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Mining Association Rules for Neurobehavioral and Motor Disorders in Children Diagnosed with Cerebral Palsy

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Abstract

Children diagnosed with cerebral palsy (CP) appear to be at high risk for developing neurobehavioral and motor disorders. The most common disorders for these children are impaired visual-perception skills and motor planning. Besides, they often have impaired executive functions, which can contribute to problematic emotional adjustment such as depression. Additionally, literature suggests that the tendency to develop these cognitive impairments and emotional abnormalities in pediatric CP is influenced by age and IQ. Because there are many other medical co-morbidities that can occur with CP (e.g., seizures and shunt placement), prediction of what percentages of patients will incur cognitive impairment and emotional abnormality is a difficult task. The purpose of this study was to investigate the associations between possible factors mentioned above, and neurobehavioral and motor disorders from a clinical database of pediatric subjects diagnosed with CP. The study resulted in 22 rules that can predict negative outcomes. These rules reinforced the growing body of literature supporting a link between CP, executive dysfunction, and subsequent neurobehavioral problems. The antecedents and consequents of some association rules were single factors, while other statistical associations were interactions of factor combinations. Further research is needed to include children's comprehensive treatment and medication history in order to determine additional impacts on their neurobehavioral and motor disorders.

Keywords

rule association mining; cerebral palsy; pediatric psychiatric disorder; pediatric neurobehavioral disorder

I. Introduction

Cerebral Palsy (CP) is a nonprogressive group of disorders of motor and posture caused by brain injury that may occur during the prenatal, perinatal and/or postnatal period [1]. The

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prevalence of CP has remained stable over time and is estimated to occur in four out of 1,000 births equally between males and females [2]. CP is the most common motor disability of childhood that often co-occurs with other medical morbidities. Evidence has shown that children with low birth weight (<1500 g) are at high risk for CP [3]. The underlying etiologies of CP vary, but a global assault on the brain development is generally implicated.

General symptoms of CP vary depending on type, severity, and limb involvement but may also include tremors, muscle weakness, rigidity, ataxia, gait abnormalities, and gross and fine motor difficulties. Additionally, there are many medical morbidities that can co-occur with CP, such as seizures, epileptic disorders, neuro-cognitive impairments, motor disability from hydrocephalus [4], mental retardation, impaired vision or hearing, and speech delay [5]. Although CP is considered to be a “static” disorder from a neurological standpoint, the physical symptoms or impairments may appear to change over-time as daily or functional tasks become more demanding [6].

Given the nature of CP and related motor impairments, psychological assessment can be a difficult task. For example, the motor impairments seen in children with CP can pose challenges with regard to reliable assessment of intellectual functioning, specifically on performance-based tasks. Therefore, neurocognitive tests that rely heavily on intact motor skills for adequate completion, but do not directly control for motor ability, are likely to be lower in this population. Although literature suggests that histories of lower birth weight, use of antiepileptic drugs, or shunt placement may contribute to cognitive and motor difficulties, there has been a paucity of research trying to statistically predict what percentages of patients will incur cognitive, motor, and behavioral problems as a result of CP.

This study, through medical history and neuro-psychological instrument scores of children diagnosed with CP, uses association rule mining (ARM) to determine meaningful relationships among age, birth weight, and cognitive, motor, and behavioral disorders. We aim to assist medical professionals to provide young children with accurate assessments and treatments. We choose ARM based on its four main advantages. First, unlike conventional statistical analysis that only indicates whether the relationship significant or not (e.g., using p-value), ARM gives each rule a confidence value that determines its strength more quantitatively. Second, a rule is composed of an antecedent and a consequent that provide a direction of the relationship. Third, the antecedent and consequent can consist of one or more factors, providing advanced knowledge of complex factor interactions instead of monotonic relationship (e.g., logistic regression) [7]. Finally, ARM accepts user-specified inputs, which ensure the interestingness of each rule to optimize the mining results.

The rest of the paper is organized as follows. In section II, we give an overview of ARM and a brief review of its applications in healthcare. In section III, we describe the details of our dataset. In section IV, we illustrate the steps of our mining process. In section V, we discuss our finding using ARM. Finally, in section VI, we conclude and suggest some possible future work.

