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EEG spectral analysis of wakefulness and REM sleep in high functioning autistic spectrum disorders

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Abstract

Objective: The aim of this study was to investigate the involvement of temporo-occipital regions in the pathophysiology of autistic spectrum disorders (ASD) by using REM sleep and waking EEG.

Methods: The EEG recordings of 9 persons with ASD and 8 control participants were recorded using a 12-electrode montage. Spectral analysis (0.75–19.75 Hz) was performed on EEG activity recorded upon two activated states: REM sleep and wakefulness.

Results: During REM sleep, persons with ASD showed a selective, significantly lower absolute beta (13.0–19.75 Hz) spectral amplitude over the primary (O_1, O_2) and associative (T_5, T_6) cortical visual areas compared to controls. Persons with ASD showed significantly higher absolute theta (4.0–7.75 Hz) spectral amplitude over the left frontal pole region (Fp1) compared to controls during evening wakefulness, but not during morning wakefulness.

Significance: The results of waking EEG are consistent with previously reported observations of neuropsychological signs of frontal atypicalities in ASD; results from REM sleep are the first EEG evidence to support the hypothesis of abnormal visuoperceptual functioning in ASD. Altogether, these results point toward atypical thalamo-cortical mechanisms subserving the neural processing of information in ASD.

Keywords: Autism; Electroencephalography; Pervasive developmental disorder; Rapid eye movement sleep; Visual cortex

1. Introduction

High functioning autism (HFA) and Asperger syndrome (AS) are included in the broader category of autistic spectrum disorders (ASD). Both clinical groups share qualitative impairments in social interaction and communication, as well as restricted, repetitive patterns of behavior, interests and activities (American Psychiatric Association, 1994). Spectral analysis of the waking EEG in ASD have shown increased slow-wave activity, reduced EEG power in frontal and temporal regions, decreased variability, and decreased inter- and intrahemispheric asymmetries relative to healthy individuals (Cantor et al., 1986; Dawson et al., 1995). Since sleep is associated with a decreased influence of peripheral sensorial input to the brain (Steriade, 2000), sleep EEG is bound to offer a signal mainly, if not solely, driven by endogenous factors and may unmask further changes in EEG activity: for example, stage 2 non-REM sleep EEG in AS is characterized by a low density of visually identified EEG spindles waves (Godbout et al., 1998, 2000).

Studies of patients with ASD using anatomical (Piven et al., 1995), brain imaging (Mountz et al., 1995; Schultz et al., 2000; Zilbovicius et al., 2000), neurochemical (Hisaoka et al., 2001) and cognitive approaches (Mottron and Burack, 2001) point toward the occipito-temporal network as being involved in the pathophysiology of ASD. Then many structures related to the visual system are activated during rapid eye movement (REM) sleep, including the extrastriate visual areas (Braun et al., 1998). The purpose of this study was therefore to assess REM sleep EEG recordings in persons with ASD, in order to verify

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whether this measure confirms the involvement of temporo-occipital regions in the pathophysiology of ASD. To control for the specificity of the expected frequency findings, we also recorded participants in the waking state.

2. Methods

2.1. Participants

Ten persons diagnosed with ASD (4 with HFA, 6 with AS) and 10 control participants were recruited. All participants gave informed consent to take part in the study and the experimental protocol was approved by the ethics committee of the hospital where the study was performed.

Patients with HFA were diagnosed by explicit checking of DSM-IV criteria for autism (American Psychiatric Association, 1994) using file information, direct standardized observation (ADOS-G module 3 or 4, Lord et al., 2000), and retrospective interview using autism diagnostic interview (ADI; Le Couteur et al., 1989). ADI and ADOS-Gs were performed by one of the authors (LM) trained to these instruments.

