EEG-NeuroBioFeedback Treatment of Patients with Brain Injury: Part 1: Typological Classification of Clinical Syndromes

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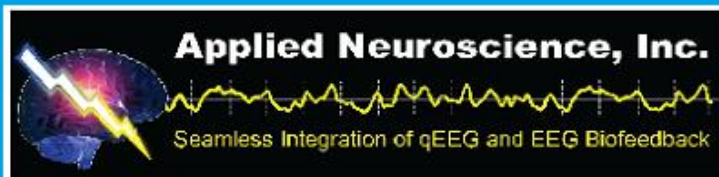
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ABSTRACT. *Background.* A group of 27 patients with brain injury were treated by electroencephalographic (EEG) NeuroBioFeedback under drug-free conditions. They were studied for distribution in classes of major syndromes for evaluation of treatment efficiency and rehabilitation rates with respect to associated EEG and other physiological changes.

Methods. A total of 48 clinical symptoms were listed, each present in at least one patient. Classes of clinical signs have been computed using both medical and statistical criteria. Claimed and presented chief complaints, secondary complaints and all associated signs were incorporated in multivariate analysis.

Results. Substantial intersection of medical and statistical distributions was observed. This provided a classification of symptoms into six

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classes representing the following syndromes of impaired functions: Q1 = motor; Q2 = language; Q3 = cognitive; Q4 = psychosocial; Q5 = pain-related; Q6(a & b) = neuropsychiatric; Q7 = metabolic.

Membership of a patient in a defined clinical class was based on a numerical index computed from: (a) a weighted coefficient for the patient's chief and secondary complaints, and (b) an index for both symptoms represented in the class and symptoms not represented in the class. Patients were unambiguously distributed in all classes except Q7.

Conclusions. Using a non-selected group of head injured patients, this work provides a rationale for the membership of each patient in a set of classes of syndromes determined by the whole set of clinical signs specifically exhibited by this group of patients. Class-average rehabilitation rates ranged from 59% up to 87% following an average 23 to 132 treatment sessions, depending on syndromes.

INTRODUCTION

NeuroBioFeedback (NBF) as a non-invasive treatment method using computer-assisted electroencephalography (EEG) for the voluntary regulation of brain activity was used in a group of 27 patients with brain injury to evaluate the efficacy of NBF in terms of clinical results (Laibow, Bounias, Stubblebine, & Sandground, 1996a). Therefore, it was interesting, from a clinical perspective, to define groups of patients who could be considered as belonging to clearly characterized clinical classes and thus to derive: (a) means for identification of clinical classes, and (b) the criteria for membership in each of these clinical classes.

Although standardized procedures are available for the diagnosis of most neuropsychological diseases, their systematic use poses problems. For example, Barkley (1991) showed, on the basis of a 14-item scale, that such laboratory measures are less efficient than observations and rating in a natural setting. Trommer, Hoeppner, and Armstrong (1988) previously reported that standard tests could provide both false positive

and false negative responses. This problem is compounded by the fact that EEG alterations can be found where no clinical signs are detectable (Jonckman, De Weerd, Poortvliet, Veldhuizen, & Emmen, 1992) so the type of lesion or functional impairment must be assessed clinically as accurately as possible prior to examination of associated EEG changes, as done by Snodgrass, Tsuburaya, and Ajmone-Marsan (1989). Diagnostic standardization is not easily achieved since some of the characteristic symptoms of a given disease may be absent while others are perceived as expected (Brown, Cathala, Castaigne, & Gajdusek, 1986).

Signs and symptoms characteristic of a given disease may be associated with other clinical indicators in the absence of a direct connection with the primary disease. Furthermore, materials available for medical practice do not necessarily provide the same possibilities as experimental research. These factors render automated classification hazardous, and the validity of neurobehavioral evaluations has been questioned even for forensic purposes (Lees-Haley, 1995). Therefore, it is essentially interesting clinically to define syndromes of clustered associated signs and symptoms presented by a given group of patients, which may assist both in diagnosis and more efficient treatment of head injured patients. Prior to our examination of the development of clinical status during the course of NBF treatment, the primary difficulty lay in determining how the cases could be subdivided into well-defined clinical categories, and how patient cases could then be objectively distributed among these categories.

The aim of this paper is to describe one solution to this problem as applied to the 27 cases presented here. This introductory study will serve as a basis for further statistical studies on associated changes in EEG and other physiological parameters.

METHOD

Initial Assessment of Patient's Clinical Status

All 27 participants in this study were outpatients, who came from various hospital centers (where they were first admitted for vascular, traumatic or combined injury) and from home care settings. Evaluation started with a review of available medical, psychiatric and rehabilitation records (including consultation with referring and/or treating physicians, care workers and staff members of programs and institutions).

Extensive medical, neuropsychological and psychosocial evaluation and history was conducted by the treating physicians.

Qualified physicians did neurological examination and neuropsychological assessment, and a Continuous Performance Test was administered (i.e., the Tests Of Variables of Attention or TOVA). Each patient was evaluated in the same manner using the same instruments, equipment and standard collection procedures. This protocol allowed a set of 48 symptoms present at least once in at least one patient to be identified. These symptoms are listed in Table 1 according to medical criteria. Since brain injury can be subdivided into acquired injury (i.e., apparently endogenous origin, such as stroke) and traumatic injury (i.e., exogenous origin, such as accidents or attack), the particular typology of injuries affecting the group of patients is given in Appendix 1, Table B. A set of pre-traumatic symptoms was also identified and listed in Table C of Appendix 1.

The pain-related class (F5) focuses on chronic pain rather than acute pain. The latter could be mediated by thalamic misinterpretation of proprioceptive and kinesthetic signs from afflicted areas (depending on thresholds of neuronal activation) and other neurologically central areas of dysfunction. It could thus arguably pertain to other classes. Class F6 consists of functions likely impaired because of the injury. Depending on specific populations of patients and on particular purposes, many alternative interpretations could be used in future studies with a similar protocol.

