**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 56063

**Manuscript Type:** CASE REPORT

**Forniceal deep brain stimulation in severe Alzheimer’s disease: A case report**

Lin W *et al.* Forniceal DBS in severe AD

Wei Lin, Wei-Qi Bao, Jing-Jie Ge, Li-Kun Yang, Zhi-Pei Ling, Xin Xu, Jie-Hui Jiang, Chuan-Tao Zuo, Yu-Hai Wang

**Wei Lin, Li-Kun Yang, Yu-Hai Wang,** Department of Neurosurgery, Joint Logistics Support Unit No. 904 Hospital, Wuxi 214044, Jiangsu Province, China

**Wei-Qi Bao, Jing-Jie Ge, Chuan-Tao Zuo,** PET Center, Huashan Hospital, Fudan University, Shanghai 200235, China

**Zhi-Pei Ling, Xin Xu,** Department of Neurosurgery, PLA General Hospital, PLA Postgraduate Medical School, Beijing 100039, China

**Jie-Hui Jiang,** School of Communication and Information Technology, Institute of Biomedical Engineering, Shanghai University, Shanghai 200444, China

**Author contributions:** Lin W drafted the manuscript, conducted the deep brain stimulation (DBS) surgery, analyzed the neuropsychological data, and designed the study; Bao WQ, Ge JJ, and Jiang JH drafted the manuscript, acquired and analyzed the PET data, and designed the study; Yang LK, Ling ZP, and Xu X revised the manuscript, conducted DBS surgery, analyzed neuropsychological data, and designed the study; Zuo CT critically revised the manuscript for important intellectual content, analyzed and edited PET data, and conceived the study; Wang YH critically revised the manuscript for important intellectual content, conducted the DBS surgery, analyzed and edited neuropsychological data, and conceived the study.

**Corresponding author: Yu-Hai Wang, MD, MNAMS, Doctor,** Department of Neurosurgery, Joint Logistics Support Unit No. 904 Hospital, No. 101 Xingyuan Road North, Wuxi 214044, Jiangsu Province, China. wangyuhai67@126.com

**Received:** May 16, 2020

**Revised:** June 11, 2020

**Accepted:** September 16, 2020

**Published online:**

**Abstract**

BACKGROUND

Forniceal deep brain stimulation (DBS) has been proposed as an alternative treatment for Alzheimer’s disease (AD). Previous studies on mild to moderate AD patients demonstrated improvements in cognitive functions brought about by forniceal DBS. Here, we report our longitudinal findings in one severe AD patient for whom the activities of daily living (ADL) rather than cognitive function significantly improved after 3 mo of continuous stimulation.

CASE SUMMARY

In 2011, a 62-year-old Chinese male with no previous history of brain injury or other neuropsychological diseases and no family history of dementia developed early symptoms of memory decline and cognitive impairment. Five years later, the symptoms had increased to the extent that they affected his daily living. He lost the ability to work as a businessman and to take care of himself. The patient was given a clinical diagnosis of probable AD and was prescribed donepezil and subsequently memantine, but no improvement in symptoms was observed. The patient then received DBS surgery. After 3 mo of continuous stimulation, the patient’s ADL score decreased from 65 points to 47 points, indicating the quality of the patient’s daily living improved distinctly. Other scores remained unchanged, suggesting no significant improvement in cognitive function. A follow-up positron emission tomography scan demonstrated perceivable increased glucose metabolism in the classical AD-related brain regions.

CONCLUSION

Based on this case we hypothesize that forniceal DBS may improve ADL through elevating regional glucose metabolism in the brain.

**Key Words:** Deep brain stimulation; Alzheimer’s disease; Fluorodeoxy glucose; Positron emission tomography; Activities of daily living; Case report

Lin W, Bao WQ, Ge JJ, Yang LK, Ling ZP, Xu X, Jiang JH, Zuo CT, Wang YH. Forniceal deep brain stimulation in severe Alzheimer’s disease: A case report. *World J Clin Cases* 2020; In press

**Core Tip:** A longitudinal case study for one severe Alzheimer’s disease patient showed that forniceal deep brain stimulation may improve the activities of daily living rather than cognitive functions after 3 mo of continuous stimulation through elevating regional glucose metabolism in the brain.

