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Perception of acoustic frequencies in (Ab) users and non-users of psychedelics: a cross-sectional analytic study via the surface web

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Abstract

Hallucinogenic substances, also known as psychedelics and entheogenic chemicals, are psychoactive substance possessing unique pharmacodynamics and pharmacokinetic properties. The literature points out some high-risk hallucinogens including those of super-potent properties active within the micro-dosing range. Psychedelics as well as several medicinal and non-medicinal chemicals can be ototoxic and can induce deafness. Our study aims to extrapolate, based on statistical inference, the existence of a potential correlation between the use of hallucinogens versus hearing loss. This study is observational cross-sectional analytic based on a survey presented to web users interacting via dedicated private groups on Facebook. The investigation will include atone (frequency) generator to test the hearing range of audible frequencies including the upper and lower limits of hearing. The study will also screen demographic parameters, and variables of interests including social and marital status, ethnicity, nationality, and pre-existing medical conditions. Hypothesis testing could notinfer any significant differences or association between the use of psychedelic substances and hearing loss. It seems that the (mis) use of psychedelics and the range of audible frequencies of (mis)users are independent of each other. However, our study has some confounding variable and limitations that will be pointed out. Future studies should incorporate animal models and controlled trials on humans to extrapolate rigour evidence concerning the potential pathophysiological effects of hallucinogens, including molecular changes, on the conductive and sensor neural mechanisms of hearing. Besides, observational studies should always attempt to be more representative, systematic, and strive to provide real-time and predictive analytics for specific populations of interest.

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Introduction

Psychedelics substances and entheogens are chemicals of hallucinogenic effects of high interest in the psychedelia-related culture (Dargan and Wood, 2013). Hallucinogens represent a unique category of psychoactive and novel psychoactive substances (NPS) (Al-Imam, 2017a; Al-Imam and Abdul Majeed, 2017). The diffusion of those chemicals on the web has been fostered by the electronic commerce phenomenon (e-commerce) existing on the surface web as well as the invisible strata of the internet, including the the deep web and the dark net illicit electronic marketplace (Ginter *et al.*, 2014; Turban *et al.*, 2015; Al-Imam, 2017a; Al-Imam *et al.*, 2017b). The booming evolution within the discipline of information and communication technologies (ICT), cybernetics, and informatics has promoted the exponential growth in e-commerce and the diffusion of diverse forms of illicit and regulated substances over the internet (Ginter *et al.*, 2014; Al-Imam *et al.*, 2017).

The central effect of those chemicals on the nervous system is stimulatory (neural stimulant and psych stimulant) via the modulation of monoamines including serotonin and dopamine neurotransmitters and their corresponding monoamine transporters (MATs) (Hanks and González-Maeso, 2012; Kolp, 2014). The effect on monoamines and MATs can be potent or super-potent. Therefore, some of these substances are effective in the microdose range. Hence, the term "micro-dosing" is implemented as in the case of Lysergic acid diethylamide (LSD), Dimethyltryptamine (DMT), and some chemical isomers of NBOMe compounds (Johnstad, 2018).The existing literature provides some evidence about high-risk psychoactive chemicals and hallucinogens (Al-Imam, 2017b; Al-Imam and Abdul Majeed, 2017). There have been documented reports of intoxication, some of which has led to catastrophic multisystem failure and even sudden death due to pharmacological, in parallel with behavioral changes which can be lead to homicide, suicidal ideation, and suicide (Dargan and Wood, 2013; Al-Imam, 2017a; Al-Imam, 2017b; Al-Imam and Abdul Majeed, 2017). The long-term use of some of these chemicals on body systems can have serious consequences and induce permanent changes including the impact on vision, hearing, cognition, personality, and behavior(Al-Imam, 2017c; Al-Imam, 2017d; Al-Imam, 2017e). There is a lack of experimental studies in the literature about the toxic effects of specific psychedelic substances on hearing (ototoxicity) leading to hearing loss and deafness. Hearing loss is physiologically classified into conductive and sensor neural deafness which can be attributed either to the loss of the ability to listen to specific amplitudes of sound waves (measured in decibel) or frequencies (measured in hertz) or due to both combined (Roth *et al.*, 2011). The particular typology of hearing loss can be accessed via audiometry and other diagnostics (Cruickshanks *et al.*, 1998; Dalton *et al.*, 2003). This study, which is purely an observational cross-sectional analysis, will attempt to extrapolate a statistical inference on the potential association of (mis)use of psychedelics and hearing perception in a specific population existing on the surface web(Facebook, 2018a; Facebook, 2018b; Facebook, 2018c; Facebook, 2018d; Facebook, 2018e). The results of this study can provide an insight guiding future attempts of research including preclinical studies, quasi-experiments, and clinical trials.

