An ontological-based monitoring system for patients with bipolar I disorder

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Abstract—Our aim is to provide a patient monitoring system that integrates a Clinical Decision Support System (CDSS) and an Electronic Health Record (EHR) that assist psychiatrists and primary care physicians to tackle existent health needs of mental illness related to the treatment and management of bipolar I disorder (BDI). Our monitoring system consists of an EHR system based on the Health Level Seven Reference Information Model (HL7-RIM) and an ontological-based CDSS leveraging the Semantic Web capabilities. Based on the evidence-based clinical guidelines and patients’ health records, the monitoring system is developed to encode and process this information and subsequently to assign recommendations of choices and alerts to clinicians for improved mental health care. Considering the clinical guidelines germane knowledge, as well as issues of patient’s health record, the monitoring system can support a personalized decision-making for bipolar I disorder longitudinal course. We propose AI-CARE as an online monitoring tool that may offer useful guidance in clinical practice.

Keywords—clinical decision support system; electronic health record; semantic web; ontology; bipolar disorder

I. INTRODUCTION

Optimal health care is a core challenge of several emerging technologies in order to promote the best health care conditions and improved health outcomes for patients living with chronic diseases, such as bipolar disorder. Toward this challenge, the advent of new scientific discoveries in medicine (genetics, epigenetics, pharmaceuticals) along with the technological explosion (medical devices, internet) enable the development of computer-based monitoring systems to aid clinicians in promoting high-quality health care and meeting the goals of “personalized medicine” [1], [2]. Personalized medicine aims to the effective adaptation of biomedical and technological knowledge to the individual features (genetic, anatomical, and physiological characteristics), needs and preferences of each patient mainly considering the difference in patient’s susceptibility to a specific disease or patient’s response to a particular medical therapy; which does not literally translate in the production of unique drugs or intelligent devices for a specific patient but rather a more targeted therapeutic intervention [2].

In the new era of personalized medicine is highlighted the need to combine “evidence-based medicine” with case based reasoning in order to enhance the health care process [3].

Evidence-based medicine refers to “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients”, while its practice implies the “integrating individual clinical expertise with the best available external clinical evidence from systematic research” [4]. In this context, CDSS systems are favorable tools to promote the practice of evidence-based medicine and clinical guidelines, in turn is a common method for CDSS [3]. These types of CDS systems, which include documented clinical knowledge, are called knowledge-based systems and provide guidance to clinical decision making [5].

In order to interpret information and derive knowledge we use Semantic Web Technologies. The concept of ontology is basic element of Semantic Web, defining a set of primitives containing [6]: concepts, relationships between concepts, described by domain and range restrictions, the taxonomy of concepts with multiple inheritance, axioms describing additional constraints on the ontology that allow to infer new facts from explicitly stated one. Semantic Web Technologies also includes the application of sets of rules that enable us to model knowledge, by inferring new implicit axioms, based on explicitly specified ones, checking for satisfiability of classes, computing hierarchies of classes and properties and checking consistency of the entire ontology.

In our implementation the existence of a domain ontology that supports decision-making is granted and so is the existence of a database supporting the patients’ information storage. In order to exploit both the advantages of the existing database and the developed domain ontology we came to develop a mapping mechanism between them, migrating database instances into ontological instances (individuals) (also called ontology population), by a query driven process of transforming the database instances that are the response to a given query.

Bearing in mind the concepts of personalized medicine and evidence-based medicine, section II presents the AI-CARE monitoring system by discussing important issues of the ontological-based CDSS development, and the architecture of the patient-centric EHR (subsection II.A and II.B, respectively), and by focusing on the alignment among Ontology and EHR entities (subsection II.C), as well as test scenarios and validation (subsection II.D). Conclusions and issues for future research are discussed in Section III.
II. AI-CARE MONITORING SYSTEM FOR PATIENTS WITH BDI

The AI-CARE monitoring system aims to provide an effective monitoring for patients with bipolar disorder.

Bipolar disorder (BD), also known as manic-depressive illness, is a severe mental illness, thought to be caused by an interaction of genetic and environmental factors. BD which is triggered by stressful life events, is often misdiagnosed and/or not sufficiently treated, and is associated with a high risk of suicide. Obviously, considering the important aspects of BD, such as the early onset, natural history, lifetime prevalence (1 to 5% in general population, estimated in different studies), mental anguish, high rate of recurrence (>90% of patients who have a single manic episode will have future episodes), and psychiatric/medical morbidity, justify the need to develop an intelligent system in order to longitudinally monitor the evolution of this complex and heterogeneous disease in bipolar patients [7].

