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# Hypothesizing Molecular Genetics of the Holocaust: Were Dopaminergic Genes Involved or Brain Wash?

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# Abstract

Numerous studies indicated that the prevalence of certain alleles of the dopamine D2 receptor gene (*DRD2*) vary across different ethnic groups. Under adverse environmental conditions, these alleles can increase the risk of developing psychiatric symptoms. Thus, we hypothesized that the prevalence of the *DRD2* gene **Taq IA** allele may serve to explain the horrific behaviours practiced by the Nazi regime. Hitler's 'Brain Washing' methods goaded his followers to carry out genocide at a time when carriers of the *DRD2TaqIA* allele (the so called 'aggressive--genotype') were significantly higher among the Aryan Germans compared to resident German Jews. It would be of interest, to genotype the Jewish Holocaust survivors, to determine whether those with the **Taq AI** allele survived in greater numbers. The hypothesis being that, greater survival may result in enhanced frequency of not only the *DRD2AI* allele but other reward gene polymorphisms among survivors. Understanding the molecular genetics of any population in terms of reward dependence and subsequent behaviours will be most beneficial in future human interaction whether negative (war) or positive (peace) in nature.

### Keywords

Holocaust; Aryan Germans; Jews; dopamine; Reward Dependence; aggression; Molecular Genetics

# Introduction

While there have been many disciplines represented in genocide studies especially those related to the Holocaust, little has been done with regard to the widely explosive field of Omics. Philosophers have suggested that, in terms of genocide, evil overcomes well [1]. We

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are cognizant of the importance of philosophical contributions to the key concepts involved in the complexities that underlie human behaviours such as the relationship between the individual and group that are central to the concept of genocide, ethical issues such as intentionality, responsibility, and concepts of good and evil, as well as societal beliefs about genocide [2]. Just as Berel Lang argued that the contribution of professional philosophers to genocide studies could be quite significant [3], we suggest here that molecular-genetic antecedents may also contribute to understanding the atrocities that occurred under the Nazi regime.

The coining of the word 'Genocide' by Raphael Lemkin led to the UN Convention on Genocide in 1948 [4]. His term signified the nullification of any innocent peoples across the globe not only the mass killings of Jews during the Holocaust. Certain countries like the Soviet Union did not treat the mass killings as a uniquely Jewish phenomenon cognizant that other groups were also executed by the Nazis [5].

Hitler's highly successful "Brain Washing" methodology included the: *dissemination* of well-camouflaged lies (propaganda), *harassment* of non-believers, *intimidation* of incorrigible dissidents and finally the *elimination* of the obstinate recalcitrant and those considered 'unworthy of life'. That many Jewish survivors went on to lead truly successful and fruitful lives attests to the remarkable resilience of the survivors of the Holocaust [6] they developed the 'Holocaust Survivorship Model' that provides an valuable framework, to help us understand how people dealt with trauma, extreme stress and what was required for them to survive, they were then able to find personal meaning in these life events, adapt, and grow [6]. According to the research of Greene's group, about sixty five percent of the Holocaust survivors scored on the high side for resilience traits. According to these investigators, seventy eight percent of the survivors in their study had engaged in processes, considered resilient. They felt they were transcendent, had engaged in behaviours that helped their personal growth and changed them during the years since the Holocaust, so that they were able to leave a legacy and contribute to their communities [6].

#### Understanding the concept of selfish genes

A brief description of the evolutionary theory first proposed by Richard Dawkins in his book called '*The Selfish Gene*' [7] will help to clarify one focus of this treatise that the gene may be the unit of evolution. Dawkins work builds on the theories of George C. Williams from his first book '*Adaptation and Natural Selection*' [8].In the 1960s W.D. Hamilton focused on the individual organism and the group rather than the concept proposed by Dawkins a gene-centred theory of evolution whereby the 'selfish gene' is replicated. Interestingly, Dawkins has suggested that from the 'gene-centred' view the more alike two individuals are genetically, the more selflessly they behave toward each other. Moreover, an organism is expected to maximize its fitness for survival by the successful replication of gene copies and rather than, by replication of an individual organism. In simpler terms, Dawkins postulated that the genes within organisms are the replicators, with the body of each organism serving as a 'survival machine' for its genes. Others like Thomas Maschler called it 'the immortal gene' [8, 9]. Finally, Dawkins suggests that successful gene combinations benefit organisms and increase the chances of the gene being propagated. Darwin discussed a theoretical

