Ivana Rosenzweig Interview

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1. You grew up in a family of medical doctors and one of your idols was your grandfather Filip. Did this medical family environment influence you during your formative teenage years and did it help you choose neurosciences as a career?

The short answer is that my *nono*, my grandfather Filip, in a way decided this for me.
A slightly longer explanation is that I was fortunate, perhaps due to my father's combative nature and penchant for going against the grain, that the most coveted surgical positions in Zagreb were out of his reach. Thus, my parents settled in Sisak, and this beautiful historical city surrounded by three rivers provided me with the best possible schooling and education that one could wish for. This is something I would, sadly, only realize decades later.
Looking back, my parents' profession (and that of many other relatives who were all also doctors) obviously must have affected my life choices and trajectory. Medicine, medical terms, even the medical way of thinking were for me all *terra familiaris*. My parents had a (sometimes annoying) habit of discussing their cases *ad libitum* during our family meals or family trips. They were both doctors caring for their patients; phone calls and visits from their patients to our family home would easily extend into the evenings, and not infrequently later into the nights. I owe to my parents, especially to my mother, my passion for learning, sometimes just for the sake of learning.
However, my parents also fervently believed that children should be treated as background noise – or if possible, as a background whisper. Against that background, my sister and I instinctively built a separate universe parallel to that of our parents. In many ways we shared with them only the physical constraints of our small flat in Sisak (Figure 1).

Figure 1. Me and my middle sister Ana. We fought a lot but we also followed each other around the world, and we still prefer to live within 5 minutes of walking distance one from another.

When my youngest sister, who was then about two years old, started struggling with various infections, metabolic upsets and a strange neurodevelopmental regression – and eventually stopped walking and talking, that small flat became even smaller. My parents contacted anyone and everyone around to try and help her, but despite all the efforts, even the very best paediatric colleagues of my mother failed to fully fathom and categorize what was happening. I presume this was one of the first domino pieces which folded in my mind, albeit in a very slow motion - that, with better knowledge and understanding of the brain and how it works, it might have been possible to do more to help my sister, and other children like her. She is now an adult, but still dependent on my parents for even the most basic self-care.
Those were difficult years and my grandparents, whilst living miles away in Split, provided all the unconditional love and moral structure that I needed and craved for. My grandfather came from a very old and politically active family. His cousins and uncles were amongst founders of the football team Hajduk; his brothers were amongst the founders of the Croatian Communist party; they formed and led the first Split's Partisan battalion during the Second World War; they were celebrated as war heroes; some of them died in concentration camps; some of them had schools in Split named after them. Some of them who survived were later imprisoned on Goli Otok, and served the sentence there for their views. And yet, my nono, despite all this revolutionary background also happened to be the most calm, peaceful, and understanding person on this planet.
During one of my visits to my grandparents in Split, my nono and I spoke for hours about my youngest sister. At some point, he looked at me and said: It is up to you Ivana, to learn about the brain. And thus I followed his advice.

2. In preparation for this interview I read the one you gave two years ago (https://korona.net.hr/pozitivne-vijesti/hrvatska-neuroznanstvenica-istrazuje-spavanje-u-mikrogravitaciji-dugotrajna-putovanja-u-svemir-morat-ce-ukljucivati-neku-vrstu-hibernacije/)
They wrote that you are a neuroscientist. How would you define that term? If I wanted to become a neuroscientist what would I have to do? Describe a prototypical neuroscientist and then tell us how did you become one.

I do not think I can authoritatively answer that question. I would say there is no strict format, but most if not all neuroscientists share the passion for understanding better the inner workings of the brain. If you insist, my abridged and doctored version of the Wikipedia page would state something along the lines that neuroscience requires a multidisciplinary approach and that it includes all specialists with distinct knowledge of the brain's physiology, biochemistry, psychology, anatomy and molecular biology of neurons, neural circuits, and glial cells and their behavioural, biological, and psychological aspect in health and disease.

