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Self-Injurious Behavior and the Efficacy of Naltrexone Treatment: A Quantitative Synthesis

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People with mental retardation, autism, and related developmental disabilities who self-injure are treated with a wide array of behavioral techniques and psychotropic medications. Despite numerous reports documenting short-term and some long-term changes in self-injury associated with the opiate antagonist naltrexone hydrochloride, no quantitative review of its efficacy has been reported. We conducted a quantitative synthesis of the peer-reviewed published literature from 1983 to 2003 documenting the use of naltrexone for the treatment of self-injurious behavior (SIB). Individual-level results were analyzed given subject and study characteristics. A sample of 27 research articles involving 86 subjects with self-injury was reviewed. Eighty percent of subjects were reported to improve relative to baseline (i.e., SIB reduced) during naltrexone administration and 47% of subjects SIB was reduced by 50% or greater. In studies reporting dose levels in milligrams, males were more likely than females to respond. No significant relations were found between treatment outcomes and autism status or form of self-injury. Results are discussed with respect to future efficacy work related to study outcomes and the pharmacological treatment of self-injury.

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Key Words: self-injurious behavior; Naltrexone; efficacy; mental retardation

Self-injurious behavior (SIB) is a clinically daunting and scientifically challenging behavior problem with profound implications for a person's general health and overall quality of life. Self-injury often leads to increased risk for institutionalization or reinstitutionalization, social stigmatization, and decreased learning opportunities. The National Institutes of Health Consensus Conference on Destructive Behavior in Developmental Disabilities generated a report estimating that the costs of care associated with the approximately 160,000 people in the United States with mental retardation and severe destructive behavior exceeded $3 billion (US) in 1989 [National Institutes of Health, 1991]. There is no reason to believe the incidence or prevalence of SIB has changed in the past 15 years [Schroeder et al., 2001]. Because of the numerous deeply disturbing qualities associated with the behavior, there is little disagreement over its significance and the need for treatment. As a consequence, people with mental retardation, autism, or related developmental disabilities who self-injure are treated with a wide array of behavioral techniques and psychotropic medications.

Clinically, SIB is a heterogeneous disorder and like other behaviorally defined disorders it is most reasonable to assume that SIB can be the consequence of a variety of etiologies that, in turn, involve a variety of environment–brain–behavior relationships. Studies of neurobiological factors associated with SIB have identified a role for opioidergic [Sandman, 1988, 1990/1991]; dopaminergic [Breese et al., 1995] and serotonergic [Cook, 1999] systems in the pathophysiology of SIB. These findings are in line with the results of a growing body of controlled psychopharmacological studies demonstrating that SIB can be reduced by agents that have actions in these neurochemical systems [Lewis et al., 1995; Sandman et al., 1999; Schroeder et al., 1995]. One of the main strategies used to test opioid involvement in the regulation of SIB has been to pharmacologically block opioid receptors by the administration of an antagonist. If self-injury is influenced or maintained by the release of endogenous opioids, then an opiate antagonist should attenuate SIB. Support for a general opioid model has come from preclinical studies that have demonstrated altered beta-endorphin levels in persons with SIB [Sandman et al., 1991]. Sandman, Hetrick, Taylor, and Chicz-DeMet [1998] subsequently showed that elevated plasma beta-endorphin levels predict differential response to treatment with opiate antagonist medications. Additional support for the opiate model in self-injury has come from controlled treatment trials of the opiate antagonist medication naltrexone [Buzan et al., 1995; Sandman et al., 1999; Symons et al., 1998].

Naltrexone hydrochlodride [*N*-(cyclopropyl-methyl) noroxymorphine hydrochloride] is an analog of naloxone and is an orally effective narcotic antagonist that has been approved by the Food and Drug Administration for use as an adjunct in treating opiate- and alcohol-dependent individuals. Although dated, in an initial review involving over 2000 cases, O'Brien et al. [1975] found that very few side effects were observed under naltrexone. In heroin addicts, reported side effects have most commonly been gastrointestinal discomfort (e.g., nausea, abdominal

