

RANDOM NUMBER GENERATION IN PATIENTS WITH APHASIA: A TEST OF EXECUTIVE FUNCTIONS

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SUMMARY

Randomization performance was studied using the "Mental Dice Task" in 20 patients with aphasia (APH) and 101 elderly normal control subjects (NC). The produced sequences were compared to 100 computer-generated pseudorandom sequences with respect to 7 measures of sequential bias. The performance of APH differed significantly from NC participants, according to all but one measure, i.e. Turning Point Index (points of change between ascending and descending sequences). NC participants differed significantly from the computer generated sequences, according to all measures of randomness,. Finally, APH differed significantly from the computer simulator, according to all measures but mean Repetition Gap score (gap between a digit and its reoccurrence). Despite the heterogeneity of our APH group, there were no significant differences in randomization performance between patients with different language impairments. All the APH displayed a distinct performance profile, with more response stereotypy, counting tendencies, and inhibition problems, as hypothesised, while at the same time responding more randomly than NC by showing less of a cycling strategy and more number repetitions.

INTRODUCTION

One of the tasks widely used for the investigation of executive functioning is Random Item Generation (abbrv. RIG; see Miyake, Friedman, Emerson,

Witzki, Howerter & Wager, 2000). In this task, the participant is requested to produce a random sequence of items which have strong, overlearned associations, such as numbers, letters of the alphabet, keys on a keyboard or semantically related words. Various studies converge in the finding that this task is executive function demanding. Particularly, inhibition and updating of working memory information are crucial for random performance (Miyake et al., 2000). To produce a random sequence the human brain needs to inhibit prepotent responses and monitor and update the responses according to a subject's concept of randomness (Miyake et al., 2000; Spatt & Goldenberg, 1993).

Human subjects are poor randomizers, exhibiting various deviations from randomness. Avoidance of immediate repetitions, too many alternations, too equally distributed items in short runs and response biases, such as counting, characterize human generated random sequences (Heuer, Kohlisch & Klein, 2005; Spatt & Goldenberg, 1993). However distorted, there are significant differences between sequences generated by healthy participants on the one hand and participants under drug or medication influence or patients suffering from a neurological or psychiatric disorder on the other (for a review, see Brugger, 1997). The RIG task has been applied to many clinical populations (for an overview, see Table 1). Most of these populations typically suffer from impairments in prefrontal cortical regions related to executive functions; accordingly, in all studies summarized in Table 1, patients performed worse than controls. They all exhibit response stereotypy. However, their performance is not attributed to the dysfunction of the same executive function. Schizophrenic patients (Rosenberg et al., 1990) and patients with Korsakoff's syndrome (Pollux et al., 1995) appear to lack the capacity to apply suitable response strategies, whereas patients with Alzheimer's disease (Brugger, Monsch, Salmon & Butters, 1996) have inhibition and control impairments.

It is established that there is a strong connection between executive functions and language processes and that language is subordinated to executive control (Alexander, Benson & Stuss, 1989). There are also executive tasks which depend highly on language processes (i.e. "inner speech"), such as the Wisconsin Card Sorting Test (Baldo, Dronkers, Wilkins, Ludy, Raskin & Kim, 2005). Neuroanatomically, these two functions share many frontal cortical regions, crucial for the elaboration of incoming linguistic information, speech initiation and production, as well as the integration, organisation and control of language and thought (Alexander et al., 1989). In an evaluation of cognitive status in patients with aphasia Helm-Estabrooks (2002) found that, apart from proper language functions, executive processes were among the most impaired functions after brain damage associated with aphasia. Against this background, it seems surprising that RIG tasks have never been administered to patients with aphasia.