3. How much exposure to neurosciences did you have during your medical school years?

Again, as with my pre-University education, I was very fortunate to study at the Medical School in Zagreb. And in parallel to my early years, when I resented the parochial settings of my childhood, I only got to fully appreciate the extent of what I had when I began teaching as a fellow at Cambridge, and even more now as an academic at the King's College London. Simply put, I genuinely believe that our grounding in preclinical subjects was second to none in Europe and most likely in the entire world.

Here I have to mention two impressive men called Ivica who influenced me enormously and helped formulate my own concept of neuroscience, i.e., what it is and what it should be. The first one was Professor *Ivica Kostović*, whom, to this day, I regard in many ways as my major mentor (Figure2).The second one who is not so well known in Croatia, was Professor *Ivica Kračun* who tragically died prematurely a few years ago(Figure 3). Like Kostović, Kračun was close to a genius, gregarious, generous, dangerous, and often quite moody. I believe that he was originally from Hrvatsko Zagorje, however, to us, he was like a Dalmatian 'Bura' storm, bigger than life, even though quite of a short physicial stature in real life. If one had to present a musical sketch of the emotions his lectures would evoke, the best approximation would be by mixing music of Wagner and Stravinsky, with sprinkling of scientific philosophy and history, only for lessons to abruptly end in a tempestuous finale of Bach's Well-Tempered Clavier. My discussions about neuroscience with him were always inspirational, uplifting and quite memorable.

4. Did you have any role models or idols that you wanted to emulate? Premedical school, medical school or thereafter?

Yes and no. I always adored *Rita Levi-Montalcini*, and in many ways, she might be the one I get to mention most often. I liked that she dared to be a different neuroscientist in the world where women were, and still are, regarded as unequal members of the society.

Figure 2. Ivica Kostović, my mentor and a great surrogate father to many of us.

Figure 3. Ivan Kračun with his collaborators in the Metabolic laboratory of the Clinical Hospital Center Zagreb,1987. Standing next to him are Ksenija Fumić, Marija Heffer and Gordana Kračun.

5. Do you still have memories of events from your student days that helped you decide about your future?

Those were difficult war and post-war years, and, to be frank, for most of my adult life I worked hard to erase some of those memories. Many of our colleagues were in a full or partial refugee status, the random bombings and shelling were continuing, and many of us had relatives who were engaged in active combat. The schisis of pretending that life goes on, and attending lectures, taking exams, whilst listening on news about Vukovar or Zadar, Petrinja, was not healthy and I am sure it took a significant toll on all of my colleagues, as well as myself. In many ways, even those not in the direct line of fire, were robbed of their youth, our brains were still developing and the epigenetic impact that those years must have left, have never been properly accounted for. We were not talking about it, and we never really talked about it even later.

When the war in Ukraine started, I called my Ukrainian friend to offer my support. However, after a few words I had to put the receiver down as I could not speak any more. This lasted for an hour, and then I started crying uncontrollably. I can not even say why, I don't think I am an overly emotional type, I just felt that something buried deep in me, something I ignored and actively worked on repressing from those years, was suddenly become unhinged in my mind.

6. Did you practice medicine upon completion of your university studies or you decided to devote yourself to science exclusively?

I did not practice medicine after graduation. I wanted to do science, pure science and nothing but science. Only after I did my PhD did I realise that, in order to know which questions to ask, I must spend some time in clinical practice. There was no other substitute for learning how to properly observe my patients and understand their problems. Like *Musil's Man Without Qualities*, I meandered never satisfied of knowing or being good enough, from doing science to clinically training in psychiatry, then neurology, then neuroradiology and eventually training in sleep medicine. I have eventually completed the full circle, from research to practice and back. Currently I am spending 50% of my time as a clinician (i.e., a sleep physician) and the other 50% as an academic neuroscientist. As my husband rightly stated it: 'If allowed, you would continue to study until your very end.' Don't tell him, but this is exactly what I intend to do.

