

Human Suicide Study, is there an Association between Suicide and Mental Illness?

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Abstract

Since suicide is a causality of a lot of human mortalities worldwide, its therapeutic study is of great medical significance. Yet human suicide predictions and preventions are still difficult until now. As a result, it needs to find out new ways of solving this dilemma. As human suicide etiological/pathologic undertaking is quite necessary, human suicide treatments can be better transformed from clinical symptom observations into new generations of therapeutics-mental illness-related diagnostics and therapeutics. In future, better clinical suicide predictions, preventions and therapeutic managements can be established via pathways of human mental illness studies.

Keywords: Psychiatric disorders; Human genome; Neural pathogenesis; Environmental factors; Bioinformatics; Medicinal chemistry; Human suicide

Introduction

Suicide is a major causality of human mortality across the world. Yet human suicide predictions and preventions are difficult to obtain. As a result, in order to find out new ways of solving this situation, human suicide etiological/pathologic study is quite necessary. Previously, human suicide was commonly regarded as a clinical symptom rather than an aspect of human mental illness-related disease that can be traceable from biological or genetic tangible existence discoveries. In order to clarify this matter of etiological/pathologic enigma, we document some events of historic literatures, medical ways of suicide probing and different types of counteractive measure promotions. After all, genetic/molecular clues available for suicidal linkage between pathogenesis and therapeutics will be established. From these avenues, better clinical suicide predictive systems and therapeutic managements would be invented in future.

Suicide Causalities

Mental disorder arguments

As suicide is not the name of disease category, the possible origin will be traced to several causalities. Human mental health problems are the most important one. From Table 1, we can see a close association between suicide and mental disorders (Table 1). Therefore, mental disorder diagnostics for suicide patients and therapeutics are exemplified.

Currently, estimated 10-20% of general human population is suffered from mental health problem and disorders. 1/4 of human beings seeking primary medical care are caused by mental illnesses, especially mood disorders. Despite high incidence, common therapeutic outcomes are generally unsatisfactory [1,2]. Mental health problems are often life-long (chronic disorder). Unfortunately, human depression (majority of human mental health problem, brain disorder) epidemics have been steadily growing in the past decades [3-6]. Varying suicide risks and rates among different types of mental diseases, such as mood depression, bipolar or dysthymia make disease interventions more complicated [7]. As a result, the costs for antidepressant therapies are rising because large proportion of human beings suffers depression

in high competitively modern society that has negative feedbacks by social isolations [8].

Other causalities

A range of social/environmental factors can decide human suicide rates and mortalities. Unveiling the interplay between insider (human genetics and chemical structures of drugs) and outsider (multifactorial economic, social, past bad habits or trauma) is the top priority [9]. However, small-range positive data from relevant medical managements have been repeated, let alone breakthroughs on this medical field. Generally, reducing from social/environmental pressure seems more beneficial than chemical drug-based therapies because so many factors affect efficacy or outcomes of drug therapeutics nowadays; outlines this matter (Table 2) [10-13].

Suicide/mental illness diagnostics generally depends on analysis of patient's mood symptom degree-depression and mania.

Suicide/Mental Illness Diagnostics

From the disease diagnosis, the symptoms of human suicide risks (hopeless feeling, self-deny and so on) are very similar with symptoms of mental illnesses (hopeless and helpless), especially mood disorder (Table 2). The outsider insults of environmental factors for suicide are also very similar with outsider insults for mental illnesses-including marriage problems or lost of jobs and so on. Since no conclusive outcomes from past suicide pathogenesis molecular/pathways have been understood and generally agreed, we hypothesized that mental illnesses may have some associations with suicide risks, events or mortalities. By human mental illness diagnostic or therapeutic studies, we may enhance out abilities for suicide predictions and preventions.

