

Original Article

Development of clinical ontology for mood disorder with combination of psychomedical information

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We have developed a new educational/clinical ontology named the “Haghighi-Koeda Mood Disorder Ontology”, which involves both medical and psychological approaches for mood disorders in order to promote the exchange of information between psychiatrists and psychologists. Data was gathered from more than 5000 articles published in journals and websites specialized in life science. We evaluated and selected articles which were related to 4 main categories of mood disorders. Using Protégé 3.4 beta, information related to mood disorders was classified by class/subclass tree in an ontological structure. Then we developed a web-based interface system on the internet enabling the implementation of the ontology. In addition, we have designed an online scale for automated diagnosis of mood disorder.

For evaluating experiments, we compare this ontology with “Decisionbase™” of which content deals with mood disorders. Evaluation was in accordance with our selected criteria via the AHP (Analysis of Hierarchical Processing) method. The results demonstrated the noteworthy superiority of our ontology. We believe that combining knowledge of medical science with that in psychological fields is a key to improving the quality of diagnosis and promoting appropriate treatment in all psychiatric disorders.

Key words: Ontology, Protégé, Mood disorders, Biomedical view, Psychological view, AHP method

1. Introduction

In recent years, medical science has made its remarkable progress, especially owing to advances in molecular genetics. As the volume of information increases subsequent to the development of medical science, classification of the knowledge and improving its accessibility becomes the inevitable task to be prioritized. Ontology is a methodology which describes the domain knowledge structure in an area of specialty, which promotes its various kinds of knowledge processing intended to provide systematic semantic links among a collection of related concepts. Ontology is currently perceived as one of the tool needed to solve problems in academic nomenclatures and terminologies related to the biomedical domain^{1,2,3}.

As expertise in each area of biomedicine grows, subsequent problems arise in communication between related areas of studies. For example, in the fields of human mental care, patients' problems are often misunderstood by counselor or psychologist due to their lack of knowledge in medicine. On the other hand, most of psychiatrists sometimes spend less time in identifying the psychological causes or aspects of the mental disease. Psychologists and physicians engaged in mental health care often have clear disagreement with each other in their diagnosis and treatment approaches.

This is partially due to the differences in their educational training: the departments of psychology in many universities do not put their main focus on providing the education in medical science in the sense

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of professional biological medicine, while psychiatrists receive the professional training mainly focused on the approach to mental diseases as physician. For better collaboration between psychologists and psychiatrists, it is essential for both groups to know more about each other's areas of expertise.

One of the feasible methods is to develop the knowledge support system which promotes the exchange of information between these two fields. A well-established ontology of the mental diseases should be developed to facilitate the mutual understanding of the expert knowledge of each field.

Decisionbase™ (<http://www.mytherapy.ca>) owns the most professional computer program for psychiatric diagnostic and record-keeping systems currently available. However, it mainly focuses on medical-psychiatric approaches as compared to psychological approaches. Hence, in this study, we developed a new educational/clinical ontology, which involves both medical and psychological approaches of mood disorders in an attempt to promote cooperation between psychiatrists and psychologists. In developing the ontology, we selected mood disorder as the subject of mental disease.

In designing our ontology, which we named the "Haghighi-Koeda Mood Disorder Ontology (HK ontology)", we took precedence in making a clear distinction between the "biomedical aspects" and "psychological aspects" of mood disorders. Like every other ontology, "hierarchical structure of the concepts" or "classification" is emphasized the most, though we also make practical approach in implementing a kind of "disease based" and "patient based" tool. Our ontology equipped with the web interface provides useful information about four main types of mood disorders. Each type of the disorders has been examined with the various criteria in the HK ontology, based on both its biomedical and psychological views.

In addition, in order to use this ontology in clinical situation and to make it comparable with Decisionbase™, an automated diagnosis scale for mood disorder was designed and linked to the web interface of this ontology-based system. After constructing the knowledge support system for mood disorder, we conducted experiments for evaluation of HK ontology in comparison with the corresponding functions of Decisionbase™ with totally 23 psychiatrists and psychologists who have considerable experience. We analyzed the results of the experiment using statistical method denoted AHP (Analysis of Hierarchical Processing).

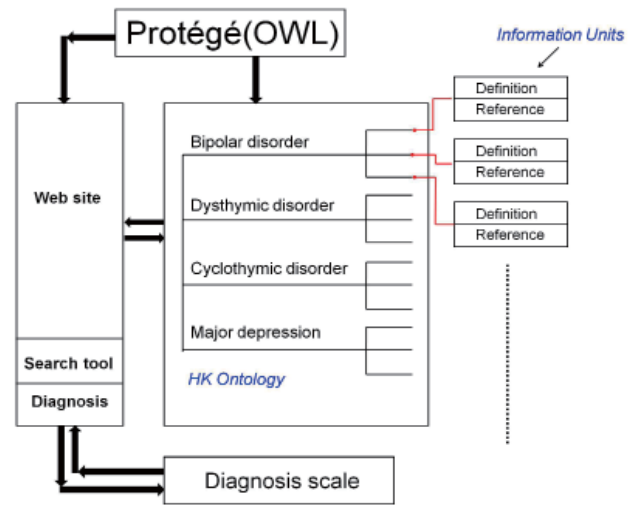


Figure 1: Schematic view of web interface structure

This web site has designed based on Protégé format and it includes search tool, diagnosis scale, hierarchical tree and information units.

2. Materials and Methods

In developing the ontology-based knowledge support system for mood disorder also equipped with diagnosing function, we used the software Protégé (Version 3.4 beta) ^{4, 5, 6}; <http://www.protege.stanford.edu> for constructing our HK ontology for mood disorder which consists the main part of our system. Protégé is the most widely used ontology-developing software and was developed at Stanford Center for Biomedical Informatics Research. We implemented this ontology into user interface system on the web to manage various operations using web-directed languages. Thus, this system possesses two formats to display the HK ontology: one is Protégé format, and the other is web-based language format, which is commonly used.

In this section, the concept of our knowledge support system, software tools and information collection method which we use in constructing our system, and also, procedures to conduct and analyze the evaluation experiments are described.

2-1. System design for our ontology-based knowledge support system on mood disorder

The following design of the structure (Figure 1) was adopted to implement our knowledge support system.

1) Ontological tree (classification tree) of the entities related to the mood disorder:

This superclass/subclass tree is the main part of the system and may be called "knowledge base," providing

the conceptual structure of the domain regarding this disease: All classified knowledge/information related to the classes/subclasses of mood disorders has embedded on the base.

2) Attached information units:

Definitions of each class/subclass concept, and list of related references to each class /subclass are attached to the nodes of the classification tree as the information unit of the class/subclass represented by the node.

3) Ontology search system implemented in web interface system:

Keyword retrieval system of concept is equipped in the web interface system to search its location in the ontological tree and to obtain the information/knowledge regarding to it.

4) HK Mood Disorder Diagnosis Scale:

Diagnosing function of the mood disorders is equipped to the system which demonstrates the certainty of diagnoses made based on the patient information typed in by the user based on the HK ontology of mood disorders.

