

Challenges Faced by Behavioral Genetic Studies: Researchers Perspective from the MENA Region

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Abstract: Background: Behavioral genetic studies are important for the understanding of the contribution of genetic variations to human behavior. However, such studies might be associated with some ethical concerns.

Methods: In the current study, ethical challenges related to studies of genetic variations contributing to human behavior were examined among researchers. To achieve the study purpose, the Middle East and North Africa (MENA) region researchers were taken as an example, where the after-mentioned ethical challenges were discussed among a group of researchers, who were the participants of an online forum. Discussions and responses of the participants were monitored and were later qualitatively analyzed.

Results: Discussions revealed that several ethical challenges, including subjects' recruitment, the difficulty of obtaining informed consents, and issues of privacy and confidentiality of obtained data as information leakage, in this case, will lead to social stigma and isolation of the participants and their immediate family members. Jordanian social and cultural norms, faith, and the tribal nature of the population were raised as a major challenge that might face conducting behavioral genetic studies in the Arab populations of the MENA. The lack of regulation related to the conduction of genetic studies, misunderstanding, and misuse of genetic information are other challenges. A full explanation of genetic research and the current and future possible benefits/risks of such research could be potential solutions.

Conclusion: In conclusion, the MENA populations are tackled with major challenges in relation to conducting research studies in genetics/antisocial behavior field/s. Establishment of guidelines related to genetic studies, capacity building, increasing public awareness about the importance of genetic testing, and enhancing responsible conduct of research will facilitate the conduct of such sensitive studies in the future in the region.

Keywords: Ethical challenges, genetic studies, human behavior, MENA, researchers, views.

1. INTRODUCTION

Antisocial behaviors are defined as angry, hostile, or aggressive acts that harm and lack consideration for others' comfort or violate their rights in which the aggressor usually has no regret for what he or she has committed [1, 2]. Such kind of condition has a variety of symptoms, which begins in preschool-aged children and continues through adulthood [3]. It has been found that around 50 percent of the adults

who suffer from antisocial behavior symptoms have acquired these behaviors since they were in elementary school, and those symptoms persisted until adulthood. Symptoms included unashamed disrepute, disregard for others, scarcity of ethical behavior, offensive to others without a sign of bother for the other, irritability, and aggression [4].

The etiology of antisocial behavior is heterogeneous, so that each condition is different from the other and the notion of the causes of antisocial behavior relies on different factors such as environmental, biological, and genetic factors [5]. Different biological factors have an implication in developing antisocial behavior, such as brain damage during pregnancy, brain hypoxia in the womb or birth, or neuropsychology

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logical dysfunction and psychosocial influences [6]. A number of studies also showed that environmental factors have a major role in the creation of antisocial behavior, especially during childhood [7]. Examples of such factors include; the person exposed to domestic violence and abused in his home, his parents being drug users, was abused during his childhood either sexually, physically, or emotionally or an unstable home environment [5, 7].

As shown by various studies, genes have an impact on childhood antisocial and aggressive behavior during childhood, and scientists have recognized specific genetic associations with antisocial behavior [8, 9]. Even with an increasing understanding of the genetic bases of human behavior, a cautious approach is warranted either in making inferences about a given individual or in considering changes to the legal system that might now take a defendant's experience and disposition into account [10, 11]. In fact, antisocial behavior had a clear genetic component and was shown to be influenced by certain genetic polymorphisms [12]. Polymorphisms in four genes have been found to be associated with an increased vulnerability for antisocial and impulsive behavior in response to aversive environmental conditions [13]. These genes include 1) MAOA that codes for monoamine oxidase A enzyme, which has an important implication in dopamine, noradrenaline, and serotonin metabolism [14]; 2) SLC6A4 gene codes for the serotonin transporter SLC6A4, which plays an important role in controlling serotonin levels in the synaptic cleft [15]; 3) COMT gene codes for catechol-O-methyltransferase, which is the main regulator of dopamine levels in synapses [16]; 4) DRD4 gene codes for the dopamine D4 receptor, which is a G protein-coupled receptor that is highly expressed in the cerebellum and plays a significant role in dopaminergic synapses [17]. In a genome-wide study of antisocial behavior in a large combined sample, it has been shown that a large number of genetic variants play a role in antisocial behavior and several variants show gender-specific effects on antisocial behavior in males and females [18]. In the current study, the ethical challenges face by genetic studies that examine genetic variations contributing to antisocial behavior were discussed in this study by taking the Middle East and North Africa (MENA) researchers as an example.

