Should we use antidepressant medications for children and adolescents with depressive disorders?

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SUMMARY

Most of the randomized controlled trials (RCT) using tricyclic antidepressants (TCAs) for the acute treatment of children and adolescents with major depressive disorder (MDD) have shown about 50% response to both TCAs and placebo. In contrast, a recent RCT found fluoxetine superior to placebo for the treatment of depressed youth. Cognitive-behavioral psychotherapy has also been found efficacious for the treatment of youth with depression. Therefore, the use of medications, in particular TCAs, as the first line of treatment for youth with mild to moderate MDD has been questioned. However, some subgroups of patients, especially those who are unable or unwilling to undergo psychotherapy and those with psychosis, bipolar depression, severe depressions, or recurrent episodes, may benefit from initial treatment with antidepressants. Further research on the *continuation and maintenance treatment* phases of depression as well as treatment for dysthymia, treatment-resistant depression, and other subtypes of depressions is warranted.

KEY WORDS

Children; Adolescents; Depression; Pharmacotherapy; Treatment.

Major depressive (MDD) and dysthymic (DD) disorders are prevalent in children and adolescents with rates of approximately 2% to 8%, respectively (Birmaher et al., 1996a). These disorders appear to have increased in prevalence and seem to be manifesting at younger ages (e.g., Gershon et al., 1987; Kovacs and Gatsonis, 1994; Lavori, et al., 1987; Ryan, et al., 1992). Depressive disorders usually produce impairment in the academic, social, and family functioning. In addition, depressed youth are at high risk for suicide, bipolar disorder, substance abuse, behavior problems, tobacco use, and early pregnancy (Birmaher et al., 1996a). These disorders are highly recurrent with a child suffering from one episode of MDD having a 70% risk of manifesting a second episode in a period of 5 years (Kovacs et al., 1984 a,b; Rao et al., 1995). Moreover, youth with DD have about 70% chance of developing an episode of MDD in a period of 5 years (Kovacs et al., 1994).

All above noted information emphasizes the need for efficacious treatments for those youth who are acurately depressed, prevention of relapses / recurrences, and prevention of development of depressive episodes in those at high risk (e.g., children with high family loading for mood disorders).

The treatment of depressed patients should begin with psychoeducation about the illness, factors associated with the onset and course, phases of treatment, and prognosis followed by psychotherapy and/or pharmacological interventions. In addition, therapy should include management of other comorbid disorders, psychosocial factors, school issues, family conflicts, and family psychopathology (for review see Birmaher et al., 1996b).

This article will review the literature on the pharmacological treatment of children and adolescents with depressive disorders. Recommendations for the acute, continuation, and maintenance treatment phases for depressed youth are made based on current literature and clinical experience.

Acute pharmacological treatment

Almost all the randomized controlled trials (RCT) of children and adolescents with MDD include the tricyclic antidepressants (TCAs), with very few investigations using the selective serotonin reuptake inhibitors

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Table 1
TCA Double-Blind Studies in Children with Major Depressive Disorder

Author	N	Diagnostic Assessment	TCA	Dose	TCA Treatment duration	Results
Petti & Law 1982	6	Clinical	IMI	Up to 5mg/kg/day	4 weeks	IMI ≈ placebo
Kashani et al., 1984	9	DSM-III	AMI	1.5 mg/kg/day	Crossover: each phase 4 weeks	AMI ≈ placebo
Preskorn et al., 1987	30	DICA/DSM-III	IMI	Up to 5mg/kg/day	6 weeks	IMI > placebo
Puig-Antich et al., 1987	38	K-SADS/RDC	IMI	Up to 5mg/kg/day	5 weeks	IMI ≈ placebo
Geller et al., 1989	50	K-SADS/RDC	NT	"Fixed" plasma level (80 ± 20 ng/ml)	8 weeks	NTP ≈ placebo
Hughes et al., 1990	31	DICA/DSM-III	IMI	?	6 weeks	IMI ≈ placebo

Note:
TCA = Tricyclic antidepressant
DSM = Diagnostic Statistical Manual
K-SADS = Kiddie Schedule for Affective Disorders & Schizophrenia
DICA = Diagnostic Interview for Children and Adolescents
IMI = Imipramine
AMI = Amitriptyline
NT = Nortriptyline
RDC = Research Diagnostic Criteria

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(SSRIs) and other classes of antidepressants (Birmaher et al., 1996b; Kye and Ryan, 1995).