2-2. Tools for making the Ontology

We used Protégé (Version 3.4 beta) for constructing our ontology-based system. Related softwares such as Protégé-OWL plugin, an OWL Wizards plugin, and an OWLViz plugin can be obtained in a single download from: <http://www.coode.org>. OWL is a multi-user document repository (knowledge base) language mainly for the purposes of publishing files/documents onto the web. Protégé is a free, open-source ontology editor and a knowledge-base framework. The Protégé platform supports two main ways of modeling ontologies via the Protégé-Frames and Protégé-OWL editors. Protégé ontologies can be exported into a variety of formats including RDF(S) OWL, and XML Schema. Protégé is based on Java, is extensible, and provides a plug-and-play environment, which makes it a flexible base for rapid prototyping and application development. Protégé is supported by a strong community of developers and academic, government and corporate users, who are making use of Protégé for knowledge solutions in areas as diverse as biomedicine, intelligence gathering, and corporate modeling. Using a practical Protégé guide created by Matthew Horridge and colleagues at University of Manchester and Stanford University 9, our ontology was developed.

As a next step, the web interface for this ontology was designed by using programming language Perl to build CGI (Common Gateway Interface). In the web

system; 1) the hierarchical tree was implemented with TreeView 4.5 software in Java Script. TreeView is a free software provided by Gubusoft Ltd. Massachusetts, USA. ; 2) The definitions, comments, and reference information were described in information units. 3) The reference information is linked to its original web page which provides the whole contents. 4) The search facility for key word retrieval is programmed in Perl Script. It finds paths from the root node to the query node. A partial match is available in this search.

We made links to PubMed using PubMed IDs. If an associated reference is an online-only article out of PubMed, then we made a link to its homepage that publishes the e-document. PubMed is a service of the U.S. National Library of Medicine that includes over 18 million citations from MEDLINE and other life science journals for biomedical articles back to the 1950s. PubMed includes links to full text articles and other related resources, enabling users to exploit the PubMed information for extended research.

2-3. Sharing aspects to make the structure of the ontology

We have two main purposes in making the HK ontology. One is to easily display the information to the unfamiliar person for the mood disorder. The other is to effectively share the new technical knowledge with physicians and clinical psychologists through the web site on the internet. To achieve such, the authors (mainly MK and MH) discussed in advance the sharing aspects in the following.

First, we collected information by classifying the 9 essential terms (Associated problems, Cause, Diagnosis, Epidemiology, Prevention, Prognosis, Symptoms, Treatment, and Types) for understanding general diseases.

Second, to promote the sharing of information between psychiatrists and psychologists in the 9 essential items, we discussed whether each item needs to be categorized as 1: the professional information on the psychiatric field, 2: the professional information on the psychological field, and 3: the common information for the psychiatrist and psychologist.

The specific terms of Associated problem and Cause were selected by categorized two aspects: the biomedical aspects (view) and psychological aspects (view). The specific terms of Diagnosis were selected by categorized three aspects: misdiagnosis as well as biomedical aspects (view) and psychological aspects (view). The specific terms of Epidemiology were selected without categorized by biomedical and

psychological aspects. We described the age, gender differences, and social background for four diseases. The specific terms concerning Prevention, Prognosis, Symptoms were selected without categorizing with biomedical and psychological aspects. In the item of Prevention, the typical references related to Prevention were collected. The information related to Prognosis was collected based on the severity of disease, the age, and medical history. The information related to Symptom and Type of disease was collected based on the international criteria of the disease and the technical book for the mood disorder.

Based on such discussion, we built the structure of our ontology.

2-4. Information collection method

In developing the ontology, top entities of four types of mood disorders have been selected based on the classification of DSM-IV⁷, a prominent reference for diagnosis of psychiatric disorders. Information related to the main tree was collected from various sources on the Internet and more than approximately 5000 articles published in professional journals on PubMed and Google Scholar sites. Collection was done by searching with the combination of search terms, "Biological/Medical/Psychiatry" + "name of disorder", or "Psychological/Unbiological" + "name of disorder". By reading the abstracts of the articles retrieved, we selected approximately 5000 articles as the source of our data. For every subclass, up to five references were listed. For finding these references, we used the search terms; "name of subclass"+ "name of disorder".

As for the fourth level in the HK ontology, we selected the specific term in the following. First, using the PubMed, the name of the disease (Bipolar disorder, Cyclothymia, Dysthymia, and Major Depression) and the term of second level in the ontology (Associated problems, Cause...) were searched. Second, if many references were selected in the Pubmed, we read the references again, and we selected the more specific term. Third, we continued to search until the searched results were within 20 references, and decided the term in third level of the HK ontology. Finally, our criterion for the selection of up to 5 references out of a number of search results was its relevancy to the specified subclass. For example, when the subclass was "excess of growth hormone" and our main class was "bipolar disorder", we preferred an article which specially focused on "excess of growth hormone and its relation with bipolar disorder". Articles which only focused on "growth hormone and its relation with bipolar disorder"

were put in lower priority.

2-5. Haghghi-Koeda Mood Disorder Diagnosis Scale

For the mood disorder diagnosis scale, we used a screening test with 5 questions based on the Hamilton depression scale. For the Mood disorders questionnaires, items were taken from the "Symptom" criteria in the HK ontology. The style of questions and answers and the scoring method were also based on the Hamilton depression scale: <http://healthnet.umassmed.edu/mhealth/HAMD.pdf>.

Haghghi-Koeda Mood Disorder Diagnosis Scale (Figure 2) was developed using XHTML⁸ transaction 1.0, PHP 4⁹, and Java-script 1.4¹⁰. As for further details, PHP was used, along with the tools mentioned above, to write a server-side code, a Java script for client side code, and an XHTML, which was used for validation of questionnaires. We used dynamic DHTML for dynamic page manipulation on the client side for instance in a screening test. The table is dynamically updated as the user answers the questions. This program works on a unix server on the server-side using a POST method¹¹ to send data between client and server.

For HTML we used a tableless layout based on XHTML specification and a CSS style sheet²². This web application works with all browsers, i.e. Firefox or Internet Explorer. The only system requirement is Javascript being the default language.

2-6 Evaluation experiment with Decisionbase™

We evaluated our ontology-based knowledge support system with Decisionbase™ with emphasis on the diagnostic function to prove its superiority to this computer program.

2-6-1. The main features of Decisionbase™

Decisionbase™ is an automated system equipped with the functions to perform:

- Psychiatric diagnosis,
- Psychiatric record-keeping (histories, progress notes),
- Brief cognitive testing (of memory, concentration, etc),
- Statistical analysis of psychiatric data.

Decisionbase™ is a kind of "server-based software"; its users can access to the psychiatric records anywhere

1* Post method is used to send complex data to other web servers.
2** CSS (Cascading Style Sheets) is a stylesheet language used to describe the presentation of a document written in a markup language. CSS defines colors, fonts, tables and images and gives facility to transfer design of one page to all pages.

Figure 2: HK Mood Disorder Diagnosis Scale

- 1. Alcohol and drug abuse**
Have you ever had a problem with alcohol?

 - Absent
 - People criticized you for drinking
 - You tried to cut down your drinking
 - Drinking alcohol as soon as you wake up in the morning
- 2. Anger**
Have you ever had a problem with anger?