No control groups were involved since head injured patients without the signs and symptoms listed in Table 1 were not available for treatment. Thus, each patient served as his own control from the beginning to the end of treatment.

The clinical status of each patient was established for chief and secondary complaints (collected for further attribution of a specific weight in the final distribution of patients in clinical classes) and for a number of associated signs, symptoms, disorders and complaints related by the patient, and/or observed by care givers, or attending physicians.

The many parameters studied on a small number of cases is a characteristic of a clinical setting, in contrast with the large number of observations made on a few cases in an experimental setting.

Chief complaints upon evaluation varied and included anxiety, attention deficit disorder (with or without hyperactivity), cognitive dysfunction (including memory loss, inattention, impaired concentration and confusion), conduct disorders (with and without psychopathic tendencies), depression, movement disorders (including paresis, paralysis,

TABLE 1. The Total Set of Post-Traumatic Clinical Symptoms as Classified for Medical Classes of Altered Functions (F1 to F7). Reference Numbers Attributed to Individual Symptoms Reflect the Chronology of Their Appearance in the Original Files. The Total Number of Observed Cases Is T Given Against the Number of Improved Ones (Imp.) Following Treatments. (S) = Syndrome.

Nr. Symptoms	Total	(Imp.)	Nr. Symptoms	Total	(Imp.)
Class F1. Motor functions					
1. Hemiparesis	8	(7)	2. Hemiplegia	8	(7)
5. Decreased tone	5	(5)	6. Increased tone	6	(6)
7. Tremor	4	(4)	8. Paresis	7	(6)
9. Paralysis	7	(6)	10. Discoordination	25	(24)
21. Muscular weakness	10	(8)	37. Limitation of movements	10	(9)
Class F2. Language					
3. Expressive aphasia	7	(7)	4. Receptive aphasia	6	(6)
43. Pervasive aphasia	17	(15)			
Class F3. Cognitive functions					
11. Memory loss	20	(19)	23. Inattention	16	(16)
25. Disorientation	11	(11)	34. Irritability	26	(22)
39. Concentration deficit	19	(18)	42. Cognitive deficit	21	(19)
47. ADD ± HD*	6	(4)	48. Disorientation to time, place and person	10	(10)
Class F4. Psychosocial disorders					
13. Impulsivity	13	(13)	14. Violence	8	(8)
15. Conduct disorders	9	(9)	38. Substance abuse	17	(13)
Class F5. Pain-related disorders					
26. Neuralgia	24	(23)	27. Headaches	13	(11)
Class F6. Neuropsychiatric impairments					
12. Insomnia	17	(15)	16. Lack of insight	17	(9)
17. Intrusive thoughts	19	(18)	22. Vertigo	24	(6)
24. Paranoia	7	(7)	35. Loss of libido	23	(19)
36. Psychic numbing	17	(9)	40. Nightmares	17	(13)
41. Depression	21	(20)	44. Emotional liability	29	(19)
45. Anxiety	15	(15)	46. Unconscious at injury	11	(0)
Class F7. Metabolic disorders					
18. Malaise	22	(21)	19. Fatigue	22	(21)
20. Lethargy	14	(13)	28. Irritable Bowel Syndrome	6	(5)
29. Weight loss	8	(2)	30. Weight gain	6	(3)
31. Excess appetite	8	(7)	32. Poor appetite	4	(3)
33. Temp. disregulation	17	(17)			

(*) evaluation upon TOVA test.

hemiparesis, hemiplegia, flaccidity and spasticity), pain (including neuralgia and headache) and visual loss. Secondary or associated complaints included those listed above plus fatigue, substance abuse, aphasia, eating and appetite disorders and limitation of movements. Chief and secondary complaints ranged from seriously problematic to totally disabling. The presence or absence of a given sign has been quoted on a

zero to three reference scale, as previously proposed by Achenbach and Edelbrock (1983) from a list of 113 items. The full list of signs and symptoms is given in Appendix 1, Table A for each patient.

Treatments and Evaluation of Rehabilitation Rates

Neither psychoactive medication, antihypertensive, analgesic nor antiseizure medications were prescribed during NBF treatment. Despite repeated urging to the contrary by the physician at the treating facility, patients generally discontinued their medications at or near the start of NBF treatment. The types of medication were: antispasmodic, anti-seizure, antidepressants, anxiolytics, steroids, nonsteroidal anti-inflammatory, bronchodilators, antihypertensives, vasopressors, laxatives and hypnotics.

NBF Protocols

NFB protocols will be described in a subsequent paper in detail.

Calculation of Rehabilitation Rates

The load of symptoms $\mathcal{L}$ which were observable initially ($\mathcal{L}_o$) and at discontinuation of treatments ($\mathcal{L}_e$) has been calculated as the proportion of symptoms exhibited by a patient (P_i), that is:

$$\mathcal{L}_a = N(S(P_{i,a})_a)_{i \in [1, N(P)]} / N(S) \tag{1}$$

with N(P) the total number of patients and N(S) the total number of symptoms affecting the whole of the set of patients (a = weighting coefficient e $\geq$ 0).

The rehabilitation rate (RR) was then evaluated by computing the number of improved symptoms in a binary manner, and calculating the following ratio:

$$RR = 100((\mathcal{L}_o - \mathcal{L}_e)/\mathcal{L}_o) \tag{2}$$

Improvement was considered positive when claimed by patient and confirmed by physicians, caregivers (including patient's family) and considered negative when this unanimity was not met. Finally, these individual rehabilitation rates were averaged for each characterized cluster of patients.

