

PAPER

Subthalamic nucleus stimulation induces deficits in decoding emotional facial expressions in Parkinson's disease

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Background: Bilateral subthalamic nucleus (STN) stimulation is recognised as a treatment for parkinsonian patients with severe levodopa related motor complications. Although adverse effects are infrequent, some behavioural disturbances have been reported.

Objective: To investigate the consequences of STN stimulation on emotional information processing in Parkinson's disease by assessing the performance of an emotional facial expression (EFE) decoding task in a group of patients before and after surgery.

Methods: 12 non-demented patients with Parkinson's disease were studied. They were assessed one month before surgery and three months after. Their ability to decode EFEs was assessed using a standardised quantitative task. Overall cognitive function, executive function, visuospatial perception, depression, and anxiety were also measured. Twelve healthy controls were matched for age, sex, and duration of education.

Results: Before surgery, the patients showed no impairment in EFE decoding compared with the controls. Their overall cognitive status was preserved but they had a moderate dysexecutive syndrome. Three months after surgery, they had significant impairment of EFE decoding. This was not related to their overall cognitive status or to depression/anxiety scores. Visuospatial perception was not impaired. There was no change in the extent of the dysexecutive syndrome except for a reduction in phonemic word fluency.

Conclusions: Bilateral STN stimulation disturbs negative emotional information processing in Parkinson's disease. The impairment appears specific and unrelated to certain secondary variables. This behavioural complication of STN may have implications for the patient's social life.

With recent advances in stereotactic surgery and improved knowledge of the basal ganglia circuits,^{1–3} bilateral subthalamic nucleus (STN) stimulation is now recognised as a treatment of choice for parkinsonian patients with severe levodopa related motor complications. The technique has positive effects on all parkinsonian symptoms,⁴ its morbidity appears to be low,² and its efficacy has been shown to be stable.^{5–6} However, certain adverse effects have been reported, including visual hallucinations, the reappearance of previous psychiatric disorders, hypophonia, and dysarthria.^{6–9}

Although the aim of functional surgery in Parkinson's disease is to provide relief from motor symptoms, the treatment also produces certain non-motor effects. Of these, the consequences on cognitive function have been most thoroughly investigated. Despite some discrepancies between the various studies, it appears that cognitive function is indeed slightly affected by chronic bilateral STN stimulation (for a review, see Fields and Troster, 2000¹⁰). The most frequently reported adverse effect is reduced word fluency. An improvement in information processing speed is also often reported.¹¹ However, the risk of global cognitive degradation is not entirely absent—some cases have been reported, particularly among the oldest patients.¹²

Behavioural abnormalities following surgery have also been described. Trépanier *et al* reported behavioural changes of a frontal nature in patients with Parkinson's disease following bilateral globus pallidus interna or STN stimulation.^{12–13} Furthermore, Bejjani *et al* reported a quite remarkable case: stimulation delivered through a contact positioned in the left STN improved the Parkinson's disease symptoms, whereas stimulation through a second contact positioned in the substantia nigra pars reticulata provoked (in the space of a few minutes) symptoms of major depression, in a patient

with no known antecedents.¹⁴ Although Houeto *et al* reported a low rate of behavioural disturbance (4/23) within the two months following surgery,⁸ these investigators underlined the need to screen parkinsonian candidates thoroughly before functional surgery, and recommended avoiding electrode implantation in patients with a history of active depression. In their recent retrospective study,⁹ they also describe certain cases in which bilateral STN stimulation leads to the development of personality disorders or worsening of previously existing psychiatric disorders. We have also reported the emergence of behavioural disturbances (such as apathy, dysthymia, or compulsive disorders) in three of nine patients with Parkinson's disease being treated with bilateral STN stimulation.¹⁵

Overall, these results thus suggest that chronic bilateral STN stimulation can disturb the functioning of the limbic baso-thalamo-cortical functional loop,¹⁶ which is involved in emotional information processing, motivation, and social behaviour.^{17–19}

To date, the disturbances in emotional and social behaviour resulting from functional surgery in Parkinson's disease have only been assessed empirically—that is, either reported through clinical observations or qualitatively assessed on clinical scales. Consequently, our aim in the present study was to investigate the consequences of chronic bilateral STN stimulation for emotion processing, by assessing the

