Effect of cannabis potency on the consumer

[Editor's note: this is an extract from Milan Röhricht's dissertation 'An overview of literature differentiating the effect of cannabis potency with regard to potential harms to the consumer'. For the purpose of clarity several sections have been omitted or published in a shortened version here. Please contact us if you would like to read the full version.]

1. Introduction

Cannabis is the most widely used illegal drug in the world, with the predicted number of users exceeding 200 million people (UNODC, 2015). Within Europe, it is estimated that a quarter of the population aged between 15-64 years have tried cannabis, with nearly 7% indicating they have consumed it in the past year (EMCDDA, 2016). This frequency of use far surpasses the use of other illegal drugs: cocaine, the second most frequently used drug, is reported to have a lifetime use of 5.1%, with only 1.1% claiming to have consumed the drug in the past twelve months (EMCDDA, 2016).

The bulk of research over recent years has established a predictive relationship between cannabis use and medical harms. Such harms cover a wide range: the risk of psychotic symptoms; cognitive dysfunction; diminished motivation; changes to brain morphology; and, many more (Broyd, van Hell, Beale, Yucel, & Solowij, 2016; Demirakca et al., 2011; Lorenzetti et al., 2015).

In particular, the investigation into the relationship between cannabis use and psychotic symptoms has a long history. In 1982, Rottanburg et al. showed an association between heavy cannabis use and a rapidly resulting psychotic illness. They stopped short of answering the growing question: 'does cannabis per se cause this psychosis or does it act as a precipitant in predisposed individuals?' (Rottanburg, Robins, Ben-Arie, Teggin, & Elk, 1982, p.1366). In a recent study, Gage and colleagues (2016) provide an in-depth review of the evidence available thus far. Whilst accounting for possible confounders, bias, inverse causalities and the like (see Murray & Di Forti, 2016 for an overview), they conclude: 'overall, evidence from epidemiological studies provides strong evidence to warrant a public health message that cannabis use can increase the risk of psychotic disorder' (Gage, Hickman, & Zammit, 2016, p. 549).

As evidence regarding potential harms accumulates, there is continuous interest in the biochemical properties of the *Cannabis sativa* L. plant responsible for these phenomena. In the 1960-70s, it was discovered that the phytocannabinoid (cannabinoid) trans-Δ^9-tetrahydrocannabinol (Δ^9-THC) is principally responsible for the psychotropic effects of cannabis (Pertwee, 2008). Since, many other cannabinoids have been sequenced; cannabis contains at least 105 known natural cannabinoids (Ahmed et al., 2015). None, however, have

been given as much attention as cannabidiol (CBD), as a result of its pharmacological difference to Δ^9-THC.

Two main cannabinoid receptors have been localised in the human body on which the various cannabinoids act as ligands: the CB-1 receptor, mainly found in central and peripheral neurons, and the CB-2 receptor, found primarily in immune cells (although it is also expressed by neurons) (Pertwee, 2008). The effects initiated by the interaction of ligand and receptor vary greatly, depending on the cannabinoid in question. Δ^9-THC has been shown to be a CB-1 and CB-2 receptor partial agonist, whereas CBD acts not only as a CB-2 receptor antagonist (by merit of an inverse agonism), but also as an antagonist of CB-1 and CB-2 receptor agonists (Pertwee, 2008). The resulting inverse effects of these two cannabinoids is of great interest for the aforementioned reason: it appears that CBD has the capacity to counteract the psychotropic effect of Δ^9-THC, and thus, more generally speaking, of cannabis.

Through these pharmacological discoveries, a major flaw in the debate surrounding the potential harms of cannabis has been unearthed: the cannabinoid profile of cannabis has not, thus far, been robustly investigated (Freeman & Swift, 2016; Potter, Clark, & Brown, 2008; Smith, 2005). Rather, it has been the *collective* outcomes of cannabis effects guiding such scientific debate and hence public policy (Romer Thomsen, Callesen, & Feldstein Ewing, 2017). Only in the last few years has new research begun to examine this variable, focussing in particular on the THC/CBD ratio of cannabis (Iseger & Bossong, 2015).

