Dynamic changes in quantitative electroencephalogram during continuous performance test in children with attention-deficit/hyperactivity disorder

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A B S T R A C T

To establish whether dynamic EEG changes in children with attention-deficit/hyperactivity disorder (ADHD) differ from those observed in controls, the authors investigated the effect of the continuous performance test (CPT) on delta, theta, alpha and beta frequency bands. High-resolution electroencephalography (EEG) was recorded during eyes-open resting and CPT performance in 16 right-handed children meeting the DSM-IV criteria for ADHD and 16 age-matched controls. Significant CPT vs. eyes-open differences in EEG activities was observed in children with ADHD. In particular, switching to CPT induced an alpha power increase in children with ADHD and an alpha power decrease in controls. This may reflect a primary deficit associated with cortical hypoarousal in ADHD. These EEG results agree with behavioral findings leading the authors to suggest that dynamic changes in neural network activities are impaired in children with ADHD.

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1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most common behavioral childhood disorder, affecting approximately 5% of children (American Psychiatric Association, 1994). The disorder comprises a variable cluster of hyperactivity, impulsivity and inattention symptoms which substantially affect the individual's normal cognitive and behavioral functions.

Quantitative electroencephalography (QEEG) techniques can be used to explore various electrical activities of the brain (Arciniegas and Beresford, 2001), particularly local synchronization of neural networks. Synchronization is related to the network's integrative capacities and the nature of its inputs and can be markedly modified by the brain's activity state. Attention impairment can therefore be monitored by QEEG.

Most studies of the electrophysiological correlates of ADHD have compared the QEEG from ADHD sufferers with those of healthy children under resting conditions. A considerable number of these studies have reported an increase in low-frequency power (predominantly in the theta band) and a decrease in high-frequency power (especially the beta1 band) in children with ADHD compared with age-matched controls (for a review, see Barry et al., 2003; for a meta-analysis, see Snyder and Hall, 2006). However, the allocation of neural resources differs when the subject directs his/her attention to an experimentally controlled situation ( Thatcher, 1998 ). It is therefore important to evaluate a neural network's ability to change from a passive to an active condition (during a cognitive task, for example (Petsche et al., 1986)).

A number of researchers (Lubar, 1991; Mann et al., 1992; Janzen et al., 1995; Monastra et al., 1999, 2001; Swartwood et al., 2003) have used EEG to investigate how children with ADHD perform various cognitive tasks (such as reading, listening or drawing). However, none of these tasks take into account inattentiveness and distractibility — the major symptoms of ADHD. Assessment of these symptoms would require tasks specifically designed to highlight attentional deficits, such as the continuous performance task (CPT) or the go/no-go task. Although some QEEG studies have been performed in healthy adults performing a CPT paradigm (Valentino et al., 1993; Arruda et al., 1999; Bearden et al., 2004), only one study has reported QEEG changes during an attentional load task in children with ADHD (El-sayed et al., 2002). These authors observed an altered QEEG activity pattern (higher levels of slow cortical activity and lower levels of fast cortical activity) in ADHD children, especially during the attentional task itself. However, the delta power and theta/beta power ratio were not reported. Given the paucity of data in the literature, it is not known how the various EEG bands change during performance of a CPT. Hence, in the present study, we set out to establish the functional reactivity of frequency-specific EEG activities during eyes-open resting and CPT in children with ADHD.

According to the hypoarousal hypothesis, inattention and hyperactivity in ADHD result from cortical underarousal (Satterfield and
Cantwell, 1974; Barry et al., 2009). This model is supported by the observation of lower skin conductance level (SCL) values in several studies (for a review, see Barry et al., 2003). In this respect, the results of EEG studies have prompted researchers to suggest that an elevated theta/beta power ratio is a marker of hypoarousal in ADHD (Mann et al., 1992; Barry et al., 2009). However, Barry et al. (2009) did not find any correlation between theta/beta power ratio and SCLs in either normal or ADHD children, but did observe that high SCLs were associated with low alpha power in both groups (Barry et al., 2009).

