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Event-related brain potentials show changed attentional mechanisms in Gilles de la Tourette Syndrome

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In many patients the Gilles de la Tourette Syndrome (TS) is associated with the childhood Attention Deficit Hyperactivity Disorder. To gain a general view of attentional processes in TS we recorded event-related brain potentials (ERPs) in 12 TS patients and in a matched control group. Four visual attention experiments with different levels of complexity were done (oddball task, pop-out experiment, figure extraction and figure conjunction task). The reaction times did not differ significantly between groups. The Tourette patients' event-related brain potentials showed an increased amplitude of the N2 component to targets in the simple oddball and pop-out experiments. While both groups had similar P3b latencies to targets in the figure extraction experiment, Tourette patients responded less accurately in the most complex figure conjunction task and had increased P3b latencies. This is interpreted as evidence for a stronger attentional effort of the Tourette patients to obtain behavioural results similar to control subjects in easy attentional tasks. Consequently, Tourette patients show a reduced performance in complex attentional tasks.

Keywords: Gilles de la Tourette Syndrome – Attention – Even-related brain potentials – Basal ganglia – Frontal lobes

INTRODUCTION

The Gilles de la Tourette Syndrome (TS) is a complex neuropsychiatric disorder which can be diagnosed in the presence of multiple fluctuating motor and vocal tics after the exclusion of other diseases (The Tourette Syndrome Classification Study Group, 1993; Singer and Walkup, 1991; Cohen *et al.*, 1988; Shapiro *et al.*, 1988; Robertson 1989; Cath *et al.*, 1992). Above chance, the Tourette Syndrome is associated with the Attention Deficit Hyperactivity Disorder (ADHD) (Knel and Comings, 1993; Comings and Comings, 1990) which is defined as the childhood combination of attentional deficits with hyperactivity (American Psychiatric Association, 1987).

Some studies have investigated different aspects of cognition in patients with the Tourette Syndrome (Georgiou *et al.*, 1995; Brookshire *et al.*, 1994; Lanser *et al.*, 1993; Burd *et al.*, 1992; Weate *et al.*, 1993; Van Woerkom *et al.*, 1994). Among the different cognitive processes, selective attention refers to the mechanism which is important for the distinction between relevant and irrelevant sensory information. Although the clinical association between TS and ADHD is well known, only a few studies have investigated attentional processes in the TS (e.g., Weate *et al.*, 1993; Van Woerkom *et al.*, 1994). Their results have important implications for the understanding of attentional deficits in the TS, but the studies were limited because they only focussed upon restricted aspects. To gain a more general view of attentional processes in the TS we compared easy and complex tasks within the same group of Tourette patients. Therefore, we recorded event-related brain potentials (ERPs) in a series of four different cognitive experiments. ERPs are tiny voltage fluctuations which can be recorded non-invasively from the intact human scalp. They are especially useful for the investigation of cognitive processes as they permit, in addition to the traditional behavioural measures, on-line recording of cerebral activity. ERPs may be described in terms of a series of positive and negative peaks or components that occur at characteristic times after the presentation of stimulus material. While some early components vary as a function of physical stimulus parameters, other components of longer latencies only appear in conjunction with specific perceptual or cognitive processes. Two of the most widely studied long latency components are the 'N2' and the 'P3b' (Hillyard and Kutas, 1983; Rugg *et al.*, 1993). Both are related to the processing of signals that belong to an attended source of input and /or provide task-relevant information (e.g., Rugg *et al.*, 1993;

Heinze *et al.*, 1992; Fitzgerald and Picton, 1983; Näätänen and Picton, 1986).

Our experiments comprised four different paradigms which have been used, in part, to characterize deficits of other patient groups (e.g. Heinze *et al.*, 1992) by means of N2 and P3b ERP-analysis.

METHODS

Subjects

Sixteen adult native German speaking subjects were diagnosed to fulfill the DSM III-R criteria for Gilles de la Tourette syndrome (American Psychiatric Association, 1987). Of these, four subjects had to be excluded from the ERP recording sessions because of excessive blink artifacts or excessive tics or because they were unable to maintain eye fixation as described below. The remaining 12 subjects were all male and had an age of 18–62 years (mean 32.9 years). Eleven subjects were right handed and one was left handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). Five of the subjects were tested during medical treatment with pimozide (2–8 mg/day, mean 5.2 mg/day). None of the patients was free of symptoms. All patients fulfilled the DSM III-R criteria for Obsessive Compulsive Disorders and three patients additionally fulfilled the criteria for Attention Deficit Hyperactivity Disorder. Twelve healthy control subjects (CG) who were recruited from the hospital staff and from patients who had suffered from a peripheral trauma but not a head trauma were matched with respect to age, sex, handedness and education.

