# Predicting Developmental Disorder in Infants Using an Artificial Neural Network

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**Abstract-** Early recognition of developmental disorders is an important goal, and equally important is avoiding misdiagnosing a disorder in a healthy child without pathology. The aim of the present study was to develop an artificial neural network using perinatal information to predict developmental disorder at infancy. A total of 1,232 mother–child dyads were recruited from 6,150 in the original data of Karaj, Alborz Province, Iran. Thousands of variables are examined in this data including basic characteristics, medical history, and variables related to infants. The validated Infant Neurological International Battery test was employed to assess the infant's development. The concordance indexes showed that true prediction of developmental disorder in the artificial neural network model, compared to the logistic regression model, was 83.1% vs. 79.5% and the area under ROC curves, calculated from testing data, were 0.79 and 0.68, respectively. In addition, specificity and sensitivity of the ANN model vs. LR model was calculated 93.2% vs. 92.7% and 39.1% vs. 21.7%. An artificial neural network performed significantly better than a logistic regression model.

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**Keywords:** Infant, Risk factor, Neural network; Developmental disability; Prognosis

## Introduction

Developmental disabilities are disorders in which there is a delay in development based on that expected for a given age level or stage of development. About 16-18% of children in various populations have developmental disorders (1,2). Early recognition is an important goal, and equally important is avoiding misdiagnosing a disorder in a healthy child without pathology. Unfortunately, the interpretation of all risk factors overall remains prone to error (3,4). Neurologic examination and diagnostic test can provide more direct evidence of developmental disorder; however, they are generally more costly, administrated with specialist, time provided and inefficient in early years of life. Efforts to develop an inexpensive method due to risk factors that can assist in the differentiation between normal and abnormal child development have met with limited success (5,6).

There has been much excitement in the scientific literature in recent years regarding artificial neural networks (ANNs) (7,8), in medicine (9), and specifically, in developmental pediatrics. ANNs are valuable tools used in the complex pattern recognition and classification tasks. They learn complex interactions among inputs and identify relations in input data that may not be apparent to human analysis (10). The most common type of ANN consists of 3 layers of processing units: the input layer, the hidden layer, and the output layer connected in sequence. ANNs are software tools with the capacity to learn. An ANN behaves like a child learning to differentiate between cats and dogs, by means of examples, under the supervision of his/her parents. An ANN can learn the relation between input variables (size, fleece, voice, behaviour patterns) and the output variable (cat or dog) by presenting multiple input–output pairs to it (supervised learning). After this learning or "training" period the ANN can "predict" the output (cat or dog) on inputs of further unknown examples (11,12). This capability is called generalisation. ANNs have shown excellent predictive accuracy in medicine even on inaccurate or incomplete input data. Recent reviews describe the many clinical applications of ANN (13-17).

Using an ANN, we aimed to: predict the developmental disorder of neonates from their perinatal

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and neonatal risk factors, and compare the net's performance with that of a logistic regression model.

## Materials and Methods

This study was conducted in the Karaj, with two millions inhabitants. The medical data were collected from a retrospective study. A total of 6150 infants' data were used in the database. The subjects consisted of 1,232 infants (1,000 without and 232 with developmental disorder) which were selected from 6,150 infants of Karaj, Alborz Province, Iran (18). The validated Infant Neurological International Battery (INFANIB) test (19-20) was employed to assess the infant's development. Information was obtained by a group of examiners (trained by the research team), by means of a questionnaire. The questionnaire had been previously evaluated for content validity and pilot studies had been carried out. The completion of the questionnaire was based on a thorough evaluation of the child's medical and health records and statements of their mothers, including prenatal and perinatal histories such as maternal age at delivery, parity, parental consanguinity, miscarriages, pregnancy complications, birth method, infant gender, neonatal and/or perinatal asphyxia, gestational age (completed weeks), birth weight, neonatal convulsion and/or postnatal epilepsy, hyperbilirubinemia leading to phototherapy or blood exchange transfusion. We use the term risk factor to refer to pre, peri and post natal biological hazards that can compromise development.

Data such as Maternal age was categorized as low risk (19-35 years old) and high risk (≤18 and >35 years old).

Preterm delivery was defined as delivery before 37 completed weeks of gestation. Gestational age duration was estimated according to last menstrual period.

The birth weight was dichotomized as high risk (≤2500 g) and low risk (>2500g).

Parity was dichotomized as high risk (primiparous, or more than 4 previous pregnancy) and low risk (1-3 previous pregnancy).

There was a special emphasis on the mother's personal and obstetric history, particularly on previous spontaneous fetal death, neonatal death, congenital malformation, cervical incompetency, miscarriage or delivery of a premature or low birth weight infant (History of high risk pregnancy). The same features and their clinical course were recorded for the current pregnancy. Complication during pregnancy meant one or more of the following risk conditions: uterine bleeding, premature rupture of membrane, poly-oligohydramnios, acute medical or surgical illness, multiple gestation, and medication during pregnancy, infections, uterine or cervical anomalies, preeclampsia or eclampsia and diabetes mellitus.