The AI-CARE monitoring system utilizes the ontological-based CDSS as part of an electronic health record in order to be beneficial to the bipolar patients, aiming to provide “the right patient with the right drug at the right dose at the right time” and tailoring the medical treatment to the individual characteristics, needs and preferences of a bipolar patient during all stages of care (diagnosis, treatment and follow-up, prevention). Also, is capable of identifying the characteristics of patient-subpopulations that do not benefit from the recommended therapy leading to new expert knowledge, new research and prospectively to new recommendations [2].

A Development of an Ontological-based CDSS

In order to develop electronic support for clinicians and health care professionals, a knowledge-based system is needed to be developed consisting of a knowledge-base that represents facts about the disorder and an inference engine that can reason about those facts and use rules and other forms of logic to deduce new facts or highlight inconsistencies.

a) Ontology

The most prominent language for implementing ontologies is Web Ontology Language (OWL). The basic structure of OWL are classes, properties and individuals, which are members of classes. OWL properties are binary relationships and are distinguished in object properties (relate two individuals) and datatype properties (relate an individual with a literal value). Also OWL can define hierarchies of classes and properties, property domain and range restrictions, value restrictions, cardinality, existential and universal quantification restrictions on the individuals of a specific class. Base of OWL is Description Logics (DL) [8].

Ontologies can be distinguished by the subject of the conceptualization, such us knowledge representation, upperlevel domain and application ontologies [9].

During the definition of a medical domain, achieving formalization of the domain terminology and categorization, is a desired result. In this attempt, formal ontologies such as SNOMED CT [10] or other formal approaches, offer great advantages in formal rigor and inference power. Nonetheless, they limit the expressiveness of the domain representation and design to an upper level description [11], [12]. Considering these limitations, our attempt to define the bipolar disorder domain integrates: (i) a vocabulary of terms along with concept definition and their inner-relationships, which is offered by formal ontologies, and (ii) a more specialized description that is geared around the concepts related to the patient condition monitoring evolving in time, as presented in Fig. 1.

In order to describe the changing aspects of the disease in terms of states, state transitions and processes, the ontology needs to be dynamic. In our implementation, we design the initial static ontology, describing the main concepts of Bipolar Disorder, using the Protégé ontology editor1. The static ontology is converted into dynamic using the CHRONOS plugin of Protégé [13]. The main concepts describing the domain of Bipolar Disorder are distinguished into dynamic entities (entities which evolve in time) and static entities (entities which do not evolve in time).

Ontology is populated with real data collected from 10 patients whose condition is monitored over a period of a few days to a year.

Fig. 1. Class Diagram.

b) Rules

We derive new knowledge from the assertions in ontology adopting Semantic Web Rule Language rules (SWRL)2, which is the most prominent language for editing such rule. A SWRL rule presents an implication between an antecedent and a consequent so that the intended meaning is: whenever the condition specified in the antecedent hold, then the conditions specified in the consequent must also hold.

An example of a treatment recommendation rule is presented, resulting into the suggestion of medical treatment. It evaluates the medication the patient is receiving and the type of symptoms the patient presents.

In the case that the patient is first diagnosed, receiving no medication and the symptoms suggest existence of a manic episode then the rule directly suggests medical treatment (Lithium, Li; Valproate, VPA; atypical antipsychotic, AAP).

1 http://protege.stanford.edu/
2 http://www.w3.org/Submission/SWRL/
Necessary information for the rule is included in the classes Personal Health Record (PHR), PatientState, Episode, Therapy, and Medicine.

The rule is expressed in DLs [8] as:

\[
\text{PHR}(\text{patientState} = \text{inEpisode}) \land (\exists \text{Episode.type = manic}) \land \text{Therapy}(\text{start Therapy with Li/VPA/AAP or combination of two medicines})
\]

The rule is expressed in SWRL as shown in Table I:

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>SWRL RULE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHR(\text{patientState} = \text{inEpisode}) \land (\exists \text{Episode.type = manic}) \land \text{Therapy}(\text{start Therapy with Li/VPA/AAP or combination of two medicines})</td>
<td></td>
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2) Documented Clinical Knowledge for BDI

Clinical practice guidelines refer to “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” according to the definition of Institute of Medicine (IOM), and are mostly relied on comparative clinical trials [14]. They are commonly utilized by the evidence-based medicine in making clinical decisions to improve the care process [5]. The scope of medication guidelines is to aid the interaction of clinicians and patients in developing the most effective treatment strategy minimizing the side effects.

a) Clinical guidelines for Bipolar I Disorder (BDI): We selected evidence-based clinical practice guidelines (e.g. Australian and New Zealand, British Association for Psychopharmacology) related to different aspects of care for BDI, as well as other systematic reviews for BD [15]. Such guidelines utilize evidence-based knowledge for treating and managed patients with BDI defined by specific clinical criteria.

b) User Scenarios for Bipolar I Disorder: Bipolar Disorder is usually classified within the context of the Diagnostic and Statistical Manual of Mental Disorders (DSM), which differentiates between bipolar I disorder, bipolar II disorder, bipolar disorder not otherwise specified (Bipolar NOS), and cyclothymia.

