

Brain potentials and self-paced random number generation in humans

Sabine Schneider^a, Gregor Joppich^b, Arie van der Lugt^a, Jan Däuper^b, Thomas F. Münte^{a,*}

^a Department of Neuropsychology, Otto von Guericke University, Universitätsplatz 2, Gebäude 24, 39106 Magdeburg, Germany

^b Department of Neurology, Medizinische Hochschule Hannover, Hannover, Germany

Received 19 April 2004; received in revised form 21 May 2004; accepted 25 May 2004

Abstract

Random number generation (RNG) requires executive control. A novel paradigm using the eight drum pads of an electronic drum set as an input device was used to test 15 healthy subjects who engaged in random or ordered number generation (ONG). Brain potentials time-locked to the drum-beats revealed a more negative response during RNG compared to ONG which had a left frontal distribution. Source analysis pointed to Brodmann area 9, which has been reported previously in a PET study and is thought to be engaged in suppression of habitual responses such as counting up in steps of one during RNG. Lateralized readiness potentials reflecting the difference in activation of the contra and ipsilateral motor cortex were smaller during ONG reflecting the ability to preprogram such canonical sequences.

© 2004 Elsevier Ireland Ltd. All rights reserved.

Keywords: Random number generation; Event-related potentials; Dorsolateral prefrontal cortex

As we produce a sequence of action over time, what we will do in the immediate future is related to what we have done in the immediate past. Humans, like any other organism, therefore have to keep track of their actions and to adapt action plans to task requirements and the changing environmental conditions. These monitoring functions are thought to be a core component of the *executive functions* [2,22]. An important paradigm to study executive functions in the control and monitoring of action sequences is random number generation (RNG). Typically, this task requires the generation of numbers in a random order, e.g. by pressing the number keys of the number block of a computer keyboard. The rate of production is often controlled by an external pacing stimulus [1]. Obviously, in trying to produce a random-like sequence the subject has to keep track of his/her past key presses and to suppress prepotent response patterns such as repetitions or counting up in ones (e.g. 1-2-3).

Lesion data suggest that the frontal lobes are important for RNG [19]. A number of studies have tried to address the neural underpinnings of random as opposed to ordered number generation using modern neuroimaging techniques [8,18]. For example, a PET study in young healthy subjects

[8] contrasting RNG and counting revealed activation in distributed cortical areas. One area that was found more active during RNG was the dorsolateral prefrontal cortex (DLPFC, Brodmann area 9) thought to be responsible for suppressing habitual responses. This view is supported by the fact that transcranial magnetic stimulation (TMS) over the left DLPFC significantly decreases randomness [7,9].

Recently, we recorded event-related brain potentials while young adults engaged either in random number generation (RNG) by pressing the number keys on a computer keyboard in a random sequence, or in ordered number generation (ONG), i.e. pressing the keys in their canonical order [10]. The most important finding in this study was a left frontal negativity peaking 140 ms after the onset of the pacing stimulus, which was observed during RNG, whenever the subjects produced a true random response. This negativity could be attributed to the left dorsolateral prefrontal cortex and was interpreted as an index for the inhibition of habitual responses. In addition, in response locked ERPs a negative component was apparent peaking about 50 ms after the key-press that was more prominent during RNG. This effect shared certain characteristics with the so-called error (related) negativity [3,4,21], an ERP component probably related to response monitoring, and was therefore tentatively interpreted as a reflection of the greater monitoring demands during random sequence generation.

* Corresponding author. Tel.: +49 391 671 8469;

fax: +49 391 671 1947.

E-mail address: thomas.muente@med.uni-magdeburg.de (T.F. Münte).

This previous study illustrated the power of the ERP technique to reveal the timing of cognitive and executive processes with a high temporal resolution [16]. Because an external pacing signal was employed as in virtually every behavioral study on RNG, stimulus and response related ERPs overlapped to some extent, however, which can cause problems in the interpretation of ERP effects. Moreover, because either the left or the right hand was used for key presses, our previous study did not allow us to record reliable lateralized readiness potentials (LRP). This lateralized part of the RP has been used as an index for specific response preparation [11]. It provides information about the timing of cognitive processes related to response preparation [15,23]. The LRP has been shown to be sensitive to movement complexity [6,25,27]. For example, Hackley and Miller [6] compared a simple movement condition requiring key strokes of the left or right index finger with a complex movement comprising successive finger taps with index, ring, and middle fingers. In this study the LRP was found to be of roughly double the amplitude in the complex as compared to the simple condition.