Construction of Patient's Indices of Membership

Mode of Elaboration of a Specific Classification

The original classification by medical classes (noted F) is a rather global one; therefore, it does not necessarily reflect particular features and interactions which can be observed between signs and symptoms within the group of patients. A statistical classification based on patients' specific symptoms has been performed and the results used for refining the original medical classification into a final form.

For the setting of final classification (Q), statistical clusters (C) were identified by multivariate analysis. Then, clusters exhibiting the maximum common parts (or intersections) with the initial medical classes were selected, and their common symptoms taken as founding representatives for new classes. The remaining symptoms were then distributed according to medical justifications in these final classes. Such tentative classification may be adjusted according to the goals of each study. It then, in turn, serves as a reference for the application of numerical indices allowing the best fit for each patient to the appropriate class.

Mode of Calculation of Patient's Indices

The principle of calculations is summarized as follows on some examples, while a formal description is given in Appendix 2.

Patients were assigned a score composed of two indices. The first one, $\Xi_k(P_i)$ for patient P_i with regard to class Q_k, denotes the matching of syndrome classes with complaints, as subdivided into major and secondary categories. For example, patient P_{29} exhibits signs 1-2 as chief complaint ($ncc_{29} = 2$, with weight $e = 3$) and sign 43 as secondary complaint ($nsc_{29} = 1$, with weight $e = 2$), out of a total $NS(P_{29}) = 36$ signs. Thus, the maximum index for any given class is $W_{max}(P_i) = (2 \times 3) + (1 \times 2) = 8$. With regard to any given class Q_k, the weighed numbers of chief and secondary complaints represented in this class for this patient ($W_k(P_i)$) divided by the maximum index provides the final index $\Xi_k(P_i)$. For example, class Q1 contains signs 1 and 2, but not 43: thus $W_k(P_i) = (2 \times 3) + (0 \times 2) = 6$, and finally $\Xi_1(P_{29}) = W_1(P_{29})/W \max(P_{29}) = 6/8 = 0.75$.

The second index $I_i(Q_k)$ allows each patient (P_i) to be given a numerical evaluation of the link of the set of all its associated signs with the set of signs defining each clinical class (Q_k). Continuing with an example of patient P_{29}, the number of signs exhibited by this patient and con-

tained in a given class (e.g., Q1) is denoted by Se: here, 10 signs of P_{29} out of 36 are represented in the list of the 10 signs constitutive of Q1. The direct representativeness to this class is thus Sr = 10/10 = 1.00. There remain 26 signs out of 36 not represented in Q1. Thus, the exclusion index is Se = 26/36 and the corresponding representativeness is (1 − Se).

These two probabilistic indices are combined into their product as I_{29} $(Q_1) = 1 \times (1 - 26/36) = 0.278$ (Figure 1). Running the same calculation for each class gives a distribution spectrum of specific values (e.g., here for Q1 to Q7):

$I_{29}(Q_1) = 0.278$; $I_{29}(Q_2) = 0.083$; $I_{29}(Q_3) = 0.170$; $I_{29}(Q_4) = 0.028$; $I_{29}(Q_5) = 0.014$; $I_{29}(Q_{6a}) = 0.0167$; $I_{29}(Q_{6b}) = 0.074$; $I_{29}(Q_7) = 0.278$.

Finally, the product of both of these indices gives a weighting value $A_{i,k}$ for putative membership of each patient (P_i) to each class (Q_k):

$$A_{i,k} = \Xi(P_i) \times I_i(Q_k) \tag{3}$$

Here one finds $A_{29,1} = \Xi_1(P_{29}) \times I_{29}(Q_1) = 0.75 \times 0.278 = 0.2085$.

The maximum value of $A_{i,x}$ determines the class x to which a patient (P_i) belongs.

RESULTS

Classification of Clinical Signs

The goal for a classification of the observed symptoms in suitable classes was to take into account both the basic medical meaning of the observed signs and the way these signs are actually clustered in statistical classes is a feature characteristic of the group of treated patients presented in this study. Figure 2 schematically illustrates the process.

Statistical Classes

A set of five principal cluster classes was computed by multivariate analysis. Table 2 indicates the distribution of symptoms among the five major statistical classes found.

FIGURE 1. The Simplest Rationale for a Calculation of Indices Allowing Membership of Patients to Be Attributed to Defined Clinical Classes.
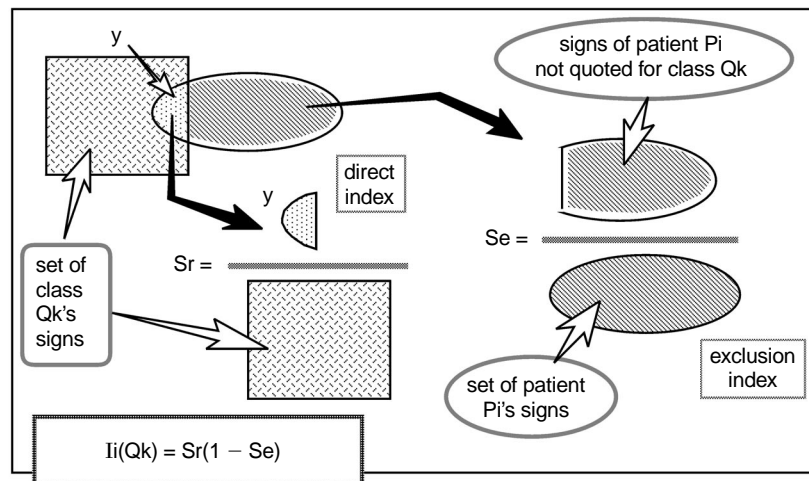
Intersection of Clinical Classes with Statistical Clusters

Common signs were examined between clinical and statistical distribution to refine the rationale of the classification. The following approaches were used. Taking the statistical clusters as reference, their largest intersection sets ($\cap$) with classes of altered functions contribute to redefining the foundation of new classes integrating both medical and statistical criteria: essentially, clusters introduce some subdivisions in, and may suggest some links between, medical classes. These results are presented as Table 3.

