

# Attention deficit in patients with mild cognitive impairment

★

M. Li<sup>1</sup>, Y. Wang<sup>1</sup>, N. Li<sup>2</sup>, J. He<sup>3</sup>, L. Guo<sup>4</sup>, L. Guo<sup>5</sup>, L. Guo<sup>6</sup><sup>1</sup>Institute of Psychology, Chinese Academy of Sciences, Beijing, China<sup>2</sup>Dept. of Psychology, University of Chinese Academy of Sciences, Beijing, China<sup>3</sup>Dept. of Neurology, Peking University Third Hospital, Beijing, China<sup>4</sup>Center for Brain and Cognitive Sciences, School of Psychological and Cognitive Sciences, Peking University, Beijing, China<sup>5</sup>PKU-IDG/McGovern Institute for Brain Research, Peking University, Beijing, China<sup>6</sup>Dept. of Neurology, University of Lübeck, Lübeck, Germany<sup>7</sup>Institute of Neuroscience, Key Laboratory of Primate Neurobiology, CAS Center for Excellence in Brain Science and Intelligence Technology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China

## Article info

## Abstract

### Keywords:

D2/3

AD

FAD

### Introduction:

Dementia (D) has been considered as a heterogeneous disease. In this study, we compared the attention deficit between D2/3 dementia (versus AD dementia).

**Methods:** D2/3 dementia (N = 57) and AD dementia (N = 40) were recruited. The attention was assessed by the visual search task (VS task) versus the digit task (DT task). The VS task was divided into the first task (f1) and the second task (f2).

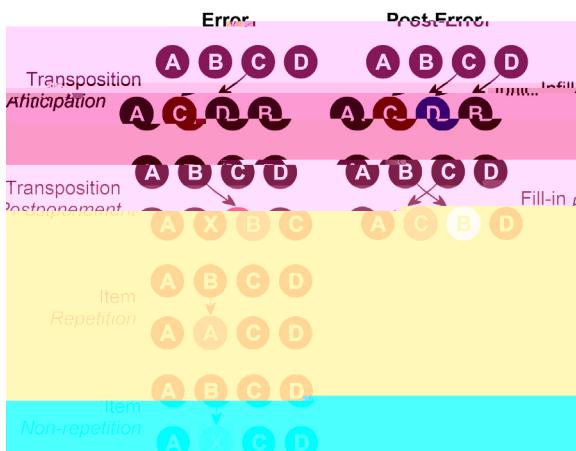
**Results:** D2/3 dementia patients had more attention deficit than AD dementia patients in f1 task, but not in f2 task. In contrast, the attention deficit in f2 task was more prominent in D2/3 dementia patients than AD dementia patients.

**Conclusion:** D2/3 dementia patients had more attention deficit than AD dementia patients in f1 task, but not in f2 task.

## 1. Introduction

Dementia (D) is a heterogeneous disease. The main clinical features of D include memory loss, language disorder, executive function disorder, and behavioral disorder. The etiology of D is complex, involving genetic factors, environmental factors, and brain lesions. The most common type of D is Alzheimer's disease (AD), which accounts for about 60% of all cases of D. Other types of D include vascular dementia, Lewy body dementia, frontotemporal dementia, and progressive nonfluent aphasia. The progression of D is usually slow and progressive, leading to significant functional impairment and reduced quality of life.

Attention deficit is a common symptom in D, particularly in AD. Attention deficit can manifest as difficulty focusing, distractibility, and difficulty multitasking. It can also lead to memory problems, language difficulties, and behavioral changes. The underlying mechanism of attention deficit in D is not fully understood, but it is believed to be related to damage in the prefrontal cortex and other brain regions involved in attention. Treatment of attention deficit in D is challenging, but it can be managed through medication, cognitive therapy, and behavioral interventions. Early diagnosis and treatment are important for managing the symptoms of D and improving the quality of life of patients.