A brief note on the terminology. There are commonly two distinct types of cannabis: the resin (secretions emitted during the flowering phase), referred to as *hashish;* and, herbal cannabis, of which two subtypes exist. Herbal cannabis grown outdoors with pollinated female plants is often called *marijuana, weed* or *bush weed*. It contains both the floral (flowers) and foliar (leaves) parts of the plant. Conversely, *sinsemilla* (from the Spanish meaning ‘no seeds’), also known as *skunk,* is grown indoors with intense artificial light using unpollinated female plants (Potter et al., 2008). This process requires only the floral part of the plant. Thus the chosen method of preparation is the major influencing factor on the resulting potency of the drug. In summary, the rank of potency from low to high is *hashish, weed, sinsemilla.*

The *potency* of cannabis is traditionally equated to its Δ^9-THC concentration (Cascini, Aiello, & Di Tanna, 2012; Hardwick & King, 2008). When defined in this way, however, the impact of CBD is neglected. Instead, only cannabis with high Δ^9-THC and low CBD concentrations should be defined as high-potency cannabis (Freeman & Winstock, 2015), and will henceforth be referred to as such. This places the THC/CBD ratio at the forefront of the definition.

The availability and consumption of high-potency cannabis is increasing worldwide (Cascini et al., 2012; ElSohly et al., 2016; Hardwick & King, 2008; Potter et al., 2008; Swift, Wong, Li, Arnold, & McGregor, 2013). For example, figures reported by Hardwick and King

(2008) showed that the market share of herbal cannabis in England and Wales increased from around 30% in 2002 to 81% in 2008. In a closer examination of such herbal cannabis samples, 97% were found to be the highly potent *sinsemilla,* containing mean Δ^9-THC and CBD concentrations of 16.2% and <0.1% respectively. The remaining 3% (imported herbal cannabis) contained mean Δ^9-THC and CBD concentrations of 8.4% and <0.1% respectively. In contrast, cannabis resin contained mean Δ^9-THC and CBD concentrations of 5.9% and 3.5% respectively. However, such cannabis only made up 16% of the market.

In light of the trend towards omnipresent *sinsemilla,* there is a growing need to understand the alignment of cause and effects with respect to the cannabinoid profile of cannabis and the potential harm to human consumers. Consequentially, the purpose of this literature review is threefold: first, to comprehensively summarise the research which has attempted to investigate this variable. Second, to interpret these findings thematically, highlighting conclusive findings and limitations. And third, to place any findings into the political and medical context, using them as a basis for a discussion on consequences which should be drawn, and future research to be carried out.

4. Discussion

4.1 Summary

This literature review set out to examine the effect of cannabis potency with regard to potential harms to the consumer. This variable has been consistently ignored in medical and political spectra, despite growing evidence of its importance. In total, twelve studies were found that set the aforementioned variable as one of their primary foci. Eight studies investigated the effect of cannabis potency on psychotic symptoms, three of which also tested for the effect on cognitive function; three studies investigated the effect on brain morphology; and, one study investigated the effect on creativity.

All in all, the twelve studies were conclusive in determining that high-potency cannabis is associated with greater harms compared to low-potency cannabis. This association was upheld in each of the four categories, albeit to a varying extent. In fact, some studies found no differences between the use of low-potency cannabis and avoiding its use altogether.

Bracketing the discussion on the medical use of cannabis and focussing exclusively on the repercussions of recreational use, the first of these two main findings, that is the association of high-potency cannabis with greater harms, was to be expected: a dose-response relationship comparable to alcohol. However, this consideration has consistently been equated to a Δ^9-THC dose-response relationship, thereby ignoring the preeminent effect of CBD altogether. As suggested in the introduction, a new definition of potency (aligned with the THC/CBD ratio) would address this shortcoming.