Materials and methods

Ethical Approval

This study has been ethically approved by the Institute Review Board (IRB) of the College of Medicine at the University of Baghdad and in compliance with the authority of the IRB meeting number seven (IRB no.7) on the 20th of December 2016.

Research design

The study is observational and cross-sectional in design aiming to infer data on hearing loss (frequencies) and the (mis)use of psychedelics.

Equipment and Materials

A tone generator (software for a hearing test of sound frequencies) is implemented in combination with a survey created via Google Forms (De la Fuente Valentín, 2009). The tone (frequency) generator was programmed using *JavaScript*. The software has built-in instructions on how to run the test to avoid erroneous results attributed to the participant's device including specification related to desktop PC, laptop, tablet devices and mobile phones, speakers, headphones, and earphones, and wireless-connected multimedia (Szynalski, 2018). Instructions also serve the purpose to minimise potential harmonic and non-harmonic distortions superimposed on the tested frequencies as well as the primary frequency. The distortions are attributed to the amplifier and speaker of the utilised computer system. This study is in connection with hearing frequencies (measured in hertz), not the amplitude of hearing (measured in decibels).

Participants

The survey web link, including the tone generator, were distributed tofive private groups of psychedelia enthusiasts and (ab)users existing on Facebook online social communication medium (Facebook, 2018a; Facebook, 2018b; Facebook, 2018c; Facebook, 2018d; Facebook, 2018e). The survey will map the demographic parameters of the participants including age, sex, ethnicity, nationality, social-marital relationship status (single or in-relation), pre-existing medical and surgical conditions, the use of psychedelics, and the type of hallucinogens. Further, data specific to the hearing test were collected including the lowest and highest limits of sound frequencies that can be perceived (heard) as well as the existence of gaps (blind spots) within the hearing range of audible frequencies.

Review of the Literature and the Level-of-Evidence

A review of the existing body of literature, with no restriction on time of publication, was conducted systematically via medical and paramedical databases including NCBI-PubMed, the Cochrane Library, Embase, EBSCO, CINAHL, Elsevier, Science Direct Research Gate, and Academia. The grey literature was also explored for data of interest. The level-of-evidence for this study is estimated to be of level-4 in compliance with the scheme of the hierarchy of evidence-based studies established by the *Oxford Center for Evidence-Based Medicine* (Howick, 2011; Greenhalgh, 2014).

Statistical Analysis

Statistical analyses were carried out via *Microsoft Excel 2016* and the *Statistical Package for Social Sciences* (SPSS v.24). The implemented statistical tests included the Student's t-test, Analysis of Variance and Covariance (ANOVA), Chi-Square test, and models Linear Regression. A confidence interval of 95% is the enacted cut-off margin for statistical significance for this study. Descriptive and inferential statistics were carried out to conclude an inference about the age and the hearing range of frequencies versus psychedelics use, sex of participants, ethnic grouping, and nationality. Additional conclusions were based on statistical analytics for age versus the hearing range of frequencies, and the existence of gaps within the audible range versus sex of the participants and the use of psychedelics.

Results

The total number of participants was one hundred and nine (n=109). Males and females contributed to 80.73% and 19.27%, respectively. Mean values were 34.62 years (age), 2.82 (number of used psychedelic substances per a participant), 46.57 Hz (lowest limit of audible frequencies), and 15772.50 Hz (highest limit of audible frequencies). The contribution of participants who are single and others who are in-relation was comparable at 51.38% and 48.62%. Concerning the chronicity of use, it was ranging from five years up to three decades, while the frequency of use was variable on the daily, weekly, and monthly basis. Besides, polypharmacy existed, using more than one psychedelics in addition to the collateral use of some medicinal chemicals, including MAO inhibitors to either potentiate the effect or the longevity of action of some hallucinogens.

