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Abnormal topography of EEG microstates in Gilles de la Tourette syndrome

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Abstract Quantitative analysis of scalp EEGs was performed on 13 patients with Gilles de la Tourette syndrome (GTS) and 25 matched controls. The analysis method was adaptive segmentation, which describes the topography and sequence of brain electric fields in continuous EEG. The GTS patients showed an abnormal increase in fields with a right-frontal/left-posterior configuration. The GTS patient's EEGs did not differ from normal controls in the average duration of the brain electric microstates, field stability and EEG carrier frequency. To find out whether the abnormal activity is similar to movement-related activity a simple and a complex motor task were performed. Both tasks led to distinct changes of brain electric activity, but not to an increase in right-frontal-/left-posterior-oriented patterns. Motor-related activity was contrasted with two auditory tasks. We conclude that GTS patient's EEG show abnormal topographic patterns of brain electric activity. Unlike other psychiatric disorders, the temporal descriptors of the EEG aspects are unaffected. The abnormal EEG patterns in GTS patients are not similar to those elicited by simple or complex movements; thus, the presence of abnormally facilitated, near-threshold motor activity in GTS patients seems not a likely explanation.

Key words Gilles de la Tourette syndrome · EEG · Adaptive segmentation · Physiology · Functional neuroimaging

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Introduction

Gilles de la Tourette syndrome (GTS) is characterized by multiple motor and vocal tics (acording to DSM-III-R), which typically wax and wane over time, but abate in later life. GTS is transmitted genetically in an autosomal-dominant pattern with high, but gender-dependent, penetrance (Eapen et al. 1993) and childhood onset. Occasionally, GTS-symptoms may arise in Huntington's Chorea or from ischemic lesions involving the basal ganglia. GTS overlaps considerably with obsessive-compulsive behavior (OCB), with 50–70% of the patients suffering also from OCB and compulsive thought. Pauls et al. (1986) have suggested that both disorders may represent alternative phenotypes of the same autosomal gene. There is also prominent comorbidity with self-injurious behavior (7–30%; Robertson and Yakeley 1993), and half of the GTS patients had a childhood diagnosis of attention deficit hyperactivity disorder (ADHD; Towbin and Riddle 1993). Neurocognitive tests have revealed that, depending on comorbidity, GTS patients are impaired in a number of cognitive and affective functions, e.g., they have reduced attention span, restlessness, concentration deficits, and diminished impulse control, but usually normal intelligence. They also suffer from severe mood swings, anxiety, and temper outbursts (Erenberg et al. 1987; Robertson et al. 1988). The underlying biological process is not known, although the mechanism of how motor and vocal behavior or thoughts are initiated, and how involuntary and voluntary acts blend into each other, is of high interest. The good response to neuroleptic drugs and increased cerebrospinalfluid (CSF) levels of monoamine transmitter metabolites (Leckman et al. 1995) suggest involvement of dopaminergic pathways. Recent SPECT investigations have reported increased dopamine-transporter levels in GTS patients' basal ganglia (Malison et al. 1995). There are no gross neuropathologic lesions apparent from CT studies. Recent MRI volumetric studies found a reduction of left lenticular nuclei volume (Peterson et al. 1993; Singer et al. 1993). Functional examinations (HMPAO-

SPECT) have revealed lower perfusion rates in the left caudate and the anterior cingulate cortex (Moriarty et al. 1995; Riddle et al. 1992). Similar brain areas have been implicated in OCB (Rubin et al. 1992; Baxter et al. 1988; Swedo et al. 1989).

Electrophysiologic studies of GTS are numerous. Most, under awake resting conditions (e.g., Volkmar et al. 1984; Verma et al. 1986; Robertson et al. 1988), found focal paroxysmal discharge and increased theta activity. Hyde et al. (1994) reported 42% of the EEGs as abnormal by IFSCEN (1974) criteria, with increased theta activity. Notably, even the more recent studies by Hyde et al. (1994), Verma et al. (1986), and Volkmar et al. (1984) evaluated the EEGs by visual inspection. Whereas Krumholz et al. (1983) have not found alterations of amplitude or latency of visual, auditory, or somatosensory potentials, Drake et al. (1992) reported that GTS patients with OCD have shorter auditory N200 and P300 latencies than controls.