 - Absent
 - Occasionally
 - Frequently
- 3. Change in appetite**
Have you ever had a change in appetite?

 - Absent
 - Eat more or less than usual
 - Strange and uncontrolled overeating or loss of appetite
- 4. Change in self confidence** *Go to: [Self esteem](#)*
Have you ever had a change in self confidence?

 - Absent
 - Mild to moderate loss of self confidence
 - Severe loss of self confidence
- 5. Cyclic mood change**
Have you ever had a persistent instability of mood?

 - Absent
 - One mild depression and one mild elation period
 - Numerous periods of mild depression and mild elation
- 6. Frequent change of residence**

 - Absent
 - Occasionally
 - Severe

Figure 2A: Part of cyclothymic disorder questionnaire

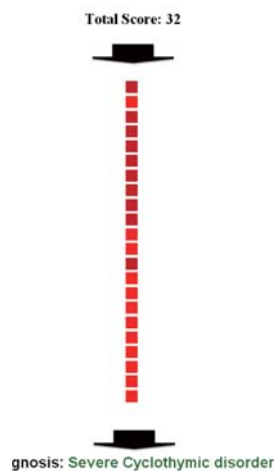


Figure 2B: Results page of the HK Mood Disorder Diagnosis Scale. Horizontal column represents the severity of the disorder. Green color represents of normal condition and red represents of abnormal condition. As much as red color goes toward darkness, problem is more severe.

in the world on the Internet. It serves its customers with data storage, online computerized diagnosis, cognitive assessment, quality of life evaluation, keeping progress-notes, filling in questionnaires. The processes in clinical situation for one patient are: creating a new patient file, completing a diagnosis assessment, completing evaluation on a quality of life scale, completing a

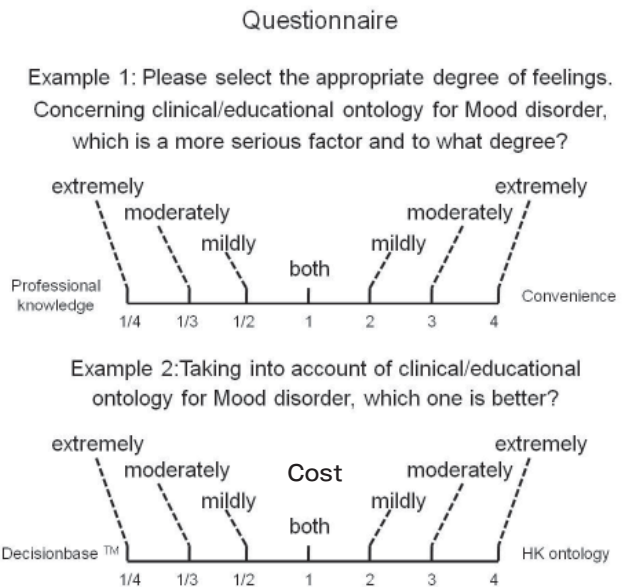


Figure 3: Some items of AHP questionnaires:

Example 1 shows that subject feels that convenience is more important for an ontology compared to professional knowledge. Example 2 shows that subject feels the HK ontology is preferable to Decisionbase™.

progress note, completing an asymptomatic progress note, browsing existing patient files, and generating statistics. Decisionbase™ is not programmed to substitute for professional diagnosis and treatment, but rather to help improve the quality of the diagnosis and treatment.

2-6-2. Subjects

The subjects enrolled in the evaluation experiments on the usefulness of the HK ontology were 23 specialists, 10 psychologists and 13 psychiatrists, most of them were staff members of Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran, and Nippon Medical School, Tokyo, Japan. Working experiences of subjects were 9.9 ± 8.0 years for psychiatrists and 8.3 ± 5.8 years for psychologists. We offered them both the HK ontology-based system and Decisionbase™ to have them examine the two for real patients. We presented the data of the one patient with severe Dysthymia to both groups (psychiatrists and psychologists), and the subjects evaluated the usefulness for the Decisionbase™ and the HK ontology. At the end of the testing period, we asked the examiners to answer to our questionnaire.

2-7. AHP method^{11, 12}

Table 1: Calculation of the Example 1 type questionnaire

	Professional Knowledge	Convenience	Information Accuracy	Additive Tools	Geometrical Average	Weight
Professional Knowledge	1	1/4	1/2	1	A	A/S
Convenience	4	1	1	1	B	B/S
Information Accuracy	2	1	1	1	C	C/S
Additive Tools	1	1	1	1	D	D/S

Table 1: We calculated the geometrical average of these scores. We then calculated the sum of four geometrical averages. Using this sum, we defined the weight of each geometrical average. For example, we calculated the geometrical average (A, B, C, D) for first layer (Table 1) using the following formula:

$$A = \sqrt[4]{1 \times 1/4 \times 1/2 \times 1} \quad B = \sqrt[4]{4 \times 1 \times 1 \times 1} \quad C = \sqrt[4]{2 \times 1 \times 1 \times 1} \\ D = \sqrt[4]{1 \times 1 \times 1 \times 1} \quad S = A + B + C + D \quad \text{Weights: } A/S, B/S, C/S, D/S$$

AHP (Analysis of Hierarchical Processing) is one of the methods to evaluate composite information objectively. We assessed the usefulness of our ontology-based system using the AHP method.

2-7-1. Questionnaire¹²

We developed a three-layer AHP model to measure the usefulness of the two ontologies Figure 3 schematically illustrates the method, which is classified into three layers. The first layer consisted of four factors: professional knowledge, convenience, information accuracy and additive tools for treatment, which were the main factors selected for evaluation. In the second layer, factors which were related to first layer were compared, such as psychological knowledge being compared to medical/psychiatric knowledge for the usefulness in patient assessment. In the third layer, the HK ontology and Decisionbase™ were compared.

Based on the AHP model, we devised 3 separate questionnaires for the 3 layers. This questionnaire had 18 questions in total. Number of questions related to the first layer was 6, that to the second layer was 4, and that to the third layer was 8. Contents of questions were related to the comparison between 2 criteria, asking the examinees which he/she thought more important. In the questionnaire 1: "professional knowledge" vs "convenience", "professional knowledge" vs "information accuracy", "professional knowledge" vs "accurate diagnosis", "convenience" vs "information accuracy", "convenience" vs "additive tools for treatment", "information accuracy" vs "additive tools for treatment". In questionnaire 2: "psychological knowledge" vs "psychiatric knowledge", "cost" vs "how to browse", "new knowledge" vs "accurate classification", "statistical analysis" vs "patient record". In questionnaire 3, style of questions was asking

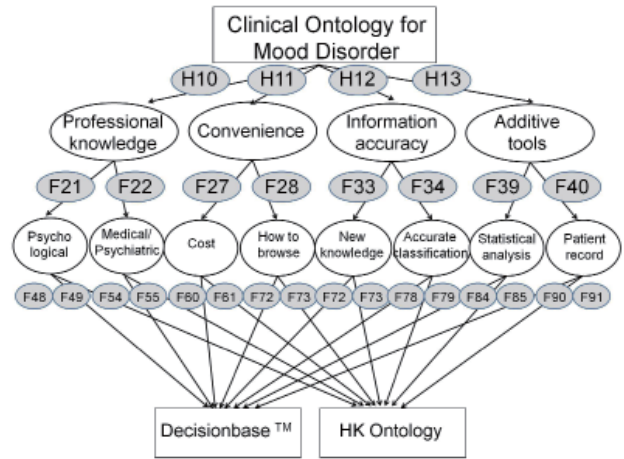


Figure 4: Analytic Hierarchical Process (AHP) model. Using this model, we evaluated some factors for comparison of the HK ontology and Decisionbase™. The first layer consisted of four factors: professional knowledge, convenience, information accuracy and additive tools for treatment. In the second layer, factors which are related to first layer were compared, such as psychological knowledge vs medical/psychiatric knowledge. In the third layer, the HK ontology and Decisionbase™ were compared.

the examinees if HK ontology or Decisionbase had priority in some criteria: the criteria compared were "psychological knowledge", "psychiatric knowledge", "cost", "new knowledge", "accurate classification", "statistical analysis", "patient record", and "how to browse".

