The Treatment of Akinesia using Virtual Images

by

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Abstract

The Treatment of Akinesia using Virtual Images

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Industrial Engineering

Parkinson's disease is characterized by three primary symptoms: rigidity, tremor, and akinesia. Akinesia refers to difficulty initiating and continuing motions, in particular ambulation. Most akinetic patients are aided by the presence of visual cues (such as bricks or cards) on the ground, which evoke a "stepping over" response; apparently, these cues can be used to fire neural ambulation programs which are otherwise unreachable except via medication.

The intent of this thesis was to investigate the effectiveness of providing visual cues which did not consist of physical objects placed on the ground, and which could easily be carried around by the patient. Ideally, such cues would allow akinetic patients a wider range of mobility with reduced medication and without the impracticality of tangible cues.

We tested both a simple laser pointing device and the Virtual Vision Sport^{TM}, a visor with a small lens mounted in front of one eye reflecting a liquid crystal display (LCD).

The study indicated a marked improvement in unmedicated gait for subjects using each of the laser pointer and images presented in the Virtual Vision visor as the stimulus. One of the subjects unexpectedly learned to improve his gait without the presence of visual cues, although this gait breaks down frequently in the presence of distractions.

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ACKNOWLEDGMENTS

This thesis represents a remarkable convergence of at least three threads: the search for treatments of akinesia in the medical community, the development of a new display technology by Virtual Vision, Inc. and the human factors research at the Human Interface Technology Laboratory (HITL). Consequently, the complete list of people to whom I am indebted is lengthy; there follows a partial list, with apologies to whomever I have not acknowledged.

The original idea behind this thesis came from T.R., a person with Parkinson's disease who also served as our first subject. This research could not have happened without him. Thanks are also due to D.L., our second subject, and the first we investigated quantitatively.

Dr. Thomas Furness, director of the HITL and professor of Industrial Engineering, is a co-inventor of the display technology commercialized by Virtual Vision, Inc. which was used in this study. He served as chair of my thesis committee, and provided many helpful suggestions during the development of the project.

Suzanne Weghorst, medical coordinator for the HITL, directed the project and served as a thesis committee member.

Denis Anson, acting instructor in Rehabilitation Medicine, played a crucial role in the study and served as a thesis committee member.

Dr. Judy Ramey, professor of Technical Communication specializing in usability testing, made her equipment available and served as a thesis committee member.

I am indebted to all of my committee members for their helpful suggestions on my thesis drafts, but particularly Denis Anson and Suzanne Weghorst.

Bob Price, research associate in Rehabilitation Medicine, allowed us to use the Biomechanics Laboratory for the quantitative part of this study and coordinated data collection and analysis.

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Dr. Phil Swanson, head of Neurology and director of the Parkinson's Disease Information and Referral Center (PDIR), and Maria Linde, coordinator of the PDIR, referred subjects for the study and provided encouragement.

Dr. George Kraft, professor of Rehabilitation Medicine, provided encouragement and suggestions concerning other important applications of the technology not covered in this thesis.

Gordon Kuenster, CEO and founder of Virtual Vision, Inc. was instrumental in providing both technical assistance and a display technology which had not yet been commercially released.

Richard Johnston and Steve Shankle from Virtual Vision, Inc. provided assistance during the trials with T.R., including the development their own test images for use in the study.

Greg Heacock, an optics engineer with Virtual Vision, has worked on prototypes for a next-generation display specifically for akinetic patients.

Toni Emerson, HITL research librarian, provided assistance with literature searches and co-authored a technical report which is the basis of Appendix B.

Ari Hollander, a fellow HITL graduate student, provided his Amiga 3000 for the qualitative study, as well as crucial programming assistance.

Dr. John Sundsten, a neuroanatomist in the Department of Biological Structure's Digital Anatomist Program, was very helpful in the preparation of anatomical illustrations.

I would like to thank my brother, Jeff Prothero, for the loan of images of his brain, which I have used in illustrations.

A “thank you” is due to fellow HITL graduate students Paul Danset and Mark Takacs who provided assistance with LaTeX.

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Last, but certainly not least, I am indebted to the HITL generally for providing an environment in which this research could be initiated and carried through to success.

To my parents, John and Joyce.

"The problem, then, is to provide a continual stimulus of the appropriate kind — and if we can achieve this we can recall Parkinsonians from inactivity (or abnormal activity) into normal activity, and from the abyss of unbeing into normal being."

Oliver Sacks [63] (p. 292)

Chapter 1

INTRODUCTION

1.1 Kinesia Paradoxa

Parkinson's disease is a progressive neurological disorder with a prevalence in the United States of 347 per 100,000, affecting 1% of people over the age of 65 [72, 69]. Parkinson's disease is the third most common neurological disease, with a mean age of onset of 58 years [32]. The disease apparently does not differentially affect specific ethnic groups. There is debate over whether it affects both genders equally [54]. The disease can have a profound negative effect on the productivity of people involved. The most debilitating symptom is that of akinesia [12], or the difficulty in initiating and substaining motion.

Most akinetic persons with Parkinson's disease are capable of near normal motion under some circumstances, an effect known as "kinesia paradoxa" [79]. Typically in such cases, more normal ambulation is made possible by providing obstacles for the patient to step over.

1.2 Virtual Vision

While the ability of visual cues to produce kinesia paradoxa in akinetic persons with Parkinson's disease is well-established in the medical community (see Chapter 2), it appears to have received little sustained attention, presumably because it appeared to provide limited therapeutic value. Obviously it would not be practical to paint two inch stripes everywhere a person with Parkinson's disease might wish to go.

The situation potentially changed in early 1993, with the development of a new, relatively low-cost[1], head-up display[2] technology by Virtual Vision^{TM} (VV).

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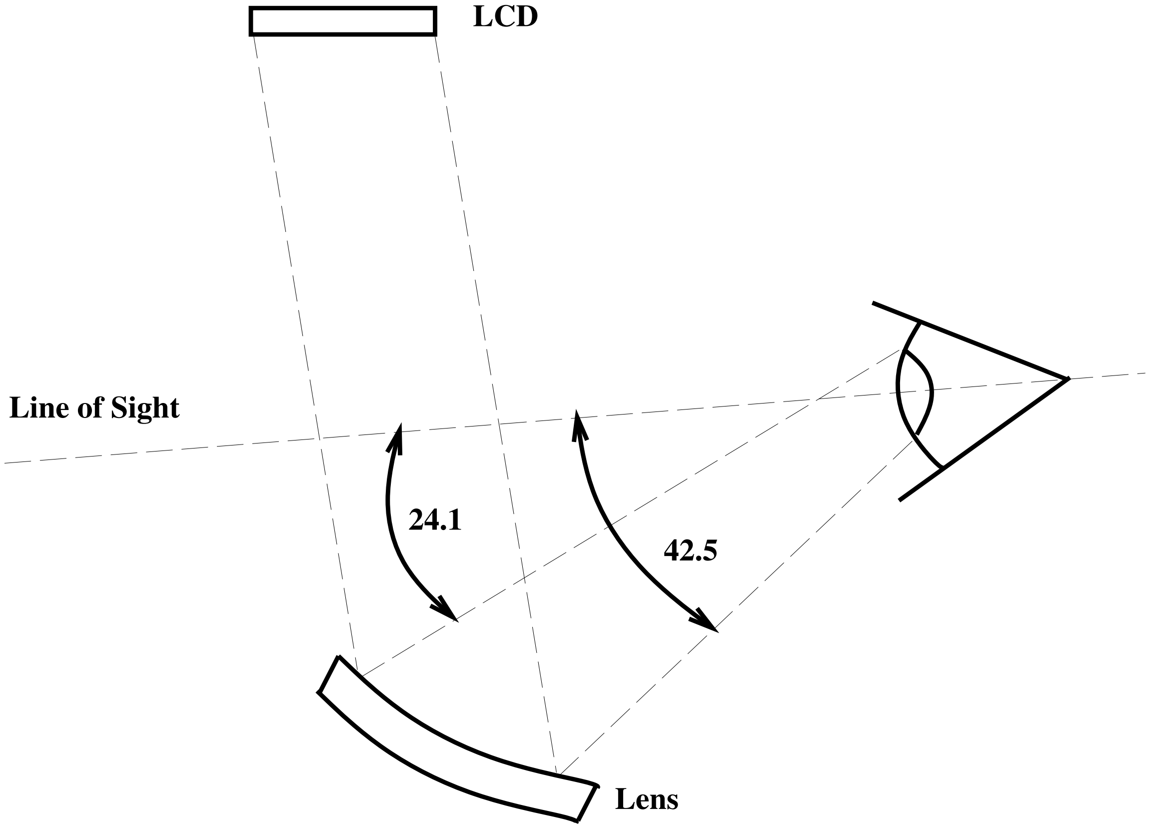
[1] Less than $1000 U.S.

[2] A head-up display is one in which information is viewed superimposed on the outside world (as by displaying on a windscreen or visor) so that the information can be read with the head erect and with the outside world always in the field of view [2].



Adapted (with permission) from Virtual Vision documentation.

Figure 1.1: Peripheral Viewing Display Angles

In essence, the VV Sport^{TM} [81] consists of a visor with a liquid crystal display (LCD) mounted above either the right or left eye. Mounted in front of the same eye, 24° below the line of sight, is a reflecting lens which projects the image from the LCD back into the eye. The LCD contains 96,600 color pixels; the lens occludes 15° by 22° of the visual field (see Figure 1.1). The rest of the visual field is left unobstructed, except for a tinted, see-thru screen. Since the Sport can be worn like sunglasses and weighs only 5 ounces, it can be thought of as providing a portable large-screen display.

Ordinarily, a display mounted less than an inch from the eye would be useless, as focus in that range would be difficult and straining. However, the lens is used to optically modify the image, causing the image to appear at a greater distance in front of the user.

The principle at work here is called "accommodation", the adjustment of the curvature of the eye's lens depending on the distance to the object being viewed. In accommodation for near vision, the ciliary muscle contracts, causing increased rounding of the lens; the pupil contracts and the optic axes converge [78].

The brain uses the amount of accommodation necessary to bring the eye into focus as one of its depth cues[3]. By collimating[4] the light rays coming out of the Virtual Vision Sport lens, the eye is made to accommodate at an apparent distance much greater than that of the display. This "fools" the brain into thinking that the image is further away than in is. Furthermore, it avoids the strain of having to re-accommodate the eye when switching focus between the display and the outside world.

Accurate accommodation is important for objects within a few feet or so; beyond about six feet it becomes less important, because the changes in accommodation for objects farther than six feet away are small [81].

Virtual Vision provides a standard reflective lens which places the virtual image six or more feet in front of the user, depending on the manufacturing tolerances of the components separating the LCD from the lens. In addition, a precision reflective lens can be adjusted to place the display focus at any distance (see Figure 1.2).

A prototype version was introduced at the 1993 Winter Consumer Electronics Show in January, and it received considerable publicity. It was at this point that T.R., who has Parkinson's disease and who has given considerable thought to visual cues, conceived the idea of using the VV Sport display to provide portable visual cues which would appear to be on the ground. Such a display might allow him to function at a lower level of medication, and therefore with less side-effects (see Chapter 2).

T.R. contacted Virtual Vision with this idea. Virtual Vision referred him to the Human Interface Technology Laboratory (HITL). That was the beginning of the research described in this thesis.

