UNDERSTANDING THE EFFECT OF LIGHT THERAPY.

Fortunately because there was such an influx of patients we were able to fill the ward that was at that time otherwise empty; people were looking for various things they couldn't find and here were a whole lot of things we weren't looking for but we found. So as they say in clinical research "no patient, no study." Lots of patients, we had a study. And they arrived in the summer time and they looked great. They were so happy and everybody looked at me and said, "You'll look pretty stupid if these people don't get depressed in the winter." And I thought, "You're right, I will look pretty stupid." But you know it's not the worst thing in the world to look stupid. And sure enough as the days got shorter, like the autumn leaves that begin to fall in a predictable way, these people began to get depressed just as they said: slowed down, difficulty waking, sleeping more, eating more especially sweets and starches, gaining weight, bad concentration, and withdrawal from friends and family and depression. One by one they became depressed. So we had a protocol in place whereby we put people through a crossover study: we gave them bright versus dim light in a random ordered sequence. And in fact even though only nine people finished the crossover there was a strong effect of the light and people realised it right away, people who really responded. It was like one of my colleagues who was the "blind rater", I was travelling at the time, I called him back, I said, "What's going on, Dave?" He said, "Listen, I don't know what your patient's on but she's blooming like a rose." So that was the beginning of the effect of light. We of course went on to replicate it several times, the light therapy work began to get replicated all over the United States as well as in Europe, in the United Kingdom and elsewhere. And people found this all over the place so that by now there are at least two strong meta-analyses showing that light therapy is a powerful antidepressant for Seasonal Affective Disorder.

05. "MEDICINE THROUGH THE EYES". THE STRUGGLE TO GET LIGHT THERAPY RECOGNISED.

You know since I had the problem myself of Seasonal Affective Disorder I began light treatment myself probably over 30 years ago. And even after years of using light therapy, as I would sit in front of the light, it would be very hard for me to believe that this light was actually influencing my mood. And I think as a culture we've been programmed to understand that medicine works when you take it as a pill. Even as children we know, "Take your medicine, here's a spoonful of sugar to make the medicine go down. Here's a pill." And so in our minds we have a very clear conception that something you take by mouth can make a difference, or an injection for that matter. We're all inoculated, it's part of the culture. But the idea that medicine could come in through the eye is still very strange to people even after all these years. It's still strange to me, I can understand how people would have difficultly really accepting it.

06. PARALLELS BETWEEN LIGHT THERAPY & COGNITIVE BEHAVIOURAL THERAPY?

Cognitive Behavioural Therapy for depression, for example, is by now widely accepted. One of the reasons I think why it's accepted is that it falls into the psychotherapy model, so people have been used to psychotherapy for a very long time. I think when Freud innovated the "talking cure" it was quite controversial and I must say when I was studying, initially to become a psychiatrist, and this was way back in the early 70s, the idea was that if you were depressed there had to be some reason harking back to your past, and this reason had to be ferretted out and rooted out. And it was Albert Ellis who actually suggested that maybe changing your thinking could make a difference. And the general idea was 'don't be ridiculous: if changing your thinking could make a difference we would have already made that difference.' But what he said was you have to do it in a systematic way. And it was really many years until Aaron Beck came up with the idea that the thinking had to be changed in certain ways and that this could be categorised in certain different types or bins. You could have fortune telling, you could have black or white thinking, you could have these various categories, and it was the systematic way of helping people lump the distorted thinking of depression that helped make it accepted. But initially it was quite outrageous the idea that you could just change your thinking because the idea at that point, by now the talking cure had become accepted, and at that point it was you had to find out what your mother had done wrong to you in order to figure out why you were depressed. And then once you figured that out that would help. So there was initially the same kind of resistance as there is whenever you have a shift in a model, and that's what has happened, and to some extent still happens in the case of light therapy for Seasonal Affective Disorder.

07. MEASUREMENT OF MELATONIN: SPECTROPHOTOMETRY & RADIOIMMUNOASSAY.

Melatonin is present in the human blood stream in teeny quantities measured in femtomoles, 10⁻¹⁵, and in the late 1970s there were not yet any radioimmunoassays that enabled people to measure melatonin in such small quantities. And at that point Dr Al Lewy, with his colleague, Sandy Marky, developed a mass spectrometer assay which enabled him to measure melatonin and that was what enabled him to show that light could suppress melatonin. But the trouble was that you could only handle relatively small numbers of samples with a mass spec. It was only later that Dr Josephine Arendt created a powerful radioimmunoassay that enabled people to measure melatonin in larger numbers of samples. And that has proved tremendously helpful in understanding that light actually has many biological functions. For example, it shifts circadian rhythms; it suppresses melatonin; it has anti-depressant effects. And so that radioimmunoassay enabled us to understand a lot about the effects of light on the brain.

