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Long-Term Changes in the Personality and Psychopathological Profile of Opiate Addicts after Nucleus Accumbens Ablative Surgery Are Associated with Treatment Outcome

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Key Words
Stereotactic neurosurgery · Nucleus accumbens · Opiate addiction · Personality · Psychopathology

Abstract
Objective: To investigate the long-term outcome and changes of the personality and psychopathological profile of opiate addicts after bilateral stereotactic nucleus accumbens (NAc) ablative surgery. ***Methods:*** 60 patients were followed up for 5 years and abstinent status and adverse events were evaluated. NAc lesion volumes and locations were obtained by postoperative MRI scans. The Chinese version of the Eysenck Personality Questionnaire (EPQ-RSC), the Symptom Checklist-90-Revised (SCL-90-R), the Beck Depression Inventory (BDI), the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the World Health Organization's Quality of Life Questionnaire – Brief Version (WHOQOL-BREF) were administered to the patients before and 5 years after the stereotactic surgery. ***Results:*** The total abstinence rate of all patients in their 5th postoperative year was 47.4%. The abstinent patients had a significantly larger lesion volume than the relapsed ones, but a larger lesion volume also increased the risk of adverse events. 5 years after surgery, the abstinent patients showed significant decreases on the Psychoticism (EPQ-P) and Neuroticism (EPQ-N) scores by EPQ-RSC, a significant decline on the Global Severity Index and the subscores in all 10 dimensions by SCL-90-R, significant decreases on the BDI and Y-BOCS scores, and significant improvements on the scores of all domains by WHOQOL-BREF, while for the relapsed patients, only the subscores of obsessive-compulsive by SCL-90-R and the Y-BOCS scores significantly decreased. Postoperative analysis revealed that the abstinent patients had a significantly better score than the relapsed ones by various instruments, and NAc lesion volumes and locations did not correlate with the outcome of any of these instruments. ***Conclusion:*** The bilateral ablation of NAc by stereotactic neurosurgery was a feasible method for alleviating psychological dependence on opiate drugs and preventing a relapse. Long-term follow-up suggested that surgery can improve the personality and psychopathological profile of opiate addicts with a trend towards normal levels, provided persistent abstinence can be maintained; relapse, on the other hand, may ruin this effect.

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Introduction

Characterized by compulsive drug-taking and drug-seeking behaviors despite negative consequences, drug addiction is a chronic relapsing brain disorder which poses a serious threat to people's health [1]. An accumulating body of studies suggested that long-term substance abuse induced abnormal changes of personality and psychopathological profile, and series of personality disorders and psychiatric syndromes were observed in addicts [2–6]. Reports showed that different abnormalities such as impulse control disorders, elevated excitability, anxiety and depression were all prevailing [2, 6]. These problems greatly affected the quality of life of the drug users, and frequently led to a variety of terrible outcomes [7, 8].

To treat these hazardous brain disorders, a lot of methods have been tried out and previous studies indicated that some of them can improve the addicts' personality and psychopathological conditions during abstinence [9–11]. However, few of the current therapies can effectively reduce the relapse rates by long-term observation [12]; if there is a relapse, it is definitely uncertain whether these short-term improvement effects on addicts' personality and neuropsychiatry can be maintained long term postoperatively.

By making a lesion in brain structures which have an intimate relationship with psychological drug dependence, stereotactic surgery showed satisfactory efficacy in reducing the relapse rate in the treatment of addicts [13]. Bilateral stereotactic cingulotomy has previously been shown to be a viable procedure to prevent relapse of drug addicts [14–16]. In a 15-month follow-up, Gao et al. [17] first reported that ablation of the nucleus accumbens (NAc) can also effectively alleviate the opiate drug psychological dependence and lower the relapse rate. However, long-term follow-up for this stereotactic surgery has not been reported.

On the other hand, how the NAc ablating surgery will influence the patients' neuropsychiatric function is still controversial. NAc was crucial for a series of processes other than addiction, such as motivation, learning, locomotion, emotional regulation and decision making [18]. This invasive ablative brain surgery has the potential to cause some negative neuropsychiatric changes. However, the outcome of detoxification brought about by the surgery may theoretically improve the patients' neuropsychiatric profile. Thus, to reveal what kind of influence this therapy had on changes of addicts' personality and psychopathological profile, good or bad, objective evidence supplied by postoperative follow-up was needed. Short-term evaluation has indicated that no significant changes can be observed for personality characteristics and psychiatric syndromes while a trend towards improvement can be detected after NAc ablative surgery [19]. However, long-term study is necessary to arrive at a more convincing conclusion.

The present study involved a 5-year prospective follow-up for the 60 patients who underwent bilateral stereotactic ablation of NAc at our institution to treat opiate dependence, in order to investigate the long-term abstinent outcome of the surgery and its possible determinants. Simultaneously, the patients' personality and psychopathological profiles 5 years postoperatively were examined by implementing various psychometric instruments and their correlated factors were also analyzed.

Methods

Ethical Considerations

The study protocol was examined and approved by the Ethics Committee of the Fourth Military Medical University in China. All the subjects and, where appropriate, their guardians, were informed in detail about the nature and duration of the study, as well as the risks and benefits of the proposed surgery. Each participant gave written informed consent. All subjects were compensated by some reduction in their medical expenses.

Participants

The consecutive 60 patients who underwent bilateral stereotactic ablation of NAc at our institution from 2003 through 2004 to treat opiate dependence were recruited into the present study. The selection criteria were confirmed heroin abuse for at least 3 years (using 0.3–1.0 g/day, by intravenous injection with or without concomitant nasal inhalation), completion of detoxification treatment preoperatively and without somatic withdrawal symptoms, negative morphine urinalysis and naloxone tests, between the ages of 18 and 50, no surgical contraindication and no major ongoing neuropsychiatric diseases. In addition, each patient had agreed not to undergo additional treatment for opiate addiction postoperatively including counseling.

Surgical Procedure

The surgical procedure was similar to that reported previously by Gao et al. [17]. Briefly, all the patients were placed in a Cosman-Robert-Wells (CRW; Radionics Inc., Burlington, Mass., USA) stereotactic frame to perform the spiral CT thin-slice scanning preoperatively. Then a set of anterior-posterior, lateral, and vertical coordinates was produced for each NAc target. Because of the individual variation, the coordinates of the NAc for each patient were different and were within the range as follows: 6–8 mm below the AC-PC line, 16–19 mm prior to the midpoint, and 5–7 mm lateral to the median line. After local anesthesia and incision, the ablation was performed by the RFG-3CF Radiofrequency Lesion Generator (Radionics) with an electrode (1.6 mm in diameter, 4-mm exposed electrode). After stereotactically placing the elec-

trode tip at the target, a low-frequency (2 Hz) followed by a high-frequency (100 Hz) stimulus was applied using an amplitude of 6–8 V. By careful monitoring of the abnormal reactions, a preliminary lesion (45°C, 60 s) was made. If no abnormal reaction was observed, a definitive radiofrequency lesion (80°C, 60 s) was carried out. If an abnormal reaction can be observed, the planned NAc lesion coordinates will be modified (by 0.5 mm in any dimensions randomly at every time of modification), and the radiofrequency lesion was carried out until the abnormal reactions disappeared.