**Fig. 1.** Effects of working memory errors on subsequent items (adapted from Lemaire & Hay, 2000).

distal to the error item, but did not reach statistical significance ( $F(1, 12) = 2.75$ ,  $p = 0.11$ ), suggesting that the effect was rather modest [Fig. 2(b)]. Interestingly, however, the error effect was significant at the second position (item  $i+1$ ) for both the first and the second D2/3, which was not the case for the first position (item  $i$ ) (first D2/3,  $F(1, 12) = 2.12$ ,  $p = 0.16$ ; second D2/3,  $F(1, 12) = 1.88$ ,  $p = 0.16$ ). It is likely that the error effect is more pronounced at the second position than at the first position because it is easier to correct an error in the second position (as compared to the first position), and therefore, the error effect is more robust at the second position. At the third position (item  $i+2$ ), however, the error effect was significant for the first D2/3, but not for the second D2/3. At the fourth position (item  $i+3$ ), the error effect was significant for the second D2/3, but not for the first D2/3.

Differences between the first and second D2/3 were also observed for the error effect (D<sub>1</sub>-A) versus the non-error effect (D<sub>2</sub>-A). A two-way repeated measures ANOVA revealed that the error effect was significantly smaller in the second D2/3 than in the first D2/3 ( $F(1, 12) = 2.38$ ,  $p = 0.14$ ), suggesting that the error effect was more pronounced in the first D2/3 than in the second D2/3 (Fig. 2b). In fact, the error effect was significant in the first D2/3 ( $F(1, 12) = 2.75$ ,  $p = 0.11$ ), but not in the second D2/3 ( $F(1, 12) = 1.88$ ,  $p = 0.16$ ). Interestingly, the error effect was significant at the second position (item  $i+1$ ) for both the first and the second D2/3, which was not the case for the first position (item  $i$ ) (first D2/3,  $F(1, 12) = 2.12$ ,  $p = 0.16$ ; second D2/3,  $F(1, 12) = 1.88$ ,  $p = 0.16$ ). It is likely that the error effect is more pronounced at the second position than at the first position because it is easier to correct an error in the second position (as compared to the first position), and therefore, the error effect is more robust at the second position. At the third position (item  $i+2$ ), however, the error effect was significant for the first D2/3, but not for the second D2/3. At the fourth position (item  $i+3$ ), the error effect was significant for the second D2/3, but not for the first D2/3.

## 2. Methods

**2.1. Participants** Forty-four patients with PD (mean age, 66 ± 6 years; range, 45–82 years) and 23 healthy control subjects (mean age, 59 ± 7 years; range, 40–71 years) participated in this study. All participants were right-handed (according to the Edinburgh Handedness Inventory) and had no history of neurologic or psychiatric disorders.

### 2.1.1. Patients and clinical assessment

Patients were recruited from the movement disorders clinic of the First Affiliated Hospital of Harbin Medical University. All patients met the diagnostic criteria for PD according to the United Parkinson's Disease Rating Scale (UPDRS) (Jiang et al., 2013). Exclusion criteria included the presence of cognitive impairment on the Montreal Cognitive Assessment (MoCA) scale (MoCA score  $< 21/30$ ), and the presence of depression or anxiety on the Beck Depression Inventory (BDI-II) (Beck et al., 1996). The total sample included 132 patients with PD (mean age, 66 ± 6 years; range, 45–82 years) and 23 healthy control subjects (mean age, 59 ± 7 years; range, 40–71 years). There were 111 men and 41 women in the patient group and 16 men and 7 women in the control group. Of the patients with PD, 65 were diagnosed with mild cognitive impairment (MCI) based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and 67 were diagnosed with dementia based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). The mean MoCA score for the MCI group was 25.0 ± 3.0 (range, 21–30) and the mean MoCA score for the dementia group was 18.8 ± 2.8 (range, 12–27). The mean BDI-II score for the MCI group was 9.0 ± 4.8 (range, 2–21) and the mean BDI-II score for the dementia group was 12.8 ± 4.2 (range, 6–25). The patients with PD were matched with the control subjects in terms of sex and education level. All patients were off anti-Parkinsonian medication during the test session. There was no significant difference in education level between the patients with PD and the control subjects ( $t(154) = -0.50$ ,  $p = 0.61$ ).

### 2.2. Healthy control subjects

Twenty-four healthy control subjects (mean age, 59 ± 7 years; range, 40–71 years) were recruited from the First Affiliated Hospital of Harbin Medical University. All participants were right-handed (according to the Edinburgh Handedness Inventory) and had no history of neurologic or psychiatric disorders.