The aim of the present study was to examine the consequences of aphasia on RIG performance. We used the Mental Dice Task (MDT; Brugger et al., 1996), which requires the simulation, in one's mind, of consecutive rolls of

Table 1. Fifteen published studies on verbal randomization performance of neuropsychological patient groups

Study	Patient group(s) [Control group(s)]	Randomization task
Rosenberg et al., 1990	23 alcoholic and 20 patients with schizophrenia [45 normal controls]	Producing digits from 1 to 10, sequence length 100
Spatt & Goldenberg, 1993	35 patients with frontal lobe lesions [20 controls] and 26 patients with Parkinson's disease [20 controls]	Producing digits from 1 to 9, sequence length 64 and 81
Pollux et al., 1995	14 patients with Korsakoff's syndrome [14 controls]	Producing digits from various response sets, sequence length not specified
Brugger et al., 1996	30 patients with dementia of the Alzheimer type [30 controls]	Producing digits from 1 to 6, sequence length 66
Robertson et al., 1996	10 patients with idiopathic Parkinson's disease [10 controls]	Producing letters of the English alphabet, sequence length 100
Brown et al., 1998	16 patients with idiopathic Parkinson's disease [8 controls]	Producing digits from 1 to 9, sequence length indefinite
Artiges et al., 2000	8 patients with schizophrenia [8 controls]	Producing digits from 1 to 10, sequence length indefinite
Leclercq et al., 2000	16 patients with severe TBI and 9 with AACoA [25 controls]	Producing digits from 1 to 10, sequence length 100
Ho et al., 2004	30 Huntington disease patients (19 symptomatic, 11 presymptomatic) [20 controls]	Producing digits from 1 to 9, sequence length 100
Hoshi et al., 2006	14 patients with schizophrenia [16 controls]	Producing digits from 0 to 9. sequence length 100
Matsukawa et al., 2006	48 patients with SLE, 58 patients with schizophrenia [39 controls]	Producing digits from 0 to 9. sequence length 100
Rinehart et al., 2006	12 individuals with autism, 12 individuals with Asperger's disease [12 controls for each clinical group]	Producing digits from 1 to 10, sequence length 20 (but 10 sequences collected)
Peters et al., 2007	26 patients with schizophrenia [59 controls]	Producing digits from 1 to 10, sequence length 100

Note: AACoA = aneurysm of the anterior communicating artery;
SLE = systemic lupus erythematosus; TBI = traumatic brain injury

a die. Generally, random *number* generation tasks are most sensitive to executive (dys)function (Towse, 1998; Heuer et al., 2005). Furthermore, an oral generation mode loads the executive higher, because the participant is required to internally represent the alternative responses (Towse, 1998). The restriction to the digits from 1 to 6 was considered to be most manageable for aphasic patients, and this number range corresponded more closely to a patient's digit span than the range of the digits 1 to 10. Finally, previous work with the MDT has clearly shown that instructions are easily understood by even moderately demented patients (Brugge et al., 1996), a precondition probably not met with the lengthy and abstract "drawing-from-a-hat" analogy, often used in randomization tasks employing all single-digit numbers.

We predicted that aphasic patients would show poorer randomization performance than a healthy control group matched to the patients with respect to age and education. We also hypothesized that patients with global or Broca aphasia would perform worse than those with Wernicke aphasia, specifically according to the measures of randomization performance that reflect the inhibition aspect of executive functions (see below, paragraph "Data analysis").

MATERIAL AND METHODS

Subjects

The experimental group consisted of twenty patients with aphasia (six women and fourteen men) recruited from various settings across the city of Thessalonica and Kavala, such as hospitals, rehabilitation centers, own home etc. Inclusion criteria were the presence of stroke accompanied by an aphasic disorder. Ten of the patients were assessed and classified by the Greek version of the *Aachener Aphasia Test* (Proios et al., 2006), while the rest were clinically assessed by speech pathologists. The patients were divided into 5 groups, with prevailing aphasic symptom as grouping criterion (see Table 2). Their age ranged from 27 to 79 years (mean 58.45, S.D. 15.25), and their years of education from 6 to 16 years (mean 10.4, S.D. 3.97). Excluding criteria were presence of dementia, a history of previous vascular incidents, traumatic brain injuries and tumors, or other neurological or psychiatric disorders. All patients were receiving speech therapy during the period of the study. One hundred and one control participants (50 women, 51 men) were selected from the general population of Thessalonica and Katerini. Their age ranged from 48 to 92 years (mean 64.17, S.D. 8.38), their years of education from 6 to 16 years (mean 8.4 years, S.D. 4.72). Neither age nor education was significantly different from the patient group. All the participants were native Greek speakers. Participants with a previous diagnosis of any neurological, psychiatric, or genetic disorder were not tested. Testing took place according to the ethical guidelines of the Declaration of Helsinki, and all participants gave written informed consent before performing the task.