Data Collection

All the patients were followed up for 5 years at 6-month intervals by methods including outpatient interviews, telephone inquiry, and letter correspondence, establishing whether the participants relapsed and whether adverse events (AEs) had appeared. In addition, the patients returned to our institution or the investigators visited the patients' homes (in the case of patients unable to return for personal reasons) postoperatively at 6 months, 1, 3 and 5 years, so that morphine urinalysis and the naloxone test could be conducted to confirm the relapse cases. Regardless of any contradictory data, positive morphine urinalysis was considered a relapse. If morphine urinalysis was negative, the naloxone test was performed; a positive naloxone test, i.e. the induction of acute withdrawal syndrome by administration of intramuscular naloxone, was also considered a relapse, regardless of other data. For each patient, psychometric instruments were conducted preoperatively to obtain the baseline scores by two experienced neuropsychologists. At the 5th year postoperatively during the face-to-face interview, all the instruments were administered again by the same two neuropsychologists who were blinded to patients' surgical details including NAc lesion volume and location parameters.

Instruments

Information on the sociodemographic characteristics was included in the structured questionnaire: age, gender, education, marital status and employment status.

The Eysenck Personality Questionnaire (EPQ) is a general personality trait scale which was developed by H.J. Eysenck in 1975. We applied the Chinese version of the EPQ (EPQ-RSC) [20] to evaluate the patients' personality status. The EPQ-RSC is an 88-item self-report questionnaire. It is a three-factor model of personality in which the three factors are Psychoticism (P), Neuroticism (N) and Extraversion (E) trait. Examples of the personality characteristics that the 3 dimensions measure are as follows: EPQ-P: aggressive, tough-minded, and lacking in empathy; EPQ-E: sociable, lively, and impulsive, and EPQ-N: anxious, emotional, and moody. Additionally, the L scale is a measure of the degree to which one is disposed to give socially expected responses to certain types of questions. A high score on this scale suggests that the respondent is engaging in impression management. A low score suggests indifference to social expectations and is usually interpreted as an indication of weak socialization [21, 22]. Each of these traits is measured by means of 24 true/false questions. The EPQ scales have been widely used for assessing opiate addicts [23], and EPQ-RSC has also been administered to Chinese heroin addicts [24]. The norm of Chinese personality characteristics by EPQ-RSC is as follows [20]: highest grade: P, N, E, L $\geq$61.5; higher grade: 56.7$\leq$ P, N, E, L <61.5; moderate grade: 43.3$\leq$ P, N, E, L <56.7; lower grade: 38.5$\leq$ P, N, E, L <43.3, and lowest grade: P, N, E, L <38.5.

Psychological symptoms were assessed by the Symptom Checklist-90-Revised (SCL-90-R), a 90-item self-report measure of global psychopathological symptoms. The Chinese version of the SCL-90 has a good reliability indicated by a Cronbach's alpha of 0.97 [25]. The instrument measures recent psychological complaints (the past 7 days) on 10 subscales: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism and additional items. Symptoms are rated on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely), with higher scores indicating more severe complaints. Scores were generated for 10 symptom subscales and an overall Global Severity Index (GSI). The SCL-90-R has been widely used for evaluating the mental health of the opiate-dependent patients [26] and also on the Chinese heroin addicts [27]. The normal values for Chinese subjects by SCL-90-R are as follows [25]: somatization: 1.37 $\pm$ 0.48; obsessive-compulsive: 1.62 $\pm$ 0.58; interpersonal sensitivity: 1.65 $\pm$ 0.51; anxiety: 1.39 $\pm$ 0.43; hostility: 1.48 $\pm$ 0.56; phobia anxiety: 1.23 $\pm$ 0.41; paranoid ideation: 1.43 $\pm$ 0.57; psychoticism: 1.29 $\pm$ 0.42, and GSI: 1.44 $\pm$ 0.43.

To measure quality of life, we used the World Health Organization's Quality of Life Questionnaire – Brief Version (WHO-QOL-BREF), which contains 26 items and 4 domains: physical, psychological, social and environmental domains. The 4-domain scores denote an individual's perception of quality of life in each particular domain. The mean score of items within each domain is used to calculate the domain scores according to the manual. Domain scores are scaled in a positive direction, scaled from 0 to 100, with higher scores indicating a higher quality of life. Validity and reliability of WHOQOL-BREF have been verified [28], and previous studies assessing the heroin users' quality of life have applied WHOQOL-BREF [29]. The Chinese version of the instrument used in the present study also showed good validity and reliability [30], and the normal values of the Chinese population by WHOQOL-BREF is as follows [30]: physical domain: 69.38 $\pm$ 10.57, psychological domain: 61.81 $\pm$ 8.41, social domain: 62.06 $\pm$ 9.18, and environmental domain: 60.63 $\pm$ 8.70.

We administered the Chinese version of the Beck Depression Inventory (BDI) to evaluate depression in the patients. This short form of the BDI consists of 13 items, and each item is rated from 0 to 3 according to the degree, which reflects the patient's state during the previous week. The BDI has a high internal consistency, reliability and validity [31]. Zhao administered the Chinese version of BDI to Chinese heroin addicts [32].

Since the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is regarded as the gold standard for assessing the severity of obsessive-compulsive symptoms [33], we administered the Chinese version of Y-BOCS to evaluate the patients. Y-BOCS comprises 10 items rated on a 5-point Likert scale ranging from 0 (no symptoms) to 4 (severe symptoms), with the total score ranging from 0 to 40. Y-BOCS has excellent interrater reliability and moderate to good internal consistency [33].

Volumetric Measurements and Location Evaluations of Lesions

The MRI scans were carried out at the 5th year postoperatively for the patients followed up to examine the postoperative condition of ablated NAc. Volumetric measurements and location evaluations of the lesions were based on the method previously reported by Hariz and Hirabayashi [34]. The maximal lateral and

anterior-posterior diameters of the lesions were measured by postoperative MRI images, their dorsoventral diameters were determined by assessing the distance between the MRI slice where the lesion began to show up and the slice where it could no longer be seen. The volume of the lesion was calculated according to the spheroid volume formula, $4/3\pi \times r \times r' \times r''$ where r, r', and r'' represented the three radii of the lesion. Furthermore, the coordinates of the center of the lesion in relation to the ventricular landmarks, and hence in relation to the original anatomical target point were measured.

Statistical Analysis

Results of the patients were presented as mean values ± standard deviation (SD; except for the enumeration data), and all analyses were conducted by SPSS 17.0. The paired-sample t test was applied to compare between the baseline and postoperative value of instrumentations, and the Wilcoxon-signed rank test was applied when two related samples represented heterogeneity of variance or did not feature the normal distribution. The two-independent-sample t test was applied to compare all the pre- or postoperative measurement data between the abstinent and relapsed or nonabstinent patients, and the correction t test was used if two samples represent heterogeneity of variance or when the two samples did not feature the normal distribution, the Mann-Whitney U test was applied. The comparisons of the lesion volume between the patients with or without AEs were done by the two-independent-sample t test as well, and the comparison of the lesion volume between the patients with different severity of total AEs was conducted by ANOVA analysis. χ^2 test was used for comparison of enumeration data as well as the incident rate of AEs between the abstinent and relapsed and nonabstinent patients. Pearson correlation was applied to analyze the correlation for the patients' NAc lesion volume and location parameters with the instrumentation values. For all comparisons, differences were considered statistically significant at $p < 0.05$.

Results

Of the 60 patients who underwent bilateral stereotactic ablation of NAc, 2 patients were excluded from analysis for seeking further treatment (residential-based treatment), 3 patients refused face-to-face interviews, and 3 patients were lost to follow-up. Therefore, complete data was available for 52 patients. Patients seeking further treatment and refusing interviews were considered treatment failures, and thus, to evaluate the major outcome, i.e. the abstinence, 57 patients were included.