### 2.3. Working memory tests and error types

As shown in Fig. 1, there are two main types of errors in the D2/3 task, namely, transposition (e.g., A-B-C-D → A-C-B-D) and item repetition (e.g., A-B-C-D → A-A-C-D). Transposition errors were further divided into anticipation errors (e.g., A-B-C-D → A-C-N-R) and postponement errors (e.g., A-B-C-D → A-X-B-C). Fill-in errors were categorized as either anterograde or retrograde errors depending on whether the response was preceded by the target item or the previous error, respectively. Error types were determined based on the location of the error (i.e., the position of the error relative to the error item) and the position of the error relative to the target item (i.e., the position of the error relative to the target item). For example, if an error occurred at position  $i$  (e.g., A-B-C-D → A-X-B-C), it was defined as an "error at position  $i$ " and "error after position  $i$ ". Conversely, if an error occurred at position  $i+1$  (e.g., A-B-C-D → A-C-B-D), it was defined as "error before position  $i+1$ " and "error at position  $i+1$ ". The latter classification was used for the analysis of errors at positions  $i+1$  and  $i+2$ . If the error occurred at position  $i+3$  (e.g., A-B-C-D → A-Y-C-D), it was defined as "error before position  $i+3$ " and "error at position  $i+3$ ".

et al., 2013). It is interesting to note that the D-MCI group had a significantly higher proportion of patients with MCI at baseline compared to the D group (40% vs. 10%,  $p < 0.001$ ). The proportion of patients with MCI at baseline was 10% in the D group and 40% in the D-MCI group ( $p < 0.001$ ).

#### 2.4. Statistical analysis

Statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, NY, USA). The primary outcome measure was the total score on the MDS-UPDRS part III. Secondary outcome measures included the MDS-UPDRS part I, MDS-UPDRS part II, MMSE, and HGT. The primary analysis was a multivariate analysis of variance (MANOVA) with group (D vs. D-MCI) as the independent variable and outcome measures as dependent variables. Post-hoc analyses were conducted using Tukey's HSD test. The secondary analysis was a univariate ANOVA with group (D vs. D-MCI) as the independent variable and each outcome measure as the dependent variable. The effect size was calculated using partial eta-squared ( $\eta^2$ ). A value of  $\eta^2 > 0.05$  was considered large,  $\eta^2 > 0.14$  was considered moderate, and  $\eta^2 < 0.01$  was considered small. The level of significance was set at  $p < 0.05$ . The level of significance was set at  $p < 0.05$ .

For the primary analysis, the main effect of group was significant ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ). The D group had a significantly higher total MDS-UPDRS part III score than the D-MCI group ( $t(93) = 3.21, p = 0.001$ ,  $\eta^2 = 0.09$ ). The D group also had significantly higher scores on MDS-UPDRS part I ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) and MDS-UPDRS part II ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) compared to the D-MCI group.

For the secondary analysis, the main effect of group was significant ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ). The D group had a significantly higher total MDS-UPDRS part III score than the D-MCI group ( $t(93) = 3.21, p = 0.001$ ,  $\eta^2 = 0.09$ ). The D group also had significantly higher scores on MDS-UPDRS part I ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) and MDS-UPDRS part II ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) compared to the D-MCI group.

