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Cognitive control and brain network dynamics during word generation tasks predicted using a novel event-related deep brain activity method

（新たな事象関連深部脳活動法により推察される語産生課題中の認知制御とプレインネットワークのダイナミクス）
Cognitive Control and Brain Network Dynamics during Word Generation Tasks Predicted Using a Novel Event-Related Deep Brain Activity Method

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Abstract

There is a growing interest in the diagnosis and treatment of patients with dementia and cognitive impairment at an early stage. Recent imaging studies have explored neural mechanisms underlying cognitive dysfunction based on brain network architecture and functioning. The dorsal anterior cingulate cortex (dACC) is thought to regulate large-scale intrinsic brain networks, and plays a primary role in cognitive processing with the anterior insular cortex (aIC), thus providing salience functions. Although neural mechanisms have been elucidated at the connectivity level by imaging studies, their understanding at the activity level still remains unclear because of limited time-based resolution of conventional imaging techniques. In this study, we investigated temporal activity of the dACC during word (verb) generation tasks based on our newly developed event-related deep brain activity (ER-DBA) method using occipital electroencephalogram (EEG) alpha-2 powers with a time resolution of a few hundred milliseconds. The dACC exhibited dip-like temporal waveforms indicating deactivation in an initial stage of each trial when appropriate verbs were successfully generated. By contrast, monotonous increase was observed for incorrect responses and a decrease was detected for no responses. The dip depth was correlated with the percentage of success. Additionally, the dip depth linearly increased with increasing slow component of the DBA index at rest across all subjects. These findings suggest that dACC deactivation is essential for cognitive processing, whereas its activation is required for goal-oriented behavioral outputs, such as cued speech. Such dACC functioning, represented by the dip depth, is supported by the activity of the upper brainstem region including monoaminergic neural systems.
Keywords
Deep Brain Activity, Alpha-2 Wave, Cognitive Processing, Dorsal Anterior Cingulate Cortex, Event-Related Deep Brain Activity Method

1. Introduction

Cognitive control is essential for performing daily activities. It allows the brain to vary adaptive behavior according to current goals and tasks, rather than remaining rigid and inflexible. Cognitive behavior is altered, in a number of neurodegenerative and psychiatric diseases, lowering the quality of life. Enormous effort has been addressed to eliciting underlying neurophysiological mechanisms of the affected individual [1]-[8]. Functional magnetic resonance imaging (fMRI) studies reveal that neurophysiological mechanisms underlying cognitive disorders involve disrupted large-scale brain networks, including the default mode network (DMN) consisting of the ventromedial prefrontal cortex (VmpFC), posterior cingulate cortex (PCC), inferior parietal lobule, and hippocampus; the salience network (SN) consisting of the dorsal anterior cingulate cortex (dACC) and insular; and the central executive network (CEN) consisting of the dorsolateral prefrontal cortex (DLPFC) and intra-parietal sulcus (IPS) [9]-[18].

To elicit mechanisms of cognitive dysfunction, there has been a significant interest in understanding networks that manage cognitive function. Recent fMRI studies have revealed a negative correlation between the DMN, a task-negative network, and the CEN, a task-positive network [19] [20] [21] [22]. However, these networks are not always anti-correlated [23] [24] [25] [26]. Such counterevidence to the conventional anti-correlation-based brain network architectures [27] is thought to originate from dynamic interactions [28]. Using a graph theory [29] [30], correlations across the entire brain have been investigated using fMRI data measured both during rest and while actively performing tasks to explore how the human brain is functionally organized [31] [32].

Although the brain intrinsically follows an anti-correlated architecture, the organized networks are reconfigurably associated with not only aging [33] but also external situations [34] [35] [36]. To understand mechanisms underlying contextual reconfiguration of brain networks, an event-related fMRI paradigm has been developed [37] [38]. Data given by this paradigm reflect temporal information associated with hemodynamics. To elicit the mechanisms, such data are desired to be integrated with data derived from more direct electrophysiological measurements including electroencephalography [39]. However, blood oxygen level dependent signals of fMRI are too slow to capture temporally changing network dynamics, compared with electroencephalogram (EEG) signals. This discrepancy interferes with the integration of fMRI and EEG paradigms.
In this study, we aimed to investigate temporal behavior of dACC for exploring the temporal dynamics of task-oriented brain networks recruited for cognitive processing. We adopted a single word generation task [40] [41] [42] following conventional trial-by-trial protocols, where subjects were asked to pronounce a semantically appropriate verb for a presented noun at each trial. It is well known that the left inferior prefrontal cortex (IPFC) and dACC are activated during word generation tasks. This activation of dACC and IPFC is attributed to semantic processing and target-oriented attention control, respectively [43]. Therefore, to elicit the dynamics of cognitive processing for generating contextual verbs, the dACC was considered as the target to measure during tasks.