Abstinence Status

Out of the 57 patients who were included to evaluate abstinence, 27 participants never used opiates again up to the 5th year after operation. Among the 25 relapsed cases, 23 were confirmed to have used opiates again by morphine urinalysis and naloxone test, and 2 confessed to have used methamphetamine after surgery. Two patients seeking residential-based treatment (1 and 1.5 years postoperatively) and 3 patients who refused face-to-face interviews were also considered treatment failures. Thus, the total abstinence rate of total patients at their 5th postoperative year was 47.4% (27/57). According to the survival curve of the abstinent patients (fig. 1), most of the relapses reported were within 2 years after surgery, while 2–5 years after the surgery, little relapse occurred.

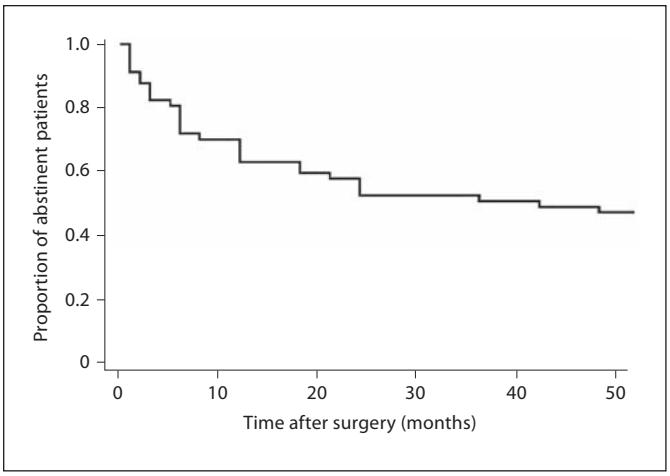


Fig. 1. Proportion of abstinent patients followed up at different time points postoperatively.

Demographic Features of Patients

As shown in table 1, there was no significant difference between the abstinent and nonabstinent patients with regard to most of the preoperative demographic and drug use characteristics, except that there was a significantly higher number of married patients among the abstinent ones compared to the nonabstinent ones ($p = 0.008$). As times goes by, a change in the patients' marital status can be observed: 3 preoperatively unmarried patients got married (2 were still abstinent and 1 got married before relapse); 5 preoperatively married patients got divorced (1 before relapse, 3 after relapse, and 1 was still abstinent), and 4 preoperatively divorced patients remarried (1 still abstinent and 3 remarried before relapse with 1 getting divorced again after relapse). The comparison 5 years after surgery showed that the number of married patients among the abstinent ones was still significantly higher than that for the nonabstinent patients ($p < 0.001$), and there are no significant changes (decrease or increase) of the postoperative marital status compared with baseline for either abstinent ($p = 0.353$) or relapsed patients ($p =$

Table 1. Baseline characteristics of the patients

Characteristics	Total patients recruited (n = 60)	Abstinent patients (n = 27)	Nonabstinent patients (n = 30)	p value[1]
Demographic characteristics				
Age, years	31.35 ± 4.85	30.15 ± 4.56	32.27 ± 5.16	0.108
Sex				
Male	56 (93.3)	25 (92.6)	29 (96.7)	N/A
Female	4 (6.7)	2 (7.4)	1 (3.3)	
Education				
Elementary school	33 (55.0)	12 (44.4)	18 (60.0)	0.502
High school	18 (30.0)	10 (37.0)	8 (26.7)	
Superior or special course	9 (15.0)	5 (18.5)	4 (13.3)	
Marriage				
Unmarried	7 (11.7)	2 (7.4)	5 (16.7)	0.008**
Married	39 (65.0)	23 (85.2)	14 (46.7)	
Divorced	14 (23.3)	2 (7.4)	11 (36.7)	
Employed	29 (48.3)	11 (40.7)	15 (50.0)	0.483
Drug use				
Drug type				
Heroin	51 (85.0)	23 (85.2)	25 (83.3)	0.206
Nonheroin opiates	9 (15.0)	4 (14.8)	5 (16.7)	
History, months	109.18 ± 41.40	101.63 ± 44.12	114.23 ± 38.77	0.256
Dosage, g/day	1.70 ± 1.29	1.72 ± 1.55	1.66 ± 1.09	0.867
Administration methods				
Sniffing only	28 (46.7)	13 (48.1)	15 (50.0)	0.889
Injection or combined others	32 (53.3)	14 (51.9)	15 (50.0)	

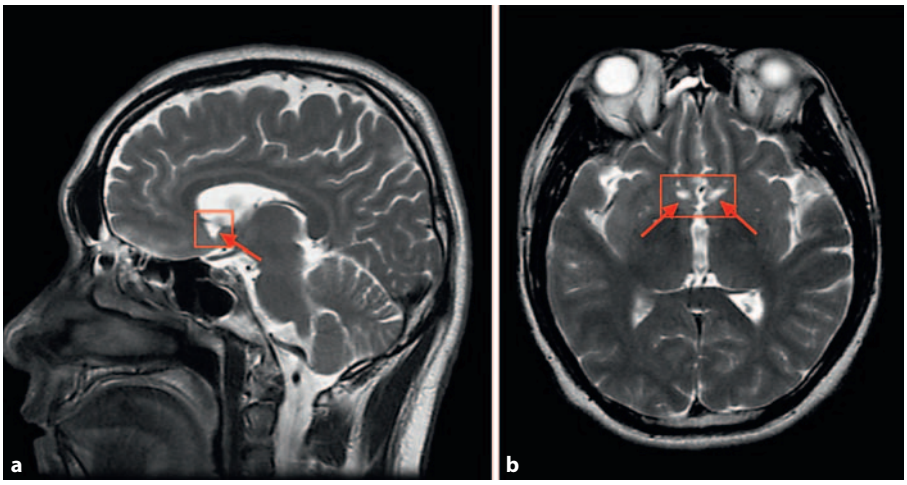
Data are presented as mean ± SD or number of patients with the percentage in parentheses. N/A = Not available.
[1] Abstinent versus nonabstinent patients. ** $p < 0.01$.

0.927). Additionally, though not statistically significant, there were also some changes in the patients' employment status within the 5 years: of the patients who stayed abstinent after surgery, the number of those in employment increased to 15 (from 11 at the baseline) at 5 years postoperatively (6 found new jobs after surgery, of whom 2 lost their jobs again), while among the nonabstinent patients, the number of those in employment increased to 17 (from 15 at the baseline) when interviewed (8 were employed before relapse, of whom 6 lost their jobs again after relapse). At 5 years postoperatively, statistical analysis showed there is still no significant difference between the abstinent and nonabstinent patients as for the employment status, with the employment ratio of 55.6 versus 56.7% (p = 0.572).

Lesion Volume and Location versus Abstinent Status

The surgical targets were all examined by MRI scanning at the 5th year postoperatively. Among the 52 patients completing the follow-up, 3 with metal components planted in their body (by other surgery after the NAc ablating neurosurgery) and 1 unable to tolerate the long scanning time (needed for NAc lesion volume and location analysis) were excluded. In addition, 1 patient seeking further treatment also arrived at hospital to undergo the scan; thus the MRI were obtained for 49 patients in total. As seen in figure 2, bilateral NAc were uniformly hyperintense on T2-weighted images, with a clear boundary, fitting in with the long-term pathological changes, i.e. liquefactive necrosis of the ablated focus with organization of the surrounding structures.

The lesion volume between the right and left NAc for all patients showed no significant difference (p = 0.986), with a mean volume of 202.80 ± 44.40 versus 202.79 ± 43.62 mm^3. As seen in table 2, on both the left and right side, the lesion volume of NAc for abstinent patients turned out to be significantly larger than that for the nonabstinent ones, with a mean volume of 220.01 ± 41.00 versus 184.87 ± 41.25 mm^3 on the right side (p = 0.004) and 220.04 ± 40.61 versus 184.82 ± 39.87 mm^3 on the left side (p = 0.004).