Statistical outliers were absent for age and the highest limit of audible frequencies (Fig. 1). However, several outliers (total of 17) were detected for the lowest limit of audible frequencies. Outliers frequencies included those from 89 Hz up to 250 Hz and were in connection with participants strictly from the Caucasian ethnicity, including males and females, from the developed countries mainly the US, UK, and the European Union. There were four main contributing ethnic groups including Caucasian (88.99%), Latin (8.26%), Asian (1.83%), and Persian ethnicities (0.92%) (Fig. 2). Participants were from twenty-five different countries.

Table 1. Descriptive and Inferential Statistics.

	Age		Lowest Freq.		Highest Freq.	
	Substance Use (Yes)	Substance Use (No)	Yes	No	Yes	No
Mean	31.78	37.03	43.18	47.71	16605.06	15030.36
St. Dev.	12.13	12.05	48.14	46.75	3226.38	3395.01
p-value	0.026 *		0.494		0.612	

*Data based on the use of psychedelics (Yes, No) versus age and the hearing range of frequencies for the participants (lowest and upper limits of audible sound frequencies).

Continued.

	Age		Lowest Freq.		Highest Freq.	
	Male	Female	Male	Female	Male	Female
Mean	35.49	31.00	45.67	50.33	15526.03	16805.33
St. Dev.	12.76	9.69	47.21	48.51	3479.12	2949.29
p-value	0.082		0.694		0.094	

*Dara based on the sex of participants versus age and the hearing range of frequencies.

Continued.

	Age		Lowest Freq.		Highest Freq.	
	Caucasian	Latin	Caucasian	Latin	Caucasian	Latin
Mean	35.56	26.78	49.08	25.67	15556.21	15556.21
St. Dev.	12.68	4.55	49.49	5.94	3508.93	1728.20
p-value	0.000 *		0.000 *		0.809	

*Data based on the ethnicity of participants versus age and the hearing range of frequencies.

Continued.

	Age		Lowest Freq.		Highest Freq.	
	UK	US	UK	US	UK	US
Mean	39.86	33.88	61.62	47.32	15324.76	15412.93
St. Dev.	12.73	13.67	63.46	46.40	3401.15	3867.18
p-value	0.065		0.306		0.920	

*Data based on the nationality versus age and the hearing range of frequencies.

The top two contributing nations were the US (37.61%) and the UK (26.61%). Other countries included Argentina, Australia, Belgium, Canada, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Israel, Japan, Lithuania, Moldova, Netherlands, Poland, Portugal, Romania, Russia, South Africa, Spain, Sweden, and Switzerland (Fig. 2). Israel was the only country from the Middle East. Other regions of the developed world are also under-represented which is in harmony with data from prior studies (Dargan and Wood, 2013; Al-Imam, 2017a; Al-Imam, 2017b; Al-Imam, 2017c; Al-Imam, 2017d; Al-Imam, 2017e; Al-Imam and Abdul Majeed, 2017).Although descriptive data does not show a potential correlation between age and the limits of perceived (audible) frequencies (Fig. 3), a proper statistical inference will later be established for this purpose. Concerning participants who were labeled as psychedelics users and non-users, the mean value was 31.78 and 37.03 years (age), 43.18 and 49.44 Hz (lowest limit of audible frequencies), 16648.24 and 15030.36 Hz (highest limit of audible frequencies).

