Application of Classification for Figure Copying Test in Parkinson's Disease Diagnosis by Using Cartesian Genetic Programming

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ABSTRACT

Previous studies have proposed an objective non-invasive approach to assist diagnosing neurological diseases such as Alzheimer and Parkinson's diseases by asking patients to perform certain drawing tasks against certain figure. However, the approach of rating those drawing test results is still very subjective by relying on manual measurements. By extracting features of the drawn figure from the raw data, which is generated from the digitized tablet that patients can draw on, we can use supervised learning to train the evolutionary algorithm with those extracted data, and therefore evolves an automated classifier to analyse and classify those drawing accurately. Cartesian Genetic Programming (CGP) is an improved version of conventional Genetic Programming (GP). As GP adapts the tree structure, redundancy issue exists as the tree develops more nodes with the evolution of the GP by mutation and crossover. CGP addresses this issue by using fixed number of nodes and arities, evolves by using mutation only. The outcome of this research is a highly efficient, accurate, automated classifier that can not only classify clinical drawing test results, which can provide up to 80% accuracy, but also assisting clinicians and medical experts to investigate how those features are used by the algorithm and how each component can impact patient's cognitive function.

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CCS CONCEPTS

• **Computing methodologies~Supervised learning by classification** • Applied computing~Health care information systems

KEYWORDS

Cartesian Genetic Programming, Clinical Drawing Test, Genetic Programming, Machine Learning

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1 INTRODUCTION

Parkinson's disease (PD) assessment is often related with motor skills test as it is recognized as a motor disorder widely [1, 2]. In addition, Parkinson's disease's non-motor symptoms, for example, memory function and sensory, are also common [2]. In a clinical drawing test, the patient will be assessed in three aspect through different tasks – motor skills, cognitive abilities and memory functions. Such drawing test is recognized by medical experts and is widely used currently. However, verdict on the final drawing result is often subjective with existential human error as it is measured manually. By using machine learning, an automated classifier can provide an objective approach on rating those drawing test results.

As a form of machine learning, evolutionary algorithm and its subset, genetic programming, provide a biologically inspired learning method through mutation and crossover from best currently known hypotheses in the algorithm [3]. By using drawing's features as input, classification as output, we can have an objective method that minimise human error by analyse the figure with smallest details to perform automated clinical drawing test classification using evolutionary algorithm.

Previous study has shown the validity of application of evolutionary algorithm on the assessment of bradykinesia in Parkinson's disease by using finger-tapping test [4]. In the finger-tapping test, two special devices were attached on patient's index finger and thumb separately. Features were extracted from these devices, resulting in a well-trained classifier with an overall accuracy of 91.05% on both hands, providing information from the test result by machine learning technique [4] for further research on how evolutionary algorithm can measure the severity of bradykinesia in PD accurately as well as differentiate early stage of PD from normality [4].

Another form of neurological disease test is clinical drawing test, in which the patient was required to perform various drawing task against certain figure, for example, figure copying and delayed recall. Several figure tests were proposed such as Clock Drawing Test (CDT) and Rey-Osterrieth Complex Figure (ROCF). Both have been proven on being effective on assisting neurological disease diagnosis [5, 6], but with lack of objective method to rate and classify those figures because of the limitation of those figures.

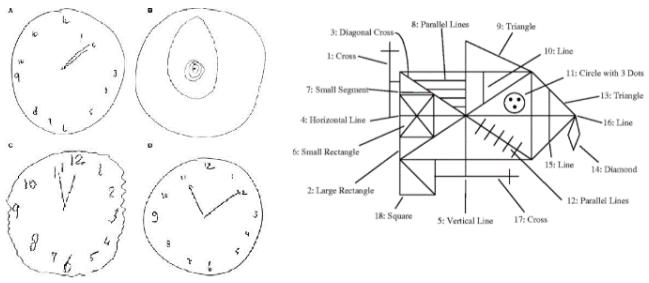

Figure 1: Illustration of CDT and Rey-Osterrieth Complex Figure, taken from [7] & [8]