The current pathogenetic model for GTS postulates dysfunction of a loop comprising dorsolateral prefrontal cortex, dorsolateral caudate, and dorsomedial pallidum, as well as VA and MD thalamic nuclei (Moriarty et al. 1995).The pathobiology of GTS is thought to be similar to OCB, where hyperactivity of motor and vocalization circuits is assumed (Insel 1992). The dysfunction underlying GTS may imply altered levels of neuronal activity in abnormally facilitated motor or premotor circuits. Alternatively, abnormal activity may result from the attempt to inhibit the abnormal movements (Moriarty et al. 1995). In either case, provided that the ensembles of cortical neurons involved are large enough, analysis of EEG should yield abnormal spatiotemporal patterns in GTS patients.

In a previous paper (Günther et al. 1996) the results of spectral power analysis of the same set of subjects were presented. The main finding was that GTS patients showed less reduction in EEG alpha power than controls when performing various tasks, which was interpreted as impaired cortical activation. However, the abnormalities could not be explained exclusively by aberrant motor function. The present report analyzes the topography and temporal sequence of scalp electrical fields. The hypothesis is that the topographic organization of EEG in GTS patients differs from that of healthy controls. In addition, if the abnormal activity is similar to the kind of activity elicited by voluntary movements, EEGs from controls and from GTS patients should differ most at rest, and less so when both groups perform movements. The data are analyzed by adaptive segmentation of continuous EEG (Lehmann et al. 1987; Strik et al. 1993, 1995). Adaptive segmentation identifies periods of topographically stable electric fields. Lehmann et al. (1987) and Wackermann et al. (1993) have demonstrated that successive brain electric fields do not blend into each other. Instead there are distinct switches from one configuration to the next. It is assumed that the epochs during which field configurations are stable (the brain electric microstates) represent distinct states of brain activity. Adaptive segmentation is thus suitable to evaluate the topographic distribution and the temporal succession of brain electric states.

Methods

Patients and controls

Thirteen patients with GTS, were recruited at the Psychiatric Hospital of Munich University. They were consecutive admissions referred for diagnosis and/or treatment of tic disorder. Written consent was obtained from each subject. Exclusion criteria were psychiatric or neurologic diagnoses other than GTS. Diagnoses were made by an expert, according to DSM-III-R criteria. Table 1 describes the patient and the control population. All patients were off medication for at least 2 weeks. A total of 25 healthy controls were matched for age and gender with the patients. All subjects were right handed.

EEg recordings

The EEGs were recorded from patients resting in a reclined chair, using 21 electrodes placed according to the 10-20 convention at the following sites: FP1, FPz, FP2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, and O2. Standardized electrode positioning was achieved by using the Electrocap (Gelimed, Munich) system. Linked ears served as reference. Impedance was < 5 kOhms. The data were amplified from 0.016–64 Hz, and stored at a sampling rate of 128 Hz. Vertical and horizontal eye movement, as well as ECG, were recorded by bipolar leads, using the same amplifier setting and stored at the same rate as the EEG signals. They were used for off-line correction for artifacts by multiple linear regression (Gratton et al. 1983). The EEGs were visually inspected and five epochs of 2 s artifact-free EEG from the center of each task were chosen for further analysis. One control EEG was lost due to artifacts.

The EEGs were acquired during a resting condition, followed by four tasks, each separated by 1 min of rest. All tesks and the rest conditions were performed with closed eyes. All instructions were given verbally and in a standardized way. After the resting period, a simple motor task was demanded. The instruction was to flex the thumb against the index finger in a slow, self-paced way for 1 min. After another resting period, the next instruction was to flex the thumb against the index finger twice, the middle finger once, the ring finger three times, the little finger twice, and then reverse the sequence. After another resting period, a simple auditory task was performed: A stereotyped Rumba-rhythm in a rising cadence was played for 1 min by binaural headphones. After a resting period of 1 min, the beginning of Mozart's "Hunting Quartet" K458 was played through the headphones for 1 min.

