

# DISCUSSION 3

Read Chapters 6 and 7 of your text. Then, select a disorder of the sensory system to discuss. You must choose a different disorder than your peers. If you would like to focus on a disorder that is not on the list, please get prior approval from your instructor.

Select a disorder of the sensory system from this list.

- Balint's syndrome

Conduct research and locate two peer-reviewed articles to support your statements. In your post

ARTICLES ATTACHED &

- Explain the symptoms of the disorder.
- Describe how the diagnosis is made (e.g., findings on brain imaging, laboratory testing, etc.).
- Discuss the neurobiological basis for the disorder (e.g., CNS structures involved and neurotransmitters).
- Describe the functional deficits associated with the disorder including how these may impact the patient's ability to carry out activities of daily living (e.g., occupational, social, recreational).
- Cite your sources in APA style as outlined in the Ashford Writing Center .



## Balint Syndrome due to Bilateral Parieto-occipital Ischemic Stroke *Parieto-oksipital İskemik İnmeye Bağlı Gelişen Balint Sendromu*

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**Keywords:** Balint syndrome, stroke, pathophysiology  
**Anahtar Kelimeler:** Balint sendromu, inme, patofizyoloji

Dear Editor,

A 50-year-old male was evaluated in our neurology clinic during a follow-up visit due to previous ischemic stroke. An interrogation of his medical history revealed that the patient had been under follow-up due to rheumatic heart disease and related aortic valve insufficiency since childhood. Due to the progression of ventricular dysfunction, a prosthetic aortic valve replacement was performed nine years ago. After this surgery, when the influence of anesthesia was over, a significant weakness in his left upper extremity was noticed. More devastatingly, he was unable to visually perceive any colored or colorless objects. However, the symptoms improved in the following one-year period and the patient was able to perceive the objects, separately. At admission to our clinic, his direct and indirect pupillary light reflexes were evaluated as normal. In addition, the visual acuity was found to be bilaterally normal. However, the patient was unable to make pursuit eye movements, as well as saccadic eye movements, which were totally absent in the left direction and moderately disturbed in right direction. Moreover, during the oculocephalic test, rotation of the eyes to the opposite direction of the head movements were observed. Ability of visual-guided reaching was defective. This was compatible with optic ataxia. In addition, the patient was able to see and read a letter but could not combine the letters to perceive a word, which was compatible with simultanagnosia. The patient could distinguish the objects separately; however, he had

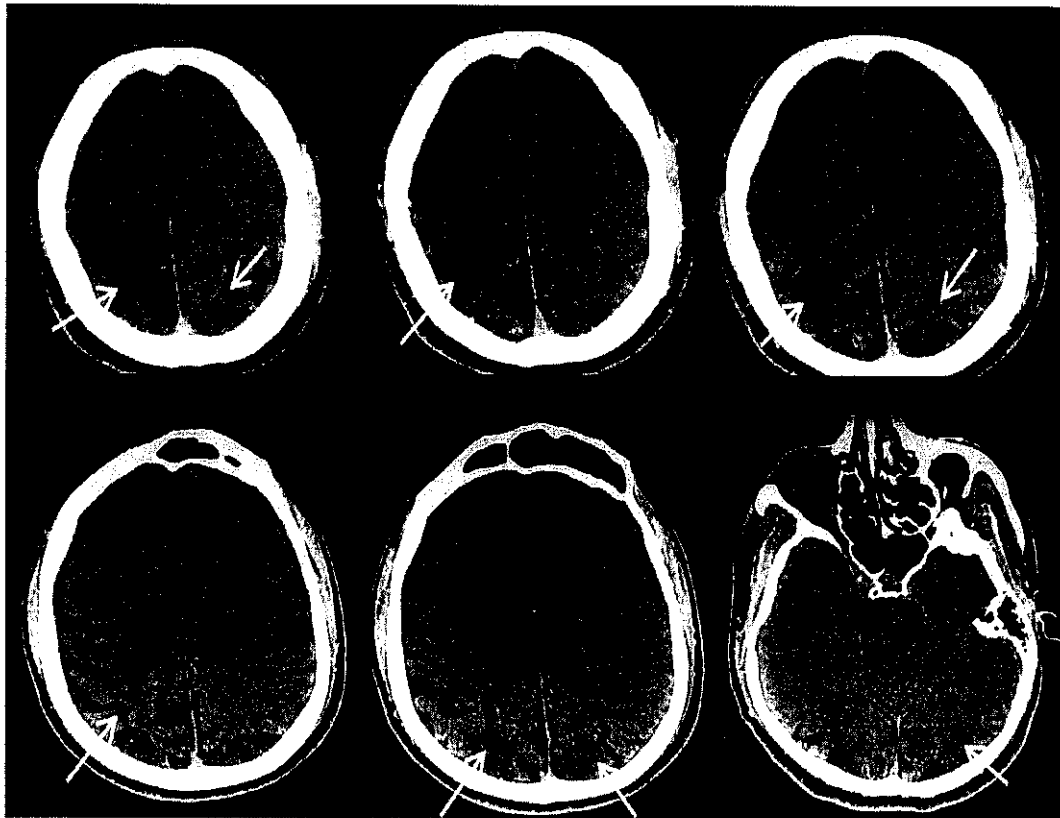
difficulty when they were visualized side-by-side or back-to-back (Video 1). Cranial tomography showed bilateral parietooccipital hypodensity, which was prominent in the left hemisphere (Figure 1). The clinical findings of severe oculomotor apraxia, optic ataxia, and simultanagnosia led to the diagnosis of Balint syndrome due to ischemic stroke.

In this letter, a rare case of Balint syndrome is presented through detailed video images of the neurologic examination. Balint syndrome, which was first described by Balint in 1909, can be defined as a clinical presentation including defects consisting of psychic paralysis of gaze, spatial disorder of attention, and optic ataxia (1). In the literature, lesions mainly affecting the bilateral occipitoparietal lobes have been attributed to causing Balint syndrome (1,2). In the author's opinion, this report gives valuable findings, presenting a smart example of this rare syndrome, which is rarely illustrated in the literature. At first clinical presentation, the patient experienced total blindness, which gradually improved during the following one-year period. In a similar report by Espay and Allen (3), a patient with Balint syndrome who presented with total blindness was described. In that report, the visual acuity of the patient improved within the first 24 hours of clinical symptomatology, which was explained in the setting of posterior reversible encephalopathy syndrome. However, the clinical triad of Balint syndrome was apparent at the follow-up evaluation. In our patient, recovery of total blindness took a much longer time.

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**Figure 1.** Cranial tomography showing bilateral parietooccipital hypodensity, which was prominent in the left hemisphere

**Video 1.** In the first part of the video, oculomotor apraxia is demonstrated. The pursuit and saccadic movements of the eye to the left are completely restricted, and movements to the right are substantially restricted. Vestibulo-ocular reflex testing revealed normal movements of the eye. In the subsequent part of the video, optic ataxia examination of the patient is illustrated. The patient has difficulty in detecting the location of the pencil and holding it. In the final section, a physical exam of simultanagnosia is demonstrated. The patient can perceive the objects correctly when they are shown separately; however, the patient has difficulty when the objects are visualized side-by-side or back-to-back

<http://www.tjn.org.tr/jvi.aspx?pdire=tjn&plng=eng&un=TJN-69862&look4=>

Future reports including long-term follow-up of these patients may provide substantial data for the underlying pathways/mechanisms of these manifestations, as well as their compensatory networks.

