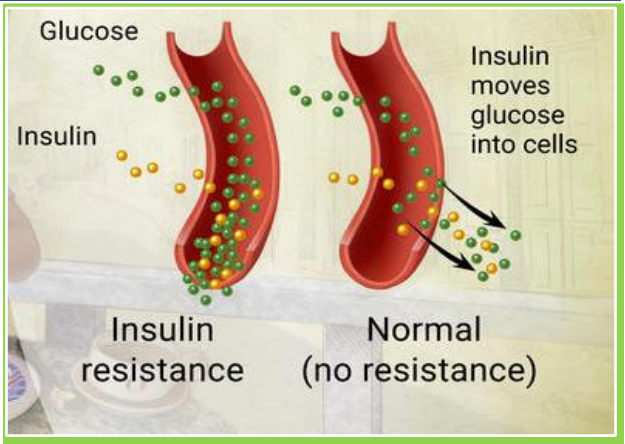
AIISH RESEARCH PROJECT

LEXICAL PROCESSING IN TYPE 2 DIABETES SH/CDN/ARF-70/2016-2017 dated 28.10.16

Dr. R. Rajasudhakar



ALL INDIA INSTITUTE OF SPEECH AND HEARING,
MANASAGANGOTHRI,
MYSORE

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ABSTRACT

Introduction: Few cognitive domains that have found to be negatively affected in individuals with type 2 diabetes are attention, memory, psychomotor speed, executive function, processing speed, complex motor function and verbal fluency (Kodi & Seaquist, 2008). A less addressed and not as well recognized complication of diabetes is cognitive dysfunction. Therefore, present study aimed to investigate the speed of information processing in semantic association task and lexical decision making task in individuals with diabetes.

Methods: Two groups participated in the present study where group 1 consisted of 60 individuals with type 2 diabetes mellitus in the age range of 40-60 years and group 2 included age and gender matched 60 individuals without diabetes. All the participants will be ruled out by screening for other associated problems. Each subject was administered two tasks, the semantic association and lexical decision making tasks. Further, reaction time and accuracy were measured.

Results: Present study found significant higher reaction time and less accuracy scores in both the tasks for individuals with type 2 diabetes than normal individuals.

Conclusions: The poorer performance in the lexical processing skills by diabetes individuals can be probably due to reduced speed of cognitive functions with the long term history of high blood sugar, though it is controlled.

Keywords: Diabetes, Cognition decline, Processing speed, Reaction time, Semantic memory.

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CHAPTER I

INTRODUCTION

Diabetes mellitus is derived from the Greek word *diabetes* meaning siphon - to pass through and the Latin word *mellitus* meaning honeyed or sweet. Diabetes mellitus is a long term chronic metabolic disorder characterized by hyperglycemias resulting in adverse effects on other organs of the body. According to American diabetes association, diabetes can be classified as type 1, type 2, gestational diabetes and other specific types of diabetes due to various causes. Type 2 diabetes is a fast growing chronic type of diabetes across the world. It is caused due to insulin resistance of the body cells which results in overproduction of insulin by β cells to such an extent where it becomes inefficient overtime to produce insulin as a result the blood sugar levels rise. Type 2 diabetes is often associated with vascular disease, renal disease and cognitive dysfunction but, the extent to which it affects the cognitive function is not clear.

However, by three indirect ways, the dysfunction or impairment in cognition is contributed due to the presence of type 2 diabetes mellitus. First, cognitive dysfunction in patients with type 2 diabetes has been correlated to inflammatory markers and increased inflammatory markers may contribute to the development of Alzheimers disease. Studies have shown that type 2 diabetes and Alzheimers disease share a common pathophysiology where patients with Alzheimers disease demonstrate increased inflammatory markers (Rosler, Wichart & Jellinger, 2001). Second, potential mechanism through which it added to cognitive dysfunction is

through disruption of the hypothalamic pituitary adrenal axis. Humans with type 2 diabetes have up regulation of the hypothalamic pituitary adrenal axis, increased serum cortisol levels. Thus, the increased cortisol seen in them might contribute to cognitive dysfunctions (Lee et al., 1999). The third potential mechanism through which type 2 diabetes mellitus may indirectly contribute to cognitive dysfunction is by promoting the formation of senile plaques that is found in Alzheimers disease which leads to death of neurons.

Many studies have explored cognitive domains affected through type 2 diabetes mellitus by considering different characteristics of the research participants with respect to age, gender and history of diabetes. The domains mainly affected were memory functions, information-processing speed, attention, executive functions and language comprehension (Ruis et al., 2004). Reduced neurocognitive speed (Fischer et al., 2009), significant differences in verbal learning and delayed recall, semantic verbal fluency, executive function and processing speed were impaired in individuals with diabetes (type 2) compared to normal individuals (Jurado et al., 2016). Further, it was also reported that the prolonged auditory and visual reaction time in individuals with type 2 diabetes compared to controls (Sidhu et al., 2015).

Our normal cognitive system includes different processes to understand information in an accurate manner. One such process is lexical processing. Lexical processing is a process of recognizing, phonemic or orthographic input

which is matched to templates in the mental lexicon and syntactic, semantic information associated with the word and is activated through lexical access. Lexical processing requires semantic memory. Lexical processing can be assessed using tasks like semantic association task and lexical decision task. In most of the studies involving participants with type 2 diabetes, cognitive domains such as processing speed, memory and so on were commonly reported to be affected. Hence, there arises a need to understand lexical processing skills in individuals with type 2 diabetes.

Need for the Study

India is one of leading countries with individuals with diabetes and is considered the diabetic capital of the world. Total number of diabetic subjects to be around 40.9 million in India and this could further rise to 69.9 million by year 2025 and 80 million by the year 2030 (Mohan, Sandeep, Deepa, Shah & Varghese, 2007). Few studies in the literature have reported slight slowness in the information processing speed in individuals with type 2 diabetes. However, the same has not been empirically verified or documented in the Indian population. Hence, the present study investigates lexical processing among individuals with type 2 diabetes in and around the city of Mysore, Karnataka, South India. Lexical processing is one of the important cognitive skills for proper communication. Thus, even mild cognitive dysfunction may hamper everyday activities. Hence, there arises the need to verify empirically, there is deficit (if any) related to lexical processing in individuals with type 2 diabetes. The present study findings would

also yield insights into need for detailed evaluation of cognitive skills in individuals with type 2 diabetes. If there are processing speed deficits present in them, it would be implemented in the assessment as well as intervention stage to provide more time duration for them to respond. In addition to the above, the outcome of the present study would shed light on planning appropriate cognitive strategies by Speech Language Pathologists during intervention. Thereby improve the quality of life in individuals with type 2 diabetes.

Objectives of the Study

- To investigate lexical processing in individuals with diabetes (type -2) and compare the same with controls using two tasks.
    i. Semantic association task (SAT)
    ii. Lexical decision task (LDT)
- To examine the gender differences in the lexical processing abilities in persons with type 2 diabetes and controls in the above two tasks.
- To examine task differences in lexical processing skills in individuals with type 2 diabetes and without type 2 diabetes (controls).

Implications of the study

- The findings of the study would augment the understanding of Speech Language Pathologist on lexical processing speed and accuracy in individuals with type 2 diabetes.

- Results of the study augment the understanding the effect of type 2 diabetes on cognitive linguistic skills.
- The study would also help in suggesting further clinical assessment and treatment and promote better healthcare to individuals with type 2 diabetes.

CHAPTER II

REVIEW OF LITERATURE

Diabetes mellitus is a long term chronic metabolic disorder characterized by hyperglycemias. According to recent estimates; India is considered the diabetic capital of the world (31.7 million) followed by China (20.8 million) with the United States (17.7 million) in second and third place, respectively. Long standing diabetes mellitus has adverse effects on different organs of the body. The long term uncontrolled diabetic complications include the diabetic retinopathy, renal problems, increase in blood pressure, skin problems and reduced speed of cognitive functions. Also, it has been observed that diabetes serves as a risk factor for cerebrovascular disease, stroke and even dementia. Thus, there arises a need to understand the effect of diabetes on cognitive skills. Type 2 diabetes is characterized by insulin resistance and thus understanding effect of insulin resistance on brain and its physiology is important to study the direct and indirect ways in which type 2 diabetes affects cognitive function.

Effect of insulin resistance in the brain

Insulin plays an important role in the cerebral metabolism and its insufficiency may indirectly affect the brain functions but the extent or speed at which it's affected is not clear. Different studies in the literature have explored the effect of insulin resistance in the brain. Hirvonen et al. (2011) investigated how insulin plays a role in brain glucose metabolism using positron emission tomography

(PET) and fluorodeoxyglucose (FDG) in two separate conditions (in the fasting state and during a euglycemic-hyperinsulinemic clam). 13 impaired glucose tolerance and nine healthy subjects were considered. Results suggested insulin stimulates brain glucose metabolism, but this effect depends on the glucose tolerance of the subjects. Insulin did not increase brain glucose metabolism in subjects with normal glucose tolerance but significantly increased glucose metabolism in patients with impaired glucose tolerance in euglycemic hyperinsulinemic clam condition, however, during fasting condition there was no difference. Thus, the effect of insulin on brain glucose metabolism is already maximal at physiological fasting. These findings suggest that patients with peripheral insulin resistance need more insulin than healthy subjects to get the maximal effect of insulin on brain glucose metabolism. Insulin in the brain also contributes to the control of nutrient homeostasis, reproduction, cognition, and memory, as well as to neurotrophic, neuromodulatory and neuroprotective effects (Blazquez et al., 2014).

