

EEG-NeuroBioFeedback Treatment  
of Patients with Brain Injury  
Part 4:  
Duration of Treatments  
as a Function of Both the Initial Load  
of Clinical Symptoms  
and the Rate of Rehabilitation

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**ABSTRACT.** Background. Twenty-seven patients with brain injury, primarily from car accidents and stroke, were treated by computer-assisted electroencephalographic NeuroBioFeedback (EEG-NBF).

Methods. Patients were distributed into five clinical classes, and changes

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The authors wish to thank the peer reviewers for their stimulating comments and constructive remarks.

in power spectra and in cardiovascular parameters were surveyed. A rationale was proposed for the calculation of the load of symptoms for each patient of each class, which in turn provided indices of rehabilitation rates.

Results. Statistically significant correlations were observed between the number of NeuroBioFeedback (NBF) treatment sessions (SN#) needed and both the initial load of symptoms (SL%) and the final rate of improvement of patients' clinical status (IMP%). When patients were considered in all five classes of defined SL%, the relationship exhibited a hyperbolic shape, although linearity could not be totally rejected, due to the variability of data. The improvement rates could be subdivided into two major classes, in which number (SN#) was hyperbolically related to the improvement rates. In addition, finger temperature responsiveness exhibited a significant correlation with the number of NBF sessions.

Conclusion. The work suggests a rationale for the prediction of the duration of treatment, by considering the patients' initial clinical status and the levels of improvement and rehabilitation considered achievable. [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <getinfo@haworthpressinc.com> Website: <<http://www.HaworthPress.com>> 2002 by The Haworth Press, Inc. All rights reserved.]

**KEYWORDS.** Brain injury, fingertip temperature, initial symptom loads, number of sessions, math models, targeted rehabilitation rates, EEG biofeedback

## INTRODUCTION

The importance of computerized EEG techniques has been addressed for both the evaluation and the long-term management and rehabilitation of patients with mild head injuries (Johnstone & Thatcher, 1991). The technique currently called NeuroBioFeedback (NBF) consists of voluntary regulation of brain activity, managed under continuous control by computer-assisted electroencephalography (c-a EEG). Applications of this technique in various forms have been reported for a wide range of injury and diseases (Shapiro, 1979; Rothberg & Surwit, 1981; Hatch & Riley, 1985). However, except for a study relating the number of sessions to the severity of seizures (Andrew & Schonfeld, 1992) and a report of the number of sessions required for clearing ADHD symptoms (Ramos, 1998), little if anything is known about the precise duration of treatment needed for more or less complete rehabilitation of

patients with various levels of injury. Theoretical work shows that NBF founded on the brain's faculty of anticipatory mental imaging predicts that the duration of treatments should be a function of initial loads of symptoms and of rehabilitation rates (Bounias, 2001). Therefore, the goal of the present study was to examine how clinical parameters could provide an objective basis for the mathematical assessment of the duration of treatments. The present work is a preliminary evaluation, which opens the way for further research on the use of these methods.

## MATERIALS AND METHODS

### Evaluation of Patients' Clinical Status

In the clinical study of traumatic brain injury (TBI), patient status is evaluated with respect to symptom checklists, which are tracked for subjective improvement during the course of treatment (Hoffman et al., 1996) and evaluation of symptom improvement based on further therapy requirements (Lasko et al., 1998). In the present study, clinical data have been examined from a set of 27 patients with brain injury treated by NeuroBioFeedback (Laibow, Bounias, Stubblebine, & Sandground, 1996). A checklist of 48 clinical signs present in at least one of the patients has been established as a reference framework (Bounias, Laibow, Bonaly, & Stubblebine, 2001).

