TeleCare of Mental Disorders by Applying Semantic Web Technology

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***Abstract*—We present the design of a decision support system aiming to provide specific telecare capabilities between health experts and patients suffering from Bipolar Disorder (BD). Bipolar Disorder is a severe and recurrent mental illness related with high morbidity and evolves constantly in time. We focus on Breakthrough Depressive Episode, a scenario that develops when a patient shows depressive symptoms during pharmaceutical treatment. Using Semantic Web Technologies we developed *SybillaTUC*, a prototype Clinical Decision Support System, able to predict the evolution of the disease for each patient, alerting the clinician on the possibility of a crucial incident suggesting optimal treatment**.

***Index Terms*—Semantic Web, Clinical Decision Support Systems, Bipolar Disorder, Breakthrough Depressive Episode.**

I. Introduction

Clinical decision support systems (CDSS) [1] are currently being applied to support health care processes. Semantic Web Technologies are currently applied to support solutions to problems of CDSS development relating to data integration, knowledge representation and reasoning [2]. The main advantage of these systems is that they can provide powerful knowledge representation and management instruments, whereas their main disadvantage is their incapability to handle information evolving in time.

CDSS are extremely useful for diseases that evolve in time, requiring constant, and for long periods of time, monitoring of patient's condition by the clinicians. We focus our attention on Bipolar Disorder (BD), a disease which is characterized by long periods of evolution (switching between opposing phases of mania and depression, often with interposing periods of apparent clinical recovery, referred to as "euthymia"), mostly recurrence of mood episodes, and different diagnosis and treatment guidelines that change often over time, preventing the providing of trustworthy medical care to patients [3]. Our aim is to predict the evolution of BD and the effects of early interventions in patients with prodromal symptoms of the disorder, to prevent a bipolar breakthrough depressive episode and suggest optimal therapies. Breakthrough depression must be distinguished from *de novo* depression; the former arises in established BD when treatment is in place, whereas the later arises in the absence of medication [4]. The introduction of Semantic Web technologies in chemical, physical and bio-informatics sciences is a promising direction for research [5]. Despite of technological achievements in information and Semantic Web Technologies during the last few years, developing computerized methods assisting to the early prevention of BD episodes is still challenging [6]. To meet this challenge we developed and implemented *SybillaTUC*, a decision support telecare system for handling patients suffering from Bipolar Disorder disease. It is designed to represent and manage information about patient's medical record and the modeling of the evolution of the disease. Combining the clinical guidelines for Bipolar Disorder with a patient's medical record, *SybillaTUC* can predict the evolution of each patient, alert the clinician on the possibility of a critical incident and propose the best treatment suggested in clinical practice guidelines.

SybillaTUC represents patient's and disease information as well as expert's knowledge by means of an ontology. *SybillaTUC* implements an ontology for modeling bipolar patients for which the breakthrough depressive symptoms are induced during lithium medication monotherapy. By using *SybillaTUC*, clinicians are provided with the means to access each patient's file information and view the evolution of their patient's condition in time. *SybillaTUC* is also designed to provide recommendations concerning the treatment that each patient should receive. For this purpose, it takes into consideration the medical guidelines that are in effect for the disease at each particular time and the patient's medical record.

The rest of this paper is organized as follows: Background information such as Semantic Web technologies and tools used for implementing the BD ontology are described in Section 2. The Depressive BD scenario implemented in *SybillaTUC* is discussed in Section 3. Implementation of the *SybillaTUC* system is presented in Section 4 followed by discussion, conclusions and issues for future research in Section 5.