Type 2 diabetes also shares a common pathophysiology as Alzheimer's disease (AD) which tends to produce cognitive linguistic deficits. Reduced insulin levels and insulin activity contributes to a number of pathological processes that characterize Alzheimer's disease (AD) such as synaptic loss, limited dendritic arborisation and memory impairment (Craft et al., 2012). Studies have found that the brains of people with Alzheimer's disease are insulin resistant which are caused by oligmers. In turn, insulin resistance may trigger Alzheimer's symptoms

by reducing the brain's ability to think and learn (Klien, 2012). Type 2 diabetes tends to increase the Alzheimer's disease associated pathologies and also high glucose concentration results in toxic effects on neurons in the brain through several mechanisms. Osmotic insults and oxidative stress and the maintenance of chronic high glucose leads to the formation of advanced glycation end products which have adverse and toxic effects on neurons (Umegaki, 2014).

Cernea et al. (2016) identified the cognitive impairment markers in diabetes (type 2) by evaluating the correlations of cognitive function with immunology, hormonal, nutritional, metabolic parameters. The Romanian edition of MoCA test was administered to test cognition, in 216 patients with T2D in the age range of 62.2 ± 7.8 years and 23 healthy control individuals in the age range of 61.6 ± 7 years. The MOCA test evaluates several cognitive domains: visuospatial, executive, naming, attention language, abstraction, delayed recall and orientation. Other pathophysiological parameters were further established: Lipids, cortisol, C-peptide, vitamin B12, high-sensitivity CRP (by chemiluminescent immunometric assay), 'hba1c', TSH, Mg (by a Cobas 6000 analyzer), glucose (by glucose-oxidase method) and leptin and adiponectin (by using enzyme-linked immunosorbent assay [ELISA] method). The MoCA in patients with Type-two-diabetes-T2D) conveyed the following results: 25% had normal cognitive function scores, 69% had mild and 6% had moderate. In contrast, in the control group, 48% had mild cognitive impairment and 52% had normal cognitive function scores. Even if there was no difference in duration of diabetes between

the three groups and patients with impairment in cognition were significantly older. Patients with diabetes (type 2) reported to have significant impairment in cognition, with decrements in the visuospatial/executive and delayed recall cognitive domains.

Male patients performed poorer than female patients in delayed recall function but better in the visuospatial/ executive, naming and language domains. Younger age and higher education correlated with better cognitive function. Subjects with diabetes (Type 2) had higher HbA1c, fasting blood glucose, triglyceride and fasting C-peptide levels. However, no other significant differences reported for laboratory parameters between the three diabetes (Type 2) groups. When serum Mg levels were compared between diabetes (Type 2) groups, there was a significant difference reported, with both cognitive impairment groups having significantly lower Mg concentration against normal cognitive group ($p < 0.05$ for both). No other significant difference was noted for laboratory parameters between the three diabetes (Type 2) groups. Serum Mg levels were significantly lower in patients with diabetes (Type 2) and positively correlated with the overall cognitive function, as well as with visuospatial, executive and naming domains. Hence, serum Mg was considered as the strong biological marker for cognitive dysfunction in T2D.

Effect of type 2 diabetes on cognitive functions

A normal cognitive system is important for processing of language. One such process is called lexical processing. It is a process of recognizing, phonemic or

orthographic input which is matched to templates in the mental lexicon and syntactic, semantic information associated with the word is activated through lexical access. It requires cognitive functions like semantic memory, association and judgment. Many tasks have been used by researchers to understand cognition and lexical processing which includes semantic association and lexical decision tasks. Many studies have used different assessment procedures to investigate the effect of type 2 diabetes on cognitive functions. The initial studies made use of different cognitive tests including pen paper tests. But, recent studies with advancement in technology have made use of various assessment procedures including fMRI, PET scan etc.

Research has suggested that type 2 diabetes is often associated with cognitive decline. Cosway et al. (2001) explored the cognitive functions and information processing using both subjective tests and event related potentials in type 2 diabetes. The study included 38 diabetic participants in the age ranges of 40 to 70 years (16 males and 22 females) and 38 healthy normal participants (15 males and 23 females). Premorbid mental ability was assessed using national adult reading test. Cognitive functions was assessed using Ravens progressive matrices that evaluated the abstract reasoning which is considered to be a good measure of fluid intelligence and general mental ability. Rey auditory verbal learning test (AVLT) was used to test short-term and long-term verbal learning and memory function. Borkowski verbal fluency test was also administered. The information processing assessment was done by measuring choice reaction time which included

movement time and decision time, inspection time and visual change detections that reflects the efficiency of the early stages of visual information processing. Event related potentials like P300 was used to measure which uses reflect the speed of neuronal events underlying information processing and the efficiency of higher cognitive processes in the brain**.** Authors reported that there was no significant difference in any area of cognitive and information processing between the two groups. However, it was noticed that increased duration of diabetes is associated with cognitive decline. All cognitive domains including memory function in elderly type 2 diabetes individuals appeared to be particularly affected promoting accelerated aging of the brain which the authors attribute to the presence of type 2 diabetes. The average P300 wave of the healthy normal group was higher in amplitude and slightly shorter in latency than the diabetes group; however, neither was statistically significant. There were no significant difference between the two groups but within the group there were differences. However the authors speculate that other diabetes related factors such as depression, hypertension, macrovascular disease, and depression may add to cognitive deficits.

Grodstein et al. (2001) examined the relationship between type 2 diabetes and cognitive dysfunctions in community dwelling women aged 70-78 years old from 1995 to 1999 using telephonic interview of cognitive status (TICS), immediate and delayed recall of the East Boston Memory Test, and verbal fluency test in 2,374 individuals of which 82 individuals were having type 2 diabetes. Women

with type 2 diabetes had lower mean scores than those without diabetes on all tests. Women with diabetes (Type 2) scored almost 1 point lower on the TICS than did those without diabetes. Overall, combined results of four cognitive tests in a global score showed, women with diabetes were twice as likely to have a low score as those without diabetes. Longer duration of diabetes and recent lack of pharmacological treatment seemed to be associated with worse performance. This study has found that having diabetes was equivalent to aging 4 years in terms of scores on general cognitive test (TICS). This study reflects a longitudinal trend of diabetes mellitus in community dwelling women and highlights the need to conduct such test to understand the extent and effects of type 2 diabetes disease progression.

There are studies reflecting effects of early stage of type 2 diabetes on cognition as well. One such study was investigated by Ruis et al. (2004). A detailed neuropsychological assessment was done which included a screening test followed by national adult reading test and other domains assessed were abstract reasoning, working memory, immediate memory and learning rate, forgetting rate, incidental memory, information processing speed, attention and executive functions, visuoconstruction language comprehension in individuals early type 2 diabetes in the age range of 50-70 years, 183 individuals with early stage of type 2 diabetes and 69 age matched controls. The study revealed that type 2 diabetes performed significantly poorly on memory functions, information-processing speed, attention, executive functions and language comprehension in the

unadjusted analyses. However, mean differences were small between the diabetes and control group. The performance on tasks for memory and information speed in diabetic patients was inversely proportional to age. This study provides insights that early stage of type 2 diabetes can cause cognitive decrements. Arvanitakis et al. (2006) explored how type 2 diabetes mellitus affects the different cognitive systems like episodic memory, semantic memory, working memory, perceptual speed, visuospatial ability, and global cognition using 19 tests in 882 individuals in which 116 individuals had type 2 diabetes in the age range of 80 to 86 years. The tests used were as follows; Episodic memory was evaluated using seven tests: Word List Memory, Word List Recall, and Word List Recognition, immediate and delayed recall of Story from the Logical Memory subtest of the Wechsler Memory Scale–Revised ; and immediate and delayed recall of the East Boston Story. Semantic memory was assessed using verbal fluency, an abbreviated version of the Boston Naming Test and an abbreviated version of the Reading Test. Working memory tests included digit span forward and backward of the Wechsler memory scale revised and digit ordering. Perceptual speed was assessed using symbol digit modalities, number comparison, and two indexes from a modified version of the Stroop Neuropsychological Test. Visuospatial ability was evaluated by two tests, items from judgment of line orientation and standard progressive matrices. Finding revealed that diabetes was associated with lower performance in two cognitive domains: semantic memory and perceptual speed. Diabetes was not associated with episodic memory, working memory, or visuospatial ability.

Yeung et al. (2009) explored the effects of diabetes (type 2) on cognitive functioning in 41 older adults with type 2 diabetes individuals in the age range of 55 to 80 years and control group in the age range of 53 to 90 years and classified them as young-old adults (YO, 53–70 years old) and old-old adults (OO, 71–90 years old). The diagnosis of type 2 diabetes was based on self report measures; follow up, objective medication data and precise biological information. Mean history of type 2 diabetes was 8 years.

Measures tested include memory, verbal fluency, executive functioning and neurocogntive speed. Neurocognitive speed task included five tests. Two of these were semantic speed tests (lexical decision, sentence verification) and two were reaction time tests. The fifth test measured perceptual speed (digit symbol substitution). The first four tests were computerized and participants had to press designated keys on the keyboard, and performance was recorded in milliseconds (ms). In Lexical decision, 30 words and 30 non words were visually presented randomly (e.g., island vs. nabion) and the participant had to identify English words. The scores were the mean latencies across the 60 trials (composed of 30 words and 30 non words). Sentence verification involved presentation of 50 sentences and the participants had to indicate whether each sentence was plausible or nonsensical (e.g., "the tree fell to the ground with a loud crash" vs. "the pig gave birth to a litter of kittens this morning"). Two outcome measures were used: the average latency of the 50 trials and the percentage of errors. Third, for the simple reaction time (SRT) test, a warning stimulus was presented in the middle

of a screen, followed by a target stimulus to which participants pressed a key. Ten practice trials were followed by 50 test trials. Ten trials were presented at a time, with randomly alternating intervals separating the warning and target stimuli. Fourth, for the choice reaction time (CRT4) test, a 2 × 2 grid corresponding with the key arrangement on a response console was presented. Each block had 10 trials, wherein the participant attended to four plus signs, one of which transformed into a square, to which the matching key was pressed. The average latency across 20 test trials was calculated.