TCAs RCT in children: As shown in Table 1, except for Preskorn et al., (1987), studies in children had not shown statistically significant differences between the TCAs and placebo. Most of these studies showed that approximately 50% of the depressed children responded to placebo. Only one study (Geller et al., 1989) showed about 20% respond to both placebo and nortriptyline (NTP) although, in contrast to other RCTs, this study included a sample of children with chronic depressions and high family loading for bipolar disorder.

TCAs RCT in adolescents: As shown in Table 2, except for Geller et al., (1990) all studies showed that approximately 50% of the sample responded to placebo. Again, Geller et al., (1990) included a sample of chronically depressed adolescents with high family loading for bipolar disorder.

Limitations of the TCA RCTs: The above noted findings need to be considered in light of the following limitations:

1) Most of the studies used small sample sizes; 2) Most of the studies include patients with mild to moderate depressions; 3) Most of the studies were done with outpatient samples and their results cannot be extrapolated to other settings; 4) Patients had comorbid disorders, in particular disruptive disorders, which may have a high placebo response (Hughes et al., 1990), and 5) The length of treatment was usually short.

To address some of the above limitations, a study including a group of adolescents with severe, chronic depression who were admitted to a state psychiatric hospital because of lack of response to previous hospitalizations, was recently conducted (Birmaher et al., 1997). At randomization, these patients had an average Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), scores of 22.4 ± 7.3, and a Beck Depression Inventory (BDI) (Beck, 1961) score of 26.6 ± 11.3. Patients had on average 3 previous psychiatric hospitalizations, 1.6 ± MDD episodes, and 50% had previous history of sexual abuse. After a period of 4 weeks of nonplacebo washout, 27 patients were randomized to placebo or a serotonergic /adrenergic TCA, amitriptyline (AMI) for a period of 10 weeks. Patients received on average 173.1 ±56.3 mg/day of AMI and at this dose the AMI + nortriptyline levels were 226.2 ± 80.8. Surprisingly, approximately 70% - 80% of both patients on placebo and patients on AMI showed

Table 2
TCA Double-Blind Treatments in Adolescents with Major Depressive Disorder

Author	N	Diagnostic Assessment	TCA	TCA Dose	TCA Treatment duration	Results
Kramer & Feiguine 1981.	20	?	AMI	200 mg/day	6 weeks	AMI ≈ placebo
Geller et al., 1990	31	K-SADS/RDC	NT	"Fixed" plasma level (80 ± 20 ng/ml)	8 weeks	NT ≈ placebo
Klein & Koplewicz., 1990	30	K-SADS/DSM-III-R	DMI	Up to 5mg/kg/day	6 weeks	AMI ≈ placebo
Kutcher et al., 1994	42	K-SADS/DSM-III-R	DMI	200 mg/day	6 weeks	DMI ≈ placebo
Kye et al., 1996	31	K-SADS/DSM-III-R	AMI	Up to 5mg/kg/day	6 weeks	AMI ≈ placebo
Birmaher et al., (unpublished results)	27	K-SADS/DSM-III-R	AMI	Up to 5mg/kg/day	10 weeks	AMI ≈ placebo

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response to treatment defined as BDI < 9, HDRS < 7, or 50% reduction on the HDRS scores. Even though the results of this study are limited because of the small sample size of patients included, given the high response rate to both AMI and placebo, future studies will require thousands of patients to show between-group significant differenes (Cohen, 1976).

