INPLASY PROTOCOL

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Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Polymorphisms and NIHL: A Systematic Review and Meta-Analyses

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Review question / Objective: **To explore the correlation between gene polymorphism and susceptibility to NIHL disease.**
Condition being studied: **The different susceptibility of individuals to the same noise exposure may be due to different genetic backgrounds. Genetic factors are known to influence an individual's susceptibility to noise in animal models. But whether it applies directly to humans is debatable. In order to explain the differences in individual susceptibility and provide a new method to predict the risk of NIHL, exploring the individual susceptibility of NIHL from the level of gene polymorphism has become a breakthrough point for many researchers to explore hearing loss, and has achieved success.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 June 2023 and was last updated on 01 June 2023 (registration number INPLASY202360003).

INTRODUCTION

Review question / Objective: **Formal screening of search results against eligibility criteria.**

Rationale: **The purpose of this study was to conduct a detailed and systematic review of the studies on the relationship between SNP and NIHL susceptibility through a large number of relevant literature searches, and to conduct a meta-analysis of SNPS to resolve these contradictory results, and to find out the genes or SNPS associated with NIHL susceptibility, so as to establish a practical and reliable prediction system.**

Condition being studied: **The different susceptibility of individuals to the same**

noise exposure may be due to different genetic backgrounds. Genetic factors are known to influence an individual's susceptibility to noise in animal models. But whether it applies directly to humans is debatable. In order to explain the differences in individual susceptibility and provide a new method to predict the risk of NIHL, exploring the individual susceptibility of NIHL from the level of gene polymorphism has become a breakthrough point for many researchers to explore hearing loss, and has achieved success.

METHODS

Search strategy: ((("polymorphism, single nucleotide"[MeSH Terms] OR "nucleotide polymorphism single"[Text Word] OR "nucleotide polymorphisms single"[Text Word] OR "polymorphisms single nucleotide"[Text Word] OR "single nucleotide polymorphisms"[Text Word] OR "SNPs"[Text Word] OR "single nucleotide polymorphism"[Text Word]) AND ("hearing loss, noise induced"[MeSH Terms] OR "hearing loss noise induced"[Text Word] OR "noise induced hearing loss"[Text Word] OR "acoustic trauma"[Text Word])) NOT ("case reports"[Publication Type] OR "Comment"[Publication Type] OR "Congress"[Publication Type] OR "consensus development conference"[Publication Type] OR "duplicate publication"[Publication Type] OR "Editorial"[Publication Type] OR "english abstract"[Publication Type] OR "observational study, veterinary"[Publication Type] OR "retracted publication"[Publication Type] OR "retraction of publication"[Publication Type] OR "Meta-Analysis"[Publication Type] OR "Review"[Publication Type] OR "systematic review"[Publication Type])) AND (humans[Filter]).

Participant or population: Noise-induced hearing loss (NIHL) patients.

Intervention: No intervention.

Comparator: Normal people without noise-induced hearing loss.

Study designs to be included: Case-control study.

Eligibility criteria: The inclusion criteria are as follows: (1) the literature on the correlation between genepolymorphism and NIHL susceptibility using case-control studyor cross-sectional study, (2) both NIHL case group and control group conform to the HWE equilibrium law, (3) the original datadirectly or indirectly provide the allele or genotype frequency ofeach SNP in the case and control group. (4) Two independent sample sets in one study are considered as two different studies. Anyone of the following situations will not be included: (1) randomized controlled experimental research, animal experimental researchor cell research; (2) Case reports, meta-analysis studies, reviews, books, conferences; (3) Incomplete information or invalid original data; (4) There are <3 studies on a gene or a SNP.

Information sources: PubMed, CNKI, Embase, Wang Fang, Web of Science and Cochranelibrary.

Main outcome(s): Seventy four papers reported 64 different genes, 26 of which were studied in at least 3 publications and only 25 polymorphisms were studied in at least 3 publications.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS) of the case-control study was used to evaluate the quality of the included study (Hwang et al.,2023) The total score of 0–5 points belongs to low quality research, and 6–9 points belongs to high quality research. The score was completed by two researchers independently, and the differences were discussed and resolved bya third person effect size and accompanying confidence intervals.

Strategy of data synthesis: Meta-analyses should generally be performed using random-effects model to estimate. Statistical heterogeneity should be assessed with I2 statistic, with values over 50% indicating substantial heterogeneity,

and publication bias should be assessed by funnel plot asymmetry and Egger's regression test. Because of the large number of NIHL susceptibility related gene polymorphisms we analyzed, in order to improve efficiency, all SNPs only compared the gene distribution differences between the case group and the control group under the allele model.All data analysis was completed using stata17.0 software, and the correlation between SNPs of each gene and NIHL risk was evaluated by combining odds ratio (OR) and 95% confidence.

Subgroup analysis: Subgroup analysis was used to identify subgroups based on race when there was great heterogeneity in some gene polymorphisms and complex mixing of race.

Sensitivity analysis: Sensitivity analysis was performed using stata to assess the stability of the pooled results.

Language restriction: Search all English and Chinese literature as far as possible.

Country(ies) involved: China.

Keywords: noise induced hearing loss, polymorphism, meta-analysis, GRHL2, CAT, EYA4, HSP70.

Contributions of each author:

Author 1 - Wang Lu was suitable for the study design, literature searches, statistical analysis, and manuscript preparation.
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