The results of the study revealed that there were no significant differences between type 2 diabetes and healthy controls except for lexical decision task and sentence verification task where the controls performed faster than type 2 diabetes individuals. Hence, authors further suggest the reason to the finding of slow processing in lexical decision and sentence verification task is that the tasks requiring quick and precise processing of new verbal information may be sensitive markers for detecting cognitive deficits in relatively milder diabetes patients.

Fischer et al. (2009) examined short term longitudinal data of healthy controls and type 2 diabetes participants. They examined 3 year longitudinal data (Wave 1; initial n = 577, Mean age = 68.29 years), (Wave 2; n = 402; Mean age = 72.08 years) and at follow-up 3 years later from the victoria longitudinal study. The present study compared only 28 diabetes and 272 controls on a comprehensive

neuropsychological battery whose presence of diabetes (type 2) was determined by a series of self-report, objective medication information and validity checks at both Wave 1 and Wave 2. The assessment of declarative memory included two tasks that are episodic memory task and a composite variable of two semantic memory tasks. Episodic memory included word recall test and two semantic memory tasks included vocabulary tests and fact recall test. Verbal fluency tasks included opposites, figures of speech, and similarities subtests. Neurocognitive speed was assessed using computerized reaction time (RT) tests, measuring the average latency over trials to attend to a signal stimulus (Simple Reaction Time, SRT, *and* four-Choice Reaction Time, CRT4*).*

The other two were computerized tasks measuring semantic speed latency which were lexical decision and sentence verification. Lexical decision scores involved 60 trials with participants indicating whether a string of letters formed a meaningful word. Sentence verification required participants to judge whether a sentence was meaningful or not. The mean latency of responses was calculated. Composite semantic speed (summed average score for Lexical Decision and Sentence Verification) and RT (summed average score for SRT and CRT4) scores were computed. Executive function assessment involved five tests, two tests representing the sub domain of inhibition and three representing the sub domain of shifting or switching. Composite variables were created by summing and averaging across constituent tests: semantic memory (fact recall, vocabulary), RT (SRT, CRT4), fluency (opposites, figures of speech, similarities), semantic speed

(lexical decision, sentence verification), and speed-intensive executive functions (CTT-2, DSS). All cognitive variables were converted to standardized z-score units. Results revealed that the first domain showing a significant deficit for the diabetes group was neurocognitive speed, with both indicators (reaction time and semantic speed). Thus neurocognitive slowing may be a hallmark of the deficits associated with diabetes in older adults. Executive function was the second domain that produced significant differences between diabetes participants and healthy controls. There were no diabetes-related effects on any measure of declarative (episodic or semantic) memory or the verbal fluency composite. The longitudinal design provided an initial opportunity to explore actual short-term change and stability in neuropsychological performance for individuals with type 2 diabetes.

Whitehead et al. (2011) systematically tested whether neurocognitive speed (mean rate) or inconsistency (intraindividual variability) was the more sensitive clinical markers of cognitive dysfunctions in type 2 diabetes (T2D). Three independent samples of initially healthy older adults are followed at 3-year intervals. The participants completed baseline testing in 2002-03 and a second wave of testing in 2005-06, yielding cross-sectional and 3-4-year longitudinal data. The final longitudinal sample comprised a T2D group (n =28; 18 females and 10 males) in the age range of 55-81 years and control group (n= 272; 188 female, 84 men) in the age range of 53-91 years.

The tasks used were lexical decision, sentence verification reaction time and choice reaction time. Computation of intraindividual means for each task, the average rate across trials was calculated in terms of intraindividual means (IM). Ims were computed as the average of each individual's raw reaction time (RT) latencies across all trials. Computation of intraindividual variability estimates were computed as the across-trial intraindividual standard deviation (ISD) about each individual's mean RT. The results revealed mean rate decrements in speeded performance across all tasks were observed for the T2D. A general trend toward moderately elevated intraindividual variability was observed in the T2D group, as compared with the control group. Based on logistic regression analyses, IM was the more effective predictor of T2D status. There was a longitudinal change pattern for IM and ISD. Two prominent speed indicators mean rate or intra individual variability were affected similarly by type 2 diabetes. Although present evidence indicates that mean rate may be more theoretically and clinically implicated. This study investigated a novel aspect of the neuropsychology of T2D and aging and explored the two prominent neurocognitive speed indicators.

Reijmer et al. (2013) explored the reason for slowing of information processing speed in 55 patients with diabetes and 50 healthy controls in the age range of 71-64 years. Premorbid intellectual ability was assessed using national adult reading test (NART). Information processing speed was assessed by the trail making test, the stroop color word test, and the subtest digit symbol of the Wechsler adult intelligence scale. Verbal memory was assessed by the immediate and delayed

task of the Rey auditory verbal learning test. Executive functioning was assessed by the trail-making test–Part B, the stroop color–word test, and a Verbal fluency test. For each domain, the raw test scores were standardized into z-scores and averaged to obtain one composite z-score per cognitive domain. They also reconstructed the white matter network of 55 non demented individuals with type 2 diabetes (mean age, 71-64 years) and 50 age-, sex-, and education matched controls using diffusion magnetic resonance imaging based fiber tractography.

The white matter consists of a complex network of fiber connections and its integrity and organization is important for understanding extent to which the brain can efficiently transfer information between regions. The findings suggested that patients with type 2 diabetes showed significant differences in local and global network connectivity relative to controls. These network abnormalities were related to slowing of information processing speed and increased cerebrovascular lesion load. This study serves as a evidence that disruption of the cerebral white matter network is related to slowing of information processing speed in patients with type 2 diabetes. This study's approach of characterizing the brain as a network using fiber tractography and graph theoretical analysis can provide new insights into how white matter abnormalities can affect cognitive function in patients with diabetes.

Espeland et al. (2013) explored whether type 2 diabetes has adverse effects on brain volumes and changes using MRI in 1,366 women, in the age range of 72–89

years and repeated scan was done after 4.7 years. Firstly, they measured regional brain volumes and ischemic lesion loads and examined whether it varied according to diabetes status. Global cognitive function was assessed with the Modified Mini Mental State (3MS) examination. Four cognitive domains were assessed verbal memory, verbal fluency, language and executive function, orientation, language and praxis. Secondly, associations between global cognitive function and brain and ischemic lesion volumes were examined. At the first examination, standardized MRI measures were obtained from 145 women with recorded diabetes and from 1,221 without; these women comprise the cross-sectional cohort. A second standardized scan was obtained for 58 of the 145 women from the cross sectional cohort with diabetes (40.4%) and for 640 of the women with diabetes (52.4%); this subset of women comprises the longitudinal cohort. The results revealed mean global cognitive function was significantly lower among women with diabetes. Lower brain volumes and greater ischemic lesion volumes were all related to poorer cognitive function. Diabetes was associated with trends toward greater progression of ischemic lesion loads and loss of total brain volumes throughout the brain but not loss of white matter during 4.7 years of average follow-up. The study sheds light on the fact that diabetes is associated with smaller brain volumes in gray but not white matter and increasing ischemic lesion volumes throughout the brain. These markers are associated with but do not fully account for diabetes-related deficits in cognitive function.

Chen et al. (2014) investigated the relationship between abnormal resting-state brain functional connectivity and insulin resistance in 30 type 2 diabetes and compared the same with 31 age matched controls in the age range of 45-70 years, with disease duration of 3 to 20 years and type 2 diabetes was diagnosed using the criteria proposed by the World Health Organization, (1999). Mini-Mental State Exam, Montreal Cognitive Assessment, Auditory Verbal Learning Test (AVLT), Complex Figure Test (CFT), Digit Span Test (DST), Trail-Making Test (TMT) Parts A and B, Clock Drawing Test (CDT), and Verbal Fluency Test (VFT) were used for measuring the following cognitive function, episodic verbal and visual memory, semantic memory, attention, psychomotor speed, executive function and visuospatial skills.

Resting-state brain functional connectivity analysis was also done which describes an interregional cooperation that can be characterized by synchronous and low-frequency (0.08 Hz) fluctuations on blood oxygen level–dependent (BOLD) functional magnetic resonance imaging (fMRI) was used to examine the correlation between the posterior cingulate cortex (PCC) and whole-brain regions. Middle temporal lobe, particularly the hippocampus and middle temporal gyrus with rich insulin receptors, is associated with insulin resistance which is responsible for memory processing. The results revealed the patients with type 2 diabetes showed significant decreases in the functional connectivity between the posterior cingulate cortex (PCC) and the right middle temporal gyrus (MTG), the left lingual gyrus, the left middle occipital gyrus and the left precentral gyrus.

Thus, the study concludes that aberrant brain functional connectivity is related to insulin resistance in type 2 diabetes.

Nazaribadie et al. (2014) assessed the executive functions and information processing in patients with diabetes (type 2) in comparison to prediabetic patients and normal subjects. The sample consisted of 32 patients with type 2 diabetes, 28 pre-diabetic patients and 30 healthy individuals in the age range of 35-60 years. Executive functions were assessed by Wisconsin Card Sorting Test (WCST). Information processing was assessed by Paced Auditory Serial Addition Test (PASAT) and sub tests of Wechsler Adult Intelligence Scale-Revised (WAIS-R). The results of this study showed that there was a significant difference among normal, diabetic and pre-diabetic groups in executive function of WCST (perseveration) and information processing. Findings suggest that diabetic patients experience decline in executive functioning. Thus, monitoring neuropsychological status besides controlling levels of blood sugar in these patients is important. This study shows that the possible link between executive deterioration and diabetes.

