A COMBINED INTERVENTION FOR EXECUTIVE DEFICITS AND ANXIETY IN

PARKINSON'S PATIENTS: A CASE STUDY

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Abstract

Parkinson's disease (PD) is a neurodegenerative disorder most commonly associated with motor symptomatology, yet often presenting with deficits in attention, executive functioning (EF; e.g., planning, mental flexibility, complex attention), anxiety, and depression, with debilitating effects on patients' quality of life. Current interventions, including pharmacological and surgical methods show efficacy in motor symptom management, yet produce equivocal results in addressing non-motor dysfunction. The goal of this paper was to describe and investigate the efficacy and patient acceptance of a nonpharmacological intervention for treatment of executive dysfunction (ED) and anxiety in PD, in the context of a case study (the case of Mr. K). Brain and Mind Fitness Program (BMFP) is a short-term intervention, consisting of a combination of cognitive remediation and cognitive behavioral therapy (CBT). BMFP was demonstrated to be fully acceptable to Mr. K, based on ratings of 4 feasibility dimensions (fatigue, effort, progress, and enjoyment). The program also proved to be efficacious in alleviating Mr. K's anxiety and depression symptoms, with benefits extending over the treatment period. BMFP, elsewhere shown to be an effective cognitive re-training of EF in PD patients, exhibited limited gains in the case of Mr. K., possibly due to his relatively intact cognitive abilities at baseline. Despite its limitations, the case of Mr. K presents a novel approach to treatment of PD non-motor symptoms and a learning opportunity for researchers and clinicians interested in expanding their knowledge across disciplines.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

`

The Scope of the Problem

Progress of civilization, including science and modern medicine has extended human life span by eliminating many causes that have killed young people (e.g., starvation and epidemics) and by treating age-related diseases. Life expectancy is increasing at an astonishing pace (Vaupel, 2010), thus by 2030, 25% of the population will be over the age of 60 (U.S. Census, 2005), although some enter very old age in good health, they then deteriorate rapidly, seemingly indicating that the rate of aging was not changed, but rather merely postponed (Blagosklonny, 2010).

As people age, the ability to defend against exogenous insults such as environmental agents diminishes and the efficiency of internal protective mechanisms (e.g. blood-brain barrier, immune system, cognitive integrity) declines. This leads to exposure of genetic vulnerabilities and ultimately, increases the risk of various medical and psychiatric diseases (e.g., osteoporosis, hypertension, renal impairment, Parkinson's disease (PD), Alzheimer's disease, anxiety, and depression; Blazer, 2003) and cognitive impairment. Many of these disorders, common in the elderly, lead to debilitating consequences for individuals and their families, and place a financial burden on our medical and long term care system. However, only recently have researchers begun to recognize the importance of prioritizing resources to address the needs of this rapidly growing age group (Reynolds & Gatz, 2003).

PD – General Overview

PD is one of the most complex diseases affecting as many as 1 to 2 % of people above the age of 60 and between 4 and 5% by the age of 85 (Burn, 2003). This neurodegenerative disorder of unknown etiology (Zgaljardic, Borod, Foldi, & Mattis,

2003) was first described by James Parkinson more than 150 years ago in his work entitled, "An Essay on the Shaking Palsy." It has been estimated that PD currently affects 1 million Americans, with a prevalence of 0.2% (Twelves, Perkins, & Counsell, 2003), expected to double within the next 20 years, as the percentage of elderly in the population grows (Chen, 2010). Age is the single most consistent risk factor. Mortality is two to five times higher among PD patients as compared to age-controls (Lang & Lozano, 1998).

PD is a chronic disease that places a substantial burden on patients and caregivers, and on society as a whole. Research shows that economic costs of PD are high, particularly for patients in advanced stages of the disease and for those with both motor and psychiatric complications (Dowding, Shenton, & Salek, 2006). The total cost associated with direct and indirect care of PD patients is estimated to be more than $23 billion annually (Table 1; Huse et al., 2005). PD patients have twice the direct medical costs of those without PD (Chen, 2010). The presence of psychiatric complications in PD, requiring a higher level of care (e.g., hospitalization, nursing homes, at-home specialized care) and increased dependence on family members, further exacerbates the financial situation.

With recent advances in medical care, PD patients are likely to live longer, which increases the probability of cognitive and emotional deterioration, with disease progression. As a consequence, they become less productive in society and eventually, a significant financial and humanitarian concern for the nation. For example, within five years of diagnosis, approximately one fourth of those still employed are no longer able to work, and over the subsequent five years, that number reaches about 80% (Spate, Germende, & Germende, 1988). It is estimated that approximately 5.2% of people in

nursing homes have PD (Marek & Jennings, 2009). With the expected increase in PD prevalence, it can be anticipated that PD will continue to exact significant economic costs (Chen, 2010). Consequently, it is important to design effective therapies for PD, with a positive impact on both individual and society as a whole (Karlsen, Tandberg, Arsland, & Larsen, 2000).

PD – Clinical Presentation

Idiopathic PD is a hypokinetic[1] movement disorder presenting with subcortical pathology, consisting of degeneration of the neuromelanin-containing neurons in the substantia nigra and in the locus ceruleus (Rowland, 2000). Studies suggest that nearly all people with PD also experience non-motor symptoms in addition to the typical motor deficits (Shulman et al., 2001; Table 2, Rowland, 2000).

To date, most progress has been made in understanding and managing the motor symptoms of PD, yet little has been done to treat the non-motor symptoms (Cole & Vaughan, 2005; Dobkin, Allen, & Menza, 2006; Feeney, Egan, & Gasson, 2005). Cognitive impairment, anxiety, and depression are examples of non-motor symptoms and psychiatric conditions common in PD, affecting as many as 60% to 80% of patients (Kulisevsky at al., 2008). The complexity in which non-motor conditions present clinically in PD patients (i.e. multiple etiologies, co-morbidity, and interaction between physical and psychological symptoms) may explain the limited research in this area. For example, many PD patients complain of short term memory loss, difficulty concentrating, fatigue, depressed mood, difficulty sleeping, muscle twitching, stiffness, or tremor, frequent urination, or sexual dysfunction (Kulisevsky et al., 2008). The causes of these presenting problems are multifaceted and may be the result of pathophysiologic changes

of a degenerative disease, exposure to antiparkinsonian treatments, or emotional reactions to living with a disabling chronic illness (Ferreri, Agbokou, & Gauthier, 2006). This paper focuses on executive dysfunction and anxiety in the context of PD and attempts to understand their role in the progression of disease and the impact they have on patients' quality of life.

Executive Dysfunction and Anxiety in PD

Although 20% to 40% of PD patients eventually develop dementia (Aarsland et al., 2003), less severe cognitive impairment is a well-recognized and common feature of the disease, present even in some newly diagnosed patients (Aarsland, Marsh, & Schrag, 2009). The risk factors associated with development of dementia in PD include increased age, duration of PD, and the stage of the PD progression. The proportion of patients with more than one specific cognitive impairment increases with the disease progression from approximately 40% in stage 1 to about 86% in stage 4 (Growdon, Corkin, & Rosen, 1990).

The most common cognitive deficits in non-demented PD patients are decrements in planning, sequencing, concept formation, and working memory (Cools, 2006; Weintraub, 2006). These cognitive abilities are usually grouped under a term called "executive functioning" (EF). The behaviors associated with EF include planning and organizing everyday tasks without distraction, initiating and maintaining goal-directed behaviors (e.g. driving, cooking, medication adherence, housekeeping), and performing tasks that involve abstract thinking and mental flexibility (Owen, 1993).Working memory (Lange & Robins, 1992) and emotion regulation (Fuster, 1997) have also been included in the EF category.

Research also suggested that executive decline (ED), commonly found in 41 % of non-demented PD patients tends to be co-morbid with neuropsychiatric disorders such as depression and anxiety (Kulisevsky et al., 2008). From a psychological perspective, it has been hypothesized that patients with cognitive decline may be more prone to develop anxiety symptoms due to difficulties in problem-solving and inability to resolve anxiogenic situations (Mast, Yochim, MacNeill, & Lichtenberg, 2004).

Up to 40% of patients with PD experience clinically significant anxiety, including panic disorder, generalized anxiety, and phobic disorders. This rate is higher than that in the general population and in groups of patients with similar physical disabilities (e.g., multiple sclerosis; Richard, Shiffer, & Kurlan, 1996). Somatic symptoms include breathlessness, sweating, chest discomfort, restlessness and dizziness. Patients also may experience fear of institutionalization, of going insane, or of dying. The precise cause of anxiety disorders in patients with Parkinson's disease is unknown. Anxiety may be a psychological reaction to the symptoms of PD; it may also be related to the neurochemical degenerative changes associated with the disease, such as progressive decreases in dopamine, serotonin, and norepinephrine levels. Anxiety symptoms can surface before any motor symptoms are noted and may be an early manifestation of PD, or a risk factor for developing PD (Weisskopf, Chen, & Schwartzchild, 2003). Along the same lines, some have proposed a pre-morbid (anxious) personality type that is more likely to be associated with the developing of PD later in life (Menza, 2000). Personality traits such as harm avoidance and reduced novelty seeking behaviors seem to be characteristics of PD patients in the pre-morbid phase and which persist after the onset of motor symptoms (Kaasinen et al., 2001).

While the timing in which anxiety and ED tend to emerge in PD is somewhat controversial in literature, their impact on patients' quality of life is undisputable. Anxiety, present in 69% of PD patients leads to excessive worry, fatigue, concentration problems, sleep disturbance, and restlessness (Kulisevsky et al., 2008). Anxiety has been associated with motor fluctuation, and like ED, is considered a significant predictor of quality of life. For example, anxiety and ED tend to negatively affect patients in many areas of their lives such as bodily comfort, emotional well-being, self-image, social, cognitive, and sexual function, communication, energy, participation in recreational and social activities (Karlsen, Tandberg, Arsland, & Larsen, 2000). ED also has been associated with the decreased ability to function in daily life (Koven et al., 2007) while anxiety has been connected with increased disability (i.e, problems with mobility, stigma, isolation; Marinus, Visser, Martinez-Martin, van Hilten, & Stiggelbout, 2003) and a lowered sense of emotional well-being in PD patients (Marinus, Leentjens, Visser, Stiggelbout, & van Hilten, 2002). Other studies found that ED has the greatest impact on their social and occupational functioning (Bassett, 2005) and a significant impact on their quality of life (Abudi, Bar-Tal, Ziv, & Fish, 1997; Brod, Mendelsohn, & Roberts, 1998; Hobson, Holden, & Meara, 1999; Schrag, Jahanshahi, & Quinn, 2000). These findings highlight the importance of addressing both cognitive and psychiatric symptoms, as they affect the ability to function in multiple domains of patients' lives. An important step in conceptualizing and designing effective treatment solutions for non-motor symptoms is to understand the degree to which PD pathology may contribute to their development.

The Neuropathology of PD

The best recognized pathological change in PD is the progressive loss of dopamine (DA) neurons in the ventrolateral tier of the substantia nigra pars compacta, directly altering the activity of motor cortico-striatopallido-thalamocortical pathways (Wichmann & DeLong, 2003; Bassett, 2005; Owen, 2004). Additionally, there are inclusions such as Lewy bodies present in locus ceruleus, nucleus basalis, hypothalamus, cerebral cortex, cranial nerve motor nuclei, and in the central and peripheral components of the autonomic nervous system (Olanow & Tatton, 1999). Research indicates that by the time motor symptoms appear, the substantia nigra has already lost approximately 60% of the dopamine (DA) neurons, and DA concentration in the striatum is approximately 80% lower than normal (Rowland, 2000). Severe dopamine depletion in dorsal striatum affects signals traveling via the nigrostriatal pathway from the striatum to the supplementary motor area (SPMA) and dorsolateral PFC. Malfunctioning of these pathways has been linked with impairment on tasks associated with affected brain areas (e.g., motor planning and sequencing, EF, source memory, and emotional regulation (Green et al., 2002; Owen, 2004, & Cools, 2006). In contrast, direct dopaminergic projections from the ventral tegmental area (VTA) to the PFC via the mesocortical pathway are relatively spared, indicating that DA deficiency in PD is rather specific (not global) to certain brain structures and neuronal pathways. This has implications in pharmachological treatment targeting motor symptoms, which has been found to have little or no effect on psycho-cognitive deficits (Drag, Bielauskas, Kszniak, Bohnen, & Glisky, 2009).

Recent imaging studies offered the possibility of capturing evidence of cognitive deficits in areas of the brain affected by PD pathology. Huang et al., (2006) found that cognitive deficiencies in PD may be expressed through a metabolic pattern (PD-related cognitive pattern, or PDCP) using fludeoxyglucose positron emission tomography (FDG PET) scans. This metabolic pattern is different than the expression of the PD-related motor pattern (PDRP). PDCP is characterized by metabolic reductions in frontal and parietal association areas and relative metabolic increases in the cerebellar hemispheres and dentate nuclei, as a potential compensatory response to the loss of dopaminergic input to the striatum. PDCP expression has been found to correlate with performance on tests of memory and EF in multiple cohorts of patients and is sensitive to early cognitive decline (Huang et al., 2007). Additionally, reduced dopaminergic stimulation of the prefrontal cortex (PFC) has also been associated with the development of anxiety disorders in PD (Levy & Cummings, 2000). Furthermore, Mentis et al. (2002) found discrete patterns of resting metabolic activity associated with cognitive and psychiatric disorders such as anxiety and depression in non-demented PD patients, suggesting the presence of a common neuro-mechanism for both (Weintraub, 2006).

Studies also indicated that DA deficiency is not the only cause of cognitive deficiencies in PD. Substantial evidence exists implicating abnormalities in other neurotransmitter systems such as cholinergic (Bohnen et al., 2006) as well as intrinsic cortical pathology (i.e., Lewy body formations) and concurrent Alzheimer's disease (Braak et al., 2005). More specifically, Kao et al. (2009) suggested that an underlying alpha-synuclein[2] pathology contributes to ED and increased depression and anxiety in PD.