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cramps, and diarrhea) and skin rash, which O'Brien et al. interpreted as part of the opiate withdrawal syndrome rather than a side effect of naltrexone per se. Meyer [1976] administered multiple doses of naltrexone ranging from 50 to 200 mg to individuals with mental retardation with no documented adverse effects. Cardiovascular and autonomic function does not appear to be impaired by opiate antagonist administration [Campbell et al., 1989; Herman et al., 1989]. The most serious potential side effect associated with naltrexone is a temporary increase in liver enzymes, which can indicate liver malfunction and damage. This effect has been reported in people who had no mental retardation and only in doses 2–3 times larger than those typical used in reported SIB treatment research. Four studies that directly monitored liver enzymes in people with developmental disabilities [Barrett et al., 1989; Bernstein et al., 1987; Campbell et al., 1989; Thompson et al., 1994] reported no signs of liver toxicity. Thompson et al. also reported no significant changes in the key vital signs of heart rate, blood pressure, or respiration associated with naltrexone administration. Overall, the relative safety of naltrexone for use in individuals with developmental disabilities has been well established and documented.

Despite many reports suggesting the efficacy of naltrexone for SIB [Casner et al., 1996; Crews et al., 1993], multiple cases of naltrexone nonresponse have been documented in controlled trials [Bodfish et al., 1994]. Even in responders the magnitude and breadth of the clinical effects of naltrexone have been questioned [Barrera et al., 1994]. Reviews of the same literature have tended to come to contradictory conclusions regarding the treatment efficacy of naltrexone for SIB, including no significant effects [McDougle, 1997] and no clinical value [Willemsen-Swinkels et al., 1995] to documented efficacy for up to 50% of individuals with SIB [Lewis et al., 1997; Sandman and Hetrick, 1995] and effective treatment for SIB in individuals with developmental disabilities over long time periods [Casner et al., 1996].

Although a relatively large research base has been synthesized concerning the behavioral treatment of self-injury [Kahng et al., 2002] and specific reviews exist regarding treatment efficacy of a variety of treatment modalities [Lundervold and Bourland, 1988; Scotti et al., 1991; Schlosser and Goetze, 1992], including research practices addressing SIB and destructive behavior [Scotti et al., 1996], no quantitative review specific to naltrexone treatment for SIB exists. Previous reviews of SIB and naltrexone treatment efficacy have been narrative and either selective [McDougle, 1997] or not specific to self-injury and developmental disabilities [Modesto-Lowe and Kirk, 2002]. The purpose of this article is to report a quantitative review of the evidence to date specific to the use of naltrexone in the treatment of SIB in individuals with developmental disabilities (e.g., mental retardation) and related disorders (e.g., autism). Conducting a quantitative review provides the opportunity to test specific hypotheses about naltrexone treatment outcomes in relation to participant characteristics and study design features.

Because of (1) a myriad of reporting inconsistencies across journals, (2) the subsequent difficulty of reliably determining effect sizes, (3) issues specific to integrating and interpreting effect sizes across group and single-subject designs [Allison and Gorman, 1993], and (4) the lack of an accepted effect size statistic from single-subject studies [Allison and Gorman, 1993, 1994; Salzburg et al., 1987; but see Scruggs and Mastropieri, 1998], we based our quantitative synthesis on a secondary data analysis technique. From the reviewed studies, individual level data were extracted, percentage change scores for comparisons from baseline to naltrexone treatment phases were calculated and treatment outcomes assigned to one of three categories as follows: (1) positive (i.e., reduced SIB), (2) negative (i.e., increased SIB), or (3) no effect in either direction. We then tested the significance of each outcome in relation to subject and study design features.

METHOD

Article Search Procedures

The overall literature search for articles was from 1983 following publication of the first report of opiate antagonist treatment for self-injury. The search used the descriptors self-injurious behavior, self-injury, naltrexone, opiate antagonist, treatment, mental retardation, intellectual disability, and cognitive impairment. The databases searched were PsychInfo and MedLine between the years 1983 and 2003. Reference lists from retrieved articles were individually searched as well to identify candidate articles.

Article Selection Criteria

Articles were included for initial review if the following four criteria were met: (1) the article's primary focus was the treatment of self-injurious behavior using the opiate antagonist naltrexone hydrochloride, (2) the article explicitly stated that participants' characteristics included mental retardation, (3) self-injurious behavior per se was measured, and (4) the article was published in a peer-refereed English-language journal. An initial pool of 48 articles was identified given our selection criteria. A second review was conducted applying two additional selection inclusion criteria: (1) the article's results were reported in a quantitative format and (2) the study was a short-term or acute treatment trial (as defined by the author but limited to 3 months or less) or contained such a phase. From this two-step screening process, 27 articles were identified for quantitative review.