7. Why did you go to Cambridge for your PhD? Why Cambridge and not some other place?

I do not believe in a 'predetermined' universe, and yet, looking back, I believe my path could have only to lead to Cambridge. Firstly, my nono Filip often spoke about Cambridge as a centre of educational excellence, and apart from his politics, I never challenged my grandfather's grand truths. Secondly, I never wanted to live in the USA, which was my husband's (then my boyfriend) first choice. Thirdly, after the war, I realised that my traumatised inner *homo politicus* needed to be in country whose people were politically frigid (or at least I perceived them to be so), and whose politics and inner workings would not interest me in the slightest, and thus, my second favourite choice, Israel, was also eventually out of the bounds.

But our personal history was sealed by our 1995 summer trip to the UK. The basic idea was to persuade my boyfriend that there were other places we could go together to study apart from the US. In those days before mobile telephones and internet, we spent four weeks in a cheap little University hostel in south London, pretty much without any contact with our families, or news from Croatia. We loved it though, we lived very frugally, rationing ourselves to a sandwich a day, and travelling for hours on the double decker buses around London whilst visiting various Universities trying to gather more information about scholarships and courses, and pretty much unaware of happenings at home.

To this day I remember the very feeling of profound happiness that overtook us both when we passed the newspaper stand one evening. This sported big headline stating that '*Oluja*' started and that Knin was ours. I fear that passer-by's must have judged us to be on drugs, as I have never since done so much jumping, shouting and crying. An overwhelming sense of primordial joy and calm overtook us - the war which claimed and tainted our best years of youth was finally and truly over. Our homeland was free, we were free.
Years later I would read *Amos Oz's* '*A Tale of Love and Darkness*', and in the passage where the author describes the highly charged emotional scene and his father's reaction to the news that Israel has gained its statehood – that was the exact emotion I recognised.

If memory serves me right, we then had too much to drink and eat, and we spent far too much. Once the elation subsided, we realised that we only had money left for a short trip to Cambridge, that being the cheapest of all our other planned trips that were to include Oxford, Bristol and Edinburgh. And so it was. We went. We stopped at the Trinity College gates. We asked if they had any information or booklets on available scholarships. A nice lady who clearly took pity on us, two dishevelled Eastern European kids , proposed that, if I wanted, she could also see if there were any Professorial Fellows still on the site so that I could talk with them. She was successful and thus I had my first and only interview with faculty members of Trinity College. It was a lovely chat about medicine, mathematics and universe and many other unrelated topics. I could not catch their names fully, and only much later did I learn that one of them was a Nobel Prize winner.

I must have impressed them in some way, as a few months later I got a letter stating that I have won a prestigious Trinity College Scholarship, which fully funded my subsequent PhD studies.

8. Are there some exciting moments from you school days, either in Zagreb or in Cambridge that you still remember? Why?

I will never forget my student exchange days in France , where I did my Gynaecology and Obstetrics rotation with my friend Tanja Buklijaš. My French was really pathetic, but Tanja, whose French was fluent, managed to arrange for both of us to be placed on the same rotation schedule.Thus we stayed together for the entire period of time. During all that time she basically served as my personal translator. We had fabulous time in France escaping the dreary and grey corridors of post war maternity wards in Croatia.

As often, one's plans, are the fool's material. The first thing we found out when we arrived to Rennes was that we were placed in different clinical groups. Second shock was when we realised that in France medical students were used to man the wards. Our third and perhaps our biggest shock was when we realised that French women expected a proper full daily examinations by their gynaecologists, a.k.a two petrified medical students from Croatia. I will leave the rest to your imagination.Two important thing that I learned in Frances were as follows: I was never meant to be a gynaecologist, and there was no chance that I would ever learn to speak French fluently.

9. You spent several years in Cambridge studying to become a clinical neuropsychiatrist. Was that an intentional detour or you felt that you must learn more clinical psychiatry in order to become a well rounded neuroscientist?