The intended experiment of applying evolutionary algorithm on analysing drawing data is to feed the algorithm with the features extracted from the raw data of the drawing result, using supervised learning to train the algorithm as an automated classifier. CDT is proven very effective on diagnosis of neurological deficits disease as it is harmless, easy to administrate, objective. Previous study by Agrell et al. [9] shows that it has a strong correlation between CDT and Mini Mental State Examination (MMSE), a questionnaire targets on investigation on mental state of patients [10], which is used extensively by clinical experts and researchers [11] in patients with various cognitive dysfunctions [9]. However, the shape of the clock makes feature extraction for the algorithm very difficult as the components in the figure are mostly distorted. Deep learning approach can address this issue by training the algorithm with original image file, but such approach cannot identify detailed features like movement disorder and hesitation. Compared with CDT, feature extraction from the ROCF is relatively easier and more accurate with its line segment structure rather than curves, but the test itself is too complicated to distinguish patients from different conditions and even from control group due to its difficulty to perform this drawing task. Thus, a figure with a simpler shape but also capable of distinguishing patients in various conditions as well as algorithm-friendly is required.

2 CLINICAL DRAWING TEST

There are three aspects when diagnosing neurological disease – motor skills, cognitive abilities and memory functions. The clinical drawing test is divided into two sub tasks – copy and delayed recall. Copy task requires patients to copy a figure which is presented to them by hand drawing. Delayed recall asks patients to draw the figure they were presented after certain time according to their memory only. In this study, both simple figure and complex figure are used in separate tests.

2.1 Simple Figure

Simple figure test uses cube figure and the drawing task does not include delayed recall because this task targets on cognitive function and motor skills only. The test subjects are 40 pupils from local elementary school with their parents' and headmaster's consent with ethical approval from the Physical Sciences Ethics Committee, the University of York. The objective of this study is to conduct simple experiment with cube figure, which tests visuospatial ability only, in order to provide evidence for further studies on complex figure tests. The range of age of those pupils is between 7 and 11 as children in this age group have rapid development of cognitive skills, such as visuospatial ability [12], which is tend to decline with the advance of cognitive impairment.

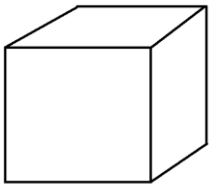

Figure 2: Cube figure presented to test subjects

Each test subject in this test is required to copy the cube figure for three times as shown in Fig. 1 on a digitized tablet with paper sheet covered to minimize external disturbance on drawing condition. Only the raw data, hand preference and test date are recorded. A total of 122 drawing samples were collected.

The purpose of this sub-task is to validate the possibility on using evolutionary algorithm to classify various drawings against their quality, before we can apply complex figure on actual neurological disease patients. Previous study has shown the clear relationship between children development and visuospatial ability [12], drawing quality tends to increase with the increase in child's age because of the development of children's visuospatial ability.

2.2 Complex Figure

Complex figure test uses a Benson figure as shown in Fig. 3. It is a combination of line and curve segments with higher requirements on line scaling and placement compared with the cube figure. Test subjects are 58 Parkinson's disease patients and 27 people in normal control group, with the age range between 48 and 82 regardless of gender and dominant hand. In this test, subjects are required to perform both copy and recall task. A total of 162 drawing samples were collected.

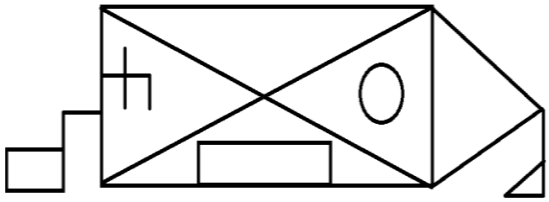

Figure 3: Benson figure presented to test subjects

3 DATA PRE-PROCESSING

Data from the stylus and tablet is recorded in the form of data stream during drawing. A set of data will be captured after a constant time gap, including pen positional coordinate, pen tilt angle and pen pressure. To feed each sample to the machine learning algorithm, number of features are extracted from the raw data. Those features are divided into dynamical and figure structural features.

3.1 Dynamical Features

Dynamical feature assesses subject's drawing in motor skills aspect. Table 1 shows features extracted for dynamical discipline.