General Analysis Procedures

This review was initially conceived as a meta-analysis, anticipating the synthesis of study level results. However, many studies were single-case designs and in many of the group designs, individual level data were reported. Articles were separated based on those containing individual subject results and those containing only group level results. All individual subject results were pooled into a combined data set for secondary data analysis. Group-level studies were reviewed narratively.

Articles resulting from the search procedures were next analyzed for subject characteristics (age, gender, cognitive level, autism status, SIB topography) and design features (naltrexone dose level, blind versus open label). For the purposes of this review, three categories of blinding were defined. Open indicated that raters or observers were aware of the subject's medication status. Single blind indicated that raters or observers were blind but other members of the research group (e.g., investigators) were aware of the subject's medication status. Double blind indicated that no members of the reported research group were aware of the subject's medication status. It should be noted that naltrexone dose level was reported as either milligrams per kilogram or milligrams alone. Because almost no studies reported the weight of their participants, it was not possible to convert studies reporting naltrexone dose in milligrams only to milligrams per kilogram to make them comparable, thus some subsequent analyses were run separately for milligram-only studies.

Results were assigned to one of three outcome categories as follows: pos-

itive (i.e., SIB decreased), negative (i.e., SIB increased), or no effect. Percentage change relative to baseline was the primary metric calculated on a per-comparison basis (naltrexone to baseline at each dose level across all subjects). Data from individuals reported in single-subject or group studies and each dose evaluated were considered as a comparison for the purpose of the analysis. Two separate outcome levels were created for the positive outcome categories. Level 1 outcome assignment was based on a reported or calculated percentage change of 5% to 49% decrease in SIB. Level 2 outcome assignment was based on a more conservative response to treatment definition with positive outcomes tallied if the percentage change in SIB was a 50% or greater reduction [Casner et al., 1996; Piazza et al., 1994].

The following method was used to calculate the reliability of the naltrexone treatment and SIB outcomes categorization process. Two reviewers independently scored a random sample of 30% of subjects from studies included in the quantitative review noting agreements and disagreements on the categories of SIB reduction. Self-injury agreements were scored when both reviewers agreed on the outcome assignment (Level 1, Level 2, increase, no change). Reliability was calculated by dividing agreements by agreements plus disagreements and multiplying by 100. Overall outcome agreement was 93%.

Statistical Analysis Procedures

Descriptive summary-level statistics were calculated on the reported demographic information within studies and on specific study-design features. Dichotomous (gender, autism status) and categorical (level of cognitive impairment, SIB topography, open/blind design) variables were analyzed using Chi-square analysis to test for statistically significant relations with study outcomes and phi to quantify the magnitude of the relation. Continuous variables (age) were analyzed using analysis of variance (ANOVA).

RESULTS

Participant and Overall Study Characteristics

The original literature search identified 48 studies in 20 different journals. After applying the additional selection criteria (see Methods), 27 articles were identified in 12 journals. The 27 reviewed studies included a total of 86 participants (see Table 1). The authors reported gender for 59% of these participants. Of the participants for whom gender was reported (n = 51), 37% were male and 63% were female. Age of persons participating was reported for 56 participants, with a mean of 27 and a range from 7 to 67 years old. All participants had a diagnosis that included mental retardation (91% severe/profound level of impairment, 2% mild/moderate level of impairment). Thirty-five percent of study participants were reported to meet diagnostic criteria for autism. The most common topography of SIB was a combination of forms covering the body (e.g., head banging, self-scratching, and self-kicking) (34% of participants), followed by a combination of forms to the face (e.g., head banging, face slapping, and face picking) (20% of participants). The majority of studies were conducted in residential treatment facilities. The most frequent milligram dose evaluated was 50 mg (43% of milligram comparisons) (see Table 2). The most frequent milligram-per-kilogram dose evaluated was 1.0 (33% of milligram-per-kilogram comparisons) (see Table 2). Nine percent of the studies were open label, 6% single blind, and 85% double blind.