Inclusion criteria for all clinical participants was a score above the ADI cut-off in the three relevant areas (social interaction, communication, and restricted interest and repetitive behaviors). Persons with AS were further characterized by an absence of language delay, echolalia, stereotyped language, or pronoun reversal. However, as commonly observed, individuals with an AS diagnosis were above the cut-off for autism using the ADI algorithm, which does not take into account the HFA vs AS distinction. Therefore, the AS subgroup cannot be considered as less typical of the Autism category than the HFA subgroup. There was no comorbidity in any of the patients, including Tourette syndrome, attention deficit disorder with of without hyperactivity, and obsessive-compulsive disorder. None of the ASD participants complained of sleep disorders and none was using medication.

Comparison participants were selected on the basis of a matching according to age, gender and full-scale IQ (WISC-WAIS). Exclusion criteria for comparison participants were a past or current history of psychiatric, neurological or other medical or sleep disorders, and/or an history of primary sleep disorder or major psychiatric illness in their first-degree relatives. All were free from CNS-acting drugs.

All participants were asked to refrain from taking any CNS-active medication for at least 14 days prior their visit at the sleep laboratory. One AS patient was unable to comply with this requirement for therapeutic reasons and was eventually withdrawn from the study. None of the participants had been exposed to neuroleptics in the 12 months preceding the recording and none had been taking benzodiazepines for the last 3 months.

Complete EEG files for waking and sleeping could be obtained from 9 persons (8 M, 1 F) with ASD ranging in age from 12 to 53 (mean = 22.2 ± 4.1 years) and 8 comparison participants (7 M, 1 F) ranging in age from 8 to 56 years (mean = 23.5 ± 4.9 years). All participants were right-handed and had a full-scale IQ ≥ 80.

2.2. Sleep and EEG recordings

Participants visited the sleep laboratory for two consecutive nights, while pursuing their regular activities during daytime. Participants had the possibility to go to bed and rise at their preferred time. The first night was used as an adaptation to recording conditions (data not used). Clinical polysomnographic assessment included the monitoring of anterior tibialis EMG (2 nights) and respiration flow (night 1). Wakefulness EEG recordings were performed with participants lying in bed, with eyes closed, prior to sleep and the next morning, during 5 min on each occasion. Evening waking EEG was recorded within 15 min before lights out and morning recordings took place 15 min following final awakening. Only results from night 2 will be reported here.

Participants were fitted with a 12-electrode montage according to the International 10–20 System (Jasper, 1958; C_3, C_4, Fp_1, Fp_2, F_7, F_8, T_3, T_4, T_5, T_6, O_1, and O_2). EEG electrodes were referenced to linked earlobes (A1 + A2) and each reference electrode had a serial 10 kΩ resistor for impedance equilibrium purposes (Pivik et al., 1993). Chin electromyogram (EMG) and electro-occulograms (EOG) were also recorded. Recordings were performed on a Grass Neurodata Model 12 polygraph equipped with model 12A5 amplifiers. Filter settings and amplification factors were as follow. EEG: 1/2 amplitude low frequency filter = 0.3 Hz, 1/2 amplitude high frequency filter = 100 Hz, gain × 1000 = 20. EEG records were digitized at a sampling rate of 128 Hz and stored on CD-ROM disks for off-line visual inspection on a computer screen.

Sleep was scored in 20 s epochs according to standard methods (Rechtschaffen and Kales, 1968), using a dedicated software (Eclipse®, Stellate Systems, Montréal). Periodic leg movements in sleep (PLMS) were scored according to standard criteria (Montplaisir et al., 2000); a PLMS index (number of leg movements per hour of sleep) >10 was considered pathological. Ten or more 10 s respiratory flow pauses per hour of sleep were considered pathological.

2.3. EEG spectral amplitude analysis

Waking EEG samples were made of 15–24 4 s segments. REM sleep EEG samples were made of 24 4 s segments, taken in equal proportions from the first three REM sleep periods. Particular attention was paid to discard EEG segments containing EOG and EMG artifacts; waking and REM sleep samples were taken during ocular quiescent periods ('tonic REM sleep'; Larsen et al., 1992). EEG

segments were grouped together as single 60–96 s long EEG samples. EEG samples were submitted to Fast Fourier Transform using cosine window smoothing, with a frequency resolution of 0.25 Hz. EEG measures were computed in four frequency bands: delta = 0.75–3.5 Hz; theta = 4.0–7.75 Hz; alpha = 8.0–12.75 Hz and beta = 13.0–19.75 Hz. Power spectral analysis was performed using a commercially available software (Rhythm® v.10, Stellate Systems, Montréal).