Color version available online

Fig. 2. MRI sagittal (**a**) and horizontal (**b**) section demonstrates bilateral NAc lesions by T2-weighted images in 1 subject. Arrows show the target zones in the NAc.

With regard to the location of the lesion focus, which were measured by the coordinate of the center of the lesion in relation to the original anatomical target point, the comparisons showed that there was no significant difference across the bilateral side of the brain in all 3 dimensions (data not shown). As seen in table 2, in all 3 dimensions, i.e. anterior-posterior, lateral and vertical dimensions, the relative coordinates of NAc lesions between the abstinent and nonabstinent patients revealed no significant difference on either the right or left side. The absolute values of the relative coordinates of NAc lesions, which illustrate the deviation of the surgical targeting, were also compared between the abstinent and nonabstinent patients, and the significant difference can be detected in the vertical dimension for bilateral sides ($p < 0.001$ for the right side and $p = 0.010$ for the left side).

Adverse Events

Information about AEs was obtained by the patients' self-reported feelings and covered 57 patients (3 patients lost to follow-up were excluded). Epilepsy and infection occurred in 1 and 5 patients, respectively, and all healed within 3 months postoperatively. A total of 39 persistent AEs were reported in 29 (50.9%) patients. Among these persistent AEs, memory deficits, weakened motivation and dysosphresia occurred most frequently and were encountered in 12 (21.1%), 10 (17.5%) and 11 (19.3%) patients, respectively. Memory deficits manifested as a weaker memory for new events; weakened motivation manifested as attenuation of motivational activities responsive to surrounding stimulus and a reduction of purposeful behavior, and dysosphresia displayed a reduction of olfactory discrimination. Additionally, 2 patients reported hyposexuality. Although over half of the patients (30/57 = 52.6%) reported a change in temperament, most changes were mildness-oriented (26 patients), while only 4 cases reported obvious impulsion-oriented temperament changes as AEs. Most of these persistent AEs started 2 weeks after surgery and gradually disappeared in the following 2 postoperative years, except for 2 patients with weakened motivation of 3 and 4.5 years' duration, and another patient with hyposexuality up to now, but all these patients reported that their AEs were tolerable.

Analysis of the lesion volume was done for the 49 patients who had an MRI scan done postoperatively, and the results showed that the AEs patients had significantly larger lesion volumes than the non-AE patients, with a mean volume of 229.10 ± 42.21 versus 175.40 ± 26.81 mm^3 on the right side ($p < 0.001$) and 229.15 ± 41.34 versus 175.33 ± 25.40 mm^3 on the left side ($p < 0.001$). As seen in figure 3a, the lesion volume also showed a significant difference between the patients with more severe AEs (multiple AEs reported for 1 patient or with at least one AE lasting more than 2 years), slight AEs (with only one AE lasting less than 2 years) and those without AEs ($p < 0.001$). Figure 3b–d showed the relationship between lesion volume and the occurrence of three types of the most frequent AEs, respectively: (1) patients with memory deficits have a significantly larger lesion volume than those without, with a mean volume of 256.25 ± 36.25 versus 189.09 ± 35.13 mm^3 on the right side ($p < 0.001$) and 255.93 ± 35.80 versus 189.16 ± 34.14 mm^3 on the left side ($p < 0.001$); (2) patients with weakened motivation have a significantly larger lesion volume than those

Table 2. Comparison of NAc lesion volume and location between abstinent and nonabstinent patients

	Abstinent (n = 25)	Nonabstinent (n = 24)	p value
Right			
Volume			
Mean ± SD	220.01 ± 41.00	184.87 ± 41.25	0.004**
Range	143.74–291.93	138.85–302.60	
Location			
X			
Mean ± SD	–0.27 ± 0.71	0.03 ± 0.64	0.134
Range	–1.50 to 1.10	–1.30 to 0.90	N/A
ABS	0.52 ± 0.24	0.67 ± 0.45	0.174
Y			
Mean ± SD	–0.26 ± 1.15	0.11 ± 1.03	0.240
Range	–2.10 to 1.30	–1.80 to 2.10	N/A
ABS	0.92 ± 0.72	0.81 ± 0.63	0.567
Z			
Mean ± SD	0.15 ± 0.42	–0.02 ± 1.08	0.482
Range	–0.50 to 1.20	–1.90 to 1.70	N/A
ABS	0.36 ± 0.26	0.93 ± 0.53	<0.001**
Left			
Volume			
Mean ± SD	220.04 ± 40.61	184.82 ± 39.87	0.004**
Range	145.14–290.16	140.64–298.57	
Location			
X			
Mean ± SD	–0.18 ± 0.70	–0.01 ± 0.61	0.386
Range	–1.40 to 1.00	–1.20 to 0.80	N/A
ABS	0.60 ± 0.38	0.52 ± 0.29	0.418
Y			
Mean ± SD	–0.21 ± 1.19	0.14 ± 0.97	0.268
Range	–2.20 to 1.40	–1.60 to 2.00	N/A
ABS	0.95 ± 0.73	0.80 ± 0.54	0.438
Z			
Mean ± SD	0.20 ± 0.52	–0.03 ± 1.01	0.329
Range	–0.60 to 1.00	–1.90 to 1.80	N/A
ABS	0.51 ± 0.19	0.84 ± 0.55	0.010*

X, Y and Z represent the lateral, anterior-posterior and vertical dimension, respectively. ABS = Absolute value; N/A = not available.

* $p < 0.05$, ** $p < 0.01$.

Table 3. The numbers of abstinent and nonabstinent patients with and without AEs

	With AEs	Without AEs	$\chi 2$	p value
Abstinent	15	12	0.449	0.503
Nonabstinent	14	16		

without, with a mean volume of 244.43 ± 48.76 versus 193.43 ± 38.05 mm^3 on the right side ($p = 0.001$) and 243.98 ± 48.57 versus 193.52 ± 37.12 mm^3 on the left side ($p = 0.001$), and (3) patients with dysosphresia and those without have no significant difference in lesion volume, with a mean volume of 218.70 ± 45.34 versus 198.19 ± 43.64 mm^3 on the right side ($p = 0.180$) and 219.75 ± 43.50 versus 197.88 ± 42.97 mm^3 on the left side ($p = 0.145$). In addition, 2 hyposexuality cases represented an obviously larger volume for both the right and left NAc lesion (one patient: 302.60 and 298.57 mm^3 on the right and left side; another patient: 291.93 and 289.26 mm^3 on the right and left side, while the mean values of all patients were 202.80 ± 44.40 and 202.79 ± 43.62 mm^3 on the right and left side).

Analysis detected no significant difference of lesion locations in most dimensions between the AEs patients and non-AEs patients, except that the patients with dysosphresia revealed a significantly deeper lesion location in the vertical dimension than those without, with a mean Z value of –0.35 ± 0.59 versus 0.19 ± 0.83 mm ($p = 0.049$) on the right side and –0.45 ± 0.51 versus 0.24 ± 0.81 mm on the left side ($p = 0.011$). In addition, the MRI of 2 patients who reported an impulsion-oriented temperament change (another 2 patients did not undergo an MRI scan) showed an obviously smaller distance to the midline (X value, one patient: –1.50 and –1.40 mm on the right and left side; another patient: –1.30 and –1.20 mm on the right and left side, while the mean X value of the total is –0.12 ± 0.68 and –0.10 ± 0.65 mm on the right and left side).