Table 1. Subject Characteristics and Study Design Features

Characteristic	Category	Frequency	%
Gender	Female	32	(37)
	Male	19	(22)
	Not stated/ascertainable	35	(41)
Age	7–27 years	33	(38)
	8–48 years	22	(26)
	49–67 years	1	(1)
	Not stated/ascertainable	30	(35)
Cognitive level	Mild/moderate impairment	2	(2)
	Severe/profound impairment	78	(91)
	Mental retardation (level not stated/ ascertainable)	6	(7)
Autism diagnosis	Yes	30	(35)
	No	55	(64)
	Not stated/ascertainable	1	(1)
SIB topography	Head banging	3	(4)
	Head hitting with fist	4	(5)
	Face slapping	2	(2)
	Multiple forms of injury to face	17	(20)
	Hitting body parts (not head or face)	4	(5)
	Biting	4	(5)
	Multiple forms (head, face, and other)	29	(34)
	Not stated/ascertainable	23	(27)
Study design	Open label	8	(9)
	Single blind	5	(6)
	Double blind	73	(85)

Table 2. SIB Treatment Outcome by Dose[a]

Dose	5%–49% Decrease	50%–100% Decrease	Increase or No Improvement	Total
12.5 mg	1 (100)	—	—	1
25 mg	1 (14)	4 (57)	2 (29)	7
50 mg	12 (34)	9 (24)	14 (38)	37
75 mg	1 (20)	3 (60)	1 (20)	5
100 mg	6 (26)	7 (30)	10 (43)	23
200 mg	—	2 (100)	—	2
0.5 mg/kg	3 (43)	1 (14)	3 (43)	7
1.0 mg/kg	3 (38)	3 (38)	2 (25)	8
1.5 mg/kg	2 (33)	3 (50)	1 (17)	6
2.0 mg/kg	3 (50)	2 (33)	1 (17)	6

Note. Row percentages are in parentheses.
[a]Tabulated data sum to greater than total number of subjects because of subjects exposed to multiple doses.

Analyses Outcomes

Descriptive

Overall, 80% of subjects (n = 69) were reported as having improvement

Table 3. SIB Treatment Outcome for Gender by Dose

	5%–49% Decrease		50%–100% Decrease		Increase or No Improvement		Total	
Dose	Males	Females	Males	Females	Males	Females	Males	Females
12.5 mg	—	1 (100)	—	—	—	—	—	1
25 mg	—	1 (14)	—	4 (57)	—	2 (29)	—	7
50 mg	3 (43)	9 (35)	2 (29)	7 (27)	2 (29)	10 (38)	7	26
75 mg	—	1 (50)	3 (100)	—	—	1 (50)	3	2
100 mg	3 (50)	3 (18)	1 (17)	6 (35)	2 (33)	8 (47)	6	17
200 mg	—	—	2 (100)	—	—	—	2	—
0.5 mg/kg	3 (43)		1 (14)		3 (43)		7	
1.0 mg/kg	3 (38)		3 (38)		2 (25)		8	
1.5 mg/kg	2 (33)		3 (50)		1 (17)		6	
2.0 mg/kg	3 (50)		2 (33)		1 (17)		6	

Note. Row percentages by gender in parentheses.
[a]Tabulated data sum to greater than total number of subjects because of subjects exposed to multiple doses.

during naltrexone treatment relative to baseline (Levels 1 and 2 combined). Forty-seven percent (n = 40) of subjects were reported to improve by 50% or greater during naltrexone treatment relative to baseline (Level 2). For dose level in milligrams only, 50 and 100 mg were associated most frequently with achieving Level 1 outcomes for males and 50 mg was most frequently associated with achieving Level 1 outcomes for females (see Table 3). Seventy-five milligrams was associated most frequently with Level 2 outcomes for males and 50 mg for females (see Table 3). For dose level reported in milligrams per kilogram, 0.5, 1.0, and 2.0 mg/kg were evenly distributed across reported Level 1 outcomes for males, whereas the 1-mg/kg dose level was associated most frequently with Level 2 outcomes for males (see Table 3: Note that no females were included in the milligram-per-kilogram studies selected for review in which gender was ascertainable).

Inferential

Outcomes (Level 1, Level 2) were compared as a function of demographic characteristic (age, gender, cognitive level, autism status, SIB topography) and study design feature (open/blind). Because 91% of subjects were reported to function in the severe to profound range of mental retardation, degree of cognitive impairment was dropped from subsequent inferential analysis.