Abbreviations: AC, anterior commissure; AMDP-AT, Association of Methodology and Documentation in Psychiatry-anxiety; DRS, dementia rating scale; EFE, emotional facial expression; MADRS, Montgomery and Asberg dementia rating scale; MMSE, mini-mental state examination; PC, posterior commissure; STN, subthalamic nucleus; UPDRS, unified Parkinson's disease rating scale; WAIS-R, Wechsler adult intelligence scale, revised

Table 1 Demographical and cognitive characteristics of the participating groups

	PD patients	Healthy controls
Number	12	12
Age (years)	57.5 (6.5)	58.7 (8.5)
Education duration (years)	12 (3.3)	12 (2.5)
MMSE score	28.8 (0.9)	29.7 (0.5)
Mattis DRS score	137.2 (4.3)	143.3 (1.2)

Values are mean (SD).
DRS, dementia rating scale; MMSE, mini-mental state examination; PD, Parkinson's disease.

performance of an emotional facial expression (EFE) decoding task in a group of patients before and after surgery. This is a commonly used procedure for evaluating emotional information processing ability. Impairment of this task has been reported following lesions in certain structures participating in the limbic baso-thalamo-cortical circuit, namely the amygdala¹⁷ and the orbitofrontal cortex.¹⁸⁻¹⁹ Moreover, several neuroimaging studies in healthy subjects have shown specific amygdala responses to presentations of everyday, or even masked, fear expressions.²⁰⁻²¹ Deterioration has also been seen as a result of basal ganglia dysfunction related to neurodegenerative disorders.²²⁻²³ We reasoned that if bilateral chronic STN stimulation does indeed have an effect on limbic baso-thalamo-cortical function, this could lead to changes in performance of an EFE decoding task.

METHODS

Population

A consecutive series of 12 non-demented patients with Parkinson's disease (five men and seven women) was selected for electrode implantation in the STN. The mean (SD) duration of the disease was 13 (2.5) years. All presented with clinical features (notably severe motor fluctuations) that met the criteria of the United Kingdom Parkinson's disease brain bank for Parkinson's disease diagnosis.²⁴ In the off-drug state before surgery, the median Hoehn and Yahr score²⁵ was 4 (range 3 to 5) and the median unified Parkinson's disease rating scale (UPDRS) III score²⁶ was 50 (40 to 72). The mean preoperative levodopa equivalent dose was 1472 (510) mg/day, range 970 to 2325.

Patients were assessed one month before and three months after surgery, while receiving their usual levodopa treatment. Both assessments were conducted when the patients were in their "best on" state. The postsurgery examination took place with the stimulator turned on.

A group of 12 healthy control subjects (five men and seven women) also participated in the study. Controls were chosen to match the patient group as closely as possible for sex, age, and education. They had no history of neurological or psychiatric illness, and their family histories were negative for Parkinson's disease or parkinsonian symptoms.

All participants were required to show a mini-mental state examination (MMSE) score higher than 27 and a Mattis dementia rating scale (DRS) score higher than 130.

Characteristics of each group are shown in table 1.

Tasks

Emotional facial expression decoding

We used two series of EFEs constructed by Hess and Blairy.^{27*} Specifically, these investigators selected facial expressions

*More information on these stimuli is available in papers by Hess *et al* and Blairy *et al*.³¹⁻³² Full technical details of the procedure for creating stimuli are available from Ursula Hess.

corresponding to happiness, anger, sadness, disgust, and fear from a series of standardised EFEs produced by two male and two female white actors (JACFEE²⁸). Based on the neutral face (0% emotional intensity) and the full blown EFE (100% emotional intensity) from the same actor, and using the Morph 1.0 computer program, the authors constructed a series of intermediate expressions differing in emotional intensity by steps of 10%. In the present study, a matrix of 2 (intensity: 30% and 70%) × 3 (emotions: anger, disgust, and sadness) × 2 (sex: one male and one female actor) stimuli (that is, 12 EFEs in total) constituted the material. A second, strictly matched series of stimuli was constructed in order to avoid learning effects: half the participants started with one series while the other half started with the second set. The EFE stimuli were presented in random order on an Apple Macintosh LCII computer screen. We selected a smaller subset of stimuli than those previously used in research into EFE judgment by clinical populations,²⁹⁻³⁰ in order to reduce the patients' fatigability: under our original experimental conditions, patients were asked to decode a series of 16 expressions: 2 (intensity: 30% and 70%) × 4 (emotions: anger, disgust, sadness, and fear) × 2 (sex: one male and one female actor). Happiness expressions had already been excluded, as even at the very low level of intensity of 20%, they are recognised with a success rate close to 100%.³¹ Nevertheless, patients with Parkinson's disease always reported fatigability, and so we chose to discard fear expressions because they are less often displayed during everyday social interactions.