These signs and symptoms were shown to constitute six major classes of general syndromes, on both medical and statistical criteria. Membership of patient cases in five of these syndrome classes was computed as indicated in Table 1, along with the following other parameters:

For each patient ( $P_i$ ), the initial load of symptoms (SL%) was calculated as the frequency of clinical signs (CS) present post-injury at evaluation. A general index of symptom loading can be defined from a relation of the following type:

$$SL_i = 100 \times \frac{\sum_a (k_i \cdot S_i)_a}{\sum_a (k_o \cdot S_o)_a} \% \quad (1)$$

with (a) indexing the sequence of symptoms, ( $S_o$ ) basic symptoms, ( $S_i$ ) symptoms observed in patient (i), and ( $k_o$ ), ( $k_i$ ) the respective coefficients specifically applying eventually to the considered class of disorders ( $k_o \geq 1$ ), ( $k_i \geq 0$ ), when specific scales of evaluation are taken in consideration.

TABLE 1. Indices of Total Disorders (Symptom Load: SL%) and of Improvement (IMP%), Total Number of NeuroBioFeedback Sessions, Listed for Each Patient Quoted by Its Reference Number. Each Patient Number, and Classes of Major Clinical Symptom, as Defined at the Bottom of Table, Denoted as Q1 to Q6.

Patient ref. nr.	SL%	IMP%	Session nr.	Clinical class
2	40.4	89.5	17	(Q 5)
4	66.7	78.1	19	(Q 3)
5	34.0	87.5	40	(Q 3)
6	27.6	84.6	40	(Q 3)
7	21.3	70	40	(Q 5)
8	42.5	85	39	(Q 6a)
9	29.8	64.3	11	(Q 6b)
10	53.2	80	124	(Q 1)
11	48.9	78.3	12	(Q 3)
12	61.7	79.3	93	(Q 5)
13	36.1	94.1	69	(Q 3)
14	48.9	60.9	17	(Q 4)
15	55.3	88.5	93	(S 4)
16	59.6	85.7	179	(Q 3)
17	36.2	81.5	40	(Q 4)
18	27.6	92.3	47	(Q 3)
19	42.5	85	19	(Q 6a)
20	74.5	97.1	167	(Q 1)
21	65.9	100	148	(Q 3)
22	38.3	83.3	75	(Q 3)
23	17	Fuzzy *	24	(Q 6b)
24	29.8	07.1	41	(Q 1)
25	63.8	86.6	158	(Q 1)
26	57.4	77.8	188	(Q 1)
27	70.2	90.9	75	(Q 1)
28	72.3	82.3	111	(Q 1)
29	76.6	91.7	193	(Q 1)

Definitions of classes of syndromes of impaired functions:

Q 1 = Motor function (N = 8 patients)

Q 5 = Pain-related functions (N = 3)

Q 2 = Language function (N = 0)

Q 6 = Neuropsychiatrically quoted functions (N = 4),  
subdivided into: - Q 6a = physiological subtypes  
(N = 2); - Q 6b = emotional subtypes (N = 2)

Q 3 = Cognitive functions (N = 9)

Q 7 = Metabolic functions (N = 0).

Q 4 = Psychosocial functions (N = 3)

(\*) "Fuzzy" means that clearing off coefficients belongs to a [0,1] interval, due to indetermination factors (for patient 23, improvement claimed by the patient was disputed by his parents). This suggests a further introduction of fuzzy set theory in modelization of the assessment of patients' status.

Here, in the absence of particular specification, the coefficients ( $k$ ) have been adjusted to zero or one (i.e., finally for patient ( $i$ ), with  $CS_i$  the cardinal of  $S_i$ :  $SL = 100 \times [(CS_{i/pre-Tr})/48]$ ), while the remaining level of unresolved symptoms is:  $RS = 100 \times [(CS_{i/post-Tr})/48]$ .

Equation (1) applied to symptoms still remaining post treatment provides parameter ( $RS\%$ ). Clinical symptoms were checked at each session, through neurophysiological and psychiatric examination of patients, both individually and by conferring with the patient's family. The improvement rate ( $IMP\%$ ) was calculated from the remaining (unresolved) symptoms ( $RS\%$ ) post-treatment, that is:

$$IMP\% = [(SS_i - RS/CS_i)] \times 100 \quad (2)$$

Taking patient four as an example, 32 signs and symptoms were recorded before treatment and seven remained at the end of treatment. Thus, from relation (1) with  $k = 0$  for symptoms not represented and  $k = 1$  for symptoms recorded without particular weighting, one gets:  $\Sigma_a(k_i \cdot S_i)_a = [16 \times (0) + 32 \times (1)] = 32$ , and  $\Sigma_a(k_o \cdot S_o)_a = 48 \times (1) = 48$ , with  $SL\% = (32/48) \times 100 = 66.7\%$ . Then,  $IMP\% = ((32 - 7)/32) \times 100 = 78.1\%$ .