We adopted an electroencephalographic (EEG) technique for numerically evaluating the activity of dACC in the derivations of the occipital EEG alpha-2 (10 - 13 Hz) power fluctuations. The occipital EEG alpha rhythms were thought to come from neocortical structures, and enormous effort had been addressed to explore which areas are correlated with the EEG alpha rhythms [44] [45] [46] [47]. More recently, it has been shown that regional activity is dependent on the frequency range of the occipital alpha-2 power fluctuations; a faster component (≥0.04 Hz) represents the metabolic activity of dACC, whereas a slower component (≤0.04 Hz) represents the upper brainstem [48]. Based on this finding, we developed an event-related deep brain activity (ER-DBA) assessment paradigm using trial-by-trial tasks. This paradigm provides event-related traces in the derivation of the arithmetic mean of alpha-2 power streams with a high time resolution of hundreds of ms. This enabled numerical evaluation of the temporal activity of dACC as a member of the deep brain structures, for the first time, beyond the capability of conventional event-related fMRI techniques.

2. Materials and Methods

2.1. Subjects

Student volunteers from the Kobe Co-medical College (grade: 1th, major: training course for speech-language-hearing therapy) were screened for their medical history declared in clinical interviews, and students currently receiving treatment for neurological and/or psychiatric disorders were eliminated. Twelve healthy subjects (6 males and 6 females; mean age 25.0 ± 1.8 years) were selected to participate in this study according to a criterion stating that subjects should be native Japanese speakers who grew up in Japan. Written informed consent was obtained from subjects according to the guidelines of the ethics committee of Kobe University Graduate School of Health Sciences.

2.2. Stimuli

A series of auditory stimuli consisting of 60 pairs of sounds S1 and S2 were used for this study (Figure 1). S1 represented the sound of a single familiar Japanese noun, while S2 was a beep sound used as a speech onset cue. Sounds S1 and S2
were separated by an interval of 1125 ms. Nouns were pronounced with natural prosodies, and each beep sound had a duration of 50 ms at 2000 Hz. Each trial comprised of an S1 and an S2 sound and was 2250 ms long.

2.3. Paradigm Design

Subjects were asked to respond to auditory instructions, according to which they were expected to repeat the noun (noun repetition task; NRT) or generate the associated verb (verb generation task; VGT) as soon as they heard the beep sound. The verbal response of each subject was recorded using a digital voice recorder. Scalp EEG of the subjects were recorded Scalp EEGs were also recorded with using Ag/AgCl electrodes arranged according to the international 10 - 20 method. The EEG recordings were carried out with a digital electroencephalograph, which provided recording channels with a 24-bit voltage resolution and a sampling rate of 512 Hz. The EEG signals were re-referenced to the mastoid electrodes (A1 and A2) and band-pass filtered in the 0.1 - 45 Hz range to eliminate artifacts. EEG recording during tasks was performed with the eyes closed.

2.4. Behavioral Performance Analysis

Verbal responses of subjects were analyzed linguistically and prosodically, and categorized into three behavioral groups: correct response (CR), incorrect response (IR), and no responses (NR) groups. The response of a subject was categorized as IR if it was linguistically incorrect, e.g., an adjective, instead of a verb, was generated by the subject or a different verb, not relatively close to the noun, was generated; or prosodically incorrect, e.g., the response exhibited an abnormal rhythm, such as stuttering or partially repeating the same word. Examples of linguistic and prosodic errors are provided in Table 1. If no response was recorded in the voice recorder, it was categorized as NR.
Table 1. Examples of error assessment.

| Stimulus | Response | Assessment                        |
|----------|----------|-----------------------------------|
| Blood pressure | High      | Grammatical error: adjective generation |
| Pine cricket  | Eat       | Perseveration: the same verb generation |
| Alarm     | s-set     | Abnormal rhythm: stuttering       |

