Prototypes and Prototypicality Measures for Diagnosis of Dysmorphic Syndromes

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Introduction. When a child is born with dysmorphic features or with multiple congenital malformations or if mental retardation is observed at a later stage, finding the correct diagnosis is extremely important. An initial goal for medical specialists is to diagnose a patient to a recognised syndrome. Genetic counselling and a course of treatments may then be established. A dysmorphic syndrome describes a morphological disorder and it is characterised by a combination of various symptoms, which form a pattern of morphologic defects. The main problems of diagnosing dysmorphic syndromes are that more than 200 syndromes are known, many cases remain undiagnosed with respect to known syndromes, usually many symptoms are used to describe a case (between 40 and 130), and every dysmorphic syndrome is characterised by nearly as many symptoms. Furthermore, knowledge about dysmorphic disorders is continuously modified, new cases are observed that cannot be diagnosed, and sometimes even new syndromes are discovered. Usually, even experts of paediatric genetics only see a small count of dysmorphic syndromes during their lifetime.

Material. Starting point to build the case base was a large case collection of the paediatric genetics of the University of Munich, which consists of nearly 2.000 cases and 229 prototypes. A prototype (prototypical case) represents a dysmorphic syndrome by its typical symptoms. Most of the dysmorphic syndromes are already known and have been defined in literature. And nearly one third of our entire case base has been determined by semiautomatic knowledge acquisition, where an expert selected cases that should belong to the same syndrome and subsequently a prototype, characterised by the most frequent symptoms of his cases, was generated. To this database we have added rare dysmorphic syndromes, namely from the journal Clinical Dysmorphology and from the London dysmorphic database [1].

Methods. We apply the Case-Based Reasoning idea of retrieving former, similar cases and subsequently adapting their solutions to the query case. Because of the variety of cases with the same syndrome it is unreasonable to search for single similar patients but for more general prototypes that contain the typical features of a syndrome. Prototypes are a generalisation from single cases. They fill the knowledge gap between the specificity of single cases and abstract knowledge in form of cases. Since doctors reason with typical cases anyway, in medical CBR systems prototypes are a common knowledge form. To determine the most similar prototype for a query patient a prototypicality measure is required.

Our system consists of four steps. At first the user has to select the symptoms that characterise a new patient. Since our system is still in the evaluation phase, secondly the user can select a prototypicality measure. In routine use, this step shall be dropped. At present there are two choices. As humans look upon cases as more typical as more features they have in common [2], distances between prototypes and cases especially consider the shared features. The first measure was developed by Rosch and Mervis [2]. From the number of common features of a patient and a prototype, the number of symptoms used for the prototype but not observed for the patient are subtracted. The second measure was proposed by Tversky [3]. Additionally the number of symptoms that are observed for the patient but are not used to characterise the prototype are subtracted from the number of common features. In the third step the chosen measure is sequentially applied on all prototypes (syndromes). Since the syndrome with maximal similarity is not always the right diagnosis, the 20 syndromes with best similarities are listed in a menu. In the fourth and final step, the user can optionally choose to apply adaptation rules on the syndromes. These rules state that specific combinations of symptoms favour or disfavour specific dysmorphic syndromes. Unfortunately, the acquisition of these adaptation rules is very difficult, because they cannot be found in textbooks but have to be defined by experts of paediatric genetics. Since nobody knows how much these rules may alter computed similarity values, the result after applying adaptation rules is a menu that contains up to three lists. On top the favoured syndromes are depicted, then those neither favoured nor disfavoured, and at the bottom the disfavoured ones. Additionally, the user can get information about the specific rules that have been applied on a particular syndrome.

Results. Since the main idea is to support diagnosis of rare syndromes, we have chosen our 100 test cases randomly but under the condition that every syndrome can be chosen only once. Firstly, we did not apply any adaptation rules, subsequently our first 10 rules were applied and finally all 18 rules were used (table 1).

Right Syndrome	Rosch, Mervis No Adaptation	Tversky No Adaptation	Rosch, Mervis 10 Rules	Tversky 10 Rules	Rosch, Mervis 18 Rules	Tversky 18 Rules
On Top	29	40	32	42	36	44
among top 3	57	57	59	59	65	64
among top 10	76	69	77	71	77	73

Table 1. Comparison of prototypicality measures before and after applying adaptation rules

Diagnosis of dysmorphic syndromes is very difficult and usually needs further investigation, because often a couple of syndromes are very similar. So, the right diagnose among the three most probable syndromes is a already a good result. Obviously, the measure of Tversky provides better results, especially when the right syndrome should be on top of the list of probable syndromes. With the number of acquired adaptation rules the quality of the program increases.

Conclusion. We have shown that an increased number of adaptation rules improves the diagnoses of dysmorphic syndromes. Unfortunately, the acquisition of them is very difficult and time consuming.

References

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