The present experiment was designed to maximize the LRP in order to take advantage of its capability to reveal the timing of motor actions during random and ordered sequence generation. To this end, the subjects had to perform RNG and ONG by hitting the drum pads of an electronic drum set arranged left and right of the subjects (Fig. 1). Furthermore, to avoid the problem of overlapping stimulus- and response-related ERP components the drum-beats were self-paced in the present experiment.

Fifteen right-handed, neurologically healthy subjects (9 women; age-range 19–32, mean 23.6), all students at the University of Magdeburg, received course credit or monetary compensation for their participation.

Subjects were tested individually while seated in a sound attenuated and dimly lit room. To the left and right of the subject two groups of four muted electronic drum pads each (clearly marked by numbers 1–8) were placed as shown in Fig. 1. The drum pads were arranged such that all of them could be reached easily. The left hand of the subject was to

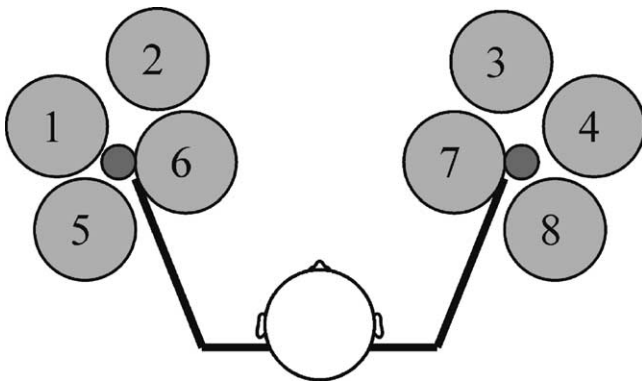


Fig. 1. Illustration of the experimental set-up. Four drum pads each were positioned left and right within reach of the subject.

be used to hit the left four pads, while the right hand was used for the four right pads. By hitting a pad, a midi signal was produced which was passed on as an event marker to the data acquisition computer.

In the experiment the subjects had to beat the 8 drum pads with the tips of fingers 2–4 in a self-paced fashion and with medium strength for 10 runs each comprising about 200 beats. In training runs they were instructed to achieve an interbeat-interval of roughly 1 s. This was accomplished by using a metronome set to 60 bpm. In five of the 10 runs the drums had to be hit in the canonical order (ONG condition, i.e. 1-2-3-4-5-6-7-8-1-2-...), while in the other five runs subjects were instructed to generate “random” sequences (RNG: e.g. 3-4-4-7-1-5-8-3-...). The order of conditions was pseudo-randomized and counter-balanced across subjects. Each run lasted approximately 3.5 min. Breaks were taken between runs as required by the participant. The entire experiment lasted about 2.5–3 h including positioning of electrodes.

Participants were asked not to speak and to minimize eye blinks, eye and body movements during the experiment.

According to Ginsburg and Karpiuk [5] there are three important factors in the description of randomness: cycling, repetition and seriation. Following Jahanshahi et al. [9] we focus on seriation in the present communication.

Seriation refers to the tendency to generate during RNG sequences with the canonical order of the numbers (e.g. 2-3-4). To describe seriation the occurrence of steps of one (e.g. 2-3, CS1) and steps of two (e.g. 2-4 CS2) as described by Spatt and Goldenberg [24] was counted. These measures take into account the length of the series. The sequence length was squared to give greater weights to longer sequences. An increase of the measure CS1 would indicate less randomness. These measures were compared with a sample of pseudorandom series generated by a computer program.

EEG was recorded from 27 scalp sites using tin-electrodes (including all standard 10/20 system positions) mounted in an elastic electrode cap. Signals were collected using a left mastoid electrode as a reference and were re-referenced off-line to the common average reference. Vertical eye movements were recorded using a bipolar montage using electrodes placed on the left lower orbital ridge and Fp1. Horizontal eye movements were monitored by using two electrodes placed on the left and right external canthus. The EEG was sampled with time-constants of 10 s and low pass filter settings 70 Hz. Signals were digitized with a sampling rate of 250 Hz (4 ms resolution). Averages were obtained time-locked to the midi-signal emitted by the drum pads for 1024 ms epochs starting 724 ms before the beat. The time period between –700 and –600 ms (with respect to the drum-beat) was used as a baseline. Trials contaminated by eye movement or amplifier blocking within the critical time window were rejected from averaging by a computer program using individualized rejection criteria.

