Relating the Efficacy of Naltrexone in Treating Self-Injurious Behavior to the Motivation Assessment Scale

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One opiate hypothesis suggests that self-injurious behavior (SIB) is related to elevated sensory thresholds. The present study examined the relationship between scores on the Motivation Assessment Scale (MAS) (Durand and Crimmins, 1988), a 16-item scale designed to determine variables that maintain SIB in developmentally delayed individuals, and response to naltrexone (an opiate blocker). High baseline levels of SIB in 20 subjects were significantly correlated with observations that SIB was maintained by need for attention as measured by the MAS. There were no significant correlations between scores on the MAS and change in SIB to the most effective dose of naltrexone (2.0 mg/kg). The present findings did not support the relationship between response to naltrexone and sensory scores on the MAS.

KEY WORDS: endorphins; mental retardation; Motivation Assessment Scale; naltrexone; opiate blocker; opiates; self-injurious behavior.

INTRODUCTION

There is no universally effective treatment for self-injurious behavior (SIB). However, recent studies have indicated that SIB is reduced by treatment with the opiate blockers naloxone and naltrexone (Herman et al., 1987; Campbell et al., 1989; Sandman 1990/1991; Sandman et al., 1990). Moreover, studies of cerebrospinal fluid (Gillberg and Terenius, 1985) and

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plasma (Sandman et al., 1990) have suggested opioid disregulation in patients exhibiting SIB.

Parallel studies have suggested that functional analysis of behavior has been useful in determining variables which maintain SIB (Repp et al., 1990; Vollmer et al., 1992). As an alternative to formal functional analysis, Durand and Crimmins (1988) designed the Motivation Assessment Scale (MAS), a 16-item scale which addresses four categories of reinforcement (sensory consequences, escape, attention, and tangibles) that may contribute to the maintenance of SIB.

The ability to predict response to naltrexone (NTX) could eliminate or shorten costly drug trials and efficiently match subjects to effective treatments. The present study attempted to relate response to naltrexone with MAS scores in order to discover if such predictions could be made using the MAS. Specifically, a prominent opiate hypothesis (Sandman, 1990/1991) postulates that SIB is the result of elevated sensory threshold and an exaggerated attempt to generate sensory stimulation. The fact that opiate blockers induce hyperalgesia (Grevert and Goldstein, 1977) and reduce SIB (Barrett et al., 1989; Herman et al., 1987; Sandman et al., 1990) is consistent with this possibility. One category of the MAS is designed to detect sensory consequences of SIB and may be used to predict response to NTX.

METHODS

Subjects and Procedures

Twenty-four subjects were enrolled in a 10-week protocol examining the efficacy of naltrexone in patients exhibiting SIB. The design involved two weeks of open placebo and eight weeks of double blind cross-over naltrexone administration. Each subject received three weeks of active naltrexone treatment, with a randomized reversal of three doses (0.5, 1.0, and 2.0 mg/kg); blind placebo was administered during the remaining five weeks.

Throughout the 10 weeks, each subject was videotaped six sessions per day (Monday, Tuesday, and Thursday) for 5 min each session; these sessions were equally divided between mornings and afternoons. Subjects were videotaped in residential, school, and recreational settings. Approximately 90 min of videotape per week was collected for each client, and scored for SIB by blind raters using a computerized observational program described by Hetrick et al. (1991). Following the conclusion of the study, research staff who were blind to treatment and responsible for gathering videotaped data over the entire study (and spent approximately 45 hr with
Response to Naltrexone and the MAS