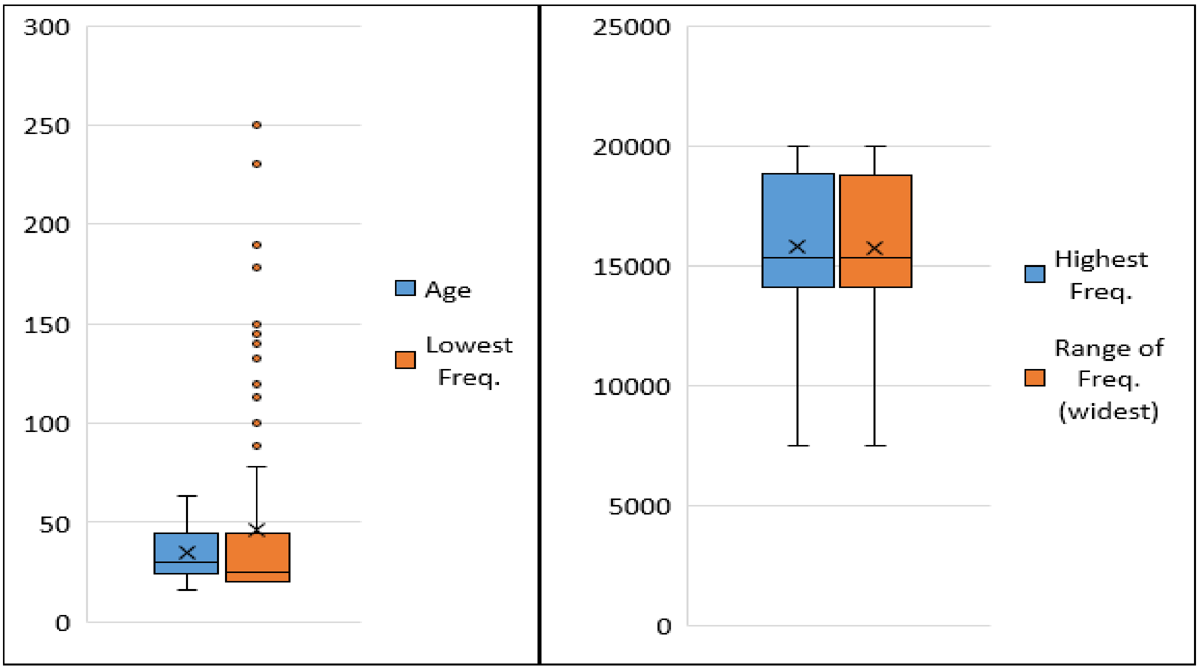

Fig. 1. Boxplot Presentation and Statistical Outliers.

Participants who had pre-existing medical or surgical condition were a minority (4.6%) who were entirely mapped within the psychedelics users group. Conditions were limited to tympanic membrane rupture-perforation and chronic otitis media. Psychedelics users contributed to 45.87% of the participants. Psychedelics included DMT, LSD, Mescaline, Mushrooms, 2C-B, DMT alone and in combination with MAO inhibitors, Psilocybin, 2C-x, 25x-NBOMe, DPT, Ketamine, LSD-1P, MDMA, Mescaline, and Psilocybin. Other chemicals of interest were cannabis, MDMA, and amphetamines. Gaps (blind spots) within the range of audible frequency spectrum were also found at which a participant was not able to hear a specific segment of frequencies.

These gaps were mapped to six participants (males and females) including three psychedelics users who were strictly from the Caucasian ethnicity from the US, UK, Canada, and Denmark. The blind spots were ranging from 8000 to 16500 Hz, and half of which were clustered in between 8000 and 9200 Hz. Only two participants (33.33%) of those with gaps had a pre-existing tympanic membrane perforation or chronic otitis media.

Linear regression shows a weak correlation of age versus the upper and lower limits of perceptible frequencies (R^2 score=0.102 and 0.0719) (Fig. 4). Concerning the use of psychedelics, users were significantly younger compared to non-users (31.78 versus 37.03, *p-value*=0.026) albeit there was also no significant differences concerning the upper and lower limits of audible frequencies for users versus non-users (Table 1).

Based on sexual differences, men and women had no significant difference neither concerning the age nor the upper and lower limits of the hearing range of frequencies. Concerning the top two contributing ethnicities, Caucasians were significantly older than Latins (35.56 versus 26.78, $p<0.001$). Caucasians also had a considerably higher lower limit of audible frequencies (49.08 versus25.67, $p<0.001$).