2. METHODS

2.1. Study Design

In the current study, a descriptive qualitative approach was used to explore the research ethics of genetic variations contributing to antisocial behavior by taking MENA researchers as an example. Researchers from MENA participated in the study as a part of the Responsible Conduct of Research (RCR) training program, which was hosted by the online learning platforms of Jordan University of Science and Technology and the University of California at San Diego, CA, USA. This program was funded by The National Institute of Health/Fogarty International Center to enhance the RCR in the MENA region. Twenty-eight researchers were

the study participants, including 18 from Jordan, 2 from Tunisia, 2 from Morocco, and one from each of the following countries: Egypt, Yemen, Iraq, Sudan, Algeria, and Gaza-Strip/Palestinian Authority. The majority of participants were faculty members (PhD holders, n=24) and 4 were MSc research assistants.

The opinions of the scientists (n=28) were collected through an online discussion forum. The forum was opened for a total of two weeks, with enough time provided by the moderator for each of the questions to motivate online discussion. The posts in the discussion (n=118) were used as a tool for qualitative analysis and were categorized into six ethical themes 1) subjects recruitment, 2) informed consent process, 3) privacy and confidentiality, 4) nature of the population (culture, norms, and regulations), 5) interpretation of the findings, and 6) Risks and benefits. An expert qualitative researcher monitored forum discussions. This process included promoting the study participants to be involved in the discussion using some provocative statements and probe questions such as “good point that needs more elaboration”, “could you explain more...”, *etc.* Such a monitoring process is effective in improving the validity of the collected data and study findings [19]. To reduce bias, a different researcher other than the one who monitored the discussion forum transcribed the collected data into different domains. In detail, the moderator was responsible for posting the main questions and probing when needed, and then he directed and facilitated the online discussion. Participation in the online discussions was voluntary and participants were informed that they have the right to withdraw at any point without penalties. All discussions in the forum were transcribed verbatim for analysis. Researchers conducted the analysis process in its original English to maintain fidelity of the results, which could be lost by early and inaccurate translation. Preliminary analysis was conducted after the end of the online discussion on the forum to get a general impression of the data. Analysis of the transcribed data was undertaken manually through the coding process and generating categories and themes by two independent researchers, who then met to overcome any inconsistency in the categorization of themes and subthemes and reach a consensus.

2.2. Ethical Approval

The Institutional Review Board (IRB) at the Jordan University of Science and Technology (IRB-JUST) approved this study. The IRB applies the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Participants gave informed consent before they participated in the forum.

3. RESULTS

Participants were asked about their opinion concerning ethical challenges for studies that examine genetic variations contributing to antisocial behavior in the Arabic populations. A total of 6 challenges were raised/discussed by the participants (Table 1). The order of challenges according to number of participants who raised/discussed them is privacy

Table 1. Main challenges of conduction of antisocial genetic research in the MENA region

Challenge	Number of Participant Who Raised/Discussed the Challenge: N (%), Out of 28
Subjects' recruitment	4 (14.2)
Informed consent	9 (32.1)
Privacy and confidentiality	16 (57.1)
Nature of the population: culture, norms and regulations	12 (42.9)
Interpretation of the findings	7 (25.0)
Risks and benefits	15 (53.6)

and confidentiality > risks and benefits > culture/norms/regulations > informed consent > interpretations of the findings > Subjects' recruitments (Table 1). Details about challenges are presented below:

3.1. Subjects' Recruitment

Several participants pointed to a challenge in recruiting subjects for this kind of research due to the sensitivity of the topic and the lack of awareness and knowledge of such studies and their test results.