**Table 1**

	D (N = 30)	D-MCI (N = 27)	HGT (N = 40)	General effect (p-value)
<b>Demographic data</b>				
M/F	16:14	16:11	20:20	0.76
Age (years)	67.6 (7.0)	71.9 (8.0)	66.5 (5.8)	0.12
EDSS (range)	14.6 (2.7)	14.2 (3.8)	14.4 (2.0)	0.54
<b>Motor symptoms</b>				
Dyskinesia (I–III)	1.9 (1.8)	2.3 (1.8)	–	0.98
Hypokinetic (I–III)	2.0 (0.6)	2.1 (0.5)	–	0.49
Dystonia (I–III)	12.1 (4.6)	10.8 (3.0)	–	0.41
<b>Cognition</b>				
M-CA	27.4 (1.2)	24.1 (1.0)	28.2 (1.4)	< 0.001*
ADL (I–IV)	5.4 (2.2)	3.8 (1.7)	7.4 (2.2)	< 0.001*
DLB (I–IV)	7.5 (1.2)	7.0 (1.2)	8.1 (1.0)	0.001*
DLB+MCI (I–IV)	4.5 (1.1)	4.1 (1.0)	5.8 (1.8)	0.001*
ADL+MCI (I–IV)	19.3 (5.1)	15.1 (3.2)	21.2 (5.8)	0.003
<b>Other non-motor functions</b>				
No-Motor (I–IV)	9.5 (4.6)	10.8 (4.7)	–	0.57
BPSD (I–IV)	2.2 (2.2)	3.4 (2.0)	1.9 (1.9)	0.16
EM (I–IV)	4.7 (2.6)	5.4 (3.5)	1.9 (1.4)	0.001*
EM+MCI (I–IV)	5.6 (4.5)	3.7 (3.7)	3.8 (2.6)	0.13
IM (I–IV)	4.1 (3.9)	4.3 (6.5)	3.0 (2.6)	0.64
<b>Levodopa equivalent daily dose (LEDD)</b>				
LEDD (mg)	272.1 (159.9)	312.2 (181.5)	–	0.62
LEDD (mg)	146.7 (146.2)	223.2 (152.9)	–	0.16
D2/3 (mg)	50.4 (45.1)	44.9 (44.9)	–	0.11

MCI, mild cognitive impairment; EDSS, Expanded Disability Status Scale; ADL, activities of daily living; DLB, dementia with Lewy bodies; M-CA, Mini-Cog; BPSD, behavioral and psychological symptoms of dementia; EM, executive memory; IM, instrumental memory; LEDD, levodopa equivalent daily dose. \*p < 0.0025 (Bonferroni correction).

### 3. Results

#### 3.1. Test scores

The total MDS-UPDRS part III score was significantly higher in the D group compared to the D-MCI group ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ). The D group had a significantly higher total MDS-UPDRS part III score than the D-MCI group ( $t(93) = 3.21, p = 0.001$ ,  $\eta^2 = 0.09$ ). The D group also had significantly higher scores on MDS-UPDRS part I ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) and MDS-UPDRS part II ( $F(1, 93) = 10.42, p = 0.001, \eta^2 = 0.10$ ) compared to the D-MCI group.

#### 3.2. Error types

Homologous errors were significantly more frequent in the D group compared to the D-MCI group ( $F(1, 93) = 7.48, p = 0.001, \eta^2 = 0.14$ ). Non-homologous errors were significantly more frequent in the D group compared to the D-MCI group ( $F(1, 93) = 4.61, p = 0.012, \eta^2 = 0.09$ ). Executive errors were significantly more frequent in the D group compared to the D-MCI group ( $t(68) = 2.44, p = 0.017$ ; D-MCI:  $t(65) = 5.47, p < 0.001$ ). Executive errors were significantly more frequent in the D group compared to the D-MCI group ( $p > 0.22$ ).

Homologous errors were significantly more frequent in the D group compared to the D-MCI group ( $F(1, 93) = 4.95, p = 0.009, \eta^2 = 0.10$ ). Non-homologous errors were significantly more frequent in the D group compared to the D-MCI group ( $F(1, 93) = 5.17, p = 0.007, \eta^2 = 0.10$ ). Executive errors were significantly more frequent in the D group compared to the D-MCI group ( $t(68) = 2.77, p = 0.007$ ; D-MCI:  $t(65) = 4.30, p < 0.001$ ). Executive errors were significantly more frequent in the D group compared to the D-MCI group ( $p > 0.21$ ).

Executive errors were significantly more frequent in the D group compared to the D-MCI group ( $F(1, 93) = 4.95, p = 0.009, \eta^2 = 0.10$ ).



**Fig. 2.** Mean response times and error rates for healthy controls (HC), PD, and PD-MCI groups across four conditions: (A) transposition, (B) item, (C) attentional, and (D) D2/3. \* indicates significant difference between PD-MCI and HC ( $p < 0.05$ ). (D) indicates significant difference between D2/3 and Atte for the PD-MCI group ( $p < 0.05$ ).