The participants' task was to correctly recognise the emotion presented and quantify its intensity. In order to achieve this, they had to rate each expression on seven point scales for each of seven emotions: happiness, sadness, fear, anger, disgust, surprise, and shame. These scales were presented in random order on the computer screen, below the facial expression, three seconds after each face was first displayed. The face was maintained on the screen until all the scales had been completed. After completion of the emotion scales, participants were also required to rate the difficulty of the task (that is, how difficult they found it to deduce the emotion portrayed by that specific facial expression). All the scales were anchored by "not at all" at one extremity and "very intensely" at the other. There was a two second inter-trial interval. Decoding accuracy was defined as the participant's ability to infer the posed emotion correctly. An expression was considered to be accurately identified if the emotion scale receiving the highest intensity rating on the emotion profile corresponded to the target emotion. Accurately identified or misidentified expressions were scored by 1 and 0, respectively.

To enable familiarisation with the procedure and use of the computer, participants completed two practice trials with the experimenter before completing the procedure individually.

Executive function

During the same session, participants also completed a set of tasks assessing executive function.

Word fluency tasks

Three different word generation tasks were administered: a phonemic task (naming as many words as possible beginning with the letter "P"), a semantic task (naming as many animal nouns as possible), and an alternating task (alternatively naming a word beginning with the letter "T" and a word beginning with the letter "V"). Each task lasted one minute and performance was assessed by the number of different words named during this period.

The Stroop word-colour test

A 50 item version of the test was applied, and comprised two trials. In the baseline condition, a list of 50 strings of five dots was presented to participants. Each string was randomly printed in one of three colours (red, blue, or green). Participants were instructed to name the colour of each string of dots as quickly as possible without error. In the interference condition, a list of 50 colour names (red, blue, or green) printed in a colour different from the word itself was presented. Participants were instructed to name the colour of the ink of each word as quickly as possible and without error.

Performance was assessed by the time in seconds needed to complete each phase, the number of errors in the interference condition, and an "interference cost" index (the difference between the time needed to complete the interference condition and the time needed to complete the baseline condition).

Letter and number sequencing task

In this task, participants were first instructed to recite the alphabet. Next, they were instructed to count forward from 1 to 26. In a third phase, they were instructed to alternatively give a letter and a number in the right order, beginning with "A" as the first letter and "1" as the first number until 26 items were produced—that is, an ideal sequence of "A, 1, B, 2, ... M, 13". The time to complete each phase was measured.

Performance was evaluated by the number of alternation errors in the third phase and by an alternation cost index corresponding to the time increase due to alternation: TB-TA, where TA is the mean time of the first two phases ($[\text{alphabet} + \text{simple counting}] / 2$) and TB is the time of the third phase.

Crossed tapping test

Participants were given a stick and asked to listen to a sound recording. They were instructed to tap twice on the table with the stick when they heard a single, brief sound, but to tap once when they heard two, consecutive, brief sounds. Both kinds of sounds were mixed. Practice trials were run before starting the actual task, which comprised 40 trials.

Performance was assessed by the number of errors.

Backward digit span

The Wechsler adult intelligence scale, revised (WAIS-R) backward digit span subtest was administered. Performance was assessed by the subtest score (marks out of 14).

Control measures

Patients were also assessed with respect to several control measures in order to prevent or minimise the influence of variables such as depression, anxiety, or visuospatial perception deficits. Depressive mood and anxiety were assessed using the Montgomery and Asberg dementia rating scale (MADRS)³³ and the Association of Methodology and Documentation in Psychiatry-anxiety (AMDP-AT) anxiety scale,³⁴ respectively. A Pillon's 15 object test³⁵ was also administered as a measurement of visuospatial perception.

Non-emotional face recognition tests were not included because deficits in this ability are uncommon in Parkinson's disease³⁶ and are usually related to cortical lesions: nevertheless, each of our patients underwent a magnetic resonance examination in order to rule out the presence of such lesions.

