

FOCUS 1 REPORT – JANUARY 2004

Disclaimer

It is our intent to provide general educational information in our publications. These publications are written by volunteers and professional staff associated with The Parkinson Alliance (PA) a not-for-profit organization. Some information is from outside sources, such as medical journals, governmental publications and Internet.

Our publications are for informational and educational use only and not an attempt to practice medicine or provide specific medical advice and should not be used to make a diagnosis, to replace or overrule a qualified health care professional's judgment. We strongly encourage patients to consult with a qualified health care professional for answers to their health questions.

Introduction

The participants in this report were involved in an earlier survey, aptly named CORE. In this first survey, the patients either filled out the questionnaire on-line or they were given or mailed a printed copy by participating facilities where surgery and adjustments are done. In some instances, help was given to patients by either the caregiver or a nurse in filling out the form.

We contacted the participants who completed the CORE survey and asked if they were interested in working with us to continue to gather information giving the patient's point of view. Forty-nine patients answered our call and completed Focus 1, the current questionnaire. We are now mailing you the summary of your responses in this paper entitled Focus 1 Report. We are very grateful for your continued interest and want you to know that you and your caregiver are performing a unique and important ground breaking function that serves the PD patient community as well as health care professionals involved with neurology, movement disorders and DBS/STN surgery.

We hope that all of you will wish to participate in follow-up surveys. The anticipated topics for the next 2 Focus Surveys are: [1] Depression, anxiety and PD, as this cluster of symptoms relate to DBS/STN and [2] Non-Motor Symptoms (NMS). As you will see in the current report, the occurrence of NMS is equal to, if not greater than the Motor Symptoms (MS) in their disruption of Activities of Daily Living (ADL). All the factors that influence the quality of life (QOL) of the PD patient who had DBS/STN will be evaluated in the social, psychological and neurological health domains.

We are also looking to recruit additional DBS/STN patients who are at least 6 months out of surgery. Please have them call our office at 1-800-579-8440.

Background

This survey has been a patient driven project, meaning that the design and data analysis was accomplished by patients interested in learning more about Parkinson's Disease (PD) as it relates to DBS/STN. Researching the current topic we noted that there is a growing interest in studying the patient's point of view and research projects are focusing on feedback from patients to help determine whether treatments are doing more good than harm or if health and quality of life are improving or worsening.

Our sample population (49 patients) included male and female participants, whose ages at diagnosis ranged from 22 to 74; they all had bilateral STN, and their age at surgery ranged from 36 to 76.

Description of Symptoms

Parkinson's disease (PD) is characterized by four cardinal motor symptoms: bradykinesia, rigidity, loss of normal postural reflexes, and tremor.¹ Deep brain stimulation of the subthalamic nucleus (DBS/STN) has expanded the choices of therapeutic treatments for individuals suffering from PD. Researchers agree that DBS/STN provides a marked improvement in the cardinal motor symptoms, but there is little information about long-term effects of this treatment. Moreover, several of the challenges for persons with PD transcend motor deficits, as non-motor deficits are also quite prevalent within this illness.^{1,2,3} In fact, it has been documented that both motor and non-motor symptoms impact quality of life.⁴ For example, one study found that postural instability, disability, depression, and cognitive impairment have the greatest influence on quality of life.⁴ The survey to which you responded addressed your experiences with the cardinal motor symptoms as well as many of the other symptoms that individuals with PD experience, including speech, cognition, memory, and problems with depression, isolation, and fatigue. We conducted a review of over 25 published studies that looked at DBS/STN, and we compared those findings with the survey that you completed.

Results

We are including several tables to assist in understanding the data we are presenting. All numerical data was converted to percentages for easier reading. To understand how to use the tables choose one of the symptoms and read across to the right. For the purpose of easier presentation, we combined the "greatly improved" and "improved" categories into one, "improved". We did the same for "declined" and "greatly declined" and left the remaining two categories unchanged. This leaves us with 4 categories for evaluation and comparison: improved, declined, no change and no symptom. For example, if you want to find the percentage of the population that improved in rigidity after the surgery, you would go to the row with rigidity in the first column and read across to the 2nd column "improved" where you will find 51%

Cardinal Symptoms:

MOTOR	Improved		Declined		No change	No Symptom
Tremor	57%		2%		14%	27%
Rigidity	51%		6%		27%	16%
Balance	24%		18%		41%	16%
Freezing	49%		8%		20%	22%
Bradykinesia	45%		6%		29%	20%

Consistent with prior research, the respondents of our survey indicated that they experienced improvement in tremor, 57%, and rigidity, 51%. Others, however, reported that these symptoms remained unchanged, tremor, 14%; and rigidity, 27%, bradykinesia, 29% and a few individuals reported worsening of these symptoms 2%, 6% and 6% respectively. There was also a group of people who did not experience these symptoms at all.

