



Dr. Ethan Russo ETHAN RUSSO

Dr. Ethan Russo is a world-renowned authority on the medicinal use of cannabis; an academic researcher, author and industry leader whose expansive knowledge of cannabis therapeutics spans history, cultures and its myriad applications for improved health and wellbeing. A board-certified neurologist and former Senior Medical Advisor at GW Pharmaceuticals, Dr. Russo is

currently Director of Research and Development of the International Cannabis and Cannabinoids Institute, a consortium of international academic institutions and private companies dedicated to promoting medical cannabis research.

In this interview, Dr. Russo shares an informed and insightful vision of how cannabis-derived medicine stands to benefit two of the more intractable neurological conditions facing older adults, Parkinson's (PD) and Alzheimer's (AD) diseases.

Abbie Rosner: If medicinal cannabis targets our endocannabinoid system (ECS), what is the involvement of that system in PD and AD?

Dr. Ethan Russo: The ECS regulates most physiological systems in the body, but above all the nervous system, where it helps to achieve the balance that allows individual nerve cells to communicate. The ECS is disrupted in both AD and PD.

Rosner: What is the research with cannabinoids and Parkinson's disease showing?

Russo: In a mouse model of PD, treatment with nabiximols (Sativex®), a cannabis-based pharmaceutical approved in 30 countries outside the USA, resulted in improvement in dopamine neurotransmitter function, and reduced oxidative stress (akin to "rust" of the nervous system), as well as leading to improvements in anxiety and self-injury behaviors.

Clinical results with treatment of PD with cannabis have been quite mixed. Cannabidiol (CBD) helped a few PD patients with psychotic symptoms, and some with a rapid-eye movement sleep disorder. Observational studies with smoked cannabis, presumably high in THC, reportedly produced acute benefits on tremor, rigidity and slow movement (bradykinesia). The best results in PD were reported in a Czech study in 2004, in which patients ate raw leaves of cannabis for as much as three months and reported significant

improvement in overall function, tremor, bradykinesia and rigidity, with few side effects.

Rosner: And what about cannabis for AD?

Russo: The story in AD is even more intriguing. Both THC and CBD have been shown to interfere with the production of abnormal toxic matter in the brain of such patients. This is quite exciting, inasmuch as synthetic drugs designed for similar purposes have yet to advance in the clinic. Both THC and particularly CBD are known neuroprotective agents that hold the potential to slow or perhaps even halt the degenerative process. On the symptom side, THC as a single agent has proven beneficial in AD patients in reducing nocturnal agitation, improving sleep and appetite. Observations of nursing home patients in California with dementia have produced similar benefits as well as reducing the need for nursing intervention and amounts of other drugs.

There are four FDA-approved pharmaceuticals to treat memory loss in AD, but all have mild benefits on a temporary basis. These are designed to increase the amount of acetylcholine, the memory molecule in the brain that becomes depleted in AD. Interestingly, the terpenoid alpha-pinene is capable of boosting acetylcholine by inhibiting its breakdown, and with fewer side effects than the conventional drugs.

Rosner: We hear a lot of talk about THC and CBD, but what about the role of terpenes?

Russo: Terpenes are aromatic compounds from plants that are important in our everyday exposure to scents and flavors. Some of these, when combined with cannabinoids, boost their effects such that the result is greater than the sum of the parts. We discussed above the role of alpha-pinene to combat memory deficits in AD and PD. Linalool, a component of lavender essential oil as well as cannabis, has been demonstrated to calm agitation in AD. The terpene limonene, common to citrus and cannabis, is a powerful

antidepressant and immune stimulator. Caryophyllene, a terpenoid with the distinction of also being a cannabinoid, is of key importance in AD, as it may help in clearance of beta-amyloid waste in the brain.

Rosner: CBD products are so popular now. But what price is paid when you remove THC from the cannabis equation?

Russo: A severe price may be paid if cannabis-based medicines are devoid of THC. It is clear from the above that THC has a major role to play in both symptomatic treatment of dementia and quite possibly in preventative benefit. The dangers of THC have been vastly exaggerated by alarmist politicians and the press, particularly in such contexts where alternatives have been extremely disappointing and are actually much more problematic. Very small doses of THC are required and their benefits outweigh any risks by healthy measures.

Rosner: You have also been a proponent of diet and other complementary approaches to cannabis.

Russo: Fascinating epidemiological studies have linked diet to degenerative diseases, especially AD. Diabetes and obesity, which are rampant in the USA, as well as trans-fats, all increase AD risk. In contrast, disease rates are lower in areas following a Mediterranean diet rich in monounsaturated olive oil and omega-3 fats from fish. We also know that daily cognitive challenges when carried into the elder years offer some protection, as does vigorous physical exercise.

An underappreciated factor in degenerative diseases is the microbiome, the bacterial content of the gut. We know that THC, rather than leading to obesity as one might surmise, rather changes the microbiome balance in the gut to favor bacteria that protect from development of obesity and the metabolic syndrome.

Great benefits may accrue to AD and PD patients through the use of probiotics (i.e., natural organic multi-culture yogurt, kefir, lacto-fermented vegetables,

and supplements in capsules) and prebiotics (vegetable matter like acacia fiber, slippery elm, burdock root and supplement in capsules) that provide an optimum feedstock for the beneficial gut bacteria.

Rosner: From where we are today, what are the best approaches for prevention and treatment of PD and AD?

Russo: The best current approaches to AD and PD beyond what the conventional pharmacopoeia offers include: aerobic activity, daily mental exercise, Mediterranean diets with use of anti-inflammatory fruits and berries, probiotics and prebiotics. From cannabis, THC, THCA, CBD, beta-pinene, caryophyllene, linalool and limonene may all have important contributions to treatment of these disorders.

Rosner: Where do you see promise on the horizon?

Russo: While the current laboratory experiments have been extremely important in establishing a foundation for cannabis-based medicines in treatment of AD and PD, it is definitely time to move the effort into the clinical arena. It is clear that these conditions are increasing in our aging populations and conventional approaches to date have been less than satisfactory. Utilization of cannabis preparations with the right mixtures of cannabinoids and terpenoids show great promise to produce better results. While these may be simply palliative in reducing drug and care burdens, there is also the possibility of making a real difference in slowing or abrogating the pathological processes in these two disorders.

The conversation has been edited and condensed for clarity.