EEG analysis

The data were automatically processed as described by Lehmann et al. (1987) and Strik et al. (1993, 1995). In short, the EEGs were

Table 1 Description of patient and control populations

	Gilles de la Tourette	Controls
N	13	26
Male/female	11/2	21/4
Mean age (years)	36.4 ± 11.3	35.2 ± 11.3
TSGS mean score (Harcherik et al. 1984)	31.3 ± 14.4	
YGTSS mean score (Leckman et al. 1989)	50.2 ± 19.8	

NOTE: TSGS and YGTS are rating scales for tic severity. Scores indicate moderate to severe disease

transformed into average reference recordings to remove spatial DC offset and digitally filtered to a bandwidth of 2-15 Hz. The rationale in choosing this frequency band was that the microstates obtained from the higher-frequency range (15–35 Hz) contribute nothing to variance explained by diagnoses and conditions, as preliminary experiments showed. For every sampling point (at 128 Hz) the global field power (GFP) was determined and the maps with maximum field strength (maximal GFP) were selected. Field topography is described by the coordinates of the two centroids indicating the center of gravity of positive and negative field areas. The coordinates are given as x- and y-values, the x value corresponding to a left–right gradient, and the y value to an anterior-posterior gradient. The units are electrode distances (10/20 system) with a left frontal origin, i.e., 1/3 describes the T3 electrode site. During each microstate the polarity of the centroids changes repeatedly, whereas the field topography remains stable. Therefore, the centroids are not designated "positive and negative", but instead "anterior and posterior". A new brain microstate is assumed, when one of the centroids moves out of a circular area (the topographic window) which was set by the preceding centroid locations. The size of the circular shaped window was determined for each subject and condition in a data-driven way as described by Strik and Lehmann (1993). The size corresponds to the precision with which the field is maintained. To render comparison of parameters depending upon window size meaningful, these were determined by employing a constant window ($r = 0.49$). The number of GFP peaks/s indicates the frequency of field strength maxima, i.e., the carrier frequency. The brain microstates are characterized by their duration (milliseconds) and their topography. The summary topography as presented in Table 2 indicates for each condition and diagnostic group the center of gravity of all centroid locations, denoted in the same x/y-coordinate system described above, the average orientation of the axis connecting the two centroids (in degrees, clockwise from ear–ear = 0°). For reasons of space, the distance between the centroids and the size of the topographic window is not given. The number of single-peak segments/s represents the frequency of fields containing only one GFP maximum. These were excluded from data analysis, because they did not contribute to variance explained. They represent noise or instances of rapid field changes (Strik et al. 1995). To obviate bias introduced by their omission, the data were also examined including the 2-35 Hz frequency range and single-peak segments. This diminished statistical effects (data not shown), thus confirming the findings of Strik et al. (1995).

Table 2 EEG segmentation data

Group	GTS ($n = 13$)[a]	Controls ($n = 25$)[a]
Average duration of EEG microstates (ms)		
Rest	129 ± 33	141 ± 48
Simple hand movement	121 ± 25	139 ± 52
Complex hand movement	111 ± 25	125 ± 38
Rhythm	116 ± 24	120 ± 29
Mozart	121 ± 32	125 ± 45
No. of single-peak segments per second		
Rest	12.7 ± 6.2	11.5 ± 4.9
Simple hand movement	14.6 ± 4.6	12.2 ± 4.8
Complex hand movement	16.2 ± 4.8	14.7 ± 6.6
Rhythm	14.6 ± 5.2	13.6 ± 4.9
Mozart	14.6 ± 5.3	13.5 ± 5.4
GFP peaks/s *(n)*		
Rest	23.5 ± 2.9	23.6 ± 2.3
Simple hand movement	23.5 ± 2.4	24.1 ± 3.1
Complex hand movement	24.6 ± 2.9	25.1 ± 3.6
Rhythm	24.3 ± 2.7	24.8 ± 3.2
Mozart	24.4 ± 2.7	24.9 ± 3.2
Centroid location x-position		
Rest	3.00 ± 0.04	2.99 ± 0.04
Simple hand movement	3.01 ± 0.05	3.02 ± 0.05
Complex hand movement	3.00 ± 0.03	3.00 ± 0.06
Rhythm	3.00 ± 0.04	2.98 ± 0.07
Mozart	3.00 ± 0.06	2.98 ± 0.08
Centroid location y-position		
Rest	3.15 ± 0.08	3.15 ± 0.10
Simple hand movement	3.15 ± 0.08	3.15 ± 0.13
Complex hand movement	3.06 ± 0.10	3.10 ± 0.11
Rhythm	3.09 ± 0.08	3.13 ± 0.13
Mozart	3.11 ± 0.08	3.10 ± 0.16
Centroid axis (clockwise, in degrees from 0° = ear – ear)		
Rest	99.3 ± 9.2	88.3 ± 13.0
Simple hand movement	99.6 ± 7.6	86.9 ± 10.1
Complex hand movement	100.0 ± 9.2	89.0 ± 9.8
Rhythm	99.9 ± 8.0	86.1 ± 20.1
Mozart	101.4 ± 10.0	95.6 ± 22.4