2.4. Statistical analysis

REM sleep spectral amplitude values (μV) from both groups of participants were compared with Mann–Whitney *U*-tests for independent samples using an alpha of 0.05. Waking EEG was compared using two groups (ASD, controls) × 2 moments (evening, morning) ANOVA and LSD post hoc tests.

3. Results

3.1. Sleep parameters

None of the participants presented a pathological sleep apnea index. No comparison participant presented a pathological PLMS index while two persons with ASD presented pathological PLMS (43.3 and 57.4 movements/hour of sleep, respectively). REM sleep parameters are shown in Table 1.

3.2. REM sleep EEG

Compared to control participants, REM sleep EEG recordings of persons with ASD showed a significantly lower absolute beta spectral amplitude over the primary (O_1: $U = 15$, $P < 0.05$; O_2: $U = 12.5$, $P < 0.03$) and associative (T_5: $U = 11.5$, $P < 0.03$; T_6: $U = 11$, $P < 0.02$) visual areas. Diminished beta spectral amplitude appears to be specific to these two regions as differences among groups did not reach significance in any of the other brain regions where similar analyses were performed (data not shown). REM sleep EEG results for significant placements are summarized in Fig. 1.

Table 1
REM sleep parameters (means ± SEM) in ASD and control participants

	ASD	Controls	*P*
Total sleep time (min)	468.6 ± 23.3	429.7 ± 26.4	n.s.
REM sleep latency (min)	96.5 ± 12.9	99.0 ± 18.9	n.s.
REM sleep duration (min)	89.0 ± 7.9	85.1 ± 8.1	n.s.
No. REM sleep periods	4.8 ± 0.3	4.8 ± 0.6	n.s.

Groups were compared with *t* tests for independent samples.

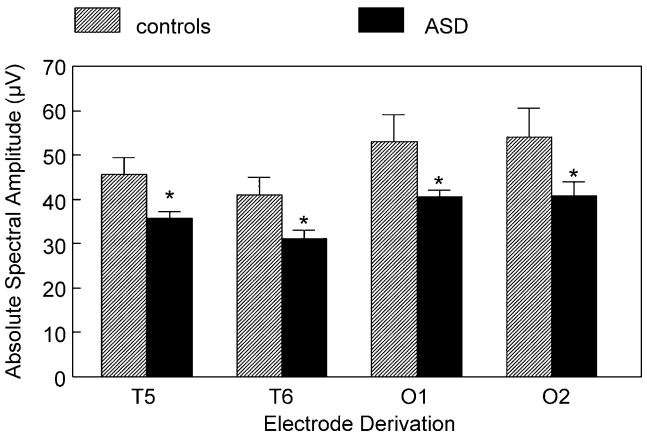

Fig. 1. Histogram representation of absolute spectral amplitude for beta frequency band on bilateral homologous electrode derivations, for significant placements in REM sleep. Stars (*) indicate a statistically significant difference ($P < 0.05$) between the two groups using Mann–Whitney *U*-tests.

3.3. Waking EEG

All EEG values are shown in Table 2. Waking EEG was analyzed using a group (ASD, control participants) by moment (evening, morning) ANOVA for each electrode placement and frequency band. Only Fp1 theta activity showed a significant difference between groups ($F(2, 28) = 3.34$, $P = 0.04$). The LSD post hoc test indicated that the difference between groups was due to evening recordings, i.e. prior to sleep. Accordingly, no difference was found between groups for EEG measures taken in the morning for any frequency band, at any recording site. Only participants with ASD exhibited a difference between evening and morning recordings, in the form of higher theta activity at the Fp1 recording site (see Table 3).

The relative locations of electrode sites showing significant differences between groups in sleep and waking EEG are depicted in Fig. 2.