**INTRODUCTION**

Alzheimer’s disease (AD), the leading cause of senile dementia, is a neurodegenerative disorder that is characterized neuropathologically by excessive β-amyloid (Aβ) retention and tau-protein accumulation. Extensive synaptic dysfunction and neuronal loss are present in the late stages, leading to consequent memory deficit and cognitive impairment[1]. While therapeutic medication approaches can fail to alter the course of AD[2], deep brain stimulation (DBS), a mature surgical treatment for various neuropsychiatric disorders[3-5], has recently been proposed as an alternative treatment for AD[6].

The fornix is believed to be an important part of the Papez circuit that is responsible for multiple memory functions[7]. Memory improvements induced by forniceal DBS (f-DBS) were first unexpectedly discovered in the treatment of a patient with an eating disorder[8]. Inspired by this phenomenon, a series of phase-I and phase II clinical trials were conducted to explore the effectiveness of f-DBS for AD patients[9-13]. These studies focused on relatively mild AD, with the exclusion criteria of a Clinical Dementia Rating (CDR) greater than 1 or a Mini-Mental State Examination (MMSE) score less than 20. However, whether f-DBS could also benefit severe AD patients has not yet been investigated. To the best of our knowledge, the patient in our case is the first severe AD patient (CDR = 2 and MMSE = 1) to undergo f-DBS.

**CASE PRESENTATION**

***Chief complaints***

In 2011, a 62-year-old Chinese male with no previous history of brain injury or other neuropsychological diseases and no family history of dementia developed early symptoms of memory decline and cognitive impairment. Five years later, the symptoms had increased to the extent that they affected his daily living. He lost the ability to work as a businessman and to take care of himself.

***History of present illness***

The patient’s MMSE[14], Montreal Cognitive Assessment Basic (MoCA-B)[15], CDR[16], and global deterioration scale scores[17] were 1, 0, 2, and 6 points, respectively, indicating that his cognitive function was greatly impaired. The patient’s activities of daily living (ADL) score[18] was 65 points, showing that multiple domains of his daily living were affected. Cerebrospinal fluid tau, ptau, and Aβ1-42 levels were all abnormal (Table 1), which was parallel with a distinctively positive [C-11] Pittsburg compound B positron emission tomography (PET) scan and an [F-18] fluorodeoxyglucose PET scan with a typical AD-like hypometabolic pattern (Figure 1A).

**FINAL DIAGNOSIS**

The patient was given a clinical diagnosis of probable AD according to the National Institute on Aging-Alzheimer’s Association criteria[19].

**TREATMENT**

The patient was prescribed donepezil 5 mg *quaque nocte*. However, no apparent alleviation of his symptoms was observed, even when he was subsequently prescribed donepezil 10 mg *quaque nocte*, and memantine 20 mg *quaque die*. Therefore, the neurosurgeons decided to accept him as a candidate for DBS at the fornix hoping to improve his impaired cognitive symptoms and quality of daily living. The study was approved by the Ethics Committee of the 101st Hospital of the People’s Liberation Army.

On March 1, 2017, the patient received DBS surgery after signing written informed consent. The electrodes were inserted 2 mm anterior and parallel to the vertical portion of the bilateral post-commissural fornix (Figures 1C and D). Continuous stimulation was delivered by the PINS stimulator system using the following parameters: C+, 1- and 5-, frequency = 130 Hz, voltage = 3.0 V, and pulse = 80 μs[9,12].