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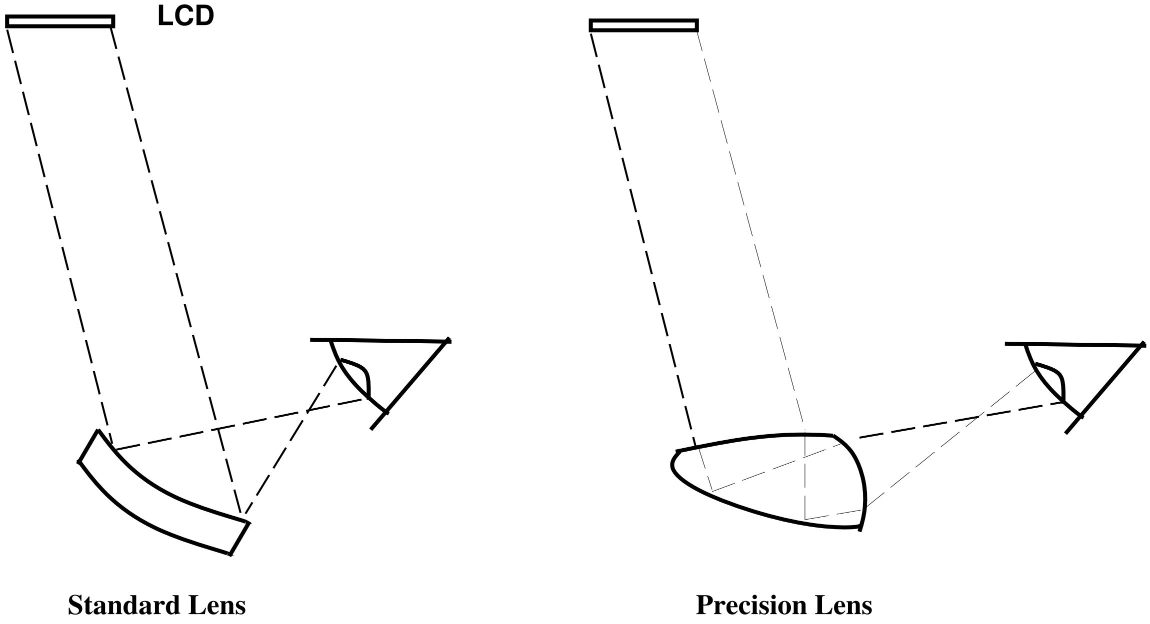
[3] Other depth cues include interposition (blocking of one object by another), linear and size perspective, texture gradients, distribution of shadows and illumination, motion parallax, and stereoscopic cues related to comparing the retinal images to the two eyes [32].

[4] "Collimation" refers to changing a divergent beam of light (from a point source) into a parallel beam, or (in our case) a near-parallel beam.



Adapted (with permission) from Virtual Vision documentation.

Figure 1.2: Reflective Lens Options

1.3 Organization

The following chapters contain a literature review and a description of an initial study undertaken to determine the effectiveness of non-tangible visual cues for producing kinesia paradoxa.

The appendices provide T.R.'s views on his trials a week or so afterwards, a survey of medical applications of virtual environments technology, and a short summary of the relevant medical background.

1.4 Contact

Questions or comments regarding this thesis may be addressed to Jerry Prothero, University of Washington, Human Interface Technology Laboratory, FJ-15, Seattle, WA 98195, or electronically to prothero@hitl.washington.edu.

Chapter 2

LITERATURE REVIEW

2.1 Overview

This chapter briefly reviews current treatments of Parkinson's disease, particularly akinesia. Some of the necessary medical background can be found in Appendix C. As this thesis represents a conjunction of the specialized fields of the medical treatment of Parkinson's disease and virtual imaging technologies, specialized terms from both of these fields are defined in the glossary section.

2.2 The Treatment of Parkinson's Disease

Parkinson's disease is related to a reduction of dopamine in the brain and damage to the dopaminergic pathway from the substantia nigra to the striatum [32]. The search for a cure for Parkinson's disease is complicated by the fact that its cause is unknown. The most prominent risk factor is age, with symptoms usually appearing after the age of 50 [8], although one third of patients develop the disease before the age of 50 and 10% before the age of 40 [27]. At present, all therapies for Parkinson's disease are palliative, and treatment failures are eventually experienced by patients given the primary antiparkinsonian drug, levodopa [8].

Tremor is the usual first symptom which leads to the patient seeking medical advice, although more subtle clues may have been present earlier [27]. Untreated, the progression of Parkinson's disease has been broken into five stages [28] (see also [27]):

Stage I The symptoms occur on one side, usually in an extremity. During Stage I, the disease is primarily an inconvenience. The median duration of illness at Stage I is about 3 years.

Stage II The disease spreads and becomes generalized. The site of onset remains most severely affected. The median duration of illness at Stage II is about 6 years [27].

> "In addition to tremor, rigidity and impaired mobility on the opposite side, during Stage II the posture may become mildly flexed with adduction of the limbs. Facial masking, monotonous and hypophonic speech, mild disturbance of gait, generalized slowness, decreased associated and spontaneous movement and easy fatigability usually begin to make an appearance. However, these signs are mild, and balance is still intact."

Stage III In this stage, "disequilibrium with impairment of balance and of postural and righting reflexes" occurs. The median duration of illness at Stage III is 7 years, but with wide variation.

Stage IV The patient begins to require help with everyday tasks such as walking, dressing, bathing and feeding. "The disease is fully developed, generalized and advanced." While other symptoms become worse, tremor may be less severe. The median duration of illness at Stage IV is 9 years with wide variation.

Stage V "The patient is severely disabled and confined to a wheelchair or bed unless aided." The median duration of illness at Stage V is 14 years.

The introduction of levodopa (L-DOPA) in the late 1960's marked a milestone in the treatment of Parkinson's disease, although the reasons for its effectiveness are not well understood [9]. Eighty-five percent of patients initially show clinically significant benefit [58] (see also [43, 62]). The effect is so noticeable that a response to it is often used as a diagnostic criteria for Parkinson's disease [26].

Unfortunately, according to Peppe *et al.* [58],

> "this salutary response generally does not last. Within a few years, the stable antiparkinsonian action of L-DOPA gives way to motor fluctuations of gradually increasing severity. In addition, abnormal involuntary movements, especially of the choreoform type, begin to spoil periods of peak drug efficacy [41]. It has been reported that two-thirds of parkinsonian patients develop one or both of these motor response complications within 6 years of L-DOPA initiation [71]."

Peppe *et al.* conclude that

> "motor response complications reflect alterations in striatal systems due to the loss of dopaminergic inputs and subsequent exposure to fluctuating dopamine levels as a result of intermittent L-DOPA administration."

At least three classes of abnormal involuntary movements can result from chronic levodopa therapy. These include choreoform movements (termed dyskinesia)[1], dystonia[2], and myoclonus[3] [37].

Dyskinesias are clearly related to the duration of high dosage levodopa therapy [36]. Boshes [3] reports finding dyskinesia in 37% of levodopa-treated patients at 6 months, in 66% of patients at 18 months, and in 70% of patients at 24 months.

Peak dosage dystonia occurs in about 10% of patients [36] (see also [55]).

Monoclonus also appears to be directly related to levodopa dosage and duration of treatment [36, 37].

Besides levodopa, another treatment for Parkinson's disease is stereotaxic surgery, which involves precisely locating structures in the brain for ablation. Stereotaxic surgery was common in the period from 1957 to 1972, but fell off sharply with the advent of levodopa [52]. This reflects the preference of patients and physicians for medication instead of surgery and the (relatively slight) risks involved in surgery.

Fahn [19] mentions that the stereotaxic thalamotomy of the 1950s and 1960s

> "was particularly effective for controlling tremor, somewhat effective for rigidity, and less so for bradykinesia. It probably had no effect on loss of postural reflexes.... The procedure did not slow progression of the disease, and elderly patients were prone to develop complications of stroke."

Stereotaxic techniques have continued to improve, however, becoming more selective and accurate, with minimal complications and side-effects [52].

A recent paper by Fahn [19] lists five directions for future treatments in Parkinson's disease:

---

[1] "A nervous condition marked by involuntary muscular twitching of the limbs or facial muscles" [78].

[2] "Impaired or disordered tonicity, esp. muscle tone" [78].

[3] "Twitching or clonic spasm of a muscle or group of muscles" [78].

Attempts to slow the progression of the disease This will proceed in two directions. The first is the investigation of trophic factors associated with the growth and nourishment of the dopaminergic nigrostriatal system. The second will look at oxidative stress, which has been proposed as a mechanism for dopaminergic neuronal death in Parkinson's disease.

Attempts to overcome complications from current therapies Particularly clinical response fluctuations associated with long-term L-DOPA usage.

Attempts to treat other neurotransmitter and chemical defects Some Parkinson's disease problems (for instance, freezing and loss of postural reflexes) do not respond to dopaminergic agents. These may be treatable with drugs acting on other neurotransmitter sites, although no such drugs are currently available.

Attempts to control symptoms by noncentral approaches Tremor may be treatable outside of the brain, by muscle injections.

Attempts to control symptoms and progression by surgical approaches In part due to problems with L-DOPA, thalamotomy is making something of a comeback, particularly for patients with intractable tremor. It may also be used to control L-DOPA-induced dyskinesias and to treat the "off" states, in which L-DOPA occasionally becomes ineffective. Two other types of surgery, stereotaxic ablative pallidotomy and surgical lesions of the subthalamic nucleus, also show promise. Fetal transplantation to provide more dopaminergic neurons is also being tried, but is very experimental.

It is also worth mentioning the recent isolation of "glial cell line-derived neurotrophic factor" (GDNF), which shows promise for keeping dopamine-producing cells alive [83], and research on the treatment of Parkinson's disease using magnetic fields [64].

2.3 Akinesia

While akinesia is the most disabling of the three primary manifestations of Parkinson's disease[4], it is poorly defined [12]. Taber's Cyclopedic Medical Dictionary defines it simply as "complete or partial loss of muscle movement" [78]. Other authors present similar definitions [32, 63, 42].

Delwaide and Gonce [12] and Imai *et al.* [31] provide more detailed lists of possible symptoms of akinesia: see Appendix C.

For the purposes of this thesis, the generic definition of akinesia as "difficulty initiating and maintaining motion" is sufficient.

2.4 Kinesia Paradoxa

The classic study on kinesia paradoxa, the ability of akinetic persons to move significantly more naturally in the presence of visual cues at their feet, is provided by Martin in 1967 [45]. Martin examined various configurations of objects such as blocks and tape to determine their effectiveness as visual cues. He concluded that:

> *Transverse lines* of almost any kind across his path are of some help to the average Parkinsonian patient, and almost the best effects are obtained from bold lines, an inch or more wide, and of a colour contrasting with that of the floor or ground. Thus white lines, one or two inches wide, and eighteen inches or so apart on a dark ground produce a pronounced, and sometimes dramatic, effect, enabling a patient who seemed unable to walk, or the shuffler on short steps, to step out strongly. It may be that *strips* of light-coloured cardboard or linoleum or merely paper are more effective, and certainly *obstacles* of the nature of pieces of wood, two or three inches high, or bricks, seem to produce the maximum effect. The influence of these stimuli may be a little greater indoors, where there are other visual points and lines of reference, than out on an open space.
>
> ...The patient may seem to be making an effort to step over the lines or obstacles, but without seeing them his voluntary effort is of no avail. Occasionally, if the patient is blindfolded, the memory of the obstacle will enable him to start, but more often this procedure fails.
>
> Usually the transverse line or obstacle is ineffective until the patient comes within stepping distance of it, i.e. so close that he can step over it.
>
> ...Zig-zag lines are less effective than transverse, and strips without contrast of colour are somewhat less effective than contrasting ones, though the difference is not great when the patient attends to them.
>
> ...A moving line, drawn along the ground in front of him, seemed to have no effect on one of our patients, and lines not on the ground

---

[4] Tremor, rigidity, and akinesia.

> (for example, on a suitably striped skirt), were also without effect. On the other hand there can be little doubt that the influence of a series of transverse lines or obstacles is at least one of the factors that enable so many Parkinsonian patients to mount stairs much better than they walk on the level.

A number of studies have also mentioned the effectiveness of an upturned walking stick in providing a cue for treating freezing episodes [15, 14, 20].

Other patients have used the trick of dropping paper balls to get started; for instances, Sacks [63] (p. 296) mentions that "Miss D."

> "had various ways of 'defreezing' herself if she chanced to freeze in her walking: she would carry in one hand a supply of minute paper balls of which she would now let one drop to the ground: its tiny whiteness immediately 'incited' or 'commanded' her to take a step, and thus allowed her to break loose from the freeze and resume her normal walking pattern... Such methods are discovered or devised by *all* gifted post-encephalitic and Parkinsonian patients, and I have learned more from such patients than from a library of volumes."