The incident rate of AEs in the patients with different abstinent statuses was compared as shown in table 3. Among the patients with AEs 55.6% (15/27) were abstinent, which is a little more than the AE rate in nonabstinent patients (14/30 = 46.7%); the χ^2 test showed that the difference between these two rates was not significant ($\chi^2 = 0.449$, $p = 0.503$). Among the total patients, the long-term abstinent patients who had never experienced AEs account for 21.1% (12/57) of the total. In addition, abstinent and nonabstinent patients with AEs accounted for 26.3% (15/57) and 24.6% (14/57) of total patients respectively, and all of these AEs were reported to be tolerable and nearly all gradually disappeared over the following 2 postoperative years. The nonabstinent patients who had not experienced any AEs amounted to 28.1% (16/57).

Personality Trait Analysis

Preoperatively, the subjects were found to have significantly higher scores on the EPQ-P, EPQ-N, and EPQ-E

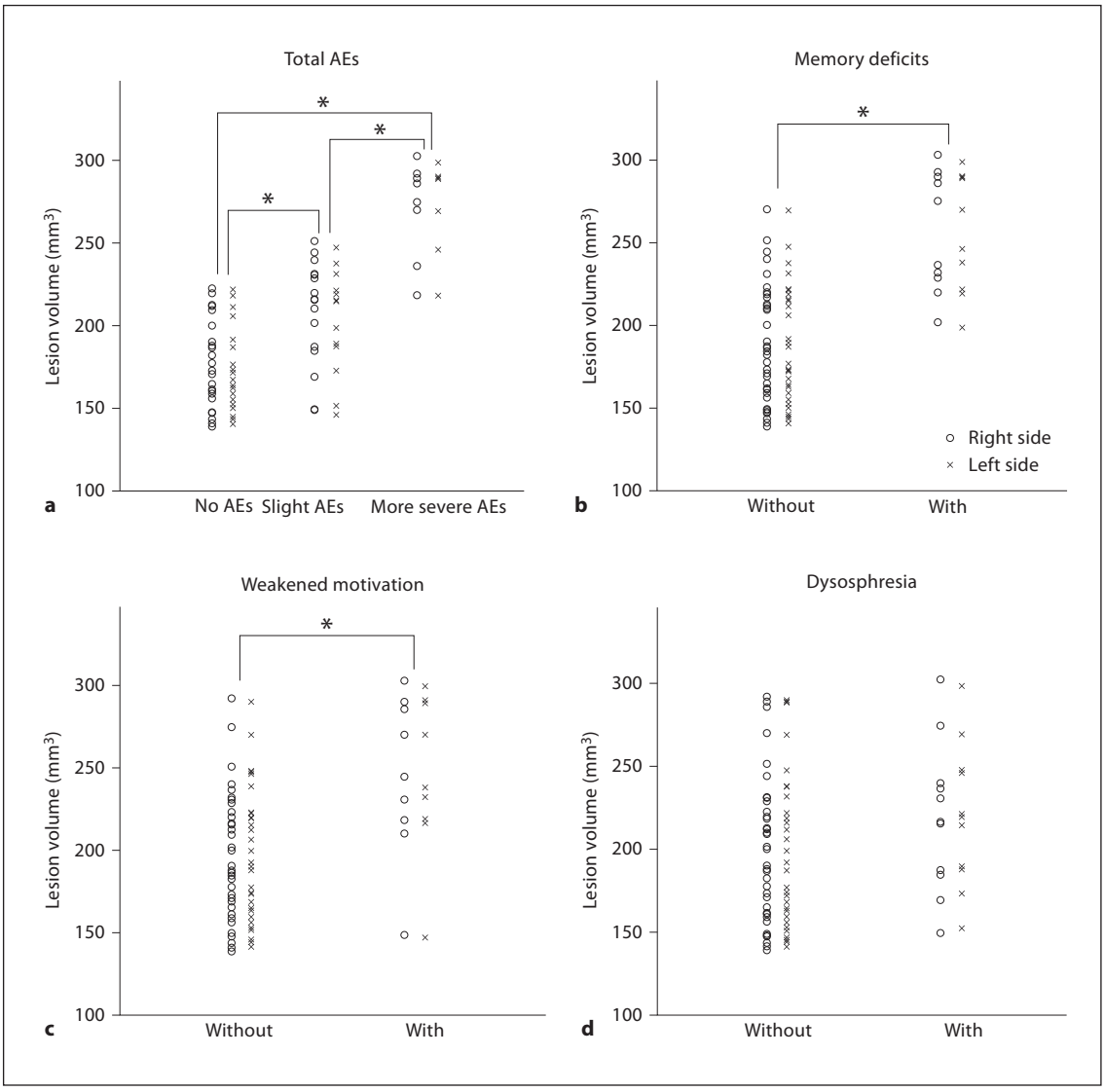


Fig. 3. Different effects of the surgery on the status of patients' AEs in relation to the lesion volume. **a** Analysis of the total AEs. **b–d** Analysis of the memory deficits, weakened motivation, and dysosphresia, respectively. Slight AEs = With only one AE lasting less than 2 years; more severe AEs = multiple AEs reported for 1 patient or at least one AE lasting more than 2 years. * $p < 0.05$.

scale, but a significantly lower score on the Lie (EPQ-L) scale in comparison to the normal population [20]. There are no significant differences between the abstinent and the relapsed patients with regard to the EPQ-RSC scores on all four scales preoperatively (table 4).

Five years after surgery, all patients' scores by EPQ-RSC decreased on EPQ-P, EPQ-N, and EPQ-E scales (table 4) with a trend toward scores of the control model, and only the decreases for EPQ-P and EPQ-N were statistically significant ($p = 0.010$ and 0.007 for EPQ-P and EPQ-N). For the scores on the EPQ-L scale which showed an increased change, no significant change was detected ($p = 0.484$).

Correlation analysis showed that there is no significant correlation between either the lesion volumes or lesion locations and the 5-year postoperative EPQ-RSC scores (data not shown). The comparison between pre- and postoperative EPQ-RSC scores revealed that scores on the EPQ-N and EPQ-P scales decreased significantly at 5 years postoperatively for the abstinent subjects ($p =$

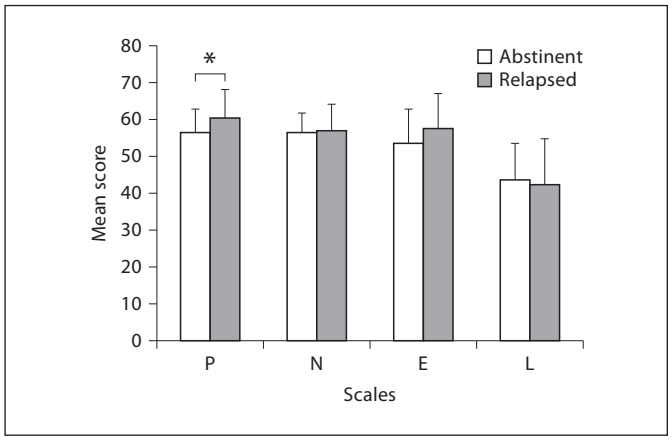


Fig. 4. Comparison of postoperative scores by EPQ-RSC evaluation on EPQ-P, -N, -E and -L scales between the abstinent patients (n = 27) and relapsed patients (n = 25) (mean values, SD). * $p < 0.05$.