For Level 1 (L1) outcomes and milligram comparisons, there was a significant effect for gender, $\chi^2(1, 51) = 7.49$, $P < 0.01$, with more males (95%, 18/19) than females (60%, 19/32) showing some improvement (5%–49% reduction) on naltrexone relative to baseline. Phi equaled 0.4 ($P < 0.01$), indicating a moderate magnitude of association. Note, however, that the gender analyses is restricted to the milligrams-only comparison because gender was not reported or ascertainable for most subjects in milligram-per-kilogram comparisons (in some group studies presenting individual data, it was often not possible to determine the gender corresponding to each participant's data, which was typically displayed graphically and assigned a number rather than a pseudonym). No significant effects were found for age, autism status, SIB topography, or the study design feature (open/blind) in relation to L1 outcomes. Seventy-three percent of subjects with and 84% of subjects without autism showed L1 improvement on naltrexone relative to baseline. Small cell sizes precluded reliable inferential analyses SIB topography and open/blind design in relation to L1 outcomes. Cross tabulations showed that the majority of individuals with head banging (100%, n = 3), head hitting fist (100%, n = 4), multiple forms directed to face (65%, n = 17), self-hitting areas other than the head (75%, n = 4), biting (100%, n = 4), and multiple forms of SIB (69%, n = 29) showed improvement during naltrexone treatment relative to baseline. Seventy-five percent of subjects (n = 8) in open and 80% of subjects (n = 73) in blind designs showed improvement on naltrexone relative to baseline. No age differences were found in relation to L1 outcomes.

For Level 2 (L2) outcomes and milligram comparisons, there was a significant effect for gender, $\chi^2(1, 51) = 6.04$, $P < 0.01$, with more males (63%, 12/19) than females (28%, 9/32) showing 50% or greater improvement during naltrexone treatment relative to baseline. Phi equaled 0.34 ($P < 0.01$), indicating a small to moderate magnitude of association. Note, however, as with the L1 outcomes analysis described above, the gender analysis is restricted to milligram comparisons only because gender was unknown for most subjects in the milligram-per-kilogram comparisons (typically because of difficulties in ascertaining the gender of each participant from group studies depicting individual results graphically). No significant effects were found for age, autism status, or SIB topography in relation to L2 outcomes. Fifty-three percent of subjects with and 44% of subjects without autism showed improvement during naltrexone treatment relative to baseline. Small cell sizes precluded reliable inferential analyses SIB topography in relation to L2 outcomes. Cross tabulations showed that the majority of individuals with multiple forms of face-directed SIB (53%, n = 17) improved by greater than 50% during naltrexone administration relative to baseline. Half of individuals with biting (n = 4) and head hitting with fist (n = 4) improved by greater than 50% during naltrexone treatment relative to baseline. No age differences were found in relation to L2 outcomes.

Narrative review of group studies

Four group studies reported aggregate data from which individual subject data were not possible to extract. These studies included a total of 62 participants, 76% of whom were male. The mean age of subjects in these studies was 17, with a range of 2 to 43. Fifty-three percent of these individuals functioned in the severe to profound range of mental retardation and 47% in the mild to moderate range of mental retardation. Results across these group studies varied. Leboyer et al. [1992] reported reduced frequency and intensity of SIB in four children at 0.5 and 2.0 mg/kg of naltrexone but not at 1.0 mg/kg. Similarly, Campbell et al. [1993] found that 1.0 mg/kg of naltrexone did not significantly reduce SIB compared with placebo in 41 children with autism and developmental disabilities. Thompson et al. [1994] found statistically significant decreases relative to baseline levels of SIB in adults at both 50- and 100-mg naltrexone doses. Finally, Taylor et al. [1993] evaluated SIB in adults as it related to a learning task, which was the primary dependent variable. Task performance varied as a function of naltrexone dose, but unspecified decreases in SIB were not associated with

changes in learning measures during the course of the study.