2.5. EEG Data Analysis

Occipital EEG alpha-2 powers were numerically extracted at both O1 and O2 sites using a digital band-pass (10 - 13 Hz) filter in a 2-s epoch. DBA index was defined as an average of two time series’ signals. The DBA index waveforms observed in a window of 2200 ms were considered as the fast component of DBA, indicating the dACC activity, whereas average DBA indices in a larger time span of >25 s corresponding to the frequency of 0.04 Hz represented the slow component of DBA, indicating the upper brain-stem activities. The slow component of DBA indices was used for explaining personal differences in cognitive performance, whereas the fast component was used for investigating network dynamics during cognitive processing.

2.6. Event-Related DBA Index Analysis

An event-related design, which can be applied to the fast component of DBA indices, was developed following a conventional event-related potential (ERP) paradigm. Additional processing was performed with data extracted in a limited time range of approximately 2 s from original DBA index data based on S1 as event markers, excluding outliers. The averaged temporal waveforms were defined as event-related (ER) DBA indices (Figure 2). Baseline correction was performed 200 ms prior to the onset of noun presentation (S1). The event-related features of dACC activities were numerically estimated using the ER-DBA indices, avoiding background spontaneous brain activities. The time resolution was expected to be approximately 0.3 s, taking into account that the alpha-2 (10 - 13 Hz) frequency band was regarded as an occupied single-sideband modulation band including temporal information [49] ER-DBA index traces under this time resolution were expected to distinguish between a few events per second.

Here, performance-dependent ER-DBA indices were used to examine the temporal dACC activity patterns during cognitive processing and elucidate the underlying network dynamics. A conventional subtraction technique used widely for analyzing ERP data [50] was applied to the two ER-DBA indices measured during NRT and VGT. The VGT was assumed to involve additional cognitive processing of memory retrieval and decision-making associated with the generation of an optimal verb. Thus, the subtracted ER-DBA indices would indicate brain activities related to additional cognitive processing during VGT [51].
Figure 2. Two time series signals of deep brain activity (DBA) index. (a) The slow component of DBA index corresponding to the frequency of 0.04 Hz; (b) The fast component of DBA index. Additional processing was performed with data extracted in a limited time range of approximately 2 s from the original DBA index data based on the onset markers of S1 as event markers, excluding outliers. The averaged temporal waveforms were defined as event-related (ER) DBA indices. Baseline correction was performed 200 ms prior to the onset of noun presentations (S1).

2.7. Event-Related Potential Analysis

Conventional event-related potential (ERP) measurement was performed with EEG signals at Cz for evaluating contingent negative variation (CNV) during tasks. The CNV, associated with the CEN during focusing of attention [52], is expected to support our claim based on the event-related DBA index analysis, which addresses roles of the dACC in cognitive processing.

2.8. Statistical Analysis

Statistical analysis of data was performed using the t-test to determine significant differences in error rate between NRT and VGT, and in ER-DBA indices among response types and groups. Statistical significance was primarily assessed by the p value (p), which was confirmed by the power and Cohen’s d value (d). Total error incidence was further evaluated by measuring the interval of stimulus number between two consecutive errors. The measured interval data were statistically analyzed to determine probability density functions (PDFs) for the error incidence. PDFs were then used to examine whether committing the error affected post-error task performances.

3. Results

3.1. Behavioral Performance Data

We assessed the behavioral performance of subjects as CR, IR, or NR for each NRT and VGT trial, according to the criteria described in Materials and Methods. Table 2 lists the assessed results for all subjects. Error rates were significantly lower for NRT than for VGT (p < 0.001) (Figure 3).
**Table 2.** Behavioral performance data recorded for 12 subjects while performing noun repetition task (NRT) and verb generation task (VGT).