Jurado et al. (2016) assessed the neuropsychological performance of a group of middle-aged participants with type 2 diabetes mellitus (T2DM) and compare it to a group of healthy adults on measures of verbal memory, verbal fluency, executive function, attention, and speed of processing.

The sample consisted of 117 functionally independent subjects (60 females, 60.2 ± 3.01 SD years of age, 12.68 ± 4.65 SD years of schooling) of which 34 were diagnosed with diabetes mellitus according to the American diabetes association (ADA) criteria, and 84 were controls without history of significant neurological, psychiatric or cerebrovascular disease. Neuropsychological examinations were conducted to assess participant's cognitive functioning. The results revealed that T2DM subjects had significantly lower scores than healthy controls in measures of verbal learning, delayed recall, semantic verbal fluency, executive function and processing speed. In multiple regression models diabetes remained strongly associated with poorer verbal memory and processing speed performance even after parsing out the effects of hypertension co morbidity and educational attainment. Findings suggest that the deleterious effects of diabetes on cognition are already present in middle-aged patients without significant cognitive complaints. Preventive measures to reduce further cognitive risk should be emphasized during routine diabetes care. The study emphasis the need of neuropsychological test in middle aged individuals with type 2 diabetes.

In the Indian context, very few studies have explored the processing speed in individuals with type 2 diabetes. Muhil et al. (2014) investigated the correlation between the glycosylated HbA1C and auditory, visual reaction time in 100 chronic type 2 diabetes of 40-60 years who are on oral hypoglycemic drugs of >10 years duration and compared with 100 age matched control group.

Chronic Type 2 diabetes mellitus (52 males & 48 females) individuals on oral hypoglycemic agents were divided into two groups. The chronic type 2 diabetic patients (with>10 y) with glycemic control i.e., HbA1C - <7 are grouped as Group-1(n=100), and those of without glycemic control i.e., with elevated HbA1C >7 are grouped as Group-II (n=100). Method of measuring reaction time was using audacity software. Visual reaction time (VRT) measurement task involved the examiner pressing the 'start' button in the component (A) which was out of the view of the subject and the subject was instructed to press the 'Stop' button in component (B) with the right index finger first as soon as he/she sees the red light in the instrument. In auditory reaction time (ART) measurement also the examiner had to press the 'start' button which was out of the view of the subject and was instructed to press the stop button with the right index finger first as soon as he/she hears the sound (1000 hertz's tone) through the head phone connected to it. Minimum five trials were given for both VRT and ART measurement. From both the study groups, chronic type 2 diabetes mellitus has prolonged Auditory and visual reaction time than the controls.

Group-II has shown more prolonged reaction time than the control and Group-I which is statistically significant. There is no significant difference of mean in study and control groups in males and females. The auditory reaction time and visual reaction time are delayed in both the study groups (GI & GII) than the controls and visual reaction time is more delayed which is similar to the findings of previous studies and it is also shown that chronic hyperglycemia favors glucose

oxidation and free radical release like peroxynitrite leading to the axonal fragmentation & degeneration of both myelinated and unmyelinated fibers, axon shrinkage, finally impair the signal transmission of nerves & delayed motor nerve conduction velocity and hence the delayed reaction time. There is significant relationship between the reaction time & glycemic control, in chronic type 2 diabetes mellitus.

Sidhu et al. (2015) compared the reaction time in twenty five individuals with type 2 diabetes since 5 years and twenty five individuals with non diabetics in the age range of 30-50 years. Auditory and visual reaction times were recorded using digital display response time apparatus (Model no 608: Medicaid: AMBALA). Three auditory stimuli (low, medium, high pitched sounds) were presented and three light stimuli (red, green, yellow) were presented. The reaction times of both were recorded in milliseconds and the lowest of the three readings was considered. There was significant increase in the visual and auditory reaction time between diabetic than non diabetic group. Diabetes mellitus affects the peripheral nerves, slows psychomotor responses and has cognitive effects on those individuals who do not have a proper metabolic control. Individuals with long standing type 2 diabetes mellitus may develop signs of autonomic dysfunction, affects somatosensory and auditory system, slows psychomotor responses and affects reaction times.

Influence of cognition in diabetes self care management

Tomlin and Sinclair (2016) investigated the influence of cognition on self management of type 2 diabetes. Cognitive functioning has shown significant correlations with many areas of diabetes self-management including diabetes knowledge, insulin adjustment skills, ability to learn to perform insulin injections, worse adherence to medications, decreased frequency of self care activities, missed appointments, decreased frequency of diabetes monitoring, and increased inaccuracies in reporting blood glucose monitoring.

Herath et al. (2016) explored the effect of diabetes treatment on change of measures of specific cognitive domains over 4 years. The sample was drawn from a population-based cohort study in Australia (the PATH Through Life Study) and comprised 1814 individuals aged 65–69 years at first measurement, of whom 211 were diagnosed with diabetes then the second follow-up in 2009-2010 (Wave 3, aged 69−72 years; n = 1973). Cognitive function was measured using 10 neuropsychological tests. The effect of type of diabetes treatment (diet, oral hypoglycemic agents, and insulin) on measures of specific cognitive domains was assessed using generalized linear models adjusted for age, sex, education, smoking, physical activity level and Body Mass Index (BMI). Assessment of cognitive function was using immediate recall (first list of california verbal learning Test) was used to measure verbal short-term memory. Wechsler Memory Scale-Digit Span Backward was used to test working memory. Spot the-word (STW) task was used to assess verbal ability. Symbol-Digit Modalities Test

(SDMT) was used to assess speed of information processing. Simple reaction time (SRT) and choice reaction time (CRT) were also performed to measure psychomotor speed and information processing speed. Trail making test (TMT), part A and part B, provided measures of processing speed and executive function (task switching). For both tests (TMT-A and TMT-B) completion time was recorded.

The results of all cognitive tests revealed higher performance to be associated with the metformin only treatment group, although these results were not statistically significant. In the longitudinal analysis, participants only on metformin (n = 76) showed significant protective effect only on performance for choice reaction time. Participants who used metformin to treat their diabetes appeared to have better cognitive function at baseline compared to those who used other forms of treatment. This effect was strongest for the domains of verbal memory, working memory, and executive function. It was noted that significant protective effect from metformin on performance for psychomotor speed over 4 years. This study emphasis on frequent usage of medication can slow the decline in the cognitive function of individuals with type 2 diabetes.

These above studies have highlighted several points of interest on the pathophysiology of cognitive dysfunction in type 2 diabetes. Its gives a holistic view and different perspectives on how the brain is affected at various regions like cellular level (neuron cells), how the brain metabolism is affected by insulin

resistance and the major structural changes in the brain. These studies have been done under different population with different sociocultural backgrounds but still the evidence suggests that there is linkage between cognitive dysfunction and type 2 diabetes is present. Most of the studies have used different assessment procedures/protocols to investigate the relation between type 2 diabetes and cognition. Earlier studies have in cooperated cognitive function and information processing tests from the neurophysiological test battery and later studies involved the usage of various event related potentials and imaging instruments like P300, magnetic resonance imaging, blood oxygen level–dependent functional magnetic resonance imaging, resting state functional magnetic resonance imaging, other computerized reaction tests. In the majority of the studies, the domains affected are memory which includes semantic memory. Type 2 diabetes individuals were shown to perform poorly in reaction time tests like lexical decision task, semantic speed tasks etc further suggesting decreased speed in information processing. Few limitations of the above studies provide valuable insights on the importance of proper education matching and premorbid intelligence matching among controls (neurotypical normal individuals) and experimental group (individuals with type 2 diabetes). It also highlights to make an account of self-report, objective medication information; medical test information of individuals with type 2 diabetes. Such studies also indicate the need to assess cognitive linguistic deficits in them. The goal of diabetes self-management is to optimize metabolic control, prevent acute and chronic complications and optimize the quality of life in them.

In this prologue, insights about lexical processing in type 2 diabetes would help in understanding whether there is difference in lexical processing skills in individuals with type 2 diabetes and controls (neurotypical normal individuals). With this background information, the present study has made an attempt to determine the lexical processing skills in individuals with type 2 diabetes.

CHAPTER III

METHOD

Participants

A total of 100 native speakers of Kannada who were divided into two groups, in the age range of 50-70 years were considered. Group I (experimental group) had 50 individuals with type 2 diabetes which included 25 males and 25 females. Group II (control group) had 50 age matched neurotypical individuals including 25 males and 25 females, participated in the study.

Inclusion criteria for group I

- Individuals should have confirmed diagnosis of type 2 diabetes mellitus by diabetologist (atleast with history of 5 years minimum). The participants in the study had a history of blood sugar for 5 to 15 years)
- Individuals should have no history of sensory issues and other neurological problems
- Individuals should have no history of alcohol and drug abuse
- Individuals should have Kannada as mother tongue
- Individuals should know to read and write Kannada
- Individuals should have minimum education of 10^{th} standard
- Individuals should pass Mini Mental State Examination (MMSE)

Inclusion criteria for group II

Individual should not have diabetes or at risk for diabetes which was confirmed by a physician/ diabetologist based on the blood glucose measurement. The Indian diabetes risk questionnaire was also administered with a cut off score of less than 30*. Individuals should have Kannada as mother tongue and should know to read and write Kannada language. Individuals who passed in Mini-Mental State Examination were considered for the study. (According to Indian diabetes Risk Score, < 30 was categorized as low risk, 30-50 as medium risk and > 60 as high risk for diabetes.)

Stimuli

The present study consisted of two tasks to assess lexical processing that is semantic association and lexical decision task**.**

Selection of stimuli

Task 1: Semantic association task

Semantic association task consisted of 120 word pairs in which 60 of the word pairs are semantically related and 60 of them are semantically unrelated. In semantically related word pair, the prime was semantically related to the target. In semantically unrelated word pair, the prime was not semantically related to the target. These words pairs were taken from Prema, Abhishek and Prathana (2013) study and is mentioned in the Appendix I.