[a] Mean ± SD

Statistical analysis

After testing for normal distribution and homogeneity of variance, the data were analyzed by multivariate repeated measures ANOVA, one for the variables describing temporal organization of the EEG, and one for topographic organization. In both designs the between-groups factor was "diagnosis," the within factor "condition," with age as covariate, followed by post-hoc univariate F-tests to locate effects. When MANOVAs indicated an (within cells) effect for the covariate, standardized regression coefficients (beta) and their significance for the covariate were calculated. Significance was assumed at $p < 0.05$. Covariance matrices were analyzed by Mauchly's test of sphericity and correction by Greenhouse-Geisser's epsilon was applied if appropriate. F-values cited represent averaged multivariate results.

Results

The effects residing in temporal properties of the signal are presented first, followed by the parameters describing field topography (Table 2). First, an analysis of all five tasks (rest, simple motor, complex motor, rhythm, Mozart) is offered. Significant main effects and first-degree interactions from this analysis are then broken down to variables and to differences between individual tasks.

Temporal parameters

There was no main effect for diagnosis on EEG segment duration, number of GFP peaks/s and single-peak segments/s ($F4,32 = 1.48$,n.s.). The condition effect was significant ($F8,29 = 4.06$, $p < 0.01$), consisting (in univariate analysis) of a decrease in EEG microstate duration ($F2,72 = 7.49$, $p < 0.001$) from rest to the simple hand movement and again to the complex movement and the auditory tasks. The number of single-peak segments per second ($F2,72 = 13.40$, $p < 0.001$) and of GFP peaks/s ($F2,72 = 13.34$, $p < 0.001$) increased from rest to movement and

auditory conditions. The interaction diagnosis × condition was not significant (F8,29 = 1.18,n.s.). When only the motor tasks (simple vs complex) were compared, the condition effect remained (F4,33 = 2.76, $p < 0.05$). Univariate statistics comparing the simple and the complex motor task indicated effects for microstate duration (F1,36 = 5.1, $p < 0.03$), for the number of single-peak segments per second (F1,36 = 8.8, $p < 0.01$), and for the GFP peaks/s (F1,36 = 10.2, $p < 0.01$). Between the two auditory tasks, no differences were found (F4,33 = 0.84,n.s.).

Topography parameters

Repeated measures ANOVA indicated a main effect for diagnosis (F4,32 = 3.34, $p < 0.02$), consisting of a 10° counterclockwise shift of the axis connecting the EEG centroids in the GTS patients (F1,36 = 13.6, $p < 0.001$). This shift was stable through all conditions (diagnosis × condition interaction: F8,29 = 1.04,ns). A significant condition effect was found (F8,29 = 3.59, $p < 0.001$) consisting of a shift in the center of gravity of the centroids to the anterior in the simple motor and auditory tasks as compared with rest and the complex motor task (F2,72 = 10.4, $p < 0.001$). Also, the distance of the positive and the negative centroids was reduced in the active tasks (both motor and auditory) (F2,72 = 5.6, $p < 0.02$). Statistical analysis (contingency tabulation) of the observed frequencies for each field class in controls and in GTS patients indicated that not a single abnormal field type was responsible; instead, a diffuse increase of right-anterior/left-posterior oriented fields prevailed in the TGS group (for reasons of space, the data describing field distribution are not given). When the simple and complex motor tasks were compared, the effect for diagnosis, loading on the orientation of the axis connecting the centroids was of the same magnitude (F1,36 = 13.9, $p < 0.001$). There was also a significant condition effect (F4,33 = 5.3 $p < 0.001$): loading on the y-position of the centroids' center of gravity (F1,36 = 18.8, $P < 0001$). When motor and auditory tasks were compared (i.e., the resting condition was excluded), the effect for diagnosis (the axis shift) was found again; there was also an effect for condition (F12,25 = 3.17, $p < 0.01$) due to a shift in centroid y-position (univariate F-test: F3,108 = 6.3, $p < 0.001$) and the distance between the centroids (F3,108 = 2.93, $p < 0.05$). Comparison of the two auditory tasks gave no significant effects.

For the covariate (age), no effect was found. There was no overall trend in any parameter related to the time elapsed since the begin of the experiment (rank correlation test).