II. Methods and Procedures

The OWL language [7] is the Semantic Web standard for crafting, publishing and sharing ontologies. Information in OWL in represented by means of binary relations (e.g., "Mr.Smith SuffersFrom BipolarDisorder"). However, dealing with the evolution of a disease (the evolution of a binary relation in general) in time turns results in ternary relations with the addition of the temporal property (e.g., "Mr.Smith SuffersFrom BipolarDisorder Between 2000 and 2010"). Representing ternary relations in the Semantic Web calls for additional methods such as the N-ary approach [8] used in this work. More specifically, *SybillaTUC* employs the SOWL approach [9] as the underlying mechanism for

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dealing with temporal information and specifically, with the evolution of Bipolar Disorder in time. A temporal relation in SOWL can involve of the 13 pairwise disjoint Allen's relations between time points or temporal intervals In addition to SOWL, we apply CHRONOS [10], a Tab-widget plug-in for the Protégé editors that facilitates handling of temporal ontologies. CHRONOS interface is consistent with the layout of the default Protégé Tabs. CHRONOS is available on the Web[1].

III. *SYBILLATUC*

A. BD: Breakthrough Depressive Episode Scenario

Long-term management focuses on maintenance of eythymia which is the primary goal, requires ongoing medication, and may benefit from adjunctive psychotherapy. Maintenance treatment is the suggested treatment of bipolar disorder during eythymia state. The goal of maintenance treatment is the prevention of future mood episodes.

Typically, maintenance treatment follows the continuation phase, in which the goal is preventing a relapse into a same episode for which acute treatment has begun [11]. Current evidence best supports the use of lithium as first-line treatment: it has been shown to prevent both manic and depressive relapse, as well as suicide in meta-analytic reviews of randomized controlled trials [12]. In this context, we assume a Breakthrough Depressive Episode scenario, where a patient suffering from Bipolar Disorder I (one or more manic or mixed episodes, or both and at least one major depressive episode) is in the state of eythymia, receives treatment with lithium, displays breakthrough depressive symptoms caused by pharmaceutical treatment and may indicate an onset of bipolar depression [3-4, 13].

Keck (2004) reports that the pharmacological decisions for effectively treating these episodes should take into account information about the mood state the patient was experiencing prior to a breakthrough depressive episode, the type of drug received and the patient's history (e.g., hospitalization, number of episodes). Clinicians should then decide on the best treatment in order to preserve the patient in the state of eythymia.

In our study, we investigate on providing recommendations to clinicians on optimal treatment of Depressive patients by leveraging information associated with a Breakthrough Depressive Episode scenario and clinical practice. As a proof of concept, we focus on a Breakthrough Depressive Episode Scenario, which is selected according to the following criteria: (a) The condition of the patient evolves in time, (b) it is relative simple regarding treatment options, compared to other potential scenarios, (c) emphasizes the importance of optimizing maintenance treatment for the prevention of mood episodes caused by treatment, (d) focuses on identifying prodromal symptoms for early intervention in BD aiming at preventing relapses or suicide attempts. Existing evidence suggests a dose-response relationship, in which higher serum concentrations of lithium provide greater protection against recurrent mood episodes. The problem of individualized dose finding in maintenance treatment, however, is that the clinician cannot predict whether a given level of lithium dose is sufficiently protective until an episode occurs [4].

In the following, we discuss recommendations based on four well established evidence-based treatment guidelines [4, 14–18]. We focus on exploiting these guidelines for improving the quality of treatment during the breakthrough depressive episode. Recommendations based on these guidelines are meant to provide a framework for clinical decision making, not to replace clinical judgment. As new evidence and additional medications become available, it is expected that treatment practices and their supported algorithms will evolve beyond recommendations [19]. According to these guidelines, a bipolar patient can be under long-term medication after having suffered one, two or three episodes depending on their severity and family history.

B. Algorithm for Breakthrough Depressive Episode

In the following, we propose an algorithm for constant monitoring for patients and for deciding best medical treatment based on patient's condition.

STEP 1: The patient receives a pharmaceutical treatment based on mood stabilizer Lithium.

STEP 2: The patient is in eythymia phase.

STEP 3: Serum Lithium tests results are in normal levels ($0.6<value<0.8$).

STEP 4: 70 days after Serum Lithium tests, prodromal symptoms appear.

STEP 5: 20 days after the appearance of prodromal symptoms, the patient undergoes his regular functional tests.

STEP 6: Serum lithium tests levels are not optimal ($0.4<value<0.6$).