Disturbances of respiration in the immediate postnatal period that have originated in the uterus, in the delivery room, or in the nursery, defined as neonatal respiratory distress syndrome (RDS).

Type of delivery was categorized into 2 groups: routine vaginal (NVD), not normal vaginal delivery (not NVD) included operative vaginal (using vacuum or forceps), or cesarean section.

The term neonatal and/or perinatal asphyxia was used when one of the following features was present: meconium-stained amniotic fluid, Apgar score (≤ 5) at 5 min or beyond, need for emergency caesarean section or for resuscitation after birth.

Neonatal convulsion, in this study was defined as a convulsion during the neonatal period based on clinical diagnosis of a physician, occurring at least once and without metabolic disorders such as hypoglycemia or hypocalcaemia, and with no need for long-term treatment with anti epileptic drugs; and converting to normal EEG after 2-3 months of treatment.

Postnatal epilepsy indicated a convulsive condition based on clinical diagnosis and EEG that resulted from perinatal insults (but not congenital, CNS infection, toxic/metabolic conditions, CNS neoplasm, and traumas). In our definition, febrile seizures are included.

Neonatal sepsis was defined as positive blood culture during the first week of life, with any organism known as causing neonatal sepsis or clinically suspected in the baby.

Parental consanguinity indicated first or second degree relation of parents.

In order to predict the infants' neurodevelopmental outcome a multilayer perceptron (MLP) was used. A MLP is a special kind of artificial neural network (ANN) and often shown to be more powerful in classification tasks than alternative statistic procedures, e.g. discriminant analysis (21). A three layer MLP was used in this study. The first (input) layer consists of 14 neurons (i.e. independents variables and factors). The second (hidden) layer is built up by examination (4-28 neurons), and the last (output) layer contains one neuron (i.e. outcome/dependent variable).

In the ANN modeling process, we randomly divided the data into two subsets: 740 patients (nearly 60%) for constructing the models (training subset) and the remaining (nearly 40%) for testing the model (as the

validation subset).

To find the best prediction model, the training process was started by a three layer MLP with 4 hidden neurons using the back-propagation algorithm (22). Based on the outcome variable, a sigmoid/logistic function was used as an activation transfer function. After training the MLP, the number of hidden neurons was increased by one until 28. In each time, the learning error prediction and concordance indexes (the percentage of normal and abnormal infants who are correctly identified as having the condition) were calculated. Finally, a three layer MLP with 14 neurons in the hidden layer was selected as the best prediction model. In the next step, testing process was made on testing data set based on this architecture.

Logistic regression (LR) and ANN models were used to analysis of data by R 2.13.0 software.

For the purpose of performance assessment and method comparison ROC (receiver operating characteristic) curves were used. The outcome predictions as delivered by both models were developmental disorder risk. The ROC curve represents a graphic display of the true-positives (sensitivity) plotted against the false-positives (1-specificity) for various thresholds that are used to define developmental disorder. For comparing the accuracy of the models' prediction, the accuracy classification table was used for the testing subset.

Inform consent was obtained from all parents whose children were studied, and the research was approved by the "Ethics Committee of the University of Social Welfare and Rehabilitation Sciences".

## Results

Of the 1,232 infants, 625(50.7%) were boys and others were girls. In addition, 1000 infants (81.2%) were normal, and others were abnormal.

The mean ± SD of age of children was 35.77±15.77 (and median age was 33 weeks). The mean ± SD of maternal age was 25.96±5.41 (and median age was 25 years). 33.2% of parents were parental consanguinity. Characteristics of infants and their mothers shown in table 1.

**Table 1.** General characteristics of the infants.

| Variable | No | Percent |
|---|---|---|
| Parental consanguinity | 409 | 33.2 |
| Maternal age (≤18 or >35) | 143 | 11.6 |
| Prematurity | 89 | 7.2 |
| Complications during pregnancy | 101 | 8.2 |
| History of high risk pregnancy | 206 | 16.7 |
| Parity (<1 or >3 ) | 663 | 53.8 |
| No NVD delivery [1] | 659 | 53.5 |
| Low Birth Weight | 214 | 17.4 |
| Asphyxia (neonatal and/or perinatal) | 109 | 8.8 |
| Neonatal respiratory distress syndrome | 125 | 10.1 |
| Icterus[2] | 145 | 11.8 |
| History of convulsion [3] | 68 | 5.5 |
| Neonatal Sepsis | 54 | 4.4 |

[1] Not normal vaginal delivery included operative vaginal (using vacuum or forceps), or cesarean section.

