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Human Suicide Study, New Insights and Drug Development

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Abstract

Suicide is still a major event of human mortality (2%) worldwide. However, no high-effective drug has been developed. Influence by diverse and complex environmental factors and pressures, suicidal treatment study grows slowly. In search of pharmaceutical options against human suicide, transition from psychoanalysis (cognitive, behavior and emotional) into psychobiology study (genetics/image) is more important. Neural-psychiatric associated study may profoundly impact on pharmacotherapy for suicide prevention and therapeutics. A great deal of neurobiological study may obtain more clinical paradigms (modern diagnosis and pharmacotherapy). In the future, clinical suicide prediction, pharmacology and therapeutics can be successful.

Introduction

Major limitations for human suicide study

Suicide is a major causality of human mortality across the world (2 % of human mortality among all disease-categories). Yet human suicides are difficult to predict, let alone immediately therapeutic control and managements [1-3]. Due to a slow progress of suicide study, no therapeutic magic bullet (high effective drug against large suicide origins and categories) has been widely benefiting worldwide. Despite a number of anti-psychiatric drugs in clinical applications, symptom control for suicide patients is diverse. We have done less from pharmaceutical sides at this stage of drug development. A long way must go through before any magic bullets can be found out. Correspondingly, patho-therapeutic relation between different suicidal causality and relevant therapeutic options proves to be quite helpful [1-3].

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Importance of etio-pathologic study

To attain a goal of excellent suicide therapeutics, it must first know the complexity of suicide etiopathology in details. However, this kind of scientific researches lags behind until now [4]. Currently, human suicide is widely predicted from clinical symptom (psychoanalysis) in patients. Growing evidence about genetic/molecular/image diagnostics may facilitate new drug developments in the future [4-9]. In order to meet etiopathologic study requirements, historic literature review, suicide symptom framing and experimental investigations of different drug categories must be looked for [4-9]. The patho-therapeutic relationships are important to note (Table 1). New drug experimental evaluation and clinical validity can be derived from these patterns of environmental and pathological combination. From different factor and categories integrations, more efficient suicide predictive and therapeutic paradigms would be emerged in the future. In this article, human suicide prevention and treatment systems are addressed [1-8].

Co-morbidity of human suicides

Key factors for suicide origins

Human suicide has been multiple co-morbidities in the clinic (Table 1). Fortunately, some therapeutic progresses have been made in the past medical investigations [9]. A great number of human suicidal mortality still exists no matter what types of financial condition of patients (either poor or rich countries). Correspondingly, financial conditions should not be over-emphasized for suicidal origin probing and effective treatment developing. Etio-pathological information is important for drug developments. At this moment, suicide events and co-morbidities are very common in therapeutic study. Thus, it suggests that co-morbidity control may reduce the events and mortality of suicide patients.

Table 1: The linkage between suicide events and co-morbidity.

Originality	Future diagnostics	Therapeutics	References
Mental disorders	Genetics/molecular/image	Drug or brain surgery	10
Personality	Temperament	Social work	11
Repeat self-harm/injure	Past episode and symptoms	Psychiatric intervene	7-8
Socioeconomic deprivation	Financial evaluation	Social/legal support	12
Chemical exposure	Brain damage	Exposure control	13
Viral infection	Brain image	Vaccine or drugs	14
Long physical handicaps	Constance suffering	Pain-killers or others	8
Alcohol/drug addictive	Paracetamol overdose	Physical exercise	9
Physiological disability	Dysfunction (old age)	Financial and social	15-16

Pathological causality for human suicides

Major suicidal emergence pathways [4];

Different types of human mental illness;

A history of past physical or psychiatric traumas;

Change of brain neural transmitter;

Chemical or drug-induced brain damages;

Old age for growing troubles and difficult in normal life (double suicide incidence and mortality);

Environmental and socio-economic burden, pressures and forces;

Human genetic changes and inheritable factors;

As mentioned above, every event of such bad experience may possibly trigger a sequence of suicide or self-harm behavior and episode, further therapeutic drugs or counteractive will be developed [11-18].

Mental disorder arguments and current scenario

Human mental disorders are the widest sources to trigger events or mortality of human suicides. Like suicide events, self-harm behaviors or repeaters, they mostly seek medication from psychiatrists. In addition, most of medical experience and benefits were coming from this special biomedical discipline (psychiatry). However, this type of biomedical study is not without challenge. Therefore, mental disorder diagnostics and therapeutics for suicide patients must be deeper understood in the clinic and developed in drug markets.