2-7-2. Evaluation by the AHP method⁹

We distributed the questionnaires to subjects. The choice of terms provided were, "both", "mildly", "moderately" and "extremely" regarding the relevance of the item to the importance of scale. When the subjects selected the midline, it meant that both factors were equally important. When the subjects selected the left end of scale, it meant that the left factor was most important. The scores from left to right are: 1/4, 1/3, 1/2, 1, 2, 3, 4. First, we calculated the geometrical average of these scores. We then calculated the sum of four geometrical averages. Using this sum, we defined the weight of each geometrical average. For example, we calculated the geometrical average (A, B, C, D) for first layer (Table 1) according to the formula; the followings are the results: $A = \sqrt[4]{1 \times 1/4 \times 1/2 \times 1}$, $B = \sqrt[4]{4 \times 1 \times 1 \times 1}$, $C = \sqrt[4]{2 \times 1 \times 1 \times 1}$, $D = \sqrt[4]{1 \times 1 \times 1 \times 1}$. Then, we calculated S such that $S = A + B + C + D$. For each layer, one table is essential. Then, weights were calculated by these portions: A/(S), B/(S), C/(S), D/(S). To confirm the accuracy of each weight, the consistency index in the questionnaire was assessed by the following equation:

Table 2: Evaluation of statistical values for Decisionbase™ and the HK ontology

		Number	Mean	SD	Mann Whitney U
total weight	Decisionbase_TM	23	0.32	0.18	P<0.001
	HK_Ontology*	23	0.68	0.17	
professional knowledge × psychological	Decisionbase_TM	23	0.06	0.02	P<0.001
	HK_Ontology*	23	0.12	0.06	
professional knowledge × psychiatric	Decisionbase_TM	23	0.05	0.03	P<0.001
	HK_Ontology*	23	0.15	0.05	
convenience × cost	Decisionbase_TM	23	0.08	0.01	P<0.001
	HK_Ontology*	23	0.32	0.05	
convenience × how to browse	Decisionbase_TM	23	0.09	0.03	P<0.001
	HK_Ontology*	23	0.32	0.07	
information accuracy × new knowledge	Decisionbase_TM	23	0.04	0.01	P<0.001
	HK_Ontology*	23	0.16	0.05	
information accuracy × accurate classification	Decisionbase_TM	23	0.03	0.02	P<0.001
	HK_Ontology*	23	0.14	0.04	
additive tools × statistical analysis	Decisionbase_TM*	23	0.18	0.05	P<0.001
	HK_Ontology	23	0.04	0.02	
additive tools × patient record	Decisionbase_TM*	23	0.14	0.06	P<0.001
	HK_Ontology	23	0.06	0.03	

Table 2: Evaluation of statistical values for Decisionbase™ and the HK ontology. A higher score for the HK ontology in the "Mean" column shows that the HK ontology is more useful overall than Decisionbase™; the P values (P<0.05) show a significant difference between scores of the HK ontology and Decisionbase™.

(Consistency Index: C.I. = $((\lambda_{max-n}) / (n-1))$ (Table 1). When we suppose the element A in each layer "a1, a2, ..., an" and suppose the weight on each layer "w1, w2, ..., wn", the pair matrix of the element of A can be supposed $A = [a_{ij}]$, $a_{ij} = w_i/w_j$, $a_{ji} = 1/a_{ij}$, $W = [w_1, w_2, w_3, \dots, w_n]$ (note: i, j = 1, 2, ..., n). In this situation, when matrix A is multiplied by weighted column vector W, the value will be $n \times W$, i.e., $A \times W = n \times W$. This formula can be changed into $(A - n \times I) \times W = 0$ (I = unit matrix). If $W \neq 0$ is correct, n has to be the eigen value of A, and W will be the eigen vector of A. Further, because the rank of A is 1, eigen value λ_i (i = 1, 2, ..., n) will be that only one eigen value is non zero and the rest zero. The sum of opposite angle's element of A is n. If the only non zero λ_i is λ_{max} , $\lambda_i = 0$, and $\lambda_{max} = n$ ($\lambda_i \neq \lambda_{max}$). The weighted vector W will be normalized eigen vector ($\sum_{i=1}^n w_i = 1$) for the maximum eigen value λ_{max} .

To determine unknown vector W, we have to calculate W' vector value, where W' is calculated by pair matrix A', which is the subject's answer to the questionnaire.

In this situation, the formula consists of $A'W' = \lambda'_{max} \times W'$ (λ'_{max} is the maximum eigen value of A'). W' will be normalized eigen vector ($\sum_{i=1}^n w'_i = 1$) for the maximum

eigen value λ'_{max} of A'. By Saaty's theorem, λ'_{max} is given by

$$\lambda'_{max} = n + \sum_{i=1}^n \sum_{j=i+1}^n \frac{(w'_j \times a_{ij} - w'_i)^2}{w'_i w'_j a_{ij} \times n}$$

$\lambda'_{max} \geq n$ is usually correct. From this formula, the Consistency Index (C.I.) can be calculated:

$$C.I. = \frac{\lambda'_{max} - n}{n - 1}$$

Concerning this formula, Saaty proposed that if C.I. is less than 0.1, C.I. is significant. So, in the present study, we used the significant value of C.I. is less than 0.1.

Using the AHP model (Figure 4), we evaluated "total weight", which was the index to judge the importance of Decisionbase™ and the HK ontology.