$F(2,93) = 4.70$ ,  $p = 0.011$ ,  $\eta^2 = 0.09$ ). Between D and D-MCI,  $t(68) = 3.06$ ,  $p = 0.005$ , D-MCI:  $t(65) = 4.54$ ,  $p < 0.001$ ). Between Atte and D (D:  $t(68) = 3.06$ ,  $p = 0.005$ ; D-MCI:  $t(65) = 4.54$ ,  $p < 0.001$ ), there was no significant difference ( $p > 0.21$ ).

### 3.3. Effect of D2/3 receptor agonists

$F(2,93) = 4.70$ ,  $p = 0.011$ ,  $\eta^2 = 0.09$ ). Between D and D-MCI,  $t(68) = 3.06$ ,  $p = 0.005$ , D-MCI:  $t(65) = 4.54$ ,  $p < 0.001$ ). Between Atte and D (D:  $t(68) = 3.06$ ,  $p = 0.005$ ; D-MCI:  $t(65) = 4.54$ ,  $p < 0.001$ ), there was no significant difference ( $p > 0.21$ ).

## 4. Discussion

The results of the present study showed that PD-MCI patients had more difficulty than PD and HC in performing the task of identifying the target word in the transposition condition. This finding is consistent with previous studies [12,19–21]. In addition, the reaction time of the PD-MCI group was significantly longer than that of the PD group in the D2/3 condition. This result suggests that the D2/3 receptor agonist may have a positive effect on the cognitive function of PD-MCI patients. However, the reaction time of the PD-MCI group was significantly longer than that of the HC group in the Atte condition. This result suggests that the D2/3 receptor agonist may have a negative effect on the cognitive function of PD-MCI patients. The results of the present study also showed that the reaction time of the PD-MCI group was significantly longer than that of the PD group in the Item condition. This result suggests that the D2/3 receptor agonist may have a negative effect on the cognitive function of PD-MCI patients. The results of the present study also showed that the reaction time of the PD-MCI group was significantly longer than that of the HC group in the Transposition condition. This result suggests that the D2/3 receptor agonist may have a negative effect on the cognitive function of PD-MCI patients.

**Table 2**

Model	$B_1$	$t$	$(BF_{10})$	Atte		$F$	$p$	$I$	$f$
				$t$	$t$				
Atte	3.34	193.54	0.25	45.69	9.95	$10^3$	6.10	$10^5$	
Atte + G <sub>1</sub>	1.77	0.21	3.58	0.13	0.65		0.23		
Atte + G <sub>1</sub> + Atte + G <sub>1</sub>	6.22	43.91	0.92	6.01	8.11	$10^3$	1.78	$10^5$	
A	1.97 $\times 10^3$	22.90	27.33	1.50	1.37	$10^5$	2.44	$10^4$	
Atte + A	0.29	0.39	0.41	0.22	0.25		0.25		
G <sub>1</sub> + A	1.00	79.91	0.11	10.53	2.68	$10^3$	1.65	$10^5$	
Atte + G <sub>1</sub> + A	0.38	0.06	0.90	0.03	0.13		0.05		
Atte + G <sub>1</sub> + A + Atte + G <sub>1</sub>	1.34	13.73	0.24	1.57	1.71	$10^3$	3.72	$10^4$	
Atte + G <sub>1</sub> + A + Atte + G <sub>1</sub>	399.36	7.62	6.88	0.41	2.87	$10^4$	4.96	$10^3$	

treatment (24). In the current study, we found that patients with D2/3 RBD were more likely than those with D1 RBD to have PD at first presentation, although the difference was not statistically significant. Our findings are in line with those of Lees et al. [21] who reported that 22% of patients with Lewy bodies and progressive nonfluent aphasia had RBD at first presentation. Interestingly, we found that patients with Lewy bodies and RBD were significantly more likely than those without Lewy bodies to have a history of stroke and/or hypertension. This finding suggests that Lewy bodies and RBD may share common pathophysiological mechanisms. For example, Lewy bodies have been associated with Lewy bodies dementia and Lewy body RBD [22]. At first presentation, Lewy bodies were found in 53% of our patients with Lewy bodies and RBD, while Lewy bodies were found in 12% of patients without Lewy bodies. Lewy bodies have also been associated with stroke [23] and hypertension [24]. Hence, Lewy bodies, stroke, and hypertension may play a role in the development of Lewy body RBD.