Table I. Subject Characteristics

| Highest Category | Description of SIB | Age and Sex | Level of Retardation | Baseline SIB | Treatment % change |
|------------------|--------------------|-------------|----------------------|--------------|-------------------|
| Attention        | Bite hand          | 23, M       | Moderate             | 1.6% of hr  | -63.22           |
| Tangible         | Bang head, pull hair | 42, F   | Severe               | 3.25/hr      | -64.4            |
| Escape           | Slaps head, bite arm, hit body | 26, M | Severe | 50/hr | 57.29 |
| Escape           | Bang/hit/slap head, hit arm | 41, M | Profound | 33/hr | -81.5 |
| Escape           | Bang/slap head, slap leg, hit arm | 50, F | Profound | 33/hr | -98.2 |
| Escape           | Slap head/face     | 26, M       | Severe               | 429/hr       | -51               |
| Escape           | Hit head           | 31, M       | Severe               | 797/hr       | +105              |
| Sens/Esc        | Bang and punch head | 36, M     | Profound             | 27.6/hr      | -37.9            |
| Sensory          | Slap head, bite arm, scratch self | 14, F | Severe | 4839/hr | -8.3 |
| Sensory          | Bang head/back, hit arm | 38, F | Profound | 27/hr | 72.28 |
| Sensory          | Bang head          | 41, M       | Profound             | 14/hr        | -29.5            |
| Sensory          | Bang head, scratch face/arm | 40, F | Profound | 28.8/hr | -23.2 |
| Sensory          | Bang/hit/slap head, hit arm | 37, M | Profound | 118.5/hr | -26.1 |
| Sensory          | Punch head         | 33, M       | Profound             | 116/hr       | -34.5            |
| Sensory          | Bite wrist         | 32, F       | Profound             | 5.5% of hr   | -100             |
| Sensory          | Hit leg and arm, pull hair | 27, M | Profound | 215/hr | -29.3 |
| Sensory          | Bang/slap head, poke eye | 31, M | Profound | 8.2/hr² | 100 |
| Sensory          | Bang/hit/slap head | 67, M       | Profound             | 3687/hr      | +2.63            |
| Sensory          | Hit shoulder       | 27, M       | Severe               | 43/hr³       | -100             |
| Sensory          | Bite hand/arm      | 37, M       | Profound             | 6.25% of hr  | -12.57           |

*Data from a second pre-treatment baseline week were substituted due to absence of SIB during week immediately preceding first treatment.

Average across multiple baselines.

Each client over the 10 weeks) completed the MAS for 20 of these subjects (see Table I for client characteristics).

For subjects with counted behaviors, such as “bangs head” and “slaps arm,” SIB was calculated as frequency per hour; for timed behaviors, such as “bites hand” or “pulls hair,” SIB was calculated as percentage of time SIB was displayed. Treatment effects were calculated as percent change from baseline (the week preceding treatment) using the following formula:

\[
\% \text{ Change} = \left( \frac{\text{Treatment SIB}}{\text{Baseline SIB}} - 1 \right) \times 100.
\]

The use of “-1” in the formula above allows a reduction in SIB to be shown as a negative figure, and an increase in SIB to be shown as a positive number. It should also be noted that this formula is directionally biased, allowing an infinite range for increase in SIB, while allowing no greater than 100% reduction in SIB.
Motivation Assessment Scale

The MAS is completed by answering questions designed to determine the likelihood of a specific behavior occurring ("never" to "always"). The MAS was completed for each subject by research staff who were also responsible for collecting the videotaped samples, and who had monitored each subject's behavior throughout the study. Scores for questions belonging to each of the four categories (four questions per category) were totaled. The category with the highest mean score is assumed to be responsible for the maintenance of SIB (Durand and Crimmins, 1988). For the purpose of analysis, category means also were ranked from one to four for each subject, with the highest category assigned a rank of one.

RESULTS

Sixty-five percent ($n = 13$) of the subjects had at least 25% reduction in SIB with the 2.0 mg/kg dose, and seven of these subjects (54%) had at least 50% reduction in SIB. For this reason only the 2 mg/kg was used for testing the opiate hypothesis.

Higher MAS attention rank correlated with higher baseline SIB ($r = .693$, $p < .01$). However, further analysis revealed that this effect was due to two subjects whose pre-treatment SIB was greater than three standard deviations above the mean. With these subjects removed from the analysis, the effect was not significant ($r = .07$). There were no significant correlations between scores on the MAS and response to the most effective dose of NTX (2.0 mg/kg).

In a second analysis, subjects were divided into a "high-response" group ($n = 7$) based on (a) at least a 50% reduction of SIB at the 2.0 mg/kg dose, and (b) a reduction in SIB at the 1.0 mg/kg dose. The remaining subjects were labeled "low/non-responders" ($n = 13$). Differences on the MAS between these groups were tested with a stepwise discriminant function analysis. There were no differences between the groups on the MAS. Univariate analysis confirmed that the groups did not differ on any of the four scales of the MAS.