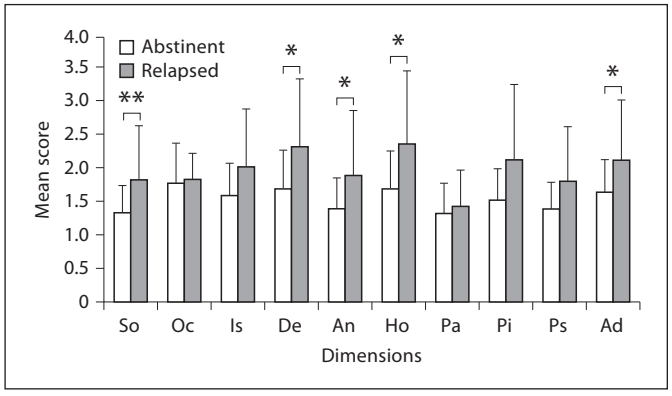


Fig. 5. Comparison of postoperative scores by SCL-90-R evaluation in the 10 dimensions between the abstinent patients (n = 27) and the relapsed patients (n = 25; mean values, SD). * $p < 0.05$, ** $p < 0.01$. So = Somatization; Oc = obsessive-compulsive; Is = interpersonal sensitivity; De = depression; An = anxiety; Ho = hostility; Pa = phobia anxiety; Pi = paranoid ideation; Ps = psychoticism; Ad = additional items.

0.002 and 0.004 for EPQ-P and EPQ-N) but not for the relapsed subjects. As seen in figure 4, the comparison of postoperative scores between the abstinent and the relapsed patients detected a significant difference for scores on the EPQ-P scale (p = 0.039).

Psychiatric Syndrome Analysis

Symptom Checklist-90-Revised

The SCL-90-R conducted preoperatively showed that the GSI and subscores on 10 factors of the total sample were all significantly higher than in the normal population [25]. The comparison of baseline scores between abstinent and relapsed patients showed no significant difference on GSI and all subscales (table 5).

At 5 years postoperatively, the GSI and all subscores significantly decreased compared to the preoperative level except on the factors hostility (p = 0.298) and paranoid ideation (p = 0.085) (table 5). Correlation analysis showed that there is no significant correlation between either the lesion volume or lesion location and the 5-year postoperative SCL-90-R scores on all subscales and GSI (data not shown).

The comparison between the pre- and postoperative scores for the abstinent and relapsed patients, respectively, was analyzed as well (table 5), and the results showed there was a significant decline of GSI and subscores in all 10 dimensions in the abstinent group. In the relapsed group, on the other hand, just the decrease of the subscore obsessive-compulsive (p = 0.043) was significant. As seen in figure 5, the comparison of postoperative scores showed that the abstinent patients scored significantly lower than those who relapsed on the subscales including somatization ($p < 0.001$), depression (p = 0.013), anxiety (p = 0.017), hostility (p = 0.012) and additional items (p = 0.043), but not on other subscales.

Table 4. Results of pre- and postoperative evaluation of EPQ-RSC

Domain	Mean score ± SD		Change		p value
	baseline	5 years	%	type	
Total					
P	60.77 ± 7.10	58.17 ± 7.54	4.28	decrease	0.010*
N	59.13 ± 6.47	56.54 ± 6.30	2.44	decrease	0.007**
E	58.27 ± 7.85	55.29 ± 9.72	5.11	decrease	0.059
L	41.35 ± 10.15	42.88 ± 11.04	3.70	increase	0.484
Relapsed					
P	60.20 ± 7.14	60.40 ± 7.90	0.33	increase	0.858
N	58.40 ± 6.57	57.00 ± 7.22	2.40	decrease	0.250
E	59.80 ± 7.70	57.40 ± 9.70	4.01	decrease	0.143
L	40.80 ± 11.15	42.40 ± 12.09	3.92	increase	0.613
Abstinent					
P	61.30 ± 7.15	56.11 ± 6.70	8.47	decrease	0.002**
N	59.81 ± 6.43	56.11 ± 5.43	6.18	decrease	0.004**
E	56.85 ± 7.86	53.33 ± 9.51	6.19	decrease	0.132
L	41.85 ± 9.32	43.33 ± 10.19	3.64	increase	0.626

P, N, E and L indicate EPQ-P, -E, -N and -L scales.
* $p < 0.05$, ** $p < 0.01$.

Beck Depression Inventory

There was no significant difference in the BDI score between the abstinent and relapsed patients before surgery (data not shown). A comparison between before and after surgery for the total patients revealed that BDI scores decreased significantly (p = 0.033), from 11.87 ± 4.05 before surgery to 10.65 ± 4.61 5 years after surgery. Postoperative correlation analysis between the lesion volume or location and BDI scores showed no significance (data not shown). A comparison between pre- and postoperative BDI scores was made, respectively, for the abstinent and relapsed patients, and the results showed that there was a significant decrease in BDI scores postoperatively for the abstinent patients (from 11.33 ± 3.44 to 8.93 ± 3.20, p = 0.010) but not for the relapsed ones (from 12.44 ± 4.62 to 12.52 ± 5.21, p = 0.951). The postoperative comparison revealed that abstinent patients obtained significantly lower BDI scores than the relapsed ones (p = 0.005), with a mean value of 8.93 ± 3.20 versus 12.52 ± 5.21.

Yale-Brown Obsessive Compulsive Scale

The preoperative comparison detected no significant difference on the Y-BOCS scores between the abstinent and relapsed patients (data not shown). Comparing with the baseline, a significant decrease of Y-BOCS scores can be detected for all three groups of patients, i.e., total (from 10.79 ± 2.99 to 9.29± 2.41, p = 0.001), abstinent (from 10.78 ± 2.64 to 9.19 ± 2.82, p = 0.020) and relapsed ones (from 10.80 ± 3.39 to 9.40 ± 1.94, p = 0.036), at 5 years postoperatively. Analysis showed that there is a significant negative correlation between the postoperative Y-BOCS scores and NAc lesion volume (r = –0.347, p = 0.012 for the right side; r = –0.316, p = 0.022 for the left side), with no correlation between the preoperative Y-BOCS scores and NAc lesion volume. The comparison between the abstinent and relapsed patients revealed no significant difference on the postoperative Y-BOCS scores (9.19 ± 2.82 vs. 9.40 ± 1.94, p = 0.752).

Quality of Life Analysis

Before surgery, the patients had significantly lower scores in all 4 domains of the WHOQOL-BREF in comparison to the normal Chinese population (n = 777) [30]. Preoperatively, the abstinent patients had a significantly higher baseline score in the environmental domain compared with the relapsed ones (38.43 ± 17.13 vs. 27.88 ± 11.66, p = 0.013), while in the other domains no significant difference could be detected. At the 5th postoperative year, the scores in all 4 domains of the WHOQOL-BREF improved significantly both for all patients and for the abstinent ones (table 6). However, the WHOQOL-BREF scores of relapsed patients did not show significant changes in all 4 domains (table 6). As seen in table 7, analysis showed that the scores of nearly all dimensions by 5-year postoperative WHOQOL-BREF scores showed no