Oliver Dragojević has a beautiful song about this, and I will only say that this restless nature of my predecessors clearly also resides in me. Having earned my PhD, I felt poorly equipped to tackle the big questions of neuroscience, without truly studying the first-hand patients suffering with these illnesses. Fortunately, these days they have excellent collated courses, which allow young clinicians to be to combine their clinical training with doing their PhD and postdoctoral research. In my time, there was no courses of that kind, and thus, I simply created my own opportunities.

10. Beside your scientific work do you still practice psychiatry?

Your question made me smile. It reminds me of my sister who used to say during our arguments that I act as a psychiatrist even in my daily private life.

I find that it is impossible sometimes to switch off, and I believe that it would be foolish, to do so. Thus, I practise my psychiatric principles every day, in every human interaction I have. Psychiatry is the only medical specialty which enables one to navigate through life's little and big challenges.

11. Why did you move to London?

We lived in Cambridge for 13 years. I did my PhD, my postdoc, I taught Physiology and subsequently I did most of my clinical neuropsychiatric training there. The decision to move to London coincided with my pregnancy with my son Jakov, and my career decision to re-enter the academic world, and specifically to enter the field of sleep medicine.

12. You are mostly known for your studies of sleep. Or am I wrong?

I work in the field of sleep neuroscience, but I hope that my best work is yet to come.

13. In order to better understand the disturbances of sleep we must first of all study normal sleep.Tell us a few things about normal sleep that the neuroscientists discovered during last few years.

Most of what we think we know, we know we do not know for sure. Sleep is such a mystical terra incognita that I still get that very important buzz of feeling extremely lucky to work in this field. Sleep allows us unprecedented insight into the inner workings of our brain, which are impossible to decipher during our wakeful moment.
If really pressed to do prepare for you my favourite list of various recent theoretical constructs/partial truths about the sleep and its function I would have to included the following: sleep rhythms as an amazing orchestral symphony that ensures that brain gets rid of toxins, warrants partiture that replays memories, stores the important memory scores in our cortex, and in turn rebuilds our brain's circuitry and software in such way so that our conscious ego may incorporate the effects of wakeful experiences. Other empirical roles of these classical sleep accords include protection of various cortical territories in the brain, for example that of visual cortex during dreaming. If we did not sleep, it is likely that our brain's inbuilt architectural neuroplasticity mavericks would re-build and re-use these cortical territories into subserving the auditory, haptic or other functional modalities.

14. Insomnia, parasomnia, obstructive sleep apnea—these are the terms for which I have some cultural understanding. Catathrenia—I had to look it up in Wikipedia, but why would one study it?? Could you impress me with a couple of similar terms that I probably never heard off? And

maybe you could also convince me that it is important to study such problems!!

Absolutely. You see, understanding how dream mentation and ambulation arise from sleep's basic physiological components has enticing, and potentially wide reaching basic neuroscientific and wider translational clinical implications. A first case in point is the rapid eye movement (REM) behaviour disorder (RBD), a relatively rare parasomnia that predicts the later occurrence of alpha-synucleinopathies such as Parkinson disease , multiple system atrophy and dementia with Lewy bodies. Unlike sleep-walkers, patients with RBD rarely leave the bed during the re-enactment of their dreams. RBD movements may be independent of spatial co-ordinates of the 'outside-world', and instead rely on (allocentric) brain-generated virtual space-maps. My group is trying to make sense of mechanisms underlying this, which could be precious for patients with dementia. A second case in point are dreams of congenitally blind people whose dreams surprisingly may comprise visual imagery, not dissimilar to that or normally sighted people. We believe that deciphering the brain mechanisms here could help utilize neuroplasticity during the sensory loss later in life, and possibly lead to ability to stimulate functional synesthesia.

15. I looked you up the data in Google Scholar and found out that 5 of your most cited papers deal with apnea. Why are you interested in apnea?