II. Association Rule Mining

A. Overview of Association Rule Mining

Association rule mining (ARM) is a method to discover meaningful relations between variables in databases. Agrawal *et al.* first introduced the concept of ARM to extract regularities between products in large-scale warehouse databases [8]. Association rules are in the form of $X \Rightarrow Y$, which means that X implies Y , where X and Y are called antecedent and consequent, respectively [9]. X and Y can consist of one or more variables. Thus the associations are not necessarily one-to-one. In its original marketing analysis, the rule $X \Rightarrow Y$ carries the semantic that if a customer buys items in X , he/she is also likely to buy items in Y . Such rules provide valuable knowledge in the decision about marketing strategies, such as promotional pricing and product placement. Association rules are widely employed in a variety of areas such as telecommunication and inventory risk management.

Two important measures—*support* and *confidence*—quantify the frequency and interestingness of an association rule. The support of an association rule is defined as the fraction of the transactions in the database that contain both X and Y :

$$\text{support}(X \Rightarrow Y) = \frac{\text{count}(X \cup Y)}{\text{Total \# of transactions in database}} \quad (1)$$

where $\text{count}(a)$ returns the number of transactions that contain a . Here $X \cup Y$ means that X and Y both occur, not either X or Y appear (i.e., set union in logical disjunction). A high support of an association rule means that a high portion of the database is applicable to the rule. The other measure of an association rule is its confidence. It indicates the percentage of transactions that contain X and Y to the records that contain X but no Y :

$$\text{confidence}(X \Rightarrow Y) = \frac{\text{count}(X \cup Y)}{\text{count}(X)} \quad (2)$$

For example, if the confidence of an association rule is 95%, it implies that 95% of the records that contain X also contain Y . In other words, confidence reveals the strength of the association.

In order to discover frequent and interesting association rules, the mining process requires users to specify two thresholds to drop infrequent and uninteresting rules, which are minimum support (Sup_{min}) and minimum confidence ($Conf_{min}$). Rules are frequent if their supports satisfy the Sup_{min} and are interesting if their confidences exceed the $Conf_{min}$. The goal of the ARM is to find all frequent and interesting rules based on these two user-specified values.

There are two main subproblems of discovering association rules [8]. The first subproblem is to find all frequent itemsets that have supports above Sup_{min} . The second subproblem is to generate interesting rules with the $Conf_{min}$ given all the frequent itemsets generated in the first sub-problem. Because the second subproblem is straight-forward, most of the research

focus on the first subproblem. The first algorithm proposed for the first subproblem is called AIS (Agrawal-Imielinski-Swami) algorithm that was introduced in their original report of the ARM [8]. Afterwards, new algorithms were proposed to improve the efficiency of generating of frequent itemsets which the Apriori algorithm is the most classic.

B. Frequent Itemsets Generating - The Apriori Algorithm

The Apriori algorithm utilizes an iterative process to generate frequent itemsets. Assuming $\{I_1, I_2, \dots, I_N\}$ are N possible items in the database. In the first iteration, the algorithm starts from counting the occurrence of 1-itemset candidates that contain only one item. 1-itemset candidates that have supports lower than Sup_{min} are pruned out and the remaining ones are called frequent 1-itemsets. In the following iterations (i.e., $k > 1$), the candidate k -itemsets are first generated by joining the frequent $(k-1)$ -itemsets. Then frequent k -itemsets are generated by pruning out candidate k -itemsets that have supports lower than Sup_{min} . The iteration continues until no more candidate or frequent itemsets can be found. The detailed description of the Apriori algorithm can be found in [10].

C. Rule Generating

After generating all frequent itemsets via the Apriori algorithm, the second subproblem is to generate interesting rules that satisfy $Conf_{min}$. For each frequent itemset I , consider all non-empty subsets of I . For each subset a , form a new rule $a \Rightarrow (I-a)$ if the ratio of $count(I)$ to $count(a)$ is above the $Conf_{min}$, and we call a and $(I-a)$ antecedent and consequent, which are the X and Y , respectively, in the equation (2).

D. Association Rule Mining in Healthcare

Association rule mining (ARM) has been widely utilized in healthcare paradigm, such as heart disease prediction, healthcare auditing, and neurological diagnosis. For heart disease prediction, Konias *et al.* presented an uncertainly rule generator (URG) that discovers rules for home-care monitoring of congestive heart failure patients [11]. Ordonez *et al.* adopted ARM in medical data and proposed an improved algorithm to constrain rules so as to speed up the mining process [12]. Auditing abusive and fraudulent healthcare behavior is another important application of ARM. Shan *et al.* utilized ARM to examine billing patterns within a particular specialist group to detect suspicious claims and potential fraudulent individuals [13]. Bellazzi *et al.* introduced temporal ARM in the context of an auditing system to facilitate clinicians' understanding of patients' behavior and improve the quality of hemodialysis services [14]. ARM also draws attentions from neurology research. Authors in [15] proposed a novel methodology for finding image-based association rules in functional single-photon emission computed tomography (SPECT) image databases for early diagnosis of Alzheimer's disease. Studies also verified that ARM can find hidden diagnosis rules of developmentally-delayed children, so as to enable healthcare professionals in early intervention of delayed psychological developments [16]. However, we are not aware of any published study investigating the ARM technology in assessment of neurobehavior and motor disorders in children diagnosed with cerebral palsy.