To summarize, research indicated that multiple pathological mechanisms seem to contribute to the presence of ED and anxiety in PD. Dopaminergic decrements in specific brain regions and pathways, cortical pathology such as Lewy bodies, and abnormalities in multiple neurotransmitter systems are possible causes of cognitive and neuropsychiatric deficits. The implications of this research are multifold. First, it shows that pinpointing the exact etiology of these symptoms is not easy, as they may be the result of either separate or combinations of any of the aforementioned pathologies. Second, cortical pathology (e.g., Lewy bodies) can only be confirmed postmortem, which makes any possibility for targeted treatment, futile. Third, the focus of the medical community for the last 50 years (Jancovic, 2008) has been in studying and treating motor symptoms, with limited (at best) effects on alleviating non-motor symptoms. That being said, there seems to be a real need in acknowledging the complexity and dynamics of cognitive and psychiatric deficits as distinct features of the disease, and thus, with different treatment requirements.

This paper proposes an intervention targeting ED and anxiety in PD. A description of the theoretical model and supporting empirical findings are presented in the next chapters. The author concludes this paper with a presentation of a clinical case study in which the proposed intervention was administered and evaluated.

Theoretical and Empirical Basis for Intervention

Treatment Modalities in PD: Benefits and Limitations

Pharmacological treatment.

To date, dopamine replacement therapy (DRT), including primarily L-dopa and dopamine agonists, is the most common treatment for motor symptoms of PD (Cato &

Crosson, 2006). DRT demonstrated equivocal results in alleviating anxiety, with most benefit in patients experiencing anxiety during "on-off"[3] states, particularly the "off" period (Stein, Heuser, Juncos, & Uhde, 1990; Vasquez et al., 1993). However, there seems to be no correlation between duration or severity of anxiety and duration of L-dopa exposure or L-dopa dosage (Stein, Heuser, Juncos, & Uhde, 1990).

Additionally, selective serotonin reuptake inhibitors (SSRIs) are commonly used as first-line of treatment for anxiety, yet patients need continuous dose adjustment to benefit from their anxiolytic effect, (Borek, Chou, & Friedman, 2007). A benzodiazepine with a short half-life (e.g.,alprazolam, lorazepam, oxazepam) is also frequently prescribed,but because most PD patients are elderly, side effects (e.g., oversedation, increased risk of falls, cognitive impairment) may compromise any anxiolytic gain (Ferreri, Agdokou, & Gauthier, 2006).

Research also produced conflicting results regarding DRT effects on cognition in PD: the results ranged from little or no improvement (Carbon et al., 2003; Cooper et al., 1992; Gotham , Brown, & Marsden , 1988; Growdon et al., 1998; Rektorova et al., 2003) to a negative impact (Shohamy, Myers, Geghman, Sage, & Gluck, 2006). One potential explanation for such variance in response to DRT came from FDG PET studies of neural pathways. One study suggested that neural pathways associated with motor and EF manifestations in PD are statistically independent and functionally segregated (Wichmann & DeLong, 2003). The motor related neural pathway (PDRP) expression was found to correlate consistently with Unified Parkinson's Disease rating Scale (UPDRS) of motor scores (Eidelberg et al., 1995; Lozza et al., 2004 and Asanuma et al., 2006) and with clinical response to parkinsonian treatment (e.g., L-dopa or subthalamic nuclei

stimulation (STN); Asanuma et al., 2006; Eckert & Eidelberg, 2005; Trost et al. 2006).

However, the cognitive related neural pathway (PDCP) expression did not correlate with

physiological descriptors of motor parkinsonism and was not modulated by the treatment

for these symptoms (Huang et al., 2007). Furthermore, Shohamy, Myers, Geghman,

Sage, and Gluck (2006) found that dopaminergic medication was associated with

impaired learning of feedback-based and incrementally acquired tasks,[4] while patients

withdrawn from dopaminergic medication performed as well as healthy controls. PD

patients on L-dopa performed worse than controls at probabilistic reversal learning,[5] a

task that implicates orbitofrontal cortex– ventral striatal circuitry, which is relatively

spared of DA loss in PD. However, they performed better than controls at attentional

flexibility tasks (switching tasks) implicating the circuitry connecting the dorsolateral

prefrontal cortex to the dorsal caudate nucleus, profoundly depleted of DA in PD (Cools,

Barker, Sahakian, & Robbins, 2001). These studies demonstrated that a systemic

administration of DRT potentially may lead to over-regulation of orbitofrontal cortex–

ventral striatal circuitry, with negative consequences in learning and EF.

DRTs are known to decrease the motor fluctuations, yet they also can produce

disturbing side effects (Table 3). Cummings (1991) found that of the patients treated with

dopaminergic agents, 30% develop visual hallucinations, 10% exhibit delusions, 10%

have euphoria, 1% have mania, 10% to 15% experience increased anxiety, 15% have

confusion periods, and a few exhibit altered sexual behavior. Another common DRT side

effect is impulse control, including compulsive shopping, eating, or gambling. Rabinak &

Nirenberg (2010) recently reported that 19 % off PD patients, previously diagnosed with

impulse control disorders due to long exposure to DRT, and who were tapered of

medication, subsequently developed severe DA withdrawal symptoms such as anxiety, panic attacks, agoraphobia, depression, dysphoria, fatigue, pain, orthostatic hypotension, and drug cravings.

As mentioned prior, there is ample evidence implicating abnormalities in other neurotransmitters systems such as cholinergic (Bohnen et al., 2006) as well as intrinsic cortical pathology (e.g., Lewy body formation, concurrent Alzheimer's disease (AD) neurofibrilary pathology; Braak et al., 2005) as potential cause of non-motor disease manifestation. Thus, the complexity of known and unknown sources of pathology leading to cognitive dysfunction in PD may explain the challenges and limitations of current medical treatments.

PD patients are often candidates for a vast cocktail of medications, including DRT and other age-related treatments. Leoni et al. (2002) found that PD patients took on average 2.4 antiparkinsonian medications (correlated with disease duration) in addition to an average of 2.4 non-antiparkinsonian medications (correlated with patient's current age). Orsini, Castelli, Kennedy & Huse (2004) found that prescription pharmaceuticals for PD patients using private insurance (including Medicare users) were the second largest financial cost ($3,148 per patient in 2002) following inpatient admissions ($9,362 per patient). On average, PD patients fill more than 20 additional prescriptions annually than healthy controls (Huse, Schulman, Orsini, 2005).

Medication adherence in PD also is another serious problem facing current medical practice, considering the high rates of suboptimal adherence[6] (60-70% over five year period; Kulkarni, 2008), and with only 10% of the patients using medication as prescribed (Leopold, Polansky, & Hurka, 2004). Various factors, including complex

dosing regimen, titration schedules, and use of multiple medications affect patients ability to be adherent. Other reasons may be due to decline in patients' cognitive abilities (e.g., memory impairment, ED; Dymek, Atchison, Harrell, & Marson, 2001; Vermeire, Hearnshaw, Van Royen, & Denekens, 2001) and physician-patient relationship (DiMatteo, 1994).

Neurosurgical treatment.

As an alternative to pharmacological treatment of PD, neurosurgical interventions have only recently gained popularity (Jankovic, 2001; Krauss et al., 2001) Targeting the improvement of motor symptomatology, thalamotomy,[7] pallidatomy,[8] and deep brain stimulation (DBS) of thalamic nuclei showed remarkable results in controlling tremors and prolonging the "on" time (Linazasoro, Blercom, & Lasa, 2003) for medically-refractory patients. However, bilateral thalamotomy was associated with hypophonia, dysarthria, and dysphagia (Jancovic & Aguillar, 2008), while DBS increased the post-surgery risk of speech impairment, postural instability, and cognitive decline (Anderson et al., 2003; Rodriguez-Oroz et al., 2005).

Psychotherapy in PD.

To date, research investigating the efficacy of non-pharmacological interventions in PD with ED and anxiety has been limited (Mohlman et al., 2010). However, there is ample empirical evidence suggesting that in general, empirically supported treatments, like cognitive behavioral therapy (CBT) are more effective for treating anxiety than supportive therapy and most medications (Mohlman, 2005; Mitte, Noack, Stell, & Hautzinger, 2005; Stanley, Beck, & Glassco, 1996). Encouraging results of previous studies proposed CBT as an effective intervention for treatment of depression and anxiety

in PD (Cole & Vaughan, 2006; Dobkin, Allen, & Menza, 2006; Feeney, Egan, & Gasson, 2005). Many PD patients with depression and anxiety tend to attribute their non-motor symptoms to psychosocial factors and endorse non-pharmacological approaches (Oehlberg et al., 2008). However, the biggest challenge consists in designing effective treatments which take into account the variability in clinical presentation of PD patients with anxiety or depression. Some suggested that a CBT model tailored to patients' needs may be probably the most effective treatment option for such patients (Dobkin, Menza, & Bienfait, 2008). The intervention presented in this paper is designed specifically for PD patients with anxiety and ED.

The Theoretical Foundation of the Brain and Mind Fitness Program

Brain and Mind Fitness Program (BMFP) is a novel integrative treatment, designed for PD patients with ED and anxiety which combines an executive skills training program derived from Attention Process Training II (APT) (Sohlberg, Johnson, Paule, Raskin, & Mateer, 2001) and CBT. The theoretical foundation supporting BMFP is based on the theory of neuroplasticity (Mesulam, 2000) and the three part model of anxiety (Lang, 1977).

Neuroplasticity is the ability of adult brain to continue to form novel neural connections and grow new neurons (neurogenesis) in response to learning or training even into old age (Garland & Howard, 2009). Neuroplasticity subsumes diverse processes of vital importance by which the brain perceives, adapts to, and responds to a variety of internal and external stimuli (Manji, Moore, Rajkowska, & Chen, 2000). Specifically, manifestations of neuroplasticity in the adult brain have been characterized as alterations of dendritic function, synaptic remodeling, long-term potentiation (LTP),

axonal sprouting, neuritic extensions, synaptogenesis, and even neurogenesis (Kolb, & Whishaw, 1996; Mesulam, 2000). Neuroplasticity provides the scientific basis for treatment of acquired brain injury with cognitive rehabilitation programs. The adult brain is not "hard-wired" with fixed and immutable neuronal circuits. There are many instances of cortical and subcortical rewiring of neuronal circuits in response to training as well as in response to injury. For instance, animal studies indicate that exposure to a challenging, enriched environment evoked a much larger regulation of adult hippocampal neurogenesis in old animals than in younger ones (Kempermann, Gast, & Gage, 2002). It is believed that APT (the cognitive remediation section of the BMFP) may work through learning and sustained cognitive activity and by promoting neurogenesis and/or synaptic expansion and re-organization.

The other theoretical model supporting BMFP is the three part model of anxiety. This model posits that anxiety can be best understood as a constellation of language behaviors or cognitions, motor acts or behaviors, and physiological events or bodily sensations (Lang, 1977). For example, people suffering from anxiety and depression tend to harbor a multitude of cognitive distortions such as all-or-nothing thinking, overgeneralization, mental filtering, disqualifying the positive, jumping to conclusions, magnification and minimization, emotional reasoning, labeling and mislabeling, "should" statements, and personalization (Burns, 1980). Research indicated that PD patients are at a greater risk for depression and anxiety as compared to healthy controls, due to attention mechanisms that are vulnerable to negative stimuli, which often leads to negative cognitive distortions (Jordi & Ring, 2002). CBT uses techniques such as cognitive restructuring to address toxic thinking by increasing the patients' awareness to the

presence of cognitive distortions in their thinking style and their impact on their emotional and physical wellbeing. Anxiety also can manifest through avoidance and angry behaviors, sleep disruption, over- or under- eating, substance abuse or dependence, or social isolation (Barlow, 2002). CBT incorporates techniques such as task hierarchy, "acting as if," or acceptance and normalization to replace such maladaptive behaviors with healthy alternatives. Additionally, in PD, physical symptoms and anxiety related symptoms often overlap and tend to sustain each other in a vicious cycle. For example, tremors tend to increase during anxious moments and decrease during relaxation (Datillio & Freeman, 2007). Thus, behavioral interventions targeting bodily sensations such as diaphragmatic breathing and progressive muscle relaxation may be deemed helpful in decreasing anxiety symptoms and improving motor symptoms in PD patients.

The Empirical Evidence Supporting the Brain and Mind Fitness Program

Cognitive training in BMFP.

As previously mentioned, presence of ED in PD is very common and is thought to have a significant negative effect on patients' overall functioning and quality of life (Karlsen, Tandberg, Arsland, & Larsen, 2000; Koven et al., 2007). Based on the theory of neuroplasticity, Sohlberg & Mateer (2000) proposed that through repeated practice, executive skills can often be improved, especially in older adults who are high functioning. Specifically, cognitive training and physical activity have shown to have an impact on the onset, severity, and progression of neurodegenerative diseases such as PD (Steiner, Wolf, & Kempermann, 2006). Poor decision-making and reduced reasoning abilities have been found in many PD patients with otherwise, preserved intellect (Damasio, 1994; Upton & Thompson, 1999). APT is a model of cognitive training,

specifically designed to enhance attention and executive skills. From a pragmatic reasons, APT was chosen because it was readily available, easy to administer, and has empirical data to support its efficacy in various patient groups, including patients with brain injury (Sohlberg, McLaughlin, Pavese, Heidrich, & Posner, 2000).

Psychotherapy in BMFP.

The CBT component of BMFP is based on a transdiagnostic approach to treatment. The overarching goal of the transdiagnostic model is to target common core pathology rather than a discrete disorder. For example, PD patients tend to present with high co-morbity of anxiety and depression (Weintraub, 2006). A transdiagnostic CBT model is ideal for PD because it is organized to address concurrently the overlapping symptoms of mood and anxiety disorders such as negative affect (Clark & Watson, 1991). Furthermore, transdiagnostic CBT is a serial treatment approach that yielded encouraging results in treating symptoms along a continuum, across multiple diagnostic categories (Norton, Hayes, & Hope, 2004; White et al., 2002). This is particularly attractive in treating PD patients, whose complex clinical presentation, involving motor and non-motor symptoms (e.g., ED, anxiety, depression, sleep disorders), often crosses multiple diagnostic categories.