Sleep apnea is such a prevalent sleep disorder, and a "somewhat conservative" approach estimated the prevalence of adult OSA in the Americas to be 170 million, or 37% of the population. Thus, as a sleep physician I would be failing my patients if I was not joining in forces trying to decipher the best treatment for this debilitating multi-system chronic disorder.

16. I like to take an afternoon nap. After I wake up I feel refreshed. I am sure that you must have an explanation for it.

I am very pleased to hear this. As a clinician I can tell you that this tells me your sleep is of good quality and that you likely also have a good sleep opportunity. What the sleep rhythms symphony does to your brain, whilst you sleep, is perhaps best not pondered upon, lest this stresses you and thus contributes to your night anxiety and subsequent sleep of lesser quality.

17. I must admit that I was mightily impressed with your published discourse on Elias Canetti in which you also mentioned Ephraim Kishon. Godot found his way even into the title of one of your papers. Chapeau—what an erudition! You mentioned in your previous interview your son as a talented pianist. Where do you find time to let for literature and music enter your life?

I do not really have time for anything – I work all the time, seriously. Most of my eruditism, if you may call it that way, comes from growing up in Sisak, where we were fully expected to know our Karamazovs and distinguish them from our Taras Bulba or The Buddenbrokes. As I have already mentioned, we have had a truly superb education, thanks to many of our esteemed teachers, with special mention of my revered and beloved teacher Tea Rimay.

The truth is, that as a parent, I do not have a choice. As any parent of even vaguely talented child, be it in sport, or music can tell you - this talent of their's sucks you into an unknown world of chauffeuring to the endless events, it makes you spend your weekends waiting outside cold during their practices, and you find you learn simply by diffusion. Therefore, even if you have never previously heard of the pianist Glenn Gould, you suddenly realize you are more than able to hold your court explaining why his rendition of Bach is superior to that of, say, Lang Lang. Supporting my son all the way while he is becoming an accomplished pianist has become an important part of my life (Figure 4)

Figure 4. My son Jakov Tvrtko Filip .He is trying his best to impersonate Horowitz. However, as a tall Dalmatian, in future life, he might be more likely confused with Richter or our own Ivo Pogorelic.

Figure 5. Svjetlana Kalanj and Katarina Ilić on one of their research visits to my London laboratory. To this day I find my University colleagues still make for the best collaborators, we always laugh a lot, and decades just melt away.

Figure 6. The neuroscience congress in Zadar.

18. Let's finish this interview with a few questions about your contacts with Croatian scientists. How, when and in which form?

My generation has slowly but firmly matured, I hope that my youthful colleagues will not resent me for describing them as mature. In any case, many of them are now either running Departments or are positioned on other high functions within the Medical School and Croatian Brain Institute and wider. In my inner sanctum, I am fortunate to count Tihana Jendričko, Zdravko Petanjek, Svjetlana Kalanj-Bognar, Vlatka Boričević and Dinko Mitrečić amongst my closest friends, all from our University days. They are people I call at times of crisis, and to whom I happily turn to when I want to brainstorm or clarify some scientific ideas (Figures 5 and 6).

19. What are you currently working on? Any neuroscience data on Covid-19?

Sleeping brain. Also, we are trying to see what that sleeping brain might do in space, during the cosmic travels and under conditions of microgravity.
With regards to Covid-19 and the brain, I think the full truth will be only known in decades to come. I am a pessimistic realist, and I see what it appears to have done to my patients. My worry started even before the current studies got published. For those that did not read them, there are suggestions that Covid-19 may affect brain directly, and cause a special set of cognitive impairments, even accelerating the aging of one's brain for up to 20 years faster than expected.
My family and I have now all had it at least several times(?!). A good percentage of my salary every month goes on placebo multivitamins, prebiotics and other supplements. Living in London, we are living within the ground zero, and our motto has to be that what will come, will come.

20. Any messages for our younger colleagues who are still studying medicine on Šalata and Rebro?

I will paraphrase Rita Levi-Montalcini:" *Above all, don't fear the difficult moments. The best comes from them".*