Regarding class F1 of impairment of motor functions, one subgroup of signs {5, 6, 8, 21, 37} was represented in C1, while a second one {1, 2, 7, 9} belonging to C2 medically contributes to the same syndrome. This class can be maintained as Q1 eventually composed of two subsets. The substantial overlapping observed for pairs (C1, F1) and (C1, F7) suggests that some sort of link might connect motor and metabolic disorders in those patient groups.

Syndrome F2 is entirely composed of the remaining subset of C2, and represents the syndrome of impairment of language functions: these signs will thus be kept together in a new class, Q2. That aphasia and part of the group of motor functions share a common statistical

FIGURE 2. Schematic Picture of the Principle of the Classification Method. Statistical Clustering Provides a Formal Justification to Further Grouping of Clinical Signs, so that the Final Result Reflects Both Medical and Statistical Relevance. Indices for Patient Membership as Illustrated in Figure 1 Are Detailed in Appendix 1.
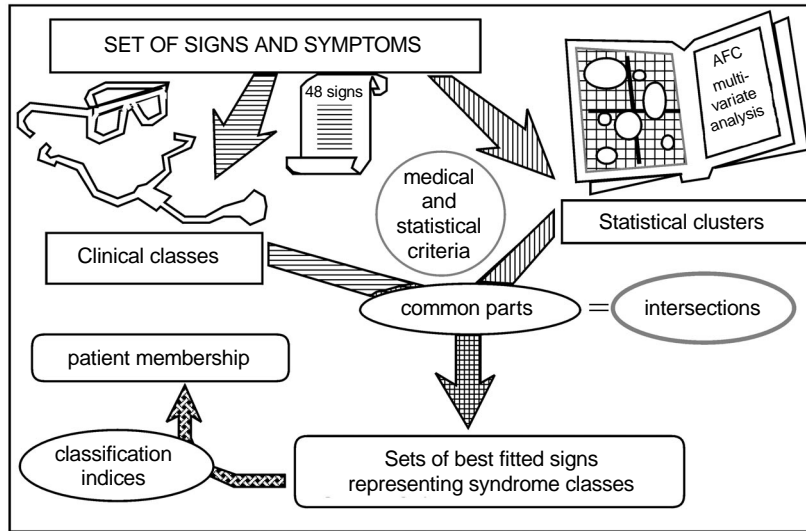
TABLE 2. Distribution of Clinical Symptoms in Statistically Clustered Classes by Multivariate Analysis.

Class N°	Symptoms N°	Nr.
C1	5-6-8-14-15-21-24-28-29-30-31-32-37-46-47-48	N = 16
C2	1-2-3-4-7-9-43	N = 7
C3	26-27	N = 2
C4	11-12-13-16-18-19-20-23-25-36-39-41-42-45	N = 14
C5	10-17-22-33-34-35-38-40-44	N = 9
		Total : SN = 48

cluster (C2) also calls attention to a possible link between these disorders. Class C3 specific of pain-related functions exactly matches with class F5: this will constitute a definitive class for pain-related syndrome, further denoted Q5.

For cognitive functions, the main group of signs {11, 23, 25, 39, 42} is gathered in C4, while two signs {47, 48} are in C1. The new class,

TABLE 3. Intersection of Clinical Classes with Statistical Clusters.

Intersecting classes	Intersections = common subsets of signs	Proportions of initial sets represented in the intersections
C1 ∩ F2 = C1 ∩ F4	= Ø	(empty intersections: full discrimination)
C1 ∩ F1	= {5,6,8,21,37}	= 50% of F1; 31.2% of C1
C1 ∩ F3	= {47,48}	= 25% of F3
C1 ∩ F4	= {14,15}	= 50% of F4
C1 ∩ F6	= {24,46}	= 16.7% of F6; 12.5% of C1
C1 ∩ F7	= {28,29,30,31,32}	= 55.5% of F7; 31.2% of C1
C2 ∩ F1	= {1,2,7,9}	= 40% of F1; 57.1% of C2
C2 ∩ F2	= {3,4,43}	= 100% of F2; 42.8% of C2
C3 ∩ F5	= {26,27} = C3 = F5	(i.e., 100% of C3) ; 100% of F5
C4 ∩ {F1, F2, F5}	= Ø	(empty intersection)
C4 ∩ F3	= {11,23,25,39,42}	= 62.5% of F3; 35.7% of C4
C4 ∩ F4	= {13}	= 25% of C4
C4 ∩ F6	= {12,16,36,41,45}	= 41.7% of F6; 35.7% of C4
C4 ∩ F7	= {18,19,20}	= 33.3% of F7; 21.7% of C4
C5 ∩ {F2, F5}	= Ø	(empty intersection)
C5 ∩ F6	= {17,22,35,40,44}	= 41.7% of F6; 55.5% of C5
C5 ∩ F1	= {10}	
C5 ∩ F3	= {34}	
C5 ∩ F4	= {38}	
C5 ∩ F7	= {33}	

Q3, will be composed of the same signs, eventually subdivided in these two subclasses. Class F4 exhibits 4 signs of which two {14, 15} are gathered in C1. The latter are maintained in the new class Q4, and the other two signs are scattered in C4 and C5, without particular statistical features. Therefore, they have been left in the same class, based on medical criteria.

The 12 signs belonging to class F6 are distributed in clusters C4 (6 signs) and C5 (5 signs). This indicates that class F6 could be redefined into two relatively important subclasses of the new class Q6: one (Q6a) with signs {12, 16, 36, 41, 45, 46} all gathered in C4, and the other (Q6b) with signs {17, 22, 35, 40, 44} all correctly gathered in C5. The exception is sign 46, clustered in C1. Since links were discerned between C1 and C4, sign 46 was tentatively affected to Q6a. A further examination shows that subclass Q6a concerns physiological aspects of neuropsychiatry disorders, while subclass Q6b concerns emotional aspects. This further validates the classification of sign 46.