### Electroencephalographic Procedures

A two channel EEG was performed using Capscan 880 or Prism V and Lexicor NRS-24 apparatus, combined with tones (through headphones) and visual (via video display) feedback of brain activity changes. Following a diagnostic session, thresholds were assigned for either inhibition (generally between 2.7 and 8 Hz, and EMG: 70-90 Hz) or reward (i.e., activation generally between 9.5 and 18 Hz). Raw data were subjected to Fourier transforms and converted into power spectra for the assessment of evolution of brain activity during the course of treatments. Protocols were as previously described (Laibow, Stubblebine, Sandground, & Bounias, 2001a) with Cz position adopted for each of these patients but two hemispherectomized cases.

## RESULTS

The two major parameters involved in individual patient's clinical status are: (a) the initial severity of the injury as assessed by the index of

symptom load before treatment, and (b) the level of improvement finally reached at the end of treatment. These two factors will be considered successively. The first one acts as a predetermined condition, while the second represents a goal that can be reached.

Decisions of treatment termination were not made solely by the medical staff since patients' employers, insurance companies and families were also involved. Thus, termination could be decided by third party payers in contrast with the advice of the medical team that further improvement could have been achieved. Other possibilities such as an assessment of cleared vs. remaining symptoms at an intermediate step may not be founded on homogeneous parameters for various patients, even belonging to the same clinical class (this point will be reviewed in the Discussion section). Therefore, the patients' status at the end of treatment was the final parameter.

#### Correlation Between Session Number and Initial Symptom Load

The study was performed comparatively from individual cases and from clinical classes. The main features are summarized here, while detailed calculations are given in the Appendix. The data illustrated in Figure 1 show that in both cases the phenomenon could be represented by a linear model, with an averaged equation of the following form:

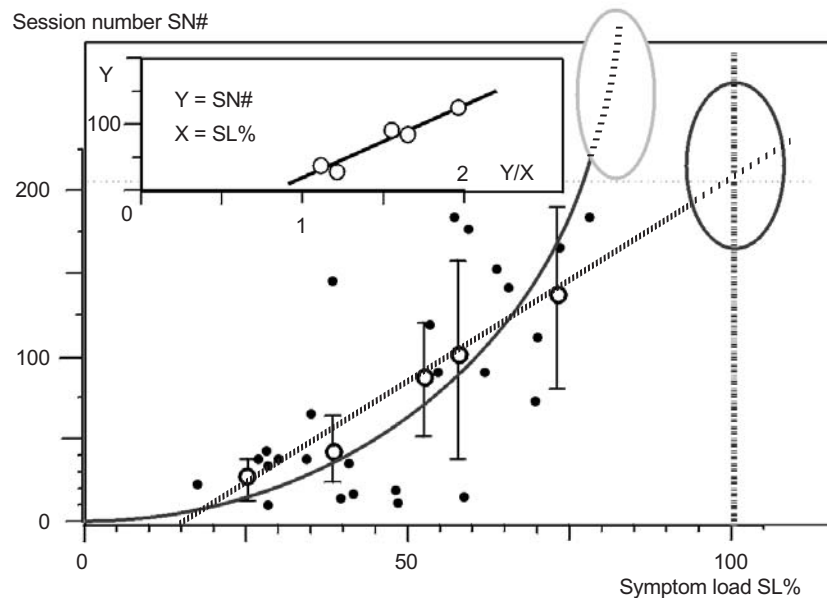
$$\text{SN\#} = (37.0 \pm 7.0) + (2.4 \pm 0.4) \times \text{SL\%} \quad (3)$$