According to the formulas of AHP, the following results were obtained:

For Decisionbase™:

$$A = H10F21F48 + H10F22F54 + H11F27F60 + H11F28F66 + H12F33F72 + H12F34F78 + H13F39F84 + H13F40F90.$$

For the HK ontology:

$$B = H10F21F49 + H10F22F55 + H11F27F61 + H11F28F67 + H12F33F73 + H12F34F79 + H13F39F85 + H13F40F91.$$

Table 2 shows the elemental statistical values, total weight and products of the first, second and third layers

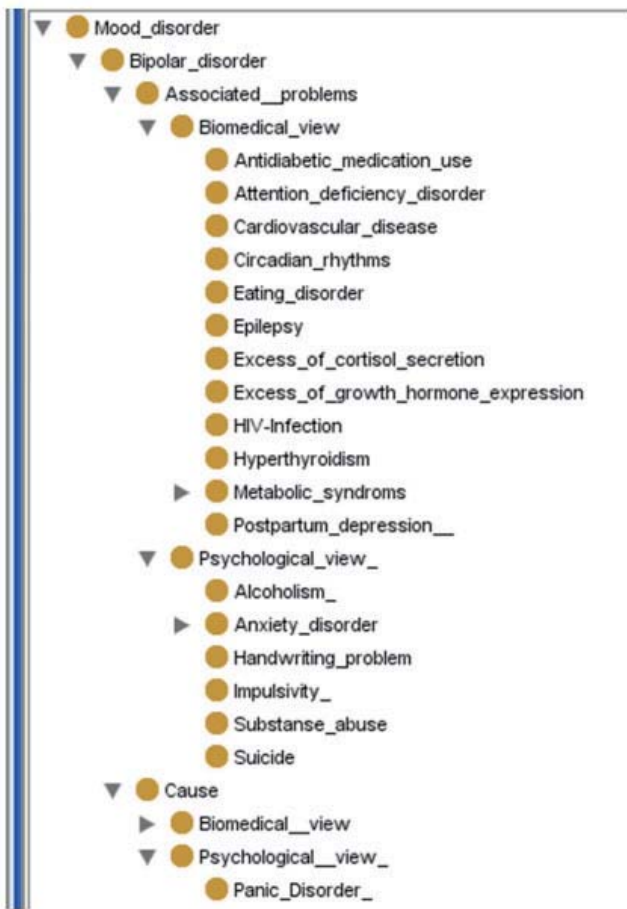


Figure 5: Protégé format: At the third level of classification, subclasses are: "biomedical view" and "psychological view" and fourth level of classification in the HK ontology varies according to the information gathered from professional articles.

(8 elements of the formula in total weight: Professional knowledge \times Psychological, Professional knowledge \times Psychiatric, Convenience \times Cost, Convenience \times How to browse, Information accuracy \times New knowledge, Information accuracy \times Accurate classification, Additive tools \times Statistical analysis, Additive tools \times Patient record): As an example, Professional knowledge \times Psychological is represented by H10F21F48 in Decisionbase TM and H10F21F49 in the HK ontology. Further, we compared elemental statistical values using SPSS No.12 software (Table 2).

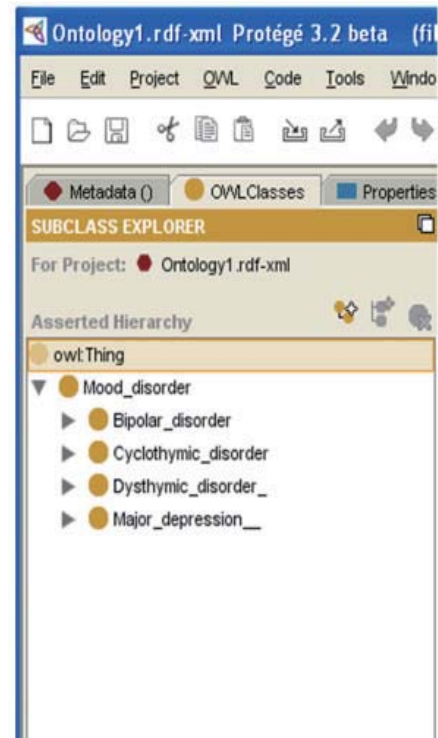
2-8. Evaluation of usefulness of the HK ontology in clinical situation

The experimental group used the HK ontology and control group did not use it. Number of subjects in each group was 10. We selected from psychologists and psychiatrists who were working in Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.

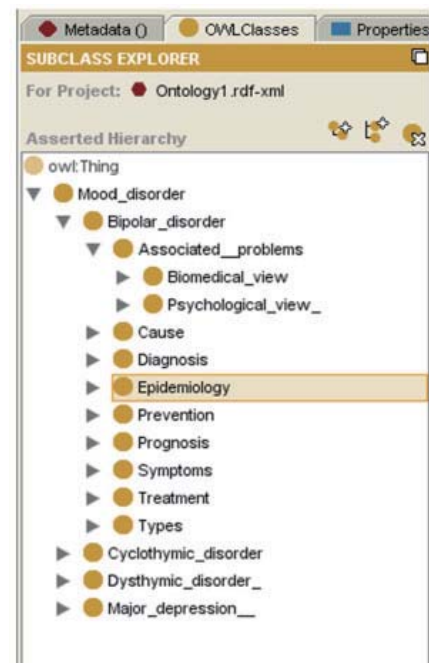
Figure 6: Protégé format: First level (A) and second level (B) classification in the HK ontology.

There are four main types of "Mood disorder": "Bipolar disorder", "Cyclothymic disorder", "Dysthymic disorder" and "Major depression". At the second level, the criteria include Associated problems, Cause, Diagnosis, etc.

A.



B.



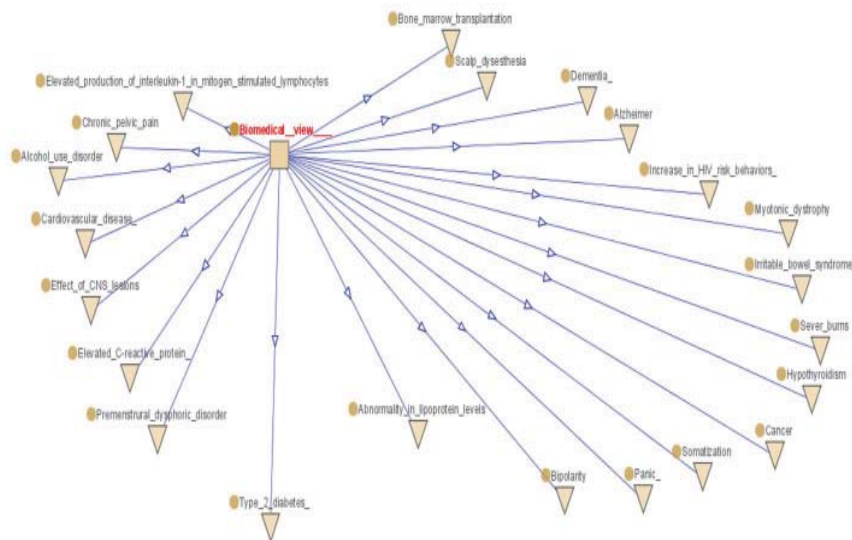


Figure 7: Protégé format: Jambalaya tree for: Dysthymic disorder > Associated problems > Biomedical view

Graphic images of the subclasses and super classes can be viewed by right clicking and selecting "show subclass tree (Jambalaya tree)" and "show subclass/superclass trees (Jambalaya tree)" from menu.