**OUTCOME AND FOLLOW-UP**

After 3 mo of continuous stimulation, the patient returned for a follow-up assessment. Interestingly, only the ADL score decreased (from 65 points) to 47 points, indicating that the quality of the patient’s daily living had improved distinctly (Tables 2 and 3). Both basic and instrumental functions were improved, especially eating meals, dressing, bathing, shopping, and clipping his own toenails, the scores for which each decreased by no fewer than 2 points. Meanwhile, the MMSE, MoCA-B, CDR, and Global Deterioration Scale scores remained unchanged, suggesting that there was no distinct improvement in cognitive function. Since the patient refused to undergo a second lumbar puncture, which he thought was quite invasive, follow-up cerebrospinal fluid tau, ptau, and Aβ1-42 results were not available. However, a follow-up [F-18] fluorodeoxyglucose PET scan demonstrated perceivable increased glucose metabolism in the classical AD-related brain regions, including the posterior cingulate cortices, superior parietal gyri, inferior parietal gyri, supramarginal gyri, angular gyri, and bilateral precuneus (Figure 1B). Semi-quantitative analysis revealed elevation of standardized uptake value ratio in these brain regions (using the global average as a reference) (Table 1).

**DISCUSSION**

According to previous mild AD studies, patients receiving f-DBS seemed to have a decreased rate of deterioration or even an improvement in cognitive functions[9]. However, the MMSE and MoCA-B scores of the patient in our case remained unchanged at 1 point and 0 points, respectively. Considering the patient’s severely impaired baseline cognitive status, the alterations in cognition and memory could have been concealed by the floor effect.

On the other hand, our results showed that the quality of daily living had significantly improved after 3 mo of continuous forniceal stimulation, as demonstrated by the ADL scale, which is consistent with similar findings in a previous f-DBS clinical trial[9]. Since the ADL score is associated with multiple cognitive domains, we believe that the recovery of the ADL scores occurred along with the recovery of hypometabolism in multiple cerebral cortical regions responsible for different cognitive functions[20,21]. Among the previously noted regions, the angular gyrus is associated with calculation and financial-skill deficit[22], whereas the supramarginal gyrus is linked to object-related sensory integration and manipulation[23]. The precuneus is associated with visuomotor control, attention, and self-processing[24]. These structures are also components of the default-mode network, which plays a critical role in executive function, memory, and goal-directed behavior[25] and thus in accomplishing complex daily activities.

**CONCLUSION**

Because the current discovery is derived from a single case observation, it is undeniable that verification in larger cohorts is required to reach a solid conclusion. It is also notable that all the previous clinical studies conducted a multi-step 1-year follow-up. Whether the alterations in clinical manifestations and the [F-18] fluorodeoxyglucose positron emission tomography of our case would be sustained after a full year of stimulation should be examined further. However, the preliminary findings in this case are promising and provide support for the future clinical application of forniceal deep brain stimulation to severe AD patients.

**ACKNOWLEDGEMENTS**

The authors would like to thank Dr Huiwei Zhang and Dr Ping Wu from PET Center, Huashan Hospital, Fudan University, Shanghai, China for their aid in image processing and Dr Jie Zhu, Dr Yi Feng, and Dr Jirong Dong from the Department of Neurosurgery, Joint Logistics Support Unit No. 904 Hospital, Wuxi, Jiangsu, China and Dr Zhiqi Mao from the Department of Neurosurgery, PLA General Hospital, PLA Postgraduate Medical School, Beijing, China for their aids in DBS surgery and post-op management.

**REFERENCES**

1 **Querfurth HW**, LaFerla FM. Alzheimer's disease. *N Engl J Med* 2010; **362**: 329-344 [PMID: 20107219 DOI: 10.1056/NEJMra0909142]

2 **Alzheimer’s Association.** 2015 Alzheimer's disease facts and figures. *Alzheimers Dement* 2015; **11**: 332-384 [PMID: 25984581 DOI: 10.1016/j.jalz.2015.02.003]

3 **Hirschtritt ME**, Bloch MH, Mathews CA. Obsessive-Compulsive Disorder: Advances in Diagnosis and Treatment. *JAMA* 2017; **317**: 1358-1367 [PMID: 28384832 DOI: 10.1001/jama.2017.2200]

4 **Rowland NC**, Sammartino F, Lozano AM. Advances in surgery for movement disorders. *Mov Disord* 2017; **32**: 5-10 [PMID: 27125681 DOI: 10.1002/mds.26636]