Table 2. Classification of 20 patients according to prevailing aphasic symptom. Note: all patients had aphasia after a first-ever stroke confined to the left cerebral hemisphere

No. of patients (N = 20)	Type of aphasia	Age (mean \pm SD, years)	Education (mean \pm SD, years)	Other neurological or neuropsychological symptoms
4	Broca's aphasia	63.75 \pm 16.17	11.5. \pm 4.12	hemiplegia
3	Wernicke's aphasia	67.66 \pm 14.74	6.0 \pm 0.00	hemiplegia
8	Anomia	62 \pm 10.08	12.0 \pm 4.14	hemiplegia, apraxia
2	Global aphasia	66.5. \pm 2.12	9.0 \pm 4.24	hemiplegia
3	Unclassified aphasia	41.33 \pm 8.08	8.0 \pm 3.46	hemiplegia

Task and procedure

Participants were required to call out a sequence of numbers from 1 to 6 in time with a metronome clicking 1 beat/sec. Specifically, they had to imagine rolling a die "over and over again, and to name the number that showed up after each imaginary roll". A practice run of 10 responses was given to make the participant acquainted with the relatively rapid response rate and to affirm that the instructions were understood. The instructions were repeated if the participant named all digits in either an ascending or descending row (the only prominent patterning of responses observed). Rather than pointing out that such an event would be rare, the instructions were simply repeated with the addition that "consecutive rolls of a die do not show any pattern in the sequence of the single digits". Although ideally the 66 responses should have been made in time with the metronome, no time constraint was employed, and even if the rhythm could not be maintained, 66 responses were reordered at whatever speed they had been elicited. The vocal responses were recorded.

Data analysis

According to a principal component analysis performed by Miyake et al. (2000), the randomization of numbers taps two basic executive functions: (1) inhibition and (2) updating and monitoring working memory information. Inhibition was captured by three measures loading high on the "prepotent associates" component (Towse & Neil, 1998). These were Adjacency (counting and backward counting in steps of one), Turning Point Index (the average length of an ascending or descending sequence) and Run Scores (variability in successive ascending or descending phase lengths). Monitoring and up-

dating was measured by Redundancy, Coupon and Repetition Gap, which all load high on the "equality of response usage" component (Towse & Neil, 1998). Redundancy reflects the ratio of ideal and observed information content based on frequencies of each digit, Coupon designates number of responses produced until all response alternatives are given, and Repetition Gap is the mean number of responses given until each digit reoccurs in the sequence.

These six indices were complemented by one further measure, i.e. Evan's (1974) RNG index because of its extensive use in the field. The RNG index is a global measure of randomness reflecting the frequency distribution of all named doublets (e.g., 1, 2; 5, 5; 6, 3). All indices were calculated using the RgCalc program (Towse & Neil, 1998).

Two between-subjects designs were used in this study. One had participant group (normal controls, patients with aphasia and computer simulations) as a between factor and the randomization indices as the dependent variable. Another comprised the 20 aphasia patients and had aphasias group (Broca, Wernicke, anomia, global and unclassified) as between factor and the randomization indices as the dependent variable.

The data were analyzed with one-way ANOVA, and the level of alpha was set at .05.

RESULTS

The ANOVAs with the aphasias patients, healthy controls and computer sequences as factors were significant for all seven indices of randomness (Adjacency [$F(2, 220) = 66.25, p<.001$], Turning Point Index [$F(2, 220) = 17.55, p<.001$], Run Scores [$F(2, 220) = 17.29, p<.001$], Redundancy [$F(2, 220) = 9.70, p<.001$], Coupon [$F(2, 220) = 49.43, p<.001$] Repetition Gap [$F(2, 220) = 46.09, p<.001$] and RNG index [$F(2, 220) = 89.04, p<.001$]. Post-hoc analyses, using Scheffe's correction, revealed that the performance of the control group and patient group was not significantly different in one index, Turning Point Index [$F(2, 220) = .720, p>.05$]. It also showed no significant difference between the computer simulator and the aphasias patients in the Redundancy [$F(2, 220) = 9.70, p>.05$] and Repetition Gap [$F(2, 220) = 46.09, p>.05$]. All other measures of randomness (Adjacency, Run Scores, Coupon and RNG index) discriminated human subject-generated (controls and patients) from computer-generated sequences (see Figures 1, 2, 3, 4).