SSRIs Randomized Controlled Trials: A study including a very small sample of adolescents with MDD did not find significant differences between fluoxetine and placebo (Simeon et al., 1990). In contrast, a recent RCT including a large sample of children and adolescents with MDD found approximately 58% fluoxetine vs 32% response on the Clinical Global Improvement scale (Emslie et al., in press). There were no age or sex effects and patients tolerated fluoxetine well.

Other antidepressant medications: A small study of depressed adolescents using low doses of venlafaxine did not find differences between this medication and placebo (Mandoki et al., 1997). Other classes of antidepressants such as nefazodone, bupropion, and monoamine oxidase inhibitors (MAOIs) have been found beneficial for treatment of adults with MDD but no RCT studies have been done with children or adolescents.

In summary, except for fluoxetine, no other antidepressant medications have been found to be different from placebo for the acute treatment of youth with MDD. Furthermore, the high placebo response shown in most of the studies questions the use of antidepressant medications as the first line of treatment for children and adolescents with MDD.

In evaluating the effects of antidepressants in children, it is also important to consider that the response to medications may be affected by developmental factors (Clein and Riddle, 1995; Kye and Ryan, 1995). For example, children metabolize medications faster than adults, and in contrast to the central serotonergic system, the central noradrenergic system appears to mature later in life (e.g., Goldman-Rakic and Brown, 1981). Also children seem to be more susceptible to suggestions and interactions with the therapist. This last issue, if found true, may explain the fact that in general youth show higher placebo response than adults (Birmaher et al., 1996b).

Continuation and maintenance pharmacological treatments

Despite the fact that childhood depression is a recurrent disorder, no continuation and maintenance pharmacological trials have been published in this population. Studies in depressed adults have shown

that all patients taking antidepressants at the same doses found beneficial for the treatment of the depression during the acute phase for a period of 6 to 12 months showed less relapses than patients discontinuing or reducing the dose of the medications (Prien and Kocsis, 1995). Similarly, studies in adults have also shown that maintenance treatment using the same antidepressant doses needed to achieve remission are necessary to prevent recurrences of major depression (e.g., Frank et al., 1990, 1993; Kupfer et al., 1992).

Preliminary recommendations and future developments

Although it is beyond the scope of this article to review the literature on the psychotherapeutic trials for youth with MDD, the few psychotherapeutical RCTs have shown about 60% - 70% response to cognitive behavior therapy (CBT) (Brent et al., in press; Clarke et al., 1995; Fine et al., 1991; Kahn et al., 1990; Kroll et al., 1996; Stark et al., 1987; Vostanis et al., 1996; Wood et al., 1996).

The fact that acute psychotherapy, in particular cognitive behavioral therapy (CBT), is as effective as fluoxetine for the treatment of MDD and in waiting for the results of ongoing RTC studies, it is prudent to first offer psychotherapy for the treatment of youth with non-complicated MDD. Thus, youth with mild to moderate depressions should be treated with at least 6 weeks of psychotherapy before starting antidepressants. Depressed youth who do not show signs of improvement during this period of time or begin to deteriorate should have a trial with a SSRI. Youth with severe depression, severe impairment in functioning, or inability or unwillingness to participate in psychotherapy, as well as patients with psychosis, bipolar depressions, or recurrent depressions that previously did not improve with psychotherapy must be administered, from the beginning of treatment, an antidepressant and, if necessary, other psychotropic medications (e.g., mood stabilizers, antipsychotics).

For those patients requiring pharmacotherapy it is recommended to initially use a SSRI. Not only has one of these medications (fluoxetine) been found to be beneficial for the treatment of youth with MDD, but SSRIs are safer in case of an overdose, the overall side effects profile is more tolerable than other antidepressants, and the once a day dose may increase compliance with treatment.

To avoid relapses, *all patients* should be offered continuation therapy for at least 6 to 12 months. At the time of discontinuation of treatment, antidepressants should be tapered over several weeks to avoid possible withdrawal side effects or relapse of depressive symptoms.

In expectation of future research, youth with two or more episodes of MDD, in particular those with highly frequent or recurrent depression, psychotic depression, or history of severe suicide attempt, should be offered maintenance treatment for 3 to 5 years and some patients should be considered for lifetime treatment.