#### Ethics

**Peer-review:** Internally peer-reviewed.

**Financial Disclosure:** The author declared that this study received no financial support.

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## Rare sequelae to some common neurological maladies: Balint's syndrome

Utkarsh Gupta<sup>1</sup>, Fariah Asha Haque<sup>2</sup>

### ABSTRACT

Balint's syndrome is a rare visuospatial disorder usually associated with bilateral and rarely unilateral parieto-occipital or just parietal lobe lesion and sometimes temporal lobe. It is characterized by triad of spatial disorder of attention/simultanagnosia, psychic paralysis of gaze/oculomotor apraxia, and optic ataxia. The most common etiologies for developing this syndrome are stroke, Alzheimer's disease, and brain trauma. A 70-year-old hypertensive male patient complained of difficulty in executing his day-to-day work. He gave history of sudden onset left-sided weakness of his body 8 months back which resolved in a period of 1 month. He complained some visual disturbances later on which he ignored. On examination, he had all the three features of Balint's syndrome as noted above. His plain computed tomography brain and skull revealed infarct in the right parieto-occipital region, lacunar infarcts in capsule-ganglionic region and multiple site of senile cortical atrophy. Radiological findings along with clinical findings and history mentioned above, the patient was diagnosed to have Balint's syndrome as a complication of brain injury in parieto-occipital area by stroke.

**Key words:** Oculomotor apraxia, optic ataxia, simultanagnosia, stroke

### Introduction

Balint's syndrome is a rare visuospatial disorder usually associated with bilateral and rarely unilateral parieto-occipital or just parietal lobe lesion and sometimes temporal lobe. It was first described by Reszo Balint in the year 1909 characterized by triad of (1) spatial disorder of attention/simultanagnosia, (2) psychic paralysis of gaze/oculomotor apraxia, and (3) optic ataxia [1]. The common etiologies for developing this syndrome are stroke, Alzheimer's disease, brain trauma, near drowning, postcardiac arrest, metastasis, eclampsia, posterior cortical atrophy (PCA), and few others [1,2]. Stroke, either ischemic or hemorrhagic, being the second most common cause of mortality worldwide resulting in approximately 6.7 million deaths annually [3,4] and Alzheimer's disease which is one of the leading causes of dementia and is a chronic neurodegenerative disease leading to other ailments such as short-term memory loss, mood swings, language difficulties, disorientation, and various behavioral issues which worsen with time [5,6], are most frequent to develop it.

Knowing the pathophysiology and the various interacting mechanism that lead to an invariable end-point of such impairment following these common neurological maladies can provide us with a window of much more refined management strategies. The more well-defined understanding

we have, the better outcome we can achieve for an individual. We herein present a case of Balint's syndrome in a hypertensive patient with unilateral affection of posterior parieto-occipital complex after suffering from stroke.

### Case Report

A 70-year-old male patient presented in our medicine outpatient department with complaints of difficulty in executing his day-to-day work such as approaching for glass of water, colliding with wall at few instances, and inability to focus his vision on what he wanted to see. He gave history of sudden onset weakness in the left side of his body 8 months back when he was trying to plough his farm land for which he was treated at a local hospital. His weakness resolved in a period of 1 month but he complained some visual disturbances which he ignored back then. At the time of admission in our hospital, he complained of being unable to do his daily work due to visual disturbances. On examination, the patient was able to read and identify individual/local alphabet or shapes, but he could not elicit global compound shapes. His global processing ability was impaired. On visuospatial analytical test, his visuospatial skills were impaired. These findings suggested the features of simultanagnosia. He was unable to reach out to various objects held by the examiner in various positions in spite of Grade 5 power in his active limb which suggested optic ataxia. The patient complained of involuntary fixation of his gaze and complained that he was unable to see as per his will which suggested of oculomotor apraxia.

He had a blood pressure of 160/110 mmHg and gave history of noncompliant anti-hypertensive treatment for the last

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15 years. He did not show features of dementia or any history of brain trauma. On radiological examination [Figures 1 and 2], plain computed tomography brain and skull revealed infarct in the right parieto-occipital region, lacunar infarct in capsule-ganglionic region, and multiple site of senile cortical atrophy. Radiological findings along with clinical findings and history mentioned above, the patient was diagnosed to have Balint's syndrome as a complication of brain injury in parieto-occipital area by stroke.

### Discussion

Various causes have been listed that may result in the development of this rare visuospatial complication. Brain injury following strokes, neurodegenerative disease such as Alzheimer's, traumatic brain damage, and intracranial tumors are few of the common preceding events [7]. Regardless of etiologies, the area in brain which is usually affected remains to be superior parietal lobule (SPL) which is located in the parieto-occipital junction [2]. Studies have shown that there is more incidence of Balint's in stroke affecting bilaterally in parieto-occipital region [7]. Balint's occurring after neurodegenerative pathology as in Alzheimer's and PCA is also suggested by involvement of occipitoparietal complex with the magnocellular visual system following detailed visuospatial analysis [8].

Visuospatial skills involve visual processing, memory abilities, and spatial processing. Spatial processing involves abilities to search the visual field, recognize different form, position, and shapes after visual processing. These spatial skills when adjoined with visual perception and finally framing them mentally using memory and other complex processes in a two-dimensional or three-dimensional configuration constitute visuospatial skills [9]. The most recent studies support the involvement of posterior parietal

lobe and also the involvement of occipital lobe with it in many instances [10]. Aleman et. al. showed the primary involvement of posterior parietal lobe rather than occipital lobe after repeated transcranial magnetic stimulations [10]. Posterior parietal lobe receives input from visual system, auditory system and somatosensory system and output are majorly sent to frontal motor cortex. The intraparietal sulcus divides it into SPL (Brodmann area 7) and inferior parietal lobule (Brodmann area 39 and 40) [11,12]. Apart from Balint's syndrome, dysfunction of posterior parietal lobe leads to apraxia or hemineglect syndrome as well. These can be assessed and differentiated after doing proper visuospatial analysis by performing various tasks. Few of the commonly performed tests are Clock test, Hooper visual organization task, Rey-Osterrieth complex figure task, Judgement of line orientation task, mental rotation test, and spatial anatomy task [9,13]. It would be more appropriate to perform comprehensive neuropsychological examination to assess different aspects such as ocular motor, visuomotor, constructional praxis, visually guided reaching, manual dexterity, visual scanning along with visuospatial abilities to be absolutely sure about all the three components of syndrome and rule out the differentials.

### Conclusion

After proper radiological imaging and visuospatial analysis along with neuropsychological testing, Balint's syndrome can be diagnosed if the patient suffers an insult in the region of posterior parietal complex and surrounding region or parieto-occipital complex. Demonstrating simultanagnosia, psychic paralysis of gaze, and optic ataxia are the key. Further localization of specific sites by neuroradiological techniques, brain electrical activity mapping, and other novel techniques are matter of ongoing research for this syndrome.



Figure 1 Computed tomography findings of Balint's syndrome 1



Figure 2 Computed tomography findings of Balint's syndrome 2

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## Authors' Contributions

Case identification, defining of intellectual content, manuscript preparation and editing, literature review and collection of media were done by both the authors Utkarsh Gupta and Fariah Asha Haque.

## Competing Interests

The authors declare that they have no competing interests

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# Seeing red: Relearning to read in a case of Balint's Syndrome

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## Abstract.

**BACKGROUND AND AIMS:** Balint's Syndrome is a rare condition, often associated with hypoxic brain damage. The major characteristic is an inability to localise objects in space, another is simultanagnosia frequently resulting in reading difficulties. We present RN, a 37 year old woman whose major problem with reading was her inability to recognise individual letters correctly in either lower or upper case. We noted, however, that she was better if the letters were shown in red type. The aims were to determine if RN could relearn letters of the alphabet, investigate whether colour affected her ability to learn, and to explore more specifically whether the red type also helped her to read words.

**METHOD:** Using a single case experimental ABA design, we first determined that the optimal font for RN was size 16. In the baseline (A) phase, we assessed her ability to read all lower and upper case letters of the alphabet in black ink. In the intervention (B) phase we used font size 16 in red ink and an errorless learning approach to teaching the letters. Sessions ran 5 times per week (20 minutes per session). The intervention was then applied to picture recognition and word reading with four sets of 10 words and corresponding pictures.

**RESULTS:** A consistent difference was noted between initial baseline and intervention. Improvement carried over when we returned to baseline.