Discussion

The study presented herein evaluates the temporal and topographic characteristics of the EEG of 13 GTS patients and of 25 controls during various cognitive states. The EEGs were analyzed by adaptive segmentation of continuous EEG (Lehmann et al. 1987; Strik et al. 1993, 1995). Adaptive segmentation describes the temporal and topographic evolution of electric fields and thus examines the functioning of brain on a spatial and temporal axis. No difference was found in the temporal dynamics of the EEG in GTS patients and controls. This distinguishes GTS from, for example, depression, with decreased microstate duration and larger topographic variance (Strik et al. 1995), and also sets GTS apart from schizophrenia, with increased duration of brain electric microstates and reduced topographic variability (Stevens et al., in press; Koukkou et al. 1994). Microstate duration indicates how long the brain maintains the same field configuration. It allows to derive the rate of switches (per time unit) between distinct electric field configurations, which was approximately 7 Hz for both GTS patients and the controls. Also, the carrier frequency of the EEG (GFP peaks/s) was similar for both groups. The main difference lay in the topography of brain electric fields. The EEGs from GTS patients showed a constant twist of the prevailing centroid locations toward right anterior and left posterior. This was not due to focal hyperactivity over a singular brain site, but to a larger number of field types with a right-anterior to left-posterior orientation was noted. The broad distribution also renders the systematic contamination of GTS EEGs by an artifact unlikely. The apparent explanation is that in GTS patients different cortical areas are activated than in normal controls. Centroid topography does not allow to localize the cortical generators unambiguously, but the data align well with those of a HMPAO-(SPECT) study by George et al. (1992), who noted that in GTS right-frontal areas are more active at rest than in normal controls.

The abnormal EEG activity in GTS patients seems not to arise from abnormally facilitated motor circuits, because it is not similar to activity elicited by movements. When motor tasks were performed, the related EEG changes were clearly discernible and comprised alterations of microstate duration, carrier frequency, and centroid topography, but not of centroid axis orientation. As a consequence, the difference between GTS patients and controls did not resolve when movements were performed. In order to establish whether the motor tasks used elicited specific EEG changes as opposed to non-specific phenomena, auditory tasks were evaluated as well. These produced patterns of activation distinct both from rest and from motor activity, whereas right-frontal/left-posterior fields in GTS patients persisted. Previous EEG studies of GTS patients have been summarized by Hyde et al. (1994). Most described a diffuse slowing, which was not evident in the present set of data (Günther et al, in press). A few (e.g., Volkmar et al. 1984) found a parietal to central focus of abnormal activity, suggesting involvement of the (anterior) cingulate gyrus (Bonnet 1982). There are more studies on the psychophysiology of the related OCB disorder, reviewed by Shagass et al. (1984a, b) and by Towey et al. 1994. Current interpretations propose generally increased cortical activity, left frontal hyperactivity, or abnormally facilitated arousal to minimal or irrelevant stimulation (Beech et al. 1983). Insel (1992) discussed

functional brain imaging, morphologic studies, and neuroanatomy of OCB thoroughly and proposed disinhibition rather than primary hyperactivity of motor circuits, which comprise cortex, caudate nuclei, globus pallidus, and thalamus. The present data suggest a disturbance beyond or other than motor loops in GTS, because the voluntary activation of motor functions did not abolish the abnormal field distribution. On the other hand, the present study evaluated only self-paced movements. Involuntary movements in GTS patients may arise differently from these, e.g., they are not preceded by a Bereitschaftspotential (Obeso et al. 1981). In our previous report (Günther et al. 1996) reduced alpha attenuation during active tasks suggested impaired, rather than abnormally facilitated, cortical activation (granted that alpha attenuation reflects cortical activation). However, attenuation of alpha activity is a relative phenomenon, and pathologic acitvity going on at rest may reduce the amount of alpha attenuation observed during active tasks. Spectral power analysis and adaptive segmentation evaluate different aspects of the EEG. The former resolves the EEG into separate spectral bands, reflecting the activity of different layers of cortical neurons (Lopes da Silva 1977; Murthy and Fetz 1992), and it integrates local activity over time. Adaptive segmentation adds the perspective of temporal dynamics and studies the global patterns of electric activity generated at each point in time. It offers a measure of how the brain peruses different functional states, and how these states differ in topography. The interpretation of the data generated by each method depends heavily on the model of brain function assumed. Herein, we understand that patterns of cortical activity, which are large enough to be recorded with relatively few (21) scalp electrodes, arise from large cortico-striatal-thalamic networks, which temporarily synchronize numerous cortical neurons into coherent activity (Alexander et al. 1986; Lopes da Silva 1991; Steriade et al. 1991). Our study may be criticized for evaluating only the 2-15 Hz EEG bandwidth. Evaluation of the data with inclusion of the higher frequencies (2–35 Hz; data not shown) indicated that they do not contribute to variance explained by diagnoses and conditions. Other evidence that the lower frequencies contain much of the information related to cortical processing is offered by Merzenich et al. (1993). Reviewing the literature on temporal information processing in the cortex they concluded that many cortical fields show "best modulation" (working) frequencies in the range of 2–5 Hz, corresponding to the 200- to 500-ms time periods known from psychophysiology experiments involving higher cognitive tasks. Merzenich et al. (1993) proposed that information is "chunked" into 200- to 500-ms sequences when processed at higher cortical levels, and that these time periods are imposed by intrinsic cortical oscillations. Similarly, Buzsaki and Chrobak (1995) have compiled evidence that information, at least in some brain areas and for some cognitive functions, is handled by theta (3–7 Hz) modulation of (40 Hz) gamma activity.