Table 1: Dynamical Features Extracted from Raw Data

Symbol	Description
$SD(V)_{figure}$	The standard deviation of figure velocity
$SD(A)_{figure}$	The standard deviation of figure angle
$SD(A)_{horizontal}$	The angular standard deviation of horizontal segments
$SD(A)_{vertical}$	The angular standard deviation of vertical segments
$SD(A)_{oblique}$	The angular standard deviation of oblique segments
$\sum(T)_{figure}$	Total time spent on the figure
$\%_{pen\text{-}up}$	The percentage of time when subject's pen is up
$\sum(T)_{hes\text{-}up}$	The total time spent on hesitating when pen is up
$\sum(T)_{hes\text{-}down}$	The total time spent on hesitating when pen is down
$\%\ (T)_{hes\text{-}up}$	The percentage of time spent on hesitating when pen is up
$\%\ (T)_{hes\text{-}down}$	The percentage of time spent on hesitating when pen is down

Standard deviation is often used to measure dispersion of a certain dataset; therefore, it can be used for stability measurement. Because there is no clear correlation between movement velocity and motor skills, we use standard deviation to measure the stability in terms of velocity. Similarly, this can be applied on angular data as a measurement of line segments straightness as Parkinson's patient often find it difficult to draw a straight line.

3.2 Structural Features

Structural features are the abstract representation of the visual figure structure. Table 2 shows features extracted for structural discipline.

Table 2: Structural Features Extracted from Raw Data

Symbol	Description
$\sum(L)_{figure}$	Total length of figure line segments
W*H	Size of the figure
W/H	Aspect ratio of the figure
$\%_{horizontal}$	The percentage of length of horizontal segments
$\%_{vertical}$	The percentage of length of vertical segments
$\%_{oblique}$	The percentage of length of oblique segments
~~$N_{segment}$~~	~~Number of segments based on pen pressure break~~[1]

Structural features include global and regional features. Global features include total length of the figure. Size and aspect ratio will be used for the algorithm to find a common pattern for the figure as well. The definition of Pen-Up is when the pen is not on the paper as the capture device has a pressure sensor. That means zero pressure reading indicates a lift of pen from the tablet. The portion of segments in terms of length in different angle groups

[1] This feature is deprecated in Benson complex figure test as the actual value varies a lot for figures with same drawing quality.

will be assessed in order to find out a distribution in portions in different classes. Hesitation is a crucial part of Parkinson's disease assessment as it may reflect a deficit in motor skills and/or visuospatial ability.

3.3 Initial Classification

Before we can use all the samples for the algorithm, we need to classify these samples that will be used for supervised learning. Currently there are two rating schemes to apply on the drawing samples.

3.3.1 Visual-based classification. A Benson-figure-test instruction manual [13] was published by the National Alzheimer's Coordinating Center in the University of Washington in 2013. This instruction has proposed a rating scheme, which is based on the structure of the Benson figure, including various components in the figure as well as general placement and scale of the whole figure.

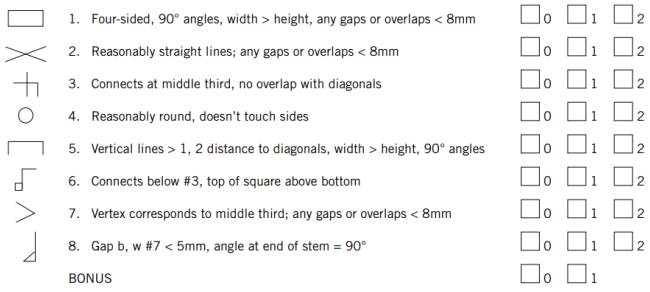

Figure 4: NACC Benson test rating scheme, taken from [13]

Apart from the eight components shown in Fig. 4, BONUS is available for reasonable placements of the components and general scale of the figure. According to this rating scheme, there is a total of 17 available marks. Because different figures with identical score has a great possibility of having completely different structural feature, those 17 marks is further classified into four classes with certain a range of score in a single class, for better training performance in the algorithm.