It should be mentioned that for ordinary Parkinson's disease, kinesia paradoxa possibly only occurs in the presence of levodopa therapy. Hardie [26] observes

> "The phenomenon of kinesia paradoxa evidently became increasingly rare as the number of postencephalitic Parkinsonian survivors[5] dwindled and it does not seem to be a feature of untreated Parkinson's disease. It was not until the advent of levodopa therapy and recognition of the remarkable 'on-off'[6] fluctuations with which it was associated that anything comparable was to be seen again."

Some of the research related to the underlying causes of kinesia paradoxa is discussed in Appendix C.

While the scope of this thesis has dictated a presentation of kinesia paradoxa strictly in terms of visual cuing, this is somewhat misleading. It seems that akinesia

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[5] Survivors of a viral epidemic active between 1916 and 1927.

[6] Fluctuations between akinetic and "normal" periods.

is related to losing the ability to sequence motor instructions internally; visual cues are one way of providing an external means of sequencing motor instructions. However, other means are also available: one is music. According to Sacks [63] (pp. 294–5),

> This power of music to integrate and cure, to liberate the Parkinsonian and give him freedom while it lasts ('You are the music/ while the music lasts', T.S. Eliot), is quite fundamental, and seen in every patient. This was shown beautifully, and discussed with great insight, by Edith T., a former music teacher. She said that she had become 'graceless' with the onset of Parkinsonism, that her movements had become 'wooden, mechanical — like a robot or doll', that she had lost her former 'naturalness' and 'musicalness'. Fortunately, she added, the disease was 'accompanied by its own cure'. We raised an eyebrow: 'Music,' she said, 'as I am unmusicked, I must be remusicked.' Often, she said, she would find herself 'frozen', utterly motionless, deprived of the power, the impulse, the *thought*, of any motion; she felt at such times 'like a still photo, a frozen frame'— a mere optical flat, without substance or life. In this state, this statelessness, this timeless irreality, she would remain, motionless-helpless, *until music came*: 'Songs, tunes I knew from years ago, catchy tunes, rhythmic tunes, the sort I loved to dance to.'
>
> With this sudden imagining of music, this coming of spontaneous inner music, the power of motion, action, would suddenly return, and the sense of substance and restored personality and reality; now, as she put it, she could 'dance out of the frame', the flat frozen visualness in which she was trapped, and move freely and gracefully: 'It was like suddenly remembering myself, my own living tune.' But then, just as suddenly, the inner music would cease, and with this all motion and actuality would vanish, and she would fall instantly, once again, into a Parkinsonian abyss.

Chapter 3

THE STUDY

3.1 Overview

As mentioned in the introduction, a new head-up display has recently been introduced by Virtual Vision, Inc. The VV Sport display subtends 15° vertically by 22° horizontally of the visual field for one eye. The rest of the visual field is unobstructed, except for a tinted, see-thru visor. The subjective impression is that the image in the display is "floating" out in front of the wearer at a distance of approximately ten feet (see Section 1.2).

Since the entire display can be worn like sunglasses and weighs only five ounces, the display itself is quite portable. The display takes NTSC format video input. Depending on how one chooses to provide the image (for instance, an 8mm videotape player), one can anticipate another couple of pounds for a beltpack (including a power supply for the VV Sport).

As pointed out to us by T.R., this display raises the possibility of a new method for treating akinesia: using the display to present a virtual image which would appear to be on the ground and which would be capable of producing kinesia paradoxa. If such a technique worked, it would provide the benefits of tangible cues, with the added advantage of portability and user control.

There are a number of basic questions which this technique raises, which were only partially addressed in this introductory work. These include:

- Is it possible to generate kinesia paradoxa using anything other than tangible objects?

- Assuming that a VV Sport display is used, should the display appear below the dominant or non-dominant eye?

- What are the field-of-view requirements? That is, how much of the patient's field-of-view does the image need to subtend, and where in the field-of-view does the image have to be?

- How important is spatial stabilization? That is, when the patient moves, how accurately do we need to shift the image so as to make it appear fixed at a given spot on the floor? Do we need a gait tracker to provide information on the patient's position, so as to adjust the image correctly?

- Does the image have to appear physically realistic? Are properties such as accurate shadows, perspective, and high resolution important?

- Is there something better than the VV Sport display for providing non-tangible visual cues? For comparison, we also tried a simple laser pointer which provides a dot image on the floor[1]. The laser pointer used was an Americraft^{TM} Tac Star^{TM}, model TSP 200. It has a two milliwatt power output and produces a red dot approximately an eighth of an inch in diameter.

The first phase of this study, conducted with one subject, was a rather informal attempt to explore the above issues. The second phase, conducted with a second subject, was intended to confirm our findings from the first phase. The second phase included a quantitative experiment conducted at the Biomechanics Laboratory in the University of Washington's Department of Rehabilitation Medicine.

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[1] As the study actually developed, we first used the laser pointer as an initiation cue, and only later as a full-fledged cue.

Chapter 4

METHODS

4.1 Overview

So far as we know, this study is the first to examine the application of head-up display technology to producing kinesia paradoxa. The primary focus, therefore, is on a qualitative exploration of the basic questions listed in Chapter 3. For this purpose, we tried as wide a range of trial conditions as we could, to get a general feel for the relevant factors, and let the results guide the unfolding of the study.

The range of stimuli fed into the VV Sport display are described in Subsection 5.1.1. Briefly, the stimuli consisted of computer animations, taped images, or a live fed from a video camera. The general idea was to provide images which moved down the screen at about the rate that the subject was walking, so as to give the impression that the image was at a fixed location on the floor.

We also ran a confirmation phase with a second subject in which we checked our conclusions. As part of that phase, we took quantitative gait measurements.

We anticipate that future studies will focus more specifically on factors addressed in a general way in this work.

The study can be seen as containing the following steps (these are described in more detail in Chapter 5).

- Exploratory Phase
  - Can virtual images provide ambulatory cues?
    - Use of actual objects in front of subject
    - Camera panning objects from above while subject walks over unobstructed floor, with camera feed to VV Sport display.
    - Pre-recorded objects played back to VV Sport display
    - Computer-generated objects played to VV Sport display
  - Field-of-view requirements

        - Determination of optimal vertical field-of-view
    - Initiating and sustaining cues
        - Use of playing card initial cue
        - Use of imaginary initial cue
        - Use of laser pointer for initial cue
    - Use of laser pointer for sustaining ambulation
    - Sustained ambulation without cues
- Confirmation phase
    - Qualitative
        - VV system with computer-generated cues
        - Laser pointer with sustained gait
    - Quantitative
        - No cues
        - Laser pointer
        - VV Sport display with no stimulus
        - VV Sport display with stimulus

4.2 Subjects

Two subjects participated in this study, T.R. and D.L. Both subjects were otherwise healthy men, aged 46 and 51 respectively, tested in an unmedicated state. In an unmedicated state and without visual cues, T.R.'s forward gait consisted of a 3–4 inch shuffle per step. His backward gait was somewhat freer. When presented with a row of dimes placed about a stride-length apart, however, he had discovered that he could walk freely or even run. A number of persons familiar with Parkinson's disease indicated that they had never before seen such a striking case of kinesia paradoxa.

D.L.'s unmedicated gait was much closer to normal, although subject to deterioration when required to count or talk, and prone to freezing in the presence of obstacles.

Both subjects have stronger symptoms on the left side.

The exploratory phase of this study was conducted with T.R. The confirmation phase was conducted with D.L.

4.3 Methods for Quantitative Experiment

The quantitative gait analysis, carried out as part of the confirmation phase, took place in the Biomechanics Laboratory at the Department of Rehabilitation Medicine, Health Sciences Building BB828 at the University of Washington. Reflective markers used as video camera targets were positioned over landmarks on the right pelvis and right lower extremities. The subject walked along a 30 foot walkway with a conductive surface which, when used in conjunction with conductive tape applied to the soles of both shoes, provided a gait event marker system for determining the spatial and temporal characteristics of gait. A videotape camera recorded the subject from the waist down. Data were taken at intervals of 40 milliseconds. For a more detailed description of the Biomechanics Laboratory, see Lehmann *et al.* [39].

Four treatment conditions were tried, in the following order: no visual cues (N), following a laser pointer spot (L), a VV Sport display with no image on (G), and a VV Sport display running a simple taped animation moving down the screen at the walking rate (V). One would expect condition G to provide the same or worse treatment value compared to condition N.

Eight trials were run for each condition. The order of the trials was not randomized; all of the trials for one condition were run before the next condition.

Due to the amount of manual labor involved in converting the raw data into analyzable form, only two of the eight trials were examined for each condition. The analyzed trials were chosen to provide uniformity across the four treatment conditions: the trials analyzed had the subject starting with the same foot and stepping on the force plate, instead of to one side of it.

The data analysis for each trial focused on a single representative stride (one step with each foot). The subject's right side, which had the reflective markers, is called the "affected" side (A); the other is called the "unaffected" side (U).

The data are organized around a series of events. The first is the heel strike of the affected side (AHS), followed by the toe strike of the affected side (ATS), the affected heel lifting off the ground (AHO), the unaffected heel striking the ground (UHS), the affected toe lifting off the ground (ATO), and finally the affected heel striking again

(AHS2), to complete the cycle.

The following data were gathered as a function of time: each of the above events; the affected knee angle; distance from the hip[1] to the floor; distance from the hip to the small toe[2]; and horizontal distance from the hip to the small toe.

Other derived data were stride length[3] and a plot comparing the time spent in each of four gait components for the affected and unaffected side. The plot gives one a measure of the symmetry of the subject's gait.

Unfortunately, data collection was centered around a force plate in the walkway which provided a very definite visual cue. It is to be expected that this reduced the apparent relative improvement for the treatment conditions by improving the "untreated" condition.

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[1] Greater trochanter.

[2] Metatarsal.

[3] A stride is one step with each foot.

Chapter 5

RESULTS

5.1 Results of Exploratory Phase

The exploratory phase was conducted at the HITL with T.R. as the subject. Our first task was to see whether virtual images would have any effect at all as ambulatory cues.

5.1.1 Can Virtual Images Provide Ambulatory Cues?

We began by using physical cues, to provide a basis for comparing the effectiveness of virtual cues. As mentioned in Section 4.2, T.R.'s unmedicated gait consists of a 3–4 inch shuffle per step.

As T.R. had indicated, placing a series of cards on the ground about 26 inches apart allowed him to walk with a normal stride length and speed, although he had to attend to the cues to do so.

The next step was to provide "real" cues indirectly through the VV Sport, instead of having T.R. see the cue directly. We trained a video camera on the row of cards, and fed the output from the video camera into the VV Sport. T.R. walked forward parallel to the cards, but with the cards out of his visual field. The video camera moved forward parallel to him, providing an indirect visual cue.

This technique produced moderately good initiation steps, but not smooth sustained ambulation. T.R. believed that the technique could have worked in principle. There were problems related to keeping a good synchronization between the motion and angle of the camera and T.R.'s motion and viewing angle.

T.R. and the HITL researchers had independently assembled collections of taped images to provide a range of test cues to be played back in the VV Sport. In addition, the HITL researchers and Virtual Vision collaborators wrote simple graphics animations, which ran on an Amiga 3000 and an IBM PC, respectively. These animations were fed live into the VV Sport.

The main advantage of the live animations was the ability to re-program them as the study proceeded. A second advantage of the Amiga 3000 was that we were able to use the output of a video camera as the background for the animation. This allowed us to test the effectiveness of matching the animation background to the floor as seen through the unobstructed part of the visor, rather than providing a black background.

The test images included film of an escalator approaching or receding, filmed movement over a tiled floor pattern, as well as static or dynamic computer animations. These animations consisted of a series of moving or static bars, grids, or flat squares. Some of the squares lay horizontally (with or without a shadow below), others vertically. We tried images with and without perspective, although we did not make an effort to precisely align the animation perspective with the real perspective the subject was seeing.

By setting the animated objects to move down the screen at about the rate that the subject was walking forward, we could give the impression that the object was at a fixed location on the floor. The animations were set to start over when they finished, thus providing a continuous visual cue.