Task 2: Lexical decision task

For lexical decision task, 120 words were chosen from Prema, Abhishek and Prathana (2013) study. Among 120 words, 60 of them were words and remaining 60 were non words. The non words were made by transposing letters of true word which is mentioned in Appendix I.

Instrumentation

The stimuli were displayed on 15 inch laptop with windows 7 operating system using freely downloadable DMDX (Automode Version 5.0.1) software (Forster & Forster 2003). The timing of the presentation of visual stimuli (word pairs) was controlled for the reaction time measures using DMDX (Automode Version 5.0.1) software.

Programming of stimuli

Task1: Semantic association task

DMDX software (version 5.0) was used for the presentation of the stimuli. Primes and targets were displayed in the centre line of the computer monitor (laptop). On white background, words were displayed in bold black letters in Kannada. The semantically related and unrelated words were displayed in random order. Each word pair consists of a prime and a target. Initially the prime appeared followed by the target. Each prime was displayed for 500 milliseconds and an inter stimulus interval (ISI) of 300 milliseconds was set following which the target was displayed for 2000 milliseconds. Duration of 4000 milliseconds was given for

participants to respond. Keyboard keys (left arrow and right arrow) were used as response mode for the participants. The left arrow in the keyboard was used to denote "yes" response (that is when word pairs [prime and target] are semantically related) and right arrow was used to denote "no" response (that is when word pairs [prime and target] are not semantically related). The reaction time (RT) was measured as the time taken from start of stimuli until subjects respond or until 4000 milliseconds. The accuracy was also measured.

Task 2: Lexical decision task

DMDX software (version 5.0) was used for the presentation of stimuli in this task. Here, words and non-words in Kannada were taken. Words and non-words were presented randomly one after the other. On white background, words and non-words were displayed in bold black letters.

Each word was presented for 500 milliseconds with inter stimulus duration of 200 ms and the participants were given 4000 milliseconds duration to respond. The left arrow in the keyboard was used to denote "yes" response (that is the displayed target word is a meaningful word) and right arrow was used to denote "no" response (that is displayed target is a non meaningful, non sense word). Both the reaction time and accuracy of the response were measured.

Procedure

All the participants were seated comfortably in a quiet room. The aim, objective and procedure of the study were explained to the participants and informed consent was obtained prior to the testing and the data was collected individually. All the participants were tested in distraction free, quiet environment with participants seated comfortably on the chair. The monitor distance was maintained at about 45 to 50 centimeters from participant's eye level.

Pilot study

A pilot study was conducted in 5 individuals to finalize the display time, the visibility of the prime and target and to finalize response mode assigned keys.

Instructions

Task 1: Semantic association task

Participants were instructed that word pairs will be presented randomly and they have to judge whether the word pair is semantically related or not. If it is semantically related, participants were asked to press left arrow denoting yes and if it is semantically unrelated then to press right arrow denoting "no" as quickly as possible. Participants were given 5 practice trials for the familiarization of the task before the experiment. Figure 3.1 shows the illustration of semantic association task with monitor display and response keys.

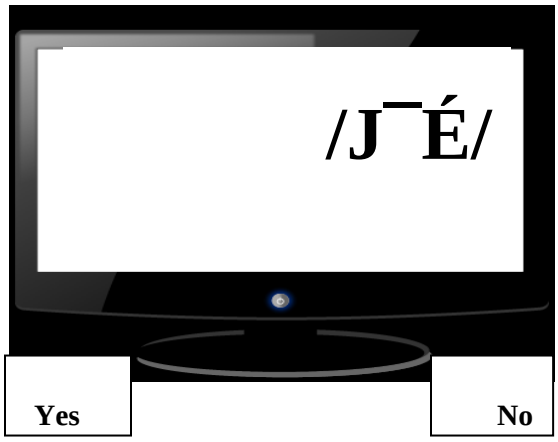

Figure 3.1: Illustration of the semantic association task with monitor display and response keys.

Task 2: Lexical decision task

Participants were instructed to judge whether the word or non-word presented has meaning or not. If the word has meaning they have to press ‘yes’ (left arrow) and if there is no meaning they have to press ‘no’ (right arrow) as fast as they can. Figure 3.2 shows the illustration of the monitor display and response keys in lexical decision task.

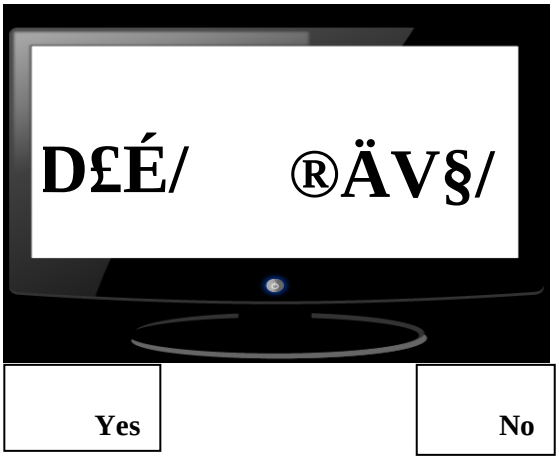

Figure 3.2: Illustration of lexical decision task with monitor display and response keys.

Scoring and analysis

Each stimuli was coded as "+n" for all related word pairs and "-n" for all unrelated word pairs and these responses were coded to the key board in a similar fashion. The responses were recorded as the participant pressed "Left arrow" for 'yes' or "Right arrow" for 'no'. All the correct responses were assigned by a "positive" value of +1 and incorrect responses were assigned by a "negative" value of -1 in the computed reaction time and "no responses" were recorded as -3000 ms.

At the completion of the task, the software automatically computed reaction time (with positive value, negative value and no responses) for each pair and this was saved as respective output file for each participant based on the responses of the respective participant. From the output files the reaction time for semantic association task was derived for every participant in the study and then these scores were averaged using excel.

Accuracy measures were analyzed for each participant for semantic association task. Correct responses were scored as “1” and wrong responses and no responses were scored as “-1”. Total number of correct responses, wrong responses and no response were calculated. The correct responses were calculated after subtracting wrong responses and no responses. The no responses were subtracted from the denominator. The average reaction time and accuracy for each of the lexical processing tasks (semantic association and lexical decision task) were separately analyzed for each participant.

Statistical analysis

All the scores were tabulated and subjected to statistical analysis using SPSS software version IBM 21. The data was subjected to descriptive statistics and the data was further subjected to normality test, the reaction time measures followed normal distribution. Hence, parametric tests were employed. An independent sample t-test was employed for between group comparison and paired sample t- test for within group comparison for reaction time measure. Accuracy measures for both semantic association and lexical decision task did not follow normal distribution. Hence, non parametric tests were employed. Mann-Whitney U test was done for between group comparison and Wilcoxon Signed Rank test for within group comparison for accuracy measure. To investigate interaction and main effect, mixed ANOVA was also employed.

CHAPTER IV

RESULTS

The present study aimed to explore and compare the lexical processing skills in the individuals with diabetes and individuals without diabetes (controls) in Mysore. The study also focused on the variation of lexical processing with respect to gender in individuals with diabetics and controls**.** The data was obtained from 100 native adult speakers of Kannada in the age range of 50-70 years and they were divided into two groups. Group I had 50 individuals with diabetes and group II had 50 individuals without diabetes. Two tasks were used to tap lexical processing that is semantic association and lexical decision task. In semantic association task, the participant has to judge as fast as possible whether the word pairs were semantically related or unrelated. If the word pairs were related, the participants has to press yes and if not related press no. In lexical decision task, the participants had to judge as quickly as possible whether the word is meaningful or not. If the word is meaningful the participants has to press 'yes' and press 'no' if it is not meaningful. The accuracy and reaction time (RT) were measured using DMDX (Automode Version 5.0.1) software. The dependent variables were reaction time and accuracy and independent variables were the groups and gender.

Following statistical measures were applied on the data;

a) Tests of normality to check the distribution of the data.
b) Non parametric tests were done for accuracy and parametric test was employed for reaction time (RT).

c) Mann-Whitney U test was used for between group comparison and Wilcoxon signed rank test was used for pair wise comparison for accuracy measures

d) Independent sample t-test was done for between group comparison and paired t test was used for pair wise comparison for reaction time measures.

e) Mixed ANOVA was administered to explore main and interaction effects of variables such as tasks, genders and groups.

The results are discussed under following sections:

1. Test of normality
2. Comparison of Reaction time
    i. Group comparison
    ii. Gender difference
    iii. Task comparison
3. Comparison of Accuracy measure
    i. Group comparison
    ii. Gender difference
    iii. Task comparison
4. Interaction and main effect

1. Test of normality

Shapiro Wilk normality test was performed to check for normality. The accuracy measures in both controls and diabetic groups did not follow normal distribution ($p > 0.05$). Hence non parametric tests were done. The reaction time measures obtained in

both the groups were found to follow normal distribution ($p < 0.05$). Hence parametric tests were further done for reaction time measures.

2. Comparison of reaction time measures

The mean reaction time scores were calculated for each participant with respect to each task and subjected to descriptive statistical analysis. Table 4.1 shows mean reaction time measure for group I (Individuals with diabetes) and group II (Individual without diabetes) in semantic association task (SAT) and lexical decision task (LDT). Mean Reaction Time (RT) of group I was higher that is they took more time than group II for semantic association task (SAT). This was observed in both males and females. Further, RT of group I was higher than Group II for lexical decision task (LDT) indicating group I takes more time than group II to respond in lexical decision task. Mean RT was higher in males when compared to females in semantic association task (SAT) in both group I and group II. Mean RT was higher in females than males in lexical decision task in both group I and group II.

