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# Linear and non-linear EEG analysis of adolescents with attention-deficit/hyperactivity disorder during a cognitive task

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ABSTRACT

*Objective:* We aimed to investigate whether electroencephalograph (EEG) dynamics differ in adolescents with attention-deficit/hyperactivity disorder (ADHD) compared with healthy subjects during the performance of a cognitive task.
*Methods:* We recorded EEGs from 19 scalp electrodes in 11 adolescent boys with ADHD and 12 age-matched healthy boys while the subjects were at rest and during a continuous performance test (CPT). The approximate entropy (ApEn), a non-linear information-theoretic measure, was calculated to quantify the complexity of the EEGs.
*Results:* The mean ApEn of the ADHD patients was significantly lower than the healthy subjects over the right frontal regions (Fp2 and F8) during the performance of the cognitive task, but not at rest. The spectral analysis showed significant differences between the two groups in the P3 and T4 regions at rest and the Fp2 and F8 regions during task performance.
*Conclusions:* The differences in EEG complexity between the two groups suggest that cortical information processing is altered in ADHD adolescents, and thus their levels of cortical activation may be insufficient to meet the cognitive requirements of attention-demanding tasks.
*Significance:* This study suggests that a non-linear measure such as ApEn is useful for investigating neural dysfunctions in adolescents with ADHD.


## 1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent childhood behavioural disorders, affecting 5–10% of all children. It persists into adulthood (Wilens et al., 2002) in approximately 4% (Biederman, 2005). The symptoms of ADHD include inattention, hyperactivity and impulsivity (American Psychiatric Association, 2000), and many patients with ADHD have lower academic or occupational performance and display a co-occurring affective illness, substance abuse or oppositional behaviour (Biederman et al., 1997; Lambert and Hartsough, 1998).

Previous electrophysiological studies of ADHD reported a relative increase in the power of the theta frequency and a relative decrease in the power of the alpha and beta frequencies in resting subjects, regardless of whether their eyes were open or closed (Clarke et al., 1998, 2001a,b; Lazzaro et al., 1998; Bresnahan et al., 1999; Barry et al., 2003; Hermens et al., 2005; Snyder and Hall, 2006). Although several electrophysiological studies of ADHD have been conducted during the performance of cognitive tasks, these studies have yielded inconsistent results owing (in part) to the different tasks employed (such as reading and drawing) (Mann et al., 1992; Janzen et al., 1995; DeFrance et al., 1996; Monastra et al., 1999; El-Sayed et al., 2002; Swartwood et al., 2003; Hermens et al., 2005; Plessen et al., 2006). In contrast, cognitive tasks such as the Stroop, go/no-go and stop-signal tasks have been used widely in functional imaging studies; the results of these studies have emphasised the importance of fronto-striatal pathways in supporting attentional processes and their contribution to the pathophysiology of ADHD (DeFrance et al., 1996; Bush et al., 1999; Rubia et al., 1999; Pliszka et al., 2006). Anatomical imaging studies have reported reduced volumes of the striatum and frontal lobe in ADHD

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patients, particularly in prefrontal cortices (Teicher et al., 2000; Castellanos et al., 2002; Sowell et al., 2003; Durston et al., 2004), as well as enlargement of the hippocampus (Plessen et al., 2006).

The inherently complex, time-evolving behaviour of neural processes in the brain can be studied using non-linear dynamics, which investigates the complex emergent phenomena underlying dynamical chaotic systems. Many non-linear measures have been successfully employed in electroencephalograph (EEG) time-series analyses, extracting meaningful information about neurophysiological processes in the brain that could not otherwise be obtained using linear analysis (Babloyantz et al., 1985; Theiler and Rapp, 1996; Stam, 2005). For example, the correlation dimension (D2) (which estimates the degree of freedom of neural processes) and the largest Lyapunov exponent (which quantifies the sensitivity of the time series to initial conditions) have been used in the analysis of EEG time-series data to identify differences in neural processing in psychiatric patients and healthy subjects (Jeong, 2004). When used to analyse EEG data, these methods can improve our understanding of the pathophysiology of ADHD (Heinrich et al., 1999, 2001). Among many possible non-linear dynamics measures, the approximate entropy (ApEn) is particularly useful for short, noisy time series because it is capable of providing a robust, model-independent, information-theoretic estimation of dynamical complexity (Pincus, 1991, 1995). Prior studies have shown that EEG-based ApEn can be a sensitive discriminator of various neurophysiological states or conditions such as sleep, anaesthesia, epilepsy, depression and Alzheimer's disease (Radhakrishnan and Gangadhar, 1998; Hornero et al., 1999; Bruhn et al., 2000; Levy et al., 2003; Abasolo et al., 2005; Burioka et al., 2005a,b). According to previous studies, the ApEn measures the complexity of the EEG and may indicate the degree of arousal (Stam, 2005). To our knowledge, no previous studies have used the ApEn to study the dynamic complexity of EEGs in ADHD patients. We believe this novel approach to EEG analysis may provide an integrative understanding of ADHD.