With regard to balance, 24% percent of the respondents of our survey indicated that balance improved after surgery, but in 18% it got worse and 41% reported no change.

The alleviation of the cardinal symptoms of Parkinson's disease via DBS/STN is well documented.⁵⁻⁹ Moreover, it is well known that the symptoms of bradykinesia, tremor, rigidity, and postural instability significantly improve after DBS/STN. Some research has found sustained improvement in motor function even 2 years after the procedure.¹⁰ Another study found that persons with advanced PD who were treated with bilateral DBS/STN had marked improvements over 5 years in motor function while off medication.¹¹ Specifically, the latter study found that tremor and rigidity improved substantially at one year and remained stable at 5 years, and painful dystonia disappeared at 5 years in most individuals. Freezing improved at one year, but this improvement was not completely sustained over time. Furthermore, most persons in the five-year outcome study were independent in their activities of daily living when assessed off medication.

Gait:

MOTOR	Improved		Declined		No change	No Symptom
Gait	47%		8%		35%	10%

Although 47% of the respondents in our study indicated that their gait improved after DBS/STN, 35% reported that their gait did not change. Only 8% of our respondents reported that their gait worsened. Prior research generally found improvement in gait after DBS/STN. One research article found that both unilateral and bilateral DBS/STN stimulation can improve walking speed by greatly increasing stride length, with only minimal change in cadence; but for some individuals, improvement in walking required bilateral stimulation.⁵ In addition, the investigators noted that bilateral DBS/STN stimulation improved gait and postural stability more than

unilateral stimulation. Another study found that DBS/STN induced an almost threefold increase in walking velocity by increasing stride length.⁶ Cadence was virtually unchanged, as in the previously mentioned study. A notation was made that the combination of both levodopa and DBS/STN further improved the participants' gait. In sum, long-term DBS/STN stimulation is effective in improving Parkinsonian gait and in some patients no additional L-dopa is required (due to the optimal placement of the DBS in the STN).⁶ It should be noted, however, that there might not be lasting effects for the improvement of gait. A 5-year outcome based study for DBS/STN revealed that while on-medication postural stability and freezing of gait worsened. These symptoms became less responsive to levodopa between years one and five after surgery.¹¹ The investigators speculated that the worsening of these symptoms is consistent with the progression of the underlying disease and would have occurred in the absence of DBS/STN.

Handwriting:

MOTOR	Improved		Declined		No change	No Symptom
Handwriting	6%		4%		22%	67%

4% of respondents in our survey did not experience improvement in handwriting. After DBS/STN, 6% showed improvement and 4% worsened. There has been limited research that has specifically investigated handwriting in PD after DBS/STN. One study examined 12 patients and revealed that continuous bilateral STN stimulation resulted in consistent improvement of handwriting in late-stage PD.¹⁵ Moreover, this study revealed that DBS/STN stimulation had a beneficial effect on highly skilled sequential hand movements. Furthermore, this research provides evidence that chronic bilateral DBS/STN stimulation facilitates appropriate dexterity and generation of force in advanced PD, and thus allows for a more automatic performance in writing movements. DBS/STN stimulation, however, did not prevent handwriting movements from becoming smaller over time in this study.

Speech and Swallowing:

MOTOR	Improved		Declined		No change	No Symptom
Swallowing	4%		24%		18%	53%
NON-MOTOR						
Speech	12%		43%		41%	4%

Although 41% of respondents to our survey reported no change in their speech after surgery, 43% indicated that their speech got worse. The results from prior research have been variable, ranging from improvement to worsening of speech. Overall, speech after DBS/STN does not improve much, although oral control has been shown to improve.⁷ One study found that the stimulation effects on speech variables were limited to modest increases in vocal intensity and a less monotone pattern of speech.¹² The less monotone pattern of speech could be caused by reduced stiffness in the laryngeal muscles, allowing improved pitch and inflection. Further, research

has found that in persons whose parkinsonian hypophonia (weak voice) is highly sensitive to levodopa, DBS/STN may induce a major improvement in speech.¹³ Research has also reported that the worsening of speech can occur with DBS/STN.¹³ In a five-year outcome study, speech worsened between the first and fifth year after surgery while on-medication.¹¹ These authors indicated that the worsening of speech is what one would have expected in the absence of specific treatment. Other research has speculated that when using excessively high stimulation parameters or with incorrect electrode location, speech difficulties may worsen;⁷ thus, it may be helpful in determining whether a speech problem is related to stimulation. Other notations in the literature indicate that parkinsonian speech problems belong to the symptoms that often are relatively resistant to levodopa therapy; hence, on average speech is not much improved with DBS/STN.¹³

Insomnia:

