DOI 10.1007/s00702-005-0337-x
J Neural Transm (2006) 113: 425–431

Journal of Neural Transmission
Printed in Austria

Self injurious behavior in autism: clinical aspects and treatment with risperidone

R. Canitano

Division of Child Neuropsychiatry, University General Hospital of Siena, Italy

Received September 19, 2004; accepted May 14, 2005
Published online August 3, 2005;

Summary. Self injurious behavior (SIB) is frequent in autistic spectrum disorders. The aim of this study was to investigate the phenomenology of SIB in a group of children with autistic disorder, and to test whether treatment with risperidone might reduce it. A group of eleven children diagnosed with autistic disorder according to the DSM-IV criteria (mean age 8.7 ± 2.2 ys) and with severe SIB were recruited for an open study of six months of treatment with risperidone. The Yale-Paris Self-Injurious Behavior Scale was used to delineate the clinical characteristics and as an outcome measure. Head-hitting and hand biting were the most frequent forms of self aggression observed. Nine children presented a mild improvement in SIB and 2 did not show any variation. A decrease in Yale-Paris Self Injurious Behavior Scale score (from M 15.1 ± 1.4 to 13.3 ± 1.4) was noted mainly due to the reduction of frequency. Side effects of risperidone were not severe.

Keywords: Self-injury behavior, autism, childhood, risperidone.

Introduction

A wide range of repetitive patterns can be observed in autistic spectrum disorders and they are considered to be core symptoms of the disorder. Self-injurious behavior (SIB) is a peculiar form of repetition and the clinical features are heterogenous and often overlap with other abnormal repetitive behaviors, such as complex tics, compulsions and rituals (Lewis and Bodfish, 1998). All these are included in the third domain of the diagnostic criteria for Autism and Pervasive Developmental Disorders (PDD) in DSM-IV, the other two major pathological domains being social-emotional disturbances and communication impairment (APA, 1994). Young age and severe mental retardation are general risk factors of SIB in addition to autism, which is a risk in itself (Bodfish et al., 2000; Murphy et al., 1999). Research on the underlying mechanisms is based on functional analysis and on the examination of the related neurotransmitter systems. Opioid, dopaminergic and serotoninergic systems are the neurobiological substrates involved in self aggression (Ernst, 2000). A dysfunction of the opiatergic system with abnormality of pain control mechanisms has been proposed. A genetically determined increase in endogenous opioids would cause pain insensitivity and the consequence would be a lack of appropriate reaction to self-injury. Alternatively, the

effect of SIB and stereotypies would be an elevated level of opiods in the blood and, as a result, a self maintaining mechanism would be activated with euphoria and analgesia secondary to high opiate tone. Whatever the underlying mechanisms, objective data are still lacking and therapeutic interventions with opioid antagonists in autism and SIB have not been convincing (Gillberg, 1995; Willensen-Swinkels et al., 1996).

The relevance of the dopaminergic system has been outlined experimentally in animals and in clinical trials in humans. In drug-induced stereotypies and SIB, stimulants dopaminergic agonists cause their onset and maintenance (Buitelaar, 1993). Animal models of self injury are based on depletion of, and later on supersensitivity to, dopamine. Interestingly, and relevant to autism, rhesus monkeys isolated in the first year of life develop markedly abnormal behaviors, including SIB, and later in adulthood showed alteration of dopamine transmission in the basal ganglia. Early social and environmental influences were shown to be very important on the developing system. In clinical studies, dopaminergic antagonists have been useful in decreasing SIB and stereotypies (Gillberg, 2000). Whether this effect is specific or only part of a general improvement in symptoms is still under debate (Pies and Popli, 1995).