Class (F7) for syndrome of impairment of metabolic functions mainly contains subset {28 to 32} of cluster C1, and subset {18, 19, 20} of cluster C4. It can be settled into class Q7, subdivided in two subclasses. Here, cluster C1 specifically gathered cases with similar pre- and post-traumatic symptoms {i.e., 28, 30, 32} into a same subclass.

Finally, seven classes and subclasses of signs noted Q1 to Q7 were adopted as summarized in Table 4.

Patient Classification and Rehabilitation Rates

The membership of patients to the various clinical classes defined above has been computed on the basis of highest $A_{i,k}$ ranks. When the calculations were achieved, neither class Q2 nor class Q7 were represented. Subclasses 6a and 6b were further generally gathered in one single class Q6, since membership was too low in each to allow statistical treatments. Table 5 provides the full classification, including the $A_{i,k}$ values.

The final set of data resulting from this classification, given in Table 6, provides the averaged rehabilitation rates reached after the given number of NBF sessions. Class Q1 contains patient {24}, a case of stroke with low level of rehabilitation due to premature discontinuation of treatment. With the exception of these cases, the remaining population of 7 patients exhibits an $86.6 \pm 7.0\%$ rehabilitation rate (i.e., a low variability, with a coefficient of variation of 0.08) after an average 145 ± 43 sessions (stroke generally deserved the higher number of sessions).

TABLE 4. Final Distribution of Clinical Signs and Symptoms of Altered Functions into Classes of Syndromes Associating Both Medical and Statistical Criteria.

N°	Syndrome classes	Nr.	Signs and symptoms numbers *
Q1	Motor	**10**	{1, 2, 7, 9}, {5, 6, 8, 10, 21, 37}
Q2	Language	**3**	{3, 4, 43}
Q3	Cognitive	**8**	{11, 23, 25, 34, 39, 42}, {47, 48}
Q4	Psychosocial	**4**	{13, 38}, {14, 15}
Q5	Pain-related	**2**	{26, 27}
Q6a	Physiological neuro-psychiatry	**6**	{12, 16, 36, 41, 45, 46}
Q6b	Emotional neuro-psychiatry	**6**	{17, 22, 24, 35, 40, 44}
Q7	Metabolism	**9**	{18, 19, 20}, {28, 29, 30, 31, 32, 33}

Total : $\Sigma N = 48$ signs

(*) Numbers correspond to signs as in Table 1.

TABLE 5. Distribution of the 27 Patients Among Clinical Classes Q1 to Q7. The Reference Number of Each Patient Is Given with Its Attached ($\Lambda_{i,k}$) Value Between Parenthesis. Classes Q2 and Q7 Are Not Filled in Practice.

Q1	Q3	Q4	Q5	Q6a	Q6b	Q2, Q7
10 (0.115)	4 (0.115)	14 (0.174)	2 (0.0714)	8 (0.075)	9 (0.060)	None
20 (0.110)	5 (0.117)	15 (0.062)	7 (0.030)	19 (0.208)	23(0.083)	
24 (0.114)	6 (0.092)	17 (0.06)	12 (0.039)			
25 (0.120)	11 (0.136)					
26 (0.078)	13 (0.071)					
27 (0.086)	16 (0.067)					
28 (0.112)	18 (0.096)					
29 (0.214)	21(0.057)					
	22(0.083)					
Number of cases N = 8	N = 9	N = 3	N = 3	N = 2	N = 2	N = 0

TABLE 6. Distribution of Patients in the Final Set of Seven Clinical Classes of Syndromes of Impaired Functions. Rehabilitation Rates Reached at Treatment Discontinuation and the Corresponding Numbers of Sessions Are Given as Mean ± Standard Deviation for (N) Values.

Subclass N°	Syndrome	Patients N°	Rehabilitation rate	Session numbers
Q1	Motor	10, 20, 24, 25, 26, 27, 28, 29	76.7 ± 28.8 (N = 8)	132 ± 54 (N = 8)
Q2	Language	None	_	_
Q3	Cognitive	4, 5, 6, 11,13, 16, 18, 21, 22	87.1 ± 7.3 (N = 9)	70 ± 57 (N = 9)
Q4	Psychosocial	14, 15, 17	77.0 ± 14.3 (N = 3)	50 ± 39 (N = 3)
Q5	Pain-related	2, 7, 12	80.0 ± 10.2 (N = 3)	50 ± 39 (N = 3)
Q6(a+b)	Neuro-psych.*	8, 9, 19, 23	58.6 ± 40.2 (N = 4) 78.1 ± 11.9 (N = 3)**	23 ± 12 (N = 4) 23 ± 14 (N = 3)**
Q7	Metabolic	None	_	_

(*) Neuro-psychiatrically quoted functions: pooled values.
(**) With patient 23 (stroke) excluded: patient's reported improvement was denied by her family, so the case was alternatively considered with null and non-null rehabilitation rate.

Subclasses Q6a and Q6b have been gathered into a single one including all kinds of impairments of neuropsychiatrically defined functions. Again, if the other particular case of a stroke with low number of sessions {patient 23} is not considered with the rest of the cases, rehabilitation rates reach a much higher value with a lower variability.

DISCUSSION AND CONCLUSIONS

As pointed out by Spurgeon (1995), "The validity of adapting existing (neurobehavioral) test batteries for use as diagnostic or screening instruments is questionable." The same work shows that these well-developed diagnostic techniques involve significant difficulties at both experimental setting and interpretation stages, and therefore can hardly be adapted to the specific features of nonselected patients.

