The One-Time Pill

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Let us imagine a medication: a generic bottle of pills. Perhaps these pills are for an acute condition that lasts a few days or perhaps they are for a chronic condition that lasts a lifetime. One might regularly self administer these pills to ensure an effective treatment. Although, we often refer to medications as pills, plural, and not pill, singular. Can we not fantasize about a treatment requiring only one administration, one pill, to see full recovery?

Perhaps the morning after pill or Botox comes to mind for muscle spasms; however, Botox doesn't scratch lifetime. Not to mention, its most popular use is for wrinkles which arguably, isn't a life-threatening condition. Few examples spring to mind since this one-time pill must carry a very distinct pharmacokinetic property: improvements in symptoms remain long after the drug is metabolized from the body. This implies that a permanent transformation in the body's physiology took place.

Fortunately, there is a field where this one-time pill might come to exist involving neurons, our psychology, and drugs: neuropsychopharmacology. The nature of our neuroplasticity and how the brain rewires itself may open the gates to such exotic treatments, particularly towards psychiatric conditions. Addiction, anxiety, depression, and post-traumatic stress disorders all beg for some fundamental rewiring of the brain. Novel psychotherapeutics, primarily psychedelics, may have an answer to help alleviate these trying conditions (Mccorvy *et al.*, 2016), (Bogenschutz & Johnson, 2016).

Psychedelics are recently showing more clinical potential and utility which function primarily as partial agonists to the 5-$HT_{1A/2A}$ serotonin receptors in the central nervous system, but may also have effects on all other serotonin receptors depending on the subtype and brain region (Bogenschutz & Johnson, 2016), (Sherwood & Prisinzano 2017). So, what about these receptors? Why should we care?

Well, 5-HT_{2A} receptor over-expression was documented as being a neurobiological abnormality associated to stress and suicidal behaviour – this was measured in post-mortem

brains of suicide victims (Pandey *et al.*, 2002). On the other hand, Mccorvy *et al.* in 2016 hypothesized that lasting symptom relief from depression with a one-time psychedelic treatment might be due to the opposite effect; 5-$HT_{1A/2A}$ receptor downregulation; assuming that downregulation of these receptors does reflect prolonged positive outcomes. If it's found that their one-time treatment provides more sustained 5-HT_{2A} receptor downregulation than chronic use of Selective Serotonin Reuptake Inhibitors, perhaps a one-time pill may well be feasible.

Changes in brain molecular biology can also reflect changes in neuronal circuitry which were seen in experiments on rats who showed that psychedelics can promote neuritogenesis, synaptogenesis, and spinogenesis; growth of axons, synapses, and dendrites respectively; thus, contributing to increased functional plasticity (Ly *et al.*, 2018). This psychedelic induced neuronal growth and plasticity compliments a 2017 study by Carhart-Harris *et al*. In their "brain on psilocybin" study, they reported that treatment-resistant depression patients; who experienced significant reductions in depressive symptoms post treatment; had decreased cerebral blood flow to the amygdala post treatment. Decreased blood flow doesn't necessarily mean rewiring of neuronal circuitry, but it gives a clue as to what's going on.

Some have even gone as far as to hypothesize that they've acted as evolutionary catalysts to human cognition. Terence McKenna's "Stoned Ape Hypothesis" discusses this plausibility of psilocybin's ancient use to claim that psychedelics spurred unnaturally rapid growth of the neocortex when psychedelic mushroom species became a part of human diets, stimulating our emergence from savagery (McKenna, 1993). It may be too far to attribute the course of human evolution to neuroplasticity inducing psychedelics, although, in terms of treating psychiatric and neurodegenerative pathophysiology's these magical molecules may have a part of the answer.

That is to say, it may be time to recognize the benefits of such a fantasy pill not forgetting to mention a one-time pill's immunity to the long-term capitalist intentions of big pharma. Society needs to endure a serious social and legal re-branding of our dreadful outlook on psychedelics, often portrayed as abusive brain-frying street drugs. Together in concert, a circus of fearful media interpretations and a general societal anxiety have unconsciously hallucinated into our realities a misguided vision of psychedelics. One that may be hindering a deeper understanding into what these molecules can do for those that need it. And right there, behind a

thick legal curtain hiding in the shadows of academia, may well be sitting a revolutionary medicine: The One-Time Pill.

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Citations

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