NON MOTOR	Improved		Declined		No change	No Symptom
Insomnia	33		6%		24%	37%

Our survey found that 27% of respondents reported that DBS/STN did not lead to changes in symptoms of insomnia. Some respondents actually showed improvement of this symptom after DBS/STN such that 10% reported a large improvement in sleep after surgery and 23% reported a mild improvement in their sleep. Only 6% of our sample reported a worsening of insomnia after DBS/STN. Despite the fact that sleep problems are common in PD, these results are difficult to compare to the published literature because sleep quality has rarely been examined in the DBS/STN literature. We found one small study of 11 patients¹⁶ that focused specifically on the effects DBS/STN has on sleep quality. The results showed that overall there was a significant improvement in self-reported sleep quality following DBS/STN. In addition, this study also measured sleep using polysomnography, which includes measuring brainwaves and behavior (e.g., movement, changes in body position) during sleep. The results showed little change in brainwave patterns and behavior, except that after surgery patients did have longer periods of continuous sleep. There was no evidence that there was a worsening of sleep after surgery. Before firm conclusions can be made regarding changes in sleep patterns resulting from DBS/STN, clearly more research needs to be done.¹⁷

Isolation:

NON MOTOR	Improved		Declined		No change	No Symptom
Isolation	22%		16%		18%	43%

Our survey found that 18% did not report a change in their level of social isolation following DBS/STN and 22% of the respondents reported an improvement in their level of social isolation. However, 16% of our respondents reported worsening social isolation after surgery (with 2% of these reporting a very large increase in their degree of social isolation). We

did not find any research that specifically examined social isolation in PD, but some studies have focused on social support as a component of quality of life. One study compared DBS/STN surgery patients to PD patients that had not undergone DBS/STN and found that ratings of social support at three and six months post-surgery were not significantly different between the two groups.⁸ The issue of social support and degree of isolation is an important one, in part because patients who are isolated and have limited social support system may have much more difficulty with the follow-up requirements of DBS/STN. Isolation and/or a lack of social support may lead to an increased risk for depression and other possible negative outcomes of surgery. Based on our survey, it appears that a sizable portion of individuals will experience an increase in social isolation and this feature must be attended to in planning for DBS/STN.

Fatigue:

NON MOTOR	Improved		Declined		No change	No Symptom
Fatigue	16%		24%		47%	12%

47% reported no change in symptoms of fatigue after DBS/STN and 16% reported an improvement in fatigue following surgery. However, 24% of respondents reported an increase in fatigue after surgery. Fatigue is difficult to assess and can be influenced by many factors, such as medication changes, “on” and “off” periods, and stimulation parameters. Studies that do report on the effects of DBS/STN on fatigue are generally in agreement with our results, which show that most patient’s level of fatigue either remains the same or improves.¹⁹ However, a subgroup of patients may be at risk for worsened levels of fatigue following DBS/STN surgery and these symptoms are probably associated with our next symptom: depression.¹⁹

Depression:

NON MOTOR	Improved		Declined		No change	No Symptom
Depression	22%		20%		27%	31%

Depression is common in PD.²⁰ The vast majority of studies we reviewed are consistent with our survey results: most DBS/STN patients experience either no change 27% or some improvement in depression 22% following surgery.²³ There is debate in the research literature about why this occurs. Common sense suggests that a significant improvement in motor symptoms following DBS/STN would naturally lead to a reduction of depression. Other researchers suggest that the procedure itself may affect the brain systems associated with depression. Still, others believe that an improvement in activities of daily living is responsible for improvements in mood after surgery. Whatever the cause, reductions in depression are commonly seen following DBS/STN. It is important to note, however, that a sizable portion of patients show a worsening of depressive symptoms following surgery and depression is sometimes cited as an adverse event.²¹ Indeed, about 20% of our survey respondents reported an increase in depression following

DBS/STN. We believe that one possible reason for increased depression after surgery relates to one’s expectations about surgery outcome. Although effective in reducing the cardinal motor symptoms of PD, DBS/STN is not a cure, and many patients may feel disappointed and frustrated when symptoms remain and/or complications occur. The best remedy for this problem is to educate oneself and one’s family about what can be expected following surgery and discuss symptoms of depression with your treatment team so that, if necessary, you can receive appropriate treatment.