ERPs were averaged for all drum-beats from the ONG and RNG conditions separately. In addition to capture the

different aspects of “random behavior”, a number of separate averages were obtained for the RNG condition: (1) repetitions: a drum pad was hit twice in a row, (2) counting up in steps of 1, (3) counting down in steps of 1, (4) “random”: all beats that could not be categorized in (1)–(3). In addition to conventional averages the lateralized readiness potential (LRP) was computed. LRPs were assessed by using C3 and C4 electrode locations, where the amplitude of the readiness potential is maximum [11]. The LRP is computed by a double subtraction as shown in the following equation:

$$\text{LRP} = \text{left hand (C4 - C3)} - \text{right hand (C4 - C3)}$$

Left and right hands refer to the response hand and (C4 – C3) is the difference in electrical potential between these electrodes [23].

For statistical analysis, mean amplitude measures were obtained and entered into ANOVA-statistics with the Huynh–Feldt epsilon correction applied as necessary. Neural generators of the brain activity were estimated by computing the cortical three-dimensional distribution of current density using the LORETA (low resolution brain electromagnetic tomography) algorithm [17] which solves the inverse problem by assuming related orientations and strengths of neighboring neuronal sources without assuming a specific number of generating sources. The “smoothest” of all possible activity distributions is thereby obtained. The version of LORETA employed here [20] uses a three-shell spherical head model registered to standardized stereotactic space [26] and projected onto the Montreal Neurological Institute standard average brain. Computations were restricted to cortical gray matter and hippocampi (spatial resolution of 7 mm, 2394 voxels) as described elsewhere [20].

The average interval of the drum-beats was very close to the target of 1000 ms with the production speed being minimally slower during ONG (1061 ms, S.E.M. 32 ms) than during RNG (1012 ms, S.E.M. 26 ms, $t(14) = 2.41$, $P = 0.03$).

The CS1 score, indicating steps of 1, was 28.9 (S.D. 8.3) per 100 drum-beats which was significantly lower than the CS1 score determined for a series generated by a computer program (47, $P < 0.01$). The CS2 score, indicating steps of 2, was 31 (S.D. 11.2) in the subjects and 44 in the computer-generated series ($P = 0.08$).

The grand average ERPs time-locked to the drum-beats are shown in Fig. 2. A negative shift emerged for the RNG versus the ONG condition which was most pronounced over left frontocentral recording sites. This shift was quantified by a mean amplitude measure in the time window –400 to –200 ms (with respect to the next drum-beat) for 5 pairs of frontocentral electrodes (F3/4, C3/4, P3/4, FC1/2, CP1/2). An ANOVA performed on these data revealed a main effect of task ($F(1,14) = 9.16$, $P < 0.009$) and an interaction effect of task by hemisphere ($F(1,14) = 9.84$, $P < 0.008$), the latter reflecting the left preponderance of the effect. Fig. 3 illustrates the its distribution by spline-interpolated isovoltage maps depicting the mean difference of the RNG and ONG ERP in the time window –400 to –200 ms. To obtain

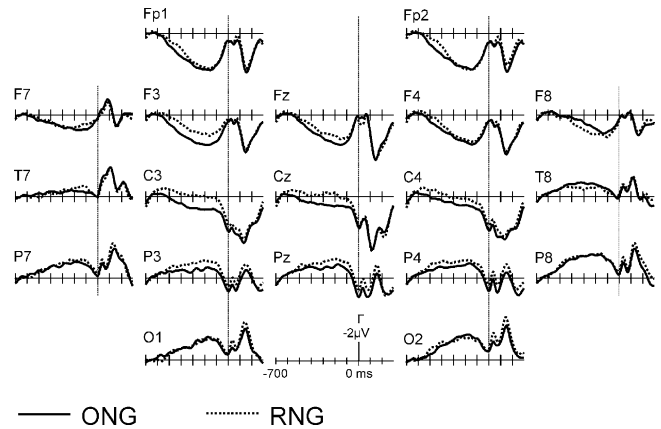


Fig. 2. Grand average ERPs time-locked to the time of the drum-beat (marked by vertical dotted line). A marked negative shift is seen for the RNG condition with a maximum over left frontocentral scalp sites.

an estimate of the neural generators underlying this effect, source analysis (LORETA) was performed on the grand average difference potential. This activity appeared to be in or near to Brodmann area 9 (coordinates of maximum activity at $t = -400$ ms, $X = -32$, $Y = 32$, $Z = 43$ mm) and is shown rendered onto brain slices of standard brain in Fig. 3.