An overall enhancement in arousal levels (including higher SCLs) occurred in healthy children during a CPT (Barry et al., 2005a,b). Based on the hypoarousal model of ADHD, it can be hypothesized that children with ADHD have trouble shifting arousal levels from resting conditions to CPT conditions. To be consistent with studies of the EEG–SCL link (Barry et al., 2004, 2005a,b, 2007, 2008, 2009), an increase in alpha activity (rather than theta/beta activity) is expected for the transition from eyes-open resting to a CPT in children with ADHD.

2. Methods

2.1. Participants

Thirty-two right-handed children participated in the study. There were 16 children with ADHD (15 boys; mean ± SD age: 9 ± 1.5) and 16 age-matched healthy children (11 boys; mean ± SD age: 8.7 ± 1.5) (see Table 1). Children with ADHD were all recruited from the pediatric neurology department at Amiens University Hospital. None had ever been treated with methylphenidate. The diagnosis was based on DSM-IV criteria and inclusion was dependent on meeting the full diagnostic criteria for the ADHD combined subtype (APA, 1994). For all participants, the Child Behavior Checklist (CBCL) (Achenbach and Edelbrock, 1983) was completed by the parents and the Swanson, Nolan, and Pelham IV Questionnaire (SNAP-IV) (Swanson et al., 1998) was filled out by parents and teachers. The diagnosis was then established after a semi-structured interview, a clinical neurological examination and a set of ADHD-oriented neuropsychological and behavioral tests (including the ADHD Rating Scale–IV (DuPaul et al., 1998), the full version of the Wechsler Intelligence Scale for Children (WISC-III) (Wechsler, 1991), Conners’ Continuous Performance Test (CPT-II) (Conners, 1998), the Attentional Capture Test (ACT) (Deltour et al., 2007) and the Stroop test (Albaret and Migliore, 1999)). These cases were reviewed independently by a pediatric neurologist and a psychologist blinded to each other’s findings and were included in the ADHD group only if both clinicians agreed on the diagnosis. Participants were administered a modified A-X version of the CPT while high-resolution EEG was recorded.

Control subjects were tested with the WISC-III, CPT-II, attentional capture and CPT-AX during recording of high-resolution EEG. Their parents completed the SNAP-IV and CBCL questionnaires, to ensure the absence of behavioral problems.

All participants had a full-scale IQ score of at least 80 and normal or corrected-to-normal vision. Exclusion criteria for all children included a history of problematic prenatal or neonatal periods, central nervous system diseases, convulsive disorders, EEG spike wave activity, sensorimotor deficits and/or learning difficulties.

The study protocol was approved by the local independent ethics committee. Parents received detailed information about the study protocol before giving their written, informed consent. After being shown the study apparatus, children verbally consented to participation. No monetary compensation was awarded.

2.2. Procedure

Participants were seated in an armchair in a quiet room and were asked to look at a computer screen placed 70 cm away. Sixty-four-channel EEG recording sessions were performed as follows: first session, eyes-closed resting (EC); second session, eyes-open resting (EO1); third session: the A-X version of the CPT; and fourth session: eyes-open resting again (EO2). During the task, the participants were instructed to press a button with their right index finger as soon as the letter “O” (warning) was directly followed by the letter “W” (the “go” condition) but not to press the button if the letter was a “non-W” (the “no-go” condition) (Fallgatter et al., 2004).

Each recording session lasted between 180 and 240 s (except for the CPT, which lasted about 10 min) with a two-minute rest period between conditions.

2.3. Recording methods

A continuous EEG was recorded, using 64 surface electrodes (Easy cap®, Berlin, Germany). The EEG was amplified by A.N.T.®, Enschede, The Netherlands DC-50 Hz filtered and recorded with a right mastoid reference at a sampling rate of 512 Hz. The impedance of electrodes was kept below 10 kΩ. The spatial positions of the 64 electrodes were digitized using a magnetic, three-dimensional position digitizer (the 3Space Fastrak® from Polhemus, Colchester, USA).

2.4. Data processing

Three parameters were used to assess each subject’s behavioral performance: (i) reaction times for correct responses; (ii) variability (standard deviation of reaction times) and (iii) the sum of errors, including the number of omission errors (i.e. no response in the “go” condition), the number of commission errors (responses occurring after stimulus presentation other than in the “go” condition) and anticipation errors (responses occurring less than 150 ms after stimulus onset).