None of the seven one-way ANOVAs within the patient group was significant (Adjacency [$F(4, 19) = .516, p>.05$], Turning Point Index [$F(4, 19) = .720, p>.05$], Run Scores [$F(4, 19) = .171, p>.05$], Redundancy [$F(4, 19) = 2.10, p>.05$], Coupon [$F(4, 19) = 1.09, p>.05$], Repetition Gap [$F(4, 19) = 2.58, p>.05$] and RNG index [$F(4, 19) = 2.49, p>.05$]).

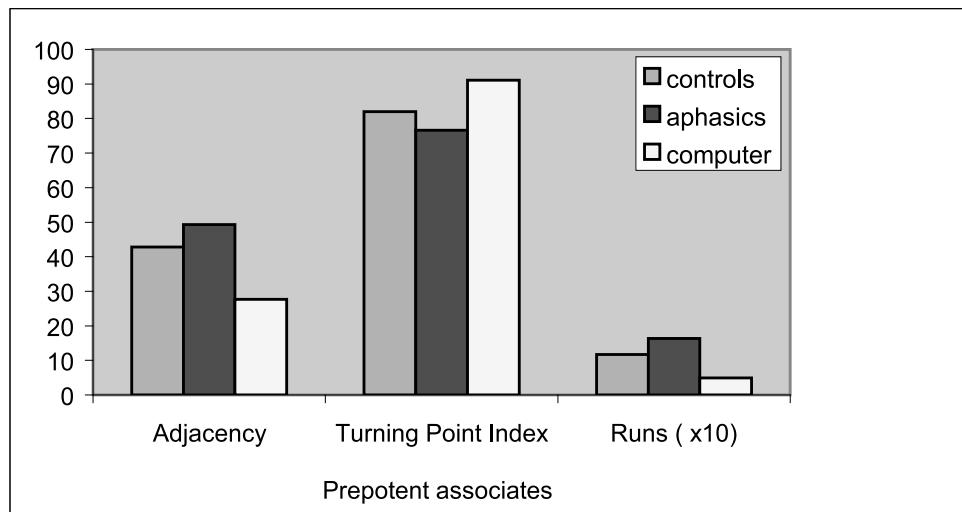


Figure 1. Mean scores for controls, aphasics and computer simulation on Adjacency, Turning Point Index and Runs

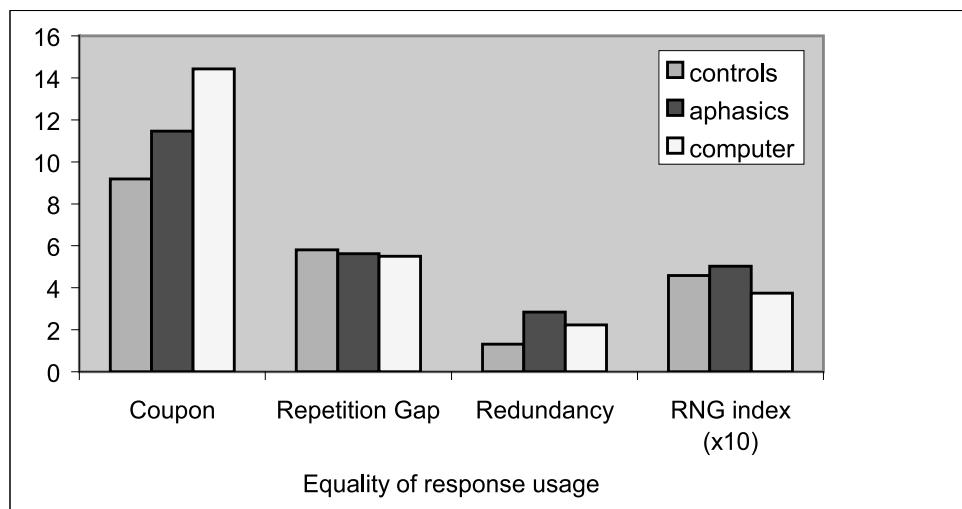


Figure 2. Mean scores for controls, aphasics and computer simulation on Coupon, Repetition Gap, Redundancy and RNG index