STEP 7: Recommendation to the clinician to improve the mood stabilizer's dosage.

STEP 8: After a week repeat tests for serum lithium.

STEP 9: Serum lithium levels are optimal ($0.6 \leq value \leq 0.8$).

STEP 10: *Check if despite the optimal serum lithium levels the symptoms persist. In that case, we have to provide an alternative pharmaceutical treatment:*

Case 1 If symptoms persist AND patient suffers from rapid cycling then Recommendation to the clinician: Add second mood stabilizer.

Case 2 If symptoms persist AND patient does not suffer from rapid cycling then Recommendation to the clinician: Add antidepressant OR second mood stabilizer.

Case 3 If symptoms do not improve then Recommendation to the clinician: exit scenario and study again patient's case file.

STEP 11: *Depending on the pharmaceutical treatment provided previously we recommend the appropriate clinical tests at an appropriate time:*

Case 1 If symptoms do not improve AND mood stabilizer has been added then Recommendation to the clinician: Do Full Blood Count (FBC) tests. After 6 months Recommendation to the clinician: Do Serum Lithium tests.

[1] http://www.intelligence.tuc.gr/prototypes.php

Case 2 If symptoms do not improve AND antidepressant has been added then After 3 months Recommendation to the clinician: Do Serum Lithium tests.

Case 3 If symptoms persist then Recommendation to the clinician: Study again patient's case file.

STEP 12: Recommendation to the clinician: Repeat serum lithium tests every 3 months and thyroid and renal tests every 6 months.

IV. IMPLEMENTATION

SybillaTUC implements a recommendation telecare system for suggesting optimal treatment to clinicians according the depressive episode scenario described above. Initially, we design an ontology representing information about the patient's profile including medical history, test results and therapy followed by the clinician. Information on the patient's condition when an episode occurs is collected as well. Below are the main concepts (entities with their properties) represented in the ontology:

- Patient (patient profile): first and last name, age, address, sex etc.
- PatientCase: the patient's medical record.
- PatientState: the patient is in eythymia or in an episode.
- PatientHistory: patient's medical history; at which age the disease appeared; if he/she has been hospitalized; the number of manic or depressive episodes has occurred; if a relative also suffers from the disease; the medication a patient may have received at previous years.
- Therapy: hospitalization and other therapeutic approaches, such as psychotherapy.
- EpisodeInfo: manic or depressive episode and it's severity.
- Diagnosis: type of the disorder-Type I or Type II - the patient is or is not suffering from rapid cycling.

Information about the medicines the patient receives as well as, the normal range levels of all medical markers and test comparisons for reaching a recommendation, are also represented. The main entities encoding this information are the following:

- Medicine (information about the medicine the patient receives): medicine name, category, dosage etc.
- StandarTests: highest and lowest optimal values of each clinical test the patient is submitted.
- Recommendations: the recommendation suggested to the clinician.

Converting the static ontology to dynamic is realized using the CHRONOS tool of Protégé (by selecting the classes to be converted from static to dynamic). When necessary, temporal intervals are assigned to temporal classes. Fig.1 illustrates the temporal ontology representing both static and dynamic concepts (evolving in time) which are important in encoding patients condition and for monitoring BD patients under Breakthrough Depressive Episode scenario. Static classes and static relations are in grey span. According to Fig.1, class *PatientCase* is associated with classes *Patient, PatientHistory, Therapy, Diagnosis, FunctionalTests, PatientState, and Recommendation* allowing the system to access easily the information of these classes when it accesses *PatientCase.* Class *PatientState* is associated with class *EpisodeInfo* allowing the system to represent knowledge on the type and the severity of an episode when a patient is in an episode state. Class *FunctionalTests* is associated with class *StandarTests* allowing the system to decide if a clinical test has optimal value or not. Class *Therapy* and *PatientHistory* are associated with class *Medicine* allowing the system to represent knowledge about the medicines that a patient may receive at the present or has received in the past.