III. Dataset Description

Our target dataset was developed from a sample of 155 patients that were seen in the clinical setting of Children's Healthcare of Atlanta (CHOA). The study was approved by Institutional Review Board (IRB) from CHOA and Emory University before the data collection. Over the course of the past 5 years (2008–2012), these patient records were placed into a database after a retrospective chart review was completed. The data was compiled and evaluated for subjects that had testing on measures of intellect, visual-motor coordination, and neurobehavioral symptoms. Finally, the data is de-identified before being processed by authors from the Georgia Institute of Technology.

A. Participants

A sample of 155 patients with CP were referred for an outpatient neuropsychological evaluation by their attending neurologist. Administrated demographic information and medical data includes age, history of seizure (*SeizureHx*), shunt placement due to hydrocephalus (*ShuntPresent*), current antiepileptic drugs use (*OnAEDs*), and birth weight (*BWGram*). The mean age is 10 years old (range 5–20 years, $SD = 3$), 19% with history of shunted hydrocephalus, and 64% have low birth weight ($BWGrams < 2500g$).

B. Procedure and Measures

The following neuropsychological instruments were administered to the subjects in this study.

Intellectual Ability—To measure the intellectual ability, one of the following scale was selected based on age of the subject: Wechsler intelligence scale for children, 4th edition (WISC-IV), Wechsler abbreviated scale of intelligence (WASI), Wechsler adult intelligence scale, 3rd edition (WAIS-III), and Wechsler preschool or primary scale of intelligence, 3rd edition (WPPSI-III). A Full Scale IQ (*FSIQ*) score was finally calculated.

Visual Motor Ability—The Beery-Buktenica developmental test of visual-motor integration, 5th edition (*VMI-5*) scale was used to assess the extent to which patients can integrate their visual and motor abilities.

Neurobehavioral Function—Two neurobehavioral function scores are considered in our target mining attributes. First, behavior rating inventory of executive function – parent form and emotional subtest (*BRIEFpEmo*) scale was used to assess emotional disorders of the subjects. Second, behavioral assessment system for children, 2nd edition – patient rating scales and depression subtest (*BASCpDep*) scale was selected to evaluate depression symptoms.

Because not all of the patients have scores of all neuro-psychological instruments, in order to increase supports of our rules, we first split the dataset into two groups. Group 1 consists of 60 patients who have both *FSIQ* and *VMI* scores, but may have missing scores of *BASCpDep* and *BRIEFpEmo*. Group 2 has 71 patients who have both *BASCpDep* and *BRIEFpEmo* scores, but may have missing scores of *FSIQ* and *VMI*. Twenty-one patients have all four types of scores and belong to the two groups.

IV. Mining Steps

The ARM process in our neuropsychological dataset is divided into six steps, which is depicted in Fig 1. It starts from generating a table that maps attributes to items. Based on the mapping table, the records are then transformed to transactions that contain of items generated in step 1. Given the user-specified Sup_{min} , step 3 generates frequent itemsets using the Apriori algorithm, and step 4 utilizes these itemsets to generate association rules based on the $Conf_{min}$. Then step 5 reduces the number of rules by filtering out redundances. Finally, the rules of items are transformed back to user-readable forms that domain experts are ready to validate. We show the detailed description of the entire process in the following section.

A. Item Mapping

All the records in our dataset have to be transformed into item-based transactions that can be processed in the mining algorithm. Categorical attributes that have values either Yes or No (i.e., *SeizureHx*, *OnAEDs*, and *ShuntPresent*) are mapped to two possible items. Instead of *Age*, which is divided into three levels, we categorize numerical attributes (i.e., *BWGrams*, *BASCpDep*, *BRIEFpEmo*, *FSIQ*, and *VMI*), in either normal or abnormal based on their values, as shown in Table I. Cut-points of the categorization are specified by domain experts or literature evidences.

B. Transaction Generation

Based on the mapping table, the dataset is transformed from attribute values to transaction items. For example, a 10-yr subject who has records of *SeizureHx*, *BRIEFpEmo*=72, *FSIQ*=60, and *VMI*=86 is transformed to a transaction of 5 items, i.e., {1,4,15,16,19}. Fig. 2 shows examples of data transformation in this step.