For animations which are either a grid or which are moving in a plane, one wants the plane to correspond to the floor when the subject views the animation through the VV Sport display. Due to the angle of the subject's gaze, this means that viewed on the computer terminal the animation must appear to be coming out of the screen. We experimented with angles ranging from 0° to 35° out of the screen[1].

The static images turned out to be essentially useless (including those produced by T.R. himself). As T.R. stepped forward, the image would appear to move forward with him, destroying the "spatial illusion" of an obstacle to be stepped over.

The film of the escalator approaching perhaps would have been effective, except that it was moving too slowly. This again removed the sense of an obstacle at a fixed location in space. Another possibility is that the escalator provided too much context which was clearly inconsistent with what T.R. was seeing in the real world (the sides of the escalator, etc.).

Although filmed as a control case for the approaching escalator, we had some hopes that the receding escalator would fire a sort of "catching up" response, but it

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[1] Assuming the subject to be looking two to three paces forward, as is true for T.R. in sustained ambulation, the optimal angle is probably around 40°.

had no effect[2].

We got our best results with animations involving simple yellow squares moving down the screen at approximately the walking rate. We tried to arrange things so that two images were in view, about two and three steps ahead of the subject[3]. This produced a series of good initiation steps, but not sustained full-stride ambulation.

Our general impression from this portion of the study was that the single most important factor was maintaining the "spatial illusion" of an object in a fixed location ("space stabilized") which needed to be stepped over.

A realistic image which did not provide spatial stabilization could not produce kinesia paradoxa. By contrast, yellow squares moving down the screen at approximately the walking rate did produce kinesia paradoxa.

Fortunately, it turned out that the space stabilization did not need to be exact, at least to achieve the level of results observed. The animations used were moving at a fixed rate in a fixed direction down the screen. Inevitable head movements and walking speed variations prevent such a technique from achieving precise space stabilization [4]. Other than at the crude level described, we did not investigate how variations in the space stabilization precision affect the quality of the gait.

We created a number on animations on the Amiga 3000 which showed that T.R. was able to switch speeds by switching his attention between different stimuli moving concurrently at different speeds in the VV Sport display[5].

It seems likely that adding realism to a properly space stabilized image will make it more effective. However, the research described in this thesis did not pursue this factor.

Using the output from a video camera trained at the floor as the background for the animations appeared to be counter-productive. It reduced the contrast of the stimulus, when compared to using a simple black background.

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[2] This is interesting, since a superficially similar use of the laser pointer did work, as discussed below.

[3] As discussed in the next section, this appears to be the region in which T.R. is looking during sustained ambulation.

[4] Precise space stabilization could be achieved by using a gait tracker and possibly a head tracker to drive the animation.

[5] In a similar way, T.R. has indicated that when walking on a gravel road he can adjust his stride length by looking for cues at the desired stride length apart.

This portion of the study was mainly a search for factors which would "leap out" as being critical. Space stabilization did so. The other factor which "leaped out" was field-of-view, to be discussed in the next section. Factors which did not appear to be as crucial (but which will need to be looked at carefully in future research) include perspective, shadows, color, vertical versus horizontal aspect ratio of stimuli, and flat versus 3-dimensional cues. We tried presenting the display beneath both the dominant and non-dominant eye, without observing a dramatic difference. Oddly enough, the angle of moving animations relative to the plane of the ground did not seem to be crucial either[6].

5.1.2 Field-of-View and Cuing Requirements

As described above, our best results in the first portion of the study were a series of initiation steps, rather than smooth, sustained ambulation. As we had suspected would be the case ahead of time, the limited vertical field-of-view seemed to cause problems.

To determine the field-of-view requirements for initiating and sustaining ambulation, we went back to using a row of playing cards spaced about 26 inches apart, viewed directly. We used the visor of a welder's helmet to block off parts of the subject's field-of-view.

The region beyond three paces ahead does not seem to be required for initiating or sustaining ambulation, at least for normal indoor walking rates. As T.R. had indicated before arriving for the study, during initiation he looks for a cue at his feet. During sustained ambulation, he is looking at cues two to three paces forward. Blocking off the region beyond one pace forward did not prevent him from initiating. However, blocking off the region from the plane of his body up to one pace forward appeared to prevent him from sustaining ambulation. Apparently the peripherally-viewed cue in this region is important.

As mentioned previously, the vertical field-of-view of the VV Sport display is

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[6] One animation, running in the plane of the screen (and therefore appearing to be moving sharply into the ground as seen in the Virtual Vision display looking two to three paces forward), was nearly as effective as another animation running nearly parallel to the ground as seen under the same conditions. The difference in effectiveness appeared to be related more to the relative speeds than to the relative angles. The angle will probably be significant for sustained ambulation.

15°. The region from two to three paces forward subtends about 10°. Therefore, the VV Sport is adequate to provide the two fovealy-viewed cues needed for sustained ambulation. It is not, however, adequate to provide the peripherally-viewed cue at about one pace forward as well.

A second problem associated with the limited vertical field-of-view of the VV Sport display is the awkward transition from initiation to sustained ambulation. To initiate one has to tilt one's head forward, so that the VV Sport can provide a cue at one's feet. To sustain, one has to tilt one's head backward, to provide a cue two to three paces forward. This is a clumsy maneuver, which makes it difficult to reach sustained ambulation.

To deal with the second problem, we decided to use the VV Sport display only to sustain ambulation, while some other method was used to initiate. We experimented with three initiation methods.

The first method used was a physical playing card, placed at the subject's feet. This was the most reliable of the three methods, but also the least convenient.

The second method was to have T.R. imagine the squares in the VV Sport display continuing off the bottom of the display until they reached his feet, but without actually looking down to see them. He would step forward when he imagined the cue reaching his feet. This was more effective than using the VV Sport display for both initiating and sustaining ambulation, but was more difficult to maintain, perhaps because it involved a greater cognitive load.

The third method tried was to use the spot from the laser pointer for the initiating cue. This also worked, and was quite convenient.

5.1.3 Use of Laser Pointer for Sustaining Ambulation

We next looked at using the laser pointer alone to both initiate and sustain ambulation. As far as we know, no previous study has looked at this stimulus source as a cue for kinesia paradoxa.

T.R. was accustomed to stepping over visual cues. This poses two problems when used in conjunction with the laser pointer. The first is that when one steps on the spot, it will appear on top of one's foot, which destroys the illusion of an obstacle needing to be stepped over. At some inconvenience, this can be dealt with by turning the laser pointer off at the appropriate moment.

A more serious problem is that after one has stepped over the laser pointer spot one no longer has a visual cue in front of one. Consequently, one has to stop to redirect the laser pointer.

Under the guidance of one of the researchers (D.A.), T.R. learned to step *to* the laser pointer spot, rather than over it. This kept the laser pointer spot continually in front of him, and therefore allowed the smoothest gait we had seen to this point in the study with non-tangible cues[7].

A drawback of the laser pointer discovered at this point was that it is not visible outside in bright sunlight.

5.1.4 Sustained Ambulation Without Cues

After an hour or so of practice, T.R. was able to sustain ambulation without the laser spot, provided that he used the spot to initiate. After another hour or so, he could both initiate and sustain ambulation without visual cues. He could in fact walk with his eyes closed. This result came as a complete surprise to all present; nor do we know of a similar case in the literature.

This new skill was retained for two or three months after the trials, although it was very fragile, breaking down in the presence of distractions. At the time, T.R. was not able to explain what the cognitive changes were which allowed him to improve his gait, beyond the statement that it had something to do with concentrating on taking a big initial step. T.R.'s excellent account of his experiences during the trials can be found in Appendix A.

Unfortunately, the general progression of his disease removed his ability to walk without visual cues or by chasing the laser pointer spot. It did not, however, affect his response to physical cues, his ability to walk by stepping over the laser pointer spot, or his ability to respond to cues in the VV Sport display.

The underlying issues here are discussed more fully in Subsection 6.4.1.

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[7] While the observable results with the T.R. trials were better with the laser pointer than the VV Sport display, T.R. believes that the mode in which he is chasing the laser spot is fundamentally different cognitively from either stepping over tangible cues, stepping over the laser spot, or stepping over the apparent images in the VV Sport display. He believes that the VV Sport display is therapeutically far more significant than the laser pointer. This is discussed in Subsection 6.4.1.

5.2 Confirmation Phase

The confirmation phase, carried out with D.L., was aimed at replicating the basic results found in the trial with T.R. It was therefore both shorter and more focused. D.L.'s unmedicated gait was much better than T.R.'s, so the differences in the various treatment conditions were less dramatic.

5.2.1 Qualitative

Using an animation which had proved effective with T.R., we were able to increase D.L.'s stride length. Since D.L. was able to initiate without visual cues, we did not face the initiation issues discussed in Section 5.1.

In the D.L. trials, we discovered that an animation moving straight down the screen of the VV Sport display is not as useful when turning corners or walking in a circle as when walking in a straight line. This is to be expected, since when turning the image does not appear to be fixed on the ground.

Chasing the laser pointer produced observable results as good or better than those with the VV Sport display[8].

Switching the laser pointer on and off as D.L. walked was sufficient to cause him to switch instantly between a better and worse gait. For D.L., there was not a learning curve associated with the laser pointer, as there had been with T.R. Nor did his gait improve over time in the absence of cues. This may be related to the relative severity of T.R.'s akinesia.

5.2.2 Quantitative

As mentioned previously, D.L.'s gait improvement was not as dramatic as T.R.'s. However, since T.R. lives in another state and was not available for the quantitative part of the study, only D.L.'s gait performance was analyzed at the Biomechanics Laboratory.

D.L. reported feeling generally looser in treatment conditions L (laser pointer) and V (VV Sport with display on) than in either condition N (no treatment) or G (VV Sport with display off).

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[8] Again, the reader is referred to Subsection 6.4.1 for a comparision of the VV Sport display to the laser pointer.

The stride length and walking speed data are shown in Table 5.1. The uncertainty in the stride length is ±5 millimeters; the time uncertainty of the foot strike data, used in the walking speed calculations, is ±20 milliseconds.

Table 5.1: Stride Length and Walk Speed

	Length (m)		Speed (m/min)		Average Length (m)	Average Speed (m/min)
Condition	1	2	1	2		
N	1.214	1.179	75.9	73.7	1.197	74.8
L	1.267	1.332	76.0	79.9	1.300	78.0
G	1.123	1.234	62.4	66.1	1.124	64.3
V	1.284	1.268	71.3	76.1	1.276	73.7

Thus, the laser pointer provided an 8.2% improvement in average stride length over the control condition, for the trials analyzed. Stride length improvement of the VV Sport with the image on over the control average is more modest, at an average of 6.4%. Of course, the small size of the sample and the presence of the force plate cue force one to treat these data with caution.

Condition V, in which the image is displayed, represents a 13% increase in stride length over condition G, in which the image is not displayed. The relatively poor results for condition G compared to both V and the control (N) may reflect the effect of occluding part of the visual field. Another possibility is that a blank screen close to the eye is perceived as a wall, and that condition G is similar to an akinetic patient becoming “stuck” in a corner.

The walking speed data does not distinguish strongly between conditions N, L, and V. The relative slowness in condition G may be due to the reasons discussed in the preceding paragraph.

We also obtained data on the percentage of time spent in each of four parts of the gait cycle for each leg (see Table 5.2)[9]. This data allows one to look at the symmetry of the gait between the two legs. The four parts of the gait cycle examined are heel

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[9] Recall from Section 4.3 that the “affected” side is the side with the reflective markers (right side).

descending, heel pressing down on the ground, heel rising, and foot swinging forward. The data are averaged over the two trials analyzed for each condition.

Table 5.2: Gait Cycle

Condition		Descending	Down	Rising	Swinging
N	Affected	4%	37%	23%	36%
	Unaffected	7%	41%	17%	35%
L	Affected	4%	36%	22%	38%
	Unaffected	6%	36%	20%	38%
G	Affected	7%	38%	20%	35%
	Unaffected	8%	38%	20%	34%
V	Affected	7%	39%	17%	37%
	Unaffected	7%	41%	17%	35%

The least symmetric gait is seen in condition N, as one would suspect. Conditions L and V provide an improvement over N, although given the sample size one can say no more than that the data are suggestive.

