Trials and training with 100 self-rated verbal reactions and a theory of sequences

Paolo Pinelli
IRCCS S. Maugeri Foundation, Veruno (NO), University of Pavia, Italy
Reprint requests to: Prof. Paolo Pinelli
Via Volta, 10 - 27100 Pavia - Italy
E-mail: ppinelli@fsm.it
Invited paper

Summary
Sequences of verbal reactions, in particular 100 self-rated reactions, were investigated in 51 normal subjects and 61 patients with different neurological disorders. The non-linear course of the sequences is highlighted, and the factors influencing the occurrence of variations are studied. Inter-individual differences in the first interstimulus intervals (ISI), and deviations between ISI and subsequent interstimulus intervals, were systematically measured and the distribution of the results analyzed in histograms: a bimodal distribution was found. Cognitive styles were classified using the Big Five Questionnaire and Matching Familiar Figure Test: a significant correlation was found between impulsive and reflective subjects and the bimodal distribution of the interstimulus intervals. The intermediary oscillations of the temporal parameters of reaction sequences were systematically analyzed, and neurological and psychological factors influencing their occurrence identified. The issues arising from these studies are incorporated into a theory of sequences in neurophysiology. Their relevance to neurorehabilitation training processes is pointed out, and the advantages of paramodular tailored training of working memory are documented.

KEY WORDS: cognitive styles, recency effects, sequences, training processes in neurorehabilitation, verbal reactions, working memory.

Introduction
Psychomotor reactions have been studied in psychophysiology laboratories and clinical departments since the end of the nineteenth century with the aim of investigating, first of all, reaction speed and response duration, and second, response accuracy and number of errors. Reaction time investigation still occupies a position of primary importance in neuroscience (1). The most common paradigm is that of the series of twelve reactions (2,3) used to obtain a statistically significant mean value in normal individuals, and to detect changes produced in different pathological conditions. Perkell (4) underlined the stochastic nature of sequences of reactions, characterized by the fact that the parameters of each reaction are unforeseeably different from those of the preceding reaction. Important neurophysiological and neuropsychological investigations of sequences of reactions have been carried out by Hikosaka et al. of the Universities of Tokyo and Kyoto and the Institute of Bethesda (5). A first batch of experiments considered the learning process of several programs of trials, at different levels of intensity, in monkeys; a second one was completed in humans and involved the examination of reaction times [in line with our multiple delayed reaction verbochronometry (MDRV) and 100 self-rated reactions (SR100) trials]. These authors found that during repeated trials performances presented many oscillations with temporary regressive worsening: the number of sets completed in 22 successive trials was: 0, 1, 2 / 1, 3 / 1, 3, 5 / 3, 5, 5 / 1, 1, 5, 5, 5, 5, 5 (the bold and divisions underline points of worsening in the sequence). The authors think that these oscillations could depend “on a variability of processes similar to those occurring within a narrower range at much shorter periods of time in 12 reactions of a single trial, and at a slightly more prolonged performance in trials of sustained attention with self-rated intervals of stimuli, responsible for perseverations and pauses”.

With regard to the large bivalent oscillations occurring during learning processes, Hikosaka et al. (5) ascribe them to the fact that “a sequential procedure is acquired through the functions of two brain systems that operate each independently of the other, in parallel networks: one occurring in a spatial, the other in a motor dimension. This happens preferentially in the earliest phase of learning for spatial operations, and in a later phase for motor operations. Memory for single elements is separately acquired in the first phase, whereas in a later phase learning concerns the sequence as a whole (effector-specific learning). The functions of both spatial and motor systems occur in closed loops formed by the basal ganglia and cerebellum, the first being involved in compensation, the second (cerebellum) in training processes”. Thus, spreading processes occur from one dimension (spatial or temporal) to the other. Subjects undergoing training do not learn single elements separately, but instead, due to chunking processes, connections of sequences with aggregations; the acquired information (memory) is partly effector-specific (for motor sequences), and partly effector non-specific (for spatial sequences). The authors speak of dual learning and hypothesize a neural architecture characterized by parallel networks, seats of excitation and inhibition processes with phases of inactivation that leave some neural centers temporarily inaccessible. The apparent dysfunction that results from this can be gathered as errors. On the
other hand, the organization in parallel networks and dual functioning means the availability of independent pathways and possible interchanging of parallel operations: a high degree of flexibility is thus assured and various combinations of multiple sequences can be acquired. Each motor sequence can then be used as an element of more complex motor sequences. Possibly, in humans, mnemonic representations of multiple sequences are orchestrated through a conscious process that produces a complex reflective behavior through internal multi-layered feedbacks.