C. Frequent Itemsets Generation (Apriori Algorithm)

The third step of the processing is to generate frequent itemsets using the Apriori algorithm on the transaction dataset. This step requires the user-specified Sup_{min} . We choose a low Sup_{min} because we are trying to find interesting rules for complex disorders that characterize very specific subgroups of subject. In addition, the low Sup_{min} allows us to run the mining process once without repeating the whole process with decreasing Sup_{min} . We are interested in rules mined from at least 6 patients; thus we choose the Sup_{min} =10% because our total sample size of Group 1 is 60 and Group 2 is 71.

D. Rule Generation

After the Apriori algorithm generates frequent itemsets, the other user-specified control, $Conf_{min}$, is used to drop uninteresting rules (i.e., support < $Conf_{min}$). Unlike small Sup_{min} in the Apriori algorithm, the $Conf_{min}$ should be high to ensure a certain level of statistical significance because there may still be rules from a small portion of the dataset but having high confidences. We choose our $Conf_{min}$ = 60%, which means that the final rules can have at least 60% of chance when the antecedent occur and the consequent will also occur.

E. Rule Reduction

Not all the mined rules are intuitively true. For example, the rule $\{FSIQ < 70\} \Rightarrow \{Age < 11\}$ should be filtered out because the *Age* attribute cannot be in the consequent. Therefore the process allows our users to specify attributes that need to be constrained to appear in a specific part of the rule. As shown in Table 1, We constrain *Age* and *SeizureHx*, *OnAEDs*, *ShuntPresent*, and *BWGram* in antecedents. *BASCpDep* and *VMI* are constrained in consequents. *FSIQ* and *BRIEFpEmo* are not constrained because they can be either in antecedents or consequents of rules. This step is commonly seen in studies using ARM in healthcare paradigm [12].

F. Readable Rule Generation

The antecedents and consequents in the generated rules are represented in item numbers (e.g., $\{6\} \Rightarrow \{16\}$), which is not user readable. Therefore the last step of our mining process is to convert rule items back to user readable attributes with values following the mapping table generated in the first step. For example, a rule $\{4, 8\} \Rightarrow \{16\}$ will be mapped to a readable rule $\{SeizureHx=Yes \ \& \ ShuntPresent=Yes\} \Rightarrow \{FSIQ < 80\}$. Fig. 3 depicts examples of transformation from raw rules to readable rules.

V. Results and Discussion

Our mined rules can predict both normal and abnormal cognitive and motor difficulties, while in this section we only present those that can predict abnormalities because they deserve more attention. Table II lists final 22 rules that can predict problematic consequents (e.g., $FSIQ < 80$). These rules were analyzed by a domain expert (i.e., neuropsychologist) to ensure their interestingness. We classify these rules according their consequents, and the rules in each group are ordered by their confidences. Fig 4. also depicts the confidences of all one-to-one rules.

A. Rules Predicting IQ Disability

History of seizure, use of AEDs, and shunt placement are all good predictors of lower IQ, and history of seizure predicts the best. Age is also a factor impacting a patient's IQ when interacting with the seizure history. According to rule 4, if an older adolescent has seizure history, his/her possibility of lower IQ is higher than children who also have seizure history but are younger. This rule confirms the implication that symptoms or impairments of CP may appear to change over-time, as daily or functional tasks become more demanding. In addition, a patient who is taking AEDs and with low emotional control, he/she may also develop low IQ. Finally, shunt placement may affect a patient's IQ when it co-occurs with seizure history or low birth weight.

B. Rules Predicting Visual Motor Deficits

Similar to IQ, AED, shunt placement, and history of seizure are all good predictors of visual motor deficits among which AEDs is the best one. In addition, lower IQ can also imply lower visual-motor integration ability when it happens alone or co-occurs with use of AEDs or history of seizure. Besides, a patient who has a combination of lower birth weight and shunt placement history may also have 72% chance of visual-motor dysfunction although

the birth weight itself cannot predict well. Finally, older adolescents with history of seizure or lower birth weight may also have lower VMI compared to those who have the same condition but are younger.

C. Rules Predicting Emotional Disorder and Depression Symptoms

As stated in rules from 20 and 21, use of AEDs and its combination with low IQ are the only two antecedents that can predict emotional disorder. Surprisingly, none of, age, history of seizure, shunt placement, or birth weight can predict emotional disorder. Besides, the level of emotional disorder in children with CP can also predict their symptoms of depression, which is shown in rule 22. This rule also supports the finding in the literature [17]; however, we cannot find other interesting rules that can predict depression symptoms.

