ARTIFICIAL INTELLIGENCE SEES THE OPIOID CRISIS AS A GENETIC DISORDER

Abstract

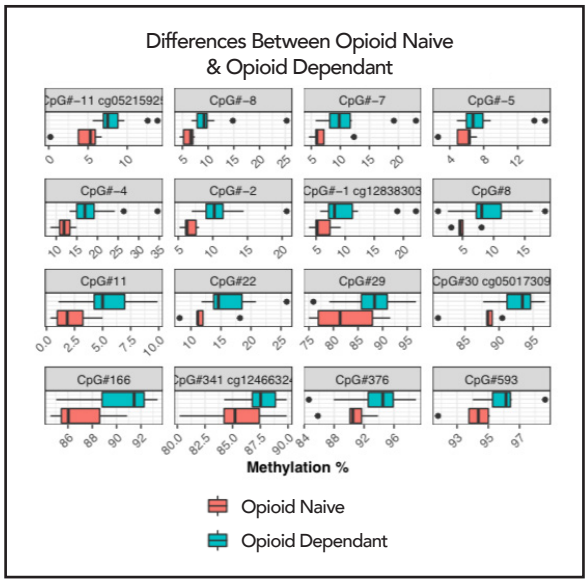
The Opioid Crisis has been hallmarked by a chronic, maladaptive, pathologic consumption of often illegal opioids. The driving force behind this dangerous activity has been attributed to an opioid craving arising from a brain disorder. An open mind will constantly consider other possibilities. We compared the DNA of the opioid dependent and against a control of the DNA of the opioid naive. Specifically, we compared the levels of DNA methylation in the OPRM1 gene between the two groups. The OPRM1 gene encodes for the main mu-opioid receptor. We used Artificial Intelligence (AI) as our arbitrator of the data. AI is a superior platform for the comparison of large datasets. AI is without bias. We are asking Artificial Intelligence to basically "learn" about the two sets of DNA. As far as "learning" within Artificial Intelligence, three broad categories of machine learning are recognized: a). reinforcement machine learning, b). supervised machine learning, and c). unsupervised machine learning. Reinforcement machine learning is useful in such activities as auto piloting a car. Supervised machine learning is useful when the available data is already "labeled" and appropriate algorithms are required such a reading a written language. Unsupervised machine learning is useful when the available data is "unlabeled" such as our data associated with DNA. The question before the machine is a simple question: does the machine see one DNA population or two? Furthermore, are any findings reproducible across a variety of software modalities? The implications of the answers are equally as simple. If the machine sees only one population, then this would be in keeping with the concept that the disorder associated with chronic maladaptive opioid consumption is a brain disease. But if the machine sees two distinct and separate genetic populations then this at least raises the possibility that the etiology of the disorder is something separate from a brain disease. In fact, this would at least raise the possibility that the etiology of the disorder could be genetic in origin.

The findings were conclusive. Artificial intelligence utilizing unsupervised machine learning identified two separate and distinct genetic populations. These findings were consistent and reproducible across a variety of software modalities. These findings raise the possibility that the etiology behind the Opioid Crisis may be genetic in origin. This would be considered a potential inconsistency with a brain disease model as an explanation of the underlying disorder.

Methods

The opioid naive data originated from individuals with no history of chronic opioid consumption (no more than two consecutive days of opioid consumption, less than twenty life time doses of opioids). The opioid dependent data originated from individuals with a history of chronic opioid consumption (greater than six consecutive months) and with at least seven symptoms present when opioid abstinence was attempted (tachycardia, mydriasis, diaphoresis, piloerection, anxiety, restlessness, joint aches, rhinorrhea, epiphora, abdominal cramps, nausea, diarrhea, excessive yawning). DNA was collected by saliva samples self-collected and submitted to the lab via the US Postal Service and at room temperature. Samples underwent targeted next gen bisulfate sequencing analysis for methylation.

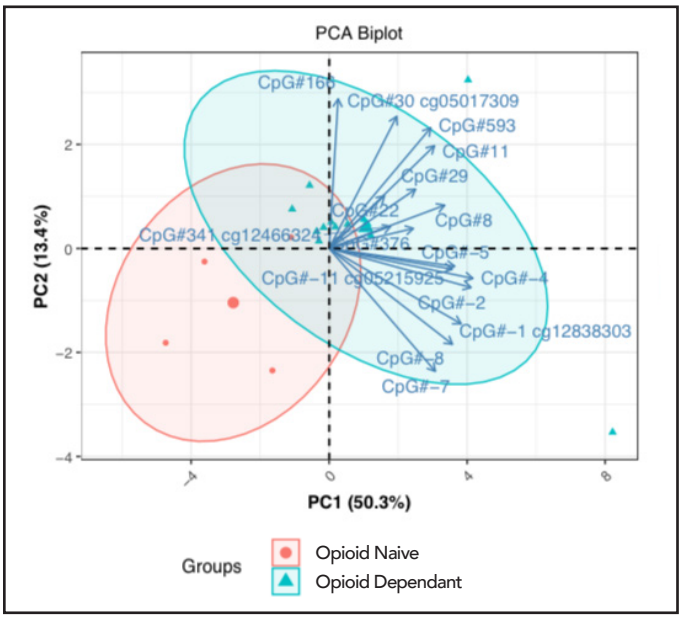
(Figure 1)