The average (\pm SD) of working experiences was 9.8 ± 8.1 years for the clinical psychologist, and 8.8 ± 6.3 years for the psychiatrist. Twenty patients were directly examined, and one patient with dysthymia was evaluated by examiners of both groups (the HK ontology and the control). We used 20 dysthymic patients who were previously diagnosed by reliable experts and had a long history of dysthymic disorder, but none of experimental and control groups had any patient information regarding the disease history, diagnosis, and treatment. The experimental group used the HK ontology for diagnosis of these patients while the control group did not. In evaluating the usefulness of the ontology (Decisionbase TM and the HK ontology), we have asked the subjects to assume the clinical situation where they are in need of searching the score of severity of the disease, the explanation of medical terms, and the search for technical terms. The subjects differentiated 4 diseases (Bipolar Disorder, Cyclothymia, Dysthymia, and Major Depression) using the HK Mood Diagnosis Scale. All subjects diagnosed Dysthymia for the patient data. In the present study, the subjects did not examine scoring of the severity of the disease, but the subjects evaluated the usefulness of the ontology

in considering the usability of the HK Mood Diagnosis Scale. We calculated the level of significance. To examine the difference of evaluation score in two groups, Fisher's exact test was used.

3. Results

3-1: Contents of the HK Ontology

The developed HK ontology for the mood disorders included 4 types of disorders and 9 criteria, 1160 terms and 620 definitions for terms. In the structure of this ontology, the "biomedical view" and "psychological view" were separately implemented for each of the related classes/subclasses (Figure 5). The "biomedical view" refers to the cellular-biological or medical contribution to the specific criterion, and "psychological view" refers to the psychological-environmental contribution to the topic. We will explain hereafter the various operations related to the ontology using the screen images in Protégé format.

By manually clicking on "OWL classes tab" in the window, the hierarchy of mood disorders appears on the screen. Then, by manually left-clicking on the triangle at the left of the phrase "Mood disorder", "Bipolar

Figure 8: Web interface of the HK ontology includes: (1) hierarchical conceptual tree; (2) descriptions associated with individual concepts and for the conceptual tree; (3) PubMed entries referred to in the HK ontology; (4) search facility for the conceptual tree (bottom left). At first, by clicking on each subclass in part 1, subclass concept of that subclass and list of references will appear in part 2 and by clicking on name of references in part 2, PubMed abstract or related page will appear in part 3. By submitting keyword in part 4, location of that term in ontology will be presented in part 2.

disorder", "Cyclothymic disorder", "Dysthymic disorder" and "Major depression", which are the main types of mood disorder in accordance with the categorization of DSM-IV, appear as subclasses (Figure 6A).

At the next level, the following attributes appear: Associated problems, Cause, Symptoms, etc. (Figure 6B). The fourth level of subclasses linked to the information units, which store the information extracted from the articles that we have searched professional databases in medical science and assessed carefully. The examples are those describing the abnormality in COMT gene, abnormality in dopamine receptor genes, etc. in relation to the mood disorders.

In Protégé format, by right-clicking on each class and subclass, then selecting "Show subclass tree (Jambalaya tree)" and "Show super class tree (Jambalaya tree)", users can obtain graphic images of the subclasses and super classes (Figure 7).

By clicking on the "Asserted super classes" window in "OWL class tab" in Protégé format, the user can

check super class for each subclass. By clicking on second figures located under "Asserted hierarchy" window in "OWL class tab", users can search the name of every class and subclass spelled out using the English alphabet and its related super class through the "conditions section" located at the bottom of Protégé page in the "OWL class" tab.

We have designed a web interface for mood disorder for clinical purpose. It is available at the following URL: <http://bio-omix.TMd.ac.jp/TMdu/>. Web-based system is composed of four windows: 1) Hierarchical conceptual tree (top-left): In this hierarchical display, users can expand and break down sub-trees as they like. Clicking one of the nodes opens a description associated with the node which is a concept in the HK ontology. 2) Descriptions associated with individual concepts: This is the definition part of the information units. 3) PubMed entries referred to in the HK ontology: This is the part that provides the reference information units. 4) Search system on the HK ontology: This is a tool to find the

location of the conceptual tree.

Mood disorder diagnosis scale include one screening test and 4 questionnaires for 4 types of mood disorders: questionnaires for major depression (20 questions), a questionnaire for cyclothymic disorder (22 questions), a questionnaire for bipolar disorder (15 questions), and a questionnaire for dysthymic disorder (35 questions). Green color in the scale represents normal condition and red represents abnormal. The darkness of red indicates the severity of abnormality. After marking answers, total score and then some general view of severity using above colors appear and at the end, scoring range and final diagnosis will appear. The URL address of the Web-based system as: <http://japan-website.com/HK> diagnosis scale, and it is linked to the HK ontology.

3-2. Statistical Evaluation

We conducted the evaluation experiments which compared the usefulness of our ontology-based system and Decisonbase™ using AHP methods. We obtained the results where the total weight of all subjects was greater in the HK ontology than in Decisonbase™. The values of C.I. in all subjects were found to be less than 0.1, meaning all C.I.s were significant. Comparing the 8 elements in the AHP method, the 6 elements of the HK ontology were found to be significantly greater than that of Decisonbase™, 6 elements (Professional knowledge × Psychological, Professional knowledge × Psychiatric, Convenience × Cost, Convenience × How to browse, Information accuracy × New knowledge, Information accuracy × Accurate classification) were significantly greater in the HK ontology than in Decisonbase™ (Mann-Whitney U test, $p < 0.05$; Table 2). On the other hand, 2 elements of the HK ontology were significantly inferior to those of Decisonbase™ (2 elements: Additive tools × Statistical analysis, and Additive tools × Patient record; Mann-Whitney U test, $p < 0.05$; Table 2). In both of psychiatrists and psychologists, total weight of HK ontology was significantly greater than Decisonbase™ (Mann-Whitney U test: $p < 0.05$). Although the group difference in the element of AHP (weight value) was statistically analyzed, there was no significant difference between psychiatrists and psychologists in the AHP scores (Mann-Whitney U test: $p > 0.05$).

When testing the usefulness of the HK ontology in clinical situations, we used two groups of clinicians, an experimental group who used the HK ontology for patient diagnosis and a control group who did not use it. The diagnostic error was 1 out of 20 for the

experimental group and 5 out of 20 for the control group. In this experiment, difference was statistically significant with significant level $p < 0.001$, and we could reduce the number of diagnosis error using the HK ontology in clinical situation.

4. Discussion

Suppose a physician is examining his/her patients, he/she may be able to list all possible medical causes related to bipolar disorder, but he/she does not have enough information on the "psychological" causes of the disease. By clicking on "psychological view" as a subclass of "cause" in the "bipolar disorder" category, the physician can instantly obtain useful information related to psychological causes of bipolar disorder, and clicking on "psychological view" in "treaTMent" enables the physician to provide useful advice regarding psychotherapy as a parallel treatMent. Likewise, by clicking on "biomedical view" as a subclass of "cause", a psychologist can find essential information related to the medical/biological causes of "bipolar disorder". Meanwhile, the physician and the psychologist can search key terms in the ontology, and read abstracts of related articles via the links provided.

In clinical situation, using "Mood disorder diagnosis scale" allows a physician to ask questions based on the items of an appropriate questionnaire, and the system automatically diagnoses the type of disorder and its severity. The physician is required, however, to use the screening test at the beginning in order to decide which questionnaire should be used for a patient.