It is surprising that the most symmetric gait is provided by condition G. This may be related to the shorter stride length and lower walking speed for this condition.

Overlaying the graphs of knee angle versus time, with the initial affected heel strikes lined up, does not reveal any substantial difference in that gait parameter for the four conditions. While the L and V conditions arguably produced a better straightening of the knee than condition N, the same is not true when compared to condition G.

The other time-dependent data similarly failed to distinguish among the four treatment conditions.

As we achieved the best results in the second and fourth treatment conditions, there does not seem to have been a systematic learning effect across quantitative trials.

Chapter 6

DISCUSSION

6.1 The Feasibility of Non-Tangible Cuing

As mentioned in Chapter 5, there is a difference between the requirements for initiating and sustaining ambulation. Initiating ambulation requires a single cue at the subject's feet; sustaining ambulation requires a series of cues stretching out in front of the subject.

It is clearly possible to produce initiation with non-tangible cues, using both a VV Sport display or a laser pointer[1].

As discussed in Subsection 6.3 below, the vertical field-of-view of the VV Sport did not seem to be adequate for smooth sustained ambulation in the trials with T.R. In these trials, the laser pointer seemed to result in a more sustained gait, in the absence of distractions. However, this result is difficult to interpret, since the laser pointer was used after the VV Sport, and T.R.'s gait changed dramatically over the course of the trials. We did not attempt to elict the behavior of stepping toward a distant stimulus using the VV Sport display.

D.L. could initiate and sustain ambulation without medication or visual cues, although with a shorter than normal stride length. Both the VV Sport display and the laser pointer resulted in an increased stride length.

6.2 Dominant Versus Non-Dominant Eye

The qualitative trials did not look carefully at the question of whether the VV images should be provided to the dominant or the non-dominant eye. We tried both eyes for both subject with positive results, but we don't have data on their relative effectiveness. One would prefer to use the non-dominant eye if possible, since it makes the display less intrusive. However, eye dominance effects may interact with field-of-view effects as the display evolves (see Subsection 6.3 below).

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[1] Both T.R. and D.L. bought laser pointers immediately after the trials.

A careful study will be necessary to tease apart the issues here, since one must also consider the fact that Parkinson's disease typically affects one side more strongly than the other. This may also play a role in determining the appropriate eye for image presentation.

6.3 Field of View Requirements

The results presented in Subsection 5.1.2 suggest that a longer vertical field-of-view for the VV Sport display is necessary, at least for more severely akinetic patients. Figure 6.1 indicates the suggested minimal extension to the field-of-view for the VV Sport. Since the minimal effective vertical field-of-view may be a function of ambulation speed (with more distant cues necessary to sustain running), the optimal design may be somewhat longer than that suggested in this frame.

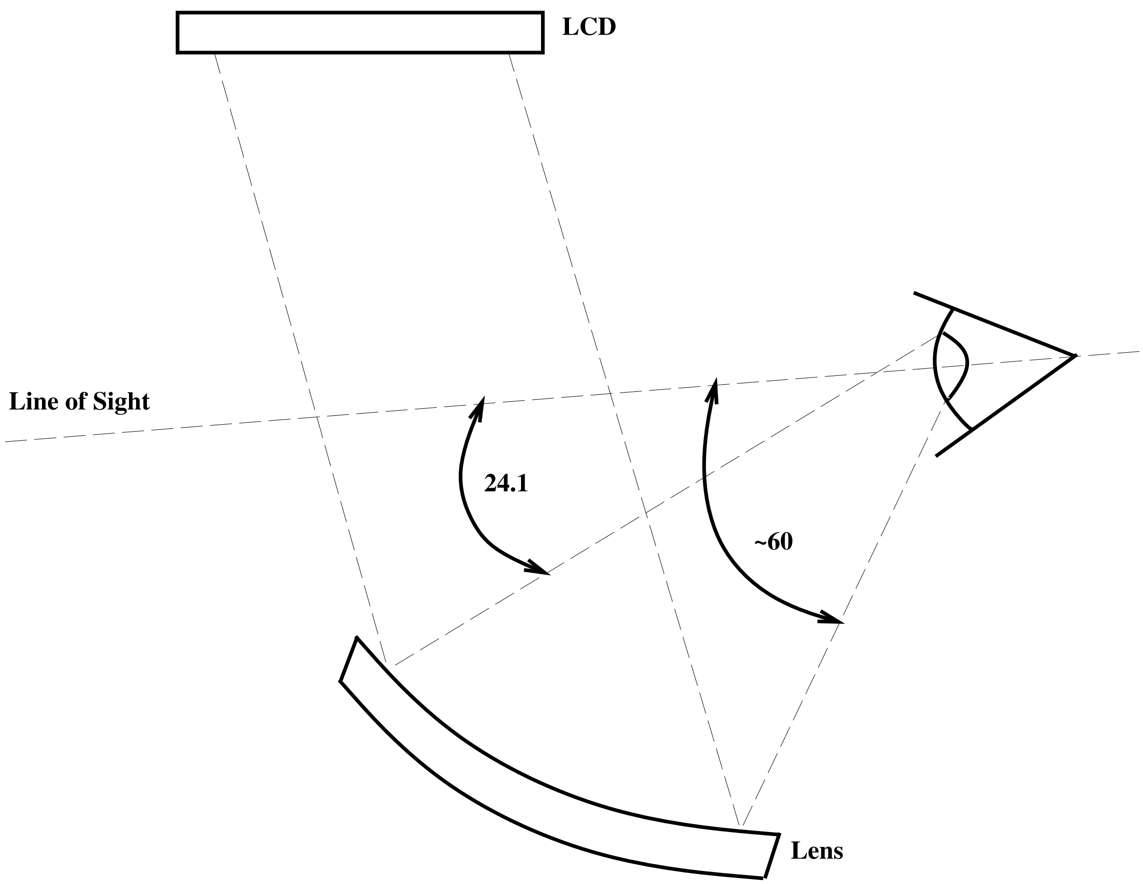
The possible advantage of a display which is wider, as well as longer, is discussed in Subsection 6.4.1.

6.4 Spatial Stabilization and Physical Realism

Spatial stabilization appears to be the single most critical factor for enabling kinesia paradoxa using the VV Sport display. It is necessary for the image to appear to be approximately stationary on the ground as the subject steps forward. Exact stabilization (for instance produced by using a gait tracker to control the rate at which images move down the display) was not attempted and fortunately does not seem to be essential, at least for the level of results achieved in this study. It is quite possible, however, that such precise space stabilization would produce better results than our approximate stabilization. We leave this for future research.

For T.R., at least, it is possible to switch speeds by attending to different stimuli in the VV Sport display. We did not try this experiment with D.L. By providing different stimuli concurrently, it may be possible to enable smooth transitions both between speeds and between directions.

Both T.R. and D.L. were able to improve their gait as a result of cues with a very crude appearance: simple squares or the spot of a laser pointer. This suggests that a highly realistic appearance is not crucial to kinesia paradoxa. However, actual playing cards remain a more effective (if less convenient) cue for both subjects than either



The suggested field-of-view for more severely akinetic patients. (Compare with Section 1.2.) 60° is an approximation: this is roughly the angle such that an image scrolling off the bottom of the display will appear at one's forward foot in peripheral vision while looking two to three paces ahead. The optimal angle needs to be determined by experiment.
Adapted (with permission) from Virtual Vision documentation.

Figure 6.1: Suggested Viewing Display Angles

the VV Sport or the laser pointer. It is to be expected, therefore, that improving the realism of non-tangible cues will increase therapeutic benefit, provided that spatial stabilization is not sacrificed.

6.4.1 Virtual Vision Display Compared to Laser Pointer

The results of this study suggest that the laser pointer produced an effect as good as or better than the VV Sport display. Given that the laser pointer is approximately ten times cheaper (roughly $100 vs. roughly $1000), lighter, and more convenient to carry around, that might seem to be the end of the story.

Things are not so simple, however, for four reasons. One factor is that we were clearly not using an ideal version of the VV Sport display, as discussed in Chapter 6. In particular, a longer field-of-view is needed, to provide peripheral cues. A wider field-of-view, to provide cues for moving smoothly in directions other than straight forward, might also be useful.

A second factor is that we almost certainly were not providing optimal cues in the VV Sport display. We have not systematically investigated what the stimulus parameters are. This is discussed more fully in Chapter 7. Furthermore, it should be possible to project much more realistic cues with the VV Sport display than are possible with the laser pointer. To the extent that more realistic cues are more effective, this provides a qualitative advantage to the VV Sport display.

A third factor is that the laser spot is not visible outside on a bright day, possibly making the VV Sport display a better outdoor solution[2].

The fourth and perhaps most interesting factor is T.R.'s perception that chasing the laser pointer spot works in a fundamentally different way cognitively than tangible cues, cues in the VV Sport display, or stepping over the laser spot, and that chasing the laser spot is fundamentally less robust and more prone to breakdown in the presence of distractions.

In Appendix C, research is presented which tentatively suggests that akinesia results from a breakdown of the brain's ability to smoothly step between the individual operations of a motor program. Visual cuing bypasses this problem by using external cues to step between operations in the motor program.

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[2] A laser spot which was clearly visible outside on a bright day might pose safety concerns.

The subjective difference between these two modalities is that the internal (noncuing) modality is unconscious, whereas the external modality requires conscious attention. The internal modality is better in that it does not require conscious attention, but for akinetic patients it is much more prone to breaking down in the presence of distractions, and also tends to degrade over time.

For T.R., unmedicated walking begins with an external cue. If he succeeds in sustaining ambulation, it becomes unconscious and internal; otherwise he needs external cues for each successive step.

T.R. claims that when he is chasing the laser spot he is operating in the unconscious modality. He is not thinking of the laser spot as an external cue; instead the spot has something to do with enabling him to maintain an adequate stride length, which seems to be essential for him to maintain unconscious ambulation. Therefore it is not surprising that using the laser pointer spot as a target to chase may break down in the presence of distractions, unlike the VV Sport display[3]. This suggests that a VV Sport display may be more suitable than the laser pointer for patients with relatively severe cases of akinesia.

As T.R.'s disease has progressed, he has lost the ability to ambulate by chasing the laser pointer spot, although tangible cues still work just as well as before and he can still use the laser pointer spot as a fixed cue to step over. This would tend to back T.R.'s claim that chasing the laser pointer spot is cognitively different from fixed cues, as provided either by real objects, the laser pointer fixated on a location, or space-stabilized images in the VV Sport display.

The trials with T.R. suggest that for more seriously akinetic patients, the current subtended vertical field-of-view of the VV Sport display is not sufficient. In addition, T.R. has suggested (Appendix A) that a modified VV Sport display covering the bottom half of the field-of-view for one eye might be more useful. This allows one to

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[3] As mentioned above, stepping over the laser spot does function as a robust external cue. However, this leads to two problems: one is that the spot appears on top of the foot, breaking the spatial illusion. This can be handled by turning the laser pointer off at the appropriate moment; in some ways this is less serious than the corresponding difficulty with the VV Sport display, in which one ideally has to make the image disappear as the foot passes over it. The second problem is that, unlike the VV Sport display, the laser pointer has to be redirected after each step, thus preventing smooth motion for seriously akinetic patients. Possibly this problem could be dealt with by developing a laser pointer with several dots which was waist-mounted and which swiveled appropriately as the patient walked.

present a range of cues covering a wide area, potentially allowing smooth motion in any direction, instead of merely straight forward.

Aside from engineering difficulties, a possible problem with such a large display is that by blocking more of the visual field, the display might interfere with the ability to perceive objects stereoscopically. This price may or may not be worth paying. T.R. agrees that a display which stretched from the straight-ahead viewing angle down to the bottom of the visor in a narrow strip would be more useful than the current arrangement, although it would not have the potential to allow smooth turning in any direction.

6.5 Shaping

A new question raised by the T.R. trials is whether the VV Sport display can be used as a rehabilitation tool, rather than simply as a prosthesis. In other words, is it possible to train akinetic patients to become less dependent on visual cues, through a process of slowly reducing the realism of the visual cues provided? This process would be an instance of what is known as "shaping" in the psychological literature [44].