Presently, we provide user diagnostic and treatment scenarios for the clinical presentation of BDI (at least one manic or mixed episode). Diagnostic scenarios consider specific information of screening and assessment tools and persons’ medical/family and past psychiatric history. Diagnosis of bipolar I disorder follows the established criteria of the DSM-IV or DSM-V for a manic or depressive episode along with their severity, considers the psychiatric or/and medical comorbidities and hinders misdiagnosis, especially with unipolar disorder (major depressive disorder).

Based on the aforementioned evidence-based guidelines [15], the diagnostic scenarios are designed to guide the clinicians during the diagnosis procedure (mental state examination, initial evaluation considering the differential diagnosis, assiduous psychiatric examination addressing the different patterns of BD emergence, unobserved comorbidities and related disorders) and the diagnostic accuracy when patients fail to respond to treatment [15]. Also, we developed the user scenarios for BDI treatment options following the dynamic disease course.

The ontology-based CDS system provides diagnosis and treatment recommendations related to the patients’ mental state (acute episodes, euthymia), alerts related to crucial mood swings and medication noncompliance, preventive care reminders about monitoring procedures (e.g. extrapyramidal symptoms, lithium serum levels, weight gain, diabetes screening, hyperlipidemia assessment), and warnings related to changes in symptom complex, as well as assists clinicians with decision-making and in developing a personalized disease management.

Longitudinal monitoring of bipolar patients is performed by the developed system to evaluate the presence or absence of symptoms, psychiatric and/or mental comorbidities, medication adherence, and to identify therapeutic drug safety and tolerance. Warnings have been placed in decision nodes with relevant annotation from the literature in order to yield the appropriate hints and alerts to the clinicians on real-time and at the time of care. The monitoring functionality can be further enriched by means of inputs received from biosensors (i.e. biosignals) and smartphone applications (e.g. voice analysis) accompanied by inputs (paper-based and electronic-based data like life charting) from the user's environment (family, carers) or the user himself.

The ontology-based CDS system is highlighted as a crucial component of the patient-centric EHRs for BD. It is implemented using a networked EHR platform, whether the knowledge is available from a repository outside the local site and is accessed, but not incorporated into the local EHR.

B. Architecture of a Patient-centric EHR

Consistent with the conceptual view of longitudinal monitoring of patients with BD, we created an Electronic Health Record (EHR) for bipolar patients. It encloses five of the essential components of the EHRs: (i) administrative processes, (ii) health information and data, (iii) communication and connectivity, (iv) results management, and (v) decision support [16].

The ontology-based CDS system delivered with the EHR as depicted in the platform architecture of Fig. 2 will provide clinicians with suitable tools achieving a better day-to-day clinical decision making.
The architecture of the integrated platform consists of four main tiers (Fig. 2) namely, a) Presentation tier, b) Application tier, c) Intelligence tier, and d) Data tier.

![Platform Architecture – Tiers](image)

1) Presentation tier: The first tier, called presentation tier, is the top layer of the integrated platform. This layer is responsible for exchanging information between the general stakeholders and the system. Its main focus is to provide advanced usability and visualization functionality along with a simple and rich graphical user interface (GUI), in order to present the stored information to the end users. Since it is responsible for the interactions between users and the system, it provides access to the EHR through the web browser and among other useful graphical user interface components it makes statistical graphs available for use for intuitive visualization of the current status of patients in terms of episodes and substance administration over time (Fig. 3).

![Graph presenting patient’s episodes with respect to the substance administration over time](image)

2) Application tier: In the middle of the tier platform, there is the application tier. This is in charge of the control of the system’s operations, achieved by performing detailed processes. It consists of three sub-tiers: (i) Business logic, (ii) Security and (iii) Data access.

The operations of the business logic sub-tier concern the processing of a heterogeneous information data set. Some of the core functionalities that stand out are the support in retrieving patients’ information; exporting patients’ data into XLS format file; the dynamic clinical forms generation; the retrieval and process of data for the visualization of diagrams; the comparison of patient’s re-examination data and printing capabilities. Furthermore, the business logic sub-tier is responsible for providing a robust working environment, coping with errors during execution and continuing the system’s operation despite the potential input inconsistencies. That is done mainly by preventing users from entering erroneous input, guiding them towards its proper use and performing in a satisfactory way, such that it does not intercept user’s flexibility, agility and operability (i.e. ICD-10, NOM).