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Worldwide; totally 15,629 cases		UK; totally 4,859 cases	
Mood disorders	35%	Mood disorders	42%
Substance disorders	22%	Schizophrenia	20%
Personality disorders	12%	Personality disorders	11%
Schizophrenia	11%	Alcohol dependent	9%
Anxiety disorders	6%	Drug dependent	4%
		Anxiety disorders	3%
Other disorders	14%	Other disorders	11%

Table 1: The linkage between suicide and other diseases [1].

Contents	Different categories of diagnosis and therapeutics		
	Unipolar	Bipolar I	Bipolar II
Nominations	Depression	Mania	Depression + Mania
Symptoms	Symptom-based diagnostics (Score index and so on)		
Current diagnosis	Genetics-, molecular- or visual-based diagnostics		
Under investigations	Diagnosis from multi-disciplinary		
Future diagnostics	Antidepressants? Such as (SSRIs)	Mood stabilizers Anti-Psychotics	Antidepressants + Mood stabilizers
Therapeutics	Controversy	Side-effects for long-term Utilities	Lack of systematical Clinical assessments
Drawbacks			

Table 2: General procedures for mood disorder diagnostics and therapeutics.

Symptom checklist for diagnosis of depressive episode

- Persistent low mood¹
- Loss of interest or pleasure¹
- Fatigue or low energy¹
- Disturbed sleep
- Poor concentration or indecisiveness
- Poor or increased appetite
- Suicidal thought or act
- Agitation or slowing of movement
- Guilt or self-blame
- Low self-confidence

Major checklist for diagnosis of mania symptoms

- Flight of ideas
- Distractibility
- Risky decision-making

Following scenarios are general data of possible suicide/mood problems from diagnostics into therapeutics. Detail diagnostic information can be found in Diagnostic and Statistical Manual of Mental Disorder-from DSM-I to DSM-V of mood problems and Hamilton Depression Rating Scale (HAM-D) of suicide risks.

The major pathways of disease therapeutics

- (i) Increase the support and backup of patients. Thus patients may go through outside stressors;
- (ii) Cognitive-behavior therapy;
- (iii) Chemotherapeutic agents or drugs;

¹Represents the especial importance.

(iv) Cut off access to suicide tools from patients at high suicide risks.

The cognitive-behavior is the widely utilized therapy in mental illness treatments, which is largely based on psychiatrists-patients conversations.

For targeted chemotherapy applications, etiologic or pathogenesis mechanisms and molecular processes must be fully understood [12-13]. To attain this goal, etiological/pathologic/phenotypic quests for diagnostic updating are the first step. Following scientific pathways are noteworthy. In most serious patients, chemical drug therapy is needed.

Suicide Origins and Pathologic Linkages

Overall, diagnostic or therapeutic model updating must be useful from environmental/pathological information-seeking medications from multi-disciplinary [14]. To attain this goal, genetic-/molecular/visual-based diagnostics by clinical teamwork is the key.

Currently, some effective clinical suicide/mental health problem interventions come from environmental condition benefiting rather than long-term drug utilities. At this stage, widely used drugs have some toxicity by long-term utilities. Equally, antidepressants or others are sensitive to some parts of patients and it even induces suicide events in other population [15-21]. This is an important discovery. We previously explained as a matter of human genetic predisposition variations [20-23]. To completely solve this dilemma, etiological/pathological tangible causalities must be found out. Although its medical significance is big, the genetic/molecular/morphologic-based pathogenesis information needs to be greatly updated. Quick diagnosis of suicide/mental illness is no easy a task owing to symptom similarity (depression or mania) between normal humans and mental health problem patients. Let alone capture the disease stages and types. Yet modern biological techniques and systems (genomic/omics) are advantage at these items of pathogenesis diagnosis [24-27].