**CONCLUSION:** Using red type and an errorless learning approach enabled RN to re-learn letters of the alphabet and read words she was previously unable to read. This did not however generalise to her everyday life.

Keywords: Balint's Syndrome, hypoxia, acquired dyslexia, reading

## 1. Introduction

Balint's Syndrome is a rare condition, often associated with hypoxic brain damage. Balint (1909) described the syndrome as a psychic paralysis of visual fixation. There are three main indications of this condition typically seen in patients. The first is that of a fixed gaze (ocular apraxia). This is seen as

an inability to scan the entire visual field despite the patient presenting with normal eye movement, intact visual fields, and intact reflex motility. The second clinical feature is optic ataxia. Patients with optic ataxia present with an inability to integrate visual and hand coordination (Ayuso-Peralta et al., 1994). The third feature which, arguably, is considered the crux of Balint's Syndrome, is simultanagnosia, which Thaiss and DeBleser (1992, p. 602) described as "impaired simultaneous perception". This is noted as reduced attentional field leading to the patient only being able to interpret one object or part of an object at any one time. It is this clinical feature that

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frequently results in reading difficulties (Balint, 1909; Humphrey et al., 1994; Karnath & Zihl, 2003; Rafal, 1996; Rizzo & Vecera, 2002; Shalev & Humphreys, 2002).

There is scant information on the rehabilitation of Balint's Syndrome although a few studies exist. Zihl and Kennard (1996) describe three patients in the acute stage. Intensive practice in localisation, touching and scanning was provided and attempts made to improve oculomotor functions, enlarge the field of attention and re-establish visual-spatial orientation. Minimal improvement was noted in visual exploration and fixation but there was no recovery of the spatial disorder. Looking at more functional rehabilitation, Al-Khawaja and Haboubi (2001) worked with a 41-year-old man with Balint's Syndrome following a bilateral stroke. Treatment involved practising functional tasks that increased in complexity over time. The patient developed strategies such as tactile feedback to help him direct his gaze to objects. Again, it is difficult to know whether passage of time or intervention helped but it seems likely that giving the patient confidence to engage in everyday activities facilitated the development of one or more compensatory strategies.

Gillen and Dutton (2003) worked with a 10-year-old boy with Balint's Syndrome. He had sustained meningitis when he was three years old. The first step was educational, helping the boy and his parents to understand and acknowledge his problems. He was encouraged to use his strengths and abilities to compensate for his difficulties and to ask others to provide him with information in a way that it was easiest for him to assimilate. He was helped to keep his environment uncluttered (e.g. leaving out only one pair of shoes) and to use hearing, touch, and proprioception to locate objects instead of relying primarily on vision. One year later, although he had not improved on objective testing, he had learned to cope better with his disability in that his performance at school, his self-esteem, his confidence and his behavioural problems had all improved (see also Toyokura & Koike, 2006).

Wilson (2009a) spent several months working with Malcolm, a man who developed Balint's Syndrome following anoxic damage. The initial step again involved explaining to Malcolm and care staff the challenging, subtle nature of his problems. This information was repeated in a letter to be passed to new acquaintances. Three months were spent unsuccessfully trying to improve his ability to localise objects. He was then helped to compensate either by presenting one object at a time on his wheelchair tray or by

making objects more distinguishable (he was much better at choosing one object from another if they maximally differed in colour, size or shape).

These studies show that improvements are difficult but possible for patients with Balint's Syndrome, especially when the interventions are tailored to deal with their specific problems. In that sense, using single-case experimental designs (SCEDs) is warranted in this field, whereas the use of *appropriate* SCEDs (Kratochwill et al., 2010; Tate et al., 2013) can be helpful for establishing cause-effect relations. Considering the rehabilitation process for patients with Balint's Syndrome, it would make sense that the focus of intervention is based on the main characteristics of the syndrome; the improvement of visual scanning, the development of integrated visual and hand co-ordination, and the improvement of the integration of visual elements.

The overarching aim of this study was to explore whether a cognitive rehabilitative approach using an errorless learning approach and compensatory strategies for visual impairment could improve the ability to recognise single letters and be integrated words with matching pictures thus improving reading in a patient with Balint's Syndrome.

## 2. Method

### 2.1. Participant

We present RN, a 37 year old woman who was attending a neurorehabilitation hospital 5 days a week for therapeutic intervention. RN sustained an acquired brain injury as a result of complications following the birth of her second child. RN has a diagnosis of Balint's Syndrome and Apperceptive Agnosia. She had been referred to Neuropsychology for assessment and intervention during which time she reported her main desire was to be able to read to her children. During the assessment it was noted her major problem with reading was her inability to recognise individual letters correctly in either lower or upper case. We noted, however, that she was better if the letters were shown in red type. The aims were to determine if RN could relearn letters of the alphabet, investigate whether colour affected her ability to learn, and if the red type also helped her to read words. A subsidiary aim was to determine whether learning to recognise single words might help in supporting her recognition of visually presented objects in the form of pictures.

## 2.2. Design and procedure

Using a single-case experimental ABA design, we first determined that the optimal font for RN was size 16. In the baseline (A) phase, we assessed her ability to read all lower and upper case letters of the alphabet in black ink. In the intervention (B) phase we used font size 16 in red ink and an errorless learning approach to teaching the letters. Errorless learning is a teaching technique whereby people are prevented, as far as possible, from making mistakes while they are learning a new skill or new information. This can be carried out in a number of ways such as providing spoken or written instructions or guiding the person through a task. The principle is to minimise the possibility of erroneous responses. The reason for this is that in order to benefit from our mistakes (trial-and-error learning), we need to be able to remember those mistakes. People with memory problems have difficulty remembering their errors and, therefore, cannot correct them. Thus, erroneous responses may be strengthened or reinforced (Wilson, 2009b). Sessions ran 5 times per week (20 minutes per session). The intervention was then applied to word reading with 4 sets of words that had meaning to her and her environment. Following the reading phase we implemented the same intervention with pictures of the learned words both in a single presentation i.e. only picture and then in a matching task i.e. picture and corresponding word.

Each phase utilised a single case experimental ABA design and errorless learning, and consisted of 5 sessions per week. Each intervention also included a follow up phase at approximately 3 months. However by this stage RN's attendance had reduced to a weekly session so the follow up was completed over 2-3 sessions.

## 3. Results

### 3.1. Comparing the initial baseline to the intervention phase

The first step in single-case data analysis is visual inspection, due to the amount of useful information it provides about several data features, as well as its usefulness for guiding the analysis and the validation of its results (Parker, Cryer, & Byrns, 2006). The initial visual inspection of the data suggested that most initial baselines were stable, with some exceptions (i.e., the errors for upper case letters), and that practically

all intervention phase data shown a progressive improvement, that is, a downward trend. Taking these data characteristics into account, we decided to use analytical techniques that quantify both the change in level and in slope, while they also account for initial baseline trend whenever it is present – piecewise regression (Center, Casey, & Skiba, 1985-1986) and the slope and level change procedure (SLC; Solanas, Manolov, & Onghena, 2010). We decided to use both techniques instead of choosing one due to two reasons: (1) the computations are performed in a different way: on the basis of least squares estimation in piecewise regression versus using differencing and computing average differences in SLC; and (2) the changes in level are conceptually different: immediate change in the first intervention phase measurement occasion is quantified by piecewise regression versus average change in level (once change in slope is controlled for). The results of using these analytical techniques are presented in Table 1 and will be commented alongside visual analysis.

Regarding the alternatives for data analysis, an option for obtaining overall estimates for the immediate intervention effect and change in slope, as well as empirical Bayes individual estimates, would have been to use multilevel models (Moeyaert, Ferron, Beretvas, & Van den Noortgate, 2014). However, we did not perform such an analysis, given that for most of the A<sub>1</sub>-B comparisons the amount of measurements available was smaller than the smallest series length for which evidence on this technique's performance is available (Ferron, Bell, Hess, Rendina-Gobioff, & Hibbard, 2009). Moreover, it is not clear that it conceptually makes sense to use a two-level model with a single participant for whom several different outcomes are measured longitudinally.