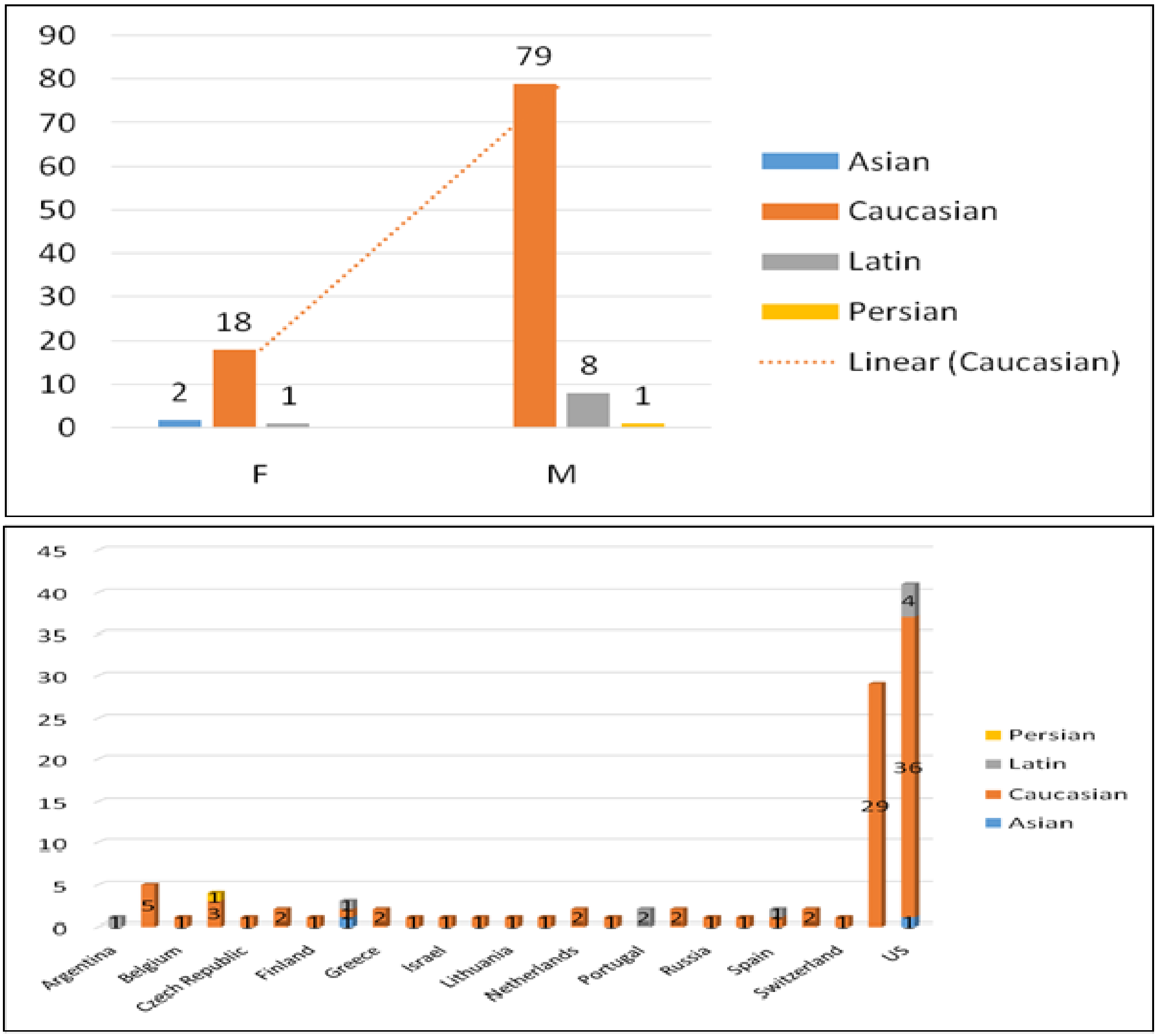

Fig. 2. Ethnic Grouping versus Sex (above) and Nationality (below).