Various transdiagnostic CBT protocols demonstrated success previously in treating patients with anxiety and depression (Barlow, Allen, & Choate, 2004; Norton, Hayes, & Hope, 2004). The CBT protocol proposed here follows a transdiagnostic model that also led to significant improvement in anxiety symptoms of older adults, in several earlier pilot studies (Mohlman et al., 2003; Mohlman & Gorman, 2005).

BMFP – A combined intervention.

Ample research indicated that sound executive skills might be required for an optimal use of CBT (Hariri, Bookheimer, & Mazziotta, 2001; Mohlman, 2005; Mohlman and Gorman, 2005). Cognitive training has been used in treatment as a complement to psychotherapy. For example, cognitive training has been successful in enhancing the use of psychotherapy for patients with brain dysfunction resulting from cranial radiation therapy (Butler & Copeland, 2002) and stroke (Murray, Keeton, & Karcher, 2005); and psychiatric disorders such as schizophrenia (Bell, Bryson, Greig, Corcoran, & Wexler, 2001; Lopez-Luego, & Vasquez, 2003; Silverstein et al., 2005), major depression (Siegle, Ghinassi, & Thase, 2007), and substance abuse.

Specifically, Mohlman (2008) indicated that the combination of APT and CBT, versus CBT alone showed greater improvement in executive skills and reduction in anxiety in older adults diagnosed with generalized anxiety disorder (GAD). Mohlman (2008) suggested that the reasoning behind combining APT and CBT is twofold. First, the combined intervention is intended to strengthen patients' abilities to engage in complex cognitive control of negative affect; second, practice of skills under situational demand (e.g., in the presence of distracters) might assist patients in applying the therapeutic techniques to real life situations.

Mohlman (2008) further indicated that specific executive skills that facilitate the use of CBT are based on different types of attentional skills: sustained, alternating, focused, and divided attention. It is expected that engaging in rigorous exercises of APT would lead to enhanced attention and executive skills, and increase the chance the clients will benefit from the subsequent CBT sessions (Hariri, Bookheimer, & Mazziotta, 2001;

Mohlman, 2005; Mohlman and Gorman, 2005). For instance, cognitive restructuring in CBT requires patients' ability to sustain attention for an extended period of time, in which they can identify and attend to target thoughts (e.g., negative cognitions) among distracting noise (e.g., other thoughts and competing stimuli). Hence, it is expected that patients make use of sustained and selective attention while engaging in cognitive restructuring. Similarly, the ability to alternate attention among different thoughts, emotions, and bodily sensations is also essential for proper use of CBT. Alternating and divided attention (i.e. multitasking) are particularly important skills that PD patients need if they were to successfully appraise and distinguish between the physical PD related symptoms and the symptoms produced by anxiety or depression. The last APT session of BMFP was designed to target the improvement of critical thinking and logic, also important components of EF. Mastery of these skills is essential for a great implementation of CBT (especially during cognitive restructuring and task hierarchy).

BMFP Protocol

BMFP, as described here, begins with five, weekly, 120-minute APT sessions, followed by five, weekly, 90- minute CBT sessions. To date and to the best of author's knowledge, a different version of BMFP, featuring the same modules but in reverse order (CBT first and APT second) achieved encouraging results in anxiety reduction and limited improvement in retraining of cognitive skills in a PD patient (Mohlman et al., 2010). The implementation of this BMFP version (APT first and CBT second) is totally novel and considered experimental.

To exemplify the implementation of BMFP, we present a case study of a patient, considered to be representative of the PD population. The patient has co-morbid anxiety

and depression and a relatively preserved intellect, yet challenging reasoning abilities. A detailed description of the patient's presenting problems, history, and behavioral observations are detailed in Chapter III.

Case Presentation

Mr. K is a 58-year-old Caucasian male who was diagnosed with PD in 2001. He grew up in Texas, but lived most of his adult life in New York and New Jersey. After his divorce in 1980, he moved to New Jersey and began a long term relationship with Ms. R, his current partner. Although they never officially married, they have lived together in Central New Jersey since 1984. Mr. K and his partner have five adult children and two grandchildren. Mr. K retired in March, 2008 on the basis of disability related to PD. He self-referred to BMFP as a result of a recruitment flyer posted in his PD support group.

History of Presenting Problems

Mr. K became interested in the BMFP because he often found himself worrying, being unable to relax, and feeling depressed. He never received a formal diagnostic of a psychological disorder, yet he feels depressed and anxious most of the time. Mr. K explained that his worries are related to monetary issues and loss of control over his life, as PD progresses. He fears that he will no longer be helpful to his family and will end up in a nursing home, once PD takes over his life.

Mr. K also reported a decline in his cognitive abilities, especially in memory, attention, and concentration. For example, Mr. K stated that he has had difficulties remembering names, details of conversations, and has to re-read information due to forgetting. He also reported that his cognitive difficulties affected his work as a computer programmer and forced him into early retirement. Mr. K also felt frustrated and angry

because of his physical PD related limitations. He had feelings of helplessness and hopelessness, especially when comparing his past accomplishments with current functioning.

Mr. K also reported significant changes in his quality of life due to physical symptoms related to PD. For example, his muscles often become rigid throughout his body, he had muscle spasms and painful jerks. This has disturbed his sleep and limited his daily physical activities. PD has also affected the quality of his speech, as he often had trouble verbally articulating. Additionally, he complained about difficulties with handwriting and performing other activities (e.g., tying his shoes, changing an electrical outlet, and painting) which require fine motor dexterity.

Medical History

Mr. K was diagnosed with PD in 2001, at the Movement Disorders Clinic of the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson hospital (UMDNJ-RWJ). His current Hoehn & Yahr score, reportedly 3, indicates that Mr. K still can function independently despite the presence of bilateral motor symptoms and postural instability (McNamara, 2009).

Prior to PD diagnosis, Mr. K reported that Ms. R observed changes in his gait and movement of his arms. For example, she noted that Mr. K had a stooped gait and decreased arm swing when walking. Over the past eight years, Mr. K noticed a visible increase of parkinsonian motor symptoms, which unfortunately are not completely controlled by his DRT. He needs constant adjustment of medication dosage in order to derive maximum benefits and to control his "on-off" cycle. Mr. K's current medication

includes: Stalevo (L-DOPA), 150 mg, three times a day, Sinemet (L-DOPA), 1 mg per day, Symmetrel (Amantadine), and Provigil (stimulant).

In addition to PD, Mr. K's medical history is significant for epilepsy in childhood and youth, which went into remission for over 20 years. He also has scoliosis, and osteoporosis, which exacerbate his PD motor symptoms, causing loss of equilibrium and tendency to fall forward. More recently, Mr. K was diagnosed with Ocular Myasthenia Gravis,[9] whose symptoms are well managed by medication and special eye glasses.

Socioeconomic History

Mr. K comes from a religious family of Jewish descent. Mr. K is the younger of the two siblings in the family. His brother currently lives in California and has a limited contact with Mr. K.

Mr. K 's childhood memories are reportedly "foggy," partly due to heavy epilepsy medication. However, he remembers growing up in a cold and difficult familial environment. His father was unreasonably demanding and a person who was hard to please. According to Mr. K, his father had a low opinion of his intellectual abilities and despised him, especially during the epilepsy attacks. Mr. K's parents divorced when he was eight years old, and his father consequently re-married. The relationships between Mr. K and his father never improved much over the years. When his father passed away two years ago, he left behind a significant financial debt which, in part had to be covered by Mr. K.

His mother suffered from multiple sclerosis and passed away five years ago. Mr. K remembered his mother being strapped to a wheelchair and very depressed in her latest years of life. Regrettably, he did not visit his mother often in the latest years, and she died

alone and demented in a nursing home in New Jersey. Mr. K's familial environment and problematic relationships with his parents have probably had a negative impact on his thinking schema and have increased the chance for development of anxiety and depression.

Mr. K reported that he had always been a good student. He loved numbers, math, and science and had very good grades in most subjects. After one year of college, Mr. K left Texas and moved in with his uncle in New York. He explained that his move allowed him to be more independent. He began working as a paralegal in a law firm, but after a few years, he returned to school and graduated from Hunter College, in 1982. Despite a modest financial remuneration and meager intellectual stimulation, Mr. K continued his work at the law firm for another three years. He stated that, up until he met Ms. R, he had no financial goals, no personal ambitions, and lived his life one day to the next.

In 1985, Mr. K applied for a certification program in information technology (IT) at a major university in the urban Northeast. He did not graduate, yet he was successful in gaining employment in the IT field. Mr. K's career developed mostly as an IT consultant, programmer, and IT manager. He worked as an independent consultant for companies such as Merrill Lynch and United Postal Services (UPS) until 2004. Soon after, Mr. K's began working part time mainly due increased fatigue and motor and cognitive deterioration related to PD. He worked part time until March, 2008 when his contract was terminated on basis of disability.

Mr. K married at age 24 and had a son. He and his ex-wife had a difficult four-year relationship that ended with a long and stressful divorce in 1980. Mr. K stated that his marriage was plagued by financial difficulties and by his wife's recurrent episodes of

severe depression and mania. After divorce, his ex-wife gained full custody, which made Mr. K's relationship with his son feel cold and "patchy." For the following 16 years, he would have sporadic visitations with his son and awkward interactions with his ex wife. His son moved in with Mr. K, after his mother's death. Mr. K stated that it took another 16 years for him and his son to slowly re-build their relationship.

Mr. K met Ms. R four years after divorce. Mr. K stated that his relationship with Ms. R has tremendously changed his life for the better. Mr. K explained that Ms. R had engendered in him a sense of responsibility for his new family (Ms. R's four children) and a new outlook on the future. As a consequence, Mr. K changed jobs, returned to school, and started a career. Mr. K feels that Ms. R is his "pillar of strength" and "the most important person" in his life. Mr. K currently prides himself in having a close and supportive family. Ms. R's adult children live close by and maintain great contact with both of them. He wished that he could also have such close relationship with his biological son.

Socially, Mr. K and Ms. R have always had a rich and satisfying life. They used to love to entertain guests at their house. However, over the past year, he felt physically and mentally exhausted and limited in what he could do to prepare for parties, as he used to do in the past.

Assessment of Presenting Problems

To assess Mr. K's mood, both self and clinician-rated instruments were used in order to control for overlap of PD and anxiety related physical symptoms, and potential overestimation of psychiatric symptoms, found on some anxiety scales (e.g., BAI; Higginson, Fields, Koller, & Troster, 2001). Thus, Mr. K completed a battery of self-

reported questionnaires including the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986), the Beck Anxiety Inventory (BAI; Beck & Steer, 1990), a trait scale of the anxiety inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), and the Beck Depression Inventory (BDI; Beck & Steer, 1987). His endorsements on these measures indicated that Mr. K has moderate to severe levels of anxiety and depression (Table. 4). Mr. K also completed two clinician-rated measures, the Hamilton Scales for Anxiety (Ham-A; Hamilton, 1959) administered with the Structured Interview Guide for the Hamilton Anxiety Rating Scale (SIGH-A; Shear et al., 2001), and Hamilton Scales for Depression (Ham-D; Hamilton, 1960) administered with the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D; Williams, 1988). The results on both HAM-A and HAM-D also indicated elevated symptoms of anxiety and depression at baseline.

To assess his cognitive abilities, Mr. K completed a battery of neuropsychological tests comprised of the Stroop Color-Word Interference Test (Trenerry, Crosson, DeBoe, & Leber, 1989), Controlled Oral Word Association Test (COWAT; Benton & Hamsher, 1976), Trailmaking Test (Army Individual Test Battery, 1944), and several subtests from the Wechsler Adult Intelligence and Memory Scales, 3rd Edition (i.e., Digit Span, Verbal Paired Associates, Similarities, and Digit symbol coding; Wechsler, 1997). The Mini Mental State Exam (Folstein, Folstein, & McHugh, 1975) and the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983) were utilized in the pre-treatment period as screener instruments for dementia. Despite subjective complaints of memory and concentration problems, Mr. K's test scores ranged in the high average to very superior range, indicating no cognitive impairment (Table 5). This discrepancy between subjective

reports and objective performance is not uncommon for people who suffer with depression and anxiety and who report cognitive difficulties. Therefore, Mr. K was considered a good candidate for BMFP, despite his intact cognitive profile. Furthermore, cognitive training is thought to be beneficial in cognitively unimpaired older adults, as is stimulates the brain and helps "fight off" aging (Mohlman et al., 2010) which in case of Mr. K is being accelerated by the neurodegenerative process of PD.

Assessment of feasibility and patient acceptance of APT was also a target of investigation during Mr. K's treatment. To date, there are few published studies investigating efficacy of cognitive training in PD patients (Mohlman, Chazin, & Georgescu, in press). Some have shown promising results in improving verbal fluency and logical memory in mildly impaired PD patients, following a 12-session computerized intervention (Sinforiani et al.,2004); others described significant progress in working memory of PD patients following 10-session executive skill intervention (Sammer et al., 2006). However, only one study by Mohlman, Chazin, & Georgescu (in press) assessed feasibility and patient acceptance of APT. Mr. K was a participant in this study and his subjective training experience provided vital information about APT feasibility, whose desired effects depend on substantial amount of practice, sustained effort, and persistency.