4. Discussion

The main finding of this research is that, compared to control participants, persons with ASD show lower beta activity during REM sleep over cortical visual areas. Given the converging evidence suggesting that the beta range of EEG activity best represents the activation of neural networks involved in the control of REM sleep (Merica and Blois, 1997), this finding supports and extends our previous observation of poor REM sleep control in patients with AS (Godbout et al., 2000). Since parieto-occipital areas are thought to be related to dreaming visual contents (Solms, 1995, 1997, 2000), this finding can also be related to the poor quality of REM sleep dream content observed in AS (Daoust et al., 2001; Godbout et al., 1998).

Table 2
Mean (± SEM) absolute spectral amplitude of evening (top panel) and morning (bottom panel) waking EEG recordings in ASD and control participants

	ASD				CNTL			
	Delta	Theta	Alpha	Beta	Delta	Theta	Alpha	Beta
Evening								
C3	94.0 ± 8.5	86.3 ± 13.4	119.9 ± 16.4	62.3 ± 7.7	86.9 ± 16.6	69.7 ± 9.9	95.4 ± 10.5	76.6 ± 14.3
C4	94.6 ± 7.8	80.3 ± 9.8	110.6 ± 14.7	58.3 ± 7.1	94.7 ± 21.3	67.7 ± 7.2	92.3 ± 10.8	88.7 ± 16.7
Fp1	107.7 ± 11.1	74.3 ± 7.2*	91.2 ± 10.2	52.8 ± 4.2	98.4 ± 15.3	54.1 ± 4.8	77.4 ± 8.4	61.6 ± 10.9
F7	79.6 ± 5.9	56.9 ± 6.2	69.0 ± 9.7	43.7 ± 4.0	72.3 ± 7.2	48.0 ± 4.3	67.9 ± 7.1	66.7 ± 19.6
T3	75.9 ± 12.7	62.0 ± 13.2	84.7 ± 22.7	49.9 ± 8.8	63.3 ± 15.4	50.2 ± 12.1	71.0 ± 13.7	52.5 ± 9.4
T5	92.4 ± 15.2	84.9 ± 15.6	167.9 ± 43.9	69.0 ± 12.4	77.7 ± 17.0	64.2 ± 11.4	140.7 ± 28.4	75.2 ± 10.6
O1	100.6 ± 10	86.4 ± 12.0	195.6 ± 34.1	77.1 ± 11.7	102.6 ± 19.4	76.9 ± 8.6	195.7 ± 31.4	103.0 ± 17.6
Fp2	103.5 ± 10.9	72.3 ± 7.3	90.5 ± 10.6	52.9 ± 4.0	97.7 ± 16.1	54.7 ± 5.3	77.6 ± 8.6	62.3 ± 11.2
F8	78.9 ± 6.9	58.3 ± 6.5	68.0 ± 9.7	44.1 ± 3.8	71.6 ± 7.7	49.4 ± 3.7	61.3 ± 3.5	57.1 ± 9.5
T4	66.3 ± 10.9	57.0 ± 12.9	74.3 ± 18.0	50.1 ± 7.2	57.7 ± 11.2	43.6 ± 6.1	62.6 ± 7.6	53.0 ± 8.8
T6	87.9 ± 18.4	84.1 ± 20.2	163.4 ± 49.5	66.7 ± 15.5	81.0 ± 17.5	63.7 ± 13.4	141.3 ± 28.0	79.0 ± 14.6
O2	86.4 ± 21.4	80.7 ± 18.2	188.7 ± 38.5	90.4 ± 18.3	83.4 ± 14.7	72.6 ± 10.1	218.4 ± 43.7	128.4 ± 24.8
Morning								
C3	89.1 ± 12.2	74.0 ± 8.4	99.1 ± 13.4	51.1 ± 4.9	79.3 ± 15.0	71.6 ± 9.9	98.4 ± 9.7	75.0 ± 13.4
C4	84.0 ± 8.8	72.6 ± 9.0	98.4 ± 18.0	51.6 ± 6.3	84.0 ± 14.3	72.5 ± 8.5	98.8 ± 7.7	69.6 ± 12.0
Fp1	98.7 ± 7.1	58.7 ± 5.4	72.3 ± 11.5	41.0 ± 3.5	80.5 ± 10.8	52.7 ± 3.4	76.6 ± 7.1	49.4 ± 6.8
F7	71.9 ± 7.1	48.7 ± 4.6	57.3 ± 7.8	38.9 ± 4.7	67.9 ± 10.1	47.5 ± 4.9	62.1 ± 6.7	46.4 ± 6.1
T3	59.9 ± 5.4	46.3 ± 4.5	52.3 ± 6.2	38.6 ± 5.0	58.0 ± 9.8	44.4 ± 5.0	57.6 ± 4.9	49.9 ± 8.0
T5	92.0 ± 17.8	78.1 ± 14.4	111.6 ± 15.4	54.3 ± 6.2	83.0 ± 15.0	66.0 ± 11.8	121.8 ± 21.0	99.8 ± 38.6
O1	92.0 ± 8.8	77.3 ± 9.2	159.0 ± 35.6	64.0 ± 7.7	96.1 ± 15.2	77.9 ± 10.2	178.4 ± 20.3	83.9 ± 10.3
Fp2	93.6 ± 4.8	57.3 ± 5.8	72.7 ± 12.3	41.3 ± 3.5	77.4 ± 8.0	53.3 ± 3.6	77.8 ± 6.7	50.8 ± 6.9
F8	72.0 ± 6.8	50.6 ± 5.7	59.7 ± 10.4	39.7 ± 4.3	66.0 ± 9.8	49.6 ± 4.4	64.9 ± 5.8	50.3 ± 7.3
T4	60.6 ± 11.8	49.4 ± 8.6	55.7 ± 7.8	43.0 ± 4.8	55.6 ± 6.4	44.3 ± 4.2	57.6 ± 3.4	42.6 ± 5.6
T6	87.9 ± 24.1	79.0 ± 17.7	104.4 ± 15.8	51.9 ± 7.1	72.5 ± 13.1	57.2 ± 9.6	112.7 ± 17.6	59.7 ± 9.4
O2	84.0 ± 21.9	71.6 ± 12.1	157.0 ± 29.9	74.4 ± 10.2	108.6 ± 18.8	88.3 ± 15.5	196.0 ± 26.5	88.4 ± 11.1