Current convention for psychiatric intervention against mental disorders

Prevalence of mental disorders in human population

Currently, a prevalence of mental health problems globally (approximately 1/5 to 1/4 of human populations) have been categorized. A certain ratio (20-25 % in the clinic) of which is associated with suicidal events, especially mood disorders either depression or mania. Apart from high suicide incidence worldwide, mental disorders are often life-long even by the assistance of available therapeutics [19-21]. Unfortunately, human mood disorder prevalence continues to grow over the past decades due to global economic crisis and higher-rate of people isolation.

Clinical diagnostic and therapeutic norm

Variability of therapeutic benefits and outcomes may happen in people with different mental diseases, such as autism, schizophrenia, mood disorders (depression, uni-polar or bi-polar) and/or neurobiological deficits [1,19-21]. Since most of

the mental illnesses are chronic diseases, curable therapeutics against mental disorders is still a medical dream. Drug developments (magic bullet discovery) against mental disorder are desperately needed [22-24]. In order to accomplish this challenge, it needs modern diagnostics and therapeutics to support in the clinic [25].

Psychoanalysis for suicide risks and treatments

Generally, psychoanalysis and treatment (cognitive-behavior therapy plus several drugs) is dominant clinical mental disorder treatment until now. Psychiatrists review and treat patients at risk from analysis of patient's cognitive, behavior and emotional changes. This pattern of clinical trials widely happens in the clinic and less-likely seeks technology of modern biology (genomics, epi-genetics, proteomics, transcriptomics and metabolomics). This norm disappoints a lot of doctors and patients. Proposal for dramatic renovation becomes lauder and lauder [25]. Yet, difficult is huge for associating from experimental discovery unto clinical applications [25-27].

Pathologic association between suicide ideation (psychiatric) versus molecular biology (neural) for human suicides

A similarity and diversity between psychoanalysis and modern biological data is difficult to be considered at same levels. From the diagnostic sides, the symptoms between human suicide risks (psychiatric review) and mental disorders (neural biology or brain image) are different in knowledge and technology, which needs to find a new leverage and balance for suicide treatments and drug developments. The outsider influence and pressures for suicide risks are also very similar (marriage problems, romance failure, lost of jobs and so on) [17-18]. That calls for convergence different diagnostic systems into an identical one of different calibers and sources.

Since little is known about suicide ideation progress in molecular basis (genetic/molecular pathways for every suicidal event), it suggests that neural biology for mental illness study (especially human mood problem) may be an inter-phase between suicide risks, events or victims versus sequentially biological aberrant (genomics, epigenetics, proteomics and metabolomics) [10]. By human mental illness diagnostic or therapeutic systems in hands, it may possibly enhance our capabilities for suicide prediction, prevention and therapeutics in the future.

New perspective

Currently, human suicide study is observed from its surface (suicide rates and events). However, the great differences between suicidal rates and biological etiology are largely unknown to us. In the following sectors, we provide our insights into suicide etiopathology, neural biology, therapeutic paradigms and effective drug developments in the future.

Neurobiology for suicide origin and risks

Current knowledge

Today, little pathogenesis/pharmacological knowledge for suicidal origin and therapeutic benefits is not well received in biomedical areas and basis. Without biomedical disciplines of pathologic/pharmacological information, the origin-targeted therapy cannot be fully applied in the clinic. Owing to this obvious therapeutic shortcoming, modern suicide diagnostics has been called for [26]. Correspondingly, advancing knowledge of etiopathogenic-therapeutic relations between human suicide mortality and therapeutic benefits must be obtained. In the past, this world lacks significantly achievements in these psychiatric knowledge, therapeutic conventions and drug developments.

Further insights into convention transition

To make a dramatic transition of human suicide diagnosis and therapeutics from psychoanalysis into molecular biology-based drug developments, neurobiological study is important and unavoidable. Following sections address this domain of human suicide study in genetic and molecular ways and levels.

Neural transmitter as drug targets

Neural transmitters (chemicals or neural peptides) are well known targets for clinical psychiatric diseases diagnosis, therapeutics and drug developments [22-25]. More recently, this area of drug developments has been widely recognized for human suicide study and clinical applications. At this moment, several chemical neural transmitters are utilized for drug developments, especially Selective Serotonin Reuptake Inhibitors (SSRIs) and dopamine secretory/activity inhibitors that are the widest drug development categories [18-20].