DISCUSSION

The purpose of this quantitative review was to synthesize the treatment efficacy literature specific to studies evaluating the opiate antagonist medication naltrexone hydrochloride for the treatment of self-injury among individuals with mental retardation and related developmental disorders. Overall, 80% of individuals with predominantly severe or profound mental retardation in published reports from which individual-level data could be extracted and pooled for analysis showed reductions in self-injury during short-term treatment with naltrexone. Forty-seven percent of the total pooled sample showed clinically significant reductions of 50% or greater during naltrexone treatment relative to baseline. Outcomes (i.e., changes in SIB as a function of naltrexone treatment) were not reliably related to age, autism status, or SIB topography. For milligram-only comparisons, males were more likely than females to show improvement and clinically significant improvement. Improvement and clinically significant improvement were most likely at almost any of the dose ranges in milligrams for males but tended to be restricted proportionately to higher doses for females.

Several important delimitations and limitations of this review should be noted. The data set reflects what has been reported. The corollary to this is what has not been reported cannot be analyzed. In many of the group studies reporting individual results, we were unable to reliably "map" demographic variables (e.g., gender) onto individual outcomes because of reporting practices in which individual subjects were identified numerically but with gender unspecified. More generally, it should be stated again that given a myriad of reporting inconsistencies and differences across studies and the fact that two distinct study methodologies (group design, single subject) were being evaluated, calculating effect sizes and integrating across studies was not a realistic option. We considered conducting separate meta-analyses for group and single-subject studies but this did not seem viable given a relatively small study sample size in each category and corresponding limited power. It appeared that because the majority of group studies provided access to individually based results a valid secondary-data analysis could be conducted based on a pooled data set of individual subject outcomes across studies.

Creating one pooled data set, however, may raise concerns about ignoring within-study dependencies embedded in the studies comprising the data set. This issue is based on observations that group-study outcomes may be influenced by higher-order nesting factors (e.g., classroom) that interact with the independent variable (e.g., classwide reading instruction outcomes). In the present analysis, however, it is unknown whether dependencies of this kind were operative. Unlike conventional group design treatment studies in which all subjects in an assigned group are exposed to the same level or levels of the independent variable at the same time for the same duration (in principle, at least), the majority of individuals in this pooled study sample received naltrexone at different levels, in different sequences, and for different durations. Considering this, each subject functioned at least in part as an independent replication of a test of the drug's effect.

An additional issue specific to quantitative reviews includes the notion of quality control of the studies reviewed. At the outset, we delimited our search to only studies that were quantitative but set no restrictions on the nature of the design or related features. Overall, however, the reported study designs were of relatively high quality. The majority ($>$ 85%) of studies or comparisons relied on some form of direct measurement of self-injury and included baseline and placebo-control conditions embedded in single or double-blind conditions (91%).

In terms of the substantive outcomes reported and summarized above, and based on the studies in which gender could be identified (95% of the milligram comparisons had specific gender information), it appears that males were more likely to be naltrexone responders than females regardless of age or autism status. Why more males than females with developmental disabilities may be responsive to opiate antagonist treatment is not clear, but it (i.e., a gender effect) is consistent with other reported clinical applications of naltrexone [Covey et al., 1999], although here females were more responsive than males when treated for smoking. Similarly, there are reported gender-linked differences in the expression of physical dependence and related opioid-mediated responses (i.e., analgesia) in nonhuman [Cicero et al., 2002] and human study samples [Kest et al., 2000]. To the degree that SIB is an opioid-mediated behavior, opiate antagonist treatment outcome differences by gender would be predicted. Considering the data in this analysis were limited to one subset of naltrexone comparisons, future work should test explicitly for gender differences.

Although there have been reports suggesting that specific SIB topographies (head banging, hand biting) [Herman et al., 1987; Thompson et al., 1994] may be more responsive to treatment with naltrexone than others (body hitting, skin picking), the data reviewed here neither decidedly refute nor support this notion. In many cases, the distinct topography of an individual's SIB was unspecified. Of those that were reported, it appeared that a wide range of topographies were both minimally and clinically responsive during naltrexone treatment, although, on balance, the highest proportion of responsive topographies tended to involve head-directed SIB. But, here again, the numbers tend to be small and therefore should be interpreted with caution.

Although not included in the quantitative review because of differences in the metric that would need to be calculated and its interpretation within the context of acute or short-term trials (i.e., efficacy versus maintenance), it is important to note that positive long-term effects of naltrexone treatment for self-injury of 1 year or greater have been reported [Casner et al., 1996; Crews et al., 1993; Sandman et al., 2000]. Predicting who is most likely to be a long-term responder is complex and emerging evidence indicates that it may depend on an individual's initial response to acute naltrexone treatment, suggesting that there are individual differences in sensitivity to opiate antagonists [Sandman et al., 2000]. Such findings further support that importance of reporting individual subject-level data in medication treatment studies.