It is not clear whether the experience of using the VV Sport display played an essential role in helping T.R. to learn new ambulatory skills, or whether he could have jumped directly to using the laser pointer. At the time, he thought that the VV Sport display might have been useful as an intermediate step which forced him to think more about the visual cues.

Viewed as a rehabilitation tool, therefore, the limited vertical field-of-view may be an advantage, in that it forces the subject to depend less on the external representation of the visual cues, and more on their imagined extrapolation beyond the display field.

6.6 Discussion of Quantitative Experiment

The quantitative study revealed an 8.2% increase in stride length using the laser pointer and a 6.4% improvement using the VV Sport display for the subject tested, based on two trials analyzed per condition.

The walkway used during the experiment contained a force plate which provided a very definite visual cue. It is reasonable to think that this improved the "untreated" case, resulting in a smaller improvement than would have been expected otherwise.

The subject, D.L., has typical Parkinson's disease symptoms with mild akinesia. Given that T.R. and D.L. both showed improvements in gait length using both the laser pointer or the VV Sport display, it is reasonable to believe that these results will generalize to other akinetic subjects. However, the percentage improvement is likely to vary considerably if other subjects are run. In particular, if we had done a quantitative study of T.R., the improvement from a festinating gait of 3-4 inches per step to a fairly normal initiation step would have been an order of magnitude larger than that seen for D.L.

The most important result of the quantitative study is that the apparent improvement in stride length seen in the qualitative studies can (within the limitations of a small sample size) be confirmed using rigorous measurement techniques.

6.7 Conclusions

For D.L., and presumably generally for patients with less severe akinesia, a laser pointer seems to be sufficient, at least for indoor situations. For more severe cases of akinesia, as discussed in Subsection 6.4.1, a modified VV Sport display may be more effective than a laser pointer.

Chapter 7

FUTURE RESEARCH

This study has demonstrated the effectiveness of both a laser pointer and the VV Sport display as a method for providing portable, non-tangible visual cues for akinetic patients. A comparison of their relative effectiveness and possible modifications can be found in Subsection 6.4.1. The results are sufficiently encouraging to justify a more extensive study.

The work done so far has demonstrated that non-tangible cues are capable of producing kinesia paradoxa, and has clarified some of the associated issues. A program of study should address at minimum the following questions:

Confounding factors Having run only two subjects to date, we know little about the variability of the effectiveness of different sorts of cues. Future quantitative studies will have to involve controlling more carefully for visual cues than was possible for the current study. For studies performed in the University of Washington's Biomechanics Laboratory, it should be possible to cover the force plate with a material which is both plain (to provide no visual cues) and conductive (so that foot strike information can be recorded). Either metalized mylar or wire screening over a formica^{TM} sheet would probably work.

Inter-subject variability Again because of the small sample size, we know very little about the affect of variables such as progressive state of the disease, age, etc.

Different hardware configurations As discussed in Chapter 6, a different design for the VV Sport display would probably have been more effective, in particular one with a longer vertical field-of-view. A laser pointer which projected multiple spots might also be advantageous.

Monocular display preference The question of whether the display should be presented below the dominant or non-dominant eye, and whether the decision is affected by which side is more affected by Parkinson's disease, needs to be investigated.

Visual cue stabilization The parameters of the visual cues presented in the head-up display need to be examined systematically. It seems clear that the most crucial issue is spatial stabilization, i.e., providing an image which appears to be fixed on the ground. However, we do not know how accurate this stabilization has to be, particularly across subjects. We produced approximate stabilization by choosing the rate at which images moved down the VV Sport display to approximate the walking rate of the subject. It is quite possible that more precise stabilization, driven by a gait tracker, would produce better results.

Visual cue realism We have not explored to what extent a more realistic appearance (images which look like real bricks, etc.) would improve the effectiveness of a space stabilized cue, nor whether images with an apparent depth would be significantly more effective than flat images. In the T.R. trials we tried horizontal and vertical polygons as well shadowed boxes, without noticing a difference, but did not look at these factors systematically.

Shaping The extent to which T.R.'s experience of learning new ambulatory skills can be replicated needs to be resolved with future trials.

A practical assistive device must deal with two issues: speed and direction determination; and graphics generation. We envision a product which could be strapped to one's waist and in which speed and direction could be controlled by dials or a joystick. Images could either be generated in real-time by a simple graphics unit, or else played back from a waist-mounted CD-ROM player. The images would be fed into the VV Sport display (or something similar).

Perhaps the most striking aspect of this research was that, quite by accident, we taught T.R. significant (if unfortunately short-lived) new ambulatory skills. The fundamental process may have been that we provided him with visual cues which were steadily less realistic, and as a result he gradually became less dependent on them.

It would seem that underlying this success is the plasticity of the human nervous system: while one cognitive technique for doing some task (in this case walking) may be most natural or obvious, other techniques are also possible. By gradually moving away from the current technique (in this case, relying on tangible visual cues) we are able to develop new techniques.

In general, one can imagine using virtual environments to gradually change a task which a subject can do into one which the subject cannot currently do. In the process, the subject may be able to learn a completely new way of tackling the problem. The potential for facilitating this type of shaping may turn out to be an important contribution of virtual environments to medicine.

GLOSSARY

Most of the medical definitions come from Taber [78].

ABLATE: To remove, especially by incision.

ACCOMMODATION: The adjustment of the eye for various distances whereby it is able to focus the image of an object on the retina by changing the curvature of the lens.

ADDUCTION: Movement of a limb or eye toward median plane of body or, in case of digits, toward axial line of a limb.

AKINESIA: Complete or partial loss of muscle movement.

ATHETOSIS: Slow, writhing movements of the fingers and hands, and sometimes of the toes.

BALLISM: Violent, flailing movements.

BASAL GANGLIA: Five large subcortical nuclei (the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra) involved with controlling movement.

BRADYKINESIA: Extreme slowness of movement.

BRAIN STEM: A joint term for the medulla oblongata, pons, and midbrain, which form a “stem” connecting the brain hemispheres to the spinal column.

CEREBELLUM: Modulates motions and takes part in motor learning.

CHOREA: A nervous condition marked by involuntary muscular twitching of the limbs or facial muscles.

CILIARY MUSCLE: Smooth muscle whose contraction allows the lens of the eye to assume a more spherical shape, thus accommodating for near vision.

CT: Computed tomography.

DOPAMINE: A neurotransmitter implicated in Parkinson’s disease.

DYSKINESIA: See chorea.

DYSTONIA: Impaired or disordered tonicity, esp. muscle tone.

FESTINATION: Abnormal and involuntary increase in speed of walking in an attempt to catch up with the displaced center of gravity due to the patient's leaning forward.

FIELD-OF-VIEW: That portion of space which the fixed eye can see.

FOVEA: The central part of the visual field, approximately a degree across, which provides the sharpest vision.

FREEZING: See akinesia.

GLOBUS PALLIDUS: One of the basal ganglia nuclei.

HEAD-UP DISPLAY: A head-up display is one in which information is viewed superimposed on the outside world (as by displaying on a windscreen or visor) so that the information can be read with the head erect and with the outside world always in the field of view [2].

HITL: Human Interface Technology Laboratory.

HMD: Head-mounted display.

HYPOTHALAMUS: Regulates autonomic, endocrine, and visceral functions.

KINESIA PARADOXA: Transient episodes of near-normal movement and of gait in particular in otherwise severely akinetic subjects [26].

LCD: Liquid crystal display.

L-DOPA: See levodopa.

LEVODOPA: A drug which has shown considerable effectiveness in treating Parkinson's disease. A form of a metabolic precursor of the natural neurotransmitter dopamine.

MEDULLA OBLONGATA: Lower part of the brain stem, controlling automatic functions such as digestion and breathing.

MICROGRAPHIA: A disorder in which a subject can begin writing normally, but in which the writing becomes increasingly small as the subject progresses.

MIDBRAIN: Connects the pons and cerebellum with the brain hemispheres. Controls various motor and sensory functions.

MRI: Magnetic resonance imaging.

MYOCLONUS: Twitching or clonic spasm of a muscle or group of muscles.

NIGROSTRIATAL: Concerning a bundle of nerve fibers that connect the substantia nigra of the brain to the corpus striatum.

NTSC: A video signal standard established by the National Television Standards Committee.

ON-OFF PHENOMENON: Changes in medical effect associated with varying levels of levodopa in the bloodstream.

OXIDATIVE STRESS: Overactivity of some biochemical pathway producing an excess of free radicals which react with and gradually destroy neurons.

PARKINSON'S DISEASE: A chronic nervous disease characterized by a fine, slowly spreading tremor, muscular weakness and rigidity, and a peculiar gait.

PONS: Connects the medulla oblongata and cerebellum to the upper portions of the brain.

POSTENCEPHALITIC PARKINSON'S DISEASE: A form of Parkinson's disease which can be particularly potent and which can strike all age groups, caused by a viral infection. Epidemic between 1916 and 1927.

RIGIDITY: tenseness; immovability; stiffness; inability to bend or be bent [78].

SPACE STABILIZATION: The illusion that a virtual object has a fixed location in space.

SPINAL CORD: Center for reflex action, routing station for all nerves to the trunk and limbs.

STEREOPSIS: Vision in which things have the appearance of solidity and relief as though seen in three dimensions, due to retinal disparity of images to the eyes.

STEREOTAXIS: A method of precisely locating areas in the brain; use of this technique is essential in certain neurosurgical procedures.

STRIATUM: Joint term for the caudate nucleus and putamen, which together form the input portion of the basal ganglia.

SUBSTANTIA NIGRA: One of the basal ganglia nuclei.

SUBTHALAMIC NUCLEUS: One of the basal ganglia nuclei.

THALAMUS: Receives all sensory input except olfactory. Serves as the interface from the rest of the central nervous system to the cerebral cortex.

TREMORS: Rhythmic, involuntary, oscillatory movements.

TROPHIC: Concerned with nourishment. Applied particularly to a type of efferent nerves believed to control the growth and nourishment of the parts they innervate.

VIRTUAL ENVIRONMENTS: displays which attempt to present information in ways which are natural or intuitive to human users. Usually space-stabilized relative to the axis of orientation.

VV: Virtual Vision^{TM}, Inc.

VIRTUAL VISION^{TM}, INC.: A company started in 1992 which markets the Virtual Vision Sport^{TM}.

VIRTUAL VISION SPORT^{TM}: A head-mounted display consisting of a lens reflecting an LCD display mounted on a visor. The lens is mounted 24° below the line of sight of one eye and occludes 15° vertically by 22° horizontally of the visual field.

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Appendix A

T.R.'S SUMMARY

In a letter to Suzanne Weghorst dated May 20th, 1993, T.R. provided us with his impression of his trials with the VV Sport display and laser pointer.

> I thought I would just give you my impressions of my two days at your facility. I have purchased a laser light and have been practicing my new skills. Currently I am about at the same point as when you last saw me.
>
> Prior to visiting the HIT lab my chief complaint was akinesia while unmedicated or during frequent off periods. I was almost completely immobile in this state relative to ambulation. I could take slight festinating steps of 3 – 4 inch length. I believe the experience at HIT has enabled me to "learn" new motor skills which hopefully will continue to grow as I exercise them. Currently my unmedicated ambulatory skills are as follows. About 80% of the time I can initiate ambulation via conscious effort by targeting a spot that forces me to extend my stride length beyond its normal range. After that I can establish a steady cruising gait about 60% of the time. I can maintain that gait, intermittently, on an unconscious, automatic level which shifts to a conscious level when external stimuli invade such as approaching obstacles or turns in direction. This ambulation breaks down frequently as a result of external stimuli and has to be re-established. It is also difficult to initiate in an obstructive (e.g. a doorway or a short hallway) environment. Acceleration and deceleration is also disruptive. It seems that changes in speed are best accomplished by slowing down the speed of the stride without shortening its length.
>
> Ambulation with tangible cues (or presumably virtual images of tangible cues) is still easier, and more reliable. A grid of playing cards spaced 26–28 inches apart allows me omnidirectional ambulation with ease albeit on a conscious level. This type of cued ambulation is much less fragile relative to external stimuli and consequently allows easier navigation around

obstacles. However, the necessity to remain in the fully conscious mode is a drawback. Any significant inattention to the cue results in breakdown of ambulation.