Abnormality of the serotoninegic system has been demonstrated in autism and the basic mechanisms and pharmacological effects of serotoninergic agents have been the object of much concern (Chugani et al., 1999). Elevated blood levels of serotonin have been detected in approximately one third of individuals with autism, but it has not yet been determined whether this finding is caused by a derangement of brain serotonin metabolism or if it reflects an increased metabolic rate at a peripheral level (Cook and Leventhal, 1996). Furthermore, a modulatory action of serotonin has been observed on dopamine transmission in the corticostriatal circuits involved in stereotypies and SIB. Serotonin depletion leads to self aggression in animals and exacerbation of stereotypies in autism (Sivam, 1996). Consistent with these findings, serotonin reuptake inhibitors have been useful in treating self injury, repetitive behaviors and mood disorders in autism (King, 2000).

Atypical neuroleptics are mixed antagonists blocking both dopaminergic (D1, D2, D3, D4) and serotoninergic receptors (5HT2A). The high ratio of 5HT2A to D2 receptors that characterize them is likely to be implicated in the therapeutic effect and in the low incidence of extrapyramidal side effects (Meltzer, 1995). Among the atypical neuroleptics, risperidone has been introduced in the treatment of autistic spectrum disorders with the purpose of reducing behavioral disorders such as hyperactivity, stereotypies and self aggression (Buitelaar and Willensen-Swinkels, 2000). Though currently there is still little data available, most studies have reported benefits in symptomatic components, also at a young age (Masi et al., 2001, 2003; Mc Dougle et al., 1997; Nicolson et al., 1998; Perry et al., 1997). A recent large controlled study demonstrated the efficacy of risperidone on target symptoms of autistic spectrum disorders (Research Units in Pediatric Psychopharmacology Autism Network, 2002). Information about safety, efficacy and long term effects are emerging but are still limited (Malone et al., 2002; Zuddas et al., 2000). The aim of this study was to thoroughly analyze the clinical features of SIB in a group of children with autistic disorder and to test whether treatment with risperidone might be effective in reducing it.

Methods

Subjects

The study group was composed of 11 children, 7M and 4F of age M = 8.7 SD ±2.2 under evaluation as inpatients at the Division of Child and Adolescent Neuropsychiatry of the General Hospital of Siena, a tertiary care referral center for pervasive developmental disorders. All subjects received a diagnosis of Autistic disorder according to DSM-IV criteria. Eight children had

severe mental retardation 3 had moderate mental retardation. SIB was the relevant additional clinical feature for children to be recruited in the study. None of the children had associated metabolic or genetic disorders. Patients 7 and 10, both females, suffered from epilepsy, one having an atypical absences of seizures at the time of evaluation and the other free of seizures for the past two years. Both were taking anticonvulsants, case 7 valproic acid 20 mg/kg, case 10 phenitoin 4 mg/kg and valproic acid at a dosage of 15 mg/kg.

Physical and laboratory examination

A general physical and neurological examination was carried out at baseline; weight and blood pressure were measured, laboratory exams included complete blood cell counts, liver and renal function tests, serum aminoacids, electrocardiogram and electoencephalogram. After six months all these laboratory tests and a clinical examination were repeated.

Assessment

The children were evaluated, independently, by two child neuropsychiatrists a careful clinical observation was performed in two sessions and the diagnosis of Autistic disorder was made according to the DSM-IV criteria. A standardized assessment was conducted as follows:

Childhood Autism Rating Scale (CARS) was administered to support the clinical diagnosis and to follow-up the patients undergoing the treatment (Schopler et al., 1980). This is a 15 item scale for measuring autistic behaviors; the cut-off score for autism is 30, while progressively higher values correspond to the increasing severity of the disorder, with mild to moderate autism up to 37 and severe from 37 to 60.

The Yale-Paris Self-Injurious Behavior Scale (YAPA-SIB) was administered to assess SIB. The scale is divided in two parts: the *lifetime pattern* referring to every period in which SIB were present and the *current pattern* which rates the worst period in the past month with three domains of assessment forming three subscales. Subscale A: measures Severity, Frequency and Duration. Severity scores vary from 1 when SIB is absent to 7 when it is at maximum expression with major concern for safety. Frequency scores from 1 when absent to 7 when continuous, and Duration scores from 1 when SIB is absent to 7 when the current observed behavior lasts for more than one year. Subscale B: is list of body parts for indicating topography. Subscale C: Context describes emotional circumstances, concurrent behaviors and different where SIB occurs. In this study only the *current pattern* part of the scale was considered and rated (Tordjman et al., 1999).