Following each in-session and homework exercise, Mr. K was asked to complete log (feasibility) sheets (Appendix D) by answering questions about level of fatigue, effort, progress, and enjoyment he experienced during the APT exercises. Research has showed that perceived *progress* has been identified as a motivating factor and a critical variable associated with APT efficacy and utility (Sohlberg et al, 2001). *Enjoyment* is

generally thought to contribute to motivation (and indirectly to treatment outcomes) by promoting and sustaining willingness to continue and persist in activities (Reeve, 1989). Additionally, Sohlberg et al. (2001) suggested that training needs to be sufficiently *effortful* in order to facilitate reorganization of cortical function and optimal acquisition of attentional skills, as well as feelings of competence. *Fatigue,* commonly associated with frontal lobe dysfunction in PD (Abe, Takanashi & Yahagihara, 2000) and expected as feature of ED (Mohlman, Chazin, & Georgescu, in press), needs to be constantly monitored and managed during APT administration in order to derive maximum benefits (Sohlberg et al, 2001).The APT feasibility was measured as feedback collected within session and at home, on a 6-point Likert scale across four dimensions: fatigue, effort, progress, and enjoyment. Criteria for feasibility were established *a priori* to reflect expectations that training should be somewhat (but not exceedingly) effortful and enjoyable, without being overly fatiguing, and should elicit from patients a sense of progress in improving EF. The target range for effort was expected to fall between "1 = A little" and "4 = Very much", fatigue was expected to be lower than "4= Very much," and progress and enjoyment were expected to fall between "1 = A little" and "5 = Extreme." (Appendix C; Mohlman, Chazin, & Georgescu, in press.

Behavioral Observations

Mr. K arrived early at all assessment and treatment sessions. His physical appearance was older than his actual age, predominately due to his vivid parkinsonian motor symptoms. For example, he exhibited a bilateral resting tremor of the hands, more pronounced in the right hand and during moments of high anxiety (i.e., test taking). He had a shuffling, short-stepped gait, a stooped posture, and diminished arm swing. His

face displayed a slight mask-like expression. Sometimes, he exhibited hypophonia[10] and slight dysarthria.[11] His handwriting was slow with a significant presentation of micrographia[12] (see Appendix A).

Mr. K also displayed flat affect and limited eye contact during the baseline assessment sessions. His expressive language style was abrupt, with short sentences and a lack of detail. His thought process seemed rigid, yet no evidence of thought disorder was present. His affect improved throughout the treatment period and subsequent assessment sessions, as he became more comfortable and interested in treatment. A graphic depiction of his self-reported mood over the intervention period is presented in Figure 1. Notably, the trend of his self- reported mood matches the behavioral observations of his affect during the assessment and treatment sessions. As treatment progressed, Mr. K also became more talkative and volunteered personal information with increased ease.

Mr. K took the entire treatment process very seriously. He displayed a great interest in actively participating in BMFT, both in sessions and at home. In one instance, Mr. K became very upset and almost rude in response to an unplanned change in clinician's schedule; that demonstrated both his vested interest in the program and his inflexible thinking style. Overall, the interaction between Mr. K and the treating clinician was positive and productive. Despite his slow warm-up period, Mr. K maintained a friendly demeanor and did his best to work on sensitive or difficult issues of his life (i.e., challenging his thoughts during the cognitive restructuring sessions of CBT).

Despite his unique attributes, Mr. K was fairly representative of the PD population in early and medium stage of the disease, from both physical and psychological presentation. Thus, his participation in BMFP seemed appropriate and was

expected to produce an improvement in mood, decrease in anxiety and avoidance behavior, and increase in daily functioning. His cognitive profile was less common, as his cognitive scores ranged from high average to superior. Therefore, BMFP was not expected to produce any significant improvements in his cognitive skills. However, the overall improvement in his psychological symptoms was expected to have a positive overflow effect on his cognitive functioning, especially in areas of self-reported difficulties.

Case Formulation

Mr. K's complaints of depressive thoughts, excessive worrying, his anger, and perceived cognitive decline may be explained by several different interrelated factors. It is conceivable that interaction of a genetic predisposition, long life experience with severe and chronic pathology (e.g., epilepsy, PD, myasthenia gravis), aging, life stressors, and psychological vulnerabilities (e.g., limited copying skills, anxiogenic, and depressive core beliefs) may have played an important role in development of his anxiety and depression (Barlow, 2002).

Regardless of what caused Mr. K's current mood disorders, several maintaining factors were identified and became target for treatment. Mr. K frequently engaged in excessive worrying and self-deprecating thinking, leading to avoidance and anger behaviors, which in turn fed back onto anxiety and depression. The fear of losing control over his life, as PD progresses, was pervasive in his thinking schema. Core beliefs such as "I am a failure if I am not perfect" fueled his cognitive processes, promoting feelings of inadequacy and insecurity. His dichotomous thinking often led to overgeneralization and exaggeration of his physical limitations (e.g., "If I can't run as I used to, it means that

I cannot exercise at all"). He avoided physical exercise, potentially losing opportunities to make himself feel better physically and emotionally (Blumenthal & Gullete, 2002). He disqualified positive experiences in his life, believed that he was "weak and unlovable", and worried that will end up alone, just like his mother. His anger, turned mostly inward, maintained his depressive thinking and had a negative impact on him socially, leading to withdrawal from many functions he had previously held (e.g., function planner, negotiator of the family; Table 6).

Mr. K also reported decline in attention, processing speed, and memory, which are common complaints in PD patients (Aarsland, Marsh, & Schrag, 2009). Even though neuropsychological exam found no underlying cognitive deficits at baseline, he may in fact already been experiencing a decline in higher cognitive functions (i.e., ED), presently exacerbated by anxiety and depression. Research showed that sensitive biomarkers, indicative of cognitive decline in PD are being expressed and captured with FDG PET technology very early in the disease progression, with or without the presence of clinically observed cognitive dysfunction (e.g., neuropsychological test results; Huang et al., 2008). Mohlman et al. (2010) discussed how ED is known to be associated with maladaptive symptom perceptions in PD, and to predict non-response to CBT. This paper investigates the efficacy of BMFP, featuring the implementation of APT modules before the CBT. It is expected that any gains obtained by Mr. K during the APT sessions will facilitate the efficacy of subsequent CBT sessions, ultimately leading to decrease in anxiety and depressive symptoms.

Course of Intervention and Assessment of Progress

The design of case study is presented in Figure 2. After completing one-month baseline period during which no treatment was administered, Mr. K began the active treatment phase. He attended a total of ten treatment sessions in a university-based psychology clinic, led by a doctoral student (the author) with extensive training in both APT and CBT; the first five session were 120–minute sessions of APT, followed by five 90 to 120-minute sessions of transdiagnostic CBT. Mr. K's mood was evaluated at 4 points: pre and post baselines and immediately and after 6 weeks post treatment.

The APT sessions targeted four types of attention, commonly thought to be disrupted in PD: sustained, selective, divided, and alternating. The fifth session focused on improving logical reasoning skills, an important component of EF (see Table 7 for a session-by session description). Tasks were administered in ascending order of complexity, such that basic cognitive skills were constantly stimulated while newer, more complex ones were targeted and exercised. For example, during the 1st APT session, Mr. K was required to listen to auditory stimuli presented on compact disks (CDs) and to press a buzzer to identify target stimuli (e.g., round, rectangular objects, and holidays). Alternate tasks, such as rapidly re-arranging words in a sentence in alphabetical order, or re-arranging numbers in increasing order, were also used during this session. Mr. K practiced on similar tasks during the 2nd session of APT, however, his work took place in the presence of "live" distracters (e.g., ripping paper, turning on and off the light, clinician reading an article). Mr. K had no trouble attending to his tasks and ignoring all distractions in the room with the exception of article reading, as he found himself briefly shifting his attention to the article.

Session 3 of APT required Mr. K to attend simultaneously to two or more tasks, which he found less enjoyable and more difficult than the other APT sessions. For example, Mr. K. did math calculations of various degrees of complexity while identifying target auditory stimuli presented on the CD. He also rapidly read a paragraph for comprehension while underlying target words (e.g., words ending in "-ing") His feedback about this session indicated that he felt challenged to the point where it was "no fun anymore." Session 4 focused on teaching Mr. K how to rapidly switch his attention from one task to another. For example, he was asked to re-arrange a 1st sentence in alphabetical order and a 2nd sentence in reverse order of words. He was then to keep track of whether to alphabetize or reverse subsequent sentences until he reached the end of the list (about 15 sentences). Mr. K enjoyed these tasks very much and asked for copies of sentences to practice at home. The last session in APT included exercises of logic (e.g., induction, deduction, and reasoning), selected from LSAT preparation manuals. Mr. K performed very well on all tasks as they reminded him of programing work he used to do for a living. Overall, Mr. K's reaction to most APT tasks was positive: he was engaged, had fun with some of them, and did not give up when challenged. According to APT feasibility criteria (see "Assessment of Presenting Problems"), the clinician had to constantly adjust the level of difficulty, so Mr. K could derive full benefit from APT exercises. Following the APT manual, the clinician selected increasingly more difficult tasks based on Mr. K's feedback and performance. For example, the clinician selected CDs in which the audio stimuli were presented at faster speeds, or added extra distractions in the room, or selected the more difficult paragraphs for reading, etc. A high functioning patient such as Mr. K was both challenging and rewarding to work with

because it required the clinician to be attentive, flexible, and creative in her approach

with Mr. K, while following the APT protocol.

Throughout all APT sessions, Mr. K. practiced exercises in two 45 minute blocks,

separated by a five-minute break and followed by completion of log sheets (see Appendix

D, for examples). Independent at-home practice included extensions of in-session

assignments as well as exercises meant to facilitate transfer and generalization of skills to

real life activities and situations (e.g., simultaneously cooking and playing Sudoku, or

walking while engaging in mental calculation; Mohlman, Chazin, & Georgescu, in press).

The remaining time in each session was spent checking in, reviewing previous week's

homework, building rapport, and assigning subsequent week's homework. Mr. K

attended and fully participated in all APT sessions. He also completed all his homework

including the generalization task, where he had a chance to practice the specific type of

attention taught in session (see Table 7, the Homework column).

As previously discussed, Mr. K was asked to assess the feasibility of APT by

completing log sheets (Appendix D) about how effortful, fatiguing, enjoyable the task has

been and how much progress he has made. Mr. K reported average scores in the higher

end of the feasible range for effort (3.34) and fatigue (2.50), and in the lower end of the

feasible range for progress (1.94) and enjoyment (2.13; see Figure 3). A detailed analysis

of Mr. K's feedback on feasibility indicated that he experienced a high level of fatigue

and a lower level of enjoyment with the increase in task difficulty (Figure 4). His

perceived progress was less variable (2 to 2.25 range), with the exception of session 3

(Divided Attention). During this session, Mr. K was involved in multitasking exercises,

which he found to be most challenging (e.g., timed article scanning with target

identification, solving arithmetic problems while listening to a CD exercise, or semantic categories identification while listening to a CD exercise). For Mr. K., session 3 (divided attention) was effortful (3), fatiguing (3), he perceived he made minimal progress (1) with very little enjoyment (0; Figure 5). It is possible that Mr. K's perfectionistic, dichotomous, and negative thinking (e.g., "I can't do these exercises well, therefore I will never be as good as I used to ") may have contributed to his low ratings of progress and enjoyment during this session.

Despite some low feasibility scores, that were still within the target range, Mr. K reported to have had a positive experience during the first five weeks of the treatment. He enjoyed the exercises, the homework, and the regularity of coming to session on a weekly basis. His superior cognitive abilities and natural inclination towards logic and "brain-power" activities (e.g., Sudoku, computer programming, etc) placed a high demand on the clinician's ability to keep him challenged and interested at all times.

CBT modules included psychoeducation, relaxation and diaphragmatic breathing training, mood monitoring, cognitive restructuring, creation of task hierarchies, and other techniques to address the physiological, cognitive, and behavioral aspects of negative mood, particularly anxiety. CBT was found to be efficacious in treating anxiety and depression in PD population (Dobkin, Allen, & Menza, 2006; Feeney, Egan, & Gasson, 2005; Cole and Vaughan, 2005; Mohlman et al., 2010). Therefore, a formal assessment of feasibility of CBT section was not necessary. Informally, Mr. K's active participation in sessions and homework compliance gave sufficient data to support feasibility for this CBT protocol. For example, Mr. K completed six out of six homework assignments, for

which he received a rating of 2.0 on a 0 to 3 scale, indicating that he completed all assignments correctly and on time.

Mr. K's participation during in-session CBT exercises also was exemplary, despite the challenge. In contrast to his ease in doing the APT work, Mr. K had trouble identifying his negative thoughts and challenging them during cognitive restructuring. The clinician had to constantly motivate Mr. K to engage in such novel and difficult process. After much effort and hard work, Mr. K identified a number of distorted thoughts that negatively influenced his feelings and behaviors (see Table 4). Following the metaphoric "onion peeling" lesson, Mr. K made significant progress in looking beyond his surface thoughts, and identifying deeper schemas that pervaded his thinking pattern (Appendix B). With Ms. R's collateral session, Mr. K learned to engage successfully in cognitive restructuring and to correct some of the thinking errors he repeatedly made. For example, he constantly compared his present "weak" state with his "almost perfect" past. Ms. R corroborated this account. He discounted all positive in his current life and highlighted his limitations. He recognized that his thinking brought about feelings of helplessness, self pity, and tremendous fear for a disastrous future. Mr. K and Ms. R agreed to participate in a behavioral modification task, in which each would pay a penalty ($0.25) every time they engaged in past/present evaluation. Subsequently, Mr. K reported feeling relief from not having to live up to his perfectionist expectations. His success was highly dependent on Ms. R's support, as he was looking for evidence against his unfounded worries. He also reported that techniques like "so what?" and " acting as if" were very helpful, as they were easy to remember each time negative thoughts crossed his mind.

Mr. K also learned to use diaphragmatic breathing and progressive muscle relaxation (PMR) to improve his sleep quality and decrease pain and muscle spasm especially during the night. While practicing the relaxations techniques, Mr. K noticed that his hand tremor decreased significantly, a fact that was also observed and confirmed by the clinician during the CBT sessions. Another goal for Mr. K was to resume physical exercise. To do so, Mr. K used a task hierarchy technique, in which a targeted activity (e.g., going to the gym) was broken down hierarchically in small, more manageable tasks, and less likely to be avoided. For example, he decided to prepare his gym equipment (e.g., clothing, special braces, water bottles, etc.) the night before and "act as if" this was part of a regular routine. This made it easier for him in the morning because he did not have to make a decision (i.e., to go or not to go) especially when his motivation was low, he felt tired, and his physical symptoms were acute. He also sought additional external motivators such as "it will make Ms. R happy if I go" and "I will learn about the business aspect of fitness and help my son to set up a new fitness center."