Drawing on animal and human studies, Insel (1992) argued that OCB patients are possibly impaired in their ability to disregard internal cues. Interestingly, 70–80% of GTS patients report distinct sensory experiences immediately preceding the tics (Lang 1993). These observations suggest also that cortical circuits other than motor are involved in GTS. Pfurtscheller and Neuper (1992) have reported desynchronization of alpha activity before and during motor performance over primary and supplementary motor areas. Our data do not permit direct comparison, but the acceleration of the carrier frequency during active tasks may reflect activity-related synchronization with higher EEG frequencies. The decrease in microstate duration from rest to simple and again to complex movements indicates that during the tasks the brain peruses more functional states per time unit than at rest. Nashmi et al. (1994) evaluated regional shifts in EEG power by Laplacian operators and also noted differential activation in simple and complex motor tasks. The fact that this relationship was unimpaired in GTS patients suggests normal functional adaptability.

In summary, both hypotheses were confirmed: The topography of cortical activity is abnormal in GTS, and the underlying pathophysiology is not explained by abnormal activity of the type (normally) elicited by voluntary movements. Either there are other circuits involved, or the abnormal activity is related to the suppression of involuntary movements. The results combine well with spectral power analysis (Günther et al, in press) and SPECT data (Moriarty et al. 1995; Rubin et al. 1992), which have emphasized alterations in basal ganglia function. The alteration in large scale activity patterns reported herein are consistent with the assumption of basal ganglia dysfunction, because large-scale cortical phenomena are probably mediated by subcortical processes (Lopes da Silva 1991; Destexhe and Babloyantz 1991). Further studies, e.g., whether the EEG changes reported herein are state or trait, and how they change under pharmacotherapy, may shed more light on GTS pathobiology.

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References

Alexander GE, De Long MR, Strick PL (1986) Parallel organisation of functionally segregated circuits linking basal banglia and cortex. Annu Rev Neurosci 9:357–381

American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders (DSM-III-R), 3rd ed, revised. American Psychiatric Association, Washington, DC

Baxter L, Schwartz J, Maziotta J, Phelps ME, Pahl JJ, Buze BE, Fairbanks L (1988) Cerebral glucose metabolic rates in nondepressed patients with obsessive–compulsive disorder. Am J Psychiatry 145:1560–1563

Beech HR, Ciesielski KT, Gordon PK (1983) Further observations of evoked potential in obsessional patients. Br J Psychiatry 142: 605–609

Bonnet KA (1982) Neurobiological dissection of Tourette syndrome: a neurochemical focus on a human neuroanatomical model. In: Friedhoff AJ, Chase TN (eds) Gilles de la Tourette syndrome. Raven Press, New York, pp 77–82

Buzsaki G, Chrobak JJ (1995) Temporal structure in spatially organized neuronal ensembles: a role for interneuronal networks. Curr Opin Neurobiol 5:504–510

Destexhe A, Babloyantz A (1991) Deterministic chaos in a model of the thalamo-cortical system. In: Babloyantz A (ed) Self-organization, emerging properties and learning. Plenum Press, New York, pp 127–150

Drake ME Jr, Hietter SA, Padamadan H, Bogner JE, Andrews JM, Weate S (1992) Auditory evoked potentials in Gilles de la Tourette syndrome. Clin Electroencephalogr 23:19–23

Eapen V, Pauls DL, Robertson MM (1993) Evidence for autosomal transmission in Tourette's syndrome. United Kingdom cohort study. Br J Psychiatry 162:593–596