Clinical Global Impression (CGI) for global improvement was scored at the end of the study. This is a single item ranging from 7 very much worse to 1 very much improved. The children scoring at least 3 (improved) were considered to be responders. Mental level was measured with Leiter International Performance Scale because the majority of children 9 of 11 had poor language skills.

Study design

An open-label study with risperidone was conducted for a period of six months. The starting dosage for all patients was 0.25 mg titrated at weekly intervals according to clinical response and side effects, with a maximum dosage of 0.05 mg/kg/die. The mean dosage was 0.6 mg, SD $\pm$0.2. Parents were contacted by phone after the children were discharged, usually one week after they had started the treatment, and then again each month for obtaining information on tolerability and clinical effects. The Institutional Review Board of the University General Hospital of Siena approved the protocol. Informed consent was obtained from parents for the administration of risperidone to their children.

Statistical analysis

A descriptive analysis was performed using matched paired t-tests to compare, at baseline and at the end of the study, the scores of the Current YAPA-SIB, subscale A: Severity, Frequency and Duration and those of CARS. Data are presented as mean and SD and the significance level of all analyses was set at 0.5. All tests were two tailed.

Results

All subjects were treated with risperidone as indicated and none of them dropped out due to unwanted effects and/or non-compliance with therapy. CARS scores varied from M 40.1, SD $\pm$4.9 to M 36.1, SD $\pm$4.7 with a $p = 0.0003$. On the basis of the global improvement item of the Clinical Global Impression Scale, 6 children scored 2 (much improved), 3 children scored 3 (minimally improved), and these were considered as responders. Two patients did not show any variation of symptoms and were defined as non-responders.

The current YAPA-SIB subscale (severity, frequency and duration) decreased from a baseline score of 15.1 M, $\pm$1.4 SD, to a score

	Diagnosis	SIB	Mental level	Risperidone
1 M 8.8 ys	Autistic Disorder (AD)	Head-hitting	Severe mental retardation (MR)	1mg (0.05mg/kg)
2 F 9.6 ys	AD	Hand-biting	Severe MR	1mg (0.04mg /kg)
3 M 9.6 ys	AD	Head-hitting	Severe MR	1mg (0.02mg/kg)
4 F 10.5 ys	AD	Hand-biting	Moderate MR	1.5mg (0.03mg/kg)
5 M 12.4 ys	AD	Hand-biting	Moderate MR	1mg (0.02 mg/kg)
6 M 7.2 ys	AD	Head-hitting	Severe MR	1mg (0.03 mg/kg)
7 F 8.6 ys	AD	Nose-hitting	Severe MR	0.50mg (0.025mg/kg)
8 M 6.3	AD	Head-hitting	Severe MR	0.50mg (0.025mg/kg)
9 M 7.0	AD	Hand-biting	Moderate MR	0.50mg (0.02mg/kg)
10 F 5.7	AD	Lips-biting	Severe MR	0.50mg (0.025mg/kg)
11 M 11.6	AD	Hand-biting	Severe MR	1.5mg (0.04 mg/kg)

Fig. 1. Clinical characteristics of patients

of 13.3 M, SD $\pm$1.8, reaching a statistical significance of $p<0.001$; the most important varying factor was frequency, from 6.3 M, SD $\pm$0.5 to 5 M, SD $\pm$0.8, $p<0.001$. Intensity did not change significantly, from 2.1 M, SD $\pm$0.8 to 2.0 M, SD 0.7 and global duration of SIB was unchanged, as shown in Fig. 1 and Table 1.