Looking at the number of errors committed with lower case letters (Fig. 1; constructed using the SCDA plug-in for R; Bulté & Onghena, 2012), the intervention is associated with an immediate improvement (3.91 errors less according to piecewise regression; net level change  $-4.58$  according to SLC) and the number of errors is gradually reduced in subsequent measurement occasions during the intervention phase ( $-0.76$  less per measurement occasion according to piecewise regression and  $-0.64$  according to SLC). For upper case letters, the intervention is associated with an immediate improvement (2.20 errors less according to piecewise regression; net level change  $-0.57$  according to SLC). However, the improvement is less steep (0.70 according to piecewise regression and 1.05 according to SLC) during the intervention

Table 1

Results for the A<sub>1</sub>B comparison obtained using piecewise regression (Center, Skiba, & Casey, 1985-1986) and the Slope and level change procedure (SLC; Solanas, Manolov, & Onghena, 2010)

Data	Regression immediate change	Regression change in slope	SLC change in slope	SLC net change in level
Errors lower case	-3.91	-0.76	-0.64	-4.58
Errors upper case	-2.20	0.70	1.05	-0.57
Words: Animals	-1.70	-1.70	-1.67	-1.75
Words: Food	-3.20	-0.80	-0.75	-3.30
Words: Instruments	-3.00	-2.90	-3.00	-2.80
Words: Utensils	-1.20	-2.10	-2.00	-1.40
Pictures: Animals	1.10	-0.40	-0.50	1.25
Pictures: Food	-3.20	-0.80	-0.75	-3.30
Pictures: Instruments	0.86	-1.70	-1.50	0.47
Pictures: Utensils	0.00	-1.30	-1.25	-0.10
Matching: Animals	-1.97	-1.30	-1.50	-1.67
Matching: Food	0.53	-1.00	-0.75	0.03
Matching: Instruments	-0.20	-0.80	-1.00	0.20
Matching: Utensils	-2.20	-0.40	-0.25	-2.50

Note. SLC – slope and level change.

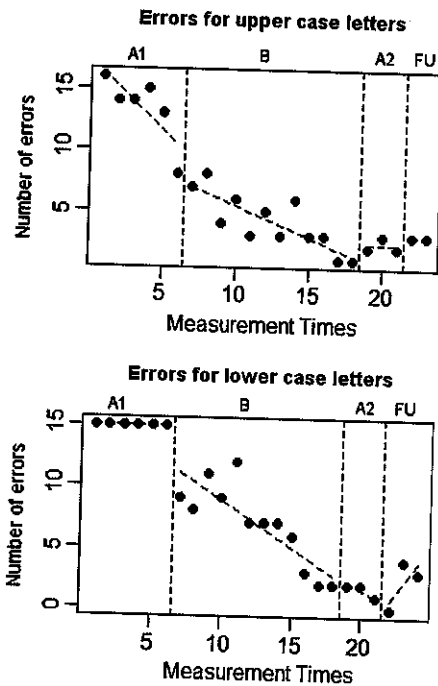


Fig. 1. Errors committed for upper case letters (upper panel) and lower case letters (lower panel). Dashed lines represent ordinary least squares regression lines fitted to each phase separately. A1 – initial baseline; B – intervention; A2 – second baseline; FU – follow-up.

phase that during baseline. In general, the intervention is apparently effective, but to a greater degree of lower case letters.

Similar change in performance is observed when looking at words (column 1 in Fig. 2) referring to animals and food. However, the effect for food is larger: immediate reduction of 3.2 vs. 1.7 according to piecewise regression; net level change of 3.3

vs. 1.75 according to SLC. For words referring to instruments and utensils, what is clear is the change in slope (e.g.,  $-2.9$  according to piecewise regression;  $-3.0$  according to SLC for instruments). However, the ordinary least squares trend lines superimposed on the graph should be interpreted with caution for the baseline phases, as with only two values it is actually not meaningful to talk about trends. In general, the intervention is effective for words as well, given that by the end of the intervention practically no errors are committed.

Regarding pictures (column 2 in Fig. 2), the data for pictures for animals do not clearly suggest an improvement, as the baseline trend seems to continue without changes into the intervention phase (an immediate increase of 1.1 errors according to piecewise regression and average deterioration of 1.25 errors according to SLC, but a steeper improvement). For pictures for food, a clear effect can be seen, both in terms of an immediate change and a change in slope (an approximate reduction of 3.20-3.30 errors per measurement occasion according to both procedures). The data patterns for pictures for instruments and utensils are similar, suggesting a gradual improvement (i.e., a change in slope of approximately 1.5 errors less per data point).

Finally, regarding the matching between words and pictures (column 3 in Fig. 2), for animals and food the data patterns are similar: an initial improving baseline trend gets steeper (e.g.,  $-1.3$  according to piecewise regression and  $-1.5$  according to SLC for animals) indicating a faster improvement than in absence of intervention. For instruments, the intervention phase trend fitted does not represent well the data, as can be seen from column 3 in Fig. 2, but at

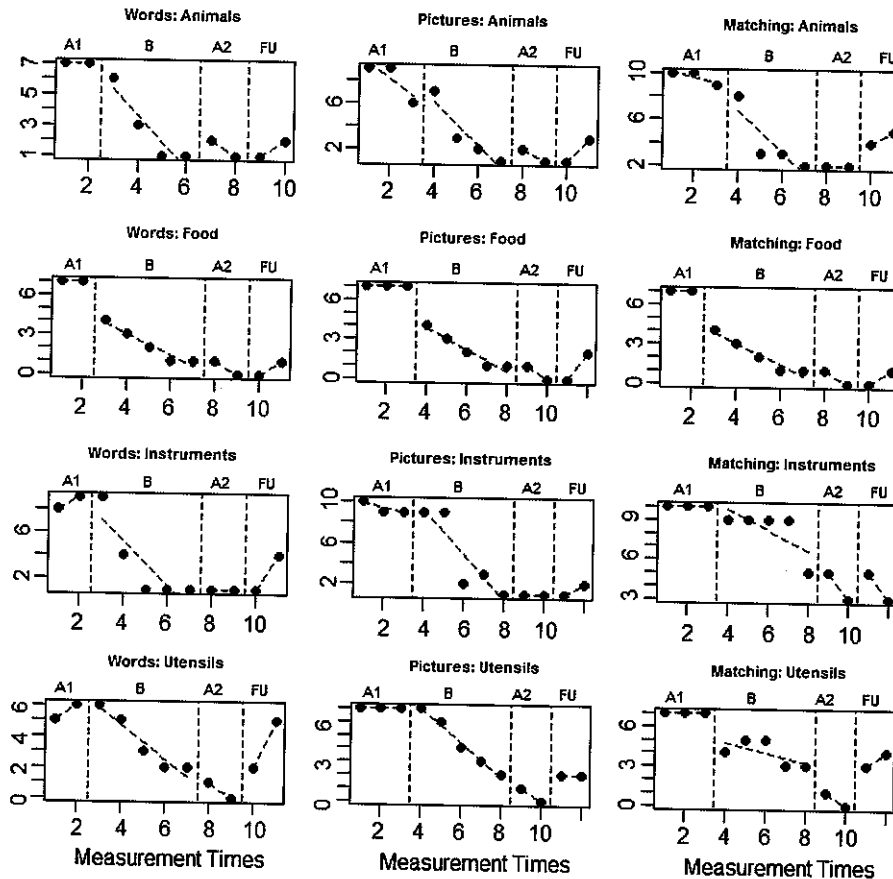


Fig. 2. The ordinate in all figures represents the number of errors committed in four different types of words (column 1), pictures (column 2), and matching (column 3). Dashed lines represent ordinary least squares regression lines fitted to each phase separately. A1 – initial baseline; B – intervention; A2 – second baseline; FU – follow-up.

least the quantifications of slope change indicate the fact that a reduction in errors is observed. For utensils, it is clearer that there both a change in level and a not very steep change in slope ( $-0.4$  according to piecewise regression and  $-0.25$  according to SLC). In general, there is an improvement associated with the intervention, although errors are not completely eliminated.