In our attempts to reach an improved classification, we had previously performed a statistical clustering in the space of patient's quantitative parameters including age, gender, delay between trauma and treatment, duration of treatment, load of initial symptoms, EEG, cardiac and other parameters. No significant result emerged from this quantitative setting, whereas, clusters appeared when the qualitative set of clinical signs was used alone.

This is consistent with the need for conceptual non-metric clustering previously discussed by Matthews, Matthews, and Landis (1995). As pointed out earlier, a clinical setting is typical of large dimensional numbers against a low number of observations. This is what precluded any classification from physiological parameters. Indeed, in our results, patient clusters contain subjects of various ages, age at trauma, etc., and are distributed into male and female in classes Q1 and Q2. These clusters are therefore representative of natural sets of people with brain injury, in which age or gender do not necessarily exert a significant influence on occurrence probability or outcome.

Statistical clusters allowed subclasses, mainly Q6a and Q6b, to be identified, the first one being more representative of physiological features and the second one of emotional signs. Classes Q1 and Q3 are filled with the highest numbers of patients, and both male and female are nearly equally represented. Interestingly, the other clusters contain either male only (Q4) or female only (Q5, Q6a, Q6b). This sexual dimorphism was strictly coincidental, and may suggest the hypothesis of an unexpected relationship between gender and frequency of some

types of brain injury in the studied group. This point should be the object of further survey.

No patient was assigned to class Q7 of metabolic syndrome. Metabolic disorder diagnoses are usually based instead on biochemical tests (Carter, Watson, Midgley, & Logan, 1996). Reciprocally, some metabolic criteria may account for neurophysiological diseases, like glucose metabolism as an indicator of dementia associated with Parkinson's or Alzheimer's diseases (Herholz, 1995). However, these methods exhibit a rather low specificity and narrow range of characterization, while diagnosis based on DNA screening remains a difficult process not yet readily available for current medical practice (Chen, Taranenko, Zhu, & Allman, 1996). It is thus not surprising that neurophysiological assessment did not select brain-injured patients for the metabolic disorder class.

A measure of the alteration of voluntary movements was performed by Folstein, Jensen, Leigh, and Folstein (1983), providing a scale for the evaluation of the severity of disorders. However, for the same type of disease (namely the case of Huntington's disease), severity initially appeared uncorrelated with EEG responses (Scott, Heathfield, Toone, & Margerison, 1972). However, it was eventually found to correlate following more recent works of Bylsma et al. (1994), using a set of standard tests for neuropsychological measures. Clinical rating allowed learning disability in children to be related to theta, delta and fronto-central beta frequencies (Gasser, Mocks, Lenard, Bacher, & Verleger, 1983). In this case, multivariate analysis was used for EEG powers, instead of clinical signs. EEG neurofeedback improved ADHD symptoms assessed by WISC-R performance, in children and adolescents, and TOVA scores were found better in correlation with decreases of theta activity (Lubar, Swartwood, Swartwood, & O'Donnell, 1995). Here, this can be related to our class Q3, in which patients reached about 87% improvement with an average of 70 sessions, that is, about five to six months of treatment.

The rationale used for this classification selected the whole set of vascular lesions in class Q1, including a case of complete right hemispherectomy (patient 29). It is worth mentioning that the second case of complete (left) hemispherectomy (patient 10) has been also included in the same class, which appears to point to the robustness of the method.

The results presented here appear to confirm that some clinical associations observed, such as the link of ADD with right hemisphere (Voeller, 1986) may not be represented in particular cases. ADD (sign

47) was not identified in the case of patient 29 who suffered from a right hemispherectomy.

The coefficients of variation for rehabilitation rates are rather low, in contrast with the numbers of sessions. This means that the number of NBF sessions required to reach a given level of rehabilitation depends on variables whose identification and determinism will be discussed in the fourth paper of this series, "Duration of Treatments as a Function of Both the Initial Load of Clinical Symptoms and the Rate of Rehabilitation," appearing in Volume 6 (1) of this journal.

As a perspective, it should be noted that the classification proposed here is a simplistic form of a more sophisticated approach which would take into consideration the fact that memberships of patients in defined classes is not an absolute. Attributions may float between several clinical classes, just as clinical classes may float between several sets of signs. Therefore, the problem deserves further attempts at treatment through the fuzzy sets theory, as this was tentatively done for optimizing the choice of a medication on the basis of symptom recording (Rakus-Andersson, 1999), while a model through the Formal Concept Analysis theory, which is also linked to fuzzy set theory (Wolff, 1999), is also under consideration.

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APPENDIX 1

TABLE A. Distribution of Clinical Signs Evaluated as Chief Complaints, Secondary Complaints and Associated Signs, Among the 27 Patients. Symptoms Are Designated by the Same Numbers as in Table 1. This Table Includes Additional Symptoms Which Were in Some Cases Claimed by Patients After Substantial Improvements Were Noted Post Treatment.

Patients ref. nrs.	Chief complaints	Secondary complaints	Associated signs observed in the same patients
2	26-27	19	10-11-13-16-17-18-22-23-25-28-31-33 to 36-39-41-42 •
4	39	38	3-4-10 to 20-22-23-25-28-31-33 to 36-39-41-42 •
5	39	26-27	10 to 13-17-18-19-22-33-34-36-42-43-47 •
6	39	26-27	10-11-16 to 19-22-33-34-35-42 •
7	26-27	37	10-18-22-25-33 to 36-38 •
8	41	45	10-11-16 to 20-22-26 to 28-31-33 to 35-40-42-44 •
9	45	11	10-16 to 19-22-26-27-33-35-38-40-44 •
10	8	37	1-2-6-10-12-14 to 16-22-23-26-33 to 36-38 to 46 •
11	42	11	10-16 to 20-22-23-26-27-31-34 to 35-37 to 41-43-44-46 •
12	42	26-27	6-11-16 to 23-28-31-33 to 36-38-40-41-43 to 45-47 •
13	42	11	10-12-22-23-26-33 to 35-38 to 41-43 to 45 •
14	15	38	10 to 14-17-19-22-26-31-33-35-37-39 to 41-43 to 45-47 •
15	27	38	10 to 19-21-22-26-31-33 to 37-39 to 41-43-44 •
16	11	41	10-12 to 19-22-23-25-26-29 to 31-33 to 40-42-43 •
17	23	14	10 to 13-15 to 17-22-24-26-33 to 35-37 to 47 •
18	41	47	10-11-22-23-26-34-35-39-40-42 to 44-46 •