General procedure

The experiments discussed herein were part of a larger study examining different neuropsychological aspects of Gilles de la Tourette Syndrome. Subjects were seated in a comfortable chair with a headrest and were instructed to relax. For each experiment, training runs were administered to ensure that subjects understood the tasks. Before each experimental run, they were reminded to minimize blinking and ocular movements as much as possible and during the runs, subjects were required to fixate a cross in the center of the screen. Whenever eye-movements were detected through monitoring of the electro-oculogram (see below), the subjects were reprimanded. The subjects were instructed to respond as quickly and as accurately as possible to all target stimuli by pressing a button held in the dominant hand. All stimuli were presented white on a dark gray background of the video screen which had a fixation cross in the center.

Experimental designs

Experiment 1: oddball task. This so called 'oddball experiment' has been used extensively to study cognitive processes (e.g. Rugg *et al.*, 1993; Picton, 1992; Segalowitz and Barnes, 1993) and is one of the simplest selective attention tasks. It comprises the easy discrimination between targets and non-targets which are serially presented one after another. Some resulting ERP components can be used to measure the 'attentional effort' required to perform the categorization (Fitzgerald and Picton, 1983; Näätänen and Picton, 1986).

Circles and crosses which subtended 0.5 degrees of visual angle were serially presented at the position of the fixation cross. Figure 1 shows the stimuli of this and the subsequent experiments. The duration of stimulus presentation was 100 ms, the inter-stimulus interval varied randomly between 900 and 1700 ms (rectangular distribution). The task was to indicate the presence of a circle (probability $p = 0.25$) on the screen by pressing a button. The number of runs was calculated to yield approximately 100 targets after artifact rejection.

Experiment 2: pop-out experiment. The 'pop-out experiment' comprises two different simple visual elements (so called target and non-target 'pop-out' stimuli, with one of them requiring buttonpresses) which are interspersed within a number of distractors. The stimuli containing pop-out features are randomly intermixed with non-target stimuli consisting only of distractors. Upon presentation, both types of pop-out stimuli are thought to be automatically perceived as different from the distractors. Thus, they allow to investigate the automatic processing of simple visual features with and without overt responses (Hillyard *et al.*, 1990; Luck and Hillyard, 1988).

Each stimulus display consisted of eight bars, distributed randomly across the monitor within an imaginary rectangle 14° wide and 10° high. There were three types of bars: vertical solid bars, vertical open bars and horizontal open bars. The vertical (horizontal) bars subtended a visual angle of 0.3° width (height) and 1.6° height (width). There were three types of stimulus arrays: standard arrays with eight solid vertical bars, non-target pop-out arrays with seven vertical solid bars and one vertical open bar, and target pop–out arrays with seven vertical solid bars and one horizontal open bar (for examples, see Fig. 1). Standards ($p = 0.5$), non-target pop-outs ($p = 0.25$) and target pop-outs ($p = 0.25$) were presented in random order with a stimulus duration of 750 ms and an interstimulus interval randomly between 1350 and 1650 ms. The subjects had to respond to the target pop-outs containing the horizontal open bar.

Experiments 3 and 4: figure extraction and figure conjunction. These experiments addressed the mechanisms