5 **Sprengers M**, Vonck K, Carrette E, Marson AG, Boon P. Deep brain and cortical stimulation for epilepsy. *Cochrane Database Syst Rev* 2017; **7**: CD008497 [PMID: 28718878 DOI: 10.1002/14651858.CD008497.pub3]

6 **Viaña JNM**, Vickers JC, Cook MJ, Gilbert F. Currents of memory: recent progress, translational challenges, and ethical considerations in fornix deep brain stimulation trials for Alzheimer's disease. *Neurobiol Aging* 2017; **56**: 202-210 [PMID: 28385550 DOI: 10.1016/j.neurobiolaging.2017.03.001]

7 **Nowrangi MA**, Rosenberg PB. The fornix in mild cognitive impairment and Alzheimer's disease. *Front Aging Neurosci* 2015; **7**: 1 [PMID: 25653617 DOI: 10.3389/fnagi.2015.00001]

8 **Hamani C**, McAndrews MP, Cohn M, Oh M, Zumsteg D, Shapiro CM, Wennberg RA, Lozano AM. Memory enhancement induced by hypothalamic/fornix deep brain stimulation. *Ann Neurol* 2008; **63**: 119-123 [PMID: 18232017 DOI: 10.1002/ana.21295]

9 **Laxton AW**, Tang-Wai DF, McAndrews MP, Zumsteg D, Wennberg R, Keren R, Wherrett J, Naglie G, Hamani C, Smith GS, Lozano AM. A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease. *Ann Neurol* 2010; **68**: 521-534 [PMID: 20687206 DOI: 10.1002/ana.22089]

10 **Smith GS**, Laxton AW, Tang-Wai DF, McAndrews MP, Diaconescu AO, Workman CI, Lozano AM. Increased cerebral metabolism after 1 year of deep brain stimulation in Alzheimer disease. *Arch Neurol* 2012; **69**: 1141-1148 [PMID: 22566505 DOI: 10.1001/archneurol.2012.590]

11 **Fontaine D**, Deudon A, Lemaire JJ, Razzouk M, Viau P, Darcourt J, Robert P. Symptomatic treatment of memory decline in Alzheimer's disease by deep brain stimulation: a feasibility study. *J Alzheimers Dis* 2013; **34**: 315-323 [PMID: 23168448 DOI: 10.3233/JAD-121579]

12 **Lozano AM**, Fosdick L, Chakravarty MM, Leoutsakos JM, Munro C, Oh E, Drake KE, Lyman CH, Rosenberg PB, Anderson WS, Tang-Wai DF, Pendergrass JC, Salloway S, Asaad WF, Ponce FA, Burke A, Sabbagh M, Wolk DA, Baltuch G, Okun MS, Foote KD, McAndrews MP, Giacobbe P, Targum SD, Lyketsos CG, Smith GS. A Phase II Study of Fornix Deep Brain Stimulation in Mild Alzheimer's Disease. *J Alzheimers Dis* 2016; **54**: 777-787 [PMID: 27567810 DOI: 10.3233/JAD-160017]

13 **Ponce FA**, Asaad WF, Foote KD, Anderson WS, Rees Cosgrove G, Baltuch GH, Beasley K, Reymers DE, Oh ES, Targum SD, Smith GS, Lyketsos CG, Lozano AM; ADvance Research Group. Bilateral deep brain stimulation of the fornix for Alzheimer's disease: surgical safety in the ADvance trial. *J Neurosurg* 2016; **125**: 75-84 [PMID: 26684775 DOI: 10.3171/2015.6.JNS15716]

14 **Zhang Z,** Hong X, Li H. The mini-mental state examination in the Chinese residents population aged 55 years and over in the urban and rural areas of Beijing. *Zhonghua Shenjingke Zazhi* 1999; **32**: 149-153 [DOI: 10.3760/j.issn:1006-7876.1999.03.006]