In a telephone conversation with Dr. Carolyn Tanner of the Calif. Parkinson's Research Center (who has done extensive research on P.D.), she expressed her opinion that the above findings, if valid, were unique and qualitatively different. She was very interested to learn more about the VV glasses.

training stages:

1. real world visual cues (playing cards)

2. VV glasses with various scrolling images

3. VV glasses with scrolling images plus real world static initiating cue

4. as in step #2 but with mental extrapolation of scrolling image to provide initiating cue

5. laser light pen as static initiating cue

6. laser light pen as kinetic initiating cue (scrolling the target to my feet)

7. chasing the light pen spot (target is about 26-28 inches in front of feet)

8. #7 but turning off the light pen after gait is established

9. unassisted ambulation conscious attention to stride length

10. #9 with periods of automatic gait

11. ? total automatic gait (as yet unattainable)

In spite of my apparent progress ambulation remains extremely vulnerable to external stimuli and thus breaks down frequently. I have great difficulty inside my home, negotiating around tight corners and kitchen chairs. However, yesterday at the local high school track I was able to walk and then run a 1/4 mile without difficulty. Even full sprinting was possible. Visual cue walking remains significantly superior relative to initiating and sustaining gait, and ignoring external stimuli. If these limitations cannot be overcome by practice, then I believe the Virtual Vision glasses are by far the best option for trying to deal with this problem.

> The following are a couple of suggestions as to what I believe would make the Virtual Vision glasses effective.
>
> **1.** the screen must superimpose over the entire southern hemisphere of the field of vision
>
> **2.** "objects" should be spaced at simulated stride length in the foreground
>
> **3.** as a substitute for a scrolling image, a stroboscopic on/off effect might be effective.
>
> Thank you again for all your efforts on my behalf.

At the time he wrote the above letter, he felt that he had learned something fundamentally new. He thinks now that it was more a working out of a latent potential, which he could have achieved in some other way.

Unfortunately, while T.R.'s new ambulatory skills lasted for a couple of months, they seem to have been removed by the general advance of his disease. Despite the advance in severity of his akinesia, however, the strong visual cuing effect remains intact. This is to be expected if one accepts the theory that visual cues bypass the basal ganglia (see Appendix C).

T.R.'s suggestions regarding an improved VV Sport display for prosthetic purposes are discussed in Subsection 6.4.1.

Appendix B

MEDICINE AND VIRTUAL ENVIRONMENTS

B.1 Overview

This appendix briefly reviews developments in the medical applications of virtual environments technology. While it puts the research described in this thesis in context, this appendix is independent of the rest of the text.

There is considerable disagreement over what should and should not be covered by the term "virtual environments." A definition in terms of interface considerations might be based on interactive three-dimensional displays, whether visual, aural, tactile, force-feedback, or some combination of the above.

Another definition, coming from a psychological viewpoint, centers around the idea of "presence": a virtual environment is one which substantially convinces the participant that he/she is "in" the environment being presented.

More difficult than defining what virtual environments are is defining what they are not. The term usually excludes interactive, screen-based computer graphics with a 2-D mouse. But what about the above with a 3-D mouse? Or a workstation which provides a 3-D display using (for instance) shutter-glasses, but which provides only a limited range of movement? What about virtual objects overlaid on a natural scene?

As with any definition, the goal should be to define the term in such a way as to include a significant self-related body of thought and work, while excluding unrelated or tangentially related material. For the purposes of this appendix, it seems best to use a loose definition in terms of intent: "virtual environments" are displays which attempt to present information in ways which are natural or intuitive to human users, and which make use of natural human sensory and interaction modalities.

Thus, we do not arbitrarily include or exclude traditional interactive computer graphics from this definition; but graphical displays which are truly 3-D and which have 3-D interaction devices are in terms of the above definition "better" virtual environments, in that they come closer to natural human sensory and interaction modalities.

As a practical matter, ordinary computer graphics as applied to medicine will not be discussed in this appendix, simply because the topic is too huge to be treated well in a limited amount of space. Instead, the focus is on "true" 3-D displays and interactions.

While a great deal of work has been done on the application of virtual environments to medical problems [61, 50, 59], most is of a preliminary nature.

One possible breakdown of medical applications of virtual environments is into visualization (or, more generally, sensing) tools, simulation tools (either for training or pre-operative planning), and assistive technology tools. Visualization tools are systems which attempt to provide medical data in a readily understandable way. Simulation tools are aimed at teaching procedures, most commonly (at present) surgical procedures. Visualization and simulation tools are intended primarily for the care-giver; by contrast, assistive technology tools attempt to provide new abilities to clinical patients.

Current computing limitations force a trade-off between level of detail and level of interaction. Visualization tools tend towards a very high level of detail but not necessarily much interaction, whereas simulators tend to emphasize interactivity at the expense of detail.

We will consider each of the three areas below. In terms of the above division, the work described in this thesis falls into "assistive technologies".

B.2 Visualization Tools

One area in which 3-D interactive displays are making inroads is minimally invasive or "key-hole" surgery [80, 11, 61]. This surgery relies on inserting (for instance) light through one small hole in the body, a telescope through a second, and surgical tools through a third. By minimizing the amount of tissue cut, this form of surgery reduces the trauma done to the patient during surgery. Minimally invasive surgery was introduced in 1987; by 1992 it was used for about 85% of gallbladder operations performed in the United States [16]. A problem has been that the surgeon is typically provided with only a two-dimensional display, whereas operative procedures take place in three dimensions. At least four companies are competing to provide the third dimension: International Telepresence in Vancouver, Canada, American Surgical in Boston, U.S.A., Storz in Tuttlingen, Germany, and Wolf in Knittlingen, Germany [16]. International Telepresence provides the third dimension by looking through a single lens from different angles; the other three companies use two lenses.

Latent Image [22] has a process for converting 2-D images to 3-D images for tasks such as processing diagnostic images and medical illustration and training. The process involves performing a parallax shift of the image and then "patching" missing information, using either other images of the same objects or human intervention. As with synthesizing color from black-and-white pictures, the result is not necessarily accurate, but is useful for some tasks.

The Mayo Clinic has developed COMPASS^{TM}, a stereotactic computer interactive robotic technology which allows CT and MRI based volumetric tumor resection [34].

Integrated Surgical Systems [56] has been developing a system which combines computer-based medical imaging and CAD/CAM for hip replacement operations using image-guided robotics. In a preliminary phase, the surgeon inserts three locator pins into the patient which act as markers to define a bone coordinate system. CT scans are used for preoperative planning. The surgery is planned by manipulating 3-D images of the femur and the implant. During surgery, the robot uses the locator pins to convert the planned operation into an actual operation.

The University of North Carolina has composited live camera video images with ultrasound images transformed to correspond to the viewer's current position. The effect is an image which appears stationary inside a patient as the observer changes position [1].

Several organizations are building detailed three-dimensional models of the human body. In the short-term, these models fall under the category of visualization tools, because they tend to be too huge for affordable computational engines to support at useful levels of interaction. As computational prices continue to fall, however, it is to be expected that a wide range of simulators will be built using these models.

The United States National Library of Medicine has underway the Visible Human Project [75], which aims to be the most comprehensive digital record of the entire human body ever assembled, stored at millimeter resolution. The project will make use of data from CT, MRI, and photographs of millimeter-thick slices.

The University of Texas Medical Branch at Galveston (UTMB) and Lincom Corporation are developing an anatomical virtual environment which is intended to enable medical students and surgeons to emerse themselves within a specific region of the human body [57]. This is viewed as a first step towards a simulator for complex, high-risk surgical procedures. Currently, the system uses the Marching Cubes algorithm on CT and MRI scans to create a polygonal representation[1]. Since current workstations cannot manipulate these images in real-time, they are stored on laser disks which can be sequenced to provide stereoscopic images.

The Digital Anatomist Program at the University of Washington's Department of Biological Structure has been developing a digital model of the human body for over ten years [76, 5, 4, 17, 47, 48, 60, 74]. This project has taken a labor-intensive approach to developing 3-D anatomical models. Beginning with 2D tissue sections, contours are hand-digitized by anatomists, then combined by computer into 3-D shapes which can be displayed as computer graphics. As opposed to "raw" CT or MRI pictures, the result is that the computer has a detailed knowledge of where the anatomically significant boundaries are. This process has been colorfully described by the departmental chair as "teaching a computer anatomy"[2].

The Vesalius Project at Colorado State University [46] is similar to the Digital Anatomist Program.

Stanford's Electric Cadaver [85] is a Hypercard program on the Apple Macintosh that uses the Bassett slide collection of photographs of anatomic dissections, plus line drawings as the main image source for learning about anatomy. It does not contain 3D images or animations.

B.3 Simulation Tools

A number of groups are working on environments for simulating surgical procedures [68, 67, 65]. These environments provide (at this stage) a crude computational patient model, together with more-or-less realistic instruments for manipulating the environment. Realistic simulations will depend on the development of faster computational engines as well as better input and display devices.

Ixion markets training devices for endoscopic surgery [29]. The set-up consists of a combination of "videographics" (stored video sequences) with endoscopic instruments

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[1] A "polygonal representation" represents an object as one or more 2-D surfaces built up out of polygons. By contrast, a "voxel representation" consists of a set of 3-D components.

[2] In the interest of openness and avoiding confusion, I should mention that my father John and brother Jeff are both members of the Digital Anatomist Program.

operating with force-feedback inside a manikin.

Dartmouth [10] has been developing a finite-element model of skeletal muscle than simulates the non-linear force characteristics of skeletal muscle. The ultimate goal is to create a computational model of the entire patient.

The Silas B. Hays Army Hospital [66] has developed a primitive surgical simulator for the abdomen, using 3-7,000 polygons with no tactile display or force feedback.

Ian Hunter of McGill University is reportedly developing an excellent eye surgery simulator [30], although the details have not yet been published.

B.4 Assistive Technology Tools

Greenleaf Medical Systems has been using the DataGlove^{TM} and DataSuit^{TM}, originally developed by VPL Research, for measuring human motion. These devices measure changes in the light flowing through fiber optic cables to record movements in 3-D. Application development areas include measuring upper-extremity motion (useful, for instance, for studying Repetitive Strain Injury), allowing physically impaired individuals to perform complex actions by interpreting and converting simple hand gestures, and as a communication device linked to a voice synthesis system [25, 24, 23].

The Rehabilitation Service of San Raffaele Hospital, in Milan, Italy is using virtual environments to address the problem of patients who have difficulty maintaining a sense of balance. The sense of balance results from information gathered from three sensory systems: visual, labyrinthic (inner ear) and proprioceptive (awareness of posture). Patients suffering from ataxia may have poor proprioceptive cues; in this case, they may become over-dependent on visual cues for maintaining balance. This is unfortunate, since visual cues do not carry full-body information, and because reaction to visual information is relatively slow (upwards of 100 milliseconds). The Rehabilitation Service is investigating the possibility of training patients to be less dependent on visual cues by supplying "bad" visual cues in a virtual environment [50, 51].

Stanford University [38, 50] has been working on a "Talking Glove" which will convert hand movements by the non-vocal into speech-synthesized spoken words.

Burdea *et al.* [7] report on using a force-feedback glove to aid therapists in measuring hand motions. Similar work is reported on by Warner [82], although without force feedback.

Appendix C

MEDICAL BACKGROUND

C.1 General Brain Anatomy

The central nervous system is broken into six main components [32]:

Spinal cord Center for reflex action, routing station for all nerves to the trunk and limbs.

Medulla oblongata Controls automatic functions such as digestion and breathing.

Pons and Cerebellum The pons conveys movement information from the cerebral hemispheres to the cerebellum; the cerebellum modulates motions and takes part in motor learning.

Midbrain Controls various sensory and motor functions.

Diencephalon Contains the thalamus and the hypothalamus. The thalamus is the interface from the rest of the central nervous system to the cerebral cortex; the hypothalamus regulates autonomic, endocrine, and visceral function.

Cerebral hemispheres Contains the cerebral cortex, the basal ganglia, the hippocampus, and the amygdaloid nucleus. The basal ganglia are involved with motor performance; the hippocampus, with memory; and the amygdaloid nucleus with autonomic and endocrine responses as they relate to emotional states.