Among suggested solutions to this challenge are creating more awareness about genetic studies, proper genetic counseling, and highlighting potential benefits.

One participant stated that “participants always concentrate on the direct benefit of research”.

Another participant said, “The lack of interest of the participants in such studies will pose an obstacle in recruiting”. However, one participant suggested a solution for the recruitment challenge: “Development of effective interventions based on genetic testing could promote motivation to participate.”

3.2. Informed Consent Process

Participants discussed the reasons why informed consent in genetic studies in Arab populations is difficult to obtain, and whether this difficulty (if any) applies only to antisocial studies or for all types of research, and how this problem can be solved?

Three members agreed that “the hardest part is achieving the consent form”.

One participant stated that “..... As the information gained from genetic testing will be retraced to the whole family, thus, submitting the consent will be very hard to achieve ...”.

Most members also stressed that informed consent is required and participants need to have a full explanation of the current and future possible benefits/risks of such research in order to convince the population of signing the consent form.

For example, one member stated, “I think genetic counseling is one way to deliver information. I think an explanation and understanding of some of the human behavior

by participants would encourage them to accept informed consent and participation in such studies.”

Another member said “The main ethical challenge in antisocial studies is the high risk of stigma and its devastating consequences that need to be stated in the consent form.”

3.3. Privacy and Confidentiality

Others highlighted matter of privacy and confidentiality of medical information of the study participants as the leakage in most cases would lead to stigmatizing related individuals, including socially isolating them and creating negative psychological effects on them.

A female member (S.A) said “Confidentiality breach and disclosure of such information generated by genetic studies can associate some families with some genetic diseases (even if rare) in the form of the social stigma that can lead to isolation and all psychological consequences.....”

Such information might be used inappropriately by private insurance companies by depriving/ refuse to cover persons from stigmatized families.”

One male member pointed to the shared nature of genetic information and highlighted that breaching confidentiality can also harm the relatives of participants.

The member stated “..... Being afraid of breaching confidentiality and privacy.....These genetic findings might affect negatively the carrier (relatives of the person who has the genetic condition.”

3.4. Nature of the Population: Culture, Norms, and Regulations

Two participants stressed the importance of Jordanian social norms, culture, faith, and the tribal nature of the population, which might form an obstacle in conducting antisocial genetic-related studies in the Arab populations, including Jordan.

One member stated, “The culture and norms of the Jordanian community could be a major barrier for such genetic tests as people not prepared and are threatened by antisocial consequences”.

Another example: “societies in the Middle East should be prepared to accept the results of genetic studies, this needs a time that is not short. Researchers should play a

great effective role in this, simplified lectures, debates, and discussions involving different spectra of the society, implanting the culture of “no discrimination” and even “Drama” and social media can participate in changing the ideas of the societies.”

Another two members stated that “If the study holds conflict with participants’ religious beliefs then it will be almost impossible to recruit the required population”.

Examples related to the lack of regulation related to the conduction of genetic study as an obstacle are “The question of who should be entitled to have the right to access and use such stigmatizing information/records related to families in the population”.

“There is a need to have regulations monitoring the process of such studies due to the fear of having a social misunderstanding of the real purpose behind conducting such studies.”

3.5. Interpretation of the Findings

Misunderstanding and misuse of genetic information are highlighted by several as major challenges.

For example:

“If such studies proved a direct relation of the “warrior gene” to antisocial behavior then violent individuals will try to get away with punishment by blaming it all on their bad genes”. “Authorities might blame the genes for all antisocial behavior and crimes and disregard other criminating factors.”