### 3.2. Comparing the initial baseline to the second baseline and the follow up phase

For the comparison between the initial baseline and the remaining conditions in which intervention was no longer provided, we decided not to choose piecewise regression or SLC, as the application of both is meaningful only when adjacent phases are compared, given that the first phase's trend is compared to the subsequent phase's trend and projections in nonadjacent phases are not warranted. An option for obtaining overall estimates for the difference between, on the

one hand, the initial baseline ( $A_1$ ) and the second baseline ( $A_2$ ) and, on the other hand, the initial baseline ( $A_1$ ) and the follow up (FU) was to use the recently proposed  $d$ -statistic (Hedges, Pustejovsky, & Shadish, 2012, 2013). Nevertheless, we decided not to use this index, given that the amount of measurements being compared (2-3 per phase) is too small for such a procedure developed on the basis of large-sample statistical theory.

Moreover, the conditions compared showed little variability, as visible from Figs. 1 and 2, and thus the use of simple indicators such as the arithmetic mean and the median is justified.

The fact that the second baseline scores represent an improvement compared to the initial baseline (an average reduction ranging from 6 to 13 errors less) and, at least visually, show no important difference from the preceding intervention phase, suggests that the intervention effect is enduring. The comparison between follow up and initial baseline shows the number of errors is smaller at later stages (i.e., a better

performance: an average reduction ranging from 3 to 10 errors less), but this performance achieved during intervention phase and second baseline is deteriorated for most outcomes. All means and mean differences between conditions are available from the first author upon request.

#### 4. Discussion

This article describes a single-case study of a 37 year old woman who presented with Balint's Syndrome and its core features of 1) failure to localise objects in space (optic apraxia), 2) inability to voluntarily look into the peripheral field (optic ataxia) and 3) despite adequate visual acuity unable to process more than one stimulus at a time (simultanagnosia). This occurred following an acquired brain injury as a result of complications following the birth of her second child. The patient, RN, during a neuropsychological assessment, reported that her main goal was to be able to read.

Given RN's desire to relearn to read, the reported rehabilitation programme commenced. It consisted of visuoperceptual training together with an errorless learning approach. Her rehabilitation programme was individualised following the recognition of appropriate font size and colour of letters, in this case red.

The initial phase of the programme took into consideration that patients with Balint's only recognise one object or part of an object at a time. Therefore RN was taught to recognise individual letters of the alphabet both in lower and upper case. The results indicate that the intervention was effective. It was noted that she was able to read upper case more easily than lower case letters.

Following RN successfully learning individual letters, the next phase of the intervention was to engage integration of these into individual words. Word sets were developed using categories pertinent to RN's environment. Once again results indicate efficacy of the intervention for 3 of the 4 categories. Given RN's goal was to be able to read, a further intervention phase of matching visual cues (i.e., pictures) to words was commenced. Similar results were obtained with significant improvement being noted in 3 of the 4 sets. At follow up the results indicate that the effects of the intervention were enduring. Overall, the results suggest it is reasonable to propose that the rehabilitation protocol used was effective.

RN's goal was to be able to relearn to read. Whilst she was able to learn to read both single letters and

category based words, generalisation to her everyday life was not noted. RN is still unable to read a book or newspaper and does not appear to be able to notice the words she has learnt in the context of a sentence.

The main strength of this study is that it recognised the need that the rehabilitation of visual field disorders is often idiosyncratic and highly individualised and has to be tailored to the patient's unique combination of deficits and preserved functions as well as to the functional impairment that is to be rehabilitated. In the case of RN developing the intervention around specific font size and colour had a clear positive impact and also considering categories relevant to her life arguably increased compliance and motivation.

When considering limitations of the study it could be argued the current study could have been performed using a multiple-baseline design across behaviours, in this case, across types of words. The staggered implementation of the intervention for each type of words would have provided a stronger experimental evidence for the causal effect of the intervention. This is especially so, given that in the A<sub>2</sub> phase of the ABA design we did not expect the behaviour to return to A<sub>1</sub> levels; A<sub>2</sub> was rather used to explore whether the effects of the intervention are maintained. Practical considerations, in particular change of staff, precluded this as it would have elongated each stage.

#### 5. Conclusion

Whilst we conclude that the intervention had a positive result it is clear that in providing rehabilitation for patients with visuoperceptual deficits such as Balint's Syndrome a more holistic approach needs to be considered. Whilst reducing the already impoverished attentional visual field to single letters/words in order to support RN's relearning, her ability to flexibly shift attention from one level of processing to another i.e. single object to complex multi objects remains impaired. RN finds this outcome frustrating. Not considering the 3 clinical features of the condition together is arguably the main weakness of this study. This issue needs to be considered in future interventions for both RN and other similar patients.

#### Conflict of interest

The authors have no conflict of interest to report.

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# Assignment 3:

For this week's assignment, you will complete the Background (including a literature review) and Significance sections of your grant proposal following the [Grant Proposal Guidelines](#) (Links to an external site.). See the [Sample Grant Proposal Template](#) (Links to an external site.) as an example and use it as a template for your Grant Proposal. The more complete your assignment is, the more feedback you will receive for the Final Project. In addition, you will create the References page for your proposal by taking the sources from your Week Two annotated bibliography and converting them into a standard [APA-formatted References list](#) (Links to an external site.). Be sure to include at least five more peer-reviewed sources on your References page (so that you have at least 15 sources as required for the Final Project).

I have attached the annotated Bibliography  
From the week Two assignment \*  
PLEASE include 5 more <sup>(References)</sup>. I HAVE  
also included a sample Paper as  
an Example. For this assignment

Annotated Bibliography

Angelia Bell

Psy 625

Professor Donaghy

### **Specific Aim**

Dementia is psychophysiological disorder that causes deterioration in thinking, behavior, and memory, and the ability to conduct daily activities. Although the disorder is mainly common among older adults, researchers believe that it is not associated with normal ageing processes, thus it can sometimes be an indication of psychophysiological syndromes, which implies that there is room for research-based prevention and treatment approaches (World Health Organization, 2019). As such, this project for grant request is aimed at conducting further research on the causes, manifestation and appropriate interventions that can Research has proven that dementia as social, economic, physical, and psychological impacts on the lives of its victims, including their family members, and can also interfere with their careers.

#### **Aim 1**

The first aim of the study is to investigate the different causes of dementia, and to examine their manifestation in different parts of the brain though the aid of magnetic resonance imaging (MRI) scans of the brain.

#### **Aim 2**

The second aim is to conduct different tests among substantial number of respondents in different socioeconomic contexts, to determine the disparities among the sample, and to recommend the best interventions for each category in the emerging themes. Research has shown that there are different other causative factors that increase vulnerability to dementia apart from old age and traumas that affect the brain. They include but not limited to: smoking, lack of enough exercises, alcohol, unhealthy diet, high blood sugar level, and low-density lipoprotein cholesterol, depression, and cognitive inactivity.

The study to be conducted will uncover different causes of dementia, how they are manifested among different individuals, and the best interventions for different cases of the disorder. The study will also unveil new dimension in the diagnosis of the disorder depending on the causative agent and propose appropriate proactive approaches through which dementia can be managed across different categories of people and stages of the disorder.