role for a 'Sympatin' gene to ensure evolutionary success; a gene form that promotes survival elements like competitiveness, aggression, and risk taking. Carriers of this gene according to Darwin had a competitive advantage, being *not noble* and not willing to share but with a better chance of survival [10]. Over 150 years later, this hypothesis is that the 'Sympatin' gene maybe the *Taq* AI allele a variant of the dopamine D2 receptor (*DRD2*) gene. In genetic studies the *Taq* AI allele a variation has been associated with a number of survival-like behaviours [11, 12].

#### Mapping survival--like behaviours and dopaminergic activity

It is well known that Nazi doctrine was promoted throughout German schools starting at a young age and continuing throughout their secular education. Young Germans were imbued with the ideas of Niche about the Arian super—race. These ideas gave impetus to the attempted annihilation of Jews. However, the potential role of the association of dopamine receptor polymorphisms with childhood aggression may be another important element. In this regard, [13] found that children who carried specific *DRD2* gene alleles had significantly increased aggressive behaviour in a Hungarian patient [13].

Imbalances in the central dopamine system including genes that regulate other reward neurotransmitters like serotonin are important in the development of borderline personality disorder. Recently [14] demonstrated that young adult carriers of a number of DRD2 polymorphisms show impulsive and aggressive self-damaging behaviours. While these results are interesting the significant association was with DRD4 –616 CC allele and rs1800497 was not found to have significant association in Hungarian patient group in terms of personality. However other work by Kazantseva et al. [15] shows significant effects of ANKK1/DRD2 Taq1A on Neuroticism (p=0.016) and of SLC6A3 rs27072 (DAT1) on Persistence (p=0.021) in both genders. The association between ANKK1/DRD2 Taq1A A2/A2-genotype and higher Novelty Seeking and lower Reward Dependence was shown in men only (p for gender interaction=0.018) [15].

This result is also supported by work from Blum's group, whereby, in a blinded clinical trial, a positive correlation was observed with *DRD2* and dopamine transporter (*DAT1*) gene variations and pathological violence in adolescents [16]. In another study of young adults with extremely aggressive behaviours, the investigators also found a positive correlation with both *DAT1* and *DRD2* polymorphisms [17]. In addition, similar impulsive behaviours were found in family members of these pro bands suggesting an inherited passage of aggressive–like genes (possibly the 'Sympatin' gene). To be clear while it has been 150 years since Darwin in his works suggested the possibility of a survival gene ('Sympatin' gene) it is proposed herein that the gene referred to be Darwin could be related to the DRD2 A1 allele. However this polymorphism (rs1800497) resides in the ANKK1 gene which interacts with the biological activity of DRD2 receptor [11–13] (also seehttp://www.ncbi.nlm.nih.gov/SNP/snp\_ref.cgi?rs=1800497).

It is noteworthy that dopaminergic neurons are involved the behaviour of muricide (killing) rats [18] found that a deficiency of dopamine, determined by chemically induced degeneration of dopamine neurons in the olfactory bulb, may be related to rodent killing aggression in rats. While homicide and aggressive behaviours are multi-factorial, genetics

may play a prominent but undetermined role. However, it is becoming clear that the genes that govern reward gene regulation in the limbic system, especially for dopamine and serotonin predispose individuals to homicidal behaviour [19]. Specifically [19] found an association between a variant on the Catechol –Methyl-Transferase (COMT), responsible for clearance of synaptic dopamine, and homicidal behaviour in Schizophrenics. Moreover, [20] systematically showed that four genes involved in dopamine function associated with violent criminal behaviour in boys. Volkow's group was the first to report that variants for the Mono Amine Oxidase A (MAOA) gene that result in an inability to clear dopamine in both the synapse and mitochondria, are associated with aberrant aggression [21]. In contrast, deficits at the molecular level, including carrying the *DRD2*AI allele, result in low dopamine receptors and a super sensitivity that occurs, when activated by an abusable substance like alcohol, leads to very aggressive behaviour [22–29].