*$P < 0.05$ (see text and Table 3). Data is expressed in μV (mean ± SEM).

Quantified EEG analysis is known to reflect thalamo-cortical and cortico-cortical neurophysiological activities (Steriade et al., 1990, 1993). The present results thus suggest atypicalities of thalamo-cortical communications involving primary/associative visual areas in persons with ASD. In an MRI study of individuals with ASD, Tsatsanis et al. (2003) recently reported that, while thalamus volume as such was indistinguishable among clinical and comparison individuals, the correlation between thalamus and cortex volume was significant only in typically developing individuals. Together with observations of increased brain size in HFA (for reviews, see Bauman and Kemper, 1994; Fombonne et al., 1999), this suggests that thalamic volume does not vary according to brain volume in HFA. Such a pattern is deemed to influence the organization of cortical pathways leading to atypical connections between cortical and subcortical regions, some of which could contribute to the significant differences found in the present study.

Our second finding is a higher left prefrontal theta activity in ASD participants compared to controls upon evening recordings. This further supports the involvement of frontal network in the pathophysiology of autism as demonstrated by diminished fronto-striatal gray matter volume (McAlonan et al., 2002), increased frontal lobe cortex volume (Carper and Courchesne, 2000), hypoactivation of the frontal lobes during rest (Ohnishi et al., 2000; Zilbovicius et al., 1995), abnormal prefrontal metabolite concentration using in vivo proton magnetic resonance spectroscopy (Murphy et al., 2002), and diminished activation in dorsolateral prefrontal cortex and posterior cingulate cortex during a spatial working memory task (Luna et al., 2002). At the behavioral level, an involvement of prefrontal regions is consistent with impaired ability in switching across mental sets and, more generally, in