Patients ref. nrs.	Chief complaints	Secondary complaints	Associated signs observed in the same patients
19	41	45	10 to 12-17 to 19-22-26-27-29-30-33 to 35-38 to 40-43-44-46 ●
20	37	42	1 to 3-5-6-10 to 13-15 to 27-34 to 36-38-39-41-4 3 to 46 ●
21	27	39-42	10 to 13-15 to 26-28-29-31-32-34 to 36-38-40-41-43 to 45 ●
22	39-42	31	11 to 13-18 to 20-23-27 to 29-41-45-46 ●
23	37	10	11-26-29-30-34-36-40-44 ●
24	9	8	10-17 to 21-29-30-35-36-41-42 ●
25	8	3-4	1-2-5 to7-17 to22-24-26-33-34-36-38-40 to 44-47-48 ●
26	7-9	26-27	2-11-12-17 to 23-25-31-34-35-37-39 to 41-45 ●
27	7	3-43	14-5-8 to 13-16-18 to 23-25-27-29-32-34-37-39-41-42-44-45 ●
28	9	3-4-43	1-6-8-10-11-13-14-16-18 to 27-29-32-34-35-37-39-41-42-44 to46-48 ●
29	1-2	43	3-4-6 to 14-16 to 25 27-34-36-37-39-41-42-44 to 46-48 ●
Weights:	3	2	1 /● 0

TABLE B. Typology of Injuries Presented by the Group of Patients. Each Number Is Referring to One Patient as in Table A.

Category	Types of injury	Patients numbers	Detectable organic lesions
Acquired	Stroke	{23,24,25}	None
	Stroke	{26,	(Optic neuritis + Sarcoidosis)
		27,	(Seizure disorders + Hemiparesis)
		28}	(Subdural hematoma + Hemiplegia),
External	Car accidents	{2,5,6,7,9,13,16,19}	None
External	Car accidents	{4,	Trauma + Substance abuse
		20	Cardiac arrest + Anoxia
		29}	Subdural hematoma + Right hemispherectomy
External	Fall and related	{8,12,11,14,17}	None
		{21	Three TBI + Schizoaffective disorder
		22}	Subdural hematoma + Hypertension
External	Forceps	{18}	Crushing trauma
External	Gunshot	{10}	Left hemispherectomy
External	Fight	{15}	None

APPENDIX 1 (continued)

TABLE C. Pre-Traumatic Symptoms Listed in the Group of Patients with Brain-Injury. Patients Are Designated by the Same Reference Numbers as in Table A. Numbers Added in Brackets Refer to Post-Traumatic Signs as Listed in Table 1.

Pre-symptoms	Patient ref. nrs.	Pre-symptoms	Patient ref. nrs.
Insomnia (12)	4,21,26,28	Misc. subst. abuse (38)	4,20,21
Violence (14)	4,20,21	(Alcohol + Cocaine) (38)	4,20
Conduct disorders (15)	4,20,21	Depression (41)	4,20,21,26,27
Paranoia (24)	4,20,21	Anxiety (45)	4,20,21,26,28
I.B.S. (28)	20,21	Allergies	20,21,22,25,26
Excess weight (30)	22,28,15	Hypertension	27
Anorexia (32)	21	Phys. DX	25
		School failure	4,20,21

APPENDIX 2

INDICES OF MEMBERSHIP DETERMINATION

1. Definitions

Sets will be denoted $\{X\}$ and their cardinal $N(X)$. Let $\{P\pi\}_{\pi = 1 \mapsto N(P)}$ the set of patients P, with here a cardinal $N(P) = 27$, and $\{S\sigma\}_{\sigma = 1 \mapsto N(S)}$ the set of clinical symptoms S, with here a cardinal $N(S) = 48$. Then, $\{S(P_i)\}_{i \in (1,N(P))}$ denotes the set of symptoms exhibited by patient P_i. The latter is a mapping SP: $P_i \mapsto S(P_i)$ of $\{P_\pi\}$ on $\{S_\sigma\}$. The following relations found the system:

$$\forall S_j \in \{S_\sigma\}, \exists Pi, S(P_i) \supseteq S_j \tag{1a}$$

$$\{S(\{P_\pi\}_\pi)\} \supseteq \{S_\sigma\} \text{ (cover of } \{S_\sigma\} \tag{1b}$$

$$\cap \{S\{P_\pi\}, S_\sigma\} \neq \mapsto \tag{1c}$$

These relations mean that a sign must be encountered at least once in at least one patient, and that any sign affecting one patient must be found in the definition of at least one clinical class.

Remark. The space of these sets is bounded, finite, discrete and Hausdorff separate: therefore, it constitutes a compact space, in the topological sense. This relates to previous findings that mental images can be formed from the space of neuronal connections if, and only if, it is a compact space (Bounias, 2001).