15 **Chen KL**, Xu Y, Chu AQ, Ding D, Liang XN, Nasreddine ZS, Dong Q, Hong Z, Zhao QH, Guo QH. Validation of the Chinese Version of Montreal Cognitive Assessment Basic for Screening Mild Cognitive Impairment. *J Am Geriatr Soc* 2016; **64**: e285-e290 [PMID: 27996103 DOI: 10.1111/jgs.14530]

16 **Morris JC**. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 1993; **43**: 2412-2414 [PMID: 8232972 DOI: 10.1212/wnl.43.11.2412-a]

17 **Reisberg B**, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Psychiatry* 1982; **139**: 1136-1139 [PMID: 7114305 DOI: 10.1176/ajp.139.9.1136]

18 **Chen P**, Yu ES, Zhang M, Liu WT, Hill R, Katzman R. ADL dependence and medical conditions in Chinese older persons: a population-based survey in Shanghai, China. *J Am Geriatr Soc* 1995; **43**: 378-383 [PMID: 7706627 DOI: 10.1111/j.1532-5415.1995.tb05811.x]

19 **Jack CR Jr**, Albert MS, Knopman DS, McKhann GM, Sperling RA, Carrillo MC, Thies B, Phelps CH. Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 2011; **7**: 257-262 [PMID: 21514247 DOI: 10.1016/j.jalz.2011.03.004]

20 **Vidoni ED**, Honea RA, Burns JM. Neural correlates of impaired functional independence in early Alzheimer's disease. *J Alzheimers Dis* 2010; **19**: 517-527 [PMID: 20110598 DOI: 10.3233/JAD-2010-1245]

21 **Landau SM**, Harvey D, Madison CM, Koeppe RA, Reiman EM, Foster NL, Weiner MW, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. Associations between cognitive, functional, and FDG-PET measures of decline in AD and MCI. *Neurobiol Aging* 2011; **32**: 1207-1218 [PMID: 19660834 DOI: 10.1016/j.neurobiolaging.2009.07.002]

22 **Griffith HR**, Stewart CC, Stoeckel LE, Okonkwo OC, den Hollander JA, Martin RC, Belue K, Copeland JN, Harrell LE, Brockington JC, Clark DG, Marson DC. Magnetic resonance imaging volume of the angular gyri predicts financial skill deficits in people with amnestic mild cognitive impairment. *J Am Geriatr Soc* 2010; **58**: 265-274 [PMID: 20374402 DOI: 10.1111/j.1532-5415.2009.02679.x]

23 **Naito E**, Ehrsson HH. Somatic sensation of hand-object interactive movement is associated with activity in the left inferior parietal cortex. *J Neurosci* 2006; **26**: 3783-3790 [PMID: 16597731 DOI: 10.1523/JNEUROSCI.4835-05.2006]

24 **Boly M**, Balteau E, Schnakers C, Degueldre C, Moonen G, Luxen A, Phillips C, Peigneux P, Maquet P, Laureys S. Baseline brain activity fluctuations predict somatosensory perception in humans. *Proc Natl Acad Sci* 2007; **104**: 12187-12192 [PMID: 17616583 DOI: 10.1073/pnas.0611404104]

25 **Eichele T**, Debener S, Calhoun VD, Specht K, Engel AK, Hugdahl K, von Cramon DY, Ullsperger M. Prediction of human errors by maladaptive changes in event-related brain networks. *Proc Natl Acad Sci* 2008; **105**: 6173-6178 [PMID: 18427123 DOI: 10.1073/pnas.0708965105]

**Footnotes**

**Informed consent statement:** Informed consent to publish was obtained from the patient.

**Conflict-of-interest statement:** All the authors of this article declare that there is no conflict of interest regarding the publication of this article.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/Licenses/by-nc/4.0/