(a) **Noun repetition task (NRT)**

| Subject ID | Response (%) | Error trial |
|------------|--------------|-------------|
|            | CR | IR | NR | IR | NR |
| 1          | 58 (96.7) | 0 (0) | 2 (3.3) | — | 2, 27 |
| 2          | 60 (100)  | 0 (0) | 0 (0) | — | — |
| 3          | 57 (95.0)  | 3 (5.0) | 0 (0) | 29, 37, 47 | — |
| 4          | 55 (91.7)  | 5 (8.3) | 0 (0) | 2, 3, 21 | — |
| 5          | 58 (96.7)  | 2 (3.3) | 0 (0) | 1, 2 | — |
| 6          | 59 (98.3)  | 1 (1.7) | 0 (0) | 40 | — |
| 7          | 59 (98.3)  | 1 (1.7) | 0 (0) | 1 | — |
| 8          | 60 (100)  | 0 (0) | 0 (0) | — | — |
| 9          | 59 (98.3)  | 1 (1.67) | 0 (0) | 47 | — |
| 10         | 59 (98.3)  | 1 (1.67) | 0 (0) | 18 | — |
| 11         | — | — | — | — | — |
| 12         | 59 (98.3)  | 1 (1.67) | 0 (0) | 1 | — |

*b*Numbers indicated for each response represent the number of times that response was given by the subject out of a total of 60 trials. Numbers in parentheses indicate the percentages. CR: correct response, IR: incorrect response, NR: no response

(b) **Verb generation task (VGT)**

| Subject ID | Response (%) | Error trial |
|------------|--------------|-------------|
|            | CR | IR | NR | IR | NR |
| 1          | 44 (73.3)  | 1 (1.7) | 15 (25.0) | 28 | 5, 7, 12, 14, 17, 19, 20, 23, 24, 26, 39, 45, 50, 51, 55 |
| 2          | 40 (66.7)  | 12 (20.0) | 8 (13.3) | 2, 9, 14, 19, 20, 21, 32, 33, 44, 48, 50, 57 | 1, 24, 36, 38, 39, 51, 53, 60 |
| 3          | 38 (63.3)  | 20 (33.3) | 2 (3.3) | 1, 2, 5, 11, 15, 24, 26, 29, 32, 33, 36, 39, 47, 51, 55, 59, 60 | 16, 17 |
| 4          | 40 (66.7)  | 5 (8.3) | 15 (25.0) | 3, 28, 30, 52 | 5, 19, 20, 23, 24, 33, 37, 39, 44, 45, 47, 55, 56, 58, 60 |
| 5          | 43 (71.7)  | 13 (21.7) | 4 (6.7) | 1, 20, 24, 27, 28, 30, 34, 38, 39, 45, 54, 58, 60 | 7, 12, 33, 53 |
| 6          | 50 (83.3)  | 3 (5.0) | 7 (11.7) | 27, 28, 43 | 24, 33, 36, 39, 45, 51, 60 |
| 7          | 38 (63.3)  | 22 (36.7) | 0 (0) | 1, 14, 23, 24, 26 - 30, 31, 33, 38, 40, 43, 45, 47, 48, 53, 55, 56, 58, 60 | — |
| 8          | 45 (75.0)  | 15 (25.0) | 0 (0) | 14, 17, 20, 24, 25, 30, 32, 39, 50, 51, 53, 55, 56, 58, 59 | — |
| 9          | 30 (50.0)  | 15 (25.0) | 15 (25.0) | 6, 7, 14, 16, 19, 28, 30, 32, 33, 37, 40, 51, 52, 58 | 8, 20, 23, 24, 26, 27, 36, 39, 44, 45, 53, 55, 59, 60 |
| 10         | 36 (60.0)  | 20 (33.3) | 4 (6.7) | 9, 15, 19, 22, 24, 26 - 30, 33, 36 - 39, 45, 53, 56, 58, 60 | 10, 14, 32, 54 |
| 11         | 46 (76.7)  | 6 (10.0) | 8 (13.3) | 10, 14, 15, 23, 30, 45 | 19, 24, 31, 36, 38, 39, 51, 53 |
| 12         | 44 (73.5)  | 15 (25.0) | 1 (1.7) | 19, 20, 22 - 24, 27 - 29, 32, 33, 39, 44, 45, 58 - 60 | 14 |
3.2. Event-Related (ER) DBA Indices

The ER-DBA index waveforms were derived from DBA index data of all subjects in a window of 2200 ms by arithmetic mean We found that the waveforms calculations. Waveforms exhibited performance differences (Figure 4(a)). The CR group showed a dip below the baseline just posterior to the onset of the auditory noun presentations (S1). The group also produced a mild increase several hundreds of ms prior to the arrival of the speech cues (S2). The IR group showed a sharp increase above the baseline accompanied with a negligible dip. By contrast, the NR group showed a steep dip spanning the entire time slot between the two auditory cuing signals of S1 and S2. We also calculated the ER-DBA waveforms for CR and IR groups of NRT (Figure 4(b)). A comparison between CR groups of NRT and VGT revealed significant differences ($p < 0.001$) with the dip for CR group of VGT being significantly deeper than that of NRT (Figure 4(c)).