Table 5. Results of pre- and postoperative evaluation of SCL-90-R

Dimension	Mean score ± SD		Change		p value
	baseline	5 years	%	type	
Total					
GSI	2.05 ± 0.54	1.77 ± 0.63	13.66	decrease	<0.001**
So	2.02 ± 0.65	1.59 ± 0.68	21.29	decrease	0.001**
Oc	2.12 ± 0.59	1.83 ± 0.50	13.68	decrease	0.002**
Is	2.01 ± 0.61	1.82 ± 0.74	9.45	decrease	0.020*
De	2.26 ± 0.76	2.02 ± 0.87	10.62	decrease	0.023*
An	1.98 ± 0.64	1.65 ± 0.78	16.67	decrease	0.001**
Ho	2.15 ± 0.73	2.04 ± 0.91	5.12	decrease	0.298
Pa	1.78 ± 0.67	1.40 ± 0.49	21.35	decrease	0.005**
Pi	1.97 ± 0.63	1.83 ± 0.90	7.11	decrease	0.085
Ps	1.91 ± 0.63	1.61 ± 0.66	15.71	decrease	0.001**
Ad	2.25 ± 0.63	1.89 ± 0.75	16.00	decrease	0.001**
Relapsed					
GSI	2.09 ± 0.69	2.00 ± 0.74	4.31	decrease	0.170
So	2.03 ± 0.84	1.85 ± 0.81	8.87	decrease	0.411
Oc	2.14 ± 0.70	1.87 ± 0.36	12.62	decrease	0.043*
Is	2.12 ± 0.69	2.05 ± 0.88	3.30	decrease	0.554
De	2.35 ± 0.91	2.36 ± 1.01	0.43	decrease	1.000
An	1.96 ± 0.77	1.93 ± 0.95	1.53	decrease	0.638
Ho	2.13 ± 0.77	2.41 ± 1.08	13.15	increase	0.112
Pa	1.79 ± 0.78	1.45 ± 0.55	18.99	decrease	0.055
Pi	2.03 ± 0.75	2.15 ± 1.12	5.91	increase	0.435
Ps	1.96 ± 0.79	1.83 ± 0.81	6.63	decrease	0.166
Ad	2.26 ± 0.74	2.15 ± 0.89	4.87	decrease	0.404
Abstinent					
GSI	2.02 ± 0.38	1.55 ± 0.40	23.27	decrease	<0.001**
So	2.02 ± 0.42	1.35 ± 0.40	33.17	decrease	0.001**
Oc	2.10 ± 0.48	1.79 ± 0.61	14.76	decrease	0.021*
Is	1.92 ± 0.51	1.60 ± 0.49	16.67	decrease	0.014*
De	2.18 ± 0.60	1.70 ± 0.57	22.02	decrease	0.004**
An	1.99 ± 0.50	1.39 ± 0.46	30.15	decrease	0.001**
Ho	2.16 ± 0.71	1.70 ± 0.55	21.30	decrease	0.004**
Pa	1.77 ± 0.56	1.35 ± 0.44	23.73	decrease	0.003**
Pi	1.93 ± 0.50	1.53 ± 0.49	20.73	decrease	0.001**
Ps	1.87 ± 0.44	1.41 ± 0.39	24.60	decrease	<0.001**
Ad	2.23 ± 0.54	1.65 ± 0.48	26.01	decrease	<0.001**

Subscores on 10 dimensions: So = somatization; Oc = obsessive-compulsive; Is = interpersonal sensitivity; De = depression; An = anxiety; Ho = hostility; Pa = phobia anxiety; Pi = paranoid ideation; Ps = psychoticism; Ad = additional items.

* p < 0.05, ** p < 0.01.

Table 6. Results of pre- and postoperative evaluation of WHOQOL-BREF

Domain	Mean score ± SD		Change		p value
	baseline	5 years	%	type	
Total					
Physical	49.08 ± 16.01	58.10 ± 18.73	18.4	increase	0.005**
Psychological	40.05 ± 15.70	45.03 ± 19.80	12.1	increase	0.046*
Social	41.03 ± 18.88	54.17 ± 19.00	32.0	increase	0.001**
Environmental	33.35 ± 15.55	46.94 ± 21.01	40.7	increase	<0.001**
Relapsed					
Physical	45.98 ± 17.48	48.57 ± 13.32	5.6	increase	0.501
Psychological	35.80 ± 10.61	34.67 ± 11.71	3.2	decrease	0.694
Social	37.67 ± 17.70	44.67 ± 16.29	18.6	increase	0.127
Environmental	27.88 ± 11.66	30.38 ± 12.55	9.0	increase	0.182
Abstinent					
Physical	51.96 ± 14.24	66.93 ± 18.86	28.8	increase	0.002**
Psychological	43.98 ± 18.61	54.63 ± 21.07	24.2	increase	0.016*
Social	44.14 ± 19.72	62.96 ± 17.19	42.6	increase	0.002**
Environmental	38.43 ± 17.13	62.27 ± 14.58	69.2	increase	<0.001**

* $p < 0.05$, ** $p < 0.01$.

Table 7. Correlation analysis between WHOQOL-BREF scores and lesion volumes and locations

	Physical		Psychological		Social		Environmental	
	r	p value	r	p value	r	p value	r	p value
Right								
Volume	0.336	0.018*	0.224	0.122	0.138	0.345	0.228	0.115
Location								
X	–0.117	0.422	0.023	0.875	–0.212	0.144	–0.044	0.761
Y	–0.069	0.639	0.126	0.388	–0.037	0.798	–0.018	0.903
Z	0.134	0.358	0.104	0.475	0.180	0.215	0.090	0.540
Left								
Volume	0.345	0.015*	0.231	0.111	0.135	0.356	0.232	0.109
Location								
X	–0.069	0.637	0.081	0.579	–0.094	0.522	0.049	0.738
Y	–0.066	0.651	0.127	0.384	–0.045	0.759	–0.023	0.877
Z	0.159	0.274	0.170	0.242	0.188	0.196	0.150	0.303

* $p < 0.05$.

significant correlation with the lesion volume or location parameters, except that only the physical quality of life score was significantly positively correlated to the lesion volume on the right ($r = 0.336$, $p = 0.018$) and the left side ($r = 0.345$, $p = 0.015$). The comparison of 5-year postoperative scores revealed that abstinent patients obtained a significantly better quality of life in comparison with those who relapsed in all 4 domains, with scores of 66.93 ± 18.86 versus 48.57 ± 13.32 ($p = 0.001$) in the physical domain, 54.63 ± 21.07 versus 34.67 ± 11.71 ($p < 0.001$) in the psychological domain, 62.96 ± 17.19 versus 44.67 ± 16.29 ($p = 0.001$) in the social domain, and 62.27 ± 14.58 versus 30.38 ± 12.55 ($p < 0.001$) in the environmental domain.

Discussion

The present study first reported the long-term outcome of bilateral NAc ablative stereotactic neurosurgery in the treatment of opiate addiction and the postoperative evaluation of addicts' personality and psychopathological profile. The abstinent patients accounted for 47.4% of the total at the 5th postoperative year, suggesting that this novel surgical therapy could prove, after long-term observation, to be a ponderable approach for preventing relapses. The results of 5-year postoperative psychometric instruments showed that the NAc ablative neurosurgery can improve the personality and psychopathological profile of opiate addicts as well as their quality of life, and the change in the patients with sustained abstinence was particularly significant. In relapsed subjects, this improvement was not obvious, indicating that the reuse of opiates may impair the trend towards a normal personality and mental health in the patients brought about by the surgery.

Lots of attempts have been made to treat opiate addiction, and most of the current therapies showed excellent efficacy of detoxification; however, the high relapse rate always meant failure of treatment [12]. With the rapid development of functional neurosurgery, the stereotactic ablation of nucleus which has a close relationship with drug addiction demonstrated satisfactory efficacy in preventing relapse [13]. The surgical targets were mostly the crucial component of the mesocorticolimbic dopamine system, and the NAc was a promising one, because of its pivotal role in this addiction-related system [35–37]. Gao et al. [17] reported that ablation of the NAc significantly decreased the relapse rate (compared with other currently used therapies) 6 months postoperatively, which implied that the partial ablation of NAc can prevent the relapse by rectifying the pathological changes of the addiction-related neurocircuitry induced by the long-term administration of opiates.

The present study involved more patients; the 5-year follow-up showed a nearly 50% abstinent rate, and the MRI scans provide the opportunity to analyze surgical factors which may predict the relapse outcome. A previous study indicted a close correlation between the size of the stereotactic lesion and the symptomatic results of pallidotomy and thalamotomy [34]; our study also suggested that a much larger NAc lesion volume strongly predicts abstinence. In addition, the large deviation of the surgical targeting in the vertical dimension seems to be related to a worse outcome, indicating that the accuracy of NAc targeting is also crucial for a better relapse-preventing effect. It has been established that social and family factors also influence the prevention of relapse [38]. Our study confirmed that the relapsed patients are less frequently married than the abstinent ones, which suggests that better family support and care is an important nonsurgical factor which also predicts a better outcome of surgery.