The information to be managed by this tier is patients’ clinical and demographic data, users’ personal data and access credentials, user roles, users’ access to patients, informed consent documents files, substance administration data and information that concern the dynamic data entry clinical forms. The functionality in this section addresses consistent terminologies/ vocabularies/ standardized transactions, data correctness, and interoperability (i.e. ICD-10, NOM).

The significance of security for the integrated platform is vital since it manages sensitive data when at the same time it is accessed by a variety of users which as stakeholders they have different roles and responsibilities according to their position and skills. The heterogeneity that characterizes those users raises the necessity of utilizing a Role Based Access Control (RBAC) [17] mechanism to regulate user actions within the system. These roles can guarantee that no user can perform ineligible acts.

Moreover, encryption/ decryption mechanisms are used to further secure users’ passwords and patient’s sensitive data. Data stored in an encrypted way can ensure the confidentiality in case that a third party breaches the database access. Users’ credentials are stored in an encrypted unidirectional way. That means that passwords are not decryptable and thus cannot be recovered. On the other hand, all patients’ sensitive data (data that can be used for identifying the patient) are stored in an encrypted bidirectional way within the database, allowing them to be decrypted, since the identification of the patient is required.

Finally the Secure Socket Layer (SSL) [18] protocol is utilized in order to preserve the secure data exchanged through a public-and-private key encryption mechanism which includes the use of a digital certificate.

The data access sub-tier handles all the logic regarding data storage and management. That is achieved by providing an abstract interface by using Data Access Objects (DAO) and thus delivering specific data operations without exposing details of the database. Finally, data persistency is achieved by adopting the Object Relational Mapping (ORM), which solves object-relational impedance mismatch problems by replacing direct persistence-related database accesses with high-level object handling functions.
3) Intelligence tier: The intelligence tier basically corresponds to the knowledge-based system, described in section A, offering knowledge extraction from the existing patient information and concluding into clinical decision support through treatment recommendations and alerts.

4) Data tier: The bottom tier is the data tier, which constitutes the database server of the integrated platform to store all the information data. In that way, data is kept neutral and independent from the rest of the tiers, offering improved scalability and performance. The design of the relational database model was based on HL7-RIM1, which is the cornerstone of the HL7 Version 3 development process and provides to the database a flexible and extensible structure.

C. Alignment of the Ontological-based CDSS and the Patient-centric EHR

The main contribution of this paper is the assignment of the ontology entities to the EHR entities, in order to enable communication and connectivity among the ontological-based CDSS and the patient-centric EHR [19].

The EHR records longitudinally the patient health information, including demographics, contact information, clinical data (e.g. patient’s personal, medical, and past psychiatric history, mental state examination, laboratory and data, and electronic diary mood reports, drug information), diagnosis, patient’s diagram (visualization of the current and/or previous status of patients in terms of episodes/disease state and drug administration over time), as well as an up-to-date drug database. The EHR supports indirectly the developed ontology-based DCSS leading to advanced health care quality.

Moreover, in order to achieve the integration between the ontology and the database, a mapping mechanism able to define the correspondences between the entities of the database and the ontology schema, is needed. Although relational databases are based on closed-world assumption whilst ontologies use open-world semantic, at a conceptual level, a database and an ontology are semantically related and correspondences are established between the database components and the ontology components. For instance, an attribute in a relational database schema may correspond to a property in an OWL ontology.

In our approach, a naïve mapping procedure is adopted retrieving data from SQL queries, through JDBC4, applied over the source database and reformulates the results, in terms of the target ontology, through OWL API5. Such mapping specifies the ontology population from the data in the database.

Fig. 1 depicts a simplified conceptual view of the mapping process. As a simplified model, it does not show the complex nature of its components (e.g. database, tables, or ontology classes), rather the interaction between DB Model and Ontology Model, which is feasible through a mapping procedure with OWL API.

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3 http://www.hl7.org/implement/standards/rim/cim
4 http://www.oracle.com/technetwork/java/javase/jdbc/index.html
5 http://ontapi.sourceforge.net;
In our study, we align an ontological-based CDSS and a patient-centric EHR providing an on line monitoring tool, which seek to support psychiatrists and mental health professionals in tailor evidence-based practice in day-to-day clinical decision making for the longitudinal monitoring of each bipolar patient. Apart from the test and validation, the ontology population is an ongoing process. In the future, we aim to adjust the monitoring system for other types of BD and for epilepsy. The presented AI-CARE ontological-based monitoring system combines both personalized and evidence-based medicine in order to promote the care process for the patients suffering from bipolar I disorder.

REFERENCES