A further contribution to clarifying the occurrence of oscillations during learning has been provided by Bekker et al. (6) of the University of Utrecht, The Netherlands, who applied the psychophysiological methodology of evoked brain potentials: event-related brain potential (ERP), frontal selection positivity (FSP), contingent negative variation (the O or orientation wave, and the E or expectancy wave), lateralized readiness potential (LRP), and reaction times in go-no-go tasks at different go probabilities. They identified neuropsychological parameters correlated with various complex cerebral functions, and specified the role of excitatory and inhibitory activation (subthreshold LRP), expectation and preparatory processing, degree of sensitivity associated with the perceptive ability to discriminate between target and non-target, and conflicts and biases that influence the response decision. All these variables were correlated with the presence of errors made during the subjects' continuous performance of the task. The authors proposed an evaluation of oscillations by means of systematic analyses of the "different probability of occurrence of the second stimulus" in all the various investigated responses. They underlined "the complexity of the central processes involved: excitatory and inhibitory (with subthreshold LRP), expectancy (preparatory processes), degree of sensitivity (perceptive ability to discriminate between target and non-target), degree of conflict, and biases (in the decision to answer) that generate omission or execution errors".

**Neurophysiological research on the dissolution-reformation sequence**

Wiese et al. of the University of Duisburg-Hessen in Germany (7) have analyzed the different components of the Bereitschaft Potential (BP) in the evolution of the sequelae of traumatic prefrontal lesions. The BP decreases and temporarily extends within 8 weeks of the trauma owing to a reduced neural input to the prefrontal cortex from the premotor structures and reduced motor preparation. At 12, 26 and 52 weeks after the trauma there is recovery of i) the controlateral negative slope (NS), and ii) the controlateral motor potential (MP) appearing 100 ms before the movement in such a way that the potential correlated to the movement, and the BP+NS+MP compound, appear completely normalized.

The course of these dissolutions and reformations (losses and recovery of operational abilities) was different from one case to the next. This variability could depend not only on different degrees of cerebral impairment, but also on various psychological factors that can modify the level of cerebral excitability: oscillations in intentional attention and degree of cognitive effort, passages from intentional to more automatic performances requiring shorter execution times.

**Some rules discovered in the sequences of 12, 100 and 2000 reactions**

In 1960, Bertelson et al. (8), followed by many other researchers, carried out a study with series of 100 to 2000 psychomotor reactions, and investigated the variations occurring in the reaction parameters within the sequences. Bertelson and Renkin (9) found that the mean latency time was 85 ms faster in trials of series containing repetitions of previous stimuli than in series that did not contain these repetitions. However, other researchers (10) found that recency effects could increase the reaction times. Lance (11), on the contrary, observed that recency effects could be both positive and negative: reaction time (RT) values were longer when the active stimulus was repetitive, and on the contrary shorter when the stimulus was different from the previous one; but RTs were also shorter when two or more repetitions were present. The conclusion was that the preparation set is not a constraint in the different trials, but differs from one experimental condition to another with different multiple combinations of biases related to the perceptions and to the response, and to the local history of the stimulation sequence.

Further experiments were carried out with the purpose of substituting the subjects' biases with some bias deliberately introduced by the examiner. These cues were used to mark stimuli with a very high probability of being presented in that trial; in this way, the subject was less drawn to consider other events that had occurred in previous trials. In very refined experiments, LaBerge et al. (12) demonstrated that the introduction of the predictive cue before the stimulus elicits a powerful bias not only on that particular stimulus, but also in its modality and on the associated response. The sequential effects occurring from one trial to another in cued conditions were markedly less than those obtained in control, non-cued conditions.