(i.e.,  $y = a + b \times x$ )

For the entire set of patients, the calculated number of sessions (SN#) required for an average percentage of improvement  $\text{IMP\%} = 77.8 \pm 23.6\%$  with an average initial symptom load  $\text{SL\%} = 48.3 \pm 17.2\%$  ( $N = 27$  patients), would consistently attain 78.9 sessions back from the equation, corresponding to an average 78.4 sessions actually performed. The above equation gives an expected maximum number of sessions  $\text{SN\#}_{\text{max}}$  ranging from 166 to 266 sessions for  $\text{SL\%} = 100\%$ , for an improvement rate of 78 percent to 83 percent, regardless of specific scales and not considering the relative importance of particular symptoms.

Table 2 provides the class-related values of all parameters. It is interesting to note that the curve may suggest an alternative hypothesis of a hyperbolic response. This interpretation is supported by the correct linearization of the responses by transformation of the hypothetic hyperbole equation into a linear form (calculations given in the Appen-

FIGURE 1. General relationship between session number (SN#) and the initial symptom load (SL%) for a 78% improvement rate. Filled circles (●) denote individual cases; empty circles (○) denote the averaged session numbers ( $\pm$ SD) for a set of five classes of initial symptom load (i.e., 10-30% [N = 5]; 30-50% [N = 7]; 50-60% [N = 5]; 60%-70% [N = 4]; 70-89% [N = 4]). The inner frame shows the Eadie-Hanes plot whose linearity supports the hyperbolic hypothesis. Elliptic frames indicate extrapolation areas.



dix), as shown by the inner frame of Figure 1. In this case, there would be no theoretical upper boundary to the needed number of sessions for the maximum initial symptom load  $SL_{\max} = 100\%$ .

However, experimental values of SN# averaged for each class were not statistically different from the corresponding theoretical points situated on the regression line (see details in the Appendix). Therefore, the linearity of the response could not be rejected: this means that further data analysis is required before the question is completely clarified.

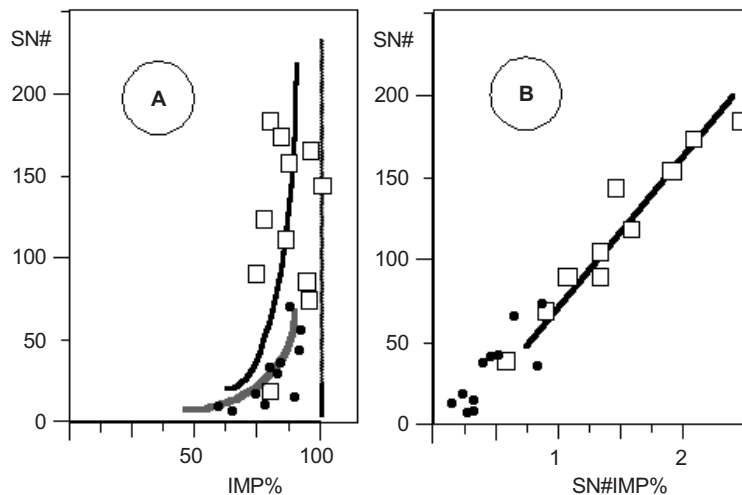
#### Correlation Between the Number of Sessions and the Rate of Improvement

Figures 2 A and 2 B show two cases of relationships between the percentage of improvement reached and the number of sessions applied for

TABLE 2. Centered Classes of Symptom Load (SL#), Corresponding Values of Session Number (SN%), Applied and Improvement Rates (IMP%) Obtained. Number of Patient Cases (N).