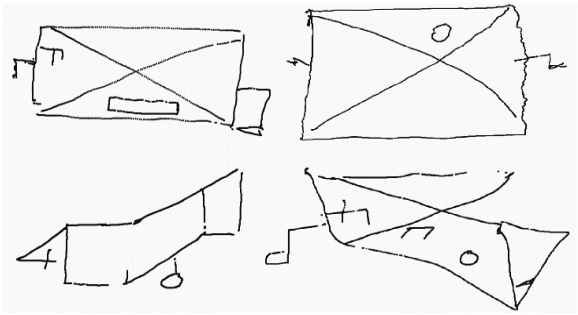

Figure 5: Part of the class 1 drawings, showing wide variety of structures in lower class drawings

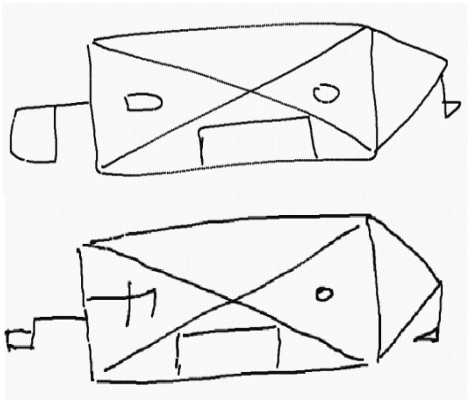

Figure 6: Two similar figures with marginal marks in their respective class (Upper in class 2, lower in class 3)

However, one known downside of this classification scheme is samples with marginal mark in different classes may be very similar in terms of the drawing quality as this scheme rates the figure based on the number of components, making it more difficult for the algorithm to distinguish marginal samples. Furthermore, especially in lower classes, figures in the same class may differ dramatically as shown in Fig. 5, making the algorithm having difficulty in finding patterns for low class drawings.

Cube figure rating is based on Bremner et al.'s study [12]. The original classification scheme proposed eight classes. For this study, those classes are regrouped into three classes based on their features as the number of samples in each class is not enough for detailed classification training. In addition, the regrouping is performed according to the shared characteristics in those classes, which is further described in figure 8.

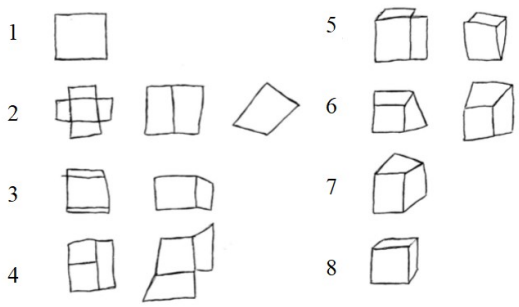

Figure 7: Bremner's cube classification scheme, taken from [12]

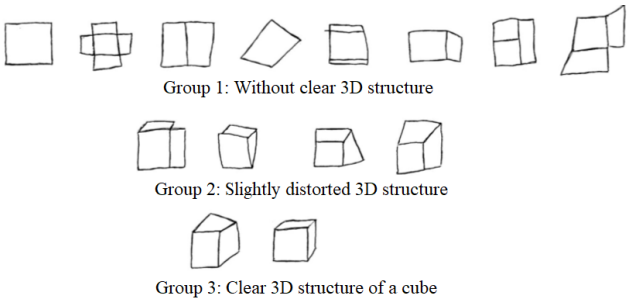

Figure 8: Regrouped cube classification scheme based on Fig. 7

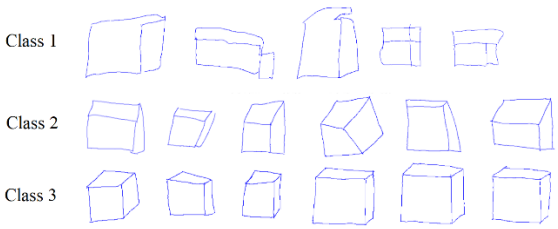

Figure 9: Sample drawings from different groups

3.3.2 Condition-based classification. Apart from using classification based on the Benson figure rating for the algorithm training, samples can be classified based on test subject's condition in four classes: control group and three Parkinson's stages: Parkinson's disease-Normal Cognitive (PD-NC), Mild Cognitive Impairment (PD-MCI) and Dementia (PD-D), in ascending order in terms of severity. There are several cognitive tests are conducted on patients along with Benson figure test, including Montreal Cognitive Assessment (MoCA), a screening component-based assessment for cognitive disorder detection [14], and Clinical Dementia Rating (CDR), a numeric scale to measure dementia symptom's severity. Patients are classified to those PD stages by their MoCA score and CDR. As different condition has different effects on patients and hence, the drawing quality, it addresses the issue induced by the visual-based classification that marginal samples may not be distinguished correctly.