Kirby, in 1980 (13), in an important paper published as a chapter of the book Reaction Times by Welford (14), reviewed and completed this research, seeking to investigate the origin of the oscillations in time of single or choice reactions in sequences prolonged until 1000 actions. He interpreted the repetitive and alternating effects as depending on a double matrix: a) cerebral processes with excitability modifications following previous excitations; b) psychological factors of expectancy and prediction that imply activations of short term memory (STM) and working memory (WM).

De Brabander (15) and Davidson (16) applied, to the study of the modalities of different kinds of sequences, the theories of complex systems and the theory of chaos in line with the principles of entropy.

With reference to knowledge on cerebral functions in the year 1996, the problem was brought clearly into focus by Goodin (17): “It is possible that changes in the functional state of the brain, occurring slowly with respect to ISIs (of a few seconds) commonly used in studies, may have determined the speed of response on a particular trial. The nature and basis of such changes cannot be determined from the present experiments” (simple and
choice reactions to acoustic stimuli with specified movements of the fingers of the ipsilateral and crossed hand as response. On the other hand, Goodin himself hypothesized and found theoretical and experimental clues that may provide the key to the problem. "On theoretical grounds such changes may be chaotic, may follow other (non chaotic) rules, or may result from a continuous but randomly varying function. Regardless of the basis for the significance of the observed correlations (between one reaction n and the n-1), the experimental results indicate that subtle alterations in the function of the brain, independent of the external stimulus and nature of any required task, govern in part the timing of the response to the external stimulus. Moreover the functional states must be changing during the course of each experimental condition to produce the response latency distributions that had the appearance of simple randomness, in fact, highly correlated".

**Training with processes of working memory**

Application of serial reactions in which there is involvement of processes of WM has been carried out in the field of neurorehabilitation since 1999, starting with Klingberg whose work at the Karolinska Institute involved young patients affected by attention-deficit/hyperactivity disorder (18).

Training of WM in an even larger field of neurological disorders has been applied by us at the IRCCS Institute of Veruno (Novara, Italy) in the past two years. Our study started in 1985 with diagnostic functional assessments through tests based on series of verbal reactions (19). The verbal channel was chosen instead of the usual manual key-pressing modality for practical and theoretical reasons: the correspondence between the stimulus and the response is more direct; the range of possible stimuli and reaction modalities is wider owing to the – uniquely human – copiousness of speech; and the technical system required was simpler and more flexible. The subjects' performances consisted mainly of delayed reactions that imply the involvement of processes of WM. These performances are task-independent: therefore, recourse to the verbal channel would not imply a limitation of the examination to the field of speaking, but would also involve the other psychomotor channels as esclave-executing systems.

The series of reactions, on the part of the subjects, are of three different types: i) 12 examiner-rated reactions; ii) 100 self-rated reactions (corresponding to training of working memory); iii) 2000 reactions carried out in different sessions twice weekly for a month.

We took into consideration not only the final result as a sign of possible improvements through learning, but also all the variations and oscillations of the reaction parameters during the trials and training sessions.

The findings of these measurements and evaluations were analyzed, also taking into consideration regular or chaotic sequences of variations. The resulting criteria and orders of the sequences led us to formulate a theory of sequences that differs from the theories of probability, i.e., that sequences imply a role of neuropsychological learning and different psychological attitudes.

Cognitive styles are a main factor influencing sequence modalities. According to Klapp (20) "The measurement of reaction times is often used to quantify the performance of cerebral processes such as attention and memory. This measure is compared to normality values obtained from samples of subjects that are homogenous for age, education and other variables which can affect the measure. The psychological condition and in particular the cognitive style too could affect the measure of reaction times. Cognitive style is usually evaluated by means of qualitative scales obtained with the administration of a questionnaire that, with respect to psychophysiological evaluation, has the disadvantage of being subjective, time consuming, and of producing little quantitative information. The effectiveness with which the two processes, INT (Internal structure) and SEQ (Selective Sequence of Queuing) are utilized varies from one subject to another, this variance being attributable to different cognitive styles".