08. STATUS OF SAD INTERNATIONALLY. SCANDINAVIA.

It's curious that Seasonal Affective Disorder was originally described in North America, in fact Washington DC is not that far north, it's like the middle of America more or less. And I remember asking a Scandinavian colleague early on whether Seasonal Affective Disorder existed in Sweden. And he responded, I thought quite wittily when he said, "Either nobody has it or everybody has it." And initially there was a lot of interest in Seasonal Affective Disorder in Sweden, and I remember going to visit Sweden and sitting in one of their light rooms. It was this beautiful room with light reflected off every wall and off the ceiling and we even had to wear these white surgical scrubs and

boots so that nothing would do anything other than reflect light, and the whole thing was this sort of beautiful white glow, and I felt better just after five minutes of sitting there. They never really took to these light fixtures or light boxes which we have used more commonly in the United States and which have been used in the United Kingdom and elsewhere. So there was a lot of interest at that time but I think one of the problems is when you recognise a problem and see this exists, and a huge percentage of people have the problem. Then if you've got a socialised medical system you are theoretically responsible for now treating the problem or providing funding to treat the problem. So at this point I would say if you ask a Swede, "Is there anybody or does SAD exist in Scandinavia?" depending on whether they're responsible for funding it or not they may once again say, "Either everybody has it or nobody has it."

09. CARING FOR PATIENTS. FUNDING & FINANCIAL ISSUES. ENGAGING WITH THE WIDER MEDICAL COMMUNITY.

Well, it's an interesting problem when you deal with something that's very common. For example, I saw recently an article that a certain European court decided that obesity is a disability. Now if obesity is a disability there are now an awful lot of people who have to be accommodated. For example, larger chairs, elevators, parking coupons to park closer to their office and so on and so forth. So I think what happens in a nationalised healthcare system is people have to be very careful about what they call an illness and what they call a disability because once they define something as an illness and a disability then the treatment becomes an entitlement and then you're talking about a lot of money. So I think when you've got a national health system that becomes an issue and I think that's been a factor in the NICE conclusion, for example, NICE, National Institute of Clinical Excellence, has decided that light therapy is not fully proven to be effective in Seasonal Affective Disorder, so it's not eligible to be funded by the national health system. And likewise in Sweden there's not currently funding for light therapy. In the United States the healthcare is a much more heterogeneous patchwork of reimbursement. So some insurance companies have actually reimbursed for light therapy and others have not. In general though for a one-time cost, one can get a lot of mileage from a single light therapy fixture. So what's happened in the case of Seasonal Affective Disorder is that the population of people affected by the condition has actually driven treatment to a large extent. People have actually gone to their doctors, informed the doctors, educated the doctors, requested the treatment, or in many cases regulatory organisations like in the United States have kind of turned a sort of blind eye towards light therapy fixtures and people just treat themselves. I think this is a shame because when you're dealing with depressed people that sometimes it really helps to have a doctor on the case because the light therapy may not work by itself, it may need to be helped along with medications and so I think that an educated medical community would be a wonderful thing, and I hope that part of the accomplishments of our all talking together will be to once again re-engage physicians and other clinicians in the interesting condition of Seasonal Affective Disorder which is so eminently treatable.

10. SAD: MAN & NATURE.

I think perhaps one of the problems in terms of SAD being accepted by the medical community is that it falls into so many different categories. Poets have written about the effects of the seasons on their spirits, Emily Dickinson comes to mind with her "certain slant of light, winter afternoons that

oppresses like the heft of cathedral tunes." Why would we want to treat a poet with light, you might ask? So the artistic side comes into play. Then there are all the animals with the seasonal rhythms, hibernating hamsters, hibernating bears. Maybe we should just allow ourselves to hibernate a little bit in the winter. Maybe everybody is a little "under the weather." Why make it into a pathology? And so there are many contingencies of people who compete for interest in this particular phenomenon. But I think as a clinician and as a doctor, when you see suffering you need to treat suffering. And many people with a winter problem, whether you call it SAD or whether you call it "seasonal pattern" or whether you call it the winter blues, they suffer. They lose relationships, they lose jobs, they feel despairing, they don't fulfil their goals and dreams and ambitions because half the year they're not their best selves. When you see suffering you need to treat it and you need to treat it with anything that works with the fewest side effects. And that's really where I'm coming from. Let's forget these different contingencies and these different interest groups and just focus on a person and a problem and alleviate suffering in every way we can.

11. 30 YEARS OF SAD. LOOKING TO THE FUTURE.

Well, it is 30 years since our original paper came in in which we described Seasonal Affective Disorder and when people talk about it now they talk about it as though it's part of the language that has always been part of the language. If I ever tell somebody that I described Seasonal Affective Disorder it seems ridiculous because only dead people have coined any new terms and this should be part of the language and what am I doing walking around, is the kind of response that I get. So 30 years makes a very big difference between a novel syndrome that hardly anybody has heard of, and a syndrome where there are 3 million web enquiries every month about the condition. So what will happen in 30 years? I think in 30 years it will just be accepted that a lot of people don't feel great during the winter and they use more light to treat it and nobody thinks twice about it and most of it happens outside of the doctor's office because so much is known about it. And the only people who end up in the doctor's office are those where light and the regular self-help things haven't worked because there will be too many people with a recognised problem for it all to end up in the physician's office.

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