On the other hand, there were no differences based on nationality versus age and upper-lower limits of the hearing range. There was no significant association between the sex of participants versus the existence of gaps (blind spots) within the hearing range (p=0.229). A significant association was also absent for the use and non-use of psychedelics versus the presence of blind spots (p=0.516), and the presence of statistical outliers (89 to 250 Hz) versus use and non-use of psychedelics (p=0.261). No significant association was found between the existence of mathematical outliers of hearing frequencies (upper and lower limits) versus the presence of gaps (0.781). Finally, an inference was made for participants with upper limits of hearing more and less than 8000 Hz versus the use and non-use of psychedelics (p=0.275), and the existence of blind spots (p=0.845). Accordingly, it can be concluded that the use of psychedelic substances and the ability to hear specific frequencies (lowest and highest limits, and gaps) are independent of each other. However, psychedelics users were considerably younger than non-users. Besides, significant inter-ethnic variabilities between Caucasians and Latins are evident concerning age and the lower limit of audible frequencies though these differences were not correlated with the use and non-use of hallucinogens and entheogens.

Discussion

Prior studies have concluded data concerning high-risk psychoactive substances including DMA/DOX, MXE, Mescaline, Methylone, Synthetic Cannabinoids, GHB, Benzodiazepines, NBOMe, 2C-B, DMT, Ketamine, Opioids, Adderall and Vyvanse, Heroin, Methamphetamine, LSD, MDMA, and Cocaine (Al-Imam, 2017d). Additional data on incidents of intoxications-deaths retrieved via literature review and drug for a found that these events can be categorised into intoxication, chronic morbidity, near-death event, pharmacological fatality, behavioral fatality, suicide, auto mutilation, and homicide(Dargan and Wood, 2013; Al-Imam, 2017a; Al-Imam, 2017b; Al-Imam and AbdulMajeed, 2017). The majority of the incidents took place in the developed world, particularly in the United States, the United Kingdom, Western Europe and Scandinavia including Germany and the Netherlands, Poland, as well as Australia, Canada, and Japan (Al-Imam, 2017b; Al-Imam, 2017d). These data are in synchrony with our study which also confirms the under-representation from the Middle East except for Israel. The majority of victims were adults in the 2nd to the 4th decades of life.

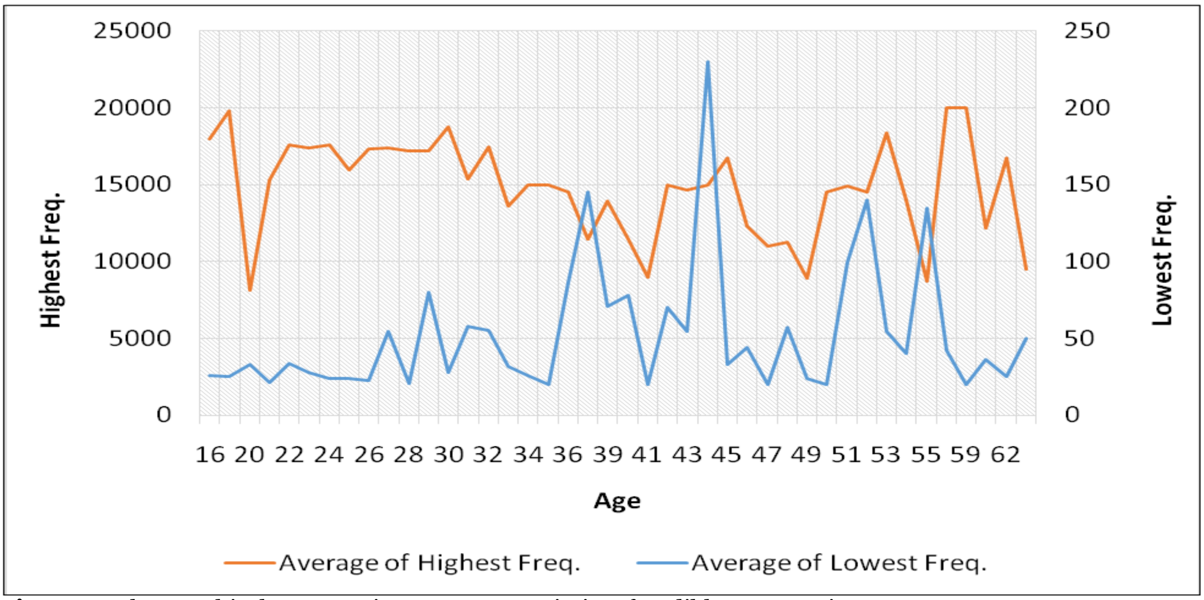

Fig. 3. Combo Graphical Presentation: Age versus Limits of Audible Frequencies.