The present study deals with MDRV and SR100 in 51 normal subjects and 61 patients with neurological disorders. In addition, we examined 6 normal subjects and 11 patients during training of WM. The main research regarded the RT and ISI oscillations occurring during the sequences, and their correlations with cognitive styles and functional neurological states.

**Materials and methods**

Table I summarizes the profile of the 51 normal control subjects.

| Male/Female | 22/29 |
| Mean age in years (range) | 46±17 (18-82) |
| Education in years (range) | 14±6 (4-30) |

The 61 patients (42 males and 19 females; age: 29-87 years; education: 5-18 years) enrolled in the study included 32 with Parkinson’s disease (PD), seven with essential tremor, four cases of cerebral vasculopathy (two in whom symptoms were limited to dysarthria), five patients with confusional syndromes due to cranial trauma, three with mental deterioration (two of mild degree and one more severe), three cases of chronic fatigue syndrome, two cases of pseudo-tetany, one case of severe migraine, two cases of depressive syndromes, one case of psychoneurotic syndrome and one case of schizophrenia.

**Multiple delayed reaction verbochronometry**

Reactions with immediate responses to single and choice stimuli (Rim). We measured two temporal parameters: time latency and word duration in the response. In reading reactions the following stages were considered: i) visual perception time; ii) visual-ideographic transfer time; iii) sequential programming time; iv) adaptation of the invariant patterns to constraint-specific conditions (buffers, WM); v) articulatory neuromotor execution time.
The range of variability within a single task (stochastic system) requires that a series of 12 reactions be obtained from the subject in each trial, so that statistically reliable mean values and standard deviations can be calculated.

In a few cases, besides the series with /mare/ /mu/v/, other series, with /clan/ and /clue/ stimuli, were performed.

Naming reactions. Two images (/mu/v/, wall; and /mare/, sea) were shown on a PC screen after an acoustic warning stimulus (800 ms), while the subject continued “breathing in” (inspiratory phase). The picture had to be named aloud immediately after the presentation of the task stimulus. As responses, acousticoGram, through a microphone, and surface oral (orbicularis oris) and sometimes oromandibular EMG responses were recorded. In a few trials, electroglottograms (EGG) and oromandibular kinetograms were also recorded.

Reactions with delayed responses to single stimuli (Rd). The response had to be given, at the appearance of a “go” stimulus, after an interval had elapsed from the presentation of the task stimulus: the intervals (0.1, 0.5, 1.5, 4 or 10 s) were randomly paired. The differences in latency time of reactions carried out at different foreperiods (i.e., intervals between the stimulus and the go-signal) and those of the immediate responses provide some clues concerning the central programming versus executive processes, and concerning occurrence of facilitation of the corticospinal executive system, in line with the development of intermediary processes of WM (Fig. 1).

The experimental model presents four lines of research involving factors that affect RTs: i) the influence exerted by the degree of response accuracy; ii) the individual cognitive style; iii) limits of endurance (central fatigue) and other kinds of change in cerebral excitability; iv) heterochronicity occurring within associative systems and projective systems of the brain in disseminated demyelinating diseases.

Once these factors have been ascertained in the single case, we are in the right condition to isolate the intrinsic factors affecting the order of sequences.

The accuracy of the response can be assessed following an evaluation based on the patterns of EMG responses (21). This evaluation provides an important indication of the correct execution of the trial: when the EMG pattern corresponded to a high degree of accuracy, the subject was invited to repeat the trials, and we took into consideration only the velocity of the reaction and disregarded the accuracy of the response.

The influence of cognitive styles (in particular reflective styles) can be ascertained in SR100 by measuring the distribution of the first interstimulus intervals (ISIs), in which the influence of personal psychological attitudes is more relevant, and of the ISI variations within the sequence; we then correlated the histograms of the results with different cognitive styles.

Training of working memory

The training sequences were established in each patient on the basis of the MDRV results, with reference to the neural functions better preserved after pathological injuries. They consisted of, first, the delayed reaction that the patient was able to perform with normal effect of facilitation, and second, the SR100 sequence.