Table 4.1: *Mean and standard deviation (SD) of reaction time in both controls and diabetes for semantic association and lexical decision tasks*

		SAT		LDT	
		Diabetes (Group I)	Controls (Group II)	Diabetes (Group I)	Controls (Group II)
Males	Mean (msec)	1263	1146	963	905
	SD	249	235	162	164
Females	Mean (msec)	1170	1129	975	934
	SD	187	275	142	188

(*SAT: Semantic association task and LDT: Lexical decision task)

i. Group comparison

Independent sample t test was employed for between group comparison, that is between group I and group II for task 1 (semantic association task) and task 2 (lexical decision task). There was no significant difference in reaction time between group I and group II in semantic association task, $t(98) = 1.65$ $p > 0.05$. Also, in lexical decision task, there was no significant difference in reaction time between group I and group II, $t(98) = 2.05$ $p > 0.05$. Though there was no significant difference statistically between group I and group II, but the mean RT was relatively higher in group I compared to group II.

ii. Gender difference

Since there was no significant difference between group I and group II in reaction time. Hence, overall males and females irrespective of groups were compared using Independent sample t-test. The results revealed irrespective of groups there is no difference in reaction time between males and females in semantic association, $t(98) = 1.15$, $p > 0.05$ and in lexical decision task, $t(98) = 1.10$, $p > 0.05$.

iii. Task comparison

Paired sample t-test was employed to understand difference between semantic association task and lexical decision task within groups. Within males irrespective of groups there was a significant difference in reaction time between two tasks $t(49) = 12.65$, $p < 0.05$. Also, in females irrespective of groups similar finding was observed, $t(49) = 7.38$, $p < 0.05$. Within group II, $t(49) = 9.25$, $p < 0.05$ and group I, $t(49) = 9.66$,

$p<0.05$ irrespective of gender also there was a significant difference in reaction time between semantic association and lexical decision task.

Within group I males, $t(24) = 9.93$, $p<0.05$ and group I females, $t(24) = 4.97$, $p<0.05$ and within group II males, $t(24) = 7.98$, $p<0.05$ and within group II females, $t(24) = 5.37$, $p<0.05$, there was significant difference of reaction time between semantic association and lexical decision task found.

3. Comparison of Accuracy

Descriptive statistic was carried out to calculate the mean, standard deviation and median of accuracy in both controls and diabetic groups in the two tasks that is semantic association and lexical decision tasks. Table 4.2 describes the mean, standard deviation and median of accuracy measures in semantic association task (SAT) and lexical decision task (LDT) in group I and group II.

Table 4.2: *Mean, standard deviation (SD) and Median values of accuracy measures in semantic association and lexical decision tasks*

		SAT		**LDT**	
		Diabetes (Group I)	Controls (Group II)	Diabetes (Group I)	Controls (Group II)
Males	Mean	91	94	96	97
	SD	4	3	3	2
	Median	91	94	97	98
Females	Mean	92	94	95	96
	SD	3	3	3	2
	Median	92	93	96	96

(*SAT is semantic association task and LDT is lexical decision task)

Mean and Median accuracy scores of group II was higher than group I for semantic association task (SAT) indicating group II were more accurate compared to group I.

Standard deviation was more in group I (diabetes) than group II (Controls) which indicates more variability of accuracy scores in group I. In both group I and group II, there was not much differences in mean accuracy scores between males and females in semantic association task and in lexical decision task.

i. Group Comparison

Mann Whitney U test was done for between group comparison that is, between group I and group II. Results of Mann Whitney U test revealed that there is a significant difference found between group I and group II in semantic association task. That is, in semantic association task, group II had higher accuracy scores when compared to group I. In lexical decision task also, there is a significant difference found between the group I and group II. That is, in lexical decision task, group II had higher accuracy scores when compared to group I. Table 4.3 shows the results of Mann Whitney U test for between group comparisons.

Table 4.3: *Results of Mann Whitney U test for between group comparison (Group I Vs Group II)*

Task	**|Z|**	**p value**
Semantic association task	3.85	<0.001*
Lexical decision task	2.62	0.009*

(* indicates significance at 0.05 level)

ii. Gender difference

In group I (individuals with diabetes), there is no significant difference in accuracy scores between males and females in semantic association task and lexical decision task. A similar finding was found in group II for semantic association task. However, in group II there is a significant difference in accuracy scores between males and females for lexical decision task. Also, mean accuracy scores are higher in males compared to females in group II for lexical decision task. The table 4.4 shows the accuracy comparison between males and females in group I and group II for semantic association and lexical decision task.

Table 4.4: *Results of Mann Whitney U test for between group comparison (Males Vs Females) in group I and group II*

	Group I		**Group II**	
TASK	**/Z/**	**P**	**/Z/**	**P**
Semantic association task	0.61	0.53	0.67	0.49
Lexical decision task	1.23	0.21	2.13	0.03*

(* indicates significance at 0.05 level)

From table 4.5, Mann Whitney U test revealed that there is a significant difference in accuracy scores between group I and group II for semantic association task and lexical decision task in males. From table 4.6, there is a significant difference in accuracy scores between group I and group II in semantic association task. But in lexical

decision task there is no significant difference in accuracy scores between group I and group II in females. Table 4.5 shows the comparison between diabetes and control in males for semantic association and lexical decision task and table 4.6 shows the comparison between group I and group II in females for semantic association and lexical decision task.

Table 4.5: *Results of Mann Whitney U test in males for group comparison for the two tasks*

Task	**/Z/**	**p**
Semantic association task	2.87	0.004*
Lexical decision task	0.004	0.038*

(*indicates significance at 0.05 level)

Table 4.6: *Results of Mann Whitney U test in females for group comparison for the two tasks*

Task	**Z**	**p**
Semantic association task	2.50	0.01*
Lexical decision task	1.65	0.10

(*indicates significance at 0.05 level)

ii. Task comparison

Wilcoxon Signed rank test was used for task comparison. In group I and group II irrespective of gender, there is a significant difference in accuracy scores between two

tasks (/Z/ =5.58, $p < 0.05$). Lexical decision task accuracy scores were better than semantic association task. In general, both in group I and group II, the lexical decision task is superiorly performed than semantic association task. In group I, males (/Z/ = 4.30, $p < 0.05$), and (/Z/ = 3.63, $p < 0.05$) females, there is statistically significant difference in accuracy scores between two tasks. Lexical decision task accuracy scores were better than semantic association task. In group II, males (/Z/ = 3.78, $p < 0.05$) , and (/Z/ = 3.65, $p < 0.05$) females, there is significant difference in accuracy scores between two tasks Lexical decision task accuracy scores were better than semantic association task

4. Main and Interaction Effect

Mixed ANOVA was used to examine main effect and interaction effects with tasks (semantic association task and lexical decision task) as a within-subjects factor and groups (diabetic versus control) and gender (males and females) as between-subjects factors. The results revealed a main effect for task, F (1, 96) = 187.94, $p < 0.05$ and there was an interaction effect found between tasks and gender, F (1, 96) = 16.74, $p < 0.05$. But no interaction effect was seen for tasks x groups; gender x group and task x gender x groups. All other main effects and interactions were non-significant.

CHAPTER V

DISCUSSION

The present study aimed to investigate lexical processing in individuals with type 2 diabetes (group I) in comparison with individuals without type 2 diabetes (group II). The main objective of the study was to compare lexical processing skills using semantic association task and lexical decision task in both group I and group II. Also, to examine the gender differences in the lexical processing abilities in persons with type 2 diabetes and controls in the above two tasks. Lexical processing using semantic association and lexical decision task was measured in terms of accuracy and reaction time measures in both group I and group II. Accuracy measures and reaction time were analyzed statistically.

The results of the present study reveals several points of interest; ***Firstly, there was no significant difference for reaction time between individuals with type 2 diabetes and individuals without type 2 diabetic in both tasks that is semantic association and lexical decision task***. However, the controls had faster mean reaction time compared to diabetes which implies that they had slight slowness in lexical processing compared to controls. This finding is consensus with various findings in literature. Cosway et al. (2001) explored the cognitive functions and information processing speed using both subjective tests and event related potentials in type 2 diabetes and age matched controls. Results revealed no significant difference in the area of information processing speed and cognition between the two groups which is also found in the present study. Ruis et al.

(2004) explored many cognitive functions in which information processing speed was assessed and the results revealed that type 2 diabetes had reduced information processing speed than controls, though the mean difference between them was small as like in the present study. Yeung et al. (2009) explored cognitive functioning in 41 older adults with type 2 diabetic individuals and control group. There were 5 tasks of which two were semantic speed tests (lexical decision and sentence verification) and other two were reaction time tests. The fifth test measured was perceptual speed test (digit symbol substitution). The results of the study revealed that there were no significant differences between type 2 diabetes and healthy controls in terms of reaction time and perceptual speed. But there was a relative difference found between type 2 diabetes and healthy controls for lexical decision task and sentence verification task that is, the controls performed faster semantic speed than type 2 diabetes individuals. Jurado et al. (2016) study also found individuals with diabetes had lower scores than healthy controls for processing speed and poor verbal memory. Many studies in literature have investigated the probable cause for slowness in information processing speed. Reijmer et al. (2013) determined the reason for slowing of information processing using a diffusion magnetic resonance imaging based fiber tractography and found disruption of the cerebral white matter network is related to slowing of information processing speed in patients with type 2 diabetes.