3.3. ERPs

Calculations based on the conventional arithmetic mean paradigm were respectively done in the Cz deviations using data of all subjects for all behavioral groups (CR, IR, and NR) of VGT. The calculated ERP waveforms were represented in a time window of 2200 ms prior to the arrival of the auditory noun stimulus (S1) in 200-ms intervals (Figure 5(a)). The ERP waveform was characterized for all groups by sustained broad negativities. No significant differences were determined between these waveforms; however, the CR group enhanced the negativity compared with the other performance groups. The ERPs
Figure 4. Event-related analyses on DBA index data. (a) CR (n = 335), IR (n = 101), and NR (n = 51) data for VGT. The CR group showed a dip below the baseline [***: p < 0.001 (p = 1.9e−20), power = 1]. The dip of the IR group was not significant (p = 0.42, power = 0.13); (b) CR (n = 554) and IR (n = 15) data for NRT; (c) Comparison of DBA indices between CR groups of NRT and VGT [***: p < 0.001 (p = 1.2e−13), d = 0.52]. n, sample size; d, Cohen’s d.

were also calculated in the same electrode deviations for the CR group of NRT (Figure 5(b)). Similar broad negativities were obtained following sustained negativities.

3.4. Subtraction Analyses

ER-DBA index and ERP waveforms. The CR group of NRT was used as a control for subtraction processing (Figure 6). The ER-DBA index waveform produced a broad sustained negativity covering the entire time range from the onset of the noun presentations (S1) to the arrival of the speech cues (S2), whereas the ERP
Figure 5. Event-related potential (ERP) waveforms. (a) ERP waveforms calculated for different three CR (n = 221), IR (n = 66), and NR (n = 35) behavioral groups of VGT; (b) ERP waveform calculated for the CR (n = 460) group of NRT. n, sample size.

Figure 6. Conventional subtraction analysis for the ER-DBA index (a) and the ERP waveforms (b).

waveform showed negativity in a limited range between S1 and S2.

3.5. Personal Differences

We were especially interested in errors committed during VGT, because this task was associated with higher-order cognitive functions. Therefore, we investigated personal differences in behavioral performance based on the DBA index of each subject. The average DBA index showed a strong negative correlation with the total error rate including IR and NR groups, and a strong positive correlation with the dip depth of the ER-DBA index waveform of the CR group (Figure 7(b)).
Figure 7. The average DBA index at rest versus (a) the total error rate and (b) the dip depth. The errors included both IR and NR. (a) $r$ (Pearson’s correlation coefficient) = −0.63, $p < 0.05$ ($p = 0.03$); (b) $r = 0.90$, $p < 0.001$ ($p = 5.2e^{-5}$).

4. Discussion

4.1. Cognitive Processes Predicted by the Dip in ER-DBA Index Trace

We found that ER-DBA index traces exhibited a dip immediately after the onset of the auditory word (noun) presentations for correct responses during the VGT (Figure 4(a)). As the fast component of DBA index reflects the dACC activity, the dip in ER-DBA indicates deactivation of dACC. The duration of the dip was approximately 600 ms, which suggests that optimal verb retrieval was performed during the dip. The IPFC associated with the frontotemporal network is deactivated during semantic processing and word retrieving [53] [54]. A previous electrocorticogram (ECoG) study revealed that the PCC is also deactivated during semantic processing [55]. Together, these data suggest that dACC and IPFC are co-deactivated during optimal verb retrieval, further indicating that dACC is coupled with IPFC. This co-deactivation of dACC and IPFC is thought to originate from direct memory access with word processing under the speed-accuracy tradeoff condition for achieving the best task performance [56] [57].