SL# classes	Center $\pm$ SD	(N)	SN% $\pm$ SD	IMP% $\pm$ SD
10-30	25.1 $\pm$ 5.7	5	31.2 $\pm$ 13.3	73.0 $\pm$ 10.4
30-50	37.7 $\pm$ 4.6	7	43.7 $\pm$ 22.3	88.1 $\pm$ 4.0
50-60	54.7 $\pm$ 3.8	5	93.3 $\pm$ 73.6	78.9 $\pm$ 8.9
60-70	64.9 $\pm$ 2.7	4	104.5 $\pm$ 63.8	86.0 $\pm$ 10.1
70-80	73.4 $\pm$ 2.8	4	136.5 $\pm$ 53.4	90.5 $\pm$ 6.1
Average	51.2 $\pm$ 19.7		81.8 $\pm$ 43.7	83.3 $\pm$ 7.2

FIGURE 2. A. Direct plots of session numbers (SN# in ordinate) versus the rates of improvements (IMP% in abscissa), for two classes average initial symptom load. (●): Class SL = 25-50% (N = 10) (rectangles): Class SL = 50-75% (N = 9). Hyperbolic responses are suggested by the shape of the curves in both cases:  $y = \alpha \cdot x / (IMP_{max} - x)$ . B. Transformation of the direct plots of session numbers (y) versus improvement rates (x), under the hypothesis of a hyperbolic response:  $y = IMP_{max} \cdot (Y/x) - \alpha$ . The two classes of initial symptom load exhibit complementarity, consistent with the relation shown on Figure 1: Higher symptom loads demand higher session numbers for a given rehabilitation rate.



two classes of initial symptom load (classes 25 to 50 percent and 50 to 75 percent). These data come from a population of various patients with brain injury including males and females of various ages. Despite these scattered conditions, the results significantly demonstrate that the number of sessions is statistically determined for a given initial load of symptoms by the percentage of improvement taken as a goal.

Let  $y$  = session number (SN#) and  $x$  = improvement rate (IMP%). Then, since  $y = 0$  for  $x = 0$  (i.e., no improvement was noted before treatment in the observed cases) and the maximum rate of improvement is  $IMP_{\max} \leq 100\%$ , the system can be represented by the following equation:

$$y = \alpha \cdot x / (IMP_{\max} - x) \quad (4)$$

Parameters can be calculated again by using the Hanes transform (5), which allows fitting by linear regression:

$$y = IMP_{\max} \cdot (y/x) - \alpha \quad (5)$$

(i) In the first class of initial symptom load (i.e., class 25 to 50 percent concussion, without stroke), the correlation is significant even before transformation:  $r = 0.780$  ( $t = 3.5$ ;  $p = 0.0078$ ). This class exhibits the following average parameters: symptom load:  $SL = 38.5 \pm 8.5\%$ ; session number:  $SN\# = 33.4 \pm 18.4$  sessions; improvement rate:  $IMP = 81.3 \pm 10.9\%$ .

Fitting the data to equation (5) gave the following regression/correlation parameters:  $r = 0.9898$  ( $t = 19.6$ ;  $p = 0.2 \times 10^{-6}$ );  $a = 5.7 \pm 2.0$ ;  $IMP_{\max} = 99.3 \pm 5.0\%$ . The experimentally determined limit of the improvement rate is therefore statistically equal to the theoretical level of 100%.

(ii) The second class of initial symptom load (i.e., class 50 to 75 percent, including stroke), also exhibit a significant correlation before transformation:  $r = 0.659$  ( $t = 2.48$ ;  $p = 0.04$ ). This class exhibits the following average parameters: symptom load:  $SL = 63.5 \pm 7.9\%$ ; session number:  $SN\# = 127.5 \pm 137.0$  sessions; improvement rate:  $IMP = 85.5 \pm 9.1\%$ . Fitting again the data to equation (5) gave the following values for regression/correlation parameters:  $r = 0.9486$  ( $t = 7.9$ ;  $p = 0.0001$ );  $a = 18.2 \pm 18.2$  (i.e., the curve correctly reaches origin);  $IMP_{\max} = 98.6 \pm 12.4\%$ .