DISCUSSION

Reduction in SIB by naltrexone was not significantly related to the sensory consequences category of the MAS. High baseline levels of SIB were significantly correlated with observations that SIB was maintained by
need for attention as measured by the MAS. However, this relationship was not reliable when outliers were removed.

The present findings in 20 subjects treated with naltrexone did not support the hypothesis that response to naltrexone was related to sensory scores on the MAS. This finding suggests that the MAS may not be sensitive to the sensory aspects of SIB proposed by the opiate hypothesis, or that the MAS may not be a reliable or valid instrument for assessment of the variables which maintain SIB (as suggested by Newton and Sturmey, 1991; Zarcone et al., 1991). It is also possible that naltrexone response was only loosely related to the self-stimulation hypothesis; patients may engage in SIB to stimulate a release of endogenous opiate peptides (Sandman, 1990/1991), rather than sensory stimulation alone. These peptides have been shown to be euphorogenic (Belluzzi and Stein, 1977) and may provide internal reinforcement which maintains SIB. The MAS may be insensitive to this type of internal reward seeking.

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REFERENCES

Barrett, R. P., Feinstein, C., and Hole, W. T. (1989). Effects of naloxone and naltrexone on self-injury: A double-blind, placebo controlled analysis. Am. J. Ment. Retard. 93: 644-651.
Belluzzi, J. D., and Stein, L. (1977). Enkephalin may mediate euphoria and drive-reduction reward. Nature 266: 556-558.
Campbell, M., Anderson, L. T., Small, A. M., Locascio, J. J., Lynch, N. S., and Choroco, M. C. (1989). Naltrexone in autistic children: A double-blind and placebo controlled study. Psychopharmacol. Bull. 26: 1-18.
Durand, V. M., and Crimmins, D. B. (1988). Identifying the variables maintaining self-injurious behavior. J. Aut. Devel. Dis. 18: 99-117.
Gillberg, C., and Terenius, L. G. (1985). Endorphin activity in childhood psychosis. Arch. Gen. Psychiatry 42: 780-783.
Grevert, P., and Goldstein, A. (1977). Effect of naloxone experimentally induced ischemic pain and on mood in human subjects. Proc. Nat. Acad. Sci. 74: 1291-1294.
Herman, B. H., Hammock, M. K., Arthur-Smith, A., Egan, J., Chatoor, I., Werner, A., and Zelnik, N. (1987). Naltrexone decreases self-injurious behavior. Ann. Neurol. 22: 550-552.
Hetrick, W. P., Isenhart, R. C., Taylor, D. V., and Sandman, C. A. (1991). ODAP: A stand-alone program for observational data acquisition. Behav. Res. Meth. Inst. Comp. 23: 66-71.
Newton, J. T., and Sturmey, P. (1991). The Motivation Assessment Scale: Inter-rater reliability and consistency in a British Sample. J. Ment. Def. Res. 34: 472-474.
Repp, A. C., Singh, N. N., Olinger, E., and Olson, D. R. (1990). The use of functional analyses to test causes of self-injurious behavior: Rationale, current status and future directions. J. Ment. Def. Res. 34: 95-105.
Sandman, C. A. (1990/1991). The opiate hypothesis in autism and self-injury. *J. Child Adol. Psychopharmacol.* 1: 237-248.

Sandman, C. A., Barron, J. L., and Colman, H. (1990). An orally administered opiate blocker, naltrexone, attenuates self-injurious behavior. *Am. J. Ment. Retard.* 7: 93-102.

Sandman, C. A., Barron, J. L., Chicz-DeMet, A., and DeMet, E. (1990). Plasma b-endorphin levels in patients with self-injurious behavior and stereotypy. *Am. J. Ment. Retard.* 7: 84-92.

Vollmer, T. R., Iwata, B. A., Smith, R. G., and Rogers, T. A. (1992). Reduction of multiple aberrant behaviors and concurrent development of self-care skills with differential reinforcement. *Res. Devel. Dis.* 13: 288-299.

Zarcone, J. R., Rodgers, T. A., and Iwata, B. A. (1991). Reliability analysis of the motivation assessment scale: A failure to replicate. *Res. Devel. Dis.* 12: 349-360.