Comparisons of ERPs to responses of the RNG task reflecting presumably different randomness (counting up in steps of 1, counting down in steps of 1, “random”) revealed no systematic effects.

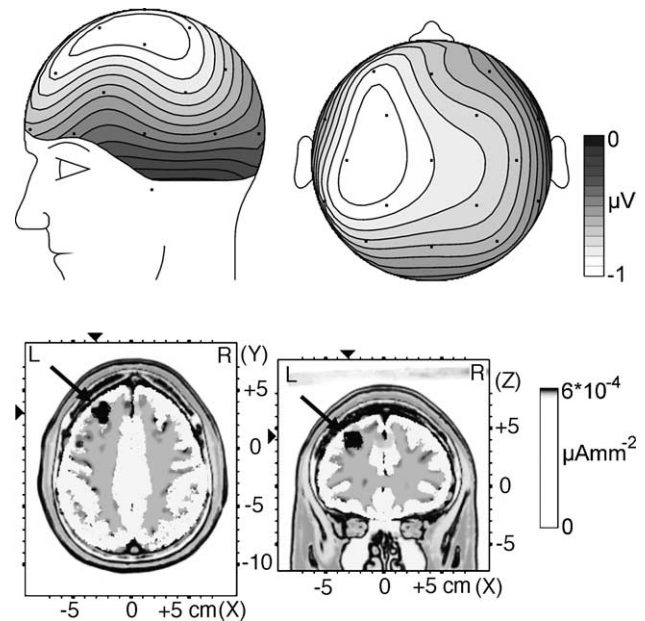


Fig. 3. Upper panel: spline interpolated isovoltage maps. Depicted is the mean amplitude difference between the ERPs in the RNG and ONG conditions in the time window –400 to –200 ms (relative to the next drum-beat). A clear left dorsolateral frontal negativity emerges. Lower panel: estimation of the neural generators using the LORETA program suggests a main source in the Brodmann area 9. Arrows point to the activation maximum (black).

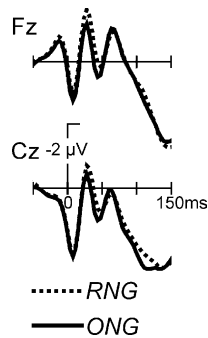


Fig. 4. Response-locked ERPs (averaged mastoid reference) for the first 150 ms after the drum-beat. A negativity peaking at 30 ms is slightly larger in the RNG condition.

The electrophysiological activity immediately following the drum-beat is shown in Fig. 4. A negative peak is seen at about 30 ms, which is slightly larger in the RNG condition. This difference was significant (mean amplitude 20–50 ms, Fz & Cz electrode, $F(1,14) = 5.19$, $P = 0.039$).

The LRPs are shown in Fig. 5. Clearly, LRPs for responses made with a different hand than the previous one were associated with a larger LRP than same hand responses. Also, LRPs from the RNG task were larger than those from the ONG task. LRPs were quantified in the –200 to –150 ms time window with regard to the drum-beat. An ANOVA with factors task (ONG versus RNG; all responses) and response hand (same versus different) revealed main effects task ($F(1,14) = 5.05$, $P = 0.041$) and response hand ($F(1,14) = 4.92$, $P = 0.044$) with no interaction. Again, comparisons contrasting responses of presumably different “randomness” from the RNG condition (see the preceding text) did not reveal any significant differences in this time window.

The present study used a modified RNG task to record event-related brain potentials. The fact that no external pacing signal was used successfully avoided contamination of the ERPs by components related to the pacing stimulus, while the rate of number production was quite regular. Moreover, the use of drum pads positioned within the reach of the left and right hands led to the generation of reliable LRPs.

LRP responses were larger in the RNG condition. Previously, it has been shown in a variety of settings that the LRP

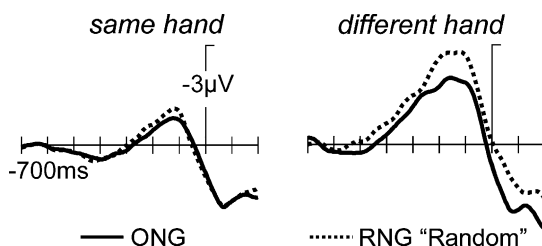


Fig. 5. Response-locked lateralized readiness potentials from C3/C4 scalp sites. The time of the drum-beat is marked by the vertical line. A marked difference in amplitude is seen between responses carried out with a different hand than the previous response and drum-beats made by the same hand. Also, LRPs were larger during RNG compared to ONG.

is sensitive to the complexity of the movement to be performed [6,25,27] and thus the smaller LRP in the ONG-task comes as no surprise. In these previous tasks the complexity manipulation entailed the preparation of sequential movements of several fingers versus the preparation of the successive movement of a single finger for example and was thus clearly different from the ONG/RNG manipulation used here. The smaller LRP for responses carried out with the same hand as the preceding response is easily explained by the fact that the motor cortex can remain active in this case.

