Vegetative State: Early Prediction of Clinical Outcome by Artificial Neural Network

L. Pignolo[1], F. Riganello[1], A. Candelieri[2] and V. Lagani[2]

[1] S. Anna Institute, RAN – Research on Advanced Neuro-rehabilitation, Crotone, Italy

[2] Laboratory for Decision Engineering and Health Care Delivery
Department of Electronic Informatics and Systemistics
University of Calabria, Cosenza, Italy

Abstract. Residual brain function has been documented in vegetative state patients, yet early prognosis remains difficult. Purpose of this study was to identify by artificial Neural Network procedures the significant neurological signs correlated to, and predictive of outcome. The best networks test set accuracy was 70%, 72% and 70% for the entire patients' group and the posttraumatic and non-posttraumatic subgroups, respectively. The method accuracy does not reflect a perfect classification, but is significantly far from the random or educated guess and is in accordance with the results of previous clinical studies.

1 Introduction

The Vegetative State (VS) is a clinical condition characterized by the absence of awareness (of self and environment), voluntary or purposeful behavioral responses to external stimuli, and communication in the severely brain damaged. Subjects in VS are otherwise awake, often with wakefulness-sleep cycles [1, 2, 3, 4, 5, 6]. Recovery (with varying residual disabilities) occurs only in a portion of patients; resources, staff, logistics and costs requirements for the care of these subjects are imposing irrespective of outcome. Purpose of this study was to identify by artificial intelligence procedures a significant model supporting decision in the early prognosis of VS subjects [7, 8]. It should be noted in this regard that evidence-based neurology indicates significant neurological signs correlated to, and predictive of outcome. Prognosis can be modeled as a regression, classification or survival analysis problem by traditional statistics or machine learning techniques [9]. This study is purposed to demonstrate that reliable classification models predictive of the vegetative state outcome prognosis can be obtained by Artificial Neural Networks (ANN) techniques. Section 2 of this paper outlines dataset and pre- processing; Section 3 describes the experimentation protocol for the training of classification models; Sections 4 and 5 summarize and comment the results.

Pignolo L., Riganello F., Candelieri A. and Lagani V. (2009).
Vegetative State: Early Prediction of Clinical Outcome by Artificial Neural Network.
In *Proceedings of the 5th International Workshop on Artificial Neural Networks and Intelligent Information Processing*, pages 91-96
DOI: 10.5220/0002264300910096

2 Data Collection and Pre-processing

2.1 Data Collection

Three hundred and thirty three subjects in VS consecutively admitted to the dedicated semi-intensive care unit of the S. Anna – RAN Institute (Crotone, Italy) over a 9-year period (April 1998–March 2006) were considered retrospectively. The VS was clinically defined in all subjects compliant to the criteria suggested by the Multi-Society Task Force and the guidelines of the London Consensus Conference (Multi-Society Task Force, 1994).

For each patient, were entered in the dataset: age, sex, etiology of brain injury (posttraumatic or non-posttraumatic), rating at the Glasgow Coma Scale (GCS) [10] at admission, and twenty-two neurological signs of established relevance in coma and VS [11] (Tables 1) assessed by the attending physician at two-week intervals following procedures and criteria predefined as intrinsic to the UNI ENI ISO 9001:2000 quality standards. Each sign was present or absent (binary attribute). The subjects' condition at discharge was measured by the Glascow Outcome Scale (GOS): GOS_1=death; GOS_2=vegetative state exceeding 1 year in duration; GOS_3=recovery, with severe disabilities; GOS_4=recovery, with mild disabilities; and GOS_5=full recovery or recovery with minimal disabilities not interfering with the everyday life [12]. The GOS is widely used in the evaluation of the VS outcome, but the subject's assignment to any GOS class is subjected to misclassification [13] which could affect the training of classification models. Therefore, the first two classes and the latest two classes of GOS were combined into the GOS_{1-2} and GOS_{4-5} classes respectively, with a resulting sharper separation among classes. The prediction of outcome was estimated at admission and after 50, 100 and 180 days after admission.