#### Annotated Bibliography

**Annear, M. J., Toye, C., McInerney, F., Eccleston, C., Tranter, B., Elliott, K. E., & Robinson, A. (2015). What should we know about dementia in the 21st Century? A Delphi consensus study. *BMC geriatrics*, 15(5), 1-13.**

Annear et al. (2015) explore different ways through which healthcare experts in neuroscience can reach consensus regarding how the classification of different forms of dementia and their corresponding symptoms. The study was prompted by the increase in the number of experts in neuroscience, and the increase in the scope through which dementia is currently being classified to establish consistence in the classification of disorder and contemporary knowledge of it. The researchers collected three rounds of data from experts in neuroscience in a Delphi study that was conducted online. The experts selected a set of 36 statements about the disorder that were fundamental for understanding dementia, which were placed in different categories. The largest category concerned aspects of care for dementia victims, and what their caregivers should understand; symptoms of dementia; assessment and diagnosis criteria; and treatment and intervention plans (Annear et al., 2015). The study is significant in care for dementia patients since it has established guidelines of care and classification of the nature of the disorder, which

increases accuracy in diagnosis and care for dementia patients. The classification can also be used to develop community educational programs.

**Harrison, J. K., Fearon, P., Noel-Storr, A. H., McShane, R., Stott, D. J., & Quinn, T. J.**

**(2015). Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a secondary care setting. *Cochrane Database of Systematic Reviews*, (3), 1-54.**

Harrison et al. (2015) discusses the extent to which informant questionnaire for cognitive decline in the elderly (IQCODE) can be applied reliably to accurately determine the likelihood of dementia development among people who have not yet developed dementia but are classified as high-risk population, such as the elderly or people who have suffered from stroke. The study approach involved searching databases for studies in which respondents were required to respond to questionnaires, and libraries such as PubMed and Cochrane databases. The questionnaires were mainly tailored to suit cognitive tests, screening, and vulnerability to dementia. Although the search yielded significant results that could be used for future studies on dementia development over time, the authors conclude that the studies that were assessed could not be used to accurately develop precise recommendations about the use of IQCODE for dementia diagnosis. The study is crucial for the understanding the gap that exists in dementia studies, especially in the detection phase where early interventions can be implemented.

**Haslam and Sabah. (2013). Preservation of person-specific knowledge in semantic memory disorder: a longitudinal study in two cases dementia. *Journal of Neuropsychology*. 2013(7). 132-138.**

The article provides results of a study on semantic dementia done over a period of six years involving two respondents. Haslam and Sabah (2013) studies the way progressive semantic dementia is expressed in patients by analyzing magnetic resonance images (MRI). The initial semantic knowledge and person-specific knowledge of the respondents was the same in the beginning of the study. However, after a period of six years, there were significant changes in the memory capacities of the respondents in that there was double dissociation in which semantic knowledge had changed whereas person-specific knowledge did not change. The results of the study prove the speculation that the right hemisphere plays a big role supporting person-specific knowledge. The findings of the study can be used to explain why person-specific knowledge is preserved whereas general semantic knowledge is lost using the concept of double dissociation. Nevertheless, the research used only two participants, which lowers the reliability of the findings.

**Killin, L. O., Starr, J. M., Shiue, I. J., & Russ, T. C. (2016). Environmental risk factors for dementia: a systematic review. *BMC geriatrics*, 16(1), 175-203.**

Following the unexplainable causes of dementia after other risk-factors such as old age and stroke have been identified, Killin, Starr, Shiue and Russ (2016) examine environmental risk factors that could trigger the development of dementia among non-vulnerable populations. The authors conduct searches in databases such as Web of Science and PubMed for research articles about environmental risk agents for dementia. The authors excluded studies that combined dementia with other studies. The result of the search exposes air quality, poisonous metals and other substances, and occupational risk factors. The leading environmental risk factors were exposure to aluminum, pesticides, magnetic and electric fields, silicon, and deficiency in vitamin D (Killin et al., 2016). The study is important in analyzing root causes of dementia in that it

unifies studies on the environmental causative agents, which makes it possible to plan for preventive approaches that can minimize the occurrence of dementia through restricting the use of such causative environmental agents.

**Lewczuk, P., Riederer, P., O'Bryant, S. E., Verbeek, M. M., Dubois, B., Visser, P. J., ... & Jack Jr, C. R. (2018). Cerebrospinal fluid and blood biomarkers for neurodegenerative dementias: an update of the Consensus of the Task Force on Biological Markers in Psychiatry of the World Federation of Societies of Biological Psychiatry. *The world journal of biological psychiatry*, 19(4), 244-328.**

The article discusses the current state of events regarding blood biomarkers and cerebrospinal fluid in the assessment, diagnosis, and treatment for people with dementia. Since the integration of Alzheimer's disease into dementia spectrum is one phenomenon that Lewczuk et al. (2018) site as aspects that can bring confusion in the diagnosis of dementia since some practitioners can apply multiple interventions where only one is necessary. Biomarker techniques are a range of technologies that have been advanced in recent times to for early identification of neurodegenerative disorders. The authors discuss different types of biomarkers, which include but not limited to: predictive biomarkers applicable in pre-clinical stages; diagnostic biomarkers used in accurate differential diagnosis; prognostic biomarkers applied in prognostic processes and probabilistic healing (Lewczuk et al., 2018). Different ethical issues have been highlighted regarding the use of recently modeled biomarkers, which include but not limited to: dilemma concerning disclosure of biomarker status regarding risk-benefit analysis that can cause uncertainty; and interventional studies require disclosure of prognosis biomarkers applied, which can cause anxiety to patients, or make them change their mind. The article can used to gain current information concerning the current state-of-the-art interventions.

**Na, R., Yang, J. H., Yeom, Y., Kim, Y. J., Byun, S., Kim, K., & Kim, K. W. (2019). A Systematic Review and Meta-Analysis of Nonpharmacological Interventions for Moderate to Severe Dementia. *Psychiatry investigation, 16(5), 325-336.***

The article provides alternative nonpharmacological approaches that neuropsychologists can apply to treat people living with dementia, especially during the early stages of the disorder, or its mild forms. Na et al. (2019) raise concerns that pharmacological interventions do not work effectively as expected, thus nonpharmacological interventions should be explored. Through literature search in credible databases such as PsycINFO, Na et al. (2019) performed meta-analyses on randomized controlled trials, and further applied the inverse variance method to estimate standardized mean difference. The results suggest that non-pharmacological interventions improved the daily quality of lives of people living with dementia. Such nonpharmacological therapies include but not limited to music, light therapy, and exercise therapy. This study is important since it can be used to select appropriate nonpharmacological interventions that caregivers can utilize for people with mild to medium forms of dementia. It can also be used to break overreliance on pharmacological treatment that sometimes impact negatively on the dementia victims.

**Orrell, M., Yates, L., Leung, P., Kang, S., Hoare, Z., Whitaker, C., ... & Pearson, S. (2017). The impact of individual Cognitive Stimulation Therapy (iCST) on cognition, quality of life, caregiver health, and family relationships in dementia: a randomised controlled trial. *PLoS medicine, 14(3), 1-22.***

Orrel et al. (2017) studies the effects of the individual cognitive stimulation therapy (iCST) on different aspects of life of people living with dementia. The main aspects of

consideration are: the quality of life; cognitive abilities; socioeconomic relationship; and psychological health of caregivers. The authors applied the single-blind-pragmatic randomized controlled trial across eight study regions. The findings of the research indicate that there is no significant effect caused by iCST on the quality of life, and the cognition among people living with dementia. This suggestion goes against the findings of some researches that have linked good relations between caregivers and dementia victims with high quality of life of dementia victims. Nevertheless, the authors found that the iCST improves caregivers' quality of life and improves personal relations between caregivers and dementia patients. The study findings can be used to provide justification for the use of iCST in giving caregivers motivation and strengthening the relationship between caregivers and patients.