Erenberg G, Cruse RP, Rothner AD (1987) The natural history of Tourette's syndrome: a follow-up study. Ann Neurol 22:383–385

Gerorge MS, Trimble MR, Costa DC, Robertson MM, Ring HA, Ell PJ (1992) Elevated frontal blood flow in Gilles de la Tourette syndrome: a ^{99}Tcm-HMPAO SPECT study. Psychiatry Res 45:143–151

Gratton G, Coles M, Donchin E (1983) A new method for off-line removal of ocular artfact. Electroencephalogr Clin Neurophysiol 44:735–741

Günther W, Müller N, Trapp W, Haag C, Putz A, Straube A (1996) Quantitative EEG analysis during motor function and music preception in Tourette's syndrome. Eur Arch Psychiatry Clin Neurosci 246:197–202

Harcherik DF, Leckman JF, Detlor J, Cohen DJ (1984) A new instrument for clinical studies of Tourette's syndrome. J Am Acad Child Psychiatry 23:153–160

Hyde TM, Emsellem HA, Randolph C, Rickler KC, Weinberger DR (1994) Electroencephalographic abnormalities in monozygotic twins with Tourette's syndrome. Br J Psychiatry 164:811–817

IFSCEN (1974) A glossary of terms commonly used by clinical electroencephalographers. Electroencephalogr Clin Neurophysiol 37:538–548

Insel TR (1992) Toward a neuroanatomy of obsessive-compulsive disorder. Arch Gen Psychiatry 49:739–744

Koukkou M, Lehmann D, Strik WK, Merlo MC (1994) Maps of microstate of spontaneous EEG in never-treated acute schizophrenia. Brain Topogr 6:251–252

Krumholz A, Singer HS, Niedermeyer E, Burnite R, Harris K (1983) Electrophysiological studies in Tourette's syndrome. Ann Neurol 14:638–641

Lang AE (1993) Premonitory ("sensory") experiences. In: Kurlan R (ed) Handbook of Tourette's syndrome and related tic and behavioural disorders. Dekker, New York, pp 17–26

Leckman JF, Riddle MA, Hardin MT et al. (1989) The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Psychiatry 28:566–573

Leckman JF, Goodman WK, Anderson GM, Riddle MA, Chappell PB (1995) Cerebrospinal fluid biogenic amines in obsessive-compulsive disorder, Tourette's syndrome and healthy controls. Neuropsychopharmacology 12:73–86

Lehmann D, Ozaki H, Pal I (1987) EEG alpha map series: brain micro-states by space-oriented adaptive segmenation. Electroencephalogr Clin Neurophysiol 67:271–288

Lopes da Silva FH (1991) Neural mechanisms underlying brain waves: from neural membranes to networks. Electroencephalogr Clin Neurophysiol 79:81–89

Lopes da Silva FH, Storm van Leeuwen W (1977) The cortical source of the alpha rhythm. Neurosci Lett 6:237–241

Malison RT, McDougle CJ, van-Dyck CH, Scahill L, Baldwin RM, Seibl JP, Price LH, Leckmann JF, Innis RB (1995) 123beta-CIT SPECT imaging of striatal dopamine transporter binding in Tourette's disorder. Am J Psychiatry 152:1359–1361

Merzenich MM, Schreiner C, Jenkins W, Wang X (1993) Neural mechanism underlying temporal integration, segmentation and input sequence representation: some implications for the origin of learning disabilities. In: Tallal P, Galaburda AM, Llinas RR, Euler C von (eds) Temporal information processing in the nervous system: special reference to dyslexia and dysphasia. Ann NY Acad Sci 682:1–22

Moriarty J, Costa DC, Schmitz B, Trimble MR, Ell PJ, Robertson MM (1995) Brain perfusion abnormalities in Gilles de la Tourette's syndrome. Br J Psychiatry 167:249–254

Murthy VN, Fetz EE (1992) Coherent 25- to 30-Hz oscillations in the sensorimotor cortex of awake behaving monkeys. Proc Natl Acad Sci USA 89:5670–5674

Nashmi R, Mendonca AJ, MacKay WA (1994) EEG rhythms of the sensorimotor region during hand movements. Electroencephalgr Clin Neurophysiol 91:456–467

Obeso JA, Rothwell JC, Marsden CD (1981) Simple tics in Gilles de la Tourette's syndrome are not prefaced by a normal premovement EEG potential. J Neurol Neurosurg Psychiatry 44:735–738