Training exerts some degree of facilitation on several functions that are directly or indirectly associated with processes of WM: i) the level of vigilance particularly with regard to appraisal of the warning stimulus; vigilance undergoes many oscillations with reference to perceptive discrimination that we can measure as the following difference: time latency of the choice reaction (tRab) minus time latency of simple reaction (tRa) [i.e. tRab-tRa]; ii) the level of purposeful attention and associated facilitation processes can be measured by the tRd/tRim ratio, i.e. the ratio of the time of the delayed reaction to that of the immediate reaction: the value of tRd in normal conditions is lower than that of tRim, owing to the facilitation occurring during the foreperiod on the corticospinal system, whose threshold is lowered, even if always within a range of subliminality.

Criteria of evaluation of oscillations in SR100

We distinguished three degrees of variation in the ISI times between one reaction and the next (two points in the SR100 diagrams) (Fig. 2): i) minimal variations (Min.), be-
We classified the oscillations as follows: (i) intermediary variations (Interm.), between 26 and 160 ms and (ii) maximal variations (Max.), between 161 and twice the mean value of ISI. Oscillations greater than double the mean value are classified as pauses and can reach values as high as 5 seconds.

The variations in latency time occurring during the SR100 sequence between one reaction and the next have been attributed to the subject's attempting to calculate recency effects through an activation of STM channels and possibly WM processes (13).

Criteria of evaluation of oscillations in paramodular tailored autotraining. We classified the oscillations as follows: Min.: from 1 to 30 ms; Interm.: between 31 and 60 ms; Max.: > 61 ms.

Some modes of investigation in the 12 examiner – rated reactions (ER12), 100 self-rated reactions (SR100) and 1000 sequences of reactions. In sequences of 12 reactions, in spite of the small number of events in Poisson sequences, a certain deterministic intrinsic auto-organization occurs that makes the oscillations converge to produce a significant mean value.

In SR100 the course of the sequences following the first twelve shows marked deviations from that of previous oscillations (within 12 α); we can thus consider the first 12 reactions (12 α) as separate from the subsequent groups of 12 reactions (12 α). By measuring the deviation in the 12 α group appearing between the first ISI and the subsequent ISI (Δ 1 – 2 of 12 α) and the deviation between the mean value of 12 α and that of the subsequent 12 α groups, we identified some segments in the sequences that appeared chaotic and others that appeared more regular.

Psychological investigations

We applied the Matching Familiar Figure Test (MF) and the Big Five Questionnaire (BFQ).

The MF presents 20 items in which one stimulus is used as the model. The subjects must compare the model to six other stimuli which are similar but not identical to each other. Only one figure is identified by the subject as identical to the model. Latency and number of errors made by the subject at each item are recorded.

The BFQ consists of 120 multiple-choice items that evaluate the five big factors: Energy (24 items), Friendhip (24 items), Conscientiousness (24 items), Emotional Stability (24 items) and Open-mindedness (24 items). Each factor contains two sub-dimensions: e.g. Emotional stability contains the sub-dimension emotional control (Ce) and impulse control (Ci).

A lie scale of 12 items is used as a control to evaluate the presence of social ingenuity, social desirability or dissimulation. In all scales, higher scores (range 30-70) indicate a greater presence of the investigated variable. The investigations were carried out with the informed consent of the subjects and the approval of the Veruno Medical Center Ethics Committee.

Results

The main results of our research on sequences of verbal reactions concern: i) ER12 reactions and correlation with cognitive styles; ii) distribution of SR100 reactions in seemingly chaotic and more regular sequences and correlation with cognitive styles; iii) the occurrence of oscillations during the WM trials.

Findings in normal subjects

ER12 reactions and correlation with cognitive styles. In 26 normal subjects (age 18-81 years, education: 5-18 years) we found 12 cases (group 1, G1) with tRa<tRab and 13 cases with tRa=tRab, plus a further case with tRa:tRab.

The mean value of tRa in G1 was 380±70, while the corresponding value in G2 was 490±65. The mean value of tRab was 480±60 in G1 and 490±70 in G2. The difference in the Ra parameters between the two groups was significant (p<0.03).

The two groups showed statistical differences in two psychological variables: Ci (a sub-dimension of the BFQ, concerning the capacity of impulse control) and tm (the mean latency of responses to stimuli in the MF) (Table II).