The total number of symptoms gathered by the complete set of patients is:

$$N(S(P)) = \Sigma_i N(S(P_i))_{I \in [1,N(P)]} \tag{2a}$$

that is, in the presence of repeated symptoms in various patients:

$$N(S(P)) \geq N(S) \tag{2b}$$

Denote by $Q_k = H_k(S) = \{Q_k\}_{k \in (1, N(S))}$ the set of classes of symptoms. It should be noted that sup $k = N(S)$. To this set is associated the set of patient groups belonging to each symptom class: $\{Q_k,(P_h)\}_{h \in (1, N(P))}$.

The numerical indices can be derived from these definitions: first, an index directly reflecting the representativeness of symptoms in the defined classes, then a reciprocal index specifying the occurrence of non-represented symptoms, and lastly a global index combining the previous two.

2. Indices for Specific Complaints

Let the set of classes $\{Qk\}$ and a patient Pi. Then, $N_{cci,h}$ and $N_{sci,h}$ respectively denote the numbers of chief (cc) and secondary (sc) complaints claimed by Pi that belong to a class Qh. If the weighting coefficients attributed to (cc) and (sc) are e_{cc} and e_{sc} (here ecc = 3 and esc = 2). Then :

(i) the actual value for Pi in class Qh is

$$X_h(P_i) = [e_{cc} \times N_{cci,h} + e_{sc} \times N_{sci,h}] \tag{3a}$$

(ii) the maximum value for Qh is the case where the total number of (cc) and (sc) would belong the considered single class, here Qh. Thus

$$\max\{X_h(P_i)\} = [e_{cc} \times N_{cci} + e_{sc} \times N_{sci}] \tag{3b}$$

and finally :

$$\Xi_h(P_i) = [e_{cc} \times N_{cci,h} + e_{sc} \times N_{sci,h}]/[e_{cc} \times N_{cci} + e_{sc} \times N_{sci}] \tag{3c}$$

Each patient thus has such an attribute for at least one class. Relation (3c) precludes the risk that a patient could be affected into a class where his chief or secondary complaints would not be represented. However, in an extended form, this relation could include all the other associated signs (as) with their weight e_{as} (here $e_{as} = 1$) so that more generally:

$$*\Xi_h(P_i) = \{m \in \{cc, sc, as\} \mid \Sigma[e_m \times N_{m,h}]/\Sigma[e_m \times N_m]\} \tag{3d}$$

3. Index of Full Associated Symptoms

This index could be limited to the signs other than those included in (cc) and (sc). However, the latter completely contribute to the constitution of clinical classes, and therefore have not been discarded here, while they received the same weight as the others (that is: e = 1). This index involves two components.

3.1. Representativeness to Concerned Clinical Class

Call $y_{i,k}$ the particular signs among those of the set of symptoms exhibited by patient Pi which also belong to the set of symptoms $S(Q_k)$ defining class Q_k. Thus:

$$y_{i,k} = \{S(P_i)\} \cap \{S(Qk)\} \tag{4a}$$

$$\text{Sup}\{S(P_j)\} = \{S(F_k)\} \tag{4b}$$

Denote by x_k the total number of symptoms defining class Q_k, otherwise: $x_k = NS(Q_k)$. Then, a direct representativeness index is given by

$$Sr = y_{i,k}/x_k \tag{4c}$$

Remark 1: Relation (4c) can be extended to include of the number of patients further attributed to class k, i.e., $N(P(Q_k))$ in an attempt to derive an index of the strength of memberships. In this case:

$$y = \Sigma_i y_i, \tag{4d}$$

$$x = N(S(Q_k)) \times N(P(Q_k)) \tag{4e}$$

$$\delta_{i,k} = y_{i,k}/x \tag{4f}$$

3.2. Representativeness to Concerned Patient

Let NSP_i the total number of signs exhibited by patient P_i. Then, $(NSP_i - y_{i,k})$ signs of P_i do not pertain to $S(Q_k)$ and an exclusion index is defined by S_e:

$$S_e = (NSP_i - y_{i,k})/NSP_i \tag{5a}$$

The direct representativeness equivalent of S_e is $(1 - S_e)$. Otherwise, $(1 - S_e) = y_{i,k}/NSP_i$. The final index is the product of the two complementary ones defined above:

$$\mathbf{I}i(Qk) = Sr(1 - Se) = y_{i,k}^2/x_k \times NSP_i \tag{5b}$$

Remark 2. $\mathbf{I}i(F_k)$ would consistently equal 1 if patients exhibited exactly all signs of their class and no other sign.

Remark 3. The set of all symptoms gathered by all patients of class F_k is: $N(S(PQ_k))$, where $PQ_k = P(Q_k)$. Taking $S\# = N(S(PQ_k))$ instead of $N(\cap(PQ_k))$, will minimize the value of the final index. Then, one can write an index of representativeness of a set of patients $\{Pj\}_{j \in (1,NP)}$ as attributed to a class Q_k by using:

$$(S\# - y) = N(\mathbf{C}_{S(Qk)}(S(PQ_k))) \tag{6a}$$

where $\mathbf{C}_A B$ denote the complementary of B in A (i.e., the set of members of A not belonging to B), and

$$z = (S\# - y)/S\# \tag{6b}$$

that is, in terms of equivalent of representativeness:

$$\rho = (1 - z) \tag{7}$$

4. Global Index

The final numerical index attached to one patient in one clinical class was posed as:

$$\mathbf{A}_{i,k} = \mathbf{I}i(F_k) \times \mathbf{\Xi}(P_i) \tag{9a}$$

This relation can be used in the following way as the probe for identifying the patients belonging to a given class of clinical symptoms:

$$P_i \in Q_h \Leftrightarrow \mathbf{A}_{i,h} = \max\{y_{i,k}^2/x_k \times NSP_i\}_{k \in [1,N(Q)]} \tag{9b}$$

This model can be adapted to various clinical classes and to various types of injury or diseases. It allows adjustment according to the requirements or purposes characteristic of each study. The objectivity of the system resides in that it defines exactly the options chosen by the practitioner.