Methodology used to measure clinical outcome of BMFP are described in Chapter VI. Regardless of treatment results, it is important to reiterate that Mr. K participated fully in both in-session and at home exercises, was motivated, and persisted in doing the work even when was challenging (e.g., APT session 3, or cognitive restructuring). His endorsements indicated that BMFP was both feasible and acceptable.

<div align="center">**Clinical Outcome**</div>

Clinical outcome of BMFP was measured across two dimensions: cognition and mood. Mr. K demonstrated improvement on both dimensions, as compared to the baseline. The outcome measures of high level cognition were assessed with

neuropsychological tests of EF (see Chapter III for a description of the instruments). In order to establish a baseline of his cognitive level, Mr. K was evaluated at two separate times, one month apart. The average of test results obtained during the two baseline evaluations constituted Mr. K' s pre-treatment EF level. In general, the average of two baseline results is preferred to a single baseline evaluation, because it attenuates the potential for score variability due to practice effects, regression to the mean, characteristics of the test taker (e.g., motivation, emotional state, test comprehension level, health), elements of the environment (e.g., temperature and lighting of the testing room), degree of rapport with the clinician, and temporary aspects such as attention lapses or memory retrieval failure (McCaffrey & Westerveldt, 1995). With the exception of a single outlier performance on one attention measure (digit backwards), Mr. K's pre-treatment results were stable across baselines (Table 8).

Pre and post results of measures of attention and EF are displayed in Table 5. As compared to pre-treatment phase, Mr. K's post-treatment results indicated minimal improvement (at best), with slightly higher scores observed in areas of associative memory and verbal learning. All other performances remained stable after treatment, with scores ranging within the high average to very superior range. A further analysis of composite scores, investigating Mr. K's verbal versus non-verbal abilities demonstrated a slight improvement in the executive domain mediated by verbal abilities (Table 9). Despite Mr. K's report of cognitive decline, his neurocognitive profile, evaluated by objective neuropsychological measures, indicated intact EF abilities at baseline, with a non-significant improvement post- treatment, possibly due to a ceiling effect.

Mr. K's subjective report of control of mental abilities was captured on a daily rating of perceived attentional control (0 to 8 Likert scale; Appendix D) throughout intervention period. His endorsements reflected minimal variability, with overall results within in the average range (Figure 1) The trend is compatible with that captured by objective assessments, and it demonstrated no significant change (increase or decrease) in both perceived or objective cognitive abilities pre and posttreatment. Notably, there was a mild discrepancy between subjective assessment of cognitive abilities (average range) and results on objective measures (high average to superior), suggestive of a possible devaluation of own abilities, common in patients with PD (Bassett, 2005). It also is possible that anxiety and depression contributed to a poorer estimation of cognitive abilities at baseline and throughout treatment period, leading to a perceived functional impairment far worse than it was in reality (Shiba et al., 2000).

Mr. K's mood, evaluated by clinician and self-reported measures, showed a more dynamic trend as compared to his EF profile. Relative to baseline, Mr. K's post-treatment results indicated a considerable reduction in scores on three out of four anxiety measures (BAI, ASI, and HAM-A; Table 4). These gains were maintained throughout the six week period, following treatment (see HAM-A results at Follow-up, Table 4). According to the "responder" criteria (Himadi, Boyce, & Barlow, 1986), defined a priori based on studies of late life GAD (Mohlman, 2004), Mr. K was classified as a responder to treatment, demonstrating at least 20% reduction in results on at least 75% of anxiety measures (Mohlman et al., 2010). In addition, Mr. K exhibited a reduction on measures of depression (BDI, and HAM-D), which were not specifically targeted by BMFP. However, the use of transdiagnostic CBT, or simple activation due to involvement in a

regular schedule (e.g., coming to sessions weekly, engagement in homework, etc.) may also explain the reduction in depressive symptoms.

Mr. K also completed a daily self-reported evaluation of pleasant feelings, anxiety, and depression (Appendix D). Mr. K's self-reported mood ratings showed little improvement (half a point to a point) throughout treatment period (Figure 1). Just as with cognitive results, there is a notable discrepancy between objective (clinician administered) and self-reported measures of mood, with the later depicting less improvement. Studies suggest that a subset of patients with PD exhibit poor self-awareness and self-concept and that these difficulties may be linked to frontal lobe dysfunction (McNamara, Durso, & Harris, 2006). It is also likely that these discrepancies reflect biases in self-evaluation or reporting, specifically a tendency to perceive or portray symptoms as more severe than they actually are. Many PD patients exhibit a pattern of low perceived control and self-efficacy (Marinus, Leentjens, Visser, Stiggelbout, & van Hilten, 2002; McQuinlan, Licht, & Licht, 2003) and lower outcome expectancies for future self, even when compared to other populations with neurodegerative diseases (Frazier, Cotrell, & Hooker, 2003). These processes are thought to contribute to greater psychological distress, poorer coping, and reduced quality of life (Thommessen et al., 2002).

Notably, most gains in mood were perceived and reported by Mr. K during the APT module (Figure 6). Future studies should investigate whether this pattern is replicable in other patients, which would suggest that APT may offer secondary gains, such as mood improvement. In Mr. K's case, APT exercises were particularly appealing, as it gave him the opportunity to apply his professional skills (as a computer

programmer) and derive satisfaction from intellectual stimulation. With one exception (session 3), he reported enjoyment doing the APT work, both in session and at home, as perhaps it allowed to use his abilities, in spite of PD. It is likely that his attitude and successful engagement during APT increased his self-esteem and ultimately led to improvement in mood. The gains in anxiety, depression, and feeling pleasant, as perceived by Mr. K were maintained until the end of treatment, with few exceptions. The exceptions refer to unexpected circumstances described in later in the paper.

In summary, BMFP showed the biggest gains in mood, as reported by clinician-administered measures and mood rating inventories. Mr. K's EF skills, as measured by neuropsychological tests, showed only minimal improvement, complicated by a possible ceiling effect.

Interpretation of Clinical Results

As previously mentioned, Mr. K was representative of PD population for which BMFP was intended. His clinical profile, including physical symptoms and psychiatric and his cognitive complaints met the selection criteria for this study (see Case Presentation). However, baseline neuropsychological measures revealed that Mr. K was cognitively intact. Mr. K was motivated and committed to work for the entire duration of the intervention. Treatment outcome was within expectations in terms of reduction in anxiety symptoms, yet it reflected only a minimal improvement in EF. (see Chapter VI). Mr. K's depressive symptoms also improved, due to an unexpected effect of BMFP. Objective and subjective measures of mood and EF, used throughout treatment period, captured clinical outcome, yet it also was necessary to consider Mr. K's personal characteristics and complicating factors in order to have a complete analysis of results.

Mr. K endorsed most progress in mood symptoms during the APT phase. This was followed by an opposite trend, showing a relative increase of anxiety and depression during week two and three of CBT (Figure 6), time in which Mr. K and Mr. R underwent an unexpected biopsy screening. Anticipatory fear of biopsy procedure, as well as waiting for the results generated anxiety and feelings of helplessness for Mr. K. His feelings were captured in daily mood records. Biopsy results were negative for both Mr. K and Ms. R., yet the stressful experience of going through such event disrupted the positive pattern of recent gains in mood and temporarily "confirmed" some of Mr. K's deep seeded cognitive schemas of vulnerability, helplessness, and bleak outlook for future. On the positive side, this circumstance created the opportunity for Mr. K to practice CBT in a crisis situation.

Additionally, Mr. K had the opportunity to use professional skills during APT, which generated a certain amount of enthusiasm and interest, and ultimately lead to decrease of anxiety and depression during the first half of BMFP. He continued to stay engaged during CBT phase, yet he may have experienced an exacerbation of mood symptoms, as most people do, during first psychotherapy sessions (Weinberg, 1984). Thus, Mr. K's premorbid inclinations and interests also are likely to account for the discrepancy in mood symptom relief noted during BMFP phases.

Mr. K's intact EF profile at baseline was maintained throughout treatment and ultimately resulted in post-treatment EF scores within the high average to very superior (Tables 5 & 9). This profile, measured by objective neuropsychological tests and reinforced by Mr. K's subjective report of control over attentional abilities, resulted in a minimal improvement in EF, post-treatment. However disappointing these results were,

they may be explained by a ceiling effect reached by Mr. K's superior cognitive abilities. Nonetheless, the incongruity between his cognitive complaints and test results is worth remembering, as it may be explained by potential limitation of objective measures to capture day-to-day cognitive struggles, or by a feature of PD, leading to exaggeration of symptoms, especially in the context of mood disorders. The clinical complexity of PD, in which the motor symptoms and EF are negatively affected by anxiety and depression (Menza & Dobkin, 2006; Dattillio, 2005) make it challenging for patients to tease apart the source of their difficulties.

Overall, the combination of APT and CBT demonstrated efficacy in improving Mr. K's anxiety and depression symptoms and only minimal improvement of EF. Given K's high functioning cognitive profile at baseline, it is difficult to determine APT's efficacy in improving EF. However, the case of Mr. K demonstrated that APT could be beneficial if it helped him get engaged in an intellectually stimulating activity with subsequent positive effects on depression and anxiety symptoms. APT also appeared helpful because it taught Mr. K how to use his attentional skills during every day activities (see examples of generalized homework exercises; Table 7) and provided him with new ideas about creating intellectually "fun" exercises (e.g., LSAT type, reading paragraphs of a book searching for certain target words, doing mental math calculation while exercising, etc). Mr. K demonstrated significant progress in identifying and correcting some of his negative thinking, by using cognitive restructuring and behavioral modification techniques. Mr. K's case also demonstrated CBT's effectiveness during a crisis situation (e.g., biopsy testing period), when Mr.K made successful use of relaxation techniques to alleviate his fear.

Follow-Up

Mr. K was contacted six weeks after termination of treatment. The HAM-A was administered by phone (score displayed in Table 4). Mr. K's post-treatment gains in anxiety symptoms were maintained, yet he continued to endorse physical symptoms which were difficult to categorize as either anxiety or PD related (e.g., muscle pain, stiffness, twitching, jerks, urinary and sexual dysfunction, unsteady voice, and grinding of his teeth) . However, a qualitative difference between his follow-up and baseline scores was noticed. For instance, at follow up, Mr. K did not endorse any more fears (e.g., fear of being left alone) and his sleep improved to a certain degree. He no longer reported concentration and memory problems, nor had he any episodes of heart racing. His depression went fully into remission.

Overall, Mr. K stated that his participation in BFMP was beneficial to him, and he felt better equipped to manage his anxiety and depression after having completed the program. For example, he often used the relaxation techniques to help him sleep and the expression "So what!" became a constant companion of his thinking, freeing him from perfectionistic standards, he could not achieve. He and Ms. R also were more aware and caught themselves before engaging in the detrimental past/present comparison. Mr. K remained physically active, by continued his physical exercises he began during treatment and by doing house work. Overall, Mr. K stated that he enjoyed the program, and he specifically announced his willingness to participate in future similar programs.

Intervention Implications of the Case

The case of Mr. K showed that BFMP was feasible, acceptable, and somewhat beneficial. He maintained his motivation and remained engaged throughout the treatment

period, by participating actively in all in-session exercises and completing his homework. The case also demonstrated that BMFP is efficacious in terms of mood improvement (i.e., reduction in anxiety and depression), yet was limited in proving its beneficial cognitive effect. Mr. K's baseline high functioning EF profile, his premorbid skills and interests, and the biopsy during treatment period influenced the clinical outcome (e.g., minimal EF improvement) and accounted for an unexpected pattern of results (i.e., significant mood gain during APT, followed by a temporary setback during CBT). These patterns indicate the importance of carefully tracking life events when evaluating treatment efficacy.

Despite limited cognitive improvement, Mr. K's case added valuable information to a limited body of literature regarding efficacy of cognitive rehabilitation in PD. It has been suggested that a lack of skill loss over time is in and of itself an improvement in certain clinical populations, such PD and other progressive neurological disorders (Troster et al., 2007). Future studies may need to evaluate outcome less stringently, and regard more positively stable results, as Mr. K exhibited after 20 weeks of intervention. It is further recommended to continue to test efficacy of APT in BFMP in a larger sample, including subjects with a more typical PD-related cognitive difficulties at baseline (i.e., variable attention and working memory, decreased processing speed, and ED). Future studies may include a stricter inclusion criterion at baseline, such that it will only allow participation of patients with a decline in cognitive profile, as measured by objective neuropsychological tests. Exclusion criterion of dementia should be maintained. This slight change in recruiting criteria may eliminate the potential for post-treatment ceiling effect and increase the chance of demonstrating efficacy of APT, as part of BMFP. It also

would help discern whether APT administration before CBT is associated with increased cognitive abilities, allowing patients to take full advantage of CBT skills.

Following APT phase, Mr. K maintained his gains in mood throughout the treatment and follow- up periods. The complicating factors described earlier did not compromise the efficacy of treatment in spite of a temporary escalation of anxiety and depression symptoms reported during the CBT phase. Mr. K learned to use relaxation techniques and cognitive restructuring to deal with the frightening experience of biopsy, and was ultimately able to reduce his anxiety and depression. The overall improvement in mood throughout the entire BFMP demonstrated that APT/CBT combination was indeed efficacious for Mr. K. Furthermore, it demonstrated that CBT alleviated increased levels of anxiety and depression during crisis. These results also add to the slowly growing body of literature demonstrating efficacy of CBT for treating non-motoric symptoms of PD (Dobkin et al., 2006; Dreisig et al., 1999; Feeney et al., 2005; Mohlman et al., 2010).