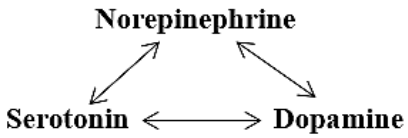

Figure 1: Interaction and activity of neural transmitters and functional regulation.

Genetic or molecular study for suicide-associated genes

Genetic exploration of different mental disorders is promising for human suicide study, yet difficult one until now. It has been reported that approximately 400-1000 human genes are participating and associated with psychiatric symptoms and disorders possibly including suicidal events and repeats [27]. As a result, a biological complexity of human genes makes it difficulty for completely clinical validity at this stage. Proposed pathway for complex genetic study is shown in (Figure 2). Currently, most single genes associated with human mental disorders are commonly in statistically insignificant manner. Large volume of Genome Wide Association Study (GWAS) data may help to stratify important genes and sequences in the future. Genomic study of mental disorders has been massively carried out previously [27-28]. Approximately 20-30 genetic alleles have been associated between mental illness patients and normal people (odd ratio, OR=1.4-1.5) in genome-wide associate study (GWAS) [29]. If we continue to drafter human genomes for large suicidal population, some genetic alleles will be stratified in the near future. The human genome draft explosion more recently will make a difference in mental and suicide genetic study and clinical applications.

Figure 2: Outlook of human suicide study from biological or pathologic disciplines.

Brain image

Brain image technology and knowledge are advancing in the fastest pace, especially in neurobiological investigations and clinical diagnostic explorations [30-34]. Nowadays, much of human physiological activity and disability can be localized in special areas of human brains (different cerebral location and cellular/tissue types). In the future, major breakthroughs can be made in many areas of human suicidal and psychiatric study *via* scientific investigations of human brain images.

Suicide diagnosis, system comparisons

Symptom checklist and modern diagnostics

Checklist of psychoanalysis between human suicide risks and mood disorders is overlapped in many clinical symptoms and score rating. Genetic/molecular-based diagnosis can improve therapeutic quality of this respect in the clinic (Table 2 & Figure 3). Between human suicide and mental illness diagnostics, patient's symptoms are very similar (such as helpless, self-deny, risk-taking and many others). This is why we associate these two mental problems in the same place [10]. Psychoanalysis can be applied by Diagnostic and Statistical Manual of Mental Disorder from DSM-I to DSM-V of mood problems and Hamilton Depression Rating Scale (HAM-D) for suicide risks. In these two diagnostic tables, many symptoms are overlapped.

Table 2: Diagnostic transition from psychoanalysis unto molecular image systems.

Psychoanalysis	Neurobiology	Modern diagnostic
Cognitive	Neural transmitters	Brain image
Behavior	Genetics (400-1000 genes)	Biomarkers
Emotional	Prognostic biomarkers	Genomics
Risky-decision	Molecular characterization	Proteomics
Social processing ability	Different cellular types	Metabolomics
Regulatory	Neural circuits/axis	Whole-exome sequencing
Language problem	Cell signals	Microarray
Intelligent disability	Different cerebral location	Chromatography
Mood disorder	Electrophoresis	Computerized tomography

From Table 2 and Figure 3, the evolution of human suicidal risk diagnosis can be seen in system transition (Table 2 and figure 3).

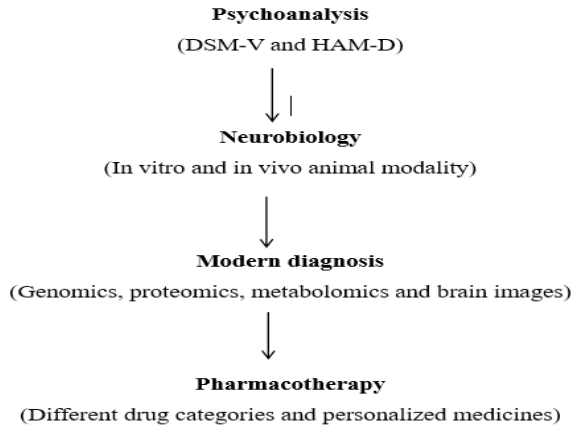

Figure 3: Diagnosis and therapeutic evolutions in human suicide study.