Suicide/mental illness may undergo long-terms latency and evolution. Once a patient seeks medical advises, the disease may have been initiated for several years. The earliest medical interventions may be paradigms for symptom controls and/or better disease managements if possible. Diagnostics of diseases by modern techniques may be a shortcut for achieving this goal in early literatures. At least 90% of suicide subjects suffer from mental illnesses. 15% of depressed subjects have attempted suicide at least once life-long. 20-50% schizophrenia patients have at least one suicide episode in whole life-time [28]. Understanding the relationship between suicide and mental illnesses is a future trend for suicidal event predictions and preventions.

Etiological/Pathologic Knowledge and Modern Drug Development Establishment

Bioinformatics studies consist of a number of different categories of biological information, such as transcriptomics, proteomics, and metabolomics and so on. Although bioinformatics in suicide risk predictions has been initially studied, no marked breakthrough has been achieved until now [24]. Along with other technologies, various chemical drugs supported by modern techniques, such as SSRIs-kind of targeted antidepressants are going smoothly nowadays.

Methodologies in advance

The best candidate genetic or molecular information for suicide/mental illness therapy predictions are unclear now. Genetic associations between drug-active and drug-toxic genes (molecules)

might be optimized by in-depth scientific investigations towards the core of patient's suicides and self-injuries. Adapting new techniques into the clinical suicidal studies is indispensable and noteworthy. Other current achievements relating chemical drug developments and clinical applications are partly offered in followings (Table 3). Some of these new techniques have already been widely utilized in mental disorder drug studies and licensing.

Technical Supportive Systems

Generally speaking, a proper treatment of the central nervous system diseases is not a easy task. In many suicide cases, mental disorder diagnostics is complex in pathological patterns, long-term suffering and a wide variety of therapeutic options. Once a person has been diagnosed with moderate-to-severe mental disorder, he/or she will usually have to take drug medication lifelong because this is a chronic disease now. Thus, relationships between pathogenesis and therapeutics in modern ways must be established. Theoretically, this recent model of therapeutics is possible, yet long way to go [28]. In our opinion, Personalized Medicine (PD) of suicide/mental disorders by Pharmacogenetics (PG) data is still immature now. It is rarely seen a high quality of genome/bioinformatics/visual diagnostic system in general hospitals. But new techniques and statistical analytical systems are gradually coming into the reality now.

Diagnostic/therapeutic relationship buildup

Currently, the drug selections for mental health problems are still decided by symptom-index systems rather than many objective data (genomic/bioinformatics/visual), let alone social/economic/habit factors or conditions. Since symptom-indexed systems are subjective rather than objective, integrating disease progression status by modern techniques (genetics/bioinformatics/visual) is important. In order to achieve such a goal, great deal of foundation studies of both neural-psychiatry profiling and target therapeutics must be undertaken first.

The polymorphisms of drug targets or toxicity genes in patients' genomes must be identified and verified for PG utilities. Similarity and diversity relationship among suicide risk, mental disorder severity, chemical drug metabolism and target drug (signal-, receptors and

so on) must be understood. Useful patents or licensed drugs can be promoted into clinical utilities.

A great number of patient's genomic predisposition has been accumulated after the advent of Next-Generation-Sequencing (NGS) technologies. Accumulating and comparisons between inheritable disease-cases and normal human population by GWAS (Genome Wide Association Study) data is general pathway for neural/mental illness therapeutics and toxicity/risk predictions [29-33]. GWAS of chemical or biotherapy might have profound impacts on science and technology developments. By taking GWAS, larger than ten genetic allele variations between normal humans and mental disordered patients has been found (>500 patient genomic samples). GWAS is a basic pathway for translating novel therapeutics from bench to the bedside. To make greater leaps, GWAS of chemical drug therapy must be studied as early as possible. The statistical analysis of genomic data and therapeutics relates with sample size. To our understanding, biomedical students are not adept with these processes. Many post-genome analysis needs to be explained by a few world-leading institutes, universities or biological companies [34-35]. Our humble imagination suggests that genome sequencing working and research forces might be gradually changed from biomedical major students into mathematic or physics major students or scholars [36-37]. The contributions by mathematics and physics students or scholars for genomic sequencing may be more significant than biomedical majored students because of larger genomic data manipulations or analysis demanding in GWAS [38-39].