VI. Conclusion

Although literature suggests evidences that may contribute the understanding of cognitive, motor, and behavior difficulties in children diagnosed with cerebral palsy (CP), it is a difficult task to statistically predict what percentages of patients will incur the abnormalities given the nature of the diseases. This article presents our study on mining association rules from medical data and neuropsychological test scores. We propose our motivation of using association rule mining. We then illustrate our mining process that can deal with categorical medical data and numerical test scores, showing how to generate association rules from a variety of patient data. We construct a mapping table to transfer the dataset to minifiable transactions, and finally use it to interpret the mined rules to user-readable forms. The process allows domain experts to apply constraints to avoid redundant results. Our mined association rules provide useful quantitative knowledge of patients who have comorbid diagnoses and their risk for neurobehavioral concerns, motor deficits, and lower overall cognitive potential. Several rules of one-on-one relationships confirm medical and literature knowledge with high accuracy, while other rules can predict complex and interesting factor interactions.

A. Future Work

This work could be extended in several directions. One of the disadvantages of association rule mining is its fixed minimum support and minimum confidence throughout the mining process. Changes in these two values may dramatically vary the number of final rules. One of our ongoing improvements is to develop a partially automatic support and confidence adjustment. In other words, the process can optimize the two values on each attribute based on the user's initial inputs. Additionally, unlike logistic regression, association rule mining lack the ability to provide significance information for individual attributes within a rule. One potential future improvement would be combining association rule mining with logistic regression or other clustering or classification methods [18]. Finally, we will include more comprehensive factors from medical and treatment history to determine their additional impacts. For example, currently we only count if a patient uses antiepileptic drugs (AEDs), but in the future we will consider the types of AEDs, such as Depakote and Dilantin, etc. Similarly, in addition to emotional disorders and depression symptoms, BRIEF and BASC scales also include scores of other subdomains (e.g., plan/organize, working memory, and

monitor in BRIEF). All of them will be considered as potential factors in our future association rule mining process.

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Fig. 1.
Steps of association rule mining in neuropsychological dataset

Fig. 2.
Examples of transformation from raw dataset to transaction dataset.

Fig. 3.
Example of transformation from raw rules to readable rules.

Fig. 4.
Confidences of 1-on-1 association rules of negative consequents.

TABLE I

Item Mapping Table

Category	Value	Item	Category	Value	Item
Age ^a	<11	1	BASCPDep ^c	<60 ^{nor}	12
	11–15	2		>60 ^{abn}	13
	>15	3	BRIEFpEmo ^{ac}	<60 ^{nor}	14
Seizure Hx ^a	Yes	4		>60 ^{abn}	15
	No	5	FSIQ ^{ac}	<80 ^{abn}	16
OnAEDs ^a	Yes	6		>80 ^{nor}	17
	No	7	VMF ^c	<80 ^{abn}	18
Shunt Present ^a	Yes	8		>80 ^{nor}	19
	No	9			
BWGrams ^a	<2500	10			
	>2500	11			

^a antecedent-only attribute

^c consequent-only attribute

^{ac} antecedent or consequent attribute

^{nor} normal value

^{abn} abnormal value

TABLE II

Mined Association Rules of Negative Consequents

rule	Antecedent	Consequent	Sup %	Conf %
1	SeizureHx=Yes	FSIQ<80	36	84
2	OnAEDS=Yes		22	83
3	ShuntPresent=Yes		12	70
4	Age>=15 & SeizureHx=Yes		10	67
5	OnAEDS=Yes & BRIEFpEmo>60		15	65
6	ShuntPresent=Yes & SeizureHx=Yes		13	64
7	ShuntPresent=Yes & BWGrams<2500		13	64
8	OnAEDS=Yes	VMI<80	24	88
9	OnAEDS=Yes & FSIQ<80		22	81
10	ShuntPresent=Yes		14	81
11	SeizureHx=Yes		34	80
12	FSIQ<80		41	80
13	SeizureHx=yes & FSIQ<80		31	72
14	ShuntPresent=Yes & BWGrams<2500		12	70
15	Age>=15 & SeizureHx=Yes		10	67
16	Age>=15 & BWGrams<2500		10	67
17	OnAEDS=Yes	FSIQ<80 & VMI<80	22	81
18	SeizureHx=Yes		31	72
19	ShuntPresent=Yes		10	60
20	OnAEDS=Yes	BRIEFpEmo>60	17	71
21	OnAEDS=Yes & FSIQ<80		15	65
22	BRIEFpEmo>60	BASCpDep>60	28	68