Genomic drafting and molecular diagnosis in the clinic

Diagnostic-therapeutic relation for human suicide must be balanced upon both environmental and pathological characters. To attain this goal, genetic-/molecular/brain-image diagnostics is the key. Currently, collection of large genetic information of suicide is a modern challenge for biomedical aspects of therapeutic study.

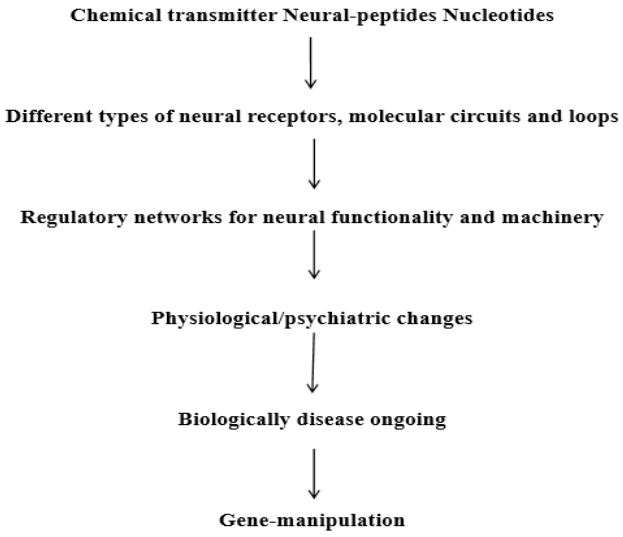

Figure 4: Biological pathways for neural functions, psychiatric abnormality, modern diagnosis and therapeutics.

Pharmacological insights in the clinic

Several types of neural-associated drugs and clinical options have been widely utilized in the clinic [35-39]. It ranks in the 4th place in new drug licensing number in the US [40]. However, it is far from final success until now. New types of anti-suicide drugs (magic bullets targeting most cases of suicide patients) must be developed or wisely utilized in the clinic (including personalized medicine or precision medicine) [41-42]. Antidepressants especially Selective Serotonin Reuptake Inhibitors (SSRIs) is one of the widest used drugs for many depressed and suicide patients. They are commonly cost-effective now. However, SSRIs may sometime even trigger suicide-events in children [41-44]. This is an important lesson for us. We previously associate it as a matter of human genetic predisposition variations [46-47]. To

completely solve this dilemma, neural biology and pharmacology study must follow up [48-56].

Diagnostic importance

At present, psychoanalysis for suicide/mental illness is no easy a task owing to symptom similarity between normal humans and mental disorder people. A lot of normal people have helpless feeling while many bad luck events take place. Let alone determine the disease stages and types. Yet modern biological techniques and systems (genomic/omics) are advancing at disease categorization and drug target identifications [5-8]. As we insist that modern technologies may be more suitable for the complex situations of suicide pathogenesis and pharmacotherapy study in the clinic [1-4].

Instrument invention

Apart from drug developments, some types of instrumental therapeutics, like light-therapy are also helpful for suicide reduction. In the near future, more treatment instruments may be invented and widely utilized in the clinic.

Drug development

Pharmacology and toxicology

In the past, therapeutic drugs against mood disorder are mainly neural transmitter promoters or inhibitors. To merge with new generations of modern diagnostic techniques, it provides new classes of disease targets, drug therapeutic mechanisms and clinical applications (Table 3). It suggests that drug treatment Pharmacogenomics (PG), biomarker/bioinformatics diagnostics, and brain volume/image data can be mandatory routines in the near future. To our perspective, safety issue is still important and useful from modern technology acquisition thereby new generations of drug (less undesired side-effects) may gradually go into the bedsides.

Techniques for promoting new drug applications in the clinic

A lot of biomedical techniques can be utilized in different levels of modern diagnosis, disease-categories and drug developments (Table 5). Pharmacological associations between drug-activity and drug-toxic genes/molecules may invite the prevalence of patient's suicide and self-injure risk diagnosis via biomedical issues and promote widely treatment benefits in the clinic. Adapting advancing techniques into clinical therapeutic validity and options and new generation of drug developments is unavoidable. Some new techniques in different disciplines and areas have already been widely utilized in drug developments, licensing and suicide managements in the future (Table 4).

Table 3: Different types of anti-psychiatric drugs and pharmacological characteristics [25].