Brain structural and neural-imaging studies

Since human suicide/mental illness are probably brain diseases, it is believed and partly discovered that brain image changes of both volumetric and cerebral regional compartments (prefrontal or cingulate cortex and so on) can be generally observed by brain imaging scanning by techniques of Position Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT) or functional Magnetic Resonance Imaging (fMRI) [5]. The changes in cortical and sub-cortical areas have been discovered. As a result, divergent techniques of neural imaging studies of both experimental and clinical are taken together to identify these cerebrally morphological changes and guide further therapeutic targets [6]. More recently, 70% false-positive data has been found in brain scan study [38]. It can be a technical drawback, software imperfection or en no mistake at all. As a result, whether effective drug can act on brain area changes are still an open question waiting to be answered.

Gene-environment interaction studies

Previously, we commonly believe that patient's genetic predisposition is independent of environmental conditions. Yet, it has been found since 2003 that environment impacts, such as bad past experience and trauma in early stage can modulate gene expression, especially epigenetic context in humans [28]. Many genes, molecules, receptors linking with serotonergic systems or others can be changed by different kinds of environmental insults and impacts. In early reports, epigenetic entities can be dramatically changed in mental-illness patients or sufferers after a big trauma.

Modern pharmacological studies

A number of chemical drugs (mood stabilizers, anti-psychosis, antidepressants and so on) are clinical utilized [12-13]. Two major drawbacks are present-low specificity against disease progresses and moderate-to-severity toxicities for long-term utilities. As a result, they are often utilized at the stage of patient's hospitalizations. In order to change this situation, novel animal models, state-of-the-art

Research fields	Major technologies
Biological	Gene knockout Optogenetics Genomic editing Brain volume and image study
Pathogenesis	Disease classifications Genetic-visual relations Gene knockout Gene-environment interactions
Experimental models	GEM
Genomic	SNP (Microarray) PCR-based diagnostics Genome wide association studies
Bioinformatics	Transcriptomics Proteomics Metabolomics Computational network
Drug developments	Medicinal chemistry Analytical chemistry Pharmacology Statistics
Clinical therapeutics	Cerebral image Personalized medicines Computational network

Table 3: Methodology applications and under investigations for suicide diagnosis and therapy [23].

lab instruments and equipments must be utilized. Certainly, these scientific researches need larger patient's genetic pools and GWAS between normal and mental health problem peoples.

Neuroscientists, neurosurgeons and pathologists in mental health diagnostic and treatment studies

Since suicide/mental health problem is probably a brain disease, neuroscientists, neurosurgeons or pathologists who are trained to tackle brain morphological change analysis may be the major forces to remedy neural dysfunctions [3-6,39]. Their importance is beyond doubts (Figures 1 and 2).

Conclusion

Growing attentions should be paid on different possibilities of diagnostic and therapeutic updating. The relationships between chemical, genetic, molecular, morphologic, neurologic, environmental, social and cultural factors for pharmacological and therapeutic improvements should be considered and investigated both individually and as a whole. It can be through genetics to molecular to visual or via visual to molecular to genetics. To attain this achievement, technical updating is noteworthy. Facing this challenge, searching for suicide-related biologically tangible molecules/entities is the key.