Muhil et al. (2014) conducted a study to explore visual and auditory reaction time. The authors found that the individuals with chronic type 2 diabetes had delayed reaction time compared to controls. The authors further support and relate to the

delay in auditory and visual reaction time is due to presence of hyperglycemia in type 2 diabetes which favors glucose oxidation and free radical release like peroxynitrite leading to the axonal fragmentation & degeneration of both myelinated and unmyelinated fibers, axon shrinkage and which finally impair the signal transmission of nerves and delayed motor nerve conduction velocity resulting in delay in reaction time. Sidhu et al. (2015) compared the reaction time in twenty five individuals with type 2 diabetes and twenty five individuals with non diabetics. There was a significant increase in the visual and auditory reaction time in diabetic group in comparison to non diabetic group. The authors stated that individuals with long standing type 2 diabetes mellitus may develop signs of autonomic dysfunction, affects somatosensory and auditory system, which slows down the psychomotor responses and affects reaction times.

The second finding reveals that, there was a significant difference for accuracy measures between group I and group II in semantic association task and lexical decision task. Insulin plays an important role in brain metabolism as it crosses the blood brain barrier via insulin receptors which are widely present throughout the brain (Stein et al., 1987). Hyperinsulinemia results in reduction in transportation of insulin to brain and thereby reduction in insulin activity (Shwartz et al., 1992). Reduced insulin levels and insulin receptor activity may contribute to a number of pathological processes that characterize Alzheimer's disease (AD) such as synaptic loss, limited dendritic arborisation and memory impairment (Craft et al., 2012). Insulin receptors are also found in medial temporal lobe which plays an important role in memory processing.

Semantic association task involves presentation of word pairs one after the other. The participant has to judge whether it is semantically related or unrelated by pressing appropriate response keys. Lexical decision task involves measuring how quickly and accurately the participants judge whether the visually presented stimuli is a meaningful word or a non word by pressing appropriate response keys in the keyboard. These tasks require intact semantic memory and semantic judgment as well as executive functions to make appropriate correct responses. It was observed in the present study that group I had less accuracy scores compared to group II indicating that individuals with type 2 diabetes may have an indirect effect on semantic memory. The mean difference between accuracy scores in group I and group II is relatively less and is statistically significant that is, accuracy in group II is higher than group I. Thus lexical processing deficit may be affected in group I. Arvanitakis et al. (2006) has also found semantic memory and perceptual speed related deficits in individuals with type 2 diabetes. It has also been found in a longitudinal study that women with type 2 diabetes was aging 4 years more than their actual age based on the scores on general cognitive test (Grodstein et al., 2001). In the present study individuals with type 2 diabetes were tested in the mornings in which just few minutes after their medication. The less accuracy scores (or more error rates) in individuals with type 2 diabetes is attributed to reduced insulin levels and insulin receptor activity in the body metabolism which would have influence on the lexical processing skills.

The third finding was that, there was no gender wise difference between group I and group II for semantic association task for reaction time and accuracy measure which is consensus with previous studies. Cosway et al. (2001) also found there was no significant gender difference in cognitive functions like abstract reasoning, short term and long term memory, choice reaction time and information processing speed in the individuals with type 2 diabetes. Watari et al. (2006) also found there were no gender differences among individual with diabetes (type 2) and controls as well as individuals with type 2 diabetes with depression in cognitive domains like overall cognitive function, attention, information processing speed, verbal memory and visual memory and executive functioning. Okereke et al. (2008) investigated the cognitive functions using in both men and women with type 2 diabetes and compared them to age matched controls. The results of study revealed that, there was no difference between males and females on basis of scores of telephonic interview of cognitive status (TICS) and the individuals with type 2 diabetes had lower scores in cognitive tests than individuals without type 2 diabetes.

The fourth finding was that, there was task wise difference within group I and within group II for both accuracy and reaction time measures. The accuracy and reaction time measures were better in lexical decision task than semantic association task for both group I and group II. This can be explained by the task difficulty in semantic association task in comparison to lexical decision task. In the semantic association task the prime appears first followed by the target which

requires participants to memorize the prime and then judge whether the prime is semantically related or unrelated while in lexical decision task the only target appears and the participants just has to judge whether it is a word or a non-word. The cognitive load of semantic memory is relatively more for semantic association task than lexical decision task. Thus results of the present study is in agreement with the finding craft et al. (2012) where they reported that reduced level of insulin and insulin receptors in type 2 diabetic individuals may result in poor semantic memory.

There was a main effect of task and an interaction effect found between tasks and gender. In semantic association task, females outperformed in both groups and in lexical decision task, males outperformed in both groups. The relationship between variables like different tasks and the performance difference among males and females in the present study is unknown and it hints that different linguistic tasks might be gender specific that needs to be explored further with more number of subjects and linguistic tasks.

CHAPTER VI

SUMMARY AND CONCULSION

The present study provides insights regarding lexical processing skills in type 2 diabetes. Lexical processing skills were assessed using semantic association task and lexical decision task. 50 individuals with type 2 diabetes (group I) and 50 individuals without type 2 diabetes (group II) participated in the present study. The semantic association task consisted of 60 semantically related and 60 semantically unrelated word pairs which were presented in a random order by using DMDX software where the participant had to press 'yes' if it is a semantically related word pair and 'no' if it is semantically unrelated. Lexical decision task consisted of 60 non words and 60 words which were presented in a random order. The participants had to press 'yes' if it is meaningful word and 'no' for a non word. The stimuli were presented on 15 inch laptop with windows 7 operating system using freely downloadable DMDX (Automode Version 5.0.1) software. The timing of the presentation of visual stimuli (word pairs) and monitoring of the response time were controlled using DMDX (Automode Version 5.0.1) software. The reaction time and accuracy scores were obtained for both semantic association and lexical decision task and subjected to statistical tests for group, gender and task comparison.

The results revealed that the first finding was that there was no significant difference for reaction time between individuals with type 2 diabetes (group I) and individuals without type 2 diabetic (group II) in both tasks semantic

association and lexical decision task. However, the mean reaction time in group I was higher compared to group II indicating slight slowness in individuals with diabetes in comparison with individuals without diabetes. The slowness in the semantic association and lexical decision tasks can be attributed probably to the presence of long history of type 2 diabetes.

Also, the present study found that there was a significant difference for accuracy measures between group I and group II in semantic association task and lexical decision task. This finding gives insights regarding importance of insulin activity for cognitive functions like semantic memory and judgment. The participants in the present study were tested in the morning where medicines effect has just started, which might have caused the reduced insulin activity resulting in less accuracy scores compared to controls. Also, reduced accuracy in group I can be attributed probably due to the presence (history) of diabetes for more than 5 years. Further, the present study also found that there was no gender difference in group I and group II for semantic association task for reaction time and accuracy measures which was consensus with previous studies.

In addition to the above findings, the present study also found that there was task-wise difference within group I and within group II for both accuracy and reaction time measures. This is attributed because of the complexity of the task. That is, lexical decision task is more relatively easier for both the groups than semantic association task. To conclude, both the processing speed and the accuracy rate

measures in individuals with type 2 diabetes were declined. The semantic association and lexical decision tasks of lexical processing ability was reduced in individuals with type 2 diabetes which was reflected from the present study findings. The poor performance in the lexical processing skills by them can be probably due to reduced speed of cognitive functions with the long term history of high blood sugar, though it is controlled.

Limitation

- The present study was carried out just immediately after the clients had their medication and hence the medications effect would not be there to react in the body. Hence, the effect of medication and its duration variability in body was not controlled in the present study.
- The study could be carried on more number of participants.

Future directions

- The study can be replicated by testing the participant's lexical processing skills at different time duration of the day with and with medication effect**.**
- Lexical processing skills can be assessed in first and second language in type 2 diabetes as the present scenario many of the individuals are bilingual and even multilingual.

Implications of the present study

- The results of the present study would augment the understanding of Speech Language Pathologist on lexical processing in general and semantic

association and lexical decision making skills in particular in individuals with type 2 diabetes.

- The outcome of the present study throws light on detailed profiling of cognitive skills in individuals with diabetes (type 2) and plan different strategies for intervention.
- The present study highlights the importance of monitoring cognitive status besides controlling the levels of blood sugar in these individuals and the cognitive slowness as one of the risk factor should be emphasized in the routine diabetes care, henceforth it can be controlled at the earlier stage by taking necessary steps.

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APPENDIX I

TASK 1- Semantic Association Task

Trial

S. No.	Prime	Target
1	J¯É	ªÀÄgÀ
2	WÀAmÉ	UÀÄr
3	OµÀ¢	UÀÆqÀÄ
4	zÀeÉð	ªÀÄºÀr
5	ºÀt	¸Á«gÀ

S. No.	Prime	Target
1	¸ÀÆAiÀÄð	UÀæºÀ
2	UÀÄr	UÉÆÃ¥ÀÅgÀ
3	«±ÁæAw	PÀvÉÛ
4	UÀrAiÀiÁgÀ	zÁgÀ
5	¤ÃgÀÄ	ªÉÆ¸À¼É

6	PÀªÀiÁ£ÀÄ	¹Aºà
7	zÉÆÃtÂ	CA©UÀ
8	ªÁzÀå	¸ÀAVÃvÀ
9	±ÁAw	¥ÁvÉæ
10	ºÀtvÉ	¥Áætà
11	VtÂ	¥ÀAdgÀ
12	¥ÀÅ¸ÀÛPÀ	dégÀ
13	±À§Þ	¥ÀmÁQ
14	vÉÆnÖ®Ä	ªÉÆmÉÖ
15	¥Àæ±Éß	zÁæQë
16	ZÀ½	UÁ½
17	GAUÀÄgÀ	¨ÉgÀ¼ÀÄ
1	gÀ¸ÉÛ	¨É

8		uÉ Ú
19	¨ÉPÀÄÌ	E°
20	ªÉÄnÖ®Ä	¸É Ã§ Ä
21	¤ÃgÀÄ	«Ä Ã£ À Ä
22	ªÁvÀì®å	vÁ ¬Ä
23	gÁV	ಅ ತ್ನ ಬ
24	ªÉÆgÀ	PÀ ÄgÀ Äq À
25	zÉÆqÀØ¥Àà	vÀ Az É
26	ºÀ°è	¯Á n
27	¥ÀÇeÉ	PÀ ¥À Çð gÀ
28	d£À	ªÀ Ä Æ ® A V
29	¸ÀPÁðgÀ	ªÀ Ä A w æ
30	¸ÉÆÃ¥ÀÅ	¸É Ê£ Àå