The HK ontology has two important conceptual advantages to Decisonbase™ besides to its user-friendly functions: it offers high quality "professional knowledge" and "accurate information". Latest information that is hard to obtain from published textbooks is accessible using the ontology, because most of information has been extracted from newly published articles online and it is constantly updated. Another advantage is "Mood disorder diagnosis scale" and an automatic detector of related articles. This diagnosis scale in its "Bipolar disorder", "Dysthymic disorder" and "Cyclothymic disorder" parts is unique being the first diagnosis scale developed for these disorders. The third advantage is that it contains both biomedical and psychological views in the same collection, when no existing textbook provides information from both perspectives.

We emphasize that this ontology has made two contributions: First and the most important contribution is providing extensive knowledge compared to ordinary



Figure 9: Necessity of psychological-medical ontology. It has seen in many cases that counselors and psychologists misdiagnose due to lack of medical information. The reason is that they only pass few elementary units related to medical science in "Faculty of Psychology and Educational Science". On the other hand, most of psychiatrists do not care about issues of Psychology and Educational Science, since they focus only on the medical-oriented approach in their faculties of medicine. These two groups usually have clear disagreement with each other in their diagnosis and treatment approaches.

decision support systems. The second contribution is creating a tool for diagnosis in clinical situations. Besides conceptual advantages, structural advantages of the HK ontology provide accurate classification, links to related up to date articles, and a search tool.

Unfortunately, most counselors and clinical psychologists do not have sufficient education in medical science; their therapy is limited to "psychological-philosophy-oriented" approach which is based on theories of historically prominent psychologists. Such a biased therapy is dangerous, just as intervention which depends only on medication without psychological approach can be harmful (Figure 9).

Most of the ontologies, which have been developed and established their usefulness, belong to genetics/medical sciences^{2, 3, 14, 15, 16, 17, 18}. Apart from Decisionbase™, there is almost no similar ontology to the HK ontology which has specific attention to mood disorders. Decisionbase™ has specific attention to psychiatric disorders, or more generally, UMLS^{17, 18, 19} (Unified Medical Language System) <http://www.nlm.nih.gov/research/umls>, which is a huge database that includes all terms related to medical science with their semantic interrelation. It covers some important

sources of medical information. The UMLS integrates over 2 million names for some 900,000 concepts from more than 60 families of biomedical vocabularies. We can also find information in the name of behavioral science and psychiatry in UMLS, but the information is too general for clinical usage. Technically speaking, Decisionbase™ cannot be classified as an ontology, but with no ontology related to mood disorder existing, Decisionbase™ was our choice for experiments in evaluating comparison to the HK ontology, since its contents deal with mood disorders.

The results of AHP method revealed that total weight of the HK ontology was greater than that of Decisionbase™ in all subjects when the two ontologies were compared. This result suggests that the HK ontology is a useful tool for the diagnosis and the treatment of mood disorders. The 23 examinees involved in the evaluation of two ontologies considered the HK ontology valuable for both psychological and psychiatric professional knowledge. Further, in terms of convenience and information accuracy, the HK ontology was evaluated as a feasible tool for all 23 subjects. These results indicate that the HK ontology has high performance in providing professional

Figure 10: (A and B): Structural comparison between Decisionbase™ and the HK ontology: the HK ontology follows only specific objective: to help psychologists and psychiatrists exchange information, while Decisionbase™ has various facilities for the user, the HK ontology is designed specifically for mood disorders (Figure 10A). As currently conceived, Decisionbase™ may be used by therapists in a private or hospital setting (Figure 10B). It has various applications compared to our ontology. In addition to a diagnostic system based on DSM-IV for all psychiatric disorders, it is a patient record database offering tests and statistical analysis functions.

Figure 10A

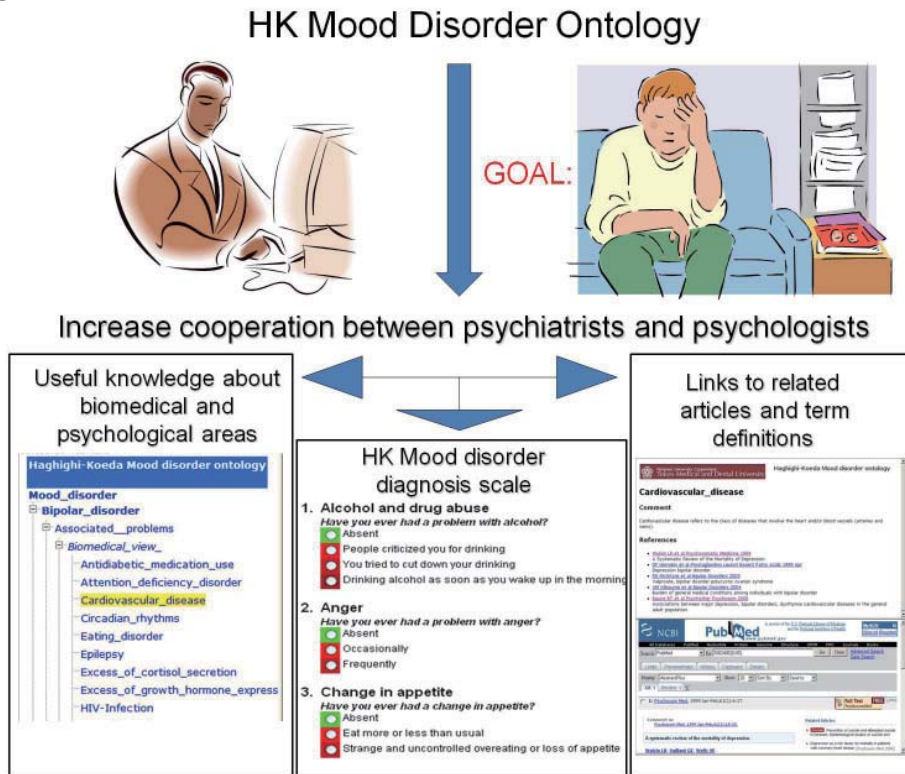


Figure 10B

1. Quality of life assessment

Please complete all of the questions below and click on "Continue" when you're done. For convenience, you may [reset](#) all answers to the first item.

Date of questionnaire completion: June 2008

Exercise	Physical Functioning	Physical Discomfort
Do you exercise regularly (e.g., walking, jogging, swimming, lifting, tennis, hiking, or gardening)?	Do you have any physical problems, such as aches, pains, or stiffness?	Do you have any physical discomforts?
<input type="radio"/> A lot	<input type="radio"/> No or little difficulty	<input type="radio"/> No or little difficulty
<input type="radio"/> Some	<input type="radio"/> Much difficulty	<input type="radio"/> Much difficulty
<input type="radio"/> Little	<input type="radio"/> Severe difficulty	<input type="radio"/> Severe difficulty

2. Progress notes

Progress Note - September/14/2008 Bill Johnson

MENTAL HEALTH SUMMARY
Bill Johnson is a 34-year-old single male, who is employed and lives at home. Primarily, Bill's recovery was stable, but today's re-evaluation is more for concern. Now Bill's overall functioning is poor.