It has also been shown that the DMN is coupled with task-positive networks, including the IPFC [19]. Hence, it is possible that the coupling between dACC and IPFC supports dACC-mediated deactivation of DMN during the verb retrieval task. Consequently, de-activation of large-scale brain networks, including SN and DMN, is thought to be essential for early-stage cognitive processing. On the other hand, such coupling increases the susceptibility of the subject to distraction by co-activation during tasks [58]. The risk is brought by excessive activation of the anterior insular cortex (aIC) responding to unpredictable stimuli [59] [60]. The IRs, given by the positive DBA index (Figure 4(a) and Figure 4(b)) corresponding to dACC activation, may be attributed to the dACC-activation-induced distraction.
We also found that whether or not the verb retrieval was successful, the dACC exhibited subsequent increase in an interval of several hundred ms from the onset of word presentation. This increase corresponds to the behavior of the ACC when a solution is hit [43]. This suggests that dACC may couple with the CEN for performing goal-oriented processing, including decision-making and motor preparation for speech. This raises the question as to why such deactivation is needed for processing information. A possible explanation of the role of “deactivation” is attributed to the function of γ-aminobutyric acid (GABA) [61], which inhibits spontaneous neural spiking with no information [62] [63] or prohibits the incoming unnecessary impulses [64] [65] [66]. Such deactivation is beneficial for highlighting target information [67]. Figure 8 illustrates a schematic diagram for explaining dACC-oriented dynamic cognitive processing supported by the above findings.

### 4.2. Temporal Dynamics Predicted by Subtraction Analyses

We further found performance-specific DBA index and ERP traces from subtraction analyses data. Figure 9 shows a schematic diagram of cognitive processing predicted during NRT and VGT. By subtracting the common processes, we obtained the difference given by the additional processes of VGT, including verb retrieval and decision-making for selecting a verb suitable to the presented noun. The negativity of the subtracted DBA index difference over the time window from the onset of the word (noun) presentation to arrival of the speech cue (Figure 6(a)) is given by sustained attention for the VGT-specific cognitive processes as mentioned above. Such durable attention is consistent with the previous finding that the working-memory remains active during tasks while the DMN is deactivated [22].

On the other hand, the negativity of the subtracted ERP trace at Cz (Figure 6(b)), reflecting the readiness potential of the motor cortex [68] [69], emerged posterior to the dip bottom of the DBA index. The temporal discrepancy between the subtracted DBA index and ERP traces indicates that the word processing and motor preparation are dissociable. This dissociation is attributed to the salience function of dACC, which regulates the motor system by immediately breaking off the coupling with the IPFC for engaging the cued speech.

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**Figure 8.** Schematic representation of performance-dependent dynamic interactions between dACC, IPFC, and CEN/motor system during cognitive processing.
Figure 9. A schematic diagram of cognitive processing predicted during the two tasks of NRT and VGT.

The flexible intra-coupling aspects of dACC with altered coupling states between the default and executive networks are essential for its salience function [70]. This flexibility supports the reconfigurable human brain networks for engaging a wide variety of cognitive demands [71] [72]. Our results are the first evidence for such network architectures.

4.3. Personal Differences

Deep brain structures are characterized by monoaminergic neural systems, especially the dopaminergic system at the ventral tegmental area (VTA) involved in the upper brainstem. This neural system is not only essential for reward [73], but also improves connectivity of large-scale networks of the human brain [74] [75] [76]. By contrast, according to small-scale network architectures [77] [78], network connectivity is dependent on the modularity of neural systems. As the number of impulses pending processing increase at the synapse with decreasing the modularity, the network connectivity is improved at the cost of metabolic stress [77] [79]. Hence, connectivity and metabolic cost are counterbalanced.

In this study, we found that the dip depth of ER-DBA index traces was positively correlated with the slow component of the DBA index (Figure 7(b)), i.e., the activity of the dopaminergic neural system at the VTA. This suggests that those who possess higher dopaminergic neural activity at rest can improve their brain network connectivity for achieving best performance during tasks against higher metabolic cost. Assuming that task performance is correlated with network connectivity, performance and metabolic cost are also counterbalanced. Hence, personal differences of cognitive behaviors are determined according to the cost of each task [80].

4.4. Error Incidence

It is known that sustained influence of errors commission is avoided by post error slowing (PES), supported by brain activation [81]. Taking into account that
performance accuracy is affected by emotional stimuli or internal motivation [82] [83], we hypothesized that the dynamic performance of the dACC promotes the brain activation associated with PES.