Table 3: Classification scheme for different PD stages

Condition	Stage
MoCA > 26	PD-NC
MoCA <= 26 && CDR < 1	PD-MCI
MoCA <= 26 && CDR >= 1	PD-D

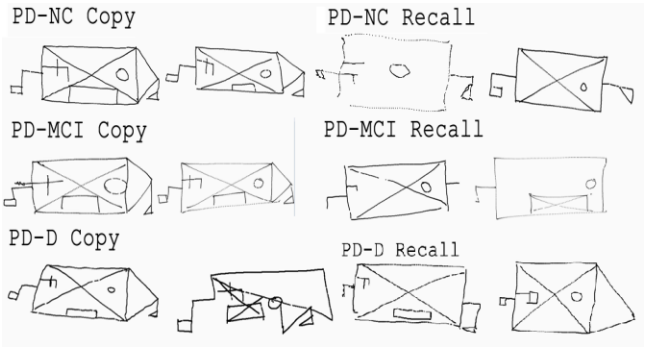

Figure 10: Samples of Benson figure drawn by patients from different PD stages

The application of this classification scheme on the cube drawing test is classifying by age. However, no demographical data were recorded during this test. Therefore, only visual-based classification will be applied on cube drawing test as the exposed downside of visual-classification on Benson figure has less effect on cube figure as the cube figure has a relatively simpler structure, as shown in Fig. 8, making it is safe to use for cube figure classification.

4 CARTESIAN GENETIC PROGRAMMING

Cartesian Genetic Programming (CGP) is an improved version of Genetic Programming (GP). It addresses the redundancy issue from GP which is caused by the binary-tree structure where a large amount of memory and computational resources are used as the tree expanding while the algorithm is evolving [15]. CGP uses a grid structure that limits the number of nodes and arities of each node and only evolves through mutation [15]. The actual form of CGP is an array of node information with node function, node connection and weighting. In general, CGP will take numerical inputs and provides outputs as computational result. Different criteria can be used to classify those outputs and as an evaluation standard for CGP.

4.1 Evaluating CGP Performance

In each generation, CGP will be evaluated by the classification accuracy on available test data set. The general process is as follows:

1. Get the total number of samples in test data set *N*;
2. Set Error counter as *E*;
3. For each sample in data set:
   a. Feed input of current sample into CGP
   b. If the output classification mismatches the expected class, Error counter *E* increments by one.
   c. Test next sample
4. CGP is evaluated by accuracy *1-(E/N)*.

The CGP chromosome with the highest accuracy among a generation will be chosen for offspring generation, until the maximum generation or the target accuracy is reached. As part of the implementation of the fitness function, there are two classification algorithms to select according to the algorithm output configuration.

4.1.1 Simple Threshold Classifier. This classifier is used for a single output CGP configuration. It requires a pre-defined number array as thresholds. The final output will be compared against the thresholds.

1. Define an incrementing integer array *A(N)*, where *N* is the number of classes;
2. For an individual sample with expected class C in data set:
   a. Get the numerical output *W* from the chromosome;
   b. If *W* is in the range of *(A(C-1),A(C)]*, it's a match, otherwise mismatch

Visual representation of this classifier is shown in Fig. 11:

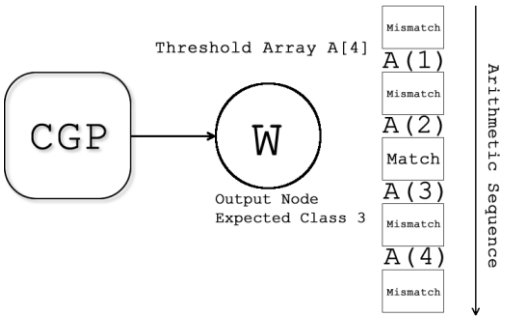

Figure 11: Visual representation of simple threshold classifier

4.1.2 Node Weighting Classifier. Node weighting classifier is an alternative solution for multiple outputs configuration as the simple threshold classifier can only handle single output scenario. The procedure is as follows:

1. Define class numbers *N*;
2. Feed inputs from a single sample into chromosome, the chromosome calculates *N* outputs to form an array *A*;
3. Find the output node with maximum value *M = max(A)*
4. If *M* is the expected class of the sample, it's a match, otherwise mismatch

Visual representation of this classifier is shown in Fig. 12:

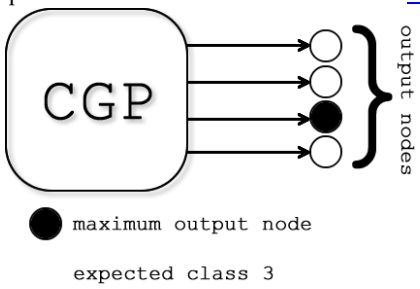

Figure 12: Visual representation of Node Weighting Classifier, showing a matching condition

4.2 CGP Configuration

CGP is a highly configurable and customizable algorithm. Most of parameters can be set prior to the training as well as the fitness and node function. Those set of parameters along with a random number seed represents a fixed evolvement process of a CGP under the circumstance that the data set remains unchanged. As the fitness is represented by the accuracy on the CGP's verdict on blindfolded dataset, best generation will be the one with the highest accuracy without overfitting. Table 3 shows CGP parameters that need to be configured before training.

Table 4: Configurable CGP parameters and description

Symbol	Description
N_{seed}	Random number seed for initialization
$N_{threshold}$	Integer array for STC
$N_{(nodes)}$	Number of nodes in the CGP
$N_{(arity/node)}$	Number of arities for each nodes
$\%_{mutation}$	Mutation rate for the evolvement of the CGP
$N_{(inputs)}$	Number of inputs
$N_{(outputs)}$	Number of outputs

4.3 Overfitting Prevention

As in other machine learning algorithms, overfitting issue needs to be addressed in CGP as well. All data set is divided into three parts: Training, Validation and Testing. Training dataset will be used to train the algorithm. Validation dataset, as an unknown dataset to the current generation, will be used to validate current generation by using a slightly lower chromosome in the generation to classify validation dataset as a solution to prevent overfitting from the training dataset. Testing dataset is used to test the chromosome with completely unknown data, which will not affect chromosome behaviour. Portion of those datasets typically are 60% of overall datasets for training, 20% for validation and 20% for testing.

In the situation that we do not have adequate number of samples for testing dataset, we need to apply K-Fold cross validation across all datasets. A convey-belt like mechanism is applied to shift data between datasets. For each fold, a fixed amount of data will be exchanged between datasets. The number of data is determined that the training dataset is to be refreshed twice when the validation is finished as described in below:

$$N_{datashift} = N_{training} * 2 / K$$

where K is the number of folds to be applied.

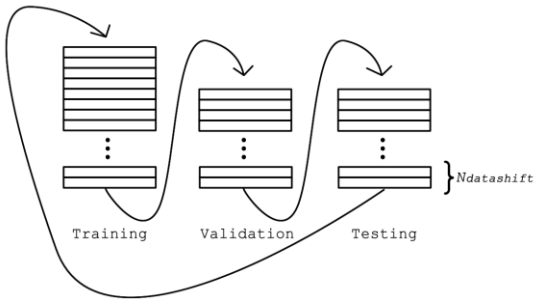

Figure 13: Illustration of data shift for K-fold cross validation on CGP

5 TEST RESULT

Cube and Benson figure task adapts different testing strategy. Cube copying task's training strategy is to mix all three categories of drawings together to train the algorithm. For Benson figure test, the algorithm will be trained pair-wise, each with different Parkinson's condition pair. For each pair, copy and recall training will be conducted separately as those tasks are aiming differently, but will share the same CGP configuration. Each pair will be trained 10 times with K-fold validation enabled and different seed, to ensure the validity of the data, which will generate 110 CGP execution results for each pair and drawing mode.