Artifact rejection was based on both visual inspection and computerized selection (the amplitude threshold detection algorithm in Eemagine® software, Enschede, The Netherlands). The threshold for electrooculographic rejection was set at 50 μV. An expert also visually appraised each epoch and decided whether or not to accept it. After artifact removal, the EEG signals were analyzed using a common hardware average reference and were then filtered between 0.3 Hz and 30 Hz, 3 dB/octave.

Although the total amount of artifact-free EEG epochs (2.5 s) varied from one participant to another, 36–48 epochs (i.e. 90–120 s of data) were randomly selected for each baseline condition. Forty-eight random epochs were selected for the CPT condition. The EEG epoch

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic characteristics and behavioral results.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADHD</td>
</tr>
<tr>
<td>GENDER</td>
<td>M = 15, F = 1</td>
</tr>
<tr>
<td>AGE</td>
<td>9 (1.5)</td>
</tr>
<tr>
<td>SNAP-IV_In</td>
<td>2.26 (0.39)</td>
</tr>
<tr>
<td>SNAP-IV_Hyp</td>
<td>2.15 (0.80)</td>
</tr>
<tr>
<td>IQ_Full</td>
<td>93.6 (9.5)</td>
</tr>
<tr>
<td>IQ_Per</td>
<td>87.8 (10.4)</td>
</tr>
<tr>
<td>ACT_RT</td>
<td>455 (106)</td>
</tr>
<tr>
<td>ACT_Var</td>
<td>158 (62)</td>
</tr>
<tr>
<td>ACT_Error</td>
<td>10 (12)</td>
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<tr>
<td>CPT-II_RT</td>
<td>53.8 (12.5)</td>
</tr>
<tr>
<td>CPT-II_Var</td>
<td>55.2 (10.5)</td>
</tr>
<tr>
<td>CPT-II_Error</td>
<td>54.9 (8)</td>
</tr>
<tr>
<td>CPT-AX_RT</td>
<td>497 (86)</td>
</tr>
<tr>
<td>CPT-AX_Var</td>
<td>193 (89)</td>
</tr>
<tr>
<td>CPT-AX_Error</td>
<td>18 (3)</td>
</tr>
</tbody>
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** p < 0.01.
* p < 0.05.

time domain was then transformed into the frequency domain using a fast Fourier transformation algorithm. The frequency bands were defined as follows: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–24 Hz). The relative power and the theta/beta power ratio of the 21 electrodes (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, Oz, O2) were calculated for each participant. Relative power is a measure of the proportion of total amplitude within a given frequency band and is therefore independent of bone thickness, skull resistance and impedance variability (Matthies et al., 1981; Nunez, 1995). Furthermore, evaluation of relative power is more discriminant than evaluation of absolute power (Barry et al., 2003).

An appropriate baseline must be defined when investigating dynamic changes in brain function during a cognitive task. Barry et al. (2007) speculated that eyes-closed and eyes-open conditions provide different EEG measurements in terms of both topography and power levels. They considered that eyes-open EEG provides a more appropriate baseline for tasks involving visual processing (Barry et al., 2007). To meet this requirement, we examined the eyes-open condition immediately before the CPT. The rationale for additional eyes-closed and eyes-open recordings was to confirm the presence of well-known EEG activities and to ensure that EEG changes were reliably associated with the task in question. Alpha power suppression when moving from an eyes-closed to an eyes-open condition is probably the best known EEG phenomenon and is particularly noticeable at posterior sites (Basar, 1997; Klimesch, et al., 2007). In contrast, beta activity increases over bilateral prefrontal and frontal regions in the eyes-open condition (Barry et al., 2007). Topographic changes in alpha and beta power under the four conditions (EC, EO1, CPT, and EO2; see Fig. 1) were therefore checked visually. In the present study, data from EO1 and CPT were compared for each group.