#### Ethnicity and Dopamine D2 receptor Gene

The evidence for differences across different ethnic groups in the prevalence of certain alleles of the DRD2 gene is ample. In 1993 [30] reported on population frequencies of the DRD2 *Taq* AI allele receptor locus. The allelic prevalence significantly varies whereby nine percent of the Yemenite Jews carried the DRD2 *Taq* AI allele, 6 percent in Ashkenazi Jews, compared to seventy-four percent of the Cheyenne American Indians and twenty-two percent among the German cohort. In fact, one variant of the DRD2 known as the rs6277C>T associated with addiction risk, was found, in a German population study, to be as high as fifty-two percent [31].However the National Library of Medicine (NLM) Hapmap Central European (CEU) population frequency of T allele is also fifty three percent (see http://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=6277). Hence the high frequency may not account for Germans only.

Interestingly, it was also determined that Germans, carrying the *DRD2Taq* AI significantly associates with extraversion [32]. In addition, it was also determined that German participants characterized by low D2 receptor density in the striatum show a high novelty seeking (thrill) behaviour. Koehler et al [32] and Mongtag et al [33] showed that in German carriers with at least one of the 66Met allele (Val66Met and Met66Met) of the BDNF SNP and one AI allele (AI/AI and AI/A2) of the DRD2 SNP are associated with the lowest grey matter volume of the anterior cingulate cortex, a site for decision making and relapse to addiction. The authors concluded that there might be an increased risk for the development of psychiatric symptoms under adverse environmental conditions. Albeit lack of direct information comparing ethnic groups we propose at the time of Hitler's rise to power, Nazism accelerated pathological aberrant behaviour against not only the Jews but other alleged "misfits" in the German society.

Other factors lend support for emotional pathology in Germans such as alexithymia. Alexithymia, a personality construct, refers to difficulties in emotional self-regulation that contribute as risk factors to several mental disorders manifest when individuals demonstrate an impoverished conscious experience of emotions. Specifically in a study by German scientists Walter et al. found that, on the subscale "Difficulties Identifying Feelings" of the total Toronto Alexithymia Scale, carriers of at least one *DRD2/ANKK1*AI allele and one

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*BDNF 66Met*, had the highest scores [34, 35]. Although Nazi indoctrination, this interesting molecular genetic fact may have had profound effects on German soldiers taking orders to kill Jews without emotion or guilt about what they have done in the line of duty. A plausible molecular -genetic hypothesis of the holocaust.

We are hereby proposing that based on this knowledge regarding molecular genetics and potential links to certain behaviours including drug seeking, aggression and even homicide in different ethnic groups we propose, the higher prevalence of the DRD2 AI, the more likely is the tendency to display these behavioural characteristics. Carriers of the *DRD2 AI* allele would have enhanced drug seeking including alcohol, and as such could become involved in violent acts, due in part, to build up of a known violent substance called Diazepam –Binding –Inhibitor (DBI) which increases post alcohol intake [27–29]. The main focus of the hypothesis, however, remains the higher frequency of the so called 'aggressive-genotype'. It is noteworthy, that in spite of Hitler's objection to any substance (tobacco, drugs and alcohol use especially in the military), there are accounts of alcohol abuse and abusive behaviour by German Soldiers [36]. Although, the German soldiers in general were not part of the Holocaust action which was driven by the SS soldiers who acted like emotionless –robots potentially due to 'aggressive—genotypes' with or without alcohol as a confounding variable.

Therefore, in accordance with this hypothesis it seems reasonable that Aryan Germans would have displayed these behavioural characteristics to a greater degree than would have German Jews. Keeping in mind that there are no records of genotyping during the early thirties, we must make assumptions which may provide an appropriate snapshot. It is well-established that severe Alcoholism has been associated with the *Taq* AI allele of the *DRD2* gene in the American population at a high rate. Therefore, when in 1982, for example, Snyder *et al.* evaluated alcoholism among the Jews in Israel who were descendants of Jewish Holocaust survives who had migrated to Israel and compared to other major either communities, found that Ashkenazi Jews have a significantly lower rate of alcoholism than both the Sephardi and Oriental groups [36]. While there are certain environmental mores (epigenetic) that load onto this, it is potentially important that various ethnic populations (Jews vs. non-Jews) may be at a higher or lower risk for a number of RDS behaviours including alcoholism depending on certain reward gene polymorphisms such as carrying the DRD2 *Taq* AI [37].