[2] Hyperbilirubinemia leading to phototherapy and/or blood exchange transfusion

[3] Neonatal convulsion and/or postnatal epilepsy

**Table 2.** Relative importance of inputs found by neural network and logistic regression modeling.

| ANN model | | LR model | |
|---|---|---|---|
| **Factor** | **Coefficient** | **Factor** | ***P*_value** |
| Low Birth Weight | 0.143 | History of convulsion [1] | 0.003 |
| History of high risk pregnancy | 0.139 | History of high risk pregnancy | 0.033 |
| Prematurity | 0.138 | Prematurity | 0.069 |
| History of convulsion [1] | 0.134 | Low Birth Weight | 0.129 |
| Neonatal Sepsis | 0.080 | Respiratory distress syndrome | 0.208 |
| Respiratory distress syndrome | 0.074 | Complications during pregnancy | 0.306 |
| Icterus [2] | 0.073 | Icter [2] | 0.308 |
| Parity | 0.060 | Asphyxia (neonatal or perinatal) | 0.328 |
| Complications during pregnancy | 0.053 | Parental consanguinity | 0.339 |
| Sex | 0.031 | Sex | 0. 401 |
| Asphyxia (neonatal or perinatal) | 0.030 | Parity | 0.451 |
| Parental consanguinity | 0.019 | Neonatal Sepsis | 0.498 |
| Type of delivery | 0.018 | Type of delivery | 0.508 |
| Maternal age | 0.007 | Maternal age | 0. 748 |

[1] Neonatal convulsion and/or postnatal epilepsy

[2] Hyperbilirubinemia leading to phototherapy and/or blood exchange transfusion

**Table 3.** Classification accuracy of ANN and LR models in testing subset of the infants.

| Status | Observed | True prediction by ANN | True prediction by LR |
|---|---|---|---|
| | N | N (%) | N (%) |
| With Movement Disorder | 92 | 36(39.1) | 20 (21.7) |
| Without Movement Disorder | 400 | 373 (93.2) | 371 (92.7) |
| Total | 492 | 409 (83.1) | 391 (79.5) |

Based on the validation set, the ANN model was used to determine the important factors. Based on importance analysis in the ANN strategy, low birth weight, history of high risk pregnancy, prematurity, neonatal and/or postnatal convulsion, neonatal sepsis, RDS, icterus leading to phototherapy or exchange transfusion, parity (<1 or >3), and complications during pregnancy were determined as ordered important factors. But in the LR analysis, neonatal and/or postnatal convulsion, history of high risk pregnancy, prematurity, and low birth weight were determined as ordered important factors (Table 2).

The results of accuracy classification table were presented in Table 3. The concordance indexes showed that true prediction of developmental disorder in the ANN model, compared to the LR model, was 83.1% vs. 79.5% and the area under ROC curves, calculated from testing data, for ANN and LR model were 0.79 and 0.68, respectively. In addition, specificity and sensitivity of the ANN model vs. LR model was calculated 93.2% vs. 92.7% and 39.1% vs. 21.7%, respectively.

## Discussion

Child's development is affected by psychosocial and biological factors (23) and by genetic inheritance. The first few years of life are particularly important because vital development occurs in all domains (24). The brain develops rapidly through neurogenesis, axonal and dendritic growth, synaptogenesis, cell death, synaptic pruning, myelination, and gliogenesis. These ontogenetic events happen at different times (25), and build on each other, such that small perturbations in these processes can have long-term effects on the brain's structural and functional capacity. Despite the vulnerability of the brain to early insults, remarkable recovery is often possible with interventions (26,27), and generally the earlier the interventions the greater the benefit (28). Neonates at risk should be identified as early as possible to decrease neonatal morbidity and mortality. Risk factors have a cumulative impact upon the development. As the number of risk factors increases, a child is put at greater risk for developmental delay (29-31). The recommendation issued by the American Academy of Pediatric (AAP) calls for early detection and intervention of any child suspected of having or known to have developmental delay and/or disorder (32).

Solely based on perinatal data, our ANN was capable of accurately predicting developmental disorder and the ANN performed better than a logistic regression model. The concordance indexes showed that the ANN model was led to more accurate predictions compared to the LR model (true prediction of developmental disorder was 83.1% vs. 79.5%).

While the logistic regression model comprised four significant items, the ANN used 14 items (table 2). The input variable selection of the ANN seems reasonable as most selected variables were reportedly associated with developmental disorder (18,33) and as all predictive variables isolated by the logistic regression analysis were also included in the ANN input variable set. Hence subtle and/or non-linear associations between input variables and developmental disorder not detected by logistic regression analysis might account for the superior performance of the ANN.

In this study, the area under ROC curves, for ANN and LR model were 0.79 and 0.68, respectively. In addition, specificity and sensitivity of the ANN model vs. LR model was calculated 93.2% vs. 92.7% and 39.1% vs. 21.7%, respectively. This means that, the ability of ANN and LR predictions to identify children without developmental disorder is similar, but the ability of the ANN predictions to identify infants with developmental disorder is better than LR predictions. Predictive models have not fared much better, and their lack of sensitivity is evidence of the complexity of the problem. The advantage of the neural networks lies in their ability to process nonlinear relationships. Because of the clinical and diagnostic complexity of neurodevelopmental disorders, correct identification of infants with developmental disorder is unlikely to depend on the presence or absence of a single defining feature. Hence, it is not surprising that standard linear statistical methodologies are relatively inadequate solutions for this type of problem. The superior

prediction capability of neural networks over LR was observed also in this study.

There are several potential limitations to the study. We relied on pre-existing data; thus we feel that information on important topics was missing in our database.

In conclusion, neural networks are able to include both quantitative and qualitative data into the same model. There are no limitations with respect to ordinal scaled data as there are in logistic regression analysis.

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