Lees et al. [21] also found that 23% of their patients with Lewy bodies and progressive nonfluent aphasia had Lewy bodies at first presentation. D2/3 RBD was found in 21% of their patients. Our results are similar to those of Lees et al. [21] in that Lewy bodies were found in 23% of patients with Lewy bodies and RBD and 13% of patients without Lewy bodies. However, the frequency of Lewy bodies in our D1 RBD group (12%) was higher than in the D2/3 RBD group (10%). We found a similar frequency of Lewy bodies in our D2 RBD group (27%) and D2/3 RBD group (28%). In contrast, Lees et al. [21] found a significantly higher frequency of Lewy bodies in the D2 RBD group (42%) than in the D2/3 RBD group (21%). It is not clear why there is such a discrepancy between our findings and those of Lees et al. [21]. One possible explanation is that the Lewy bodies in the Lewy bodies and RBD group of Lees et al. [21] were not all Lewy bodies.

Our results are consistent with those of the Mayo Clinic

## 5. Conclusion

Our results showed that Lewy bodies and Lewy bodies dementia were frequently found in patients with Lewy bodies and RBD, especially those with Lewy bodies dementia. There was a significant association between Lewy bodies dementia and Lewy bodies and Lewy bodies dementia. Lewy bodies dementia was associated with Lewy bodies and Lewy bodies dementia. Lewy bodies dementia was associated with Lewy bodies dementia. Lewy bodies dementia was associated with Lewy bodies dementia. Lewy bodies dementia was associated with Lewy bodies dementia.

## 6. Authors' roles

S.M. and M.Z. contributed equally to this work. S.M. performed the analysis and interpretation of the data and wrote the manuscript. M.Z. helped to design the study. All authors were involved in the critical revision of the manuscript for important intellectual content and approved the final version to be published.

## Funding sources

The authors received no financial support for the research and/or authorship of this article.

## Financial disclosure

The authors declare that they have no conflicts of interest or financial disclosures.

## Acknowledgments

This study was supported by grants from the National Natural Science Foundation of China (31771216 to S.M.); the National Key Research and Development Program of China (2017YFC1341104); and the Chinese Academy of Medical Sciences Innovation Project (FBT134C1 to F.M.).

## References

1. J. Steele, M. M. Fahn, B. Macdowell, K. Kurlan, C. Gilman, S. D. Adler, A. Tarsy, J. F. M. Joseph, I. Berger, R. J. Boeve, N. S. Gitter, *J. Neurology Neurosurg Psychiatry* 80 (8) (2012) 1794–1800.
2. M. A. Kahrilas, I. Bejjani, J. H. Gordon, J. F. M. Joseph, M. H. Strand, L. A. Lang, *Neurology* 78 (23) (2012) 197–104.
3. D. N. Langford, G. M. Steele, J. Bannerman, J. Kotilinek, G. Ashe, J. Lieberburg, C. Carlson, *J. Neurology Neurosurg Psychiatry* 60 (4) (1991) 444–458.
4. A. M. Arnulf, M. J. Cole, N. L. Lin, B. A. Winnick, C. D. Mors, N. R. Gersbach, K. L. Josephson, *Neurology* 42 (1992) 1727–1751.
5. J. G. McKeith, J. J. DeMattos, B. J. Stern, J. L. Emerson, A. H. Brown, C. M. Whitmer, J. M. Trojanowski, J. N. Trojanowski, *Neurology* 51 (6) (1998) 757–766.
6. J. Ma, S. Meng, H. Zhou, X. Wang, C. Zeng, Y. Li, *Neurology* 91 (13) (2018) 0197489.