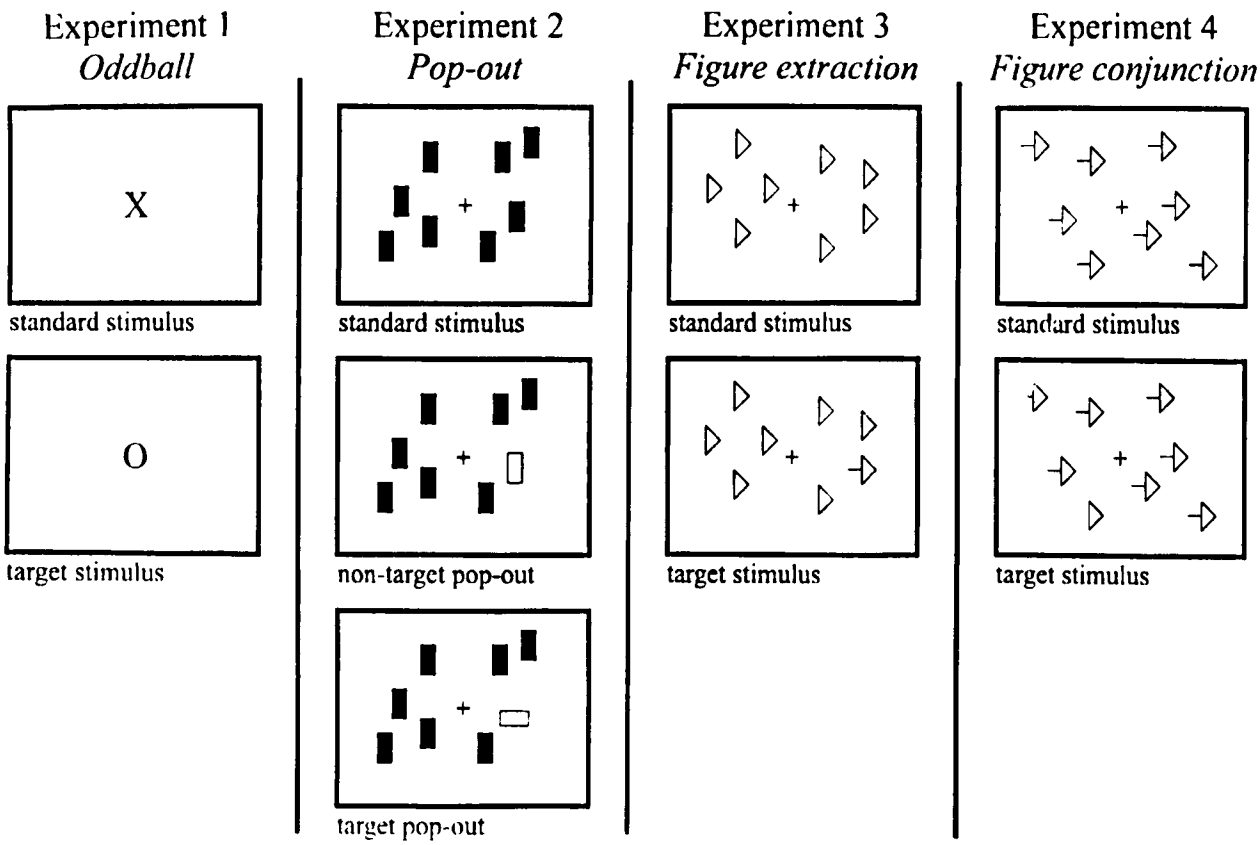

FIG. 1. Stimuli (examples) which were used in the four experiments.

of 'figure extraction' (3) and 'figure conjunction' (4). The tasks require the detection of deviant stimuli which are intermixed with a number of distractor items. While the figure extraction task comprises easy-to-detect targets, which allow the subjects to scan all presented items at once, the targets of the figure conjunction task are difficult to detect and require the serial, one by one scanning of all presented items. In contrast to the figure extraction task the figure conjunction task is viewed as a capacity limited process. Thus, a reduced processing capacity would show in changed ERPs in the figure conjunction condition whereas additional deficits in figure extraction processes would be reflected in changed ERPs of experiment 3 (e.g. Kutas *et al.*, 1977; Luck and Hillyard, 1990; McCarthy and Donchin, 1980).

The stimuli consisted of an array of eight items placed at random locations on the monitor within an imaginary rectangle 8.2° of visual angle wide and 6.5° high. There were two types of items: a triangle with one vertical left side and two oblique sides pointing to the right, and the same triangle with a horizontal line extending leftward from the vertical line as an additional feature. These two types of items were combined in two conditions. In the figure extraction condition, the triangle with the additional line was the target, while the plain triangle was the distractor. In the figure conjunction condition, the plain triangle served as target and the triangle with the line as distractor (see Fig. 1 for examples). In both conditions, half of the stimulus arrays contained a target item. The positions of the target and distractor items were randomized from stimulus to stimulus. The stimulus duration was 1.5 s, and the interstimulus interval varied randomly between 3 and 3.5 s. Both conditions were presented in separate runs with a break of 10 min between the two runs. Each run consisted of five blocks with 40 stimuli in each block. Half of the patients and controls started with the figure extraction condition, the other half with the figure conjunction condition.

EEG recording

The EEG was recorded from 19 electrodes of the International 10/20 system (Jasper 1958) referenced to an electrode located on the right mastoid. Horizontal eye movements were monitored with electrodes located on the outer ocular canthi which were referenced to one another and vertical eye movements were detected through an electrode located below the right eye which was referenced to the electrode on the right outer ocular canthus. All channels were amplified using a 10 s time

constant and processed with a bandpass filter between 0.01 and 100 Hz (half amplitude low and high frequency cut-offs), digitized at a rate of 256 Hz and stored on a harddisk.