Pauls DL, Towbin KE, Leckman JF, Zahner GEP, Cohen DJ (1986) Gilles de la Tourette syndrome and obsessive–compulsive disorder: evidence supporting an etiological relationship. Arch Gen Psychiatry 43:1180–1182

Peterson B, Riddle MA, Cohen DJ, Katz LD, Smith JC, Hardin MT, Leckman JF (1993) Reduced basal ganglia volumes in Tourette's syndrome using three-dimensional reconstruction techniques from magnetic resonance images. Neurology 43:941–949

Pfurtscheller G, Neuper C (1992) Simultaneous EEG 10-Hz desynchronization and 40-Hz synchronization during finger movements. NeuroReport 3:1057–1060

Riddle MA, Rasmusson AM, Woods SW, Hoffer PB (1992) SPECT imaging of cerebral blood flow in Tourette syndrome. Adv Neurol 58:207–211

Robertson MM, Trimble MR, Lees AJ (1988) The psychopathology of the Gilles de la Tourette syndrome. Br. J Psychiatry 152:383–390

Robertson MM, Yakeley JW (1993) Obsessive-compulsive disorder and self-injurious behavior. In: Kurlan R (ed) Handbook of Tourette's syndrome and related tic and behavioural disorders. Dekker, New York, pp 45–88

Rubin RT, Villanueva-Meyer J, Ananth J, Trajmar PG, Mena I (1992) Regional xenon 133 cerebral blood flow and cerebral technetium Tx 99m-HMPAO uptake in unmedicated patients with obsessive–compulsive disorder and matched normal control subjects: determination by high-resolution single-photon-emission computed tomography. Arch Gen Psychiatry 49:695–702

Shagass C, Roemer RA, Straumanis JJ, Josiassen RC (1984a) Distinctive somatosensory evoked potential featues in obsessive-compulsive disorder. Biol Psychiatry 19:1507–1524

Shagass C, Roemer RA, Straumanis JJ, Josiassen RC (1984b) Evoked potentials in obsessive–compulsive disorder. Adv Biol Psychiatry 15:69–75

Singer HS, Reiss AL, Brown JE et al. (1993) Volumetric MRI changes in basal ganglia of children with Tourette's syndrome. Neurology 43:950–956

Steriade M, Dossi C, Oakson G (1991) Fast oscillations (20–40 Hz) in thalamocortical systems and their potentiation by mesopontine cholinergic nuclei in the cat. Proc Natl Acad Sci USA 88:4396–4400

Stevens A, Lutzenberger W, Bartels M, Strik W, Lindner K. Increased duration and altered topography of EEG microstates during cognitive tasks in chronic schizophrenia. Psychiatry Res (in press)

Strik WK, Lehmann D (1993) Data-determined window size and space-oriented segmentation of spontaneous EEG map series. Electroencephalogr Clin Neurophysiol 87:169–174

Strik WK, Dierks T, Becker T (1995) Larger topographical variance and increased duration of brain electric microstates in depression. J Neural Transm (GenSect) 99:213–222

Swedo SE, Schapiro MB, Grady CL, Cheslow DL, Leonard HL, Kumar A, Friedland R, Rappoport SI, Pappoport JL (1989) Cerebral glucose metabolism in childhood-onset obsessive-compulsive disorder. Arch Gen Psychiatry 46:518–523

Towbin KE, Riddle MA (1993) Attention deficit hyperactivity disorder. In: Kurlan R (ed) Handbook of Tourette's syndrome and related tic and behavioural disorders. Dekker, New York, pp 89–110

Towey JP, Tenke CE, Bruder GE, Leite P, Friedman D, Liebowitz M, Hollander E (1994) Brain event-related potential correlates of overfocused attention in obsessive-compulsive disorder. Psychophysiol 31:535–543

Verma NP, Syrigou-Papavasiliou A, LeWitt PA (1986) Electroencephalographic findings in unmedicated, neurologically and intellectually intact Tourette syndrome patients. Electroencephalogr Clin Neurophysiol 564:12–20

Volkmar FR, Leckman JF, Detlor J et al. (1984) EEG abnormalities in Tourette's syndrome. J Am Acad Child Adolesc Psychiatry 23:352–353

Wackermann J, Lehmann D, Michel CM, Strik WK (1993) Adaptive segmentation of spontaneous EEG map series into spatially defined microstates. Int J Psychophysiol 14:269–283