Hypermethylation was easily identified in the opioid dependent group and on multiple CpG sites throughout the OPRM1 gene. Sixteen CpG sites were selected for further evaluation and utilizing Artificial Intelligence with unsupervised machine learning. ***(Figure 1)***

Three separate modalities of unsupervised machine learning were utilized: Principal Component Analysis (PCA), Non Metric Dimensional Reduction (NMDS), and PERMANOVA. And again, the questions were simple questions: Can unsupervised machine learning see the two genetic populations as separate and distinct and if so, do these findings hold true across PCA, NMDS, and PERMANOVA?

A). Principal Component Analysis (PCA)

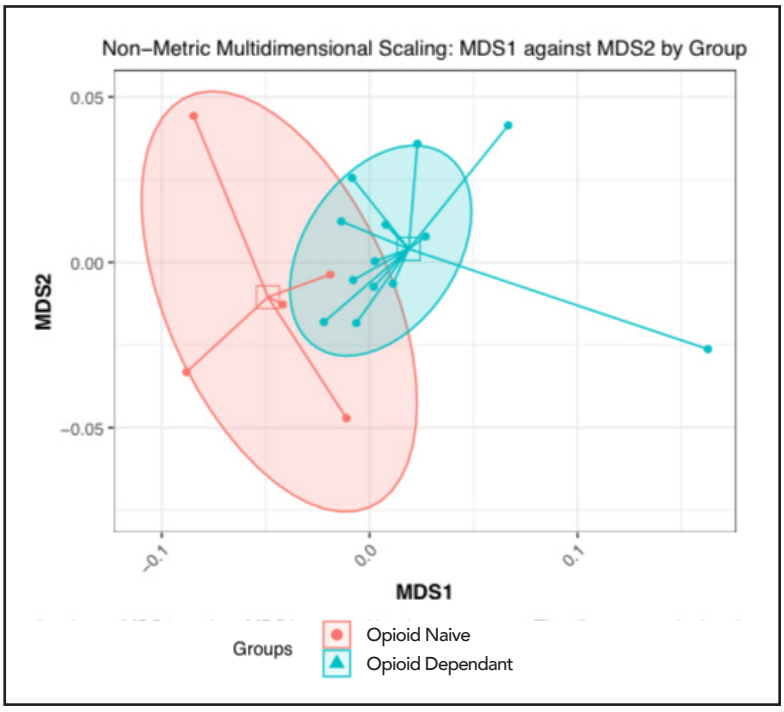


Principal Component Analysis was able to visualize two separate and distinct genetic populations.
(Figure 2)

(Figure 2)

B). Non Metric Dimensional Reduction (NMDS)

Non Metric Dimensional Reduction was also able to visualize two separate and distinct genetic populations, thus replicating the findings seen in the Principal Component Analysis.
(Figure 3)



(Figure 3)

C). PERMANOVA Analysis

(Figure 4)

Table 1: PERMANOVA Test: 10000 Permutations

	Df	SumOfSqs	R2	F	Pr(>F)
Group	1	857.3	0.2047	4.119	0.006499
Residual	16	3331	0.7953		
Total	17	4188	1		

Table 1: The PERMANOVA model was created using the 16 CpG sites as the dependent variables, and Group as the independent variable. The results show that we should reject the null hypothesis using alpha = 0.05, meaning there is some difference between the centroids/dispersions of each group ($P < 0.0065$). It is important to note that the PERMANOVA model used a distance matrix calculated by Euclidean distances. These results support the group separation seen by both the PCA biplot *(Figure 2)* and NMDS plot *(Figure 3).*

PERMANOVA Analysis supports the concept of two separate and distinct genetic populations. ***(Figure 4)***

Discussion

Artificial Intelligence is without bias. Artificial Intelligence does not have a stake in any particular conclusion. And Artificial Intelligence is able to clearly distinguish two separate and unique genetic populations - the opioid naive and the opioid dependent. This finding raises the prospect of a genetic etiology for the symptoms seen in the opioid dependent. Furthermore, this is a challenge to the widely accepted mental health basis of the brain disease model of addiction, at least in regards to the opioids.

It is long been noted that the FDA has in place a robust system for detecting mutations, changes in the DNA sequence, as the result of a drug. But critics, such as Moshe Szyf, have long voiced concerns that evaluating drugs for mutations but not evaluating drugs for epigenetic changes such as methylation leaves open a door for long range damage to occur and as a result of a drug toxicity manifesting itself as a methylation. This is a very real concern given this analysis via Artificial Intelligence.