Data analysis

After artifact rejection for exessive eye movements or amplifier blocking the ERPs were separately averaged offline for correctly detected targets and rejections of non-targets. Difference waves were calculated by subtracting the ERPs to standard stimuli from the ERPs to target stimuli. Grand-average waveforms resulted from separately collapsing the waveforms of all patients and all control subjects. The ERPs were assessed at frontal (F3, F4), central (C3, C4), parietal (P3, P4), temporal (T3, T4), temporo-occipital (T5, T6, O1, O2) and midline (FZ, CZ and PZ) 'scalp sites'. The amplitudes were assessed as mean voltages and were calculated by integrating the ERP-amplitude at each digitized timepoint over a given 'time range'. This 'time range' was centered upon the ERP components peak latency as measured in the grand-average waveform because the latencies of different ERP-components are known to vary with respect to scalp location. At frontal, central and parietal 'scalp sites' the latencies of the P2, N2 and P3b components subtended 180–270 ms, 280–340 ms and 350–650 ms post stimulus, respectively. The ERP latencies were assessed as peak latencies in case of the P1, N1, P2 and N2 components. Because the P3b component has a longer duration and, hence, a broader, less sharp peak, its latency was defined as the time required to reach 50% of its mean amplitude over the measurement window. Behavioural performance was quantified by measuring reaction time (RT) and calculating %hit scores for detection of targets.

All ERP and behavioural measures were evaluated with repeated measures analyses of variance (ANOVA). The factors for the ERP evaluation were *group* (Tourette patients vs control subjects) as between subjects factor and *stimulus category* (targets vs non-targets), *hemisphere of recording* (left vs right) and *electrode* site (left vs right) as within subject factors, excluding the factor *hemisphere of recording* for the midline electrodes. *Post hoc*, a Bonferroni-test was done to compare the three conditions of the *stimulus category* factor in the popout experiment with each other. A second ANOVA was done within the group of Tourette patients to account for possibile influences of medical treatment. Control subjects were excluded from this analysis and the factor *group* was replaced by the factor *treatment* (no medical treatement vs treatment) as between subjects factor.

Behavioural measures were analysed with the factor *group*.

All analyses were adjusted for nonsphericity with the Greenhouse–Geisser epsilon coefficient (Jennings and Wood, 1976). Because there were no significant findings for the factors *hemisphere of recording* and *electrode site* only waveforms from the midline 'scalp sites' will be presented at those sites where the experimental effects were maximal (Fz, Cz, Pz).

RESULTS

Experiment 1

Behavioural effects

Reaction times and percentage of correct answers of this and the subsequent experiments are given in Table I. For this experiment, reaction times and hit rates did not differ significantly between Tourette patients and control group.

ERP effects

Group averages for patients and control subjects are shown in Fig. 2. For the purpose of greater clarity only ERPs to targets are presented as there were no significant findings for non-targets. After the initial negative N1 and positive P2 deflections there is a fronto-centrally located negative N2 component which can be seen in the 'time range' from 280 to 330 ms and which is followed by a predominantly parietally positive P3b component between 360 and 700 ms. The N2 and P3b did not differ with respect to latency between patients and controls or

TABLE I. Response characteristics of the Tourette patients and control subjects in the four different experiments. Bold characters: significant differences between groups ($n < 0.01$)

Experiment	Tourette patients Reaction time (ms) / hit rate (%)	Control group Reaction time (ms) / hit rate (%)
Oddball	409 ± 48 / 99 ± 2	399 ± 38 / 99 ± 3
Pop-out	525 ± 63 / 97 ± 3	533 ± 61 / 98 ± 2
Fig. extraction	690 ± 75 / 88 ± 20	707 ± 106 / 87 ± 10
Fig. conjunction	847 ± 53 / **52 ± 13**	855 ± 61 / **65 ± 13**

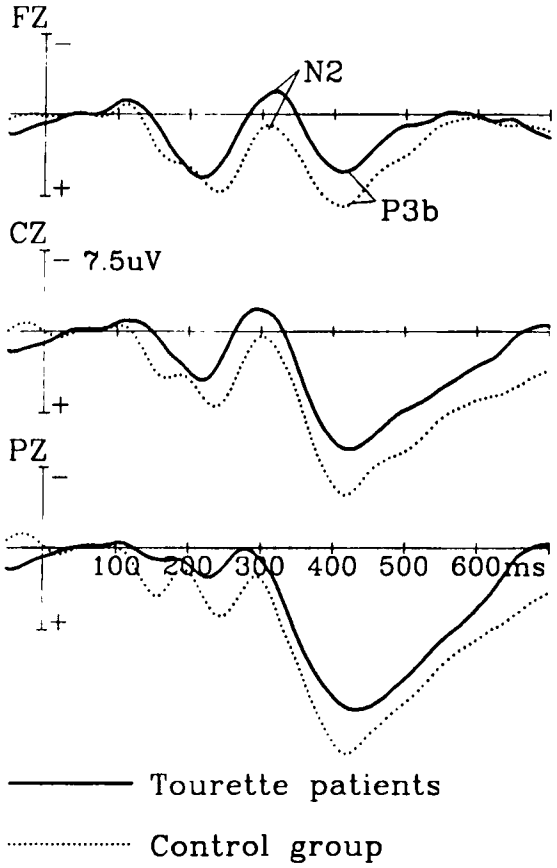

FIG. 2. Experiment 1, *Oddball*: grand average ($n=12$) ERP waveforms to targets at midline 'scalp sites'. At Fz and Cz Tourette patients (solid line) show a larger N2 amplitude compared to the control subjects (dotted line) between 280 and 330 ms post stimulus.

targets and non-targets. Both components were significantly larger for targets than for non-targets ($p < 0.001$, $p < 0.001$, respectively). Whereas the N2 component to targets was significantly larger for the Tourette patients, the P3b was larger in the control group as indexed by the interaction of the factors *stimulus category and group* ($p < 0.03$, $p < 0.01$, respectively).