Table 3
Wake mean (± SD) Fp1 theta spectral amplitude values of ASD and control (Cntl) participants, and LSD post hoc test results comparing each group and moment

		(1)	(2)	(3)	(4)
(1)	ASD evening, 74.3 ± 17.6 μV	–	0.05*	0.01*	–
(2)	ASD morning, 58.7 ± 14.4 μV	0.05*	–	–	0.40
(3)	Cntl evening, 54.1 ± 12.6 μV	0.01*	–	–	0.83
(4)	Cntl morning, 52.7 ± 10.9 μV	–	0.40	0.83	–

*$P \leq 0.05$. '–' indicates repetitive or inappropriate contrasts. Significantly higher values were found in ASD compared to controls upon the evening EEG recordings. ASD participants showed significantly higher values in the evening than in the morning.

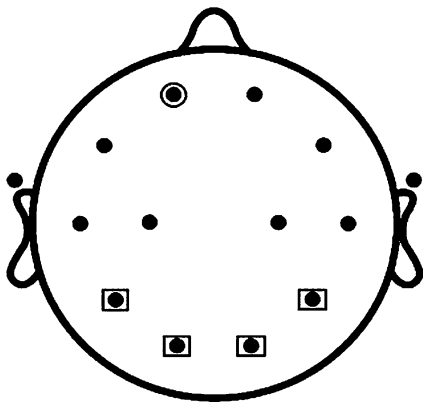

Fig. 2. Schematic representation of the EEG montage with significantly different derivations between ASD and control participants. The circled electrode site points to a significantly increased theta value for ASD patients upon the evening waking EEG recordings relative to controls. Squared electrode sites point to significantly decreased beta values for ASD patients upon REM sleep EEG recordings.

high-level controlled operation (Minshew et al., 2002). The fact that waking EEG differences were found only at bedtime needs to be further investigated. On one hand, increased EEG theta activity during waking is known to correlate with somnolence (Cajochen et al., 1997; Lafrance and Dumont, 2000); this suggests that sleep restorative functions are optimal in autism. On the other hand, theta activity is known to undergo significant diurnal variations (Lafrance and Dumont, 2000) so that an interaction involving both homeostatic (i.e. somnolence-related) and chronobiologic (i.e. clock-related) factors may play a role in the results we observed. Since cognitive performance also follows a diurnal rhythmicity (Carrier and Monk, 2000), time of day should be taken into account when frontal functions like attention and executive functions (Stuss and Benson, 1984) are tested in persons with ASD.

The present study does not replicate previous reports of increased slow-wave activity (Cantor et al., 1986) and reduced EEG power particularly in the fronto-temporal region (Dawson et al., 1995), most likely for methodological reasons. Indeed these two studies included younger participants than ours (4–12 years old, mean 7.9 ± 2.0 and 5.4–18.1 years old, mean 11 ± 4, respectively) so that maturational effect on the EEG may be involved. Another reason is that these previous studies included participants with low IQs, which challenges the specificity of such observations. Indeed, individuals with low IQs are bound to show increased delta EEG power/slowing of background activity and this could contribute to the differences between results.

The present study has its own limitations. First, since the study is 'patient-oriented', ASD participants were recruited according to their order of availability, as they presented themselves at the specialized clinic. As a consequence, one 12-year-old patient and one 53-year-old patient, both respecting other inclusion and exclusion criteria, were included. On one hand, this was compensated for by making up a group of comparison participants matched on age, in addition to gender and full-scale IQ. On the other hand, given the age range, maturational effects cannot be addressed before larger groups with a significant number of participants in different age brackets are independently analyzed and then compared using multivariate analysis. A second limitation is the number of participants. Although our 'n' compares favorably to others with the same requirements in terms of normal IQ and absence of comorbidity, our results should be interpreted with caution until confirmed by another study.