**Manuscript source:** Unsolicited manuscript

**Peer-review started:** May 11, 2020

**First decision:** June 7, 2020

**Article in press:**

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

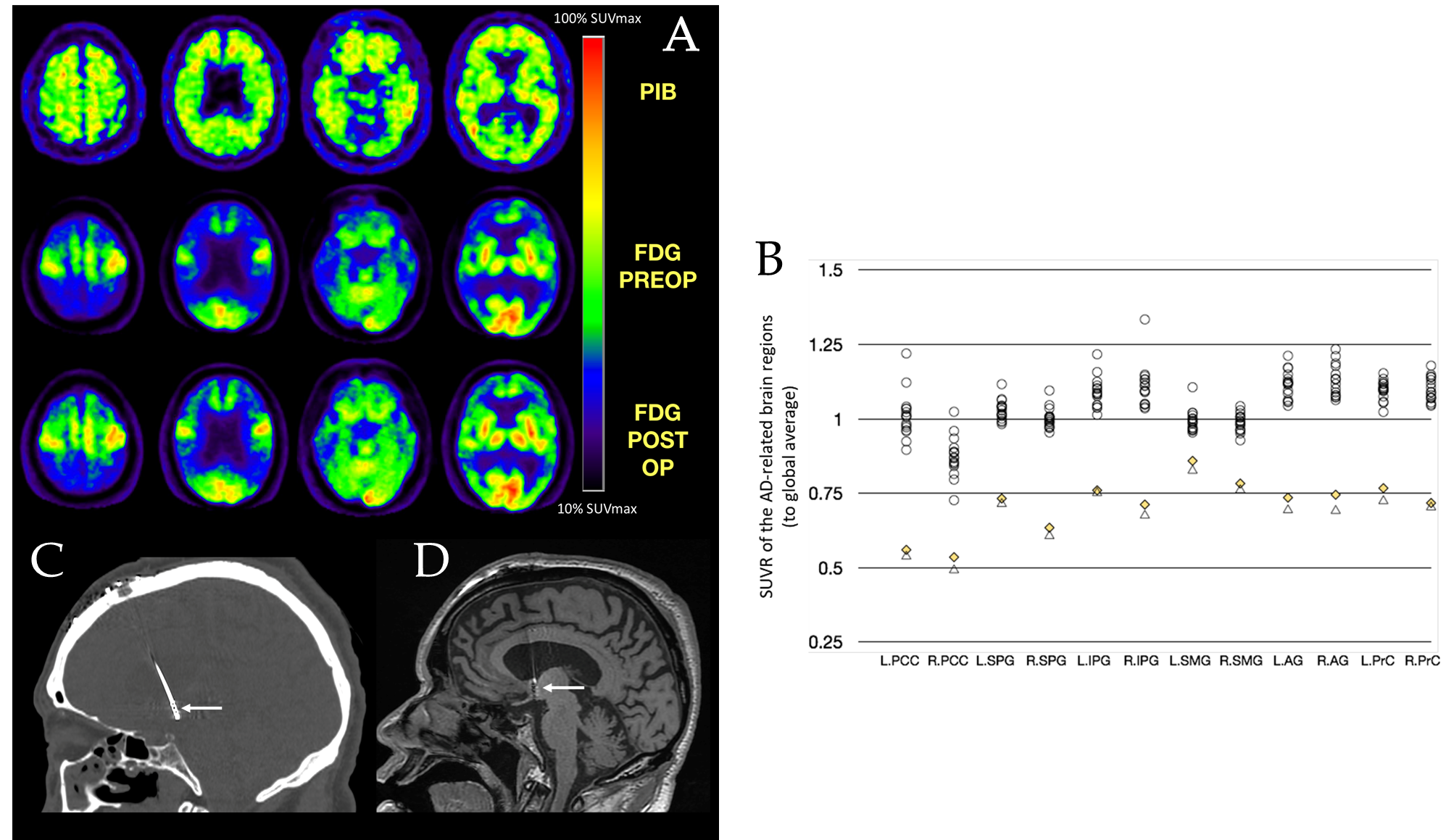
Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Vinh-Hung V **S-Editor:** Zhang L **L-Editor:** Filipodia **P-Editor:**