The experimentally determined limit of the improvement rate is therefore again statistically comparable to the theoretical level of 100%. Thus, both responses can be gathered into a single one:

$$\text{SN\#} = (12 \pm 12) \times \text{IMP\%} / [(99 \pm 9) - \text{IMP\%}] \quad (6)$$

#### A Case-Observation Connecting the Number of Sessions to Finger Temperature in Patients with Stroke

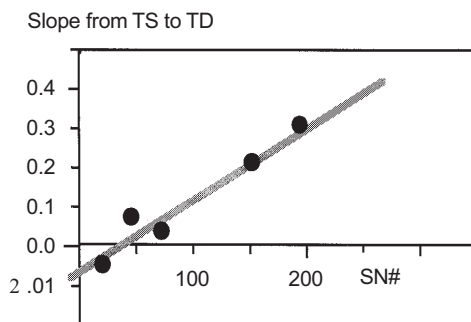
For a subset of five patients exhibiting vascular brain injury from stroke, we have observed a significant correlation between the number of treatment sessions and the responsiveness of finger temperature (Figure 3).

Let the difference  $D = (b - b_0)$  with  $(b)$  the regression slope of  $\text{FT}^\circ$  versus time during any 30-minute session,  $b_0$  at treatment start and  $b_n$  after  $(n)$  sessions. Figure 3 illustrates these results, with a calculated correlation:  $r = 0.972$  ( $t = 7.16$ ;  $p < 0.01$ ), and a slope of  $(1.82 \pm 0.25) \times 10^{-2} \text{ }^\circ\text{F} \times \text{min}^{-1} \times \text{session}^{-1}$ .

### DISCUSSION AND CONCLUSION

Taking these sets of data together, it can first be concluded that the number of sessions required is an increasing function of at least two

FIGURE 3. The increase of finger temperature ( $\text{FT}^\circ$ ) responsiveness (slopes in  $10^{-2} \text{ }^\circ\text{F} \times \text{min}^{-2} \times \text{session}^{-2}$ ) to NeuroBioFeedback, from start (TS) to discontinuation (TD) of NBF treatments, as a function of treatment duration (session number: SN#) in a subset of five patients with vascular brain injury (stroke). (Patients Nr. 23; 24; 25; 26; 27).



variables, namely the initial symptom load and the rate of improvement, which can be reached after a defined number of sessions using Cz electrode placement for all patients (except for the hemispherectomy patient where C3 was used). Using these parameters as predictive values of the number of sessions likely to be required in defined conditions is worthwhile examining carefully. The initial symptom load can take numerical values actually ranging from zero (subjects exhibiting none of the considered symptoms, although not necessarily healthy ones) to 100 percent. Although no ambiguity emerges at this level, the shape of the response of treatment duration (SN#) as a function of (SL) will be a critical factor in the evaluation of the number of sessions that will be theoretically needed to reach a given level of improvement. This will also condition any standardization of prediction procedures. Regarding the case of ADD/ADHD as a major symptom it cleared with 20 sessions (Ramos, 1998) while as a sign associated with brain injury, it cleared after an average  $47 \pm 28$  sessions (four cases) and remained in one stroke case after 158 sessions.

#### Influence of Initial Symptom Load

Finite numbers are always to be expected from the linear interpretation, which will thus give the lower boundary of predictive numerical values. From the general correlation obtained for 27 individual cases, a 100% initial load would involve a required number of sessions  $SN_{100\#} = 216 \pm 50$ , while the curve obtained with five classes would give an alternative  $SN_{100\#} = 190 \pm 20$  sessions, both for an average improvement rate  $IMP = 79 \pm 15\%$ . Note that in practice the maximum number actually used was  $SN\# = 193$  for a 91.7% improvement at a 76.6% initial load. Thus, clinical practice fairly matches the values predicted by the model. The hyperbolic model will provide either higher finite values, if the modeled limit ( $SL_{max}$ ) is found higher than 100%, or infinite values if the latter limit is  $SL_{max} \leq 100\%$ . In the present case, the predicted values would be within the range of  $531 \pm 321$  sessions (i.e., an estimated least upper bound:  $SN\# = 210$  sessions).

In the case of patients with uncontrolled seizures, the frequency of seizures at the start of treatment appeared as an index of the further possibility of control. This parameter was shown to be statistically related to the number of sessions necessary for achieving control, in contrast with the number of years seizures had been uncontrolled (Andrew & Schonfeld, 1992). This provides an alternative case of specific load con-

cerning one single symptom, while the frequency of seizures also represented a specific criterion for evaluation of the improvement rate. In contrast, our evaluation concerns a whole set of observable clinical symptoms rather than a single symptom.