Yet it is the second of these two main findings, that is, to a large extent the absence of any differences between the use of low-potency cannabis and avoiding its use altogether, which is the most striking, and in both medical and political terms the finding with the most important implications. It highlights a substantial paucity which can be subsumed under a lack of education. Several questions must be addressed: do consumers, especially young, adolescent consumers and those with a family history of mental illness (the most at-risk groups of potential harms) know which type of cannabis they are consuming? Do they know that, analogous to alcohol, there are different consequences with respect to the 'strength' of the substance; between outdoor-grown bush weed and indoor-grown skunk? Thus are they, most importantly, in a position to make an educated decision regarding the use of cannabis?

Judging from current drug-prevention programmes and official sources of information (see, for example, SAG NEIN ZU DROGEN; BZgA 'Cannabis — Basisinformation'; NHS Choices 'Cannabis: The facts', etc.), this is not the case. At best, consumers are informed of the greater risks associated with cannabis with a high Δ^9-THC concentration. However, the conventional lists of potential harms and dangers are still indiscriminately associated with cannabis per se, without taking potency into account. Scientifically speaking, such claims are false, thereby hindering consumers from making informed decisions; who are left to collate a unified picture from their own experiences and by no means accurate sources. Future programmes should therefore focus on scientifically sound facts, informing consumers of the potency-dependent risks.

Important consequences of the two main findings must also be discussed in the political realm. Lynskey and colleagues discern the problem: 'Cannabis users in unregulated markets rarely know the THC and CBD content of the products they use' (Lynskey, Hindocha, & Freeman, 2016). After years of public debate surrounding the legalisation of cannabis, the past months have seen an upsurge in the implementation of such policies, in particular in the United States where several states have now legalised both the medical and recreational use of cannabis. However, these policies have failed to take advantage of the opportunity to implement limitations according to potency-dependent risks. Although a minimum age of 21 years has been set, as of yet there is no limit to the Δ^9-THC concentration of cannabis available for purchase, along the lines of a 15% THC cap as proposed by Uruguay and the Netherlands (Englund, Freeman, Murray, & McGuire, 2017). Again drawing on the analogy to alcohol, where there are clear guidelines and restrictions as to the percent by volume available for purchase, this would perhaps be the most efficient way of preventing potential harms (Englund et al., 2017; Fischer et al., 2017).

Further, these potency-dependent risks must be considered in light of the trend towards omnipresent high-potency cannabis (e.g., Hardwick & King, 2008), as discussed in the introduction.

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4.2 Limitations

Certain limitations must be considered. Three areas are of particular importance: first, the measures used to analyse the cannabinoid concentrations; second, the recruitment strategy; and third, the samples — in particular with respect to sample size and gender.

4.3 Outlook and fields for future research

Notwithstanding the paucity of studies in this field, and thereby assuming that further research will address any doubts raised by these limitations, the results are strongly suggestive that the potency of cannabis is a major variable for potential harms to the consumer. What remains to be considered, however, is a possible inverse causality: that cannabis potency does not determine the susceptibility to a range of symptoms; rather, that the susceptibility to a range of symptoms renders the preference of consuming high-potency cannabis. This ‘chicken/egg’ problem is addressed in varying depth by many of the twelve studies included (Demirakca et al., 2011; Marta Di Forti et al., 2015; Freeman & Winstock, 2015; Morgan & Curran, 2008; Morgan et al., 2012; Schubart et al., 2011).

In the study published in 2012, Morgan and colleagues deliver the most persuading argument in opposition to inverse causality. Having deliberately set out to address this, the authors conclude ‘our preference data now allow us to rule out […] pre-existing differences that draw individuals with higher psychosis proneness to smoke low CBD cannabis’. The preference data show ‘individuals with greater psychotic-like symptoms expressed a preference for non-skunk strains’ (Morgan et al., 2012).