DIAGNOSIS

Alcohol Dependence (Alcoholism) 303.90	In Remission	Primary	ASX
Bipolar I Disorder 296.20, Manic Episode Hypomanic 310.0	In Remission	Primary	Severe Problems Walk
Conduct Disorder 301.20	In Remission	Primary	Overall Functioning
Generalized Anxiety Disorder 300.00	In Remission	Secondary	Moderate Problems Walk

PROGRESS: (Starting to talk pre-psychiatrically). Seems like he's starting to go hypomanic! (Increased need for sleep, over-enthusiasm, being over-enthusiastic)

ADDITIONAL: Five days after this was written, Bill was brought by police to hospital in a manic state. He told the psychiatrist there that he had stopped all his psychiatric medications.

3. Diagnostic assessment based on DSM-IV

Diagnostic Test Selection

Please select the diagnostic tests that you would like to take. You may select either categories to speed up testing, or questions common to different tests will be asked only once.

Date of this assessment: June 2008

Diagnostic Tests

- Adjustment Disorder (Consider in this category must be tested together) (Filter: select)
- Adjustment Disorder with Anxiety 309.24 (Filter: select)
- Adjustment Disorder with Anxiety and Depressed Mood 309.25 (Filter: select)
- Adjustment Disorder with Depressed Mood 309.24 (Filter: select)
- Adjustment Disorder with Disturbance of Consciousness 309.3 (Filter: select)
- Adjustment Disorder with Mixed Conductance 309.4 (Filter: select)
- Alcohol-Related Disorders (Consider in this category must be tested together) (Filter: select)
- Alcohol Abuse 303.50 (Filter: select)
- Alcohol Dependence (Alcoholism) 303.90, With Physiological Dependence (Filter: select)

Decisionbase™

4. Cognitive Assessments

Quality of Life Assessment

The scores are broken down into categories and are displayed below. The lower the percentile score, the better the condition.

Issue	Problems	Severity	Severity Graph	Percentile
1.3	Physical Functioning	None		38.2
12.11	Social Functioning	None		38.9
12.11	Suppression/Anxious Functioning	None		31.9
13.21	Impulsive/Anxious Behavior	None		44.4
22.24	Substance Abuse	None		72.4
22.24	Anxiety	None		37.3
22.24	Depression	None		77.4

5. Statistical analysis of patient clinical data

Quality of Life Category - Effect Size Graph

Phy Soc Occ Imp Sub Foc Dep Man Rea Int Nee Lac Ove Total

knowledge, convenience, and accurate information. On the other hand, concerning statistical analysis and patient records (additive tools), Decisionbase™ was considered a more useful tool than HK ontology. In these areas, we have to continue to improve our ontology in the future.

HK ontology aims for only one specific objective: to help psychologists and psychiatrists exchange knowledge and information while Decisionbase™ has various facilities for the users, since the HK ontology is designed specifically for mood disorders (Figure 10A). As currently conceived, Decisionbase™ may be used by therapists in a private or hospital setting (Figure 10B). It has various functions for applications compared to HK ontology. In addition to a diagnostic system based on DSM-IV, it is a patient record database offering tests and statistical analysis functions.

Comparing the mood disorder-related part in Decisionbase™ with HK ontology, the classification and information of the latter is the more precise and detailed for educational/clinical purposes. Decisionbase™ does not focus on psychological issues as much as HK ontology does. Meanwhile, HK ontology is a web-based application and free of charge, which is an advantage over Decisionbase™, which charges a fee and requires "Adobe Flash Player" installation.

5. Conclusion

We believe that combining the knowledge of medical and psychological areas is a key for reducing mistreatment of the patients and promoting the appropriate treatment of psychiatric disorders. Our new ontology provides brief and rapid information before or during a client's visit. A psychiatrist or a psychologist can find the knowledge and information which he/she needs by clicking on classes and subclasses. It is also a useful educational tool for students, patients and their families. Otherwise, searching articles for needed information would take too much time. This system was specially designed for mood disorders, so that it could be suggested that it would provide the best solution when usage is limited to this category of mental illness.

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References

1. Zhou X, Wu Z, Yin A, et al. Ontology development for unified traditional chinese medical language. *Artif Intell Med.* 2004 Sep;32(1):15-27.
2. Ashburner M, Ball CA, Blake JA et al. Gene Ontology: Tool for the unification of biology. *Nat Genet.* 2000 May;25(1):25-9.
3. Ceusters W, Smith B, Flanagan J. Ontology and medical terminology: Why description logics is not enough? Proceedings of 'Towards an Electronic Patient Record (TEPR 2003)', 10-14 May 2003, Boston, MA. US (CD-ROM publication).
4. Noy NF, Crubézy M, Fergerson RW, et al. Protégé-2000: An open-source ontology-development and knowledge-acquisition environment. *AMIA Annu Symp Proc.* 2003:953.
5. Rubin DL, Noy NF, Musen MA. Protégé: a tool for managing and using terminology in radiology applications. *J Digit Imaging.* 2007 Nov;20 Suppl 1:34-46. Epub 2007 Aug 9.
6. Horridage M, Knublauch H, Rector A et al. A Practical Guide to Building OWL Ontologies Using The Protégé-OWL Plugin and CO-ODE Tools Edition 1.0. A user manual provided by Stanford Center for Biomedical Informatics Research at the Stanford University.
7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DSM-IV, American Psychiatric Association, 4th edition, USA, 1994.
8. Ghasem nia M. HTML Guide Book, Second edition, Tehran: Naghoos; 2003.
9. Jafarnejad Ghomi E. PHP 4 Guide Book, First edition, Babol: Rayane; 2004.
10. Jafarnejad Ghomi E. Javascript Guide Book, Second edition, Babol: Rayane; 2006.
11. Gomi Y, Nogawa H, Tanaka H. Toward secure distribution of electronic health records: quantitative feasibility study on secure e-mail systems for sharing patient records. *J Med Dent Sci.* 2005 Dec; 52(4): 229-36.
12. Koeda M, Shibata T, Asai K, et al. Care policy for patients with dementia: family's decision and its impact. *Biomedical Engineering and Informatics. Proceedings of 'International Conference on BioMedical Engineering and Informatics (BMEI 2008)', Volume 2, 2008, Page(s):843-47.*
13. Rosse C, Mejino JL Jr. A reference ontology for biomedical informatics: The foundational model of anatomy. *J Biomed Inform.* 2003 Dec; 36(6): 478-500.

14. Brahler CJ, Walker D. Learning scientific and medical terminology with a mnemonic strategy using and illogical association technique. *Adv Physiol Educ.* 2008 Sep;32(3):219-24.
15. Lee KN, Yoon JH, Min WK, et al. Standardization of terminology in laboratory medicine II. *J Korean Med Sci.* 2008 Aug;23(4):711-3.
16. Bodenreider O. Biomedical ontologies in action: role in knowledge management, data integration and decision support. *Yearb Med Inform.* 2008:67-79.
17. Bodenreider O. The Unified Medical Language System (UMLS): integrating biomedical terminology. *Nucleic Acids Res.* 2004 Jan 1;32(Database issue):D267-70.
18. Bodenreider O, Mitchell JA, McCray AT. Evaluation of the UMLS as a terminology and knowledge resource for biomedical informatics. *Proc AMIA Symp.* 2002:61-5.
19. Sarkar IN, Cantor MN, Gelman R, et al. Linking biomedical language information and knowledge resources: GO and UMLS. *Pac Symp Biocomput.* 2003:439-50.