Some of the physiologic effects induced by psychoactive chemicals and hallucinogens can be permanent (Dargan and Wood, 2013; Al-Imam, 2017a; Al-Imam, 2017b; Al-Imam and Abdul Majeed, 2017).A recent case report of a teenage female from New Zealand correlated the early and long-term use of LSD and other psychedelics with inducing some permanent physiological changes including persistent mydriasis (Al-Imam, 2017b; Al-Imam, 2017e). Nevertheless, several renowned individuals including the inventor of LSD himself, the Swiss scientist Albert Hofmann, had possibly experimented with psychoactive substances including opium and cannabis (Hofmann, 1970; Hofmann, 1977). It is also documented that Aldous Huxley, the eminent philosopher and novelist, has requested his wife to administer LSD to him while lying on his deathbed suffering from a non-treatable form of laryngeal cancer (Dyck, 2015).There is a considerable lack of data based on reliable inference concerning cases of deafness induced by psychedelics and other psychoactive chemicals. However, case reports exist in connection with ecstasy, methadone, benzodiazepines, heroin, opioids, as well as polysubstance narcotic overdose (Fisman, 1991; Sharma, 2001; Christenson *et al.*, 2010; Schreiber *et al.*, 2010; Sara *et al.*, 2011; Schweitzer *et al.*, 2011; Lopez *et al.*, 2012; Church *et al.*, 2013; Saifan *et al.*, 2013; Aulet *et al.*, 2014; Novac *et al.*, 2015). The majority of these chemicals can induce sensor neural hearing loss which can be either unilateral or bilateral.

Anticipated studies of the future should integrate accurate epidemiological and digital epidemiological analyses for geographic mapping of the diffusion of psychedelics as well as surveying the subjective experiences of (ab) users on the internet who are also engaged in e-commerce activities related to those chemicals. Trends databases should also be mapped in parallel with data from blogs, e-commerce websites, and online drug for a. Statistical inference should incorporate longitudinal analysis in combination with point estimates in time in addition to confirmed cases of intoxications leading to ototoxicity and conductive-sensor neural hearing loss. Besides, the geography and chronology of the reports of interest should be interpreted in light of data extracted from of trends database. Researchers should eliminate the effects of noise attributed to confounding variables and deploy the use of multivariate analysis and logistic regression models.

Effective true interdisciplinary collaboration with ICT professionals should be attempted with an aim to eliminate information biases, related to data gathering and interpretation. Real-time and predictive analytics can lead to economic studies with resources-sparing by investing in the principles of automation in data collection and analysis via machine learning. Experimental designs using animal models and randomized controlled trials (RCTs) on humans are necessary for the advancement of evidence-based studies.