Based on Mr.K's case, BFMP deemed to be a feasible treatment of anxiety and depression in PD patients. In addition to minor modification in recruitment criteria mentioned above, future studies of BMFP may also need to provide more customization for PD population. For example, Mohlman et al.(2010) suggested the use of recording devices or therapist assistance with writing, as an alternative to the writing assignments, especially during the CBT section. As a consequence, better adherence to homework and improved quality of the assignments (e.g., improved eligibility and elimination of micrographia) may be obtained, thus increasing the overall treatment quality. Mohlman et al. (2010) also suggested that by offering more than one session of caretaker participation may have a positive impact on overall CBT effectiveness.

Defined by its intent to challenge cognitive abilities, particularly in the area of higher level cognition and EF, APT seemed at times less enjoyable than Mr. K expected (Figure 4). As mentioned elsewhere (Mohlman et al., 2010) a revision of future practice could include intermittent rewards (e.g., healthy snacks or beverages, brief shoulder massage from caretaker, unseen photos of client's pets or family members provided by spouse) and a longer rest period (> 5 min) to produce higher ratings of enjoyment.

BFMP also proved to be an economical solution due to its brief period, ease of administration, and standardization. Both APT and CBT sections were standardized and manualized, which made it easy to be transported within and outside the university clinic. Clinicians' training was relatively short and the intervention was delivered by graduate students in clinical psychology.

From a learning perspective, BFMP offered clinicians the opportunity to cross specialty fields, including neuropsychology, cognitive rehabilitation, psychotherapy, and behavioral neuroscience. Although cross-specialty training may appear as a learning bonus to many clinicians today, this may rapidly change into a common professional requirement of the future, especially when treating complex diseases such as PD. The global aging trend of rapid growth will continue and the need to understand and manage late-life diseases will have to become a priority for scientists across many professions. It is only through use of technology and continuous research that knowledge about brain-behavior relationship and related dysfunctions will flourish and new and innovative treatment solutions, as BFMP, will develop.

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Footnotes

[1] Hypokinetic: characterized by, associated with, or caused by decreased motor activity (Merriam-Webster's Medical Dictionary On-Line, http://www.merriam-webster.com/medical/hypokinetic).

[2] Alpha-Synuclein: protein that constitutes the primary structural component of Lewy body fibrils (Arima et al., 1998)

[3] "on-off" state: fluctuation of motor symptoms such as unpredictable, alternating periods of dyskinesia and immobility

[4] Learning of feedback-based and incrementally acquired task: a midbrain mediated function presumably involved in learning tasks based on repetition and feedback (e.g. learning to drive, learning to play chess, learning to cook)

[5] Probabilistic reversal learning: a type of learning that requires adaptation to new situations that appear in a probabilistic manner (e.g. a hypothetical shifting between driving in the US and UK; playing the roulette, etc.)

[6] Suboptimal medication adherence: Patients' adherence to some (but not all) medication treatment recommendations: dosage, frequency.

[7] Thalamotomy: invasive procedure involving the ablation of a selected portion of the thalamus.

[8] Palladatomy: procedure involving the surgical removal of the globus pallidus, thought to be overactive in PD.

[9] Ocular Myasthenia Gravis: autoimmune eye disorder that can occur, characterized by weakened eye and eyelid muscles. Symptoms include: diplopia (double vision), ptosis (drooping eyelids), light, nystagmus (constant involuntary movements of the eyeball in any direction), visual disturbances, and eyelid retraction, which causes an incomplete eye closure

[10] Hypophonia: a weak voice due to incoordination of the vocal muscles (Dorland's Medical Dictionary for Health Consumers. © 2007 by Saunders, an imprint of Elsevier, Inc.)

[11] Dysarthria: difficult, poorly articulated speech, resulting from interference in the control and execution over the muscles of speech usually caused by damage to a central or peripheral motor nerve. (Mosby's Medical Dictionary, 8th edition. © 2009, Elsevier.)

[12] Micrographia : tiny handwriting , or handwriting that decreases in size from normal to minute, seen in parkinsonism. (Dorland's Medical Dictionary, 2007)

Table 1

Financial burden of PD

Type of Costs	Annual Cost per PD Patient	Annual Cost per Non-PD Patient	Significant Differences between PD and non-PD patients
Direct Costs (hospital & long-term care (inpatient and outpatient), ER, outpatient medication)	$23,101	$11,247	$11,854
Indirect Costs (productivity loss, uncompensated family financial loss, reduced earnings) Unquantifiable costs (change of role in society and family, psychiatric and other co-morbid disorders, cognitive decline**.**	$25,326	No data available	2 more days in the hospital for PD patients 43 more days in long term care for PD patients 20 more filled prescriptions for PD patients
Total Costs	$48,427		

Note: Based on a study by Huse, et al., (2005) including 20,016 PD patients matched by same number of controls. The costs are reported in 2002 US dollars.

Table 2

Motor and non-motor symptoms of PD

Motor Symptoms	Non-Motor Symptoms
Primary Symptoms	*Neuropsychiatric and Cognitive Symptoms*
Tremor at rest	Bradyphrenia (cognitive slowing)
Muscle rigidity (stiffness)	Executive dysfunction
Bradykinesia (slowness of movement)	Attention & memory decline (mostly short term memory)
Gait disturbance	Language fluency decline
Muscle pain, cramps, aching, or fatigue	Anxiety
Postural instability	Depression
Secondary Symptoms	Dizziness and lightheadedness
Loss of arm swing	Sleep disturbance
Facial mask (lack of facial expression)	Fatigue
Slowed or slurred speech	Psychosis
Loss of dexterity and/or micrographia (small, cramped handwriting)	*Autonomic & Sensory Symptoms*
Akathisia (inability to sit still, restlessness)	Sexual dysfunction
Restless leg syndrome	Constipation
	Urinary Dysfunction (urgency, frequency, incontinence)
	Hyperhidrosis (sweating dysfunction
	Burning, smell loss

Table 3

Common side effects of PD pharma-medical treatment

Medical Treatment	Side Effects				
	Cognitive/Learning	**Cognitive/Psychiatric**	**Mood**	**Impulse Control**	**Other**
Dopaminergic Medication	Negative Impact on Feedback learning and probabilistic reversal learning	Hallucinations, delusions, euphoria, mania	Anxiety	Excessive shopping, eating, sexual behavior Gambling	Dyskinesia Excessive daytime sleeping leading to potential vehicle accidents
Combo Treatment: dopaminergic and anticholinergic	Negative Impact on generalization learning				
Bi-lateral Stimulation of Subthalamic nuclei	Dementia	Delirium, hallucinations	Apathy		Dyskinesia Weight gain Eye-lid opening apraxia Dysarthria

Table 4

Mr. K's pre- and post-treatment results on psychiatric measures

Anxiety	Pre-Treatment	Post-Treatment	Follow-up (6 weeks post-treatment)
BAI	34	16	-
STAI	67	64	-
ASI	34	26	-
HAM-A	25	20	22
Depression	Pre-Treatment	Post-Treatment	
BDI	32	21	-
HAM-D	24	15	-

Note. BAI = Beck Anxiety Inventory; STAI=State-Trait Anxiety Inventory ; ASI = Anxiety Sensitivity Index; Ham-A = Hamilton Scale for Anxiety; BDI = Beck Depression Inventory; Ham-D = Hamilton Scale for Depression

Table 5

Mr. K's pre- and post-treatment neuropsychological results

Test	Cognitive Skill Measured	Pre-treatment (T-scores)	Post-treatment (T-scores)
Digits Forward	Verbal working memory	70 (very superior)	71 (very superior)
Digits Backward	Verbal working memory, mental control	57 (high average)	66 (superior)
Digit Symbol Coding	Visual-motor coordination; processing speed	70 (very superior)	63 (superior)
Verbal Paired Associates (total)	Associative Memory & verbal learning	56 (average)	66 (superior)
Stroop Color-Word Interference Test	Inhibitory Control, Verbal working Memory	81(very superior)	74 (high average)
COWAT (FAS)	Verbal fluency	56 (average)	59 (high average)
Similarities	Verbal concept formation	58 (high average)	60 (high average)
Trail Making Test, Part A	Processing speed	81(very superior)	85 (very superior)
Trail Making Test, Part B	Inhibitory Control, Spatial working Memory, Mental flexibility	72 (very superior)	73 (very superior)

Note: Stroop Color-Word Interference Test, Controlled Oral Word Association Test (COWAT); Trailmaking Test and several subtests from the Wechsler Adult Intelligence and Memory Scales (i.e., Digit Span, Verbal Paired Associates, Similarities, and Digit symbol coding;

Table 6

Mr. K's cognitive style

Toxic Thoughts	Core Belief	The Impact on Mr. K
"I am afraid that someone else would be better than me at negotiating for my children"	If I am not perfect, I am worthless	Feelings of depression when perfection cannot be achieved Perfectionist thinking style, leading to fear of failure, incompetence
" I am afraid of going through life alone" "I am afraid to rely on people"	I am weak and helpless	Pervasive anxiety and low self-esteem, vulnerability; paranoid thinking style
"I can't work on house projects" "I used to be a renaissance man and I am not anymore" "I am afraid of what PD will do to me"	I am no longer a man	General depressive symptoms, anxiety, fear of losing control; angry behavior or apathy and anhedonia
"I am afraid of not being loved by anyone" "I am afraid of being rejected " "I am afraid to hold my son responsible for his misdeeds-I am afraid he will not care"	I am unlovable	Fear of abandonment, feelings of dependency, alienation from other people; depression, frustration; avoidant and angry behavior
"I am afraid of negotiating for my children"	I am a failure	Feelings of inadequacy, frustration, anger; avoidant behavior

Table 7

Summary of the Brain and Mind Fitness Program

	Module	Description of Skills Developed	Tasks	Homework
Session 1 APT	Sustained Attention	Attention Span, Mental Control, Working Memory	Rapid identification of auditory target stimuli (round objects); alphabetize sentence (alphabetical condition)	Reading and exercising for 1 hour each; organizing his email
Session 2 APT	Selective Attention	Ability to maintain behavioral set in presence of distraction	Rapid identification of target stimuli (holidays) in the presence of distracters	Watch TV & read in the company of his 3 y.o. granddaughter; find his wife in crowded place
Session 3 APT	Divided Attention	Ability to multitask	Rapid reading of a paragraph while crossing out cancellation targets, followed by answering questions about the paragraph	Attend to his granddaughter's needs while planning gardening project; count the # people with glasses while looking for his wife in the store
Session 4 APT	Alternating Attention	Ability to rapidly switch attention between multiple targets	Alphabetize sentence (rapid switch between alphabetical, reverse, and progressive conditions)	Switch between Sudoku and reading, baking and math calculations, and watching TV and reading to granddaughter
Session 5 APT	Logic	Ability to use reasoning and critical thinking	SAT like exercises	Practice previous homework and create new ones
Break				Practice previous homework and create new ones
Session 6 CBT	Three Parts Model of Emotion (physiological interventions)	Diaphragmatic breathing and progressive muscle relaxation (PMR)		Practice breathing and PMR; complete relaxation log and 3-component worksheet

Table 7 – Continued

Session 7 CBT	Three Parts Model of Emotion (cognitive interventions)	Cognitive restructuring		Practice cognitive restructuring for at least 3 toxic thoughts
Session 8 CBT	Three Parts Model of Emotion (cognitive and behavioral interventions)	Cognitive restructuring with perspective taking and reverse avoidance behaviors using task hierarchy		Complete task hierarchy for avoidance behavior (not exercising); make use of cognitive restructuring for negative thoughts
Session 9 CBT	Three Parts Model of Emotion (behavioral interventions)	Behavior modification strategies: Act "as if", "So what", sleep hygiene		Complete a worry behavior log
Session 10 CBT	Review	Review of entire skills acquired using BMFP		

Table 8

Mr. K's pre- treatment neuropsychological results

Test	Baseline 1 T Score	Baseline 2 T Score	Average T Score
Digits Forward	70	70	70
Digits Backward*	70	43	57
Digit Symbol Coding	70	70	70
Verbal Paired Associates (total)	54	57	56
Stroop Color-Word Interference Test	74	87	81
COWAT (FAS)	52	60	56
Similarities	63	53	60
Trail Making Test, Part A	74	87	81
Trail Making Test, Part B	71	73	72

Note: Stroop Color-Word Interference Test, Controlled Oral Word Association Test (COWAT), Trailmaking Test, and several subtests from the Wechsler Adult Intelligence and Memory Scales (i.e., Digit Span, Verbal Paired Associates, Similarities, and Digit symbol coding)

Table 9

Mr. K's pre- and post-treatment composite indices of executive functioning

	Index Description	Pre-treatment (T-score)	Post-treatment (T-score)
Verbal Executive Index (VEI)	Measure of EF as a function of language abilities	58 (high average)	63 (superior)
Non-Verbal Executive Index (NVEI)	Measure of EF as a function of non-verbal skills	70 (very superior)	69 (superior)
Executive Functioning Index (EFI)	Measure of EF including verbal and non-verbal abilities	64 (superior)	67 (superior)