**Possin, K. L., Kim, H., Geschwind, M. D., Moskowitz, T., Johnson, E. T., Sharon, J. S., ... & Hess, C. P. (2017). Egocentric and allocentric visuospatial working memory in premotor Huntington's disease: A double dissociation with caudate and hippocampal volumes. *Neuropsychologia*, 101, 57-64.**

The article evaluates different ways through which the brain presents information and links the channels with the likely part of the brain responsible for the activities. There are two types of spatial information that the authors use in the study, which include allocentric and egocentric information. Ellocentric information refers to individual-related data whereas allocentric relate to landmark-based coordinates. Possin et al. (2017) administers both memory coordinates to people with premotor Huntington's disease, which is closely related to caudate nucleus atrophy. The authors apply segmentation algorithm based on multiatlas approaches. The findings suggest that people with Huntington's disease had significant higher impairments on egocentric coordinates of the brain's information presentation. Caudate volumes were correlated

by egocentric accuracy, specifically the dorsolateral caudate region. Furthermore, the right part got denser afferents as compared to the left dorsolateral prefrontal cortex (Possin et al., 2017). On the other hand, the allocentric memory correlated with hippocampal capacity especially in the part posterior and intermediate regions that compactly connect with posterior parietal cortices. The study results support double dissociation, which sheds light on the how the working memory is controlled.

**Surr, C. A., Walwyn, R. E., Lilley-Kelly, A., Cicero, R., Meads, D., Ballard, C., ... & Downs, M. (2016). Evaluating the effectiveness and cost-effectiveness of dementia care mapping™ to enable person-centred care for people with dementia and their carers (DCM-EPIC) in care homes: study protocol for a randomised controlled trial. *Trials*, 17(1), 300-317.**

Surr et al. (2016) discuss methods through which relatives, friends, and caregivers for dementia patients can positively improve the quality of life of the people living with the disease. The Dementia Care Mapping (DCM) is an approach that the authors use as a dementia-control tool that can be used to give person-centered care. The authors apply multiple research approaches in study, which include but not limited to: multiple-center approach; randomized controlled trials; and Usual Care. The study is important since it explores different ways through which stakeholders can apply to determine the source and degree of agitation given that victims of dementia are easily agitated, and that agitation contributes to 90% of their non-conformity with social and work-related issues (Surr et al., 2016). Application of multiple research approaches in the study makes it more valid and makes its findings more reliable since the multiple study approach enhances data saturation, which increases the rates to which the results of the study can be generalized.

**Taylor, J. P., Firbank, M., & O'Brien, J. T. (2016). Visual cortical excitability in dementia with Lewy bodies. *The British Journal of Psychiatry*, 208(5), 497-498.**

Taylor, Firbank and O'Brien (2016) study the relationship between excitability the visual cortex and Lewy bodies among people suffering from dementia. The authors suggest that hallucinations that dementia patients often experience can be related to alterations in the visual system. Nevertheless, the authors raise concerns that cortical excitability appears normal among people with dementia with Lewy body when excitability is measured using transcranial magnetic stimulation, and functional magnetic resonance imaging stimulation of basal visual regions. The authors suggest that there occurs double dissociation regarding phosphate threshold and functional MRI regarding visual activation. The results indicate that the loss of inhibition in dementia with relation to Lewy body can be a significant predisposing factor for visual hallucinations and dysfunctions. This study is important in researches involving the association between causative factors of memory loss with cognitive abilities, which can aid in predicting dementia among vulnerable groups upon detection of related symptoms.

## Effects of Internet Based Training on Cognition in Older Adults

**Specific Aims**

The idea that maintaining high levels of cognitive activity protects the brain from neurodegeneration is not new, and much evidence has accumulated that people with high levels of cognitive ability and activity tend to maintain cognitive function well as they age (Hertzog et al. 2009). Beyond the idea of maintaining cognitive function in healthy aging, studies such as Verghese et al. (2003) found that higher levels of cognitive activity were associated with lower rates of dementia in a 21- year longitudinal study. While much of the data indicating higher levels of cognitive activity leads to better long-term function is necessarily correlational, a number of studies have begun to systematically assess the effect of cognitive interventions on cognitive function. The largest of these, the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE; Jobe et al. 2001) has found long lasting effects (5 years; Willis et al. 2006) of relatively short cognitive training activities (10 hours).

The specific aim of this proposal is to assess the effectiveness of A Fictitious Brain Training Program on research participants followed longitudinally who may be experiencing the very earliest signs of cognitive decline. Recent research tracking the trajectory of age related cognitive decline (e.g., Mungas et al. 2010) has suggested that it may be possible to identify cognitively healthy individuals at risk for significant imminent cognitive decline by examining baseline cognitive assessments or recent change, even though test scores do not reach the abnormal range.

**Background**

Techniques for maintaining and enhancing cognitive function in an increasingly aging

population are of great potential benefit to those who might suffer from Alzheimer's disease and related disorders and also to society as a whole. Higher cognitive function leads to better maintenance of activities of daily life, less need for chronic care, and direct improvements in quality of life. Research examining effective methods for cognitive enhancement is becoming increasingly prevalent and has led to a number of recent review studies, e.g., Hertzog et al. (2009), Lustig et al. (2009), Green & Bavalier (2008). These studies review evidence from both longitudinal studies of increased levels of mental activity on maintenance of cognitive function and intervention studies aimed at directly improving cognition with targeted cognitive training. For these cognitive interventions to provide widespread benefit, it is critical to identify who will gain from cognitive intervention studies and to assess methods of administering effective cognitive training.

In a large scale cognitive intervention study (ACTIVE), Ball et al. (2002) found that training increased cognitive function with as little as 10 hours of task-specific training and these gains were still evident 5 years later (Willis et al. 2006). However, none of the three types of training used in that study were found to generalize to the other types of cognitive function. Participants were trained on either verbal episodic memory, reasoning (pattern identification), or speed-of-processing (visual search skills). Gains were observed in the domain of training, but not on the other two domains. As noted by Salthouse (2006), this result is inconsistent with the strongest form of the "use it or lose it" hypothesis. However, it does hold promise for cognitive training interventions that train broadly across a wide variety of domains. The hypotheses implied by the "use it or lose it" hypothesis is that cognitive training is protective broadly against the cognitive decline associated with aging. The more commonly observed specific areas of training improvement suggest an analogy to physical fitness training: the brain should not be

thought of as a single “muscle” to be strengthened but as a collection of individual abilities that could each be improved through “exercise.” In addition, the analogy could be extended to the idea that cognitive training “exercise” should be thought of as an activity to be engaged in on a regular basis, not as a single intervention.

The cognitive training that will be used in the proposed project is based on an internet delivered set of activities designed by the company BrainExercise. The training is based on practice across a wide range of cognitive abilities, and by being highly available via the internet, is also available for regular follow-up re-training to maintain benefits. With this type of intervention, even if a cognitive intervention training does not provide a global benefit and delay decline across all types of cognition, training can be used across many areas to increase overall function. The ability to deliver cognitive training via the internet becomes important logistically since the benefit of training may depend on regular access to a broad array of cognitive activities. In the successful ACTIVE study, training was administered in face-to-face sessions requiring significant personnel and logistical support.

The issue of identifying tasks suitable for cognitive training with memory-impaired patients is an important one. In a follow-up reanalysis of the ACTIVE study data, Unverzagt et al. (2007) found that patients scoring  $>1.5$  standard deviations low on memory tests did not benefit from the verbal episodic memory training in ACTIVE. In addition to seeing cognitive training as a method for delaying or reducing the onset of memory disorders such as MCI or AD (as in Verghese et al. 2003), suitable interventions to try to rehabilitate memory function or train compensatory strategies may provide an important benefit to MCI and AD patients.

Numerous studies have suggested that elderly who are currently cognitively within the normal range, but on the lower end of the range are at risk for subsequent cognitive decline, including

the development of Alzheimer's Disease (Rubin et al, 1998; Sliwinski, Lipton, Buschke, & Stewart, 1996).

Older participants who score within normal cognitive ranges but who exhibit personal cognitive decline within that normal range are also at higher risk for the later development of Alzheimer's Disease (Villemagne et al, 2008; Collie et al, 2001). The most at-risk group of currently healthy elderly may be those who have shown some cognitive decline and are now at the bottom of the healthy range. Since this proposal is to investigate at the effectiveness of cognitive training in patients at risk for Alzheimer's Disease, the ideal comparison groups are healthy older adults who are at increased risk relative to their age group (cognitively normal, but lower scoring) and those who are cognitively normal and exhibiting no current evidence of memory impairment.