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=12)</th>
<th>Group 2 (n=14)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency time (mean and s.d.)</td>
<td>24.24±5.05</td>
<td>18.53±6.82</td>
<td>0.03</td>
</tr>
<tr>
<td>Impulse control (Ci)</td>
<td>56.91±9</td>
<td>48.64±7.61</td>
<td>0.02</td>
</tr>
</tbody>
</table>

These results seem to indicate that more reflective subjects (with tRa<tRab, subjects with a muscular set) are the ones more able to utilize SEQ programming. Conversely, impulsive subjects are more able to utilize the internal structure (INT process). So these subjects tend to perform more critically on simple reaction (Ra) trials, displaying longer RTs, because in Ra the rapidity of SEQ programming influences the latency of the response.

In one subject we found tRa>tRab. This merits special comment. The most marked change here was the increase in tRa, which in fact was the longest found in all the 26 subjects investigated. It could have been due to a high tendency to anticipate the response after the warning signals, compensated for by a higher inhibitory process. The underlying explanation could be impaired motor facilitation, probably associated with poor purposeful attention. In conclusion we have demonstrated that different cerebral processes are activated in Ra and choice reaction (Rab) trials, and that in some conditions the processes involved in Ra, particularly in the phases of preparation and programming of the response, are as complex as those in Rab.

SR100 reactions, distribution in seemingly chaotic and more regular sequences, and correlation with cognitive styles.
ISI variations. In the 12 α, marked ISI oscillations were found in a few cases, but the sequence was quite regular in the large majority. The subsequent 12 σ sequences presented some marked oscillations, with a wide range from 150 to 400 ms, particularly in the middle of the SR<sub>100</sub> sequence. However, in other cases the range was not more than 50 ms.

The distribution of the ISIs in 12 α in the 51 normal subjects, ranging from 150 to 900 ms, showed a bimodal shape with a first curve from 100 to 500 ms, and a second from 500 to 900.

Deviations in the course of the sequences. We found that the ∆ ISI 1-12 values (i.e., the difference between ISI values at the first interval and at the 12<sup>th</sup> interval) presented a bimodal shape, respectively from 50 to 100 ms (more ordered sequence) and from 100 to 200 ms (seemingly chaotic sequences), with a prevalence of impulsive subjects in the first group, and of reflective subjects in the second (Fig. 3).

The distribution of impulsive (in the first group) and reflective (in the second group) subjects was highly correlated (p = .0095).

tRab variations. The tRab showed large deviations between the first and the second ISI. The relationship between the first examiner-rated (ER) tRab and the first self-rated (SR) tRab differed markedly between subjects: sometimes SR tRab was greater, whereas sometimes, on the contrary, the ER tRab was greater, and the differences in some series of 12 were as great as 350 ms.

Oscillations during the trials of WM. The course of the paramodular tailored auto-training was non-linear showing oscillations in opposing directions. A few performances improved, others worsened, with respect to the basal conditions evaluated at the onset of treatment.

Findings in neurological disorders

The ER<sub>12</sub> reactions. A main change in neurological disorders is an inversion of the tRa/tRab ratio, with tRa>tRab. This is due to the fact that the neurophysiological substrate, at the level of the nigro-striatal pathway and basal ganglia, allowing performance of the task, becomes asymmetrically impaired. In our methodology the execution of Ra demands high activation of inhibitory processes.

For the same reasons, in patients with impairment of inhibitory processes, the value of tRd/tRim can be >0.9 in some foreperiods.

SR<sub>100</sub>, distribution of the three orders of oscillations. The mean ISI and tRab values were moderately increased in the majority of cases. But the main change in SR<sub>100</sub> was the large increase (as much as 70%) in percentage of maximal oscillations. Moreover, while the ISI in the 12 α was rather constant, the mean values of the subsequent groups of 12 in SR<sub>100</sub> showed large oscillations (from 400 to 900 ms), particularly in the most severe cases, and even from 200 to 1900 in cases of cerebral vascular damage.