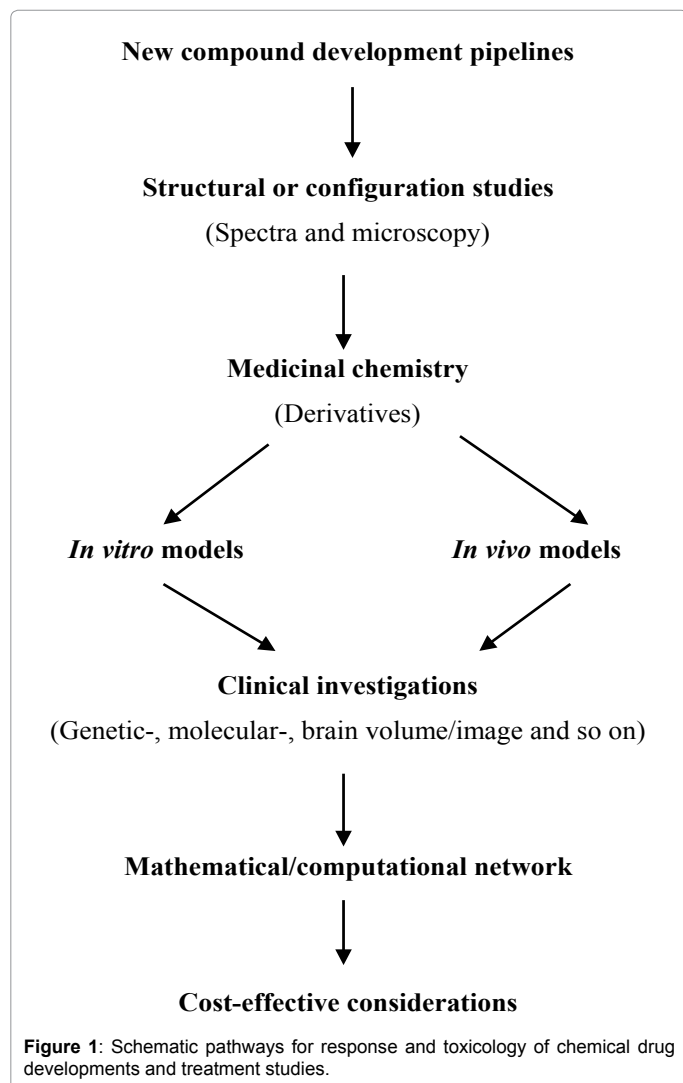


Figure 1: Schematic pathways for response and toxicology of chemical drug developments and treatment studies.

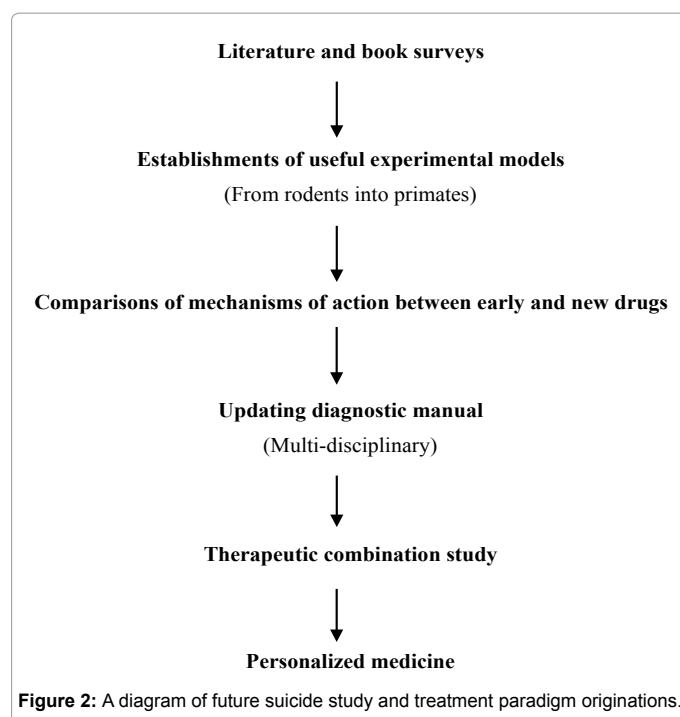


Figure 2: A diagram of future suicide study and treatment paradigm originations.

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Conflict of Interests

Authors declare there is no conflict of interests with other institutes and academies.

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