Table 1. Clinical signs assessed at two-week intervals and entered into the artificial neural network processing as potential prognostic factors.

Decerebration
Decortication
Conjugated gaze deviation
Skew eye deviation
Blink reflex
Cilio-spinal Reflex
Tactile-oral Reflex
Optic-oral Reflex
Bulldog Reflex
Grasping reflex
Corneal Reflex
Corneal-mandibular reflex
Threat reflex
Myotactic-cervical reflex
Chewing reflex
Sucking Reflex
Oculo-cephalic reflex (with disappearance of the doll's head phenomenon)
Absence of spontaneous motility
Eye tracking
Snout Rabbit sign
Half-moon pucker sign
Klippel sign

2.2 Pre-processing

Etiology of brain injury and the pathophysiology underlying VS are known to influence the outcome. The dataset inclusive of all patients and two data sub-sets of the posttraumatic (n=213) and non-posttraumatic patients were considered. Continuous numerical attributes (such as age and GCS level) were normalized in the interval [0;1] for each dataset; remaining attributes were binary and did not require pre-processing.

3 Experimentation

3.1 Parameter Configuration

The classification models were structured as classical feed-forward ANN , with one or two hidden layers and sigmoid function activation [14, 15]. The number of neurons was varied among 1, 2, 4, 6, 10, 15, 20, 25, 30 and 40 for both the first and second hidden layer. The Stuttgart Neural Network Simulator (SNSS) was used for all the experimentations [16]

The training of the ANN was performed by using the standard Back Propagation algorithm and the "Enhanced Back Propagation" algorithm. The latter introduces the previous arc weight change as a parameter for computing the new arc weight change. SNNS implements both algorithms with the Std_Backpropagation and BackpropMomentum functions. In particular, the Std_Backpropagation function requires the specification of the parameter η (learning rate) and d_{max} (maximal difference between expected and calculated output for each neuron). Besidea η, the BackpropMomentum function needs the momentum μ measuring the influence of the previous arc weight change on the current weight calculation. Table 2 shows the parameters configuration used for the training algorithms.

Table 2. Training algorithms parameters configurations.

Std_Backpropagation		*BackpropMomentum*	
η	d_{max}	η	M
0.1	0.1	0.1	0.2
0.3	0.2	0.3	0.8
0.5		0.5	
0.7		0.7	
0.9		0.9	

3.2 Experimentation Protocol

We used a Training–Validation–Test (TVT) procedure to select the best parameter configuration regulating both the network structure and the training algorithm operation. In particular, for each dataset the following steps were applied:

1. creation of training, validation and test set (see Table 3);
2. for each combination of network and training algorithm parameters:
    a. execution of 200 training cycles;
    b. evaluation of network accuracy on the validation set;
    c. if the total number of training cycles is 20000, then stop; otherwise, return to step a;
3. selection of the network with the best accuracy on the validation set;
4. evaluation of accuracy on the test set.

At the end of the TVT procedure, we obtained three trained ANN (one for each dataset) with their respective accuracy on the test set.

Table 3. Subdivision of instance among training, validation and test sets.

Dataset	*Training*	*Validation*	*Test*
NPT Dataset	80	20	20
PT Dataset	133	30	50
Entire Dataset	200	53	80

4 Results

The best networks test set accuracy was 70%, 72% and 70% for the entire patients' group and the posttraumatic and non-posttraumatic subgroups, respectively. The best parameter configurations are reported in Table 4.

Table 4. Configurations parameters of the best networks. BP: standard back propagation algorithm; EBP: enhanced back propagation; na: not applicable.

Dataset	*Entire dataset*	*PT dataset*	*NPT dataset*
1st hidden layer	30	1	6
2nd hidden layer	30	N.A.	N.A.
Training algorithm	BP	EBP	BP
η	0.7	0.1	0.7
d_{max}	N.A.	N.A.	0.2
μ	0.2	0.8	N.A.