Drug categories	Drug names	Side-effective
Tricyclic antidepressants	Amitriptyline, imipramine,domipramine, clothiepin, nortriptyline, desipramine, lofepramine	Greater
Selective serotonin reuptake inhibitors	Fluoxetine, paroxetine, citalopram, sertraline, escitalopram	Lower
Monoamine oxidase inhibitors	Phenelzine, moclobemide, tranylcypromine	Risk of drug-food interactions
Serotonin and noradrenalin reuptake inhibitors	Venlafaxine, duloxetine	Blood pressure promotion
Others	Mirtazapine, reboxetine	Over-sedate Weight-gain

Figure 4: Methodology applications and under investigations for suicide diagnosis and therapy [4].

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 Intelligent animals
Genomic	SNP (Microarray and so on) PCR-based diagnostics Genome wide association studies
Bioinformatics	Transcriptomics Proteomics Immuno-histochemistry Metabolomics Computational network
Drug developments	Medicinal chemistry Analytical chemistry Pharmacology Biological therapies Statistics
Clinical therapeutics	Cerebral image Personalized medicines Computational network Statistics Drug combination studies
Environmental pressures	Social problems Financial problems Other disease-induction (consistent pains)

Mathematical computation and artificial intelligences

Data sharing and integration is a key system of modern suicide prevention, diagnostics and treatment study (Table 5). Represents possible mathematical/computational systems for human suicide diagnostics and therapeutics including artificial intelligence system, integration of all separated data of different suicide origins risks and wide-range of biochemical diagnosis.

Table 5: Layout for computational network and AI system in the future [4].

System buildup stages	Mathematical methodology
Algebra data	Psychoanalysis and bioinformatics
Descriptive statistics	Data collection
Inferential statistics and description	Iterative, matrix
Mode building	Methodological selections
Drug evaluation data	Balance and integration
New equation and computations	Theorem establish
Workable AI	Association with computers

Outlook of futuristic suicide drug developments

A lot of important drug targets and clinical therapeutics can be pursuit including neural transmitter blocker/reuptake inhibitors, wide-range of molecular targets, genomic editing agents, signal-receptor targets, different neural cellular circuits/axis, natural chemotherapeutic drugs, herbal medicine and others. Translational work from psychoanalysis into molecular/image-based diagnosis and treatments should be emphasized in the future [60] (Figure 5).

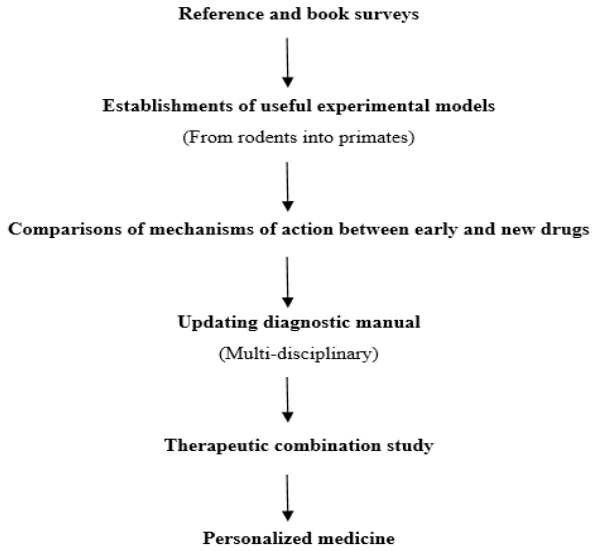

Figure 5: A schematic diagram of suicide study in animal modality and treatment paradigm in the clinic.

Besides advancing suicide etiologic/pathological knowledge, scientific accumulation can help us to develop more powerful classes of target drugs and wisely chose clinical regimes from suicide risks of outsider into biological insider. From approximately ten to thirty licensed drugs, they are more or less useful for managing some parts of patients with suicide syndromes. However, we still need to find some magic bullets (effective for more than 80% of sufferers). Only through this discovery, a great difference can be expecting.

Conclusion

New vision should be integrated into the promotional pathways of suicide prediction and therapeutics [60]. The relationships between chemical, genetic, molecular, morphologic, neurologic, environmental, social and cultural factors for pharmacotherapy should be renewed and go individually [46]. In search for suicide-related modern diagnostics in the future, biomedical study is the key. By achieving this ambitious plan, new breakthroughs are expecting. After all, we look forward to solid basis of suicide-related therapeutics in need and widely clinical application in the future.

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