Discussion

The enhanced N2 and P3b components to target stimuli replicate the results of earlier studies (e.g. Rugg *et al.* 1993; Fitzgerald and Picton, 1983). There were no significant differences between groups for the frequent non-targets, only for the infrequent targets. This indicates that in this simple cognitive task the processing of the frequent stimuli does not differ between groups. Rather, only the processing of the infrequent target stimuli is affected. While the latency of the N2 correlates with the time taken to categorize the evoking stimulus, the N2 amplitude has been taken as measure for the 'attentional effort' required to perform the categorization (Fitzgerald and Picton, 1983; Nätänen and Picton, 1986). However, such an interpretatin of the N2 needs further experimental support as there have not been any studies which directly manipulated effort and showed changes in the N2. Nonetheless, according to the above interpretation of the N2, there is no significant difference between groups to categorize target stimuli as indexed by the similar latency of the N2. Rather, the Tourette patients have to use a stronger 'attentional effort' to detect target stimuli than controls, but this stronger attentional effort resulted in similar reaction times and hit rates. These results of the N2 parallel the findings of Rugg *et al.* (1988), who found a larger N2 to target stimuli in head-injured patients. The functional significance of the P3b component is less certain. It is generally agreed that, like the latency of the N2, the peak latency of the P3b is influenced by the time required to categorize or 'evaluate' the evoking stimulus. Paralleling the results of the N2, there were no significant latency differences for the P3b components between groups. There is, however, no consensus over the functional significance of variations in P3b amplitude (Verleger, 1988). Thus, an interpretation of the P3b amplitude reduction to targets in the Tourette group remains difficult.

Experiment 2

Behavioural effects

Reaction times and hit rate did not differ significantly between Tourette patients and control group (Table 1).

ERP effects

The group averages for patients and controls are shown in Fig. 3. Concerning the latencies and amplitudes of the N1 and P2 components, there were no significant findings for the factors *group* or *stimulus category*. The peak latency of the N2 and the overall N2 amplitude did not differ between groups but there was a significant amplitude difference between the three different *stimulus category* conditons ($p < 0.01$) at the frontal and central electrodes. The Bonferroni-test indicated that this effect was due to a larger N2 amplitude for pop-out targets and pop-out non-targets as compared to standards. At the frontal electrodes, Tourette patients showed a significantly larger N2 amplitude for the pop-out targets as compared to controls (interaction of *group* and *stimulus category*, $p < 0.01$; significant Bonferroni–tests for between group comparisons of pop-out targets vs standards ($p < 0.05$) and pop-out targets vs pop-out non-targets ($p < 0.05$)). In both groups, the P3b component was largest at parietal sites and was of