2.5. Statistical analysis

Demographic characteristics were assessed using a t test and chi² test. The t test was also used to compare mean reaction times and variability for the SNAP-IV, IQ, ACT, CPT-II and CPT-Ax parameters. The numbers of errors in the ACT and CPT-Ax were compared using a Mann–Whitney non-parametric U test.

EEG data were natural-log transformed to achieve a Gaussian data distribution (John et al., 1980), which was confirmed in a Kolmogorov–Smirnov test. For the EEG bands and the theta/beta ratio, the 21 electrodes were averaged in 9 regions: left frontal (Fp1, F3, F7), midline frontal (Fpz, Fz), right frontal (Fp2, F4, F8), left central (T7, C3), midline central (Cz), right central (T8, C4), left posterior (P7, P3, O1), midline posterior (Pz, Oz) and right posterior (P8, P4, O2) regions. Statistical analysis was performed on EEG measures separately using a three-way, repeated-measures analysis of variance (ANOVA), with Group as the between-subject factor and Condition and Region as within-subject factors.

3. Results

3.1. Behavioral results

As indicated in Table 1, no significant age or gender-ratio differences were observed between the two groups, but IQ was significantly lower in children with ADHD. Within-group correlations between IQ and each of the 9 regional EEG parameters were tested but were not significant. In the CPT-Ax (i.e. during high-resolution EEG), children with ADHD did not differ from children of the control group in terms of reaction time (497 ± 86 and 503 ± 125 ms, respectively). Although children with ADHD responded more variably than controls (193 ± 89 and 148 ± 63, respectively), this difference was not statistically significant. However, the ADHD group committed a significantly higher number of errors than the control group (18 ± 13 vs. 11 ± 9, respectively; U = 84.5, p = 0.05).

3.2. EEG activity

The topographic power distributions in the alpha and beta bands are shown in Fig. 1. The relative delta, theta, alpha and beta powers and theta/beta ratio are summarized in Fig. 2.

3.2.1. Inter-condition differences in topographic EEG activities

In both groups, alpha activity was markedly higher in eyes-closed conditions than in visual input conditions (EO1, CPT and EO2), particularly at the occipital site (Fig. 1, left column). However, as depicted in the right column of Fig. 1, beta power increased during the transition from eyes-closed to visual input conditions in the right and left prefrontal and frontal regions. This focal elevation appeared to be greatest in the CPT condition.

3.2.2. Relative delta

A significant main effect was observed for Region (F = 19.35, p = 0.0001) and Condition (F = 6.79, p = 0.014). A Condition x Group
Fig. 2. Topography of relative power in each band: (D: delta; T: theta; A: alpha; B: beta; T/B: theta/beta ratio). Each row shows activity in one EEG band, separately for the ADHD (left column) and control groups (center column). In each band, the dark blue and red colors (upper) represent maximum increase and maximum decrease in power under the various conditions (from EO1 to CPT), respectively, and the lower graphs depict power changes in each region (LF: left frontal; MF: midline frontal; RF: right frontal; LC: left central; MC: midline central; RC: right central; LP: left posterior; MP: midline posterior; RP: right posterior). Pattern of between-group EEG changes (across electrodes) from EO1 to CPT are depicted in the right column. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
interaction \((F = 9.17, p = 0.005)\) and a Region x Condition interaction \((F = 3.02, p = 0.018)\) were observed, but no Region x Group interaction or Region x Condition x Group interaction was observed. These results indicate that delta power was greatest in the frontal areas. There was an overall reduction in delta power in the transition from EO1 to CPT. However, as shown in the right column of Fig. 2, this reduction was only observed in children with ADHD.

### 3.2.3. Relative theta

Significant main effects were observed for Region \((F = 26.78, p = 0.0001)\) and Condition \((F = 12.83, p = 0.001)\). The only significant interaction was a Condition x Group effect \((F = 6.67, p = 0.015)\). As shown in Fig. 2 II, theta power was highest in the midline central area. Although the CPT enhanced theta power in all regions, this enhancement was only observed in children with ADHD (Fig. 2).