Note: VEI- composite index calculated as an average of score results for VPA total (Verbal Pair Associates total), Similarities, Controlled Oral Word Association Test (COWAT); NVEI-composite index calculated as an average of score results for Trails B (Trailmaking Test), Stroop Color-Word Interference Test and selected tests of Digit Backwards, and Symbol Search of Wechsler Adult Intelligence and Memory Scales; EFI-composite index calculated as an average of score results for the executive functioning measures listed above.
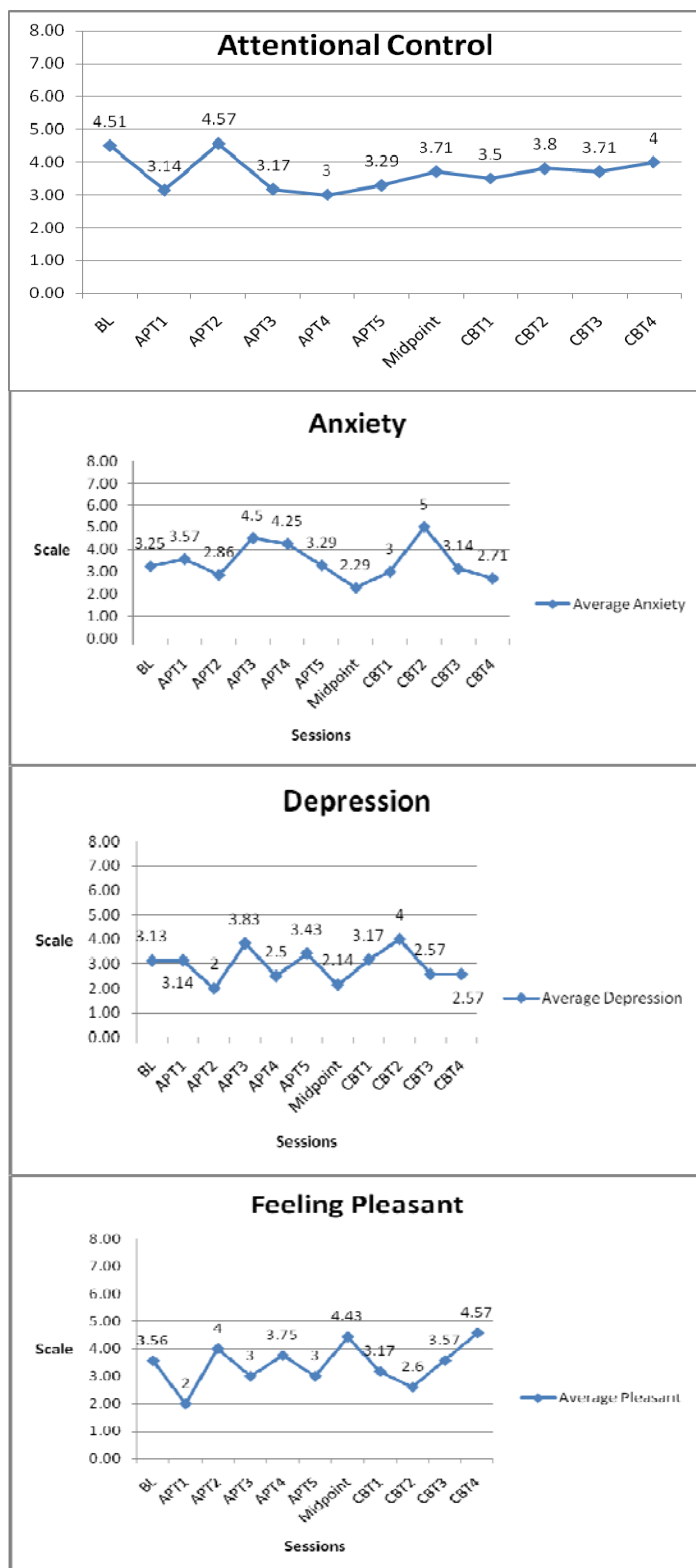
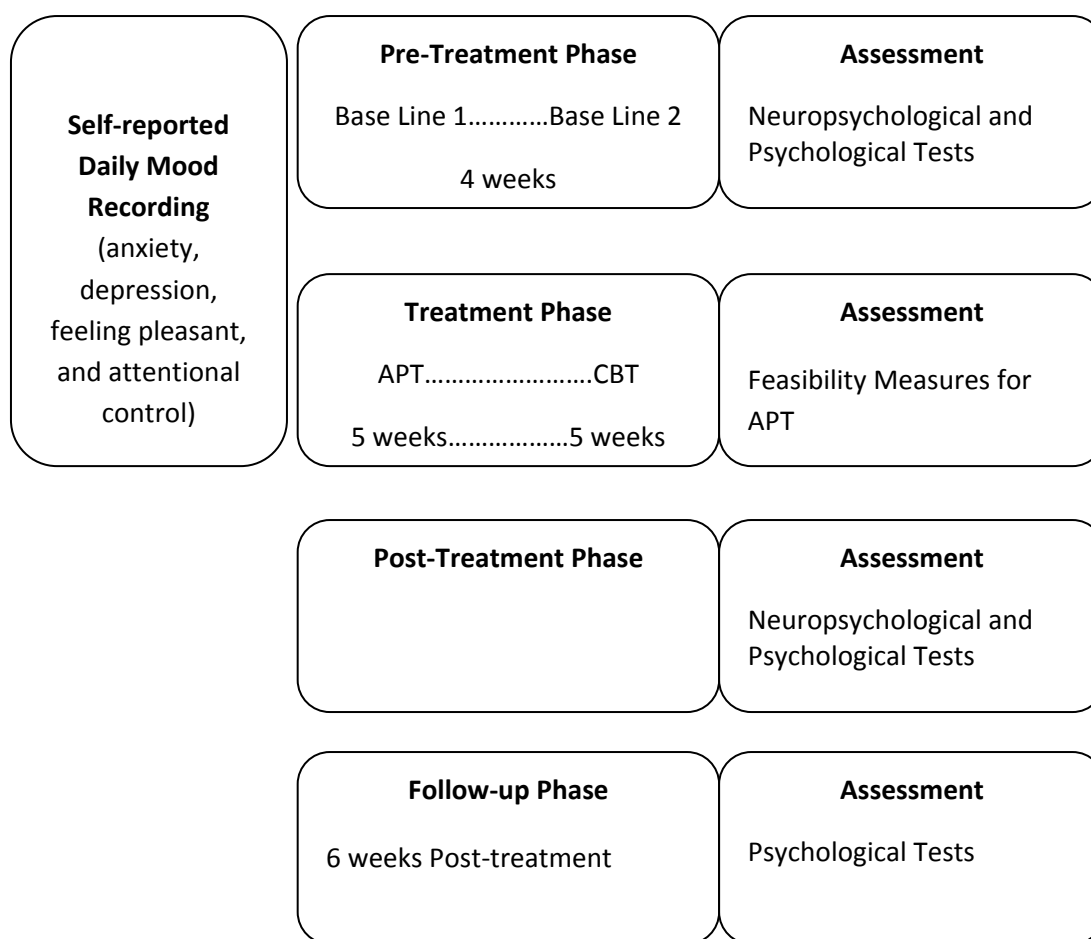Figure 1. Mr. K's self-report of daily mood and attentional control

Self-reported Daily Mood Recording (anxiety, depression, feeling pleasant, and attentional control)

Pre-Treatment Phase

Base Line 1…………Base Line 2

4 weeks

Assessment

Neuropsychological and Psychological Tests

Treatment Phase

APT……………………CBT

5 weeks………………5 weeks

Assessment

Feasibility Measures for APT

Post-Treatment Phase

Assessment

Neuropsychological and Psychological Tests

Follow-up Phase

6 weeks Post-treatment

Assessment

Psychological Tests

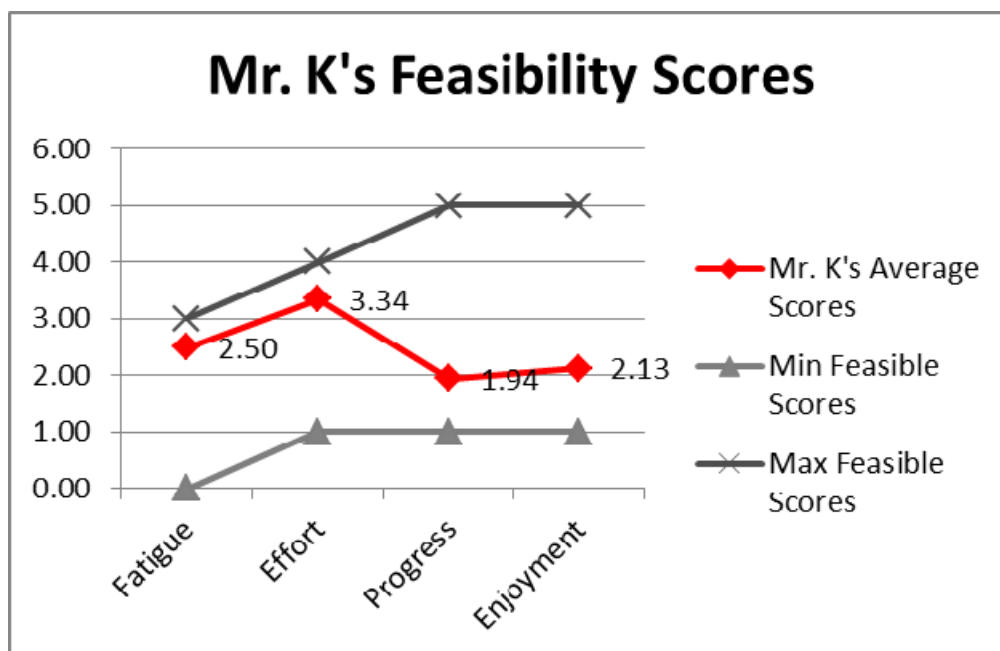Figure 2. Brain and Mind Fitness Program design

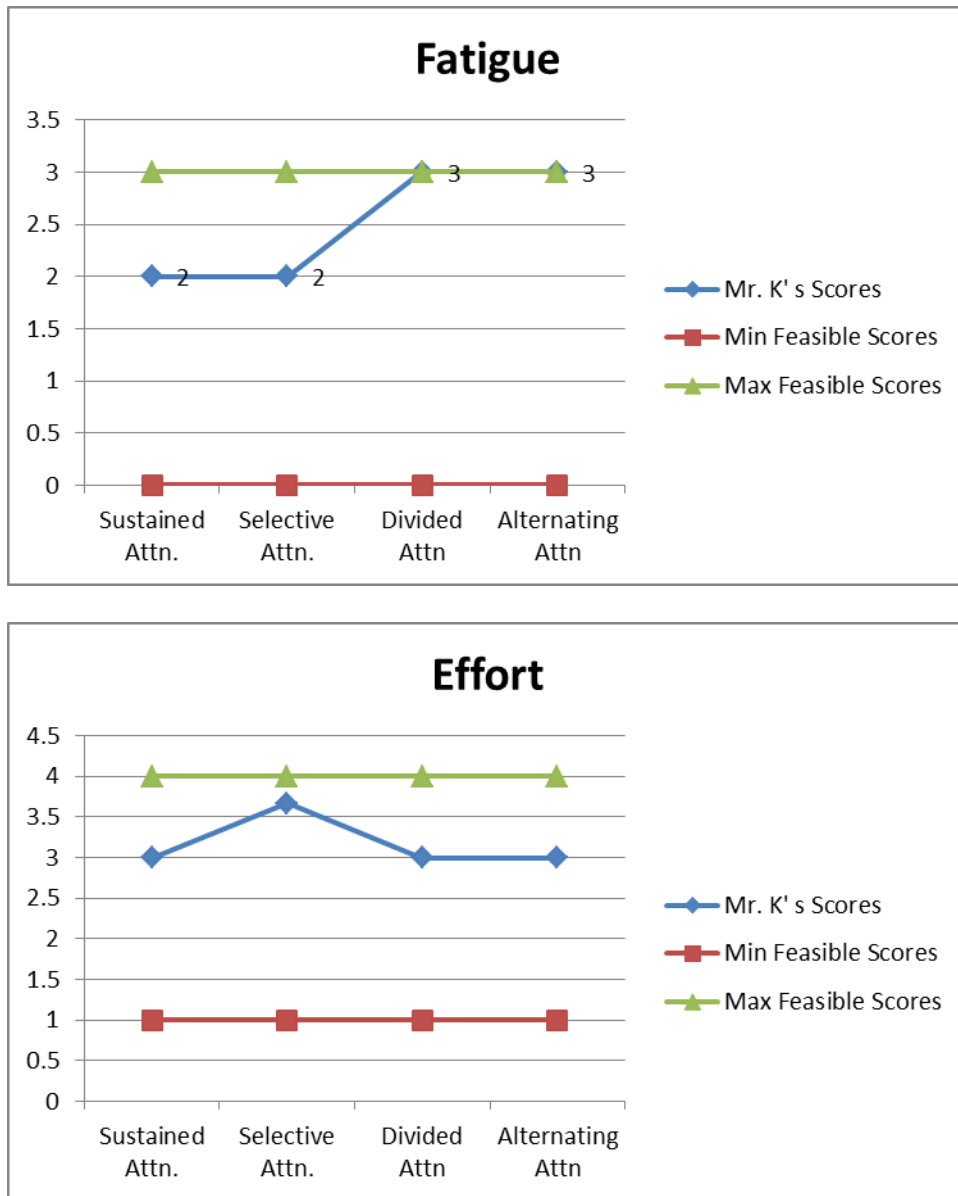Figure 3. Program feasibility and acceptability by Mr. K.'s report