Surgical procedure

Quadripolar deep brain stimulation electrodes (Medtronic, Minneapolis, Minnesota, USA) were implanted bilaterally in the STN in a single operating session. The overall methodology was similar to that previously described by Benabid *et al.*⁵ The localisation of the two selected electrode contacts (one on

the left and one on the right) was determined using the stereotactic coordinates provided by the ventriculography done at the end of the surgical procedure. The measures were transferred to the corresponding axial slice of Hassler's atlas. The subthalamic target area was determined according to Guio's geometrical diagram after performing double contrast ventriculography.

Data analysis

We used non-parametric Mann-Whitney tests to detect significant presurgery group effects on EFE decoding accuracy, decoding difficulty rating, and executive function. A 1% significance level was adopted.

In the patient group, we used non-parametric Wilcoxon tests for repeated measures to detect significant effects of surgery on the main clinical variables (motor symptom severity and levodopa dosage), overall cognitive function (MMS, Mattis DRS), EFE decoding accuracy, decoding difficulty rating, executive function, and control measures. A 1% significance level was adopted.

RESULTS

Clinical parameters

The Wilcoxon test for repeated measures revealed a significant effect of surgery on the off-drug state UPDRS part III score, which dramatically decreased to a median value of 27 (range 18 to 50) ($p = 0.008$), representing a 46% reduction. There was also a trend towards a reduction in the Hoehn and Yahr score, which decreased to a median value of 3 (range 2.5 to 4) ($p = 0.05$). The severity of motor symptoms was thus significantly reduced following surgery. The mean (SD) postoperative levodopa equivalent dosage was also significantly lowered, at 777 (323) mg/day ($p = 0.007$).

Overall cognitive function

The Wilcoxon test for repeated measures did not reveal a significant effect of surgery on the mean MMSE and Mattis DRS, which were very close to their presurgery values (MMSE, 28.22 (1.39); Mattis DRS, 136.22 (4.79)).

EFE decoding

Mean overall decoding accuracy and the decoding accuracy according to the emotion intensity and type (together with the task difficulty rating) are presented in table 2.

The Mann-Whitney tests did not show a significant group effect on either overall decoding accuracy ($p = 0.68$) or on a specific type of emotion, regardless of the expression intensity. Thus before surgery the patients had no impairment of EFE decoding. There was no group effect on the task's difficulty rating.

The Wilcoxon test for repeated measures showed a significant effect of surgery on overall decoding accuracy ($p = 0.002$); thus three months after surgery, patients had a significant impairment of EFE decoding. When the results were broken down according to the type of emotion expressed, the Wilcoxon tests revealed a significant postoperative impairment in accurate EFE decoding of sadness ($p = 0.01$) and anger ($p = 0.003$), as well as a trend towards impaired decoding of disgust ($p = 0.04$). The same pattern of results was observed regardless of the expression intensity. The patients' rating of the task's difficulty did not change following surgery ($p = 0.65$). Besides this group comparison, an examination of the individual results showed that nine of the 12 patients had a postoperative impairment of EFE decoding; the performance of the three others did not change.

Executive function

The scores for executive function are presented in table 3.

Table 2 Scores on the emotional facial expression decoding task

Variable	Controls	Before surgery	After surgery
<i>Decoding accuracy (%)</i>			
Global score**	51.5 (17.3)	52.1 (17.9)	28.8 (13.7)
<i>Accuracy by type and intensity of emotion (%)</i>			
Disgust (global score)*	43.8 (24.1)	44.8 (24.7)	31.3 (18.8)
Disgust (30%)	21.1 (22.6)	27.1 (39.1)	8.30 (19.5)
Disgust (70%)	66.5 (33.7)	62.5 (43.3)	54.2 (39.6)
Sadness (global score)**	56.3 (30.4)	62.5 (25)	29.2 (25.7)
Sadness (30%)*	58.3 (28.9)	58.3 (35.9)	29.2 (39.6)
Sadness (70%)*	54.2 (45)	66.7 (38.9)	29.6 (39.6)
Anger (global score)**	50.1 (31.7)	49 (27.9)	26 (25.3)
Anger (30%)**	30.8 (33.4)	27.1 (31)	6.3 (15.5)
Anger (70%)**	70.8 (39.6)	70.8 (33.4)	45.8 (39.6)
<i>Task difficulty rating (/7)</i>			
Global score	3.6 (0.87)	3.53 (0.78)	3.71 (1.04)

Values are mean (SD).
*p<0.05, **p<0.01.