Cognition, Memory and Decision Making:

NON MOTOR	Improved		Declined		No change	No Symptom
Cognition	2%		14%		20%	63%
Memory	6%		29%		20%	45%
Decision Making	12%		10%		12%	65%

Our survey included questions about changes in cognition (e.g., thinking, memory and decision making) before and after surgery. Although most of the respondents (between 12% and 20%) did not experience changes in cognition, memory, or decision making, a substantial portion (between 10% and 29%) reported that their cognitive, memory, and decision making abilities worsened following surgery. While the scientific research in this area is still evolving and limited in many respects (e.g., small sample sizes, few tests of cognition and memory, inconsistent findings), a few consistent findings have emerged. The largest summary of this research to date ²² indicates that following surgery, patients frequently have word finding difficulties and have less fluent speech. Speech fluency refers to how quickly one can say words and organize one’s thoughts according to a specific rule or topic. This skill relies in part on the frontal lobes of the brain, and the DBS/STN is known to activate brain pathways involved in the frontal lobes.²² The findings regarding memory changes after DBS/STN surgery suggest that declines on tests of learning and memory are not uncommon.²³ Only one study to date has compared an DBS/ STN group to a control group of PD patients that did not receive DBS/STN.²³ This study found mild declines in attention and verbal memory in the DBS/STN group compared to no change in the control group. Importantly, this study did not find that being “on” or “off” stimulation made a difference on the cognitive test performances. That is, attentional verbal fluency, and memory declines were evident when the patients were tested in either condition.

It is possible that memory problems immediately after surgery improve over time.²² One difficulty with comparing our survey results to the research literature is that, strange as it may sound, self-reported memory problems often do not correlate well with performance on objective memory tests. That is, some people believe that they have problems with their memory, but may do fine on memory tests. On the other hand, some people may not think they have memory problems, but do poorly on objective tests.

Whatever the case, both subjective and objective assessment of memory are important to consider, and it is somewhat surprising that we could not find any studies that assessed patient's self-report regarding problems with memory. Finally, it is important to point out that patients with objectively determined memory problems are often excluded from consideration for DBS/STN surgery because it is known that persons with cognitive impairments are at risk for a significant worsening of their memory after DBS/STN.²²

A few words about Dyskinesia:

It is worthwhile to address what the literature reported about dyskinesia, the involuntary movements that result from specific medications used to treat PD. One of the benefits of DBS/STN is that it allows for a reduction in the dosage of this medication. Research has found that sustained reduction in drug requirements were achieved for over 2 years after DBS/STN.¹⁰ Another study indicated that while individuals were receiving dopaminergic medication, the duration of dyskinesia and the severity of the associated disability substantially decreased at one year and remained stable at five years after receiving DBS/STN.¹¹ There is speculation that if you are still experiencing dyskinesia after surgery, you may be taking too much Sinemet or you may be highly sensitive to Sinemet. Consequently, your adjustment may need to be lowered and/or your medication might need to be modified. It is important to follow-up with your doctor about this particular issue.

Analysis

For the purpose of easier demonstration, we combined the "greatly improved" and "improved" categories into one, "improved". We did the same for "declined" and "greatly declined" and left the remaining two categories unchanged. This leaves us with 4 categories for evaluation and comparison: improved, declined, no change and no symptom. If you look at Chart 1 (Chart 1 is on a separate sheet after the Summary section) in the column for tremor you will see 57%. This means that 57% of the respondents improved in the area of tremor after surgery. Each one of those numbers refers to the % of respondents who improved in that symptom category. Keep going to the right until you reach handwriting which is 6%. You can do the same for all four categories. Only in the areas of balance and swallowing did the respondents decline. There was marked improvement in all other areas of motor symptoms.

By comparison, you can easily see that the non motor symptoms did not fare nearly as well as the motor symptoms. Refer to Chart 2 on a separate sheet after the Summary section.

Summary:

There are many limitations to the amount and the extent of research that has been conducted on DBS/STN. These include:

- Few control group comparisons.
- Variability in selection/inclusion criteria
- Small sample sizes
- Surgical complications – substantial sometimes, but rare.^{24, 25}
- Variability in surgical techniques, lack of standardization of parameters.
- Lack of long-term follow up and serial assessments.

Our conclusion is that DBS/STN is most suited to treat the motor symptoms associated with PD. Our symptom profile was consistent with the reported results in the literature. We are unable to say whether the worsening of symptoms is in fact caused by incorrectly placed electrodes in the STN or are just part of the disease's degenerative progression, or perhaps even a combination of those factors. Many more validated studies will have to be done by researchers before we will know the answers to this and many other questions.

We searched the scientific literature to find articles that are relevant to the topics we are exploring, and we compared the results of the research literature with the outcome of our patient survey. We were able to complete this project because we have both the financial and the spiritual support from The Tuchman Foundation and The Parkinson Alliance, of whom Margaret is the volunteer president. It was her search for answers about her surgery that was the driving force that put her in front of her computer as soon as she was able following her DBS surgery.

We want to acknowledge the many hours of hard work that PD patients; Rick Kramer (a DBS/STN patient) and John Wherry contributed to editing all the versions of this report. Our most recent additions to our research staff are two psychologists with PhDs who have special interest in PD, and have great analytical skills to help us sift through the mountains of research information, to review and present it in understandable language.

Margaret

Margaret Tuchman

President of The Parkinson Alliance

Publisher of *The Catalyst*, a periodic newsletter of the PA.

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