We used ApEn to study EEG complexity in adolescent boys with ADHD and in age- and sex-matched healthy subjects while the subjects were at rest and during a continuous performance test (CPT). Recent studies have proposed a conceptual framework that links reduced EEG complexity to an increased degree of dysfunction (Stam, 2005; Pincus, 2006). Therefore, we hypothesised that the complexity of the EEG time series in ADHD adolescents would be altered over frontal regions relative to healthy subjects. In addition, we expected these changes to become more pronounced during the performance of the CPT because it assesses attentional control and executive functions that are not required in the resting condition. We thus compared ApEn values between the ADHD and healthy groups in each condition and used surrogate data to determine whether the complexity of the EEGs is generated by a non-linear dynamical process. Finally, we analysed the power spectra of the EEGs in both groups because previous studies have reported abnormal profiles of EEG power spectra in ADHD patients (Abasolo et al., 2005; Pincus, 2006; Papadelis et al., 2007). Whether or not the ApEn and power spectra reveal similar (or complementary) features in the EEGs of ADHD patients is a critical issue because the association between ApEn and other general time-series characteristics is currently unknown (Abasolo et al., 2005; Pincus, 2006; Papadelis et al., 2007).

## 2. Methods

### *2.1. Subjects*

The subject group was composed of 11 ADHD adolescents between 16 and 17 years of age (mean age = 16.55 ± 0.52 years) and 12 age- and sex-matched healthy subjects (16.75 ± 0.45 years). All participants were first-year students at Hwahong High School in Suwon City, a mid-sized city located in the southern part of Seoul, South Korea. We explained the purpose of the study to all 298 first-grade male students at the school and distributed the Brown Attention-Deficit Disorder Scale (BADDS) (Brown, 1996). Subjects in the ADHD group scored in the highest 10th percentile (>75) on BADDS (30 students met this criterion), and control subjects scored in the lowest 30th percentile on BADDS (30 subjects). Subjects were excluded if their history included a neurological disorder, a brain injury, a major medical illness, mental retardation, a learning disability, psychiatric treatment, substance abuse or the use of psychotropic medication, including stimulants. A clinical diagnostic evaluation was performed on those who agreed to participate. To establish an ADHD diagnosis, the ADHD supplement section of the Kiddie-schedule for affective disorders and schizophrenia-present and lifetime version-Korean version (K-SADS-PL) was administered in person to participants and via telephone to their parents (Kim et al., 2004). The 11 ADHD patients included three with the predominantly inattentive subtype, one with the predominantly hyperactive-impulsive subtype and seven with combined-type ADHD. None of the 12 controls fulfilled the diagnostic criteria for ADHD. The parents of all children provided written informed consent for their child to participate in the study and the children too provided written assent. The study was approved by the Institutional Review Board of the Catholic University of Korea, St. Mary's Hospital.

The Korean version of the ADHD rating scale (K-ARS) for parents and teachers was used to rate the severity of ADHD symptoms (So et al., 2002). It indicates 18 symptoms of ADHD based on the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, third revision (DSM-IV-TR) diagnostic criteria; nine questions measure attentional problems and nine more measure hyperactive-impulsive problems (full range of the scale = 0–54) (DuPual et al., 1998). Intelligence quotient (IQ) was also estimated using the Korean intelligence test-primary (KIT-P), an assessment of IQ that has been standardised using a large sample of Korean high school students (Korean Institute for Research in the Behavioral Sciences, 1996). Finally, academic performance was defined as the participant's percentile ranking among other students in the same grade.

### *2.2. EEG recording*

The EEG data from ADHD and healthy subjects were recorded with a sampling frequency of 250 Hz; subjects were in an eyes-open, resting condition and performed an auditory version of the CPT-A. This task assesses attention and motor inhibitory control, requiring the subject to respond to only 1 of 10 possible stimuli (single digits ranging from 0 to 9). The task measures omission and commission errors as well as correct responses. EEG recording was performed for nine min immediately following the administration of the CPT-A. The sequence in which target and non-target stimuli were presented was determined randomly. The inter-stimulus interval was 800 ms, and the stimulus duration was 200 ms. There were 135 target stimuli and 540 non-target stimuli.

EEG recordings were collected for at least 2 min in each condition. EEG data were obtained from 19 gold-cup scalp electrodes placed according to the international 10–20 system (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz and Pz). A Neuroscan SynAmps 32-channel amplifier was used for data acquisition. EEG segments containing noise from swallowing, sweating, eye movements (detected with electrooculography) or body movements (detected using electromyography) were excluded from the analysis. All EEG data were processed using a digital Butterworth IIR band-pass filter with cut-off frequencies of 1 and 50 Hz for the eyes-open resting condition; the cut-off frequencies for the CPT-A condition were 3 and 50 Hz to reduce movement artefacts