#### Influence of the Rate of Improvement

The same types of models can be encountered here, with either a linear or a hyperbolic response, which would respectively mean that a complete rehabilitation ( $IMP = 100\%$ ) could be obtained following a theoretically finite or infinite number of sessions. Here, the data support the hypothesis of a hyperbolic response as far as the significance of correlations was much higher for the Hanes plots. The statistical model values of  $IMP_{max}$  (99.3% and 98.6%) were calculated for two classes of load, respectively, centered about the average values  $SL = 38.5 \pm 8.5\%$  and  $SL = 63.5 \pm 7.9\%$ . For an expected improvement goal of 90%, the numbers of sessions theoretically required would thus be, respectively,  $SN_{38.5\#} = 55$ , and  $SN_{63.5\#} = 190$ .

The uncertainty about the decision of treatment conclusion deserves some precautions, since in turn this uncertainty falls on the measured values of the improvement rate,  $IMP\%$ . One could for instance expect a standardized improvement rate (e.g.,  $IMP_o$ ) to be taken as a common basis for every patient. However, this might be both difficult and unwarranted for several reasons:

1. Since working with patients in regular medical practice is not the same as working in research laboratory conditions, there is no guarantee that stage  $IMP_o$  will always be reached. This would introduce biases in data interpretation by precluding statistical assessment of lack of efficacy.
2. For ethical reasons, one cannot fix an  $IMP_o$  that could eventually result in some limitation of the expectancy of a patient.
3. Assuming that full assessments of the patients' status could always be performed at intermediate steps of treatments (which may not be practically possible), since the order of symptoms clearing, as well as the associations of symptoms appearing or disappearing in the same time may differ from case to case, there is no standard stage which could be defined at present.
4. As long as the linearity of responses is not demonstrated for each case, an intermediate assessment could introduce false interpretations.

5. A correct assessment of an intermediate stage used as a standard would imply that the specific injury is both qualitatively and quantitatively known, which may not be the case, particularly when a long time elapsed between the initial trauma and the initiation of treatment. Recovery can occur after injury to the central nervous system, even if a small number of neurons remain functional as “the minimal residual structure” (Sabel, 1997). Hence, from qualitatively similar initial loads of symptoms, similar rehabilitation levels could be reached via specific treatment durations.

The present study therefore represents a provisional assessment pragmatically based on a reality observed in particular conditions. While it cannot be extrapolated to other conditions, this study raises the question and opens the way to further progress in accurate prediction of treatment duration.

#### Observations About Finger Temperature

Fingertip temperature ( $FT^\circ$ ) is related to vascular relaxation, mediated by a change in sympathetic/parasympathetic balance.  $FT^\circ$  has been reported to increase during NBF treatments (Gillespie & Peck, 1980), and improvement has been reported in the case of Raynaud’s phenomenon (Sappington & Fiorito, 1985). Here we show that in the particular case of stroke, the responsiveness of finger temperature increases with the number of treatment sessions. This provides an indication that the treatment is correctly progressing. Further research is needed to evaluate the boundaries of this phenomenon, which could also contribute to rationalization of the control of the duration of treatments by using a simple method.

In conclusion, the data obtained from a set of patients with brain injury have allowed a first modelization of session number as a function of both initial symptom load and expected improvement level. The latter can be related to other clinical and physiological parameters, and further studies should aim to compare the corresponding features in patients suffering from other kinds of injuries or diseases. We hope that this kind of work would provide an algebraic rationale for the pre-evaluation of the number of sessions that could be expected from the clinical status of a given patient. Such results, adding to the predictive index already raised by Andrew and Schonfeld (1992) could further support the goal of providing a scientific rationale for the clinical application of EEG-NeuroBioFeedback as pointed out in 1995 by Mulholland.