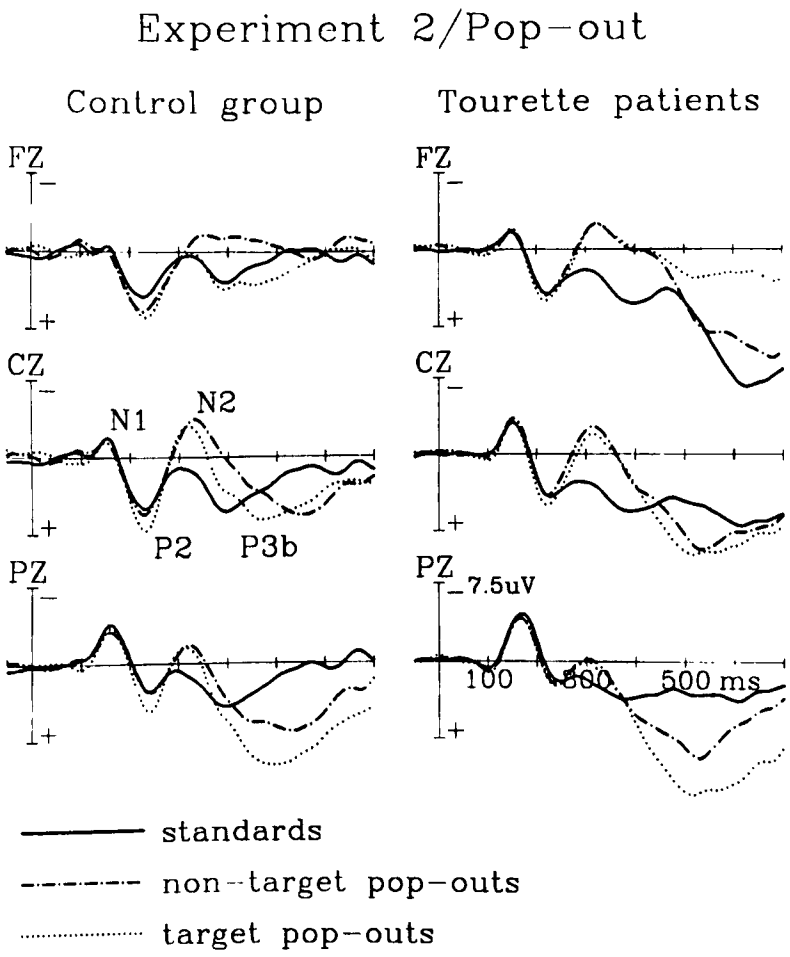

FIG. 3. Experiment 2, *Pop-out*: grand average waveforms to target pop-outs (dotted line), non-target pop-outs (dotdashed line) and standards (solid line) at midline 'scalp sites'. As in experiment 1 there is an increased frontal N2 amplitude to target pop-outs in the Tourette patient group.

maximal amplitude for the target pop-out stimuli while it was smallest for the standards. There were no significant P3b differences between groups.

Discussion

The larger N2 amplitude to pop-out targets and pop-out non-targets has also been observed in other experiments (Heinze *et al.*, 1992; Hillyard *et al.*, 1990; Luck and Hillyard, 1988). As in experiment 1 there were no significant differences between groups for the standard stimuli. Additionally, there were no significant ERP differences for the non-target popout stimuli between groups. Although the subjects did not have to respond to the non-target popout stimuli these are thought to automatically capture attention and be analyzed to some extent (Heinze *et al.* 1992). Thus, the ERP results of this experiment are evidence for an unchanged automatic analysis of simple stimulus features in patients with the TS. The pop-out targets had an increased N2 amplitude in the Tourette group. As in experiment 1, this can be taken as evidence for a stronger 'attentional effort' of the Tourette Patients to perform this simple cognitive task resulting in similar reaction times and hit rates as seen in the control group.

Experiments 3 and 4

Behavioural effects

Whereas in the figure extraction condition reaction times and hit rates did not differ between groups, Tourette patients hit rates were significantly lower in the figure conjunction condition ($p < 0.01$) with reaction times that also did not differ significantly between groups Table 1).

ERP effects

Figure 4 shows the ERP grand average waveforms to both experiments at the parietal 'scalp site' where the

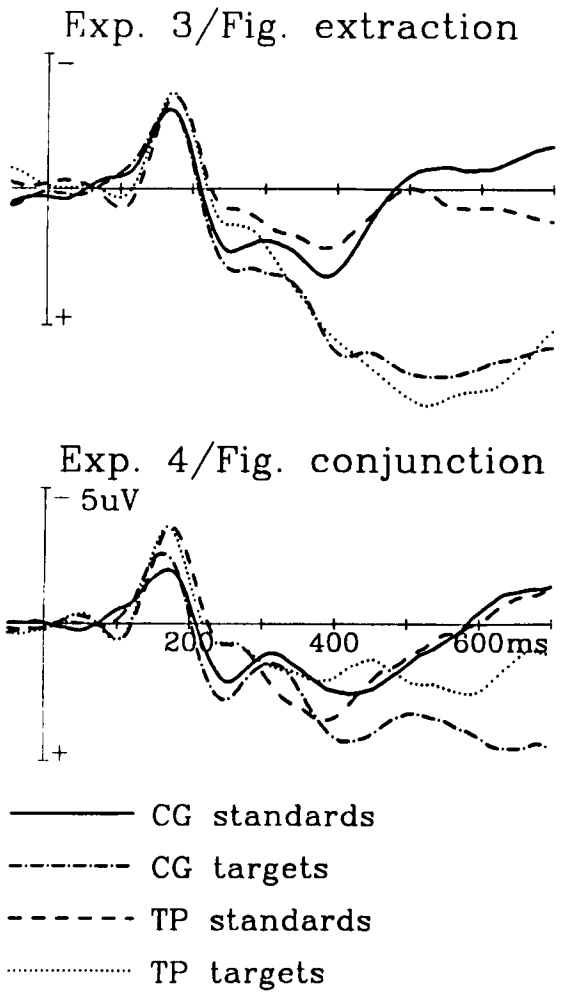

FIG. 4. Grand average ERPs to standards and targets for experiment 3 *figure extraction* (top) and experiment 4 *figure conjunction* (bottom) at the electrode Pz. TP—Tourette patients; CG—control group.