Though a larger NAc lesion volume predicts abstinence, it will also increase the risks of AEs according to our observation; therefore, the NAc lesion size should not be excessively enlarged only for a better abstinence outcome, and proper control of the NAc lesion volume is essential for the overall outcome of surgery. The AEs observed in the present study testified that NAc was also crucial for other neurobiological functions. Additionally, improving surgical accuracy is also important to decrease the AE rate, e.g. the dysosphresia, which was observed to be related to a deeper lesion location in the vertical dimension, and could be explained by the irritation of the olfactory cortex. Regarding the influence of the AEs, although several AEs had been reported, nearly all disappeared within 2 years after surgery. It is well known that perilesional edema will take time to subside and lesions may well shrink after some months [39, 40]. Accordingly, if proper NAc lesion size and targeting accuracy can be realized, it is very possible that the safety of the bilateral NAc ablative stereotactic neurosurgery can be guaranteed.

Previous reports have shown that most therapies improved the personality and psychopathological profile of addicts after detoxification which ended the effects of the opiate and so provided a better quality of life [9–11]. Considering the possible better efficacy in preventing relapse, the NAc ablative surgery has the potential to ameliorate personality and psychopathological disorders of patients, for which the present study supplied evidence.

It is commonly accepted that the long-term use of several kinds of psychoactive substance is associated with personality disorders [2, 9, 41, 42]. Among the personality characteristics of addicts, P trait acted as the powerful factor, with E and N traits making a significant contribution. In the present study, the preoperative scores of EPQ-RSC also revealed an addictive personality. On whether the surgery will influence the patients' personality profile, He et al. [19] reported that postoperative personality characteristics showed an increase in E, N and P traits in the short term, though the increase in N and E traits was not significant. However, the present study showed that scores decreased significantly in N, P and E traits with a trend toward the scores of the control model in the long term postoperatively; therefore, the changes of EPQ-RSC

scaling seemed to suggest different trends by short- and long-term evaluation. In fact, the long-term evaluation of the personality profile of patients who underwent other detoxification by EPQ test also showed a significant decrease in N and E traits [9]. We may speculate that immediate substantial changes in neurotransmitter, dopamine activity and neural pathway, and the low cortical arousal caused by the ablation of NAc, may be the chief factor for the changes of the personality profile in the short term. Actually, since the present study revealed that long-term changes of patients' personality were associated with a relapse but were not correlated with the NAc lesion volume and location parameters, we can infer that the surgical long-term effect on personality may be mainly the result of the successful abstinence while the lesions in NAc will not be the key factor.

The analysis of subscores on different scales by EPQ-RSC gave clues for establishing the detailed changes of patients' personality postoperatively by long-term observation. The EPQ-N and EPQ-P scale scores decreased significantly for the abstinent subjects, indicating that by preventing relapse, the surgery ablating the NAc can enhance the emotional stability and bring about a change to a mild temperament in the long term. For EPQ-L scales of EPQ-RSC, we could not detect a significant difference between the pre- and postoperative condition, which was the same as the short-term evaluation. A low score in L suggests indifference to social expectations and is usually interpreted as an indicator of weak socialization [21, 22]. Thus, the personality characteristic on L traits may be an irreversible change, and could not be influenced by the NAc ablative surgery.

The prevalence of psychiatric comorbidity for opiate users was described by several kinds of psychometric instruments [3, 5, 6, 43, 44]. In the present study, the results of the SCL-90-R test showed that both the preoperative GSI and the subscores on 10 factors of the patients were all significantly higher than in the control models. The previous short evaluation reported that no statistical differences were observed in postoperative mean scores in the 10 dimensions of the SCL-90-R, though the severity of patients' psychiatric syndromes declined [19]. The present study revealed that the decline of the subscores of the total patients was significant for 8 dimensions, at their 5th postoperative year, and for the abstinent patients the decline was significant for all 10 dimensions. The results suggested that the NAc ablative neurosurgery treating drug addiction has an obvious long-term positive effect on the patients' mental health conditions. However, we can observe that for the relapsed patients, only the decrease of subscores on 'Obsessive compulsion' was significant. Since the analysis also showed that the postoperative SCL-90-R scores did not correlate with the NAc lesion volume and location, the results gave evidence that the long-term change of the patients' psychopathological profile was also associated with the outcome of abstinence or relapse. Namely, if persistent abstinence can be realized postoperatively, the psychopathological profile of patients can improve greatly after the NAc ablative neurosurgery, while these effects may be erased with the occurrence of a relapse.

In addition to the SCL-90-R subscores on 'Obsessive compulsion', the Y-BOCS tests in the present study also showed that the sustained attenuation of the compulsion of patients may not be associated with whether there was a relapse, but may only be attributed to the effects of the NAc ablation, indicating that the influence of the NAc ablation on the compulsive syndrome was irreversible. As we know, in addition to drug addiction, NAc also plays a crucial role in the process of decision making and emotional regulation [45, 46], and NAc has been considered as a promising target for treatment of certain kinds of psychiatric disorders [47–49]. In particular, the nucleus has been widely used as the surgical target for the treatment of obsessive-compulsive disorders, which showed a satisfactory and sustained curative effect [48]. However, though NAc has also been used as the surgical target for the treatment of depression [49], our analysis with BDI tests showed that more negative effects on the patients' emotions as a result of relapse may offset the curative effect of the NAc lesion; thus, in our study no significant decrease of BDI scores can be postoperatively observed in the relapsed patients.

Because of the chronic and relapsing features of drug dependence which may have negative impacts on various domains of life, much more attention has been given to quality of life in the addiction research field [50]. A number of studies have indicated that opiate-dependent individuals before any treatment reported significantly lower scores in most domains of quality of life instruments compared with the general population [51, 52]. WHO-QOL-BREF evaluation in the present study showed that the scores in all 4 domains improved significantly for both the total patients and the abstinent ones at 5 years postoperatively, testifying that surgery will not worsen the patients' general quality of life.

Overall, the present study showed that the ablation of NAc will not impair the patients' neuropsychological conditions as far as the personality and psychopathological profile which are concerned in the long term. Post-

operative MRI scan showed that NAc lesions by our surgery have a mean volume of around 200 mm^3 just accounting for less than one third of the whole NAc MRI volume (mean value of around 700 mm^3) [53]; therefore, to be precise, the ablation of the NAc applied by the present surgery was a kind of partial ablation of NAc. Thus, it can be inferred that, although the ablation of NAc will induce some changes of patients' neuropsychological functions and even some side effects immediately or short term after the surgery, the compensation effect of residual NAc after the partial ablation of the nucleus could ensure the normal functions of the neural networks regulating the neuropsychological conditions. Therefore, by long-term viewing, the ablation of the NAc itself may not have a negative effect on the patients' personality and psychopathological profiles, and may even improve them if abstinence is maintained.

Conclusion

Our study initially indicated that the stereotactic ablation of the nucleus could provide a ponderable therapy that would prevent relapses when treating opiate addiction and, provided the size of the NAc lesion has been accurately assessed and targeted and there is sufficient family support, this approach has led to better outcomes. Long-term evaluation indicates that surgery itself does not negatively affect the patients' personality and psychopathological profiles even though sustained abstinence is still the key factor when assessing overall improvement.

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Disclosure Statement

The authors declare no competing financial interests.

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