A better understanding of the classificatory performance can be obtained through the analysis of the confusion matrices (see Tables 5 and 6) indicating misclassified elements. We decided to assign instances with unclear evaluation to the "misclassified" class (e.g. the same instance was assigned to two classes at the same time with similar probability).

Table 5. Entire dataset confusion matrix.

	predicted class			
real class	1_2	3	4_5	*Misclassified*
1_2	16	1	3	2
3	5	2	11	0
4_5	1	0	38	0

Table 6. Posttraumatic dataset confusion matrix.

	predicted class			
real class	1_2	3	4_5	*Misclassified*
1_2	6	0	0	3
3	0	0	7	2
4_5	0	0	30	2

Table 7. Non-posttraumatic dataset confusion matrix.

	predicted class			
real class	1_2	3	4_5	*Misclassified*
1_2	8	2	0	0
3	0	5	0	1
4_5	1	1	1	1

5 Comment

The method accuracy does not reflect a perfect classification, but is significantly far from the random or educated guess and is in accordance with the results of previous clinical studies [11]. It should be noted that class GOS_3 has a larger error estimate both in the entire dataset and in the posttraumatic sub-set. The higher misclassification depends on this class taking into account all patients with a severe motor outcome (e.g. paresis of one or more limbs), impaired consciousness (e.g. global amnesia) or both. GOS_3 can therefore be heterogeneous and ANN are unable to identify a major labeling characteristic. Interestingly, test set patients with GOS_3 in the non-posttraumatic dataset are well classified, while $GOS_{4\text{-}5}$ subjects of the same dataset are poorly classified. The limited size of the non-posttraumatic sample does not allow further investigation of such phenomenon.

References

1. Jennett B, Plum F. Persistent vegetative state after brain damage: a syndrome in search of a name. Lancet 1972;1:734-6.
2. Dolce G, Sazbon L. The posttraumatic vegetative state. Stuttgart, Thiene, 2002.
3. Laureys S. The neural correlate of (un)awareness: lessons from the vegetative state. Trends Cogn Sci 2005;9:556-9.
4. Jennett B. The vegetative state. Cambridge, UK, University Press, 2002.
5. Multi-Society Task Force on PVS. Statement on medical aspects of the persistent vegetative state. N Eng J Med 1994; 330:. 1499-1508.
6. Zeman A. Consciousness. Brain 2001;124:1263-89 (review).
7. Braakman R, Jennett WB, Minderhoud JM. Prognosis of the post traumatic vegetative state. Acta Neurochirurgica 1988;95): 49-52.
8. Schmutzard E, Kampfl A, Franz G, Pfausler B, Haring HP, Ulmer H, Felber S, Golaszewski S, Aichner F. Prediction of recovery from post traumatic vegetative state with cerebral magnetic-resonance imaging. Lancet 1998;351:1763-67.
9. Rovlias A, Kotsou S.Classification and regression tree for prediction of outcome after severe head injury using simple clinical and laboratory variables. J Neurotrauma. 2004;21:886-93.
10. Teasdale G, Jennet B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974; 2:81-84.
11. Dolce G., Quintieri M., Serra S., Lagani V., Pignolo L. Clinical signs and early prognosis: a decisional tree, data mining study. Brain Injury. 2008, 22:7, 617 — 623.
12. Jennet B., Bond M. Assessment outcome after severe brain damage: a practical scale. Lancet 1976; 1: 480-484.
13. Pignolo, L., Quintieri M., Sannita, W. G. 'The Glasgow outcome scale in vegetative state: A possible source of bias, Brain Injury, 2009, 23:1,1 — 2.
14. Holte, R.C. (1993). Very simple classification rules perform well on most commonly used datasets. Machine Learning, 11, 63–90.
15. Van Bemmel, J.H.,&Munsen, M.A. (1997). Handbook of medical informatics. Berlin: Springer-Verlag.
16. Zell, A., Mache, N., Hubner, R., Schmalzl, M., Sommer, T., Korb, T. SNNS Stuttgart Neural Network Simulator Users Manual, Version 2.0, report (1992),No. 3/92, IPVR, Universität Stuttgart.