“Members/families (in Jordan) that would be diagnosed carrying variants/genes related to causing antisocial behavior will be highly stigmatized, due to the fact that antisocial behavior is always connected to mental illness in Jordanian society”.

“Such research will end up being a tool for destroying others’ lives by stigmatizing them with a specific genetic trait which states that this person has the potential possibility of committing a specific antisocial behavior, consequently condemning them for what they might do and not for what they did”.

3.6. Risks and Benefits

Major discussions related to antisocial genetic research were focused on issues related to benefits/risks from the conduction of such studies. Two members shared opposite opinions concerning whether genetic polymorphisms would increase the possibility of an individual to have an untreatable genetic disorder. Meanwhile, one member recommended that it is not worth it to tell the subject that they hold a good possibility to an untreatable genetic disorder, whereas the other said that knowing such a possibility will create extra awareness within that subject, who in turn will avoid specific behavior which will prevent further and future complications.

One member stated, “If a patient is susceptible to develop an untreatable disease, s/he may benefit from avoiding

other factors that could contribute to increasing the risk, the management can be provided early and some complications may be prevented.”

Another member stated, “Do you think that research aiming at genetic testing for the susceptibility for behavioral and cognitive disorders is a waste of money and resources or could it lead to preventative approaches?”

Two members stated that, “Financials should be aimed towards the other affecting factors such as environmental factors and dysfunctional families for that they are easier to identify”, One member mentioned that “Genetic testing of the behavioral disorders is not a waste of money for that preventive measures can be taken should the genetic susceptibility be identified”.

More examples: “Genetic testing for study purposes could reveal certain genetic predispositions for some disease which predisposes participants to social stigma, social isolation, and psychological problems in eastern communities (e.g. Jordan)”.

“Revealing information about the existence and relation of a gene to the antisocial behavior among a specific population will create a stigmatizing effect which in turn will negatively affect such population, and therefore researchers should think twice when it comes to conducting such research in Jordan”.

4. DISCUSSION

The behavioral genetics is an important topic in genetics, which focuses on investigating the link between genes and criminal and aggressive behaviors and their relations with the surrounding environment [20]. During the last years, growing pieces of evidence exposed the significant impact of both genes and the environment on an individual’s antisocial behavior that changed the views toward antisocial behavior concepts. Moreover, understanding the causes of antisocial behavior would set the stage for prevention interventions that could significantly reduce the crime rate [21]. In the current study, a group of MENA researchers examined ethical challenges related to studies of genetic variations contributing to antisocial behavior in the Arab populations. The main challenges discussed included the recruitment of subjects, informed consent process, risks and benefits, privacy and confidentiality, and interpretations of findings and culture.

The first challenge discussed by the researchers is related to recruitments of subjects due to the sensitivity of the topic and lack of awareness about genetic testing in the Arab populations. In a study that was conducted on genetic factors that contribute to epilepsy, the decline-to-participate rate among eligible subjects was about 84%, which has been attributed to confidentiality and lack of compensation [22]. The recruitment of subjects to cancer genetic studies and clinical trials for genetic diseases was also a challenge [23, 24]. Thus, enhancing the awareness of the MENA populations about the importance of genetic studies can improve the recruitment of participants in such studies.

The second main challenge was a violation of a patient's confidentiality and privacy by genetic testing. In a study that investigated the attitudes of healthcare professionals toward behavioral genetic testing for antisocial behavior, the majority of study participants were against genetic testing unless treatment was obtainable. Participants were worried about probable harm, such as exposing patient's confidentiality that may lead to social stigma and racial discrimination [25]. Similar findings were reported in previous studies that highlighted the potential of genetic data in exposing personal/family information such as one's parent, sibling, and children [26-28]. Maintaining participants' confidentiality and privacy will enhance the trust in researchers and will ultimately increase participation in genetic studies.