5.1 Cube Copying Task

A simple training was conducted on cube copying data. After all the data were separated into three parts, a total of 25 samples, with 5 in class 1, 10 in class 2 and 10 in class 3 are used as testing dataset. Hence, K-fold validation is not applied as there's enough data for testing and validation. Table 5 shows the parameter used for CGP for the cube copying test:

Table 5: CGP configuration for Cube Copying Test

Symbol	Value
N_{seed}	1234
$N_{(nodes)}$	20
$N_{(arity/node)}$	5
$\%_{mutation}$	8%
$N_{(inputs)}$	9
$N_{(outputs)}$	1

With this configuration, the algorithm managed to evolve a chromosome with a training accuracy of 68.5% and validation accuracy of 68%. Test dataset reaches an accuracy of 76%, which is good enough to conduct further test on Benson figures considering the lack of samples, but the training and validation scores can be further improved by using K-fold cross validation and using extra features from the Benson figure test to the cube copying test. By using simple threshold classifier, two threshold values were set at 100 and 200. Fig. 14 shows the ascending trend of training accuracy.

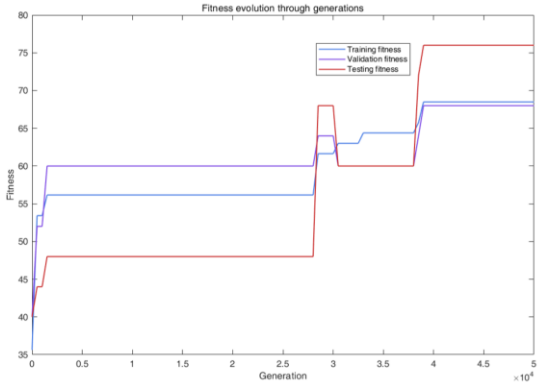

Figure 14: Illustration of CGP fitness evolution during training

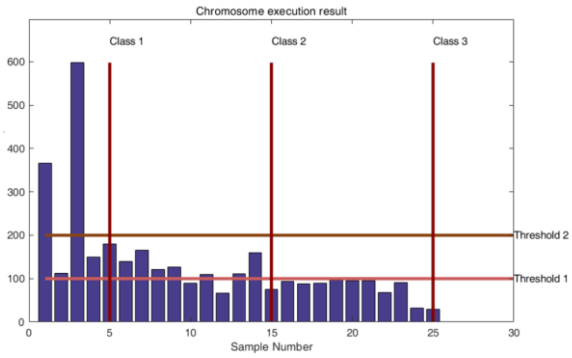

Figure 15: Chart to compare CGP output and expected output

5.2 Benson Figure Task

5.2.1 Subjective assessment result. All of patients' drawings are assessed according to the NACC Benson test rating scheme in Fig. 4. The assessment result indicates that the recall task has better performance than the copy task in terms of distinguishing patients from different stages, as shown in Fig. 16. The scores are divided into three tiers according to their minimum and maximum score. In each PD stage, the leftmost bar represents the worst drawing quality, the middle one indicates mediocre performance and the rightmost bar is the portion of the near-perfect drawings. According to Fig. 16, patients tend to perform well in copy task, which makes this task seems useless in classifying patients in different stages. However, recall task distinguishes patients better than copying task, with a vivid increase of height on the leftmost bar while the PD stage advances, and a decrease in the portion of high-quality drawings. However, as it is a subjective assessment method, we expect to see a different result in CGP classification of those drawings where both copy and recall task can distinguish patients from different stages.