experimental effect was maximal and where the latencies were measured. Target stimuli elicited a large P3b component between 350 and 700 ms post stimulus (significant main effect of *stimulus category*, $p < 0.001$ for both experiments). Earlier ERP components did not differ significantly between groups or for the *stimulus category* factor. Different from the results of others (Heinze *et al.*, 1992; Luck and Hillyard, 1990) both groups did not produce large N2 components. The mean P3b latencies of the difference waves did not differ significantly between groups in the figure extraction condition. In contrast, P3b latencies were significantly longer for the Tourette patients than for the control group in the figure conjunction condition (figure extraction TP 521 ms ± 30 ms, CG 530 ms ± 25 ms; n.s.; figure conjunction TP 618 ms ± 27 ms, CG 565 ms ± 25 ms, $p < 0.001$).

Discussion

The results are similar to those obtained by Luck and Hillyard, (1990) and Heinze *et al.*, (1992) with longer P3b latencies in the figure conjunction condition as in the figure extraction task. In accordance with these findings, others have interpreted the P3b latency as a function of stimulus recognition processes and decision confidence (Kutas *et al.*, 1977; McCarthy and Donchin, 1980) implicating longer recognition processes and a lower decision confidence for the figure conjunction task. This was also reflected in reaction times and response rates which were worse in the figure conjunction task. Response characteristics and ERPs show no differences between Tourette patients and the control group for the figure extraction task. Thus, this is evidence for an undisturbed figure extraction process within the Tourette group. In contrast, the TP have impaired figure conjunction processes as indexed in longer P3b latency in the conjunction task. Thus, as such a figure conjunction process is viewed as a capacity limited process (Heinze *et al.*, 1992; Luck and Hillyard, 1990), this experiment provides evidence for a reduced processing capacity in Tourette Syndrome.

Effects of medical treatment

There were no significant differences between the treated and the untreated group of Tourette patients with respect to behavioural performance or ERP–analysis.

Intersubject variability

An important issue for the interpretation of the above experimental effects is intersubject variability: can the observed pattern be seen in the majority of patients, or are the effects in the grand average the composite of diverse patterns in different patients? Another related question is whether the control and patient groups have comparable intra-group variabilities. Figure 5 shows the grand average ERP waveforms to targets and the standard error of mean for all experiments at the electrode Pz. The variability within control and patient groups is comparable.

GENERAL DISCUSSION

Tourette patients were able to perform simple attentional tasks with the same speed and accuracy as control subjects and performed only worse in the most difficult figure conjunction experiment. Nonetheless, in the sim-