Despite the fact that a great proportion of depressed youth show remission of symptoms, functioning may continue to be impaired due to concurrent psychiatric disorders (e.g., ADHD, anxiety) which also require proper pharmacological and/or psychopharmacological management. For example, a child with MDD and ADHD should be treated with an antidepressant and a stimulant or an antidepressant that targets both disorders (e.g, a TCA, bupropion, venlafaxine). In addition, psychosocial issues, school problems, psychological "scars" secondary to the depression, family conflicts, and psychopathology will need complete assessment and treatment (e.g., Asarnow et al., 1994; Beardslee et al., 1993; Brent et al., 1993; Brown and Lewinsohn, 1984). Furthermore, parents will need help and recommendations of how to manage the child during a period where he/she is usually more irritable, defiant, and oppositional.

Studies focusing on subtypes of depression such as atypical, seasonal, psychotic, premenstrual which may respond to specific treatment (e.g., light, MAOIs) are indicated (see Birmaher et al., 1996b; Swedo et al., 1997). Also, research in the primary prevention of depression for youth at high risk for depression, namely youth with subsyndromal depressive symptoms and children from depressed parents, are warranted (Clarke et al., 1995; Jaycox et al., 1994). Finally, investigations in the treatment of youth with dysthymia is imperative because these children and adolescents are at high risk to develop MDD and other psychiatric disorders (Kovacs et al., 1994).

References

1. Asarnow, J.R.; Tompson, M.; Hamilton, E.B.; Goldstein, M.J. & Guthrie, D. - Family-expressed emotion, childhood-onset depression, and childhood-onset schizophrenia spectrum disorders: is expressed emotion a nonspecific correlate of child psychopathology or a specific risk factor for depression? **J. Abnorm. Child. Psychol.**, 22: 129-146, 1994.
2. Beardslee, W.R.; Salt, P.; Porterfield, K. e col. - Comparison of preventive interventions for families with parental affective disorder. **J. Am. Acad. Child. Adolesc. Psychiatry,** 32: 254-263, 1993.