A different challenge that the researchers raised is related to the risks and benefits of the study. Some of the researchers doubted concerning applications of the findings and if interventions are available for subjects at risk of antisocial behavior. In a previous study, disagreement regarding the usefulness of such studies was reported. Some participants indicated that genetic testing could provide an early indication for parents about the problems children may face in the near future, which enables them to take their preventative decision early. On the other hand, some participants were concerned about potential risks for such testing that include misinterpretation of the findings, false positives, false negatives, and the danger of stigmatization that potentially comes along with a positive test result [29, 30]. With respect to the interpretation of data, which was also discussed by researchers in the current study, it is worth to mention that environmental risk factors have also been identified in influencing antisocial behavior. Actually, environmental factors tend to contribute largely to antisocial outcomes when compared to genetic ones. This is because variations in the environment seem to significantly affect an individual's gene expression *via* mechanisms that involve epigenetic changes. This will complicate the understanding and prediction of an individual's behavior [31, 32].

Social norms, culture, faith, and the tribal nature of the Arab populations of the MENA might be a major difficulty in conducting antisocial genetic related studies. It is not an easy task to convince people to accept the results of genetic studies, especially if the study holds conflict with participants' religious beliefs that will complicate participation in such a study. Another obstacle that may face genetic studies is stigmatizing the family diagnosed by carrying variants/genes related to causing antisocial behavior because antisocial behavior is always linked to psychological illness among the Jordanian community. The informed consent process was also among the challenges discussed by the researchers. The informed consent was also highlighted as a challenge in several previous studies [33, 34]. There is a necessity to comprehend people's beliefs, awareness, and responses toward genetic testing, which may fill the gap by explaining and clearing vague, concern, and knowledge in such research [35]. The shortage of expertise in the area of genetic counseling and the absence of regulations in most of the countries in the region will pose difficulties in resolving such a challenge.

The MENA populations are tackled with major challenges in providing comprehensive and up-to-date health services in the field of genetics [36]. These obstacles include lack of resources, a limited number of trained persons in the area of genetic testing and counseling, a misperception that genetic testing is too expensive to conduct, lack of regulations, and fear of families who have been diagnosed with a certain genetic disorder to be stigmatized within their community. Establishment of guidelines related to genetic studies, capacity building, increasing public awareness about the importance of genetic testing, and enhancing responsible conduct of research will facilitate the conduction of such sensitive studies in the future in the region.

Social behaviors are expected to be affected by strong environmental factors. In fact, the impact of the environment on gene expression *via* epigenetic mechanisms is well established [37-40]. In recent reviews, epigenetic regulation of genes involved in neuroendocrine, serotonergic and oxytocinergic pathways and their role in modulating personality and vulnerability to proactive and reactive aggressive behavior were discussed [41, 42]. Thus, behavioral genetics and epigenetics are important areas in research that help uncover the fine interaction between genes and environment and the subsequent molecular pathways that contribute to aggression in the populations.

Among the limitations of the current study is that the majority of participants were from Jordan. The study was part of a fellowship that was conducted in Jordan. It is worth mentioning that most of the MENA countries share language, culture, religions...*etc.*, and these countries suffer from the same issues regarding scientific research as explained above. Thus, the study represents the MENA region to some extent. However, expanding the study to have good representations of MENA countries is strongly recommended.

CONCLUSION

The MENA populations are tackled with major challenges in relation to conducting research studies in genetic/s/antisocial behavior field/s. Establishment of guidelines related to genetic studies, capacity building, increasing public awareness about the importance of genetic testing, and enhancing responsible conduct of research will facilitate the conduct of such sensitive studies in the future in the region.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Institutional Review Board (IRB) at the Jordan University of Science and Technology, Jordan (IRB-JUST) approved this study.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. For the procedures on humans the IRB applies the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

CONSENT FOR PUBLICATION

Participants gave informed consent before they participated in the forum.

AVAILABILITY OF DATA AND MATERIALS

Data will be made available upon reasonable request through email to the corresponding author [KHA].

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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