The Mann-Whitney tests revealed a significant group effect on most of the indices evaluating executive function. Before surgery, the patient group thus had a cognitive deficit pattern that is very typical of Parkinson’s disease—namely, preserved overall cognitive efficiency accompanied by a moderate dysexecutive syndrome.

After surgery, the Wilcoxon test for repeated measures showed a reduction in phonemic word fluency (p = 0.01) as well as a trend towards a reduction in alternating word fluency (p = 0.05). No other significant changes were observed. In addition to this group comparison, an examination of the individual results showed that seven of the 12 patients had no change in executive function after surgery, although the dysexecutive syndrome of the five others moderately worsened.

Control measures

Scores for control measures are presented in table 4.

The Wilcoxon test for repeated measures showed a significant reduction in the AMDP-AT anxiety scale score after surgery (p = 0.01). There was no change in the other control measures.

Electrode localisation

The mean coordinates of the selected contacts were laterally 5.26 (0.53) mm from AC–PC, 1.38 (0.51) below AC–PC, and 4.66 (0.45) anterior to the middle AC–PC line on the right side; and laterally 5.26 (0.53) mm from AC–PC, 0.79 (0.48) below AC–PC, and 4.73 (0.53) anterior to the middle AC–PC line on the left side.

Table 4 Scores on the control measures

Measure	Before surgery	After surgery
<i>Depression</i>		
MADRS score (/60)	8.3 (2.7)	6.5 (4.3)
<i>Anxiety</i>		
AMDP-AT score (/68)	12.1 (6.7)	6.0 (2.9)*
<i>Pillon’s 15 objects test</i>		
Time (s) to identify 12 objects	47.7 (26.5)	52.3 (26.1)

Values are mean (SD).
*Significant surgery effect (p<0.01).
AMDP-AT, Association of Methodology and Documentation in Psychiatry-anxiety; MADRS, Montgomery and Asberg dementia rating scale.

DISCUSSION

Using a quantitative standardised EFE decoding task, our results show disturbed non-verbal emotional information processing following functional surgery for Parkinson’s disease. The impairment appears to be rather general as it was observed regardless of the negative emotion expressed. Indeed, although there was only a trend towards significantly impaired decoding of disgust, the raw data showed a clear postsurgery decrease in decoding accuracy. The lack of a significant effect thus seems more related to a lack of statistical power (because of high variance and small numbers of subjects) than to the absence of a specific decrease in decoding accuracy for this emotion.

Table 3 Scores in the executive function tasks

Variable	Healthy controls	Before surgery	After surgery
<i>Word fluency</i>			
Phonemic	19.03 (4.68)	14.89 (4.61)**	12.67 (4.70)††
Semantic	22.92 (4.58)	19.75 (4.92)	17 (4.13)
Alternating	17.25 (4.51)	13.83 (2.92)**	11.91 (3.09)†
<i>Stroop word colour test</i>			
Time to complete phase 1 (s)	28.67 (4.79)	37.58 (8.57)**	38.25 (5.66)
Time to complete phase 2 (s)	49.75 (7.77)	67.92 (16.77)**	73.25 (21.43)
Interference cost index	21.08 (4.35)	30.33 (14.06)**	35 (18.26)
<i>Letter number sequencing task</i>			
Errors	0	1.08 (0.99)**	0.83 (1.19)
Alternation cost index	15.04 (4.35)	26.87 (14.79)*	32.25 (30.29)
<i>Crossed tapping test</i>			
Errors	0.25 (0.62)	3.08 (6.28)**	4.66 (8.74)
<i>Backward digit span</i>			
Score/14	7.33 (1.67)	5.67 (2.23)*	3.5 (1.31)

Values are mean (SD).
Mann-Whitney test: *p<0.05, **p<0.01; Wilcoxon for repeated measures test †p<0.05, ††p<0.01.

As visuospatial information processing deficits have been described in Parkinson's disease,^{37,38} it could be suggested that the deficit in decoding EFEs in our patients was related to a decline in perception after surgery. We can probably eliminate such a hypothesis here, because visuospatial perception abilities were monitored and no post-surgery changes were detected. However, the fact that we did not administer face processing tasks prevents us from completely discounting the possibility that the emotional information processing deficits we report were partly the result of a specific deficit in face recognition—even though such impairments are uncommon in Parkinson's disease. In contrast, the potential involvement of secondary factors such as anxiety and depression can certainly be excluded: after surgery, the mean anxiety score decreased and the MADRS scores did not change.