Figure 4. Mr. K's perceived levels of fatigue, effort, progress, and enjoyment
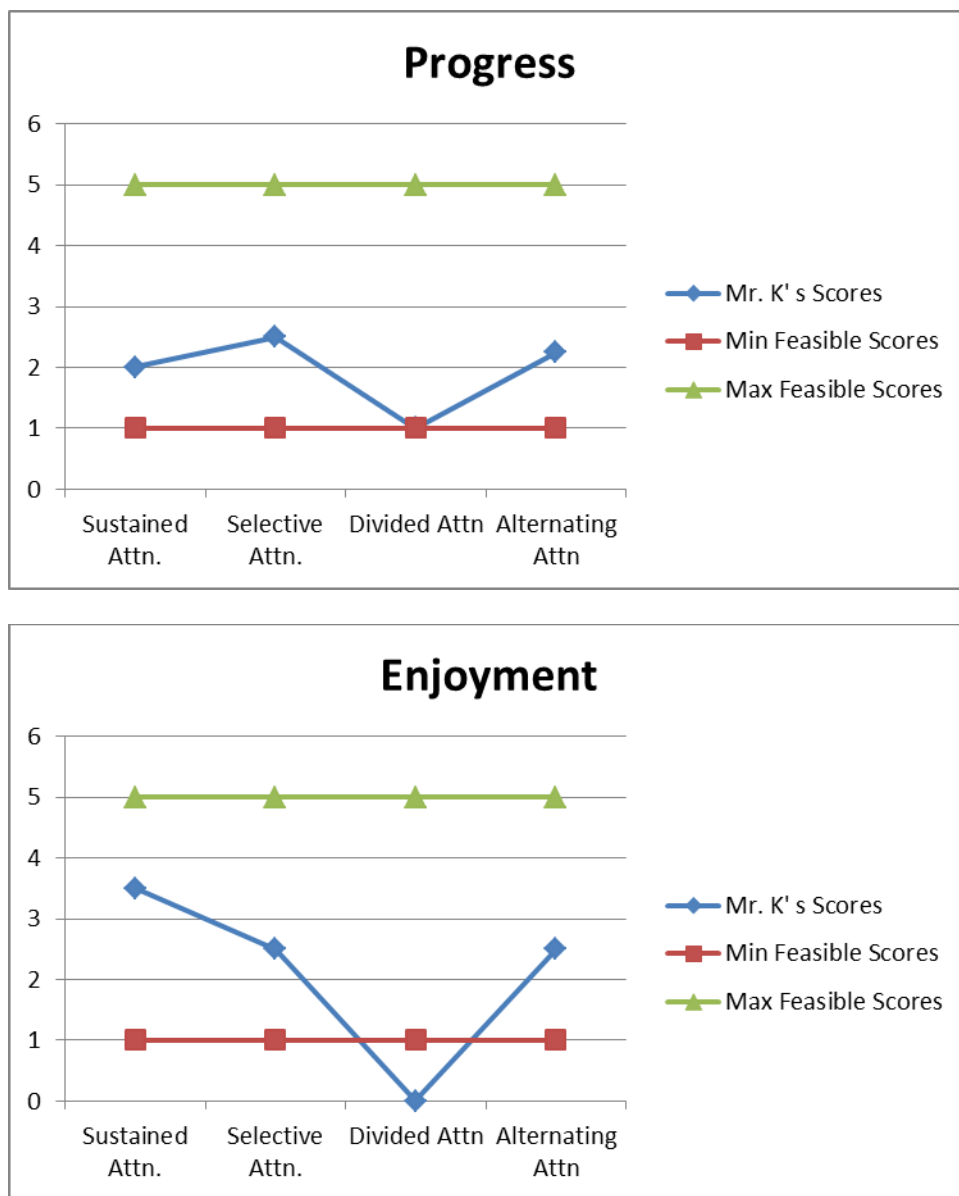
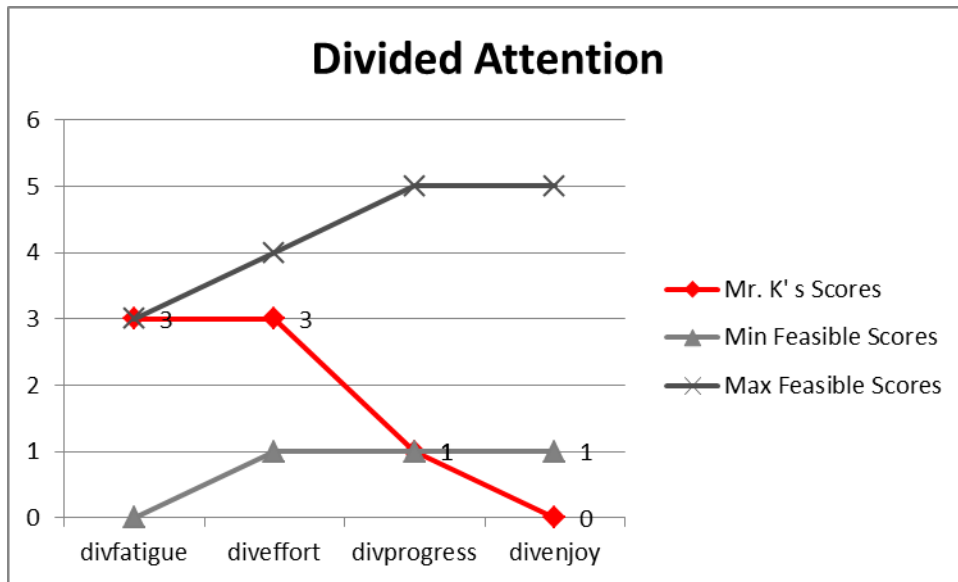Figure 4 – Continued. Mr. K's perceived levels of fatigue, effort, progress, and enjoyment

Figure 5. Mr. K's feasibility data for session 3 (divided attention)
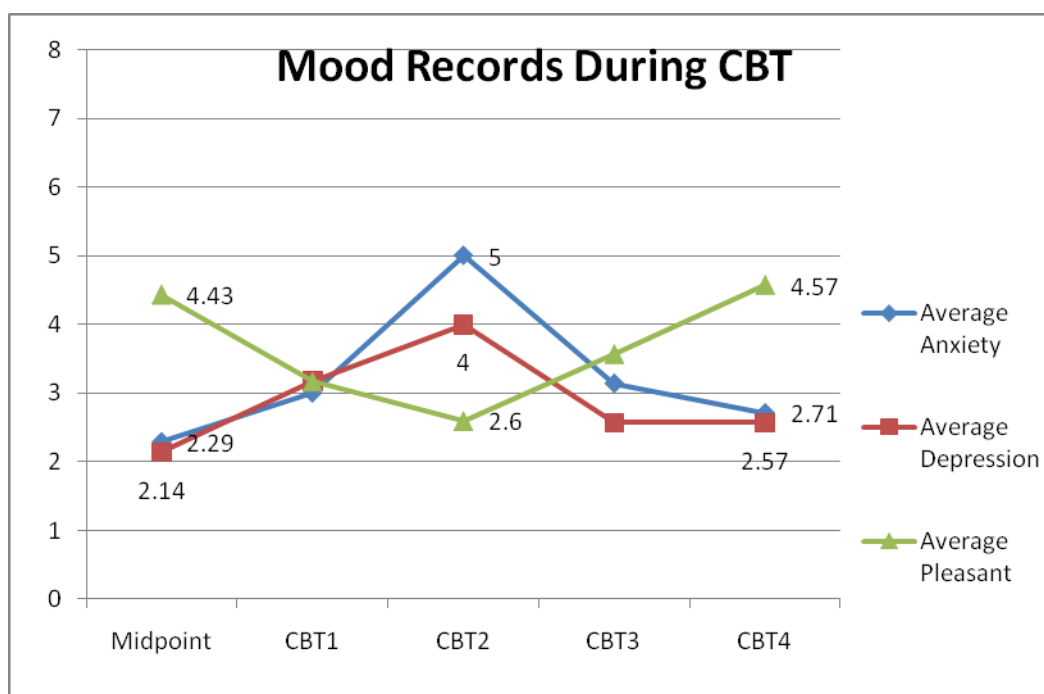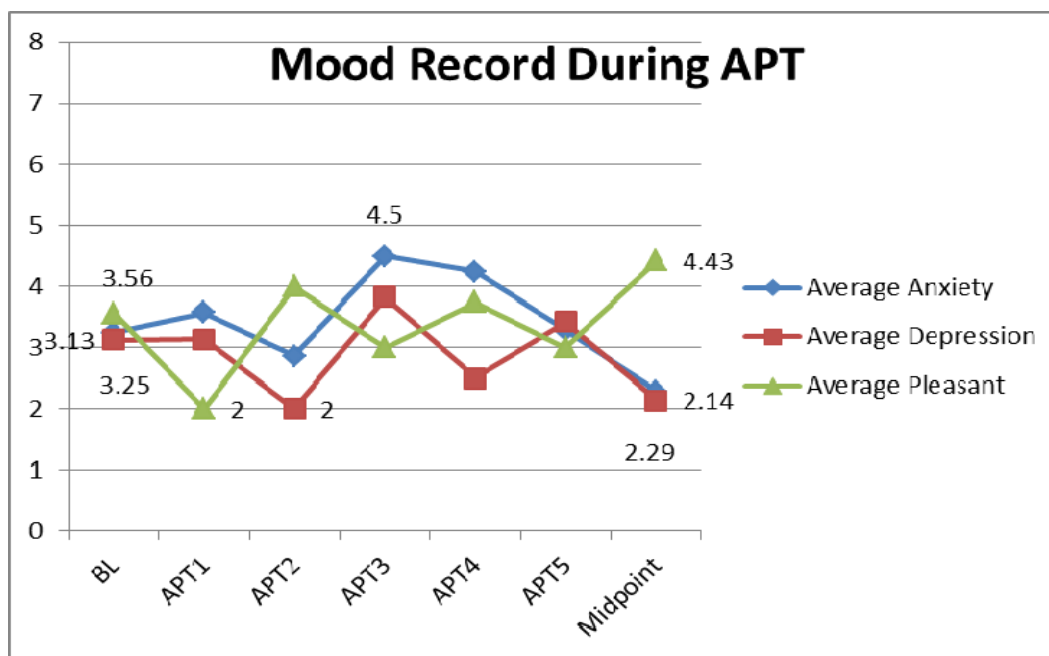
Figure 6. Mr. K's self-report of daily mood during APT and CBT

APPENDIX A

Sample of Mr. K's handwriting (example of micrographia)

THOUGHT RECORD for COGNITIVE RESTRUCTURING

1. Toxic Thought This should be a single thought, written verbatim, should include the word "I" should be written in the present tense.	2. Situation Who? What? When? Where?	3. Moods What did you feel when you had the toxic thought? Rate the intensity of each mood (0-100%).	4. Evidence That *Supports* the Toxic Thought What *facts* support your toxic thought?	5. Evidence that *Does Not Support* the Toxic Thought Try to generate 3 pieces of evidence in column 5 for every 1 piece in column 4.	6. Alternative / Balanced Thought Write an alternative balanced thought based on the evidence.	7. Rate Moods Now Write moods listed in Column 3 as well as any new moods, then rate their intensity (0-100%).

APPENDIX B

Sample of Mr. K's core beliefs, based on the "Onion Peeling Effect"

The Onion Effect

I can't do all of the projects correctly by July 4th BBQ
      I can't do all of the projects correctly
         I can't do all the projects
            A renaissance man could all the projects
               I used to be a renaissance man
                  I am no longer a renaissance man
                    I am no longer a man

I'm afraid of negotiating for Jamie and Tony
      I'm afraid of missing an important strategy
         I'm afraid they will pay more than they should
         I'm afraid of failing my daughter
         I'm afraid of failure

I'm afraid to hold Jarrad responsible for hurting me and my family
      I'm afraid to tell him I'm hurt
         I'm afraid he won't care
         I'm afraid he doesn't love me
             I'm afraid of not being loved by anyone
               I'm afraid of going through life alone
                  Loneliness is the ultimate failure
               I'm afraid of failure

I'm afraid of what PD will do to me
      I'm afraid to be an invalid because they must rely on others
      I'm afraid to rely on people
         I'm afraid of being rejected like I was as a kid
            I'm afraid of being alone and unable to care for myself
            I'm afraid of being placed in a home
               I'm afraid of being forgotten

APPENDIX C

Feasibility range for APT

	0	1	2	3	4	5
	(None)	(A Little)	(Some)	(Much)	(Very Much)	(Extreme)
Progress		■	■	■	■	■
Enjoyment		■	■	■	■	■
Effort		■	■	■	■	
Fatigue	■	■	■	■		

APPENDIX D

Example of Log Sheets

DAILY MOOD RECORD

Please use this form to rate your moods every day while you are in the Brain and Mind Fitness Training Class. Most people find it easiest to do this at night, just before bed.

```
0----------1----------2----------3----------4----------5----------6----------7----------8
None         a little        some          much         extreme
```

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control:

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control**:**

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control:

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control:

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control**:**

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control:

DATE:		DAY OF WEEK:		
Average Anxiety:	Maximum Anxiety:	Average Depression:	Average Pleasant:	Attentional Control**:**

APPENDIX D-Continued

APT Practice Log Sheet

This log sheet should be completed *after every session of practice,* both in the lab and at home. Circle a number on the scale below to answer each question.

I.D. Number: Date:

Exercises practiced:

1. Rate your level of fatigue after today's practice:
0---------------1---------------2---------------3---------------4---------------5
No   A Little   Some   Much   Very much Extreme
Fatigue Fatigue Fatigue Fatigue   Fatigue   Fatigue

2. Rate how much effort today's practice required:
0---------------1---------------2---------------3---------------4---------------5
No   A Little   Some   Much   Very much   Extreme
Effort Effort   Effort   Effort   Effort   Effort

3. Rate how much progress you made in improving your attentional abilities:
0---------------1---------------2---------------3---------------4---------------5
No   A Little Some   Much   Very much   Extreme
Progress Progress Progress   Progress   Progress   Progress

4. Rate how much you enjoyed today's practice:
0--------------1---------------2---------------3---------------4---------------5
No   A Little Some   Much   Very much Extreme
Enjoyment Enjoyment Enjoyment Enjoyment Enjoyment Enjoyment

5. Please add any other comments or thoughts about this practice session:

List of acronyms

PD: idiopathic Parkinson's disease

DA: dopamine

CBT: cognitive behavioral therapy

APT: Attention Process Training II

BMFP: Brain and Mind Fitness Program

ED: executive decline

PET: positron emission tomography

HAM A: Hamilton Scale for Anxiety

HAM D: Hamilton Scale for Depression

COWAT: Controlled Oral Word Association Test

BAI: Beck Anxiety Inventory

BDI: Beck Depression Inventory

STAI: State-Trait Anxiety Inventory

ASI : Anxiety Sensitivity Index

IT: information technology

SIGH-A: Structured Interview Guide for the Hamilton Anxiety Rating Scale

SIGH-D: Structured Interview Guide for the Hamilton Depression Rating Scale

GAD: generalized anxiety disorder

DRT: dopamine replacement therapy

L-Dopa: Levodopa

PFC: prefrontal cortex