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## APPENDIX

### Mapping of Session Number to Symptom Load

#### Study from Individual Cases

The general relationship illustrated by Figure 1 corresponds to an average percentage of improvement  $IMP\% = 77.8 \pm 23.6\%$  with an average initial symptom load  $SL\% = 48.3 \pm 17.2\%$  ( $N = 27$  patients).

A significant correlation was observed between the index of total disorders and the number of sessions needed for clearing the major primary symptoms. The corresponding parameters are the following in natural coordinates:

$$r = 0.749 \text{ (} t = 5.4; p = 2 \times 10^{-5}\text{); } a = -43.6; b = 2.60 \pm 0.48 \text{ (} N = 25\text{)}$$

that is the equation:

$$SN\# = -44 + (2.6 \pm 0.5) \cdot SL\% \quad (1)$$

This gives an expected  $SN_{\#max}$  ranging for the given improvement rate from 166 to 266 sessions for  $SL\% = 100\%$ , regardless to specific scales and not considering the relative importance of particular symptoms.

#### Study from Classes of Initial Symptoms

The data allowed five classes to be characterized, ranging from 17% to 77% of the total number of clinical signs. Table 2 provides the corresponding values of the various parameters.

By linear regression, the following values are obtained:

$$r = 0.985 \text{ (} t = 9.89; p = 0.002\text{); } a = -30.0; b = 2.2 \pm 0.22,$$

that is the equation:

$$y = -30 + (2.2 \pm 0.2) \cdot x \quad (2)$$

with  $y$  = session number ( $SN\#$ ) and  $x$  = initial symptom load ( $SL\%$ ).

This equation would involve a limit to the needed number of sessions at 100% symptom load, (i.e.,  $SN_{\#max}$  ranging from 170 to 210 not statistically different from the previous one), still regardless to specific scales and still not considering the relative importance of particular symptoms (see Figure 1).

From equation (1) and (2), the upper value of session numbers, for an average improvement rate  $IMP = 83 \pm 7\%$  would thus be estimated  $SN_{\#max} = 201 \pm 15$  sessions.

Linearity needs be tested on class 30-50, as seen on Figure 1, by comparing the experimental value to the value calculated from the regression equation, namely for  $x =$

37.7,  $y = 52.2$ . The test gives  $t = 1.01$ , which leaves significance of the difference below null hypothesis. Thus, a straight-line model remains so far acceptable.

However, this conclusion is at least partly due to the large variability of clinical parameters in as many different patients. The class-related shape of the sequence of points (see Figure 1) suggests that the actual shape could be hyperbolic, with a needed number of sessions much higher for  $SL\% = 100\%$ .

#### Testing for an Hyperbolic Model

In this case, the equation would be of the following type:

$$Y = \alpha \cdot x / (L_{\max} - x) \quad (3)$$

with  $(\alpha)$  scalar coefficient and  $(L_{\max})$  the maximum value of  $SL\%$ .

By transforming equation (3) in a similar way as the Eadie-Hanes plot of enzymic equations, one obtains the following linear form:

$$y = L_{\max} \cdot (y/x) - \alpha \quad (4)$$

Here, the least rectangle fitting is more appropriate than the least square one, since both  $y$  and  $x$  contain a dependent variable. However, with high values of correlation coefficients, the results do not differ substantially. The regression calculation allows parameters  $(\alpha)$  and  $(L_{\max})$  to be calculated:  $r = 0.960$  ( $0.005 < p < 0.01$ ),  $\alpha = 128.0$ , and  $L_{\max} = 139 \pm 25\%$ , a value not statistically different from  $100\%$  at  $p = 0.02$ .

No improvement of the correlation is obtained upon deletion of lower points, which is consistent with an exponential coefficient on  $(x)$  equal to unity.

A hyperbolic function could thus be representative of the phenomenon, and from equation (3) there would be no upper boundary to the needed number of sessions for the maximum initial symptom load  $SL_{\max} = 100\%$ .

This essentially emphasizes that the heavier the initial load of clinical signs and symptoms affecting the patient, the greater the number of sessions required for rehabilitation, eventually in a more than just proportional way.