Ibudilast May Reduce Inattention Associated with Methamphetamine Use

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Introduction

Background

- Chronic methamphetamine (MA) use is associated with numerous cognitive difficulties including deficits in learning and memory, executive ability, psychomotor function, and attention and speeded information processing (Scott et al., 2007). These deficits are evident in clinical practice.
- However, some have argued that the deficit profile of MA may be inaccurate, as many studies have not properly controlled for relevant demographic factors (Price et al., 2011). Additionally, researchers have shown that psychomotor and attention and speeded information processing deficits remain after demographic factors are controlled.
- Nevertheless, chronic MA use is associated with cognitive decline, and this may be most evident in psychomotor and attention and speeded information processing performances.

Objective

- The following analyses were conducted to discern any neuropsychological impact of Ibudilast (IB) versus placebo (P) following administration of MA.

Method

Participants

- The current study was approved by the institutional review boards of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center and UCLA and all participants consented to voluntary participation. This study was conducted within an IB safety-interaction trial.
- Participants (n = 11) were fluent in English, dependent on MA only, and free of neurological and non-MA related psychiatric disorders.

Materials & Procedure

- Participants completed assessments at baseline, when they were MA negative and pre-exposure to study medication, and prior to discharge, when they were on IB (100 mg; n = 5) or P (n = 6) 48 hours after exposure to MA (30 mg IV).
- Participants completed a brief neuropsychological assessment that included the Conner's Continuous Performance Test-II (CPT-II), a measure of sustained attention.

Statistical Analyses

- We used a threshold of $p < .05$ for statistical significance.
- Group performances on five indices of the CPT-II were contrasted with Mann-Whitney U tests.
- The groups were similar in education (U = 9.50, p = .30 , r = .31), but differed in age (U = 1.50, p = .01, r = .75), so we utilized demographically corrected T-scores for all group comparisons.

Table 1. *Sample Characteristics*

	IB *Mdn (R)*	P *Mdn (R)*	*U*	*p*	*r*
Age (years)	36.0 (9)	48.5 (13)	1.50	.01	.75
Education (years)	12.0 (5)	13.0 (5)	9.50	.30	.31
Ethnicity (frequency)					
Caucasian	2	5	-	-	-
African American	1	1	-	-	-
Hispanic/Latino/a	1	0	-	-	-
Pacific Islander	1	0	-	-	-

Note. Mdn = median, R = range; IB = Ibudilast group (n = 5); P = Placebo group (n = 6).

Table 2. *Group Differences on the CPT-II*

	IB *Mdn (R)*	P *Mdn (R)*	*U*	*p*	*r*
Omissions	42.1 (13.8)	51.5 (31.2)	7.00	.13	.45
Commissions	39.3 (15.1)	41.3 (26.4)	10.00	.36	.27
Variability	44.4 (20.0)	69.9 (24.9)	0.00	<.01	.83
Detectability	40.7 (33.4)	44.3 (27.0)	10.00	.36	.27
Perseverations	45.8 (1.2)	67.0 (190.4)	2.00	.01	.75

Note. Mdn = median, R = range; IB = Ibudilast group (n = 5); P = Placebo group (n = 6).

Results

- The variability and perseveration indices of the CPT-II were significantly different between the groups.
- Higher median T-scores (Table 2) indicate poorer performance on the CPT-II.
- The IB group showed reduced variability in response times (U = 0.00, p = .006, r = .83) and less perseverative responses (U = 2.00, p = .01, r = .75) in contrast to the P group.
- The effect sizes indicate that differences on variability and perseveration indices were large in magnitude (rs $\geq$ .5 indicate a large effect) .
- It is important to note that these differences did not exist between the groups at baseline (Us = 8.00, ps $\geq$ .190).

Conclusion

- Our results suggest that high dose IB may have a protective effect on sustained attention in the face of early MA abstinence.
- Although it is unclear whether these differences were due to improved or preserved attention, these results suggest that IB may help to improve cognitive function in early MA withdrawal.
- Data provide some support for developing MA treatments that reduce cognitive impairment.

References

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