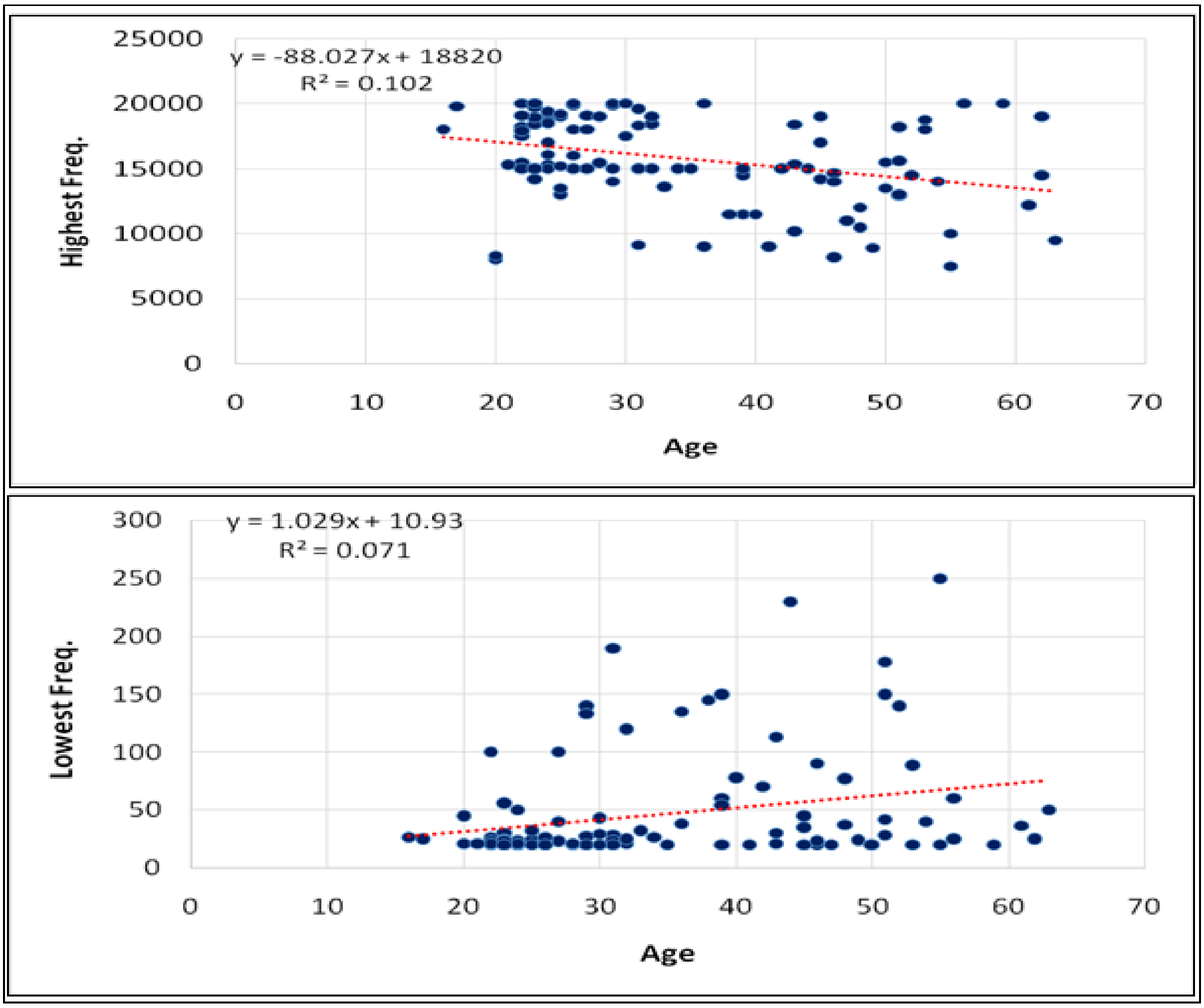

Fig. 4. Linear Regression: Age versus Upper and Lower Limits of Audible Frequencies.

These studies are required to (dis)prove the adverse effects of different hallucinogens on body systems including the cardio-respiratory and the nervous system which are well-known to be affected by amphetamines, NBOMe chemicals, in addition to performance- and cognitive-enhancing compounds (Al-Imam *et al.*, 2016; Al-Imam, 2017e; Al-Imam and Al-Imam, 2017; Catalani *et al.*, 2017).

Conclusion

The existing body of literature has a considerable deficit of experimental data on hallucinogens and their effects on hearing. Animal studies are either few or from decades ago. Human trials, including (randomised-)controlled trials, are critical to infer data of reliable evidence.

Our research venture revealed that the representation of populations from the Middle Eastis lacking except for some data originating from Israel, Turkey, and Iran. It has been concluded that the (mis) use of psychedelics and the range of audible frequencies are independent of each other. Ambitious and prospective studies should integrate automated data collection and subsequent inference to achieve real-time and predictive analytics concerning populations of interests.

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