In a previous study comparing RNG and ONG in an externally paced paradigm, we had seen a frontocentral negativity immediately following the button-press which had a frontocentral distribution and was larger for RNG during a comparatively slow production rate (1 response per 1500 ms). In the present study, a similar effect was found (Fig. 4). Again a larger negativity was seen for RNG. This response, which is similar to the error-(related)-negativity, might index the greater response monitoring demands in the RNG condition.

The most important electrophysiological finding, however, is a left frontal negativity distinguishing RNG from ONG (Fig. 2). The topographical distribution of this effect illustrated by the isovoltage maps would be consistent with an origin in the left dorsolateral prefrontal cortex. This was corroborated by the source localization (Fig. 3) which suggested a generator in Brodmann area 9.

Petrides et al. [18] found area 9 and 46 active in self-ordered working memory tasks. This location also coincides with findings by Jahanshahi et al. [8], who found BA 9 activated when PET images from RNG and ONG conditions were compared. As transcranial magnetic stimulation to the left but not the right DLPFC [7] increased the number of habitual responses (counting in steps of 1), these authors propose that this brain area is associated with the suppression of habitual counting, as it is necessary during RNG. The subjects of the current study apparently also suppressed the most habitual type of response (counting up/down in steps of 1) as the measure CS1 was significantly lower as in a computer-generated pseudorandom series. The dorsolateral prefrontal cortex is the core structure for strategic/control aspects of behavior [13,14]. For example, the DLPFC has also been found activated in an fMRI study of the Stroop paradigm in response to a cue stimulus indicating which aspect of the Stroop stimulus had to be evaluated in the particular trial [12]. These previous findings and the behavioral pattern with a low CS1 in the current study make it likely that the ERP effect observed in the present study is similarly related to these control/suppression aspects. This would suggest that this effect should be differentially modulated for responses reflecting “true” random behavior (e.g. 3-6-5) and responses reflecting habitual responding (1-2-3). Such effects could not be demonstrated in the present data set, possibly because of an insufficient signal-to-noise ratio. Such differences remain to be shown in future studies to rule out alternative interpretations of the left frontal ERP effect (e.g. planning of a motor sequence).

In our earlier study, using externally paced RNG/ONG with the number block of a computer keyboard as the input device we have described a circumscribed left-frontal negativity for RNG which also was localized to the left dorsolateral prefrontal cortex [10]. In this case the effect was of shorter duration, coincided in time with the auditory N1 component elicited by the pacing stimulus. The apparent differences in timing of the two left frontal ERP effects in the current and the previous study might partially be reconciled, as the response times to the pacing stimuli in the previous study was 417 ms, which would place the effect at about the same time with regard to the motor responses in both studies. While the left frontal modulation in our first study was seen for pacing stimuli followed by a (presumably) true random response versus pacing stimuli followed by a repetition, no systematic differences as a function of the kind of response during RNG were seen in the present study. This suggests that the present left frontal effect reflects global aspects of the RNG task and not local aspects of the specific response sequence.

Acknowledgements

Supported by DFG-grant MU 1311/11-2. We thank M. Bangert and T. Wüstenberg for technical support.

