

Ketamine이 청각 기억에 미치는 영향 : Mismatch Negativity와 정신분열병의 Glutamate 가설

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ABSTRACT

Effect of Ketamine on the Echoic Memory Process : The Mismatch Negativity and Glutamate Receptor System in Schizophrenia

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Objective : The abnormality of mismatch negativity (MMN) in schizophrenia is thought to be associated with perceptual disturbance and cognitive dysfunction. And the antagonists of the N-methyl-D-aspartate (NMDA) receptors, ketamine, can induce anomalies of psychophysiology and cognitive function as those of schizophrenia. In order to explore the role of NMDA receptors on echoic memory system, MMN under ketamine administration was analyzed. **Methods** : MMNs of Healthy 12 subjects under sub-anesthetic dose (0.65 mg/kg/hr) of ketamine administration in placebo-controlled design were recorded by 128 channel EEG. Brief Psychiatric Rating Scale (BPRS) change was also evaluated. **Results** : BPRS score was significantly increased by ketamine administration ($t = -6.655, p < 0.001$). Ketamine induced significant decrease in MMN amplitudes ($F_z, t = -2.572, p = 0.026$). Neither MMN amplitude under placebo administration nor MMN latencies under ketamine administration and placebo was changed significantly. **Conclusion** : Ketamine induced echoic memory dysfunction in healthy subjects, which is usually found in schizophrenic patients. Consequently, reduced glutamatergic activity in brain could be involved some early processes of the memory dysfunction in schizophrenia. **(Korean J Psychopharmacol 2001;12(4):322-327)**

KEY WORDS : Schizophrenia Information process · NMDA receptor · Mismatch negativity · Echoic memory.

서 론

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phencyclidine(PCP)/N - methyl - D - aspartate(NMDA) 가 glutamate 가 NMDA , NMDA ketamine MMN , Umbricht ketamine MMN Oranje 20) 0.3 mg/kg/hr , ketamine MMN 21) 0.9 mg/kg/hr , ketamine MMN (event-related potential, ERP) P300 mismatch negativity(MMN) mine PCP/NMDA 가 , ketamine MMN PCP/NMDA 가 MMN

대상 및 방법

1. 연구 대상

12 , 가 , ketamine (temporal resolution) 가 , Structured Clinical Interview for DSM- (SCID-) 2. Ketamine 투여 방법

Ketamine

(single-blind method)
ketamine(0.65 mg/kg/hr)
()
(1). ketamine
(Brief Psychiatric Rating Scale, BPRS)²³⁾
(baseline)
0.65 mg/kg/hr ketamine
(subanesthetic dosage)
(24-26)
(100 cc/hr)
BPRS MMN
ketamine
ketamine
0.26
mg/kg ketamine (bolus in -
jection) , ketamine 0.65 rate)
mg/kg/hr
ketamine 가
10
BPRS , MMN epoch
가
, ketamine (age)
) 15 50 msec MMN . MMN
30
, 2 BPRS
가
100 200 msec
MMN . MMN

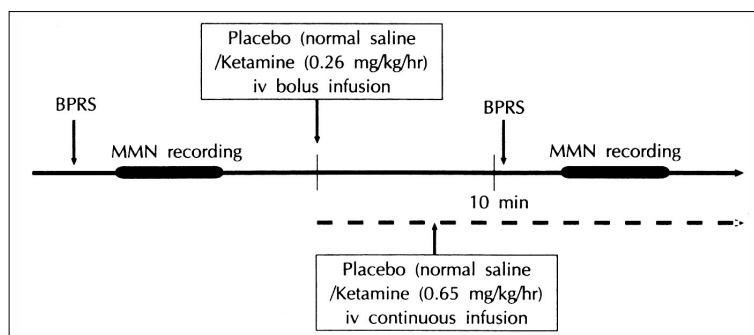


Fig. 1. Summary of the procedure to get EEG under subanesthetic dosage of ketamine or placebo.

2) 청각 Oddball paradigm의 구성
STIM (Neurosoft Inc. USA)
1600
1520 (95%,
1000 Hz, 80 dB) 80 (5%, 1200 Hz,
80 dB) , oddball paradigm

100 msec, - 10 msec,

Table 1. The changes of the Brief Psychotic Rating Scale(BPRS) scores after ketamine and placebo injections

Medication	BPRS Scores(Mean ± S.D.)
Ketamine* Pre-injection	1.00 ± 0.74
Post-injection	6.58 ± 2.64
Placebo Pre-injection	1.16 ± 0.83
Post-injection	0.75 ± 0.75

* : paired t-test, $p < 0.001$

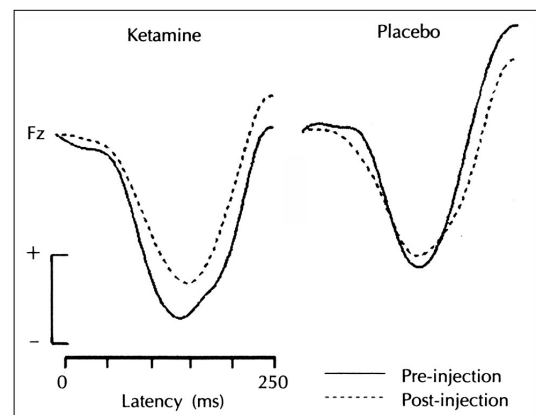


Fig. 2. Effect of ketamine and placebo injection on mismatch negativity(MMN). MMNs were shown mainly in frontal area. Amplitude of MMN under ketamine administration was decreased significantly ($p < 0.05$).

Table 2. The changes of amplitude and latency of mismatch negativity after injections of ketamine or placebo

Medication	Amplitude(Fz, V)	Latency(Fz, msec)
Ketamine Pre-injection	- 5.73 ± 2.34*	147.9 ± 26.8
Post-injection	- 4.22 ± 1.59*	149.3 ± 22.1
Placebo Pre-injection	- 3.66 ± 2.36	139.0 ± 20.9
Post-injection	- 3.91 ± 2.46	141.0 ± 24.6

* : paired t-test, $p = 0.026$

300 msec

3) 결과 분석

MMN 가 Fz MMN
Ketamine
BPRS paired t - test
($p < 0.05$) SPSS
10.0(SPSS Inc, USA)

결 과

12 28 (SD = 2.30)
17.7
Ketamine BPRS
($t = - 6.655$, $p < 0.001$),
가 ($t = 1.449$, $p = 0.175$)(1).
MMN 2 Ketamine
, Fz 가
(Fz, $t = - 2.572$, $p = 0.026$).
가 keta -
mine 가
(2).

고 찰

MMN

12,21,28 - 31)

MMN

28) 12)

32)

Javitt MMN glutamate ketamine

NMDA

(0.9 mg/kg/hr)²⁰⁾

keto(0.3 mg/kg/hr)²¹⁾

BPRS

Krystal BPRS

Mismatch negativity : Ketamine · Mismatch neg - tivity

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