Table 1. Behavioral ratings. Mean baseline and end of treatment scores

	At baseline ($M \pm SD$)	At the end ($M \pm SD$)	df	t score	p value
CARS	40.1 ± 4.9	36.1 ± 4.7	10	5.2	$p<0.01$
YAPA-SIB Global	15.1 ± 1.4	13.2 ± 1.8	10	4.6	$p<0.01$
Intensity	2.1 ± 0.8	2.0 ± 0.7	10	1.4	$p=0.1$
Frequency	6.3 ± 0.5	5.0 ± 0.8	10	5.5	$p<0.01$

CARS Childhood Autism Rating Scales, *YAPA-SIB* Yale-Paris Self Injurious Behavior Scale

On the Body part subscale, SIB were characterized by head-hitting in 4 and hand-biting in 5, and nose-hitting and lip biting in 2. The clinical features of SIB were of two types, the most frequent was self biting at hands, wrists and lips and signs of lesions were evident on examination, with callosity in the injured region, indicating chronic repeated damage in the same site. Head hitting was the second most common behavior, mainly self slapping without clinical signs but with risk of head injury given the frequency of hits. None of the children used objects damage themselves nor did they attempt more complex self-dangerous behavior. On the Context subscale there were two recurrent emotional circumstances: frustration in 5 patients and anger in 5. In some instances the distinction between the two conditions was not straightforward due to the severe communication impairment of the patients. In 2 patients the condition of isolation appeared to be the trigger factor for SIB. Anxiety was present in 7 children, while 5 had repeated stereotypies: 2 hand-flapping, 2 tip-toe walking and 1 gaze deviation.

Unwanted effects: None of the children suffered from extrapyramidal symptoms. Sedation was noted in 5 children, but it was mild in intensity and it decreased by the second week of treatment.

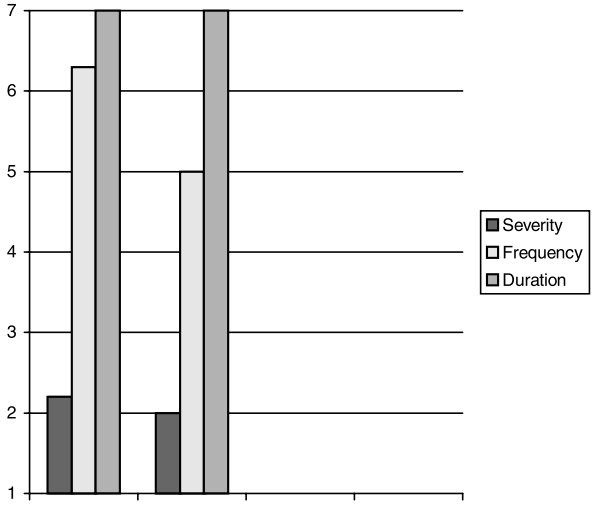

Fig. 2. YAPA-SIB scores at baseline and at the end of the trial (severity, frequency and duration subscale)

Weight gain was commonly reported during risperidone treatment at an average of 2.7 ± 0.8 kg over the six month period. One child had enuresis, which remitted after the first month of therapy.

Discussion

In the present study, the clinical presentation of SIB was characterized by head hitting and hand-biting, which are not considered specific but are frequent in autistic spectrum disorders. Aggression towards other people was neither observed nor reported by parents, consistent with the hypothesis that self-injury could be a form of pathological repetition rather than a form of lack of control over impulse. SIB intensity was moderate, none of the patients suffered from major lesions and all remained stable in a pattern characterized by skin effraction and callosity in the injured areas. Abnormal pain reactivity has been described in autism, and pain sensitivity could be preserved in the afferent pathway but pain perception and discrimination could be deranged (Gillberg, 1995). Pain reactivity was not specifically tested in this research but pain insensitivity was not detected in any of the patients at clinical examination.