The deviations in ∆ 1-12 ISI occurred in a wide range, from 50 to 5000 ms, without a significant correlation emerging with the type and severity of the disease: preliminary research seems to indicate that this is due largely to the subjects’ pre-existing biological-endogenous and psychological characteristics.

Oscillations during the trials of WM. Eleven patients performed the whole training in the course of one month: six were affected by PD, one was in stage II, the others in stage III; two patients had post-traumatic cranial syndromes: one of mild degree and one more severe; three cases were affected by cerebral vascular lesions, one mild and two more severe.

We evaluated the course of the modifications of the functional neurological state of the patients with respect to basal conditions before the training, when the clinical assessment ascertained a stationary state.

In the PD-II case no improvement was found. In one PD-III case the improvement was very marked, in another PD-III case the improvement was also marked, although less so; in another PD-III patient it was moderate, in a further one it was rather poor, and in the last one, null.

In the patient with mild cerebral vascular pathology the improvements were very marked, while in the more severe patients the improvements were moderate or small. In the two cases of cranial trauma, a moderate improvement was observed (Table III).

We observed that the cases with improvements associated with a moderate decrease in positive oscillations and marked decrease in negative oscillations showed a persistence of the improvements at the follow up carried out four months later, while in the cases with unmodified presence of negative oscillations the improvement was transitory.

The analyses of the course of variations in the 12, 100 and 2000 sequences of reactions revealed: i) some alternations between ordered and chaotic-like segments of sequence, ii) factors of auto-organization, and iii) a mixture of automatic and intentional behaviors.
In fact, we refer to three main components: i) Giambattista Vico (22) and Patricia Churchland’s (23) focusing of research on the behavioral level of human activity; ii) Levelt’s (24,25) consideration (as the core of research of sequences) of acts as complex processes that include the hierarchization of initiatives, development through bifurcations (like lighting), spreading activation and collateral inhibition; iii) Golgi and Mazzarello’s (26) principles of complexity (in the sense that one considers the whole sequence with all its internal variations, connections with multiple units and factors, rules and causality).

Our theory can be considered a specific development in the field of psychophysiology of the theories of dynamic non-linear systems (27).

On the other hand, the sequences we consider are on a different plane from that of the theory of number sequences. In fact, we refer to three main components: i) a producer of the sequence, who is a human with creative capacity; ii) a complex sequence of processes occurring within the central nervous system; iii) psychological components that can favor or hinder the flow of the sequence.

On a completely different plane dwells the praxic process. This is an essential ensemble, strictly organized in view of its aim, which is to reach, and be guided through feedbacks in the direction of, the final target. On the contrary, the sequence we analyze is characterized by repetitions and alternations among different acts which follow a possibly casual course. Moreover, the whole philosophy underlying the theory of sequences remains on a quite different plane from that of the theory of homeostasis according to Walter Cannon (28). The theory of the Harvard biologist states that physiological systems behave in such a way as to reduce variability and keep internal functions constant. At variance with this postulate, scientific investigation has demonstrated that great variations can occur even in the absence of external oscillating stimuli. The identification of spontaneous oscillation in parameters of physiological functions, which follows a chaotic course or occurs periodically, has been ascertained through two sophisticated methods: i) Fourier’s spectrum of the temporal series; ii) the delay maps or return maps method with the research of trajectory attractors (29).

In line with these considerations two main questions arise:
– How much in the sequence occurs as obligatory connection?
– How much, conversely, occurs as a kind of “curling” of primarily autonomous “quanta”?

Were we to consider reactions as points in a sequence, inserted in the ensemble of space and time with deterministic links, we could infer that recency effects play a pre-eminent role. If, on the contrary, they were exquisitely active events with intrinsic freedom, the recency effects would be negligible.

Two main fields of sequences include the processes of speaking and those of thinking. Some authors, in particular Turvey (30), have studied the role of temporal constraints of linguistic segments and acoustic patterns in speaking. At the onset of speaking, when subjects translate into words their thought or needs, there is a certain range of freedom: subjects can choose the time of their communication and modulate the tone of their speech; they can even mask their more profound intentions. But in the sequence of the natural constraint of the vocal channel, when a ramification occurs, decisions must be taken quickly at various points and each decision will condition the next one. The matrix of decisions depends on circumstances but also on the character of the subject, which varies from a rather deterministic style of conformation, to a rather chaotic impulsive emotivity. In these conditions the trajectory of all speaking processes will be non-linear.