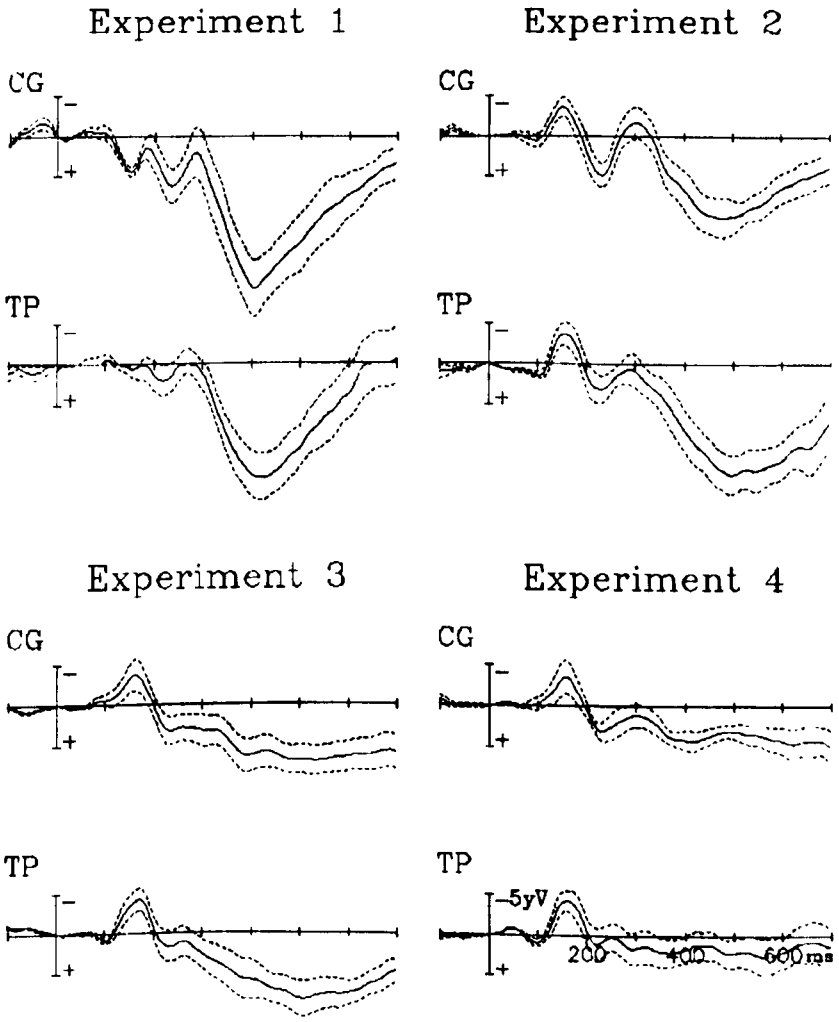

FIG. 5. Grand-average ERPs to targets (solid line) plus and minus standard error of mean (dashed lines) at the 'scalp site' Pz. The four experiments for Tourette patients and the control group are shown. TP—Tourette patients CG—control group.

ple experiments, the TP produced an increased N2 ERP component to targets, which has been taken as evidence for a stronger attentional effort to detect the targets(Fitzgerald and Picton, 1983; Näätänen and Picton, 1986). Our results are in line with such an interpretation, because the TP had an increased P3b latency to targets in the figure conjunction experiment which is viewed to test capacity limited figure integration processes (Heinze *et al.*, 1992; Luck and Hillyard, 1990) and they also showed a decreased behavioural performance in this experiment. The feature extraction mechanism was shown not to be changed in patients with Tourette syndrome. Thus, in summary there is evidence that Tourette patients have to use a stronger 'attentional effort' to obtain similar results in simple cognitive tasks than control subjects, and consequently show a reduced performance in more difficult, capacity limited processes as the figure conjunction task.

It is an important finding that the early P1 and N1 ERP components were not changed in the Tourette group in any of the experiments. These early components have been attributed to primary and secondary steps of visual information processing rather than to distinctive cognitive processes (Mangun *et al.*, 1993; Hillyard, 1993; Johannes *et al.*, 1995). Thus, these unchanged ERP components indicate that early processing of visual information is intact in Tourette patients. Hence, changed attentional processes cannot be attributed to impaired perceptual functions in TS. Therefore, it appears that the abnormality of the attention-binding process cannot be due to problems of visual perception, but rather has to act at later stages of cognitive processing. This fits well with the data of others who discussed a deficit of the frontal executive functions in TS (e.g, Bornstein, 1991; Stoetterer *et al.*, 1992). According to Duncan (1986), executive functions subsume goal-directed and future-

oriented behaviours and include planning, inhibition of inappropriate responses, organized search and working memory. These functions were partially required under the experimental conditions of this study. Thus, in this context our findings of an increased frontal N2-amplitude and partially increased P3b–latency might indicate deficits of frontal executive functions in TS.

One could argue that our findings of altered cognitive functions in TS might be due to the neuroleptic treatment of five of the 12 patients. We consider this unlikely because the comparison between medicated and unmedicated patients did not show any significant results. Although this comparison is restricted because the two groups consisted only of five and seven patients, our findings are supported by Bornstein and Yang (1991), who also did not find differences in the cognitive abilities between medicated and unmedicated TP.

Our results are in accordance with the outcomes of other behavioural experiments (Brookshire *et al.*, 1994) which also show deficits in complex cognitive processes in TS. To our knowledge, there is only one other comparable experiment examining attentional processes in Gilles de la Tourette syndrome by means of the ERP technique. In this experiment, van Woerkom et al. (1994) recorded auditory ERPs in one active and one passive auditory oddball paradigm in TP and control subjects. From an increase in negativity to standard stimuli in the passive condition compared to the active condition, the authors hypothesized TP to have an altered processing of background stimuli. Although the physical aspects of their stimuli were different from this experiment (auditory vs visual modality), our data clearly do not allow such an interpretation as we did not find any ERP differences between groups for the standard stimuli. Unfortunately, van Woerkom *et al.* (1994) do not give any data for their target stimuli. Consequently, it is difficult to define the experimental correlate of their 'background stimuli', as these can only be defined and analyzed depending upon the target stimuli. To further test our hypothesis and to compare our results to van Woerkom's data, we are currently investigating TP with a modified auditory oddball task (Rugg *et al.*, 1993) and with a dual task approach (Wickens *et al.*, 1983) as have been used elsewhere.

Our findings of an altered N2 component were restricted to the frontal and central brain regions. It is intriguing to speculate that these findings can be related to other morphological and neurochemical abnormalities of the basal ganglia and forebrain as have been demonstrated by others (Bornstein, 1991; Gedye, 1991; Braun *et al.*, 1993; George *et al.*, 1992; Sieg *et al.*, 1993; Peterson *et al.*, 1993; Singer *et al.*, 1993) supporting a frontal lobe dysfunction in Tourette Syndrome.

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