**Figure Legends**



**Figure 1** **Positron emission tomography and regional standardized uptake value ratio.** A: Positron emission tomography (PET) images of the severe Alzheimer’s disease (AD) patient who underwent forniceal deep brain stimulation. Top row: pre-operative [C-11] Pittsburg compound B PET. Middle row: pre-operative [F-18] fluorodeoxyglucose PET: hypometabolism is seen in typical AD-affected brain regions. Bottom row: post-operative [F-18] fluorodeoxyglucose PET: slight recovery of regional glucose metabolism can be seen after 3 mo of continuous f-deep brain stimulation (DBS); B: Regional standardized uptake value ratio (to global average) of 16 cognitively intact normal controls and the severe AD patient (both pre- and post-operative); C: Coronal computer tomography image (bone window), showing DBS electrode inserting into the post-commissural fornix (white arrow); and D Coronal T1 magnetic resonance image showing DBS electrode inserting into the post-commissural fornix (white arrow). L: Left; R: Right; PCC: Posterior cingulate cortex; SPG: Superior parietal gyrus; IPG: Inferior parietal gyrus; SMG: Supramarginal gyrus; AG: Angular gyrus; PrC: Precuneus.

**Table 1 Cerebrospinal fluid assessment results (upper three lines) and neuropsychological assessment results (lower five lines) before and after f-deep brain stimulation treatment**

|  |  |  |  |
| --- | --- | --- | --- |
| **Assessments** | **Preoperative** | **Postoperative at 3 mo** | **Ref.** |
| Aβ1-42 | 172.6 pg/mL | N/A | 890-2980 pg/mL |
| tau | 322 pg/mL | N/A | 103-218 pg/mL |
| ptau | 52.44 pg/mL | N/A | 28.5-42.3 pg/mL |
| ADL | 65 | 47 | 20-26 |
| MMSE | 1 | 1 | 27-30 |
| MoCA-B | 0 | 0 | 26-30 |
| CDR | 2 | 2 | 0 |
| GDS | 6 | 6 | 1 |

Aβ1-42: Cerebrospinal fluid amyloid-beta 1-42 level; tau: Cerebrospinal fluid tau protein level; ptau: Cerebrospinal fluid phosphorylated tau protein level; ADL: Activities of daily living; MMSE: Mini-mental state examination; MoCA-B: Montreal cognitive assessment basic; CDR: Clinical dementia rating; GDS: Global deterioration scale; N/A: Not available.

**Table 2 Preoperative activities of daily living**

|  |  |  |  |
| --- | --- | --- | --- |
| **Take a bus** | **4** | **Go up/downstairs** | **2** |
| Go to a place near home, within walking distance | 3 | Get on/off bed, sit down/stand up | 1 |
| Prepare meal | 4 | Fetch water to cook/bathe | 4 |
| Do the housework | 4 | Take a bath | 4 |
| Take medicine | 1 | Cut toenail | 4 |
| Eat meal | 3 | Go shopping | 4 |
| Put on/take off clothes | 4 | Go to the toilet regularly | 3 |
| Brush hair/teeth | 3 | Make a phone call | 4 |
| Wash clothes | 4 | Take care of the money | 4 |
| Walk on flat floor indoors | 1 | Be home alone | 4 |

Write down numeric points: 1 = can do it myself, 2 = have some difficulty doing but can still do it by myself, 3 = need help to do it, 4 = cannot do it at all.

**Table 3 Postoperative activities of daily living at 3 mo**

|  |  |  |  |
| --- | --- | --- | --- |
| **Take a bus** | **3** | **Go up/downstairs** | **2** |
| Go to a place near home, within walking distance | 2 | Get on/off bed, sit down/stand up | 1 |
| Prepare meal | 4 | Fetch water to cook/bathe | 3 |
| Do the housework | 3 | Take a bath | 2 |
| Take medicine | 1 | Cut toenail | 2 |
| Eat meal | 1 | Go shopping | 2 |
| Put on/take off clothes | 2 | Go to the toilet regularly | 2 |
| Brush hair/teeth | 2 | Make a phone call | 3 |
| Wash clothes | 4 | Take care of the money | 4 |
| Walk on flat floor indoors | 1 | Be home alone | 3 |

Write down numeric points: 1 = can do it myself; 2 = have some difficulty doing but can still do it by myself; 3 = need help to do it; 4 = cannot do it at all.