### 3.2.4. Relative alpha

A significant main effect was observed for Region \((F = 43.17, p < 0.0001)\). The alpha power was highest in the posterior site. The Region x Condition interaction was significant \((F = 43.17, p < 0.0001)\). The Condition x Group interaction effect was also significant \((F = 12.96, p < 0.0001)\). As shown in Fig. 2 AI, the two groups showed opposite patterns; in the eyes-open to CPT transition, the alpha power was significantly lower in controls but was enhanced in children with ADHD. No other significant main effects or interactions were observed.

### 3.2.5. Relative beta

Significant main effects were observed for Region \((F = 46.93, p = 0.0001)\) and a Region x Condition interaction \((F = 4.43, p = 0.002)\). No other significant main effects or interactions were observed. The significant main effect for Region was attributed to changes in midline regions with the lowest beta power. As shown in Fig. 2 BI, beta power increased bilaterally in the frontal region when moving from the eyes-open to the CPT condition in controls and in children with ADHD.

### 3.2.6. Theta/beta power ratio

Significant main effects on the theta/beta power ratio were observed for Region \((F = 27.37, p = 0.0001)\) and a Region x Condition interaction \((F = 4.23, p = 0.003)\). No other significant main effects or interactions were observed. These findings indicate that the theta/beta power ratio was highest in midline regions, lowest in bilateral frontal regions and highest in posterior regions, when moving from the eyes-open to the CPT condition in both groups.

### 4. Discussion

The study subjects with ADHD had a lower mean IQ but within-group correlations between IQ and EEG parameters were not statistically significant. Furthermore, Clarke et al. (2006) suggested that IQ differences between groups are unlikely to explain this type of electrophysiological finding.

Alpha and beta activities changed during the transition from eyes-closed to visual input conditions (EO1, CPT, EO2) in both groups, confirming the well-known EEG topographies reported in the literature (Basar, 1997; Klimesch, et al., 2007; see Fig. 1 in Barry et al., 2003 and Fig. 3 in Barry et al., 2007) and indicating that our results can be generalized to children in this age range and validating our EEG data.

The present study investigated dynamic changes in brain activities from eyes-open resting to a CPT condition. Our results showed that the CPT induced differences in the functional reactivity of frequency-specific EEG bands with a different effect in children with ADHD. Topographical differences between conditions were observed for the delta, alpha and beta bands and the theta/beta ratio. These changes in EEG topography indicate distinct, task-related activation processes (Vazemousavi et al., 2007; Barry et al., 2009) and, in the present study, might be associated with attention and concentration. These results suggest that specific brain structures are involved in performance of the CPT.

In line with several other studies (Matsuura et al., 1993; Kuiper et al., 1996; Clarke et al., 1998, 2002, 2003; Swartwood et al., 2003), we observed an increase in the power of the delta band during rest in children with ADHD, compared to controls. These results have been interpreted to reflect delayed functional maturation of the brain in children with ADHD (Mann et al., 1992; Matsuura et al., 1993). However, when switching from the eyes-open condition to the CPT, delta power decreased only in children with ADHD. This is the first report of dynamic delta power changes during CPTs in children with ADHD. However, this result is difficult to interpret due to the limited data available in the literature. In healthy adults, mental tasks have been shown to increase delta power but attention to the external environment decreases the level of delta activity during internal concentration (Harmony et al., 1996). In this context, delta reduction during an attentional task would support behavioral research findings in which experimental distractors impair the performance of children with ADHD during sustained attention (Xu et al., 2004).

The theta and beta power values and theta/beta power ratio are the QEEG parameters most commonly investigated in electrophysiological studies of ADHD. Most studies have reported that children with ADHD have high theta power and low beta power. The theta/beta ratio also seems to be a reliable criterion for differentiating between ADHD children and control children or between ADHD subtypes meeting DSM-IV or ICD-10 (WHO, 1992) criteria (Matsuura et al., 1993; Chabot and Serfontein, 1996; Clarke et al., 2001a,b, 2003; Barry et al., 2003; Snyder and Hall, 2006).