- 7 K.H. Kim, J.G. Hwang, H.L. Chang, K. Kim, *Neurology* 64 (3–4) (2005).
- 8 J.I. Choi, G.D. Bae, H. Cho, A. Chot, *J. Korean Neurol. Soc.* 41 (2) (2000) 101–175.
- 9 M. Meissner, A. Lohmann, F. Strobl, E. Rennert, *Cephalg. Headache* 154 (2016) 69–80.
- 10 A.M. Danner, M.J. Kao, L.A. Flitman, I.N. Hwang, F. Sano, *Migraine* 13 (3–4) (2005) 267–273.
- 11 M.M. Bhatt, J. Lai, E. Gersh, C.B. Hwang, J. Hwang, M. Lee, J.C. Hwang, A. Lohmann, F. Strobl, E. Rennert, A. Chot, *Cephalg. Headache* 12 (5) (2009) 671–678.
- 12 M.J. Hwang, G.J. Hwang, A.D. Bae, M. Meissner, A. Lohmann, F. Strobl, E. Rennert, *Cephalg. Headache* 140 (2) (2014) 339–373.
- 13 C.M. Deale, L.C. Miller, A. Deale, J. Lai, F. Bae, E. Bae, C. Hwang, M. Meissner, D. Danner, *Headache* 49 (2009) 207 (1) (2009) 35–45.
- 14 C.L. Lee, J. Lai, J. Lai, C. Hwang, G. Lee, C.E. Chung, *Headache* 50 (2010) 2649–2653.
- 15 I. Litt, J.G. Greenberg, A.I. Ziv, B.A. Hoffman, D. Goldstein, C. Gitter, B. Minkin, C.H. Auer, K. Mihaylova, C.H. Hwang, G. Danner, D.A. Lohmann, J.K. Strobl, M.C. Rennert, D.J. Bae, A. Bae, M.E. Lohmann, D. Danner, *Headache* 52 (2012) 349–356.
- 16 J.C. Danner, A. Lohmann, M. Meissner, C. Hwang, L.L. Chang, C. Gitter, G. Lee, C. Chung, M. Kim, J.K. Strobl, K. Mihaylova, J. Lai, J.A. Lee, J. Hwang, M.C.A. Lohmann, *Headache* 50 (19) (2010) 1717–1725.
- 17 K. Kim, C. Hwang, A. Lohmann, M. Meissner, D. Danner, C. Chung, A. Lohmann, D. Danner, C. Hwang, *Headache* 42 (6) (2002) 547–565.
- 18 C. Flitman, L. Chang, M. Meissner, A. Lohmann, J.M. Lohmann, *Headache* 45 (1) (2004) 115–135.
- 19 N. Bhatt, G.J. Hwang, M. Meissner, A. Lohmann, F. Strobl, E. Rennert, *Headache* 39 (3) (1999) 551–581.
- 20 C. Flitman, L. Chang, A. Lohmann, J.M. Lohmann, *Headache* 42 (9) (2002) 59–79.
- 21 M. Meissner, D. Danner, A. Lohmann, F. Strobl, E. Rennert, *Headache* 38 (4) (1998) 761–781.
- 22 K. Lee, L. Chang, C. Flitman, A. Lohmann, J.M. Lohmann, F. Strobl, E. Rennert, *Headache* 39 (E-Suppl.) (1999) 112–131.
- 23 D. Danner, J.K. Strobl, *Headache* 48 (2008) 739–749.
- 24 M. Deale, B. Lai, J. Lai, C. Hwang, G. Lee, C. Chung, A. Lohmann, F. Strobl, E. Rennert, *Headache* 55 (6) (2015) 115–142.
- 25 J.A. Greenberg, H.J. Basmajian, M. Deale, N. Jeville, C. Hwang, D. Danner, *Headache* 32 (1992) 1701–1725.
- 26 C. Flitman, N. Bhatt, A. Noh, G. Meissner, M. Hwang, D. Danner, *Headache* 50 (2010) 728–738.
- 27 D. Danner, K. J. Strobl, K. K. Lee, C. Lee, K. N. Kim, K. F. Kim, I. A. Lee, K. E. Kim, A. Chung, *Headache* 53 (2013) 317–318.
- 28 K. Kim, J. Lai, A. Lohmann, M. Meissner, D. Danner, C. Hwang, *Headache* 43 (2) (2003) 273–284.
- 29 C. Flitman, D. Danner, A. Lohmann, K. J. Strobl, I. Heffner, G. Hwang, C. Lee, L. Chang, *Headache* 52 (2012) 125.
- 30 C.M. Eich, C. Flitman, M. Meissner, H.E. Hwang, I. Heffner, G. Hwang, C. Lee, L. Chang, *Headache* 52 (2012) 376–383.