In conclusion, the present results show that persons with ASD display EEG differences with control participants and that such differences vary according to state. The demonstration of EEG atypicalities over primary/associative visual areas during REM sleep and left prefrontal cortex during waking adds to a consistent set of anatomical, functional and cognitive arguments suggesting the involvement of temporo-occipital as well as frontal regions in the pathophysiological processes at stake in the autistic spectrum.

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References

American Psychiatric Association, Diagnostic and Statistical Manual of mental disorders (DSM-IV), 4th ed. Washington, DC: American Psychiatric Association; 1994.

Bauman ML, Kemper TL. Neuroanatomic observations of the brain in autism. In: Bauman ML, Kemper TL, editors. The neurobiology of autism. Baltimore, MD: Johns Hopkins University Press; 1994. p. 119–45.

Braun AR, Balkin TJ, Wesensten NJ, Gwadry F, Carson RE, Varga M, Baldwin P, Belenky G, Herscovitch P. Dissociated pattern of activity in visual cortices and their projections during human rapid eye movement sleep. Science 1998;279:91–5.

Cajochen C, Krauchi K, Wirz-Justice A. The acute soporific action of daytime melatonin administration: effects on the EEG during wakefulness and subjective alertness. J Biol Rhythms 1997;12:636–43.

Cantor DS, Thatcher RW, Hrybyk M, Kaye H. Computerized EEG analysis of autistic children. J Autism Dev Disord 1986;16:169–87.

Carper RA, Courchesne E. Inverse correlation between frontal lobe and cerebellum sizes in children with autism. Brain 2000;123:836–44.

Carrier J, Monk TH. Circadian rhythms of performance: new trends. Chronobiol Int 2000;17:719–32.

Daoust AM, Mottron L, Godbout R. Dream content analysis in Asperger's Syndrome. Sleep 2001;24:184–5.

Dawson G, Grofer Klinger L, Panagiotides H, Lewy A, Catelloe P. Subgroups of autistic children based on social behavior display distinct patterns of brain activity. J Abnorm Child Psychol 1995;23:569–83.

Fombonne E, Roge B, Claverie J, Courty S, Fremolle J. Microcephaly and macrocephaly in autism. J Autism Dev Disord 1999;29:113–9.

Godbout R, Bergeron C, Stip E, Mottron L. A laboratory study of sleep and dreaming in Asperger's syndrome. Dreaming 1998;8:75–88.

Godbout R, Bergeron C, Limoges E, Stip E, Mottron L. A laboratory study of sleep in Asperger's syndrome. NeuroReport 2000;11:127–30.

Hisaoka S, Harada M, Nishitani H, Mori K. Regional magnetic resonance spectroscopy of the brain in autistic individuals. Neuroradiology 2001; 43:496–8.

Jasper HH. The ten–twenty electrode system of the International Federation. Electroencephalogr Clin Neurophysiol 1958;10:371–5.

Lafrance C, Dumont M. Diurnal variations in the waking EEG: comparisons with sleep latencies and subjective alertness. J Sleep Res 2000;9:243–8.

Larsen LH, Prinz PN, Moe KE. Quantitative analysis of the EEG during tonic REM sleep-methodology. Electroencephalogr Clin Neurophysiol 1992;83:24–35.

Le Couteur A, Rutter M, Lord C, Rios P, Robertson S, Holdgrafer M, McLennan J. Autism diagnostic interview: a standardized investigator-based instrument. J Autism Dev Disord 1989;19:363–87.

Lord C, Risi S, Lambrecht L, Cook EH, Leventhal BL, DiLavore PC, Pickles A, Rutter M. The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. J Autism Dev Disord 2000;30: 205–23.

Luna B, Minshew NJ, Garver KE, Lazar NA, Thulborn KR, Eddy WF, Sweeney JA. Neocortical system abnormalities in autism: an fMRI study of spatial working memory. Neurology 2002;59:834–40.

McAlonan GM, Daly E, Kumari V, Critchley HD, van Amelsvoort T, Suckling J, Simmons A, Sigmundsson T, Greenwood K, Russell A, Schmitz N, Happe F, Howlin P, Murphy DG. Brain anatomy and sensorimotor gating in Asperger's syndrome. Brain 2002;125: 1594–606.