Israel in1997, in terms of homicide rates, was amongst the top five safest countries in the world, compared to Germany, where Berlin, was amongst the top twenty worst cities in the world for homicide. However in Israel, for example, the homicide rate produced by criminal activities is relatively low: 2.4 killed per 100,000 inhabitants in a year much lower than most countries studied [38].

We are proposing that many of the Jewish survivors of the Holocaust would have carried the *DRD2Taq* AI when they immigrated to Israel in the 1940's. The Israelis of today would have an increased *Taq* AI allele prevalence and behave quite differently, more like their Aryan German counterparts during the Holocaust period. A search in the current literature did not provide any evidence of genotyping in surviving Jews and we cannot know unless

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we genotype holocaust survivors and their respective children. However, there may be some facts which could be argued in favour of investigating the possibility of enhanced *DRD2Taq* AI allele frequency in the Israel population of the 21<sup>st</sup> century.

Certainly, we have seen a lot of evidence that the current day Israelis defend themselves against enemy attacks of neighbouring Arab territories and aggression even in daily life. It is noteworthy that, in 1995, the German per 100,000 capita homicide rate was 1.7 while the Israeli per 100,000 capita homicide rate was slightly higher at 2.0. The homicide rate for Israel reached its highest rate of 3.6 in 2001 and by 2011 had dropped to 2.0 again. The homicide rate for Germany dropped to 0.8 in 2011 [39]. These numbers might reflect genetic loading in Israel for carrying the aggressive *Taq* AI allele genotype, although untested. It is equally arguable that this increase in murders by the populous, which has always included genetically unrelated Palestinians, could be due to non-genetic reasons including stress, military training, war, economics, and other environmental epigenetic elements.

#### A caveat

It is noteworthy that DNA from the modern Jewish population has not as yet been compared to ancient Judean DNA in any studies. In the absence of old DNA, geographic roots can be traced adequately using data from living populations [40, 41, 42]. Population genetics such as the Founder Effect; the presence of a selectively neutral, identical by descent allele at a high frequency in an isolated population that was carried by a founder individual or arose by later mutation, can be useful in data extrapolation. Indeed the data from living populations is in agreement with key Jewish historic events. There are traces of Northern Italian and Slavic ancestry among European Jews because intermarriage occurred before the Roman Empire outlawed conversion to Judaism. Some Ashkenazi ancestral lines in Southern European families come from these marriages. Finally, a perfect genetic corollary of Ashkenazi Jewish ancestry was demonstrated by [42] within Americans of European ancestry. Indeed, a single Jewish grandparent can be distinguished statistically from individuals without Jewish ancestry. We now know that the first migration of people out of Africa to Israel occurred over 63,000 years ago. However, to date no one has genotyped the ancestral Jewish DNA to determine whether the oldest Jews carried a higher rate of the aggressive Taq AI allele genotype which could have increased their survival chance.

# Conclusion

Limited by the absence of *DRD2 Taq* AI allele genotyping among the Jewish Holocaust survivors as well as the Nazis SS soldiers we can only hypothesize, based on recent studies in human and animal models, about the link between genetic predisposition and the horrific behaviours perpetrated during the Holocaust. However, it seems fairly convincing that during the period of the Holocaust that the differential in carriers of the *DRD2 Taq* AI allele (the so--called aggressive genotype) estimated by the older work of Barr and Kidd [30] that there was a higher percentage of *DRD2*A1 allele among the Aryan Germans compared to residential German Jews. It would be important to genotype holocaust surviving Jews across the world to determine whether there has been an enhanced frequency of not only the *DRD2*AI allele but other reward genes, including serotonin, endorphin, GABA and

other dopamine polymorphisms [43, 44, 45]. However finding such an enhanced frequency may not provide all the answers especially when you consider the environmental-epigenetic psychological factors including "brain washing" as a precursor for extermination practiced in the Nazi regime

While there is a plethora of evidence for Hitler's brain washing and resultant devastation of all Germans, [46] understanding the molecular genetics of any population in terms of reward dependence and subsequent behaviour will be most beneficial in future human interaction, both when negative and positive in nature [47].

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