As deficits in processing facial emotions have been shown to be related to cognitive impairment in brain damaged patients,^{39,40} it could also be argued that the postsurgery deficit observed here was related to general cognitive deterioration. However, as evidenced by the Mattis DRS scores, there was no change in the patients' overall cognitive efficiency after surgery. Nevertheless, we cannot exclude the possibility that despite their good general cognitive efficiency, some patients may have had an executive function impairment which influenced their ability to decode EFEs accurately. Such a hypothesis also seems very improbable as the dysexecutive syndromes within our patient group did not worsen markedly after surgery. The only significant change concerned phonemic word fluency, a frequently reported result.¹¹ However, examination of the individual patterns showed varying postoperative changes. A contingency coefficient was thus computed in order to investigate whether the decline in EFE decoding accuracy was related to a decline in executive function. Of the 12 patients, five had both a decline in EFE decoding and executive function, four had a decline in EFE decoding and no change in executive function, and the remaining three showed no change in either EFE decoding or executive function ($\chi^2 = 1.029$, exact Fisher probability = 0.204). It thus seems that the observed disturbance in emotional information processing cannot be explained by a decline in executive function. Moreover, when considering the localisation of the electrodes (fig 1), good homogeneity is observed: the three patients with no change in either EFE decoding or executive function had electrode localisations that were comparable with those of the other patients.

Our data thus extend previous results showing the involvement of the basal ganglia functional circuits in emotional information processing²²⁻⁴¹; to the best of our knowledge, this is the first study to show a worsening of non-verbal emotional information processing following a change in STN function. Animal based anatomical and physiological studies have suggested a tripartite organisation of the nigrostriato-prefrontal functional circuits in which motor, associative, and limbic cortical areas project in a segregated manner onto three distinct striatal subregions (referred to as motor, associative, and limbic striatal territories¹⁶). Our results support the animal data which suggest that this organisation is also maintained at the subthalamic level.⁴²⁻⁴³ Though the target of functional surgery is the motor neurones—that is, the most dorsolateral STN territory^{44,45}—the present results indicate that other territories are also affected. This is not surprising, given the very small size of this structure (10 mm in the mediolateral axis, 8 mm in the anteroposterior axis, and 6 mm in the ventrodorsal axis). Moreover, as the treatment in question involves deep brain stimulation as opposed to lesioning, current diffusion may occur (depending on pulse width and voltage), and this could

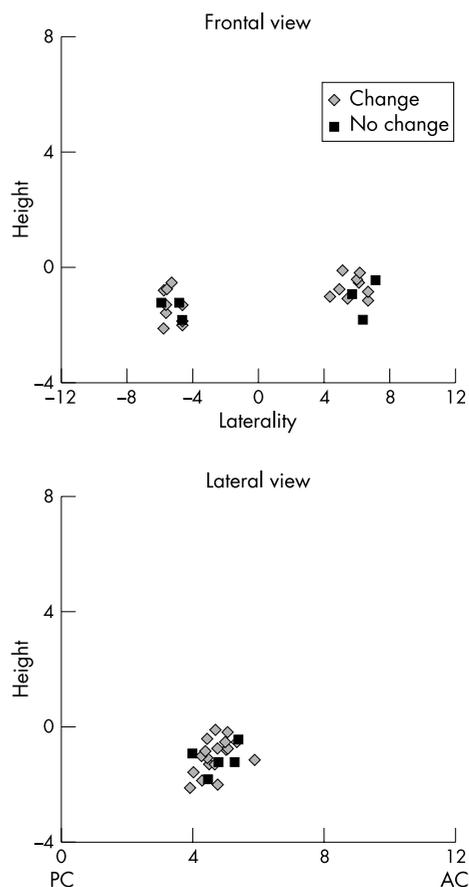


Figure 1 Distribution of the contacts of the quadripolar electrodes: the x axis gives the lateral coordinates on the frontal view and the anteroposterior coordinates on the lateral view as 1/12 of the length of the AC-PC line; the y axis represents the craniocaudal coordinates as 1/8 of the thalamic height. Black squares, coordinates of the three patients with no changes in either EFE decoding or executive function; grey diamonds, coordinates of the other patients. AC, anterior commissure; EFE, emotional facial expression; PC, posterior commissure.

account for the active effects of stimulation on territories other than motor ones.