Stressful situations are recognized as triggers of SIB in autistic spectrum disorders. The relationship between stress and stereotypies underlines the strong link with social context and with life events (Tordjman et al., 1999). The observation of patients in this study was conducted only in a clinical setting, thus the implicated social and relational factors were derived mainly from reports by parents. The majority of the children showed anxiety as a concurrent disorder and anger and frustration were associated to SIB. Severe impairment of communication also seemed to play an important role. Improving expressive tools through intensive rehabilitation should be the first step in the prevention and treatment of SIB. These

are often maladaptive reactions to communication deficits at first, later becoming an unspecific response to a wide range of life events (Bodfish et al., 2000). Therefore, pharmacotherapy should be the first step towards better compliance with psychosocial and educational programs for learning alternative behavioral patterns (Rodriguez-Abellan, 1999).

There were many methodological limitations in this study. First of all, it was an open label study with a small sample of participants. Secondly, the described behavioral variations could have been caused by the natural alternating course of symptoms and by a placebo effect. Thirdly, the long interval between clinical evaluations and ratings may not have revealed the occurrence of other uncontrolled variables. As a result we cannot draw conclusions with reference to the effectiveness of risperidone treatment, but only make some observations. There was a decrease in the frequency of SIB in this study, however intensity and duration were barely modified and none of the children showed complete remission. The role of pharmacotherapy in this outcome was uncertain, it may only be hypothesized that the mild improvement in YAPA-SIB scores was part of the treatment effect. Furthermore, the CARS rating was only approximately reduced by 10% from baseline, meaning that the basic clinical features of autism did not show substantial changes. The side effects of risperidone were not severe and no extrapyramidal symptoms were detected. Although dyskinesias are less frequent in atypical neuroleptics, they should be monitored carefully because could possibly occur with this medication (Malone et al., 2002). The low dose administered may have contributed to the safety of treatment, but it could also be the reason for minor improvement. Recent data on the treatment of autistic spectrum disorders with risperidone support its efficacy on target symptoms (Research Units in Pediatric Psychopharmacology Autism Network, 2002). Further controlled and long-term studies are awaited for confirming its safety and whether pharmacotherapy with this agent could steadily interfere with SIB and other symptomatic components of autistic spectrum disorders. At present, clinical guidelines for SIB are not yet available but are needed and therapeutic approaches are still mainly empirical. A more extensive use of evaluation scales and specific diagnostic tools could be useful for gathering further clinical information about SIB.

Acknowledgments

I am grateful to Prof. S. Tordjman coordinator of *The International Network on Self-Injury in Child and Adolescent Psychiatry – Paris* for suggesting the Yale-Paris Self Injurious Behavior Scale and for her very useful suggestions.

References

American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn (DSM-IV). American Psychiatric Association, Washington, DC

Bodfish JW, Symons FJ, Parker DE, Lewis MH (2000) Varieties of repetitive behaviour in autism: comparisons to mental retardation. J Autism Dev Disord 30(3): 237–243

Buitelaar JK (1993) Self injurious behaviour in retarded children: clinical phenomena and biological mechanisms. Acta Paedopsychiatr 56: 105–111

Buitelaar JK, Willensen-Swinkels SH (2000) Medication treatment in subjects with autistic spectrum disorders. Eur Child Adolesc Psychiatry 9 [Supp 1]: 85–97

Campbell M, Rapoport J, Simpson G (1999) Antipsychotics in children and adolescents. J Am Acad Child Adolesc Psychiatry 38: 537–545

Chugani DC, Muzik O, Behen M, Rothermel R, Janisse JJ, Lee J, Chugani LT (1999) Developmental changes in brain serotonin synthesis capacity in autistic and non autistic children. Ann Neurol 45(3): 287–329

Cook EH, Leventhal BL (1996) The serotoninergic system in autism. Curr Opin Pediatr 8: 348–354

Ernst M (2000) Considerations on the characterization and treatment of self-injurious behavior. J Autism Dev Disord 30(5): 447–450

Gillberg C (1995) Endogenous opioids and opiate antagonists in autism: brief review of empirical findings and implications for clinicians. Dev Med Child Neurol 37: 239–245