When post-error influence is avoided by PES, there is no correlation in error commission. Hence, if the random error incidence is confirmed in our experimental results, it will be appreciated that the dACC will contribute to maintaining performance accuracy during tasks.

To examine this hypothesis, we statistically analyzed error intervals, derived from the number of errors listed in Table 2. The PDFs determined for most of the subjects exhibited good correspondence ($p < 0.05$) with exponential distribution derived from Erlang distribution,

$$p(n) = \frac{\lambda (\lambda n)^{\kappa-1}}{(n-1)!} \exp(-\lambda n)$$

where $\kappa = 1$ for exponential distribution (Figure 10). The exponential PDF is derived from random stochastic processes as observed in the natural science fields addressing, for example, a many-body problem in quantum physics [84]. Hence, the random error incidence as shown in Figure 10(a) is evidential to our hypothesis.

Indeed, some subjects provided exceptional performance depicting non-exponential PDF, which was rather approximated with a higher-order ($\kappa > 1$) Erlang distribution function (Figure 10(b)). It was considered that such higher order Erlang distribution was attributed to excessive activation of the dACC, which would intensively suppress successive error commission. Hence, such exceptions still support our claim, although they are not associated with

![Figure 10](image)

**Figure 10.** Probability density functions (PDFs) of error intervals across subjects. Solid lines indicate individual data. (a) 72% of the subjects provided PDFs fitted with the exponential distribution ($p < 0.05$), corresponding to $\kappa = 1$ in the Erlang distribution, best fitted with $\kappa = 8$ of the Erlang distribution under statistical significance ($p < 0.001$).
random stochastic processes.

4.5. Limitations

This study has a few limitations. First, the study was limited to healthy subjects. Future studies should apply the novel event-related DBA index method to assess symptoms of patients with cognitive dysfunctions in clinical fields. Second, the study was limited to word-based paradigms because our primary goal is to understand cognitive processing during word retrieval. Therefore, future studies should examine the method for investigating more general cognition schemes typically including visual processing.

5. Conclusions

We investigated the dynamic behavior of dACC during word generation tasks using a newly developed ER-DBA index for elucidating mechanisms underlying SN-dominant cognitive processing. We found remarkable performance-dependent ER-DBA traces accompanied with a dip in DBA corresponding to subsequent dACC deactivation after word presentation. We also found personal dependence, according to which the DBA dip becomes stronger for those who exhibit higher average DBA index at rest. These findings suggest that the dACC is deactivated during cognitive processing from predicted task-negative regions, including the IPFC, but is activated during the execution stage with task-positive regions, including the CEN and motor system. Data also suggested that such dACC function in cognitive processing is supported by the monoaminergic neural systems at the upper brainstem region.

Future studies will be conducted to understand neural mechanisms underlying performance-based difference reflected in ER-DBA traces during cognitive tasks and those involved in cognitive impairment observed in various diseases. Hence, characterization of ER-DBA traces during cognitive tasks will be highly valuable for providing precise diagnosis of a wide range of diseases with cognitive impairment in clinical settings.

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### Appendix

#### Abbreviation Collection

| Abbreviation | Term                          |
|--------------|-------------------------------|
| CEN          | Central executive network     |
| CNV          | Contingent negative variation |
| CR           | Correct response              |
| DBA          | Deep brain activity           |
| DLPFC        | Dorsolateral prefrontal cortex|
| DMN          | Default mode network          |
| ECoG         | Electrocorticogram            |
| EEG          | Electroencephalogram          |
| ER-DBA       | Event-related deep brain activity |
| ERP          | Event-related potential       |
| GABA         | γ-aminobutyric acid           |
| IPFC         | Inferior prefrontal cortex    |
| IPS          | Intra-parietal sulcus         |
| IR           | Incorrect response            |
| NR           | No response                   |
| NRT          | Noun repetition task          |
| PCC          | Posterior cingulate cortex    |
| PDF          | Probability density function  |
| PES          | Post error slowing            |
| SN           | Salience network              |
| VGT          | Verb generation task          |
| VTA          | Ventral tegmental area        |
| aIC          | Anterior insular cortex       |
| dACC         | Dorsal anterior cingulate cortex |
| fMRI         | Functional magnetic resonance imaging |