Most studies investigating the effects of bilateral STN stimulation have concentrated on the treatment's motor efficacy; their results are broadly in concordance in showing very high efficacy for relief of parkinsonian motor symptoms, thus suggesting that STN stimulation mimics the effects of levodopa.⁴⁶ This gives rise to a puzzling situation: bilateral STN stimulation leads to dramatic relief of parkinsonian motor symptoms, has no (or at least only limited) negative consequences on cognitive function, but involves behavioural changes and disturbances in emotional information processing. Of course, it can be suggested that one important limitation of the present study is the absence of a comparison with the stimulator turned on and off. Indeed, as the levodopa treatment was significantly reduced postsurgery, we cannot rule out the possibility that this factor—rather than surgery—led to the EFE decoding impairment. Such effects may also interact. However, as far as we are aware, the specific effect of levodopa treatment on emotional information processing has been poorly investigated.

Lawrence *et al* reported that in healthy men, acute administration of a dopamine D2 class receptor antagonist (sulpiride) led to a selective disruption of the recognition of facial expressions of anger, with preserved recognition of

other emotions.⁴⁷ In healthy subjects, however, the selective disruption of one dopamine receptor family can lead to a very disruptive impairment; in Parkinson's disease, receptor families other than D2 are also affected. Hence, the question remains open, and further studies comparing performance on EFE decoding tasks in patients with the stimulator turned on and off will perhaps provide some of the answers.

We need to bear in mind that such studies also involve methodological limitations. For ethical reasons, the off stimulation assessment is usually done about one hour after turning the stimulator off. However, even after this length of time, the effects of stimulation are still partly operational: consequently, this scheme does not constitute a complete "off" condition (Pollak P, personal communication), and the actual consequences of functional surgery can be underestimated. Moreover, an effect of microsubthalamotomy cannot be excluded, and as such a procedure involves rather short periods between the examinations, this leads to an enhancement of intersession interference effects.

The differential effects of STN stimulation on the motor, associative, and limbic systems could also be explained by the involvement of different neurotransmission systems in each circuit. At present, the effects of chronic STN stimulation on non-dopaminergic neurotransmission systems remain largely unknown, and further fundamental studies are needed to shed light on this question. It is also possible that in patients with Parkinson's disease, high frequency stimulation reduces STN hyperactivity and consequently not only restores the function of the dopaminergic system in the motor territories but also disturbs the balance between the dopaminergic system and other neurotransmission systems. This could explain the difficulty in obtaining positive effects on certain non-dopa-responsive parkinsonian motor symptoms such as gait and postural disorders,⁴⁸ and the worsening of others, such as hypophonia and dysarthria,^{5 6} as well as behavioural disturbances.

CONCLUSIONS

Bilateral STN stimulation should always be considered as a possible treatment for parkinsonian patients with intractable motor symptoms. However, it can involve certain adverse (mainly behavioural) effects, and our results underline the need to bear in mind that by biasing the interpretation of the partner's emotional state,⁴⁹ STN stimulation can involve changes in the social and affective life of patients with Parkinson's disease.

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ECHO

Children surviving severe meningococcal disease have a high incidence of immune complex associated complications



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The incidence of immune complex associated complications of severe meningococcal disease such as arthritis, vasculitis, and pleuritis, has not declined despite better treatment. The documented incidence in the literature is 6–11%, although there has not been a report on a large patient group for over 20 years. A recent Dutch survey has found the incidence to be 15%.

The Dutch survey from a paediatric intensive care unit was conducted between January 1993 and August 2000. It found that of 130 survivors of meningococcal disease followed up retrospectively, 20 (15%) developed immune complex associated complications. These complications usually occur 4–10 days after initial antibiotic treatment and typically present with local clinical symptoms and a recurrence of fever.

Eighteen children had arthritis, 11 vasculitis and five pleuritis. Twelve patients had more than one complication. All had fever, leucocytosis, and increased C reactive protein. They were also found to have a significantly lower leucocyte count at admission than children who did not go on to develop any immune-mediated complications.

In patients with secondary fever or raised inflammatory parameters following meningococcal disease, immune complex associated complications should always be considered in the differential diagnosis. The high incidence found in this study compared to that reported in the literature may be due to the fact that the children studied were more severely ill. A prospective study is now needed to identify risk factors for these sorts of complications following severe meningococcal disease.

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