Gillberg C (2000) Typical neuroleptics in child and adolescent psychiatry. Eur Child Adolesc Psychiatry 9 [Suppl]: 2–8

King BH (2000) Pharmacological treatment of mood disorders, aggression and self-injury in persons with pervasive developmental disorders. J Autism Dev Disord 30(5): 439–445

Lewis MH, Bodfish JW (1998) Repetitive behaviour disorders in autism. Ment Retard Res Rev 4: 80–89

Malone RP, Maislin G, Choudhury MA, Gifford C, Delaney A (2002) Risperidone treatment in children and adolescent with autism: short and long term safety and effectiveness. J Am Acad Child Adolesc Psychiatry 41(2): 140–147

Masi G, Cosenza A, Mucci M, Brovedani P (2001) Open trial of risperidone in 24 young children with pervasive developmental disorders. J Am Acad Child Adolesc Psychiatry 40(10): 1206–1214

Masi G, Cosenza A, Mucci M, Brovedani P (2003) A 3-year naturalistic study of 53 preschool children with pervasive developmental disorders treated with risperidone. J Clin Psychiatry 64(9): 1039–1047

Mc Dougle C, Holmes J, Bronson MR, Anderson GM, Volkmar F, Price LH, Cohen DJ (1997) Risperidone treatment in children and adolescent with pervasive developmental disorders: a prospective open-label trial. J Am Acad Child Adolesc Psychiatry 36(5): 685–693

Meltzer HY (1995) Atypical antipsychotic drugs. In: Bloom FE, Kupfer DJ (eds) Psychopharmacology: the fourth generation of progress. Raven Press, New York, pp 1277–1286

Murphy G, Hall S, Oliver C, Kissi-Debra R (1999) Identification of early self-injurious behaviour in young children with intellectual disability. J Intellect Disabil Res 43: 149–163

Nicolson R, Awad G, Sloman L (1998) An open trial of Risperidone in young autistic children. J Am Acad Child Adolesc Psychiatry 37(4): 372–376

Perry R, Pataki C, Munoz Silva DM, Armenteros J, Silva RR (1997) Risperidone in children and adolescents with pervasive developmental disorders: pilot trial and follow up. J Child Adolesc Psychopharmacol 7: 167–179

Pies RW, Popli AP (1995) Self injurious behaviour: pathophysiology and implication for treatment. J Clin Psychiatry 56: 580–588

Research Units in Pediatric Psychopharmacology Autism Network (2002) Risperidone in children with autism and serious behavioral problems. N Engl J Med 347(5): 314–321

Rodriguez-Abellan J (1999) Therapeutic intervention in infantile autism and pervasive developmental disorders: self-injury and self-stimulation. Rev Neurol 28S: 130–134

Schopler E, Reichler R, De Viellis R, Daly K (1980) Towards objective classification of childhood autism: Childhood Autism Rating Scale (CARS). J Autism Dev Disord 10: 91–103

Sivam SP (1996) Dopamine, serotonin, and tachykinin in self-injurious behavior. Life Sci 58(26): 2367–2375

Tordjman S, Antoine C, Cohen DJ, Gauvain-Piquard A, Carlier M, Roubertoux P, Ferrari P (1999) Study of the relationships between self-injurious behavior and pain reactivity in infantile autism. L'Encephale 25(2): 122–134

Willensen-Swinkels SH, Buitelaar I, Van Engeland H (1996) The effects of chronic naltrexone treatment in young autistic children: a double-blind placebo contolled cross-over study. Biol Psychiatry 39: 1023–1031

Zuddas A, Di Martino A, Muglia P, Cianchetti C (2000) Long-term risperidone for pervasive developmental disorder: efficacy, tolerability and discontinuation. J Child Adolesc Psychopharmacol 10(2): 79–90

Authors' address: R. Canitano, Division of Child Neuropsychiatry, University General Hospital of Siena, Viale Bracci 1, 53100 Siena, Italy, e-mail: r.canitano@ao-siena.toscana.it; canitano@unisi.it