Related to reporting individual subject-level data is the possibility that the variance in pharmacological treatment outcomes (i.e., responders/nonresponders) may be related, in part, to behavioral mechanisms and social context effects. In 1977 Carr outlined several possible pathways through which SIB may be reinforced, including extrinsic sources of reinforcement (e.g., through positive reinforcement in the form of attention or negative reinforcement in the form of the withdrawal of demands), or that the behavior itself may produce as a consequence some form of intrinsic reinforcement (e.g., sensory stimulation, pain reduction). Considering this, Iwata et al. [1982] argued for and demonstrated that an important means of selecting a potentially effective treatment would consist of determining in advance the

variables currently maintaining the self-injurious behavior. Since this report, a technology of functional analysis has emerged and become state-of-the-art in the assessment and treatment of self-injurious behavior in people with developmental disabilities. If it is assumed that for some cases of SIB there is a physiological basis underlying maintenance, then applying functional analytic technology to subtype SIB cases would be a powerful tool to reduce the effects of environmental variance in pharmacology treatment studies of self-injury [Iwata et al., 1982; Schaal and Hackenberg, 1994; see Garcia and Smith, 2000 for an example of this application specific to naltrexone treatment].

CONCLUSION

Based on this quantitative review, there are several recommendations to consider for future work designed to investigate the efficacy of naltrexone treatment and psychotropic medication outcomes in general for the treatment of self-injury among individuals with developmental disabilities. First, individual outcomes should be reported whenever possible [see, for example, Bodfish et al., 1994] and, if doing so, information provided at the subject level should be able to be "mapped" to reported outcomes. Second, a common set of measures or, perhaps, variables measured would improve our ability to synthesize the self-injury and pharmacological treatment literature. Third, a common set of measurement procedures would also improve our ability to identify predictor variables for successful treatment outcomes [see, for example, Sandman et al., 1997].

In 1971, Sprague and Werry outlined the basic criteria for scientifically sound drug trials for treating behavior disorders in persons with mental retardation. They reviewed the published drug treatment research to that point in time and found it wanting along the majority of the suggested dimensions, including the use of standardized, valid assessment instruments. Since that time, studies continue to be conducted with an array of pharmaceuticals and numerous reviews continue to be written, but questions remain about our ability to draw firm conclusions regarding the treatment efficacy of psychoactive medications for individuals with mental retardation and related pervasive developmental disorders [Aman, 1993].

A key prerequisite for empirically valid psychopharmacological research is the use of valid and psychometrically sound assessment instruments to measure drug effects [Kalachnik, 1999; Schroeder et al., 1997; Sprague and Werry, 1971]. A number of problems exist, however, in our current state of the art, including unknown or inadequate psychometric properties associated with psychopathology assessment instruments for individuals with mental retardation [Aman, 1991], the inappropriate use of global assessment instruments as outcome measures in drug studies specific to aberrant behavior [Schroeder et al., 1997], and the problems associated with indirect measurement strategies used in psychiatric research [Rutter, 1997]. Schroeder et al. [1997] showed that the majority of instruments used to evaluate drug effects on self-injurious behavior are insensitive to changes in daily rates of target behavior and none have been evaluated for standard psychometric properties (i.e., reliability and validity) related to this application.

In chronic intractable cases of self-injurious behavior, it seems as if assessment and treatment approaches tend to assume a dichotomy between environmental and biological determinants. Among the most pressing needs are studies that clarify which people are responsive to specific medication treatments, which in turn depends on a better understanding of a given drug's mechanism of action in different environmental contexts [Thompson et al., 1991]. Based on this consideration, we suggest the following points to consider for future medication efficacy research in treatment of self-injury: (1) explore the relation between behavioral and biological markers as predictors of response to pharmacological treatment; (2) develop alternative medication evaluation protocols consistent with the nature of specific behavior problems, in specific settings not always amenable to daily direct observation, which are ethically justifiable; (3) develop empirically derived rating scale instruments that (a) consist of relevant dimensions of aberrant behavior and environmental circumstances and (b) are sensitive to behavior change; and (4) refine experimental designs that permit analysis of the interaction between neurochemical and behavioral mechanisms. ■

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