### **Significance**

The proposed research will use an online-based software company to administer a structured intervention of cognitive skill training to patients experiencing some memory decline. Prior intervention studies have typically provided cognitive training in individual or small-group environments with the patients physically present with a trainer. If interventions based on training via the internet are shown to have similar benefits, many more people can gain these benefits since the labor involved in administering this type of training is much lower. In addition, improvements in the type of training administered can be made centrally and more quickly positively impact many more patients. For the pilot intervention study proposed here, we will be working with the Brain Science division at A Fictitious Company. The Fictitious program is a home-based, computerized, cognitive training program in which a customized training plan is developed for each participant based on an initial baseline cognitive assessment and ongoing

training progress. The training plan is based on 21 different tasks that each focus on one or two of 14 different specific cognitive abilities. To collaborate on examining the effectiveness of their training plan, they are making available licenses for all study participants to access the training program without cost. In addition, all performance data on all compliance, cognitive assessments and performance on training components will be available for collaborative analysis to assess efficacy of specific training elements in our study population.

The ability to deliver cognitive training via the internet holds tremendous promise for making training benefits available widely. Concerns about the task-specificity of benefits and the need for consistent training to maintain cognitive function can be met by making training easily available at home. The proposed research will work with the cognitive science research group of the A Fictitious company to assess the effectiveness of their targeted, individually customized cognitive training methods to improve cognitive functions in patients engaged in long-term outcome research at the Brain Center at an Important University.

### **Proposed Study**

#### **Participants:**

Forty cognitively normal participants will be recruited, including 20 participants scoring 1 SD below age and IQ-adjusted norms on neuropsychological tests of memory (Rentz et al. 2004), and 20 participants scoring no worse than .5 SD below adjusted norms. Participants will be recruited from A University. The patients will be randomly assigned to two groups: intervention and waitlist (baseline) control. The intervention group will receive cognitive training via Fictitious Brain Training Program over a two month period. The waitlist control will not initially receive training. However, since we expect that the training will provide benefits to the patients, participants in the waitlist control group will be given access to the Fictitious Brain

Training Program software at the end of the protocol following the “post-training” assessment. This ensures fair and ethical treatment of groups as well as providing additional data about the effectiveness of the Fictitious Brain Training Program.

There are no major risks to patients who participate in the research. The training program is designed to be self-paced so that patients can manage fatigue or frustration. Patients may elect to stop participating in the study at any time. The potential benefits of the proposed research are considerable. The study protocol may provide a treatment to slow or reverse the cognitive decline associated with MCI (and Alzheimer’s Disease) using the internet, making this treatment broadly and inexpensively accessible.

**Procedures:**

Once identified as a candidate for enrollment, patients will be met with in person at their residence. Patients will have the training protocol described and provide informed consent if they wish to enroll. Availability of necessary internet access will be assessed. Once enrolled, patients will be provided with a license to access The Brain Training Program and a research assistant will guide them through the initial setup process. The intervention will follow the standard Brain Training Program practice: initial assessment on a range of cognitive functions followed by 24 20-minute training sessions over approximately 8 weeks. The rate of training sessions recommended is 3 sessions per week but is ultimately chosen by the patient. These sessions are followed by a re-assessment within the Brain Training Program of performance on their identified group of 14 cognitive functions.

Participants’ self-rating of quality of life will be assessed with a Quality of Life-Alzheimer’s disease (QoL-AD) scale described by Logson et al. (2002). While the current participants do not require an assessment of quality of life appropriate for cognitively impaired

individuals, all cognitive training improvement in these participants will also be compared with a group of patients who have a diagnosis of MCI and who are currently involved on an ongoing assessment of A Fictitious Brain Training Program. The same set of performance improvement instruments will be used in both studies to provide maximum comparability across all groups.

**Hypotheses & Analysis:**

The intervention group is expected to exhibit reliably higher scores on all post-training assessments than the waitlist control group. Scores on the Fictitious Brain Training Program cognitive assessments are very likely to improve reflecting the training invested in those specific cognitive tasks. Improvements on specific cognitive assessments will be compared to estimates of improved domain-specific performance available via the Brain Training Program.

For the current population of cognitively normal participants who might be showing the first signs of memory impairment, changes in self-rating of their quality of life (via the QoL-AD) will be examined carefully. While improvements in activities of daily life may not be significantly improved as these patients are not generally impaired, increases in general cognitive function may lead to better overall quality of life by improving problem solving, language comprehension and general attention skills. Improvements on this measure would be a key indicator of the potential of cognitive training to provide significant benefits to older adults.

Assessment of improvement will be made for only participants who complete the training course of 24 sessions. Performance of patients who do not complete the training will not indicate whether the training is effective at improving cognitive function. However, the drop-out rate is a key element to assess for evaluating the overall effectiveness of internet-delivered cognitive training. High rates of drop-out (e.g., >25%) may indicate that the cognitive training needs to be adjusted in difficulty to meet the needs of older adults or that additional support (e.g., more

patient contact) is needed to guide the patients through the training. An important element of the current project is the assessment of difficulty of completing the training and obtaining feedback from participants about their experiences with the online cognitive training.

### **Budget Justification**

Funding is requested for a half-time graduate research assistant to be responsible for all aspects of subject recruitment, training and data collection. Addition funding of 10% is requested for the principal investigator who will oversee the study and conduct data analysis and publication of results.

Travel funding is requested for the PI to attend one national meeting to present the preliminary results of the study. Additional travel expenses are requested to pay for costs of transportation by the research assistant to each subject's home.

Subject payment of \$50 for each subject (40 total) is requested to reimburse subjects for their participation time.

Funding is requested for an Apple Laptop computer (15" with retina display, 2.8 GHz processor, 1 TB hard drive) that will be used for data collection and analysis. Additional funding will be used to purchase the Quality of Life Scale and office supplies.

See Appendix A: Budget for detailed budget figures.

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## Appendix A: Budget

SUMMARY PROPOSAL BUDGET		FOR INSTITUTION USE ONLY	
		PROPOSAL NO.	DURATION (MONTHS)
ORGANIZATION			
PRINCIPAL INVESTIGATOR (PI)/PROJECT DIRECTOR Instructor B. Jones, PhD			
A. PERSONNEL: P/PI, Co-PIs, Faculty, Graduate Assistants, etc. List each separately with name and title.		Funds Requested By Proposer	
1. Instructor B. Jones, PhD (\$90,000/year) - 10% effort for 12 months		\$9,000	
2. Research Assistant (RA) - 50% effort for 12 months		\$25,000	
TOTAL SALARIES		\$34,000	
B. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING \$5,000.) None			
TOTAL EQUIPMENT		\$0	
C. TRAVEL 1. DOMESTIC - PI attendance at national meeting		\$1,500	
2. OTHER - Travel for RA to participants home		\$1,000	
TOTAL TRAVEL		\$2,500	
D. PARTICIPANT SUPPORT		\$2,000	
1. STIPENDS \$ 50 _____			
2. TRAVEL _____			
3. SUBSISTENCE _____			
4. OTHER _____			
TOTAL NUMBER OF PARTICIPANTS (40) TOTAL		\$2000	
PARTICIPANT COSTS			
E. OTHER DIRECT COSTS			
1. MATERIALS AND SUPPLIES- Computer for patient training, data collection and analysis		\$3200	
2. OTHER Quality of Life scale		\$1200	
3. OTHER Office supplies		\$736	
4. OTHER			
TOTAL OTHER DIRECT COSTS		\$5,136	
F. TOTAL DIRECT COSTS (A THROUGH E)		\$43,636	
G. TOTAL INDIRECT COSTS (F&A) (Rate = 37.5%)		\$16,364	
H. TOTAL DIRECT AND INDIRECT COSTS (F + G)		\$60,000	