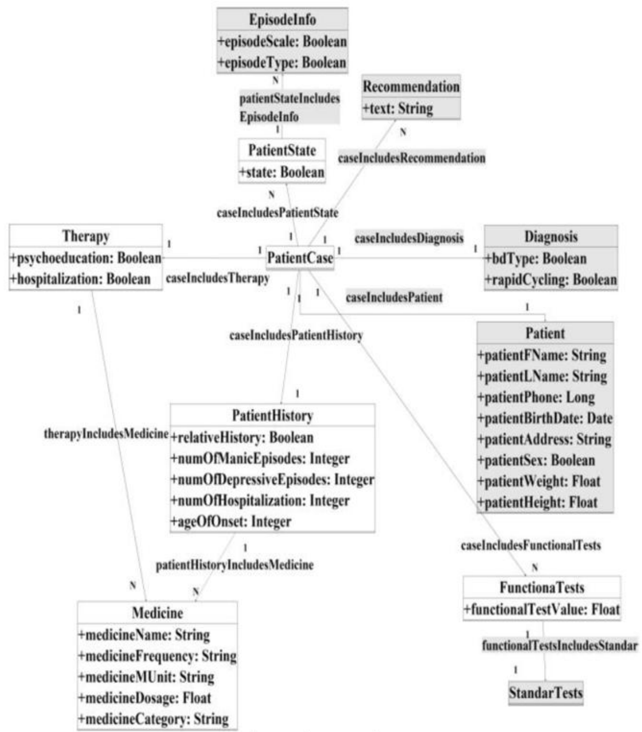

Fig 1. The Ontology

In order to provide recommendations to clinicians based on the scenario of the Breakthrough Depressive Episode presented previously, we implement a reasoning system using SWRL. For example, when a patient, who is not diagnosed with rapid-cycling (four or more mood episodes within 1 year) [15], presents depressive symptoms while his serum lithium test value is optimal, the rule should issue a recommendation to the clinician to add antidepressant or second mood stabilizer. The system issues a recommendation to the clinician based on the following rule expressed in Description Logics [20]:

PatientCase $\cap$ *∃caseIncludesDiagnosis.rapidCycling = false* $\cap$ *(∃caseIncludesFunctionalTests.functionalTestsValue* $\geq 0.6 \cap$ *<f> ∃caseIncludesPatientState.state = true)* $\rightarrow$ *Recommendation (add antidepressant OR* 2^{nd} *mood stabilizer).*

For communicating with the ontology (e. g, for populating, the ontology with new patients, updating patient's condition with new tests and their values) we created a Graphical User Interface.

V. CONCLUSIONS

We introduce *SybillaTUC*, a recommendation system for monitoring patients suffering a Breakthrough Depressive Episode. Building-upon state-of-the art technologies for representing patients, their condition and its evolution in time, the Breakthrough Depressive Episode as well as patients associated with such a scenario, are represented by temporal ontologies. *SybillaTUC* issues recommendations to clinicians for optimal handling of patients by accommodating changes of patient's condition in the monitoring processes. Reasoning over temporal concepts as patient's condition evolved in time is unique feature of *SybillaTUC*.

A. Advantages and limitations

SybillaTUC offers clinicians easy and direct access to patient's knowledge base achieving constant and individualized monitoring of a patient's condition. The system provides individualized prediction of the evolution of the disorder and treatment proposal, early warnings of patient's condition to the clinician.

For the evaluation of the system performance we worked on synthetic data. Similarly to the majority (approximately 90%) existing clinical decision support systems, is not yet tested on lab conditions and even less are tested with real trial datasets [21]. We acknowledge that this is a limitation of the present study. *SybillaTUC* can potentially become a tool for carers and family members, who are not familiar with informatic technologies**.** For example, using *SybillaTUC*, they can report mood changes observed (e.g. prodromal symptoms). *SybillaTUC* will process this information and prevent the recurrence of a new episode (depression, mania) and suicide attempt.

B. Extensions and Future Work

Extensions and future work include among others, design and implementation of more scenarios of BD such as, transition hazard from major depressive episodes to manic, mixed or hypomanic states, and malignant types of BD (rapid-cycling bipolar disorder and ultra-rapid).

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