DISCUSSION

The findings of the present study can be summarized using the two components of randomization performance as an axis. The first finding is that patients with aphasia exhibited more stereotyped responses. They counted more than controls, as indicated by Adjacency scores. They had longer successive ascending and descending sequences in the set, according to Run scores, and a much smaller number of changes between them, though not

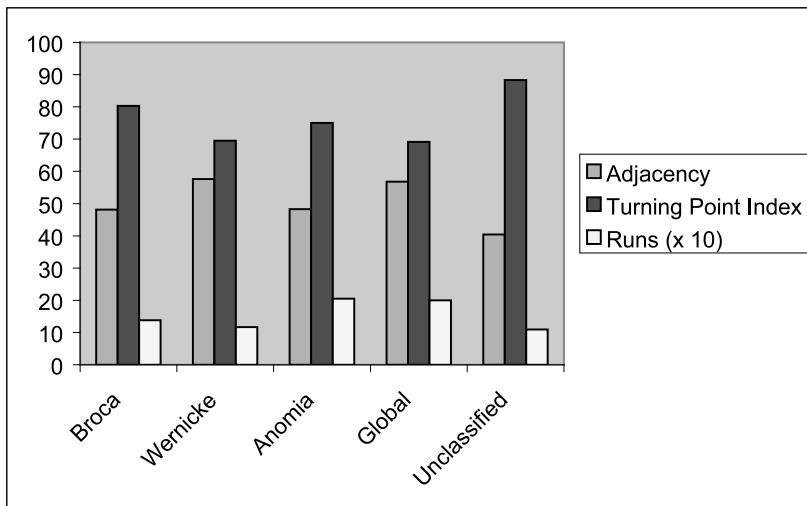


Figure 3. Mean scores for groups of classified patients on Adjacency, Turning Point Index and Runs

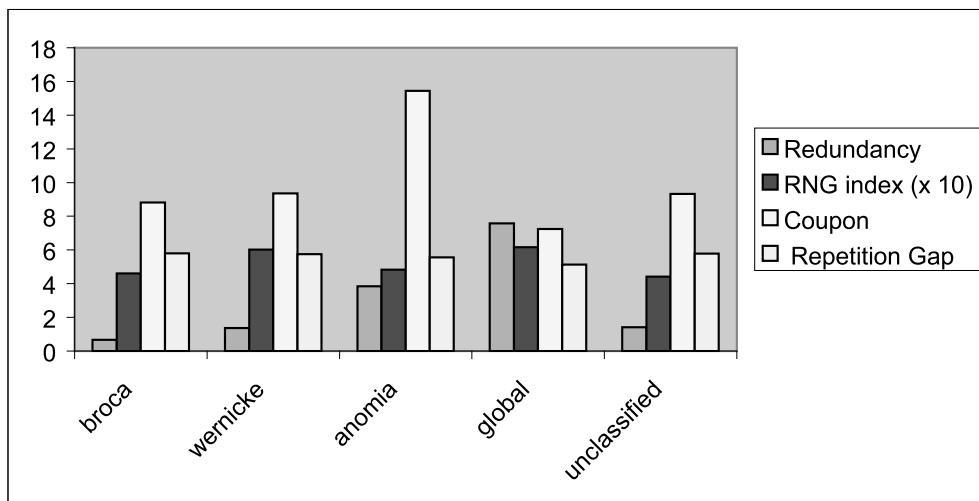


Figure 4. Mean scores for groups of classified patients on Redundancy, RNG index Coupon and Repetition Gap

significantly different from controls, as shown by Turning Point Index scores. The RNG index score is congruent with the previous measures, which demonstrate the poor performance of patients with aphasia in the "prepotent associates" component (Towse & Neil, 1998).