The logical rules of thinking are softer; the degree of freedom can be greater. At the source of its formation two fields of knowledge can compete: a passive input of external information, and the subject’s active representational creations. The discrimination between these two
fields is obtained through the production of the psychological entity of the Self. This pragmatic psychological being is subject to a wide range of variations (Pirandello’s human metamorphosis) (31). The unconscious pulsions impress a chaotic non-linearity on the sequence, while the moral law, a secondary production of thinking in Popper and Penrose’s World 3 (32,33), oscillates in a pattern of “courses and recourses”.

With more specific reference to the experimental study of sequences of verbal reactions, we have found that there is a complementary situation of casual random sequences coexisting with more ordered non-random sequences independently of their cerebral or psychological origin.

Some extrapolations

The study of the sequence has implications for the field of neurorehabilitation: we can identify the kind, order and sign of variations occurring in the course of learning and underlying neuroplastic processes; hence the examiner (and particularly the rehabilitation neurologist) can adapt the parameters external to the system.

A more general implication of the theory of sequences, understood more broadly, is that of a shift of the borders of science beyond that which can only be measured. Through analysis of the intermediary variations, partly dependent on subjective factors, we can re-integrate into scientific research the qualitative components, exquisitely human, belonging to the field of psychology. In fact, the research on the different initial ISIs and early deviations in the sequence order have demonstrated the great influence exerted by cognitive style and particularly by impulsive and reflective styles.

Moreover, the theory of sequences underlines the occurrence of chaotic, non-deterministic events, and in this way undermines the principle of certainty and predictability in science. The demonstration of chaotic phases in the sequence of mind-brain performances has proved that in the course of human events God sometimes plays dice: in fact, biological life springs from an initial chaotic sequence (28). In general, the course of biological cerebral processes and mental events follows the law of conditioned probability and more likely of Markov systems.

Some applications and developments

A main advantage of applying the principles of analysis of sequences is the possibility of replacing the poorly defined qualifications that are used in neurorehabilitation, for example, “weak or strong will”, “do your best”, “you lack the willingness/determination”; or “pay more attention to the trials”; or “resist fatigue” with a quantitative measure of the two orders of factors that affect the flow of sequences: the neural functions implied in processes of WM, and the psychological biases imprinted in the mind of the subject. In favor of this quantitative functional evaluation is the fact that a rather vague use of terms and advice could lead to the placing of excessive demands on the subject who may become frustrated and incapable of performing correctly, or, alternatively, could induce the trainer to adopt a lax attitude and to let patients perform below their capacities.

A more intensive method of training may be reached through the theory of sequences in accordance with the pulling effect of simple paired sequences (21), like the sequence of gait, associated with the training of working memory. This modality of rehabilitation is in use in our institute.

Acknowledgments

Roberto Colombo (engineer) contributed to the MDRV (technical and methodological aspects) Andrea Giordano (engineer) provided essential advice for the theoretical elaboration of the thesis discussed in this paper. Technicians Ada Patriarca and Alessandra Mazzone gave valuable assistance. Neurophysiology technicians Marco Giansella and, more recently, Isabella Napolitano collaborated on a daily basis. Psychologists, Roberta Fornara and Michele Luvaldi administered and evaluated the psychological tests. The neurologists from the clinical departments of the IRCCS S. Maugeri Foundation, Veruno, provided the clinical cases and their classification. Specialist in neuroinformatics, Luca Marchese, and neurophysiologist, Giovanni Berlucchi, made some fair comments in the analysis of sequences.

References

of Thinking and Reasoning. Los Angeles; University of California Press 2005
22. Vico GB. Scienza Nuova. Milan; Mondadori 1992
27. Prigogine I. Dall’essere al divenire. Milan; Einaudi, 1997
29. Cramer F. Caos e ordine, la complessa struttura del vivente. Turin; Bollati Boringhieri 1994
31. Pirandello L. Maschere nude. Last edition. Milan; Mondadori 1944