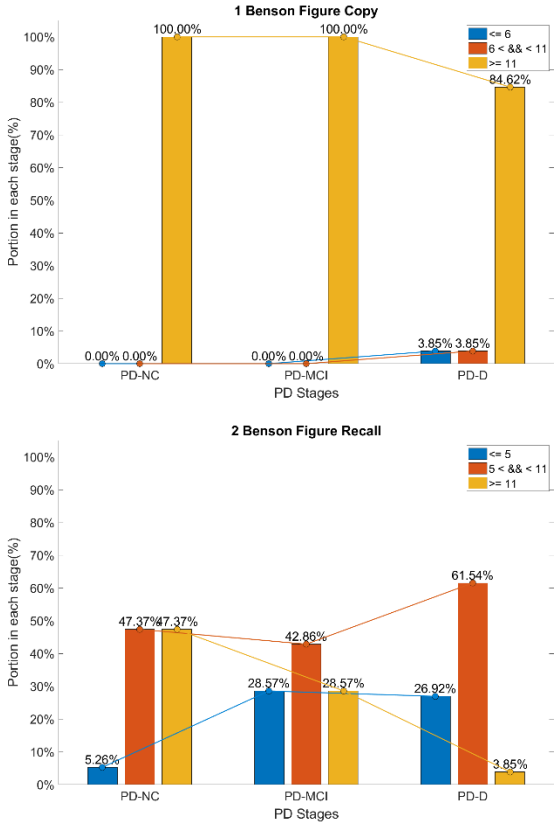

Figure 16: Distribution of scores in different Benson drawing tiers across all PD stages from conventional assessment method

5.2.2 CGP execution result. As described in the previous section, due to lack of samples, K-fold cross validation is applied in Benson figure task data training. The value of K is set as 10. For all pairs, Node Weighting Classifier is used for fitness function and classification. Only nodes and arities of CGP are different across all pairs, mutation rate is set at 8%, maximum generation is 200,000. Following is a table which shows the testing result for each dataset for each drawing mode. It includes all mean accuracies for each dataset as well as its standard deviation, which indicates CGP's stable performance from the cross validation.

Table 6: Mean of CGP classification accuracy result

PD Pair	Mode	Training	Validation	Test
NC/MCI	Copy	99.74%	85.45%	83.03%
	Recall	100%	87.82%	83.79%
	Δ	0.26%	2.37%	0.76%
NC/D	Copy	94.81%	73.44%	69.70%
	Recall	95.93%	74.95%	68.18%
	Δ	1.12%	1.51%	1.52%
MCI/D	Copy	98.89%	88.58%	83.64%
	Recall	99.03%	84.85%	79.61%
	Δ	0.14%	3.73%	4.03%

Table 7: Standard Deviation of CGP classification accuracy result

PD Pair	Mode	Training	Validation	Test
NC/MCI	Copy	0.0069	0.0835	0.0833
	Recall	0	0.0930	0.1034
	Δ	0.0069	0.0095	0.0201
NC/D	Copy	0.0548	0.1038	0.1122
	Recall	0.0477	0.0974	0.1044
	Δ	0.0071	0.0064	0.0078
MCI/D	Copy	0.0217	0.0957	0.0994
	Recall	0.0225	0.0687	0.0989
	Δ	0.0008	0.0290	0.0005

As expected in section 5.2.1, the actual CGP execution result shows that it can distinguish different classes from both copy and recall tasks, there is no significant compromises in terms of classification accuracy in copy task figures, indicating its potential in compensating the human error in subjective assessment approach. In fact, both copy and recall classification shows similar result according to table 6 and 7 with the same CGP configuration except random number seed. The cross validation performance is indicated by the standard deviation score, which shows great stability in accuracy with different folds and random number seed applied.

6 FURTHER WORKS

Support Vector Machine (SVM) is an efficient supervised learning models for dual-class data classification. Current research progress on the paper topic are using CGP for dual-class data classification. Further research can be conducted by using SVM on current datasets with different Parkinson's condition pairs to compare the performance of SVM's and CGP's. The investigation on how both algorithms process data inputs would assist clinical experts to investigate the affect elements of Parkinson's disease, in order to understand Parkinson's disease further and better.

As mentioned in section 3.3.2, numerous credited cognitive assessments are also conducted on the patients. Previous test result has only used patients' condition as classification standard. Potential research can be carried out to further investigate the correlation between the Parkinson stage, MoCA score and Benson figure score in future research.

7 CONCLUSION

Compared with traditional deep learning approach for image classification, evolutionary algorithm provided a more precise way to analyse and classify clinical drawing test, especially when the smallest detail is decisive in detecting cognitive impairment. Current diagnosis method has limitation in diagnosing early cognitive disorder. By combining machine learning and previous clinical research, this research can help clinical experts to further investigate how each aspects from the drawing have different impacts on cognitive disorder patients, thus assisting development in healthcare.

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