31	ªÉÆgÀ	Dª À Äè d£ ÀP À
32	¸ÉÊ¤PÀ	U Àr
33	gÉÆÃV	ªÉ Êz Àå
34	UÀÄwÛUÉ	ªÀ Äg Àt
35	SÉÊ¢	Dg ÀP Àë PÀ
36	PÉÆÃ±À	d£ À£ À
37	ªÀdæ	ªÀ Ä Äv À Ä Û
38	zÉÃ±À	zÀ Aq À£ É
39	PÀrªÉÄ	PÉ Æ gÀ vÉ
40	AiÀÄAvÀæ	“P É Æ ¼ É”
41	¥ÀÅ¸ÀÛPÀ	±Á ¯É
42	¸ÉÊ¤PÀ	Dg À

		A¨ sÀ
43	zÉéÃµÀ	U Àr
44	¹AºÁ¸À£À	zÁ £À
45	HgÀÄ	© Ã¢
46	«ÄÃ£ÀÄ	£É Ãg À
47	PÀªÀÄ®	gÀ PÀ Û
48	ªÀÄ¼É	Z À ½
49	UÁr	Z ÀP À æ
50	J¯É	D¹ Û
51	±À§Ý	zs Àé ¤
52	PÀgÀÄ	Cg Àª À Ä£ É
53	¸ÀA¨sÁµÀuÉ	ªÀi Áv À Ä
54	Hl	¥À jÃ PÉ ë
55	¹ÃªÉÄ¸ÀÄtÚ	§¼ À¥ À
56	wæPÉÆÃ£À	¸Á ºÀ

		¸À
57	ªÉÆÃ¸ÀA©	Qv À Û ¼ É
58	PÀÄað	ªÉ
59	NzÀÄ	PÀ gÉ
60	zÀqÀ	E wº Á¸ À
61	MqÀªÉ	ªÀ ¸À Ûç
62	PÁAqÀ	±Á ¸À Ûç
63	©ÃUÀ	C QÌ
64	gÁdå	gÁ d
65	PÀtÄÚ	PÀ £À ßq ÀP À
66	¸Á»vÀå	PÉ Æ ¯É
67	«UÀæºÀ	ªÀ Ä Æ wð
68	ªÀÄtÄÚ	PÀ ¯É
69	£ÀrUÉ	PÁ ® Ä

70	ಮಳೆ	ಛತ್ರಿ
71	¨ÉlÖ	G¥ÁAiÀÄ
72	□□ □□ಡ	C¥ÁAiÀÄ
73	PÉgÉ	PÀ¥Éà
74	ªÁºÀ£À	zÀªÀqÉ
75	PÉÆA§Ä	fAPÉ
76	¨Á¼ÉºÀtÄÚ	PÉ£Éß
77	“¨ÉÃmÉ”	²PÁj
78	MqÀªÉ	¸ÁgÀÄ
79	ºÀÆªÀÅ	ªÀÄÄ¼ÀÄî
80	E° ¨ÉAQ	¨ÉAQ
81	¨Á«	ºÀUÀÎ
82	UÀÄr¸À®Ä	gÉPÉÌ

83	¸ÁªÀiÁ£ÀÄ	CAUÀr
84	PÀÄað	ºÀªÁªÀiÁ£À
85	ºÉAUÀ¸ÀÄ	¹ÃgÉ
86	ªÉÄÃdÄ	¥ÀlÖt
87	¥Àj¸ÀgÀ	ºÀ¹gÀÄ
88	¸ÀA¦UÉ	¥ÉÇlÖt
89	§tÚ	PÉA¥ÀÅ
90	©¹®Ä	ºÀÄ§Äâ
91	ºÀÄqÀÄV	§¼É
92	ºÀ¸ÀÄ	ªÉÄnÖ®Ä
93	¨É®è	PÀ§Äâ
94	¢Ã¥À	«ÄÃ¸É
95	PÁqÀÄ	zÀlÖ
96	PÀ¼Àî	zÀgÉ

		ÆÃqÉ
97	£À¢	vÉÆnÖ®Ä
98	zÉÃªÀgÀÄ	zÀÆgÀªÁtÂ
99	eÉÆÃr	JgÀqÀÄ
100	vÀAw	PÉÆÃ®Ä
101	¥ÀÅ¸ÀÛPÀ	¥ÀÅl
102	ºÀA¢	vÀÄ¥Àà
103	©Ãd	©vÀÛ£É
104	¥ÀÅ¸ÀÛPÀ	PÀvÀÄÛ
105	¨ÉlÖ	§AqÉ
106	ªÀÄrPÉ	PÀÄA¨Ágà

107	vÀ¯É	ºÀªÀ¼À
108	¥Àl	£Á°UÉ
109	qÀ©â	PÀÄA¨Ágà
110	ªÀÄ¼É	zÉÆÃtÂ
111	D¸É	GzÉÝÃ±À
112	UÁ½	§lÖ®Ä
113	²PÀët	G¥Àz É Ã±À
114	ªÉÄÃ¯É	JvÀÛgÀ
115	ZÁPÀÄ	¸ÉÆ¥ÀÅöà
116	ªÀÄ£É	eÉÃ£ÀÄ
11	ºÉÆ¢PÉ	ZÁ¥

7		É
118	ºÀÆªÀÅ	£É Æ Ãl
119	zÁæQë	zÁ ½ A¨ É
120	UÀÄºÉ	ªÀ Ä Æ ¯É

TASK 2- Lexical decision Task

S. No.	Trial -Target stimuli
1	D£É
2	®ÄV§
3	ªÀÄ¥ÀæzÀ
4	¢Ã¥À
5	gÀPÀÛ

S.No.	Target stimuli
1	gÀÄ¤
2	ZÁPÀÄ
3	vÀmÉÖ
4	£É®
5	UÉ°èªÀÄ
6	zÀ¥Á
7	ªÀÄgÀ¼ÀÄ
8	QmÁ¥À
9	vÉgÀa
10	¥ÀÅµÀà
11	CAV
12	«PÀ
13	ºÉUÀÄ
14	±ÀªÉÃ¥Àæ
15	¨É£ÀÄß
16	£ÁåAiÀiÁ®AiÀÄ
17	gÀtQ
18	UÉ£Á°
19	lUÀgÀÄ
20	ಛತ್ತ
21	gÀÄ¸Á
22	gÀÄzÉÃªÀ
23	UÀÄªÀÄ
24	¢¼ÀºÀ
25	ªÀiÁ»w
26	¥ÉZÁ

27	±ÀgÀ§vÀÄÛ
28	gÀAUÉÆÃ°
29	D¸É
30	¸ÀgÀ
31	¸ÀT
32	¢AºÀ
33	Dl
34	°ºÀÄ
35	¸ÀªÉÆ¼É
36	ºÀA¸À
37	gÀªÀ¼À
38	¸ÁªÀÅ
39	vÀeÉÆ
40	§APÀ
41	¨sÀQÛ
42	£ÉPÉ
43	«µÀå¨sÀ
44	¯ÉPÀÌ
45	«zÉå
46	wj¹Ü¥À
47	UÀÄj
48	¨ÉAgÉ
49	£ÀÈvÀå
50	PÀ¥ÀàÅ
51	ªÀÄÆmÉ
52	®ÄPÉÆÃ
53	ºÉÆÃgÁl
54	£ÀeÁÕ£À
55	ªÀiÁ¸Àd
56	ªÀiÁgÀPÀ
57	gÀ¥ÀAd
58	¨Á«
59	ªÀiÁ°ÃPÀ
60	jPÁ²
61	eÉgÉÆ
62	£ÀuÁ
63	avÀ
64	PÀÄlÄA§
65	¢©Ã

66	ªÀ¼ÀºÀ
67	ºÉÆmÉÖ
68	PÁUÀzÀ
69	¯É²
70	eÁUÀmÉ
71	gÀ¸ÉÛ
72	£ÀzÁªÀÄvÀ
73	E¢Ý®Ä
74	ªÉÄnÖ®Ä
75	GvÀiªÀ
76	£ÉvÀÛ©
77	¯ÉPÉÆ
78	ºÀwÛ
79	¤ºÀ
80	£ÀPÀëvÀæ
81	®¥À
82	ºÀtÄÚ
83	£À±Àé
84	vÀAvÀæ÷å¸À
85	§ºÀÄªÀiÁ£À
86	eÉ¥ÀÇ
87	ZÀAzÀæ
88	gÀ¨É¼ÀÄ
89	PÀzÀ£À
90	w©
91	zsÀÄªÀ
92	PÁUÀzÀ
93	¬Ä£Á
94	¸ÀAªÀiÁ
95	¸ÀAªÀiÁ
96	QvÀÛ¼É
97	QëÃzÀæ
98	qÀ©â
99	j¥Á¼ÀªÀ
100	zÉÆÃtÂ
101	CUÀÎ
102	vÀÄªÀiÁ
103	PÀ¥ÀÅöà
104	MqÀªÉ

105	gÉ£É
106	PÀ£À¸ÀÄ
107	zÉ¸Ë
108	ªÀÄUÀÄ
109	DPÁ±À
110	VgÁ
111	gÉUÉ
112	¨sÀPÀÛ
113	wAUÀ
114	gÉÊ®Ä
115	PÉÆÃ½
116	¥ÀÅvÀæ
117	AiÀÄÄgÀ
118	«ÄAZÀÄ
119	gÁdå
120	£ÀuÁ