References

- [1] A. Baddeley, H. Emsli, J. Kolodny, J. Duncan, Random generation and the executive control of working memory, *Quart. J. Exp. Psychol. A* 51 (1998) 819–852.
- [2] A.D. Baddeley, Exploring the central executive, *Quart. J. Exp. Psychol.* 49A (1996) 5–28.
- [3] M. Falkenstein, J. Hoormann, S. Christ, J. Hohnsbein, ERP components on reaction errors and their functional significance: a tutorial, *Biol. Psychol.* 51 (2000) 87–107.
- [4] W.J. Gehring, B. Gross, M.G.H. Coles, D.E. Meyer, E. Donchin, A neural system for error detection and compensation, *Psychol. Sci.* 4 (1993) 385–390.
- [5] N. Ginsburg, P. Karpiuk, Random generation: analysis of the responses, *Percept. Motor Skills* 79 (1994) 1059–1067.
- [6] S.A. Hackley, J. Miller, Response complexity and precue interval effects on the lateralized readiness potential, *Psychophysiology* 32 (1995) 230–241.
- [7] M. Jahanshahi, G. Dirnberger, The left dorsolateral prefrontal cortex and random generation of responses: studies with transcranial magnetic stimulation, *Neuropsychologia* 37 (1999) 181–190.
- [8] M. Jahanshahi, G. Dirnberger, R. Fuller, C.D. Frith, The role of the dorsolateral prefrontal cortex in random number generation: a study with positron emission tomography, *Neuroimage* 12 (2000) 713–725.
- [9] M. Jahanshahi, P. Profice, R.G. Brown, M.C. Ridding, G. Dirnberger, J.C. Rothwell, The effects of transcranial magnetic stimulation over the dorsolateral prefrontal cortex on suppression of habitual counting during random number generation, *Brain* 121 (1998) 1533–1544.
- [10] G. Joppich, J. Däuper, R. Dengler, S. Johannes, A. Rodriguez-Fornells, T.F. Münte, Brain potentials index executive functions during random number generation, *Neurosci. Res.* 49 (2004) 157–164.
- [11] M. Kutas, E. Donchin, Preparation to respond as manifested by movement-related brain potentials, *Brain Res.* 202 (1980) 95–115.
- [12] A.W. MacDonald, J.D. Cohen, V.A. Stenger, C.S. Carter, Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control, *Science* 288 (2000) 1835–1838.
- [13] E.K. Miller, The prefrontal cortex and cognitive control, *Nat. Rev. Neurosci.* 1 (2000) 59–65.
- [14] E.K. Miller, J.D. Cohen, An integrative theory of prefrontal cortex function, *Ann. Rev. Neurosci.* 24 (2001) 167–202.
- [15] J. Miller, S.A. Hackley, Electrophysiological evidence for temporal overlap among contingent mental processes, *J. Exp. Psychol. Gen.* 121 (1992) 195–209.
- [16] T.F. Münte, T. Urbach, E. Düzel, M. Kutas, Event-related brain potentials in the study of human cognition and neuropsychology, in: F. Boller, J. Grafman, G. Rizzolatti (Eds.), *Handbook of Neuropsychology*, vol. 1, Elsevier, Amsterdam, 2000, pp. 139–235.
- [17] R.D. Pascual-Marqui, C.M. Michel, D. Lehmann, Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain, *Int. J. Psychophysiol.* 18 (1994) 49–65.
- [18] M. Petrides, B. Alivisatos, A.C. Evans, E. Meyer, Dissociation of human mid-dorsolateral from posterior dorsolateral frontal cortex in memory processing, *Proc. Natl. Acad. Sci.* 90 (1993) 877–885.
- [19] M. Petrides, B. Milner, Deficits on subject ordered tasks after frontal- and temporal-lobe lesions in man, *Neuropsychologia* 20 (1982) 249–262.
- [20] D.A. Pizzagalli, D. Lehmann, A.M. Hendrick, M. Regard, R.D. Pascual-Marqui, R.J. Davidson, Affective judgments of faces modulate early activity (160 ms) within the fusiform gyri, *Neuroimage* 16 (2002) 663–677.
- [21] A. Rodriguez-Fornells, A.R. Kurzbuch, T.F. Münte, Time course of error detection and correction in humans: neurophysiological evidence, *J. Neurosci.* 22 (2002) 9990–9996.
- [22] T. Shallice, P. Burgess, The domain of supervisory processes and temporal organization of behaviour, *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 351 (1996) 1405–1411.
- [23] H.G.O.M. Smid, G. Mulder, L.J. Mulder, G.J. Brands, A psychophysiological study of the use of partial information in stimulus–response translation, *J. Exp. Psychol. Hum. Percept. Perform.* 18 (1992) 1101–1119.
- [24] J. Spatt, G. Goldenberg, Components of random generation by normal subjects and patients with dysexecutive syndrome, *Brain Cognit.* 23 (1993) 231–242.
- [25] V. Stief, H. Leuthold, J. Miller, W. Sommer, R. Ulrich, The effect of response complexity on the lateralized readiness potential, *Z. Psychol.* 206 (1998) 305–310.
- [26] J. Talairach, P. Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*, Thieme Medical Publishers, New York, 1988.
- [27] N. Wild-Wall, J. Sangals, W. Sommer, H. Leuthold, Are fingers special? Evidence about movement preparation from event-related brain potentials, *Psychophysiology* 40 (2003) 7–16.