The medulla oblongata, the pons, and the midbrain, which form a “stem” connecting the brain hemispheres to the spinal column, are often lumped together under the term “brain stem” [78].

C.2 Motor Control Overview

Motor control occurs in a three-level hierarchy. The spinal cord is the most primitive, controlling reflex and stereotypical actions. Integration of sensory and vestibular information occurs in the brain stem, which controls posture, eye, and head motions. The apex of the motor hierarchy is the cerebral cortex, in particular the primary motor cortex, the lateral premotor area, and the supplementary motor area.

It appears that the supplementary motor area is concerned with programming sequences of movements, whereas the the premotor area is concerned with the selection of movement plans based on external cues [6].

Motor activity is also modified by the cerebellum and basal ganglia.

Both the cerebellum and the basal ganglia receive input from the cerebral cortex and send output to the cortex via the thalamus. According to Kandel *et al.* [32], the three major differences between the connections of the cerebellum and the basal ganglia are:

- The cerebellum receives input only from the sensorimotor parts of the cortex, whereas the basal ganglia receive input from the entire cerebral cortex.

- The cerebellum output goes only to the premotor and motor cortex, while the basal ganglia also project to the prefrontal association cortex.

- The cerebellum has direct ties with the spinal cord and the brain stem. The basal ganglia have little connection to the brainstem, and no direct connections with the spinal cord.

The cerebellum apparently modifies the output of motor systems to bring intention into line with performance; it acts as a comparator. It has been suggested that the cerebellum is a very large associative memory [33].

It is thought that the cerebellum regulates motion directly, whereas the basal ganglia have to do with the planning and execution of complicated motor strategies.

C.3 The Basal Ganglia

The basal ganglia are defined operationally as a set of structures whose damage causes similar sorts of motion disorders [53]: in particular, involuntary movements, muscular rigidity, and immobility without paralysis [32]. The basal ganglia are usually taken to include the caudate nucleus and putamen (jointly termed the neostriatum or striatum), the globus pallidus (or pallidum), the subthalamic nucleus, and the substantia nigra.

C.4 Basal Ganglia Components and Pathways

The striatum serves as the input center for the basal ganglia. The primary input comes from the cerebral cortex; there is a secondary input from the thalamus. Specific areas of the cortex map to specific parts of the striatum. These associations are maintained in projections throughout the basal ganglia.

The globus pallidus is broken into internal and external segments. The internal section is one of two main output nuclei of the basal ganglia, along with the substantia nigra pars reticulata [84]. The pallidal output is passed by the thalamus primarily to the supplementary motor area, and possibly also to the premotor cortex [6]. The supplementary motor area is also a major input to the basal ganglia; therefore there is a loop between the supplementary motor area and the basal ganglia.

As mentioned earlier, it appears that the supplementary motor area is involved with planning sequences of movements. The loop between the supplementary motor area and the basal ganglia therefore provides a clue to the function of the basal ganglia.

The external section of the globulus pallidus passes information within the basal ganglia, in particular to the subthalamic nucleus.

The subthalamic nucleus takes the output from the motor and premotor cortices, and from the the external segment of the globus pallidus. The subthalamic nucleus projects to both segments of the globus pallidus and to the substantia nigra pars reticulata.

The substantia nigra, along with the internal globus pallidus, is one of the two major output sections of the basal ganglia.

There are two major pathways through the basal ganglia, arising from different cellular populations of the putamen. The inhibitory direct pathway projects monosynaptically from the putamen to the motor regions of the internal globus pallidus and the substantia nigra pars reniculata [84].

The indirect pathway is inhibitory from the putamen to the external globus pallidus, inhibitory from there to the subthalamic nucleus, and excitatory to the external globus pallidus or substantia nigra pars reticulata.

It appears that the net affect of the direct pathway is to facilitate motion by exciting the supplementary motor area; the indirect pathway has the opposite effect [32].

In addition (and crucially for Parkinson's disease), there is a loop from the striatum to the substantia nigra pars compacta and back to the striatum. The return route is mediated by dopamine. Dopamine excites the direct pathway and inhibits the indirect pathway: since these two pathways have opposing effects, dopamine tends to facilitate motion. In effect, "the dopamine terminals are in a position to 'gate' the influence from cortex" [73].

There are also reciprocal inhibitory connections between the internal and external globus pallidus.

The major output of the basal ganglia, from the internal globus pallidus and the substantia nigra pars reticlata, project to three nuclei in the thalamus: the ventral lateral, ventral anterior, and mediodorsal. These thalamic nuclei in turn project to the prefrontal cortex, the premotor cortex, the supplementary motor area, and the motor cortex [32].

From an input-output analysis, therefore, the basal ganglia do not appear to generate motions directly; they take input from the cortex, modify it in some way, and pass it back to the cortex (via the thalamus).

C.5 Diseases of the Basal Ganglia

As with brain research generally, much of what is known about the basal ganglia comes from studying diseases which affect them. This section briefly outlines the range of diseases which are caused by damage to the basal ganglia.

Damage to both the basal ganglia and the supplementary motor area are correlated with impaired performance on sequential tasks [6].

The "theme" of diseases affecting the basal ganglia appears to be that the balance between the two major pathways is disturbed: the result is either involuntary movements or impairments to motion.

According to Kandel *et al.* [32], the impaired motions include "lack of movement (akinesia), slowness of movement (bradykinesia), and the shuffling gait of Parkinson's disease."

The list of involuntary movements includes

> *tremors* (rhythmic, involuntary, oscillatory movements), *athetosis* (slow, writhing movements of the fingers and hands, and sometimes of the toes), *chorea* (abrupt movements of the limbs and facial muscles), *ballism* (violent, flailing movements), and *dystonia* (a persistent posture of a body part which can result in grotesque movements and distorted positions of the body).

The major diseases of the basal ganglia are [32]:

Parkinson's disease is related to a reduction of dopamine in the brain and damage to the dopaminergic pathway from the substantia nigra to the striatum. The result is an increased output of the basal ganglia to the thalamus. The major symptoms are tremor, rigidity, and akinesia.

Huntington's disease is caused by a loss of specific striatal neurons. The result is a decreased output of the basal ganglia to the thalamus (as opposed to the increased output due to Parkinson's). As one might expect from their opposing neural behavior, Huntington's disease results in hyperkineticity, the opposite of the hypokineticity of PD.

Ballism is tied to damage to the subthalamic nucleus. It causes severe involuntary movements, which tend to slowly diminish.

Tardive dyskinesia is related to changes in the dopaminergic receptors, causing hypersensitivity to dopamine. It causes abnormal involuntary movements, particularly of the face and tongue.

C.6 Basal Ganglia Functionality

In discussing the precise functionality of the basal ganglia (which is still very much a matter for debate), it is worthwhile to introduce the idea of a motor plan. A motor plan "represents an action requiring the sequential operation of simple motor acts (or motor programs)" [6]. It seems to be generally agreed that the basal ganglia have something to do with the creation and/or execution of motor plans.

Kandel *et al.* [32] propose that the basal ganglia

- facilitate some motions, and suppress others, or
- compare motor commands with feedback from the evolving motion, or
- are involved with the initiation of internally generated movements.

As they point out, the third possibility is consistent with the difficulty persons with Parkinson's disease have in initiating motion.

Similarly, a recent paper by Kimura *et al.* [35] mentions three models for basal ganglia function in the literature.

- Denny-Brown and Yanagisawa's model [13], which posits that the basal ganglia are a "clearing-house", facilitating some cortical input while suppressing the rest.
- Marsden's model [42], that the basal ganglia handle automatic execution of learned motor programs.
- Miller and DeLong's model [49], that the basal ganglia have a motor command monitoring function.

Steg and Johnels [73] suggest that the basal ganglia are a sort of "auto-pilot":

> the basal ganglia may be regarded as the autopilot controlling on a subconscious level the coordination in a distributed computer system built up by different motor programs, and by this activity gives the environmentally well-informed pilot, the cortex, optimal conditions for integrating information and selecting the target for direct, precise, and well-prepared actions undisturbed by a multitude of internal control functions.

C.7 Recent Studies of the Basal Ganglia

A number of recent studies have investigated the range of basal ganglia motor control function. For instance, Kimura *et al.* [35] probed the striatal neurons of monkeys performing arm motion tasks, concluding that

> The majority of the striatal neurons showed activity when a particular sensory stimulus was linked to a conditioned movement or when the movement was performed in a particular context (e.g., sensorially guided or internally guided). This activity profile of striatal neurons is in strong contrast to that of pyramidal tract cells in the primary motor cortex, which show strong dependence on parameters of movement such as torque or direction [18]. Striatal neuron activity has been demonstrated to be only poorly related to parameters of movement [49].

This supports the viewpoint that the basal ganglia are tied in with the planning or sequencing of motor activities, rather than with the details of their execution.

Another study points to the relation between basal ganglia damage and rhythmic motion. Rhythmic motions can be either voluntary or involuntary (tremor). Both have characteristic frequencies, with involuntary rythmic motion being the upper bound on the speed of voluntary rhythmic motion [21]. According to Freund and Hefter [21], basal ganglia disorders affect "involuntary and voluntary alternating movements in different motor subsystems to the same extent." There is also a loss of frequency modulation for higher frequencies, known as "hastening." "At higher frequencies the patient is clamped to a particular higher frequency that actually corresponds to his/her tremor frequency [40]." Freund and Hefter conclude that "The data thus support the view that basal ganglia and the cerebellum are important for setting CPG [central pattern generator] characteristic frequencies."

Brotchie *et al.* [6] believe that they have recorded neuronal discharges in the basal ganglia which are related to switching between components of a motor plan. They recorded pallidal neuron activity in monkeys performing sequential wrist tasks. They observed phasic pallidal neuron discharge "which is influenced by the animal's preparation for movement and which appears to have a role in the performance of sequential movement tasks. Its role appears to be an internal cue which may signal the end of one movement in order that the next movement in the sequence may commence."

This phasic activity does not seem to correlate with regulating the parameters of motion; Brotchie *et al.* suggest that it appeared to be dependent on the predictability and automaticity of the movement.

Referring to studies by Schwab *et al.* [70] and Talland and Schwab [77], which deal with the performance of simultaneous motor tasks, Brotchie *et al.* argue that

> these studies demonstrated that it is not possible to perform two movements simultaneously in hypokinesia and that it is always the more subconscious movement that fails and that the more conscious movement is completed. These studies indicate that the role of the BG is important for the performance of subconscious movements and our results reveal a possible neuronal basis for this function... Our theory is that phasic activity in pallidal cells may be the internal cue used by the motor system to switch between motor programs in SMA [supplementary motor area].

The idea that the motor system is using internal cues to step between tasks is supported both by the difficulty that persons with Parkinson's disease have with sequential tasks, and (as Brotchie *et al.* point out) by the ability of Parkinson's patients to use external stimuli to partially overcome this difficulty. In this viewpoint, "visual or proprioceptive stimuli can signal the arrival at each point in a sequence, thereby providing the necessary cues for switching motor programs." This is perhaps the anatomical basis of kinesia paradoxa.

C.8 Akinesia

For the purposes of this thesis, the generic definition of akinesia as difficulty initiating and maintaining motion has been sufficient. More precise definitions have been put forward, however.

Delwaide and Gonce [12] provide a more detailed list of possible symptoms of akinesia, as follows:

- Delayed motor initiation

- Slow performance of voluntary movements
- Difficulty reaching a target with a single continuous movement
- Rapid fatigue with repetitive movement
- Inability to execute simultaneous actions
- Inability to execute sequential actions
- Negative symptoms, including
  - Disorders of postural fixation and equilibrium
  - Disorders of righting
  - Disorders of locomotion
  - Disorders of phonation and articulation
  - Disorders of arm movement
- Defective kinetic automatisms — the loss of associated movements such as arm swinging during gait, etc.

Imai *et al.* [31] list as symptoms:

- Masked face
- Loss of finger dexterity
- Loss of restless spontaneous movements of normals while sitting
- Micrographia
- Loss of arm swing in walking
- Shuffling gait
- Freezing of gait