The present results indicate widespread theta activation across the entire scalp for children with ADHD. A frontal increase in beta power was found in both groups. Since patients were treatment-naive at the time of the study, this increase in beta power cannot be due to a medication effect (Fisch, 1994). In addition, visual inspection of the raw EEG data suggested that the beta power increase could not be attributed to increased EMG signals. In fact, an increase in frontal beta power is consistent with widely reported changes during periods of increased mental or physical effort (Ray and Cole, 1985; Andreassi, 2000). These changes in beta topography most likely reflect increased activation of higher-order processing (Barry et al., 2007). Although beta power was lower in children with ADHD and was even further reduced during the CPT, these changes (vs. controls) were not significant. This finding is not in agreement with most similar studies, which report an increase in beta power and a higher theta/beta ratio (Barry et al., 2003; Snyder and Hall, 2006).

Although some studies (i.e. Chabot and Serfontein, 1996) have reported an increase in alpha power in children with ADHD, we found lower relative alpha power at baseline, in line with most studies (see Barry et al., 2003). This finding has been interpreted (Swartwood et al., 2003) as meaning that children with ADHD are unable to attend to and process visual stimuli as efficiently as healthy children. Klimesch et al. (1996) suggested that alpha synchronization during mental inactivity may be important for introducing powerful inhibitory effects, which could prevent a memory search from entering irrelevant parts of neural networks. Based on this explanation, we suggest that impaired inhibition of neural networks in children with ADHD at baseline alters not only energy demands but also control excitatory processes.

Alpha desynchronization with visual input is generally considered to be indicative of increased functional innervation of the visual system and widespread transmission of cortical and thalamocortical interactions, which arouses and activates the entire cortex to aid information processing (Gevins et al., 1997; Basar and Schurmann, 1999; Fisch, 1994; Klimesch, 1999). Recent electrodermal/EEG studies

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of arousal performed in Barry's laboratory (Barry et al., 2004, 2005a,b, 2007, 2008, 2009) support these hypotheses. Barry et al. have suggested the presence of a negative correlation between SCL and alpha power (since elevated SCL was associated with decreased alpha) in both normal and ADHD groups. Interestingly, we observed the opposite pattern in the alpha band; the CPT induced an increase (rather than a decrease) in alpha power in the children with ADHD. This finding is compatible with the hypoarousal model of ADHD and suggests the presence of a primary deficit and cortical underarousal. However, as expected, no inter-group differences in the theta/beta power ratio were observed when comparing the eyes-open condition to the CPT condition (i.e. the Group x Condition effect was not statistically significant). Barry et al. (2009) failed to observe a correlation between theta/beta and SCL and were therefore unable to provide support for theta/beta as a marker of CNS arousal. Our results might be consistent with and support this consideration. However, our results should be interpreted with caution because they were limited to EEG changes from baseline to CPT conditions. No correlation was established between EEG parameters and electrodermal measurements. Further EEG/SCL studies need to investigate the process of shifting from baseline to an attentional task in children with ADHD.

Although an opposite pattern of alpha power change from baseline to CPT conditions was observed in children with ADHD, no significant difference was observed between the two groups during the CPT itself (Fig. 2A(right)). However, the number of errors was significantly higher in the ADHD group than in the control group. If this impaired functioning is associated with cortical underarousal in this disorder and if alpha power is correlated with arousal level, what would be the implications of these findings? Our results must be interpreted according to a model in which “activation” can be separated from “arousal” (Barry et al., 2004, 2005a,b, 2007, 2008, 2009). By separating these concepts, arousal is defined as “the current energetic state” and task-related activation is considered to be “the change in arousal from resting baseline to the task” (Barry et al., 2009). In addition, specific structures in the brain are involved during a task, producing regional/focal EEG changes. It has also been demonstrated that behavioral performance may not be directly related to arousal levels and that task-related activation (rather than arousal) determines behavioral performance (Barry et al., 2005a,b; VaezMousavi et al., 2007).

In summary, children with ADHD showed opposite changes in frequency-specific EEG activities (especially in the alpha band), when compared with controls. Based on these atypical brain wave patterns, we hypothesize that dynamic changes in neural network activities related to arousal levels and that task-related activation (rather than arousal) determines behavioral performance (Barry et al., 2005a,b; VaezMousavi et al., 2007).

processing of go and no-go stimuli. Their separate analysis is beyond the scope of the present article, but should be explored in future work.

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