Merica H, Blois R. Relationship between time courses of power in the frequency bands of human sleep EEG. Neurophysiol Clin 1997;27: 116–28.

Minshew NJ, Sweeney J, Luna B. Autism as a selective disorder of complex information processing and underdevelopment of neocortical systems. Mol Psychiatry 2002;7(Suppl 2):S14–S15.

Montplaisir J, Nicolas A, Godbout R, Walters A. Restless legs syndrome and periodic limb movements during sleep. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. Philadelphia, PA: Saunders; 2000. p. 742–52.

Mottron L, Burack JA. Enhanced perceptual functioning in the development of autism. In: Burack JA, Charman T, Yirmiya N, Zelazo PR, editors. The development of autism: perspectives from theory and research. Mahwah, NJ: Lawrence Erlbaum Associates; 2001. p. 131–48.

Mountz JM, Tolbert LC, Lill DW, Katholi CR, Liu HG. Functional deficits in autistic disorder: characterization by technetium-99m-HMPAO and SPECT. J Nucl Med 1995;36:1156–62.

Murphy DG, Critchley HD, Schmitz N, McAlonan G, Van Amelsvoort T, Robertson D, Daly E, Rowe A, Russell A, Simmons A, Murphy KC, Howlin P. Asperger syndrome: a proton magnetic resonance spectroscopy study of brain. Arch Gen Psychiatry 2002;59:885–91.

Ohnishi T, Matsuda H, Hashimoto T, Kunihiro T, Nishikawa M, Uema T, Sasaki M. Abnormal regional cerebral blood flow in childhood autism. Brain 2000;123:1838–44.

Piven J, Arndt S, Bailey J, Havercamp S, Andreasen NC, Palmer P. An MRI study of brain size in autism. Am J Psychiatry 1995;152:1145–9.

Pivik RT, Broughton RJ, Coppola R, Davidson RJ, Fox N, Nuwer MR. Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. Psychophysiology 1993;30: 547–58.

Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles, CA: BIS/BRI, University of California at Los Angeles; 1968.

Schultz RT, Romanski LM, Tsatsanis KD. Neurofunctional models of autistic disorder and Asperger syndrome: clues from neuroimaging. In: Klin A, Volkmar FR, et al., editors. Asperger syndrome. New York: Guilford Press; 2000. p. 172–209.

Solms M. New findings on the neurological organization of dreaming: implications for psychoanalysis. Psychoanal Q 1995;64:43–67.

Solms M. The neuropsychology of dreams: a clinico-anatomical study. Mahwah, NJ: Lawrence Erlbaum Associates; 1997.

Solms M. Dreaming and REM sleep are controlled by different brain mechanisms. Behav Brain Sci 2000;23:843–50. See also p. 904–1018, 1083–1121.

Steriade M. Brain electrical activity and sensory processing during waking and sleep states. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. Philadelphia, PA: Saunders; 2000. p. 93–111.

Steriade M, Jones EG, Llinás RR. Thalamocortical oscillations and signaling. New York: Wiley; 1990.

Steriade M, McCormick DA, Sejnowski TJ. Thalamocortical oscillations in the sleeping and aroused brain. Science 1993;262:679–85.

Stuss DT, Benson DF. Neuropsychological studies of the frontal lobes. Psychol Bull 1984;95:3–28.

Tsatsanis KD, Rourke BP, Klin A, Volkmar FR, Cicchetti D, Schultz RT. Reduced thalamic volume in high-functioning individuals with autism. Biol Psychiatry 2003;53:121–9.

Zilbovicius M, Garreau B, Samson Y, Remy P, Barthelemy C, Syrota A, Lelord G. Delayed maturation of the frontal cortex in childhood autism. Am J Psychiatry 1995;152:248–52.

Zilbovicius M, Boddaert N, Belin P, Poline JB, Remy P, Mangin JF, Thivard L, Barthelemy C, Samson Y. Temporal lobe dysfunction in childhood autism: a PET study. Am J Psychiatry 2000;157:1988–93.