According to Miyake et al. (2000), the above scores estimate the deliberate inhibition of automatic or overlearned responses, irrelevant to the task demands, in our case, habitual counting. Counting is based on nonpropositional, automatic language, and is usually better preserved in patients with

aphasia than propositional – in this case, random number production (Lum & Ellis, 1999). From this point of view, it is not surprising that patients were more susceptible to counting than controls. According to a model proposed by Brown et al. (1998), there is an "active controller" that suppresses activation in a number-representing network with very high associative links between adjacent digits (such as 2, 3, 4 or 2, 4, 6 etc.). The limited capacity of this "active controller" in our patient group, which can no longer effectively inhibit the production of stereotyped outputs, accompanied by language impairments, may account for these results.

RNG is a complex executive task (Miyake et al., 2000) and as such, performance on it depends not only on deliberate inhibition, but also on monitoring and updating working memory information. This function is better estimated by Redundancy, Coupon and Repetition Gap measures (Miyake et al., 2000). These measures load high on the "equality of response usage" component (Towse & Neil, 1998), and demonstrate how equally response alternatives are distributed in the produced sequence. Patients with aphasia scored higher than controls on Coupon, though not higher than the computer simulator. This result points out that patients relied less on a cycling strategy. In the Repetition Gap and Redundancy scores no significant difference was found between patients and computer-generated sequences. With two out of three measures constituting the "equality of response usage" component not being significantly different from the computer generated sequences, patients with aphasia seem to be better randomizers. As far as the "equality of response usage" component is concerned, patients responded in a more random way than control participants. This finding can be attributed to a deficit in the function of monitoring and updating working memory representations. It could be because of this deficit that patients with aphasia failed to distribute response alternatives equally in the sequence, as controls did, and hence produced more random sequences.

The findings of the present study stress the dissociation between the mechanisms that lie beneath the randomization process, inhibition and, monitoring and updating. They verify the argument that RNG is a complex executive task, that it employs related but distinguishable executive functions which contribute in a different way to parameters of the task (Miyake et al., 2000). We can suggest that a good working inhibition (suppressing counting) and a defective monitoring and updating function (allowing repetitions and unable to apply cycling) would result in a random sequence. Our patients could not replicate this model due to inhibition problems.

Inhibition deficits also characterize the randomization performance of most clinical populations tested with the RIG task. Patients with Alzheimer's disease (Brugge et al., 1996), Parkinson's disease (Robertson et al., 1996), schizophrenia (Rosenberg et al., 1990), severe diffuse traumatic brain injury and vascular prefrontal damage (Leclercq et al., 2000) all exhibit response stereotypy and counting tendencies. However, the result of a patient group

responding more random than control participants, as in our study, is unique in the literature on RNG.

Despite the heterogeneity of our patient group, we found no significantly different performance patterns. We had hypothesized that patients with different prevailing aphasic symptoms would have different scores, but there was no such effect. This could be attributed to the small size of our patient group. Also, the majority of participants had no severe language impairments, except for the two global aphasics. Another factor that can account for this finding is the fact that numbers are special words (Domahs, Bartha, Lochy, Benke & Delazer, 2006). According to the "triple code" model of Dehaene (1992), humans can represent and manipulate numbers in three forms: verbal, arabic and as analogical magnitude. This makes numbers unique randomization items that could not differentiate patients with aphasia. It would be interesting for future research, however, to examine patients with different language impairments, using phonemes, or semantically or phonemically related words, as randomization items (see Taylor et al., 2005).

We examined randomization performance in patients with aphasia using a verbal task of RIG. It could be easier to apply random key pressing, a non-verbal task, but as mentioned before, this task is not sensitive to executive dysfunction (Heuer et al., 2005; Towse, 1998). Patients responded quite satisfactorily to the task: the vast majority had no problems in naming numbers, a fact that supports the finding that a selective preservation of numerals can be observed in aphasics (Domahs, Bartha, Lochy, Benke & Delazer, 2006). There was a problem in responding in time with the metronome, which surely influenced performance. However, it was inevitable that patients with aphasia, especially anomics, Brocas and global aphasics, could not respond at such a high pace as 1 response per second, and therefore we allowed them a self-paced performance.

The RNG task is a very useful tool for the exploration of executive functioning, and lacks the greatest disadvantage of executive tests: it cannot be learned, because, as Spatt et al. (1993) pointed out, there is no algorithm for successive performance. Our study showed that it is also applicable to patients with aphasia.

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