3. Beck, A.T.; Ward, C.; Mendelson, M.; Mock, J. & Erbaugh, J. - An inventory for measuring depression. **Arch. Gen. Psychiatry,** 4: 561-571, 1961.
4. Birmaher, B.; Ryan, N.D.; Williamson, D.E. et col. - Childhood and adolescent depression: a review of the past 10 years - Part I. **J. Am. Acad. Child Adolesc. Psychiatry,** 35: 1427-1439, 1996a.
5. Birmaher, B.; Ryan, N.D.; Williamson, D.E et col. Childhood and adolescent depression: a review of the past 10 years - Part II. **J. Am. Acad. Child Adolesc. Psychiatry,** 35: 1575-1583, 1996b.
6. Birhmaher, B.; Waterman, S.; Ryan, N. et col. - **Should we use antidepressant medications for children and adolescents with depressive disorders?** Florida: Boca Raton, 1997.
7. Brent, D.A; Holder, D.; Kolko, D. et col. - A clinical psychotherapy trial for adolescent depression comparing cognitive, family and supportive treatments. **Arch. Gen. Psychiatry,** in press, 1997.
8. Brent, D.A.; Poling, K.; McKain, B. & Baugher, M.A. - Psychoeducational program for families or affectively ill children and adolescents. **J. Am. Acad. Child Adolesc. Psychiatry** 32: 770-774, 1993.
9. Brown, R.A. & Lewinsohn, P.M. - A psychoeducational approach to the treatment of depression: comparison of group, individual and minimal contact procedures. **J. Consult Clin. Psychol.** 52: 774-783, 1984.
10. Clarke, G.N.; Hawkins, W.; Murphy, M. et col. - Targeted prevention of unipolar depressive disorder in an at-risk sample of high school adolescents: a randomized trial of group cognitive intervention. **J. Am. Acad. Child. Adolesc. Psychiatry,** 34: 312-321, 1995.
11. Clein, P.D. & Riddle, M.A. - Pharmacokinetics in children and adolescents. **Child and Adolesc. Psychiatr. Clin North Am,** 4 (1): 59-75, 1995.
12. Cohen, J. - **Statistical Power Analysis for the Behavioral Sciences (revised edition).** New York: Academic Press, 1976.
13. Emslie, G.; Rush, A.J.; Weinberg, A.W. et col. - A double-blind, randomized placebo-controlled-trial of fluoxetine in depressed children and adolescents. **Arch. Gen. Psychiatry,** in press, 1997.
14. Fine, S.; Forth, A.; Gilbert, M. & Haley, G. - Group therapy for adolescent depressive disorder: a comparison of social skills and therapeutic support. **J. Am. Acad. Child. Adolesc. Psychiatry,** 30: 79-85, 1991.
15. Frank, E.; Kupfer, D.J.; Perel, J.M. et col. - Three-year outcomes for maintenance therapies in recurrent depression. **Arch. Gen. Psychiatry,** 47: 1093-1099, 1990.
16. Frank, E.; Kupfer, D.J.; Perel, J.M. et col. - Comparison of full dose versus half dose pharmacotherapy in the maintenance treatment of recurrent depression. **J. Affect. Disord,** 27:139-145, 1993.
17. Geller, B.; Cooper, T.; McCombs, H.; Graham, D. & Wells, J. - Double-blind, placebo-controlled study of nortriptyline in depressed children using a "fixed plasma level" design. **Psychopharmacol. Bull,** 25: 101-108, 1989.
18. Geller, B.; Cooper, T.; Graham, D.; Marsteller, F.A. & Bryant, D.M. - Double-blind placebo-controlled study of nortriptyline in depressed adolescents using a "fixed plasma level" design. **Psychopharmacol. Bull,** 26: 85-90, 1990.
19. Gershon, E.S.; Hamovitt, J.H.; Guroff, J.J. & Nurnberger, JI. - Birth-cohort changes in manic and depressive disorders in relatives of bipolar and schizoaffective patients. **Arch. Gen. Psycniat,** 44: 314-319, 1987.
20. Goldman-Rakic, P.S. & Brown, R.M. - Regional changes of monoamines in cerebral cortex and subcortical structures of aging rhesus monkeys. **Neuroscience,** 6: 177-187, 1981.
21. Hamilton, M. - A rating scale for depression. **J. Neurol Neurosurg Psychiatry,** 23: 56-61, 1960.
22. Hughes, C.W.; Preskorn, S.H.; Wrona, M.; Hassanein, R.; & Tucker, S. - Follow-up of adolescents initially treated for prepubertal-onset major depressive disorder with imipramine. **Psycopharmacol. Bull,** 26 (2): 244-248, 1990.
23. Jaycox, L.H.; Reivich, K.J.; Gillham, J. & Seligman, M.E.P. - The prevention of depressive symptoms in school children. **Behav. Res. Ther,** 32: 801-816, 1994.
24. Kahn, J.S.; Kehle, T.J.; Jenson, W.R. & Clark, E. - Comparison of cognitive-behavioral, relaxation, and self-modeling interventions for depression among middle-school students. **School Psychol. Rev,** 19: 196-211, 1990.
25. Kashani, J.; Shekim, W. & Reid, J. - Amitriptyline in children with major depressive disorder: a double-blind crossover pilot study. **J. Am. Acad. Child. Adolesc. Psychiatry,** 23: 348-351, 1984.
26. Klein, R. & Koplewicz, H. - **Desipramine treatment in adolescent depression.** Pittsburgh: PA, 1990.
27. Kovacs, M.; Akiskal, S.; Gatsonis, C. & Parrone, P.L. - Childhood-onset dysthymic disorder. **Arch. Gen. Psychiatry,** 51: 365-374, 1994.
28. Kovacs, M.; Feinberg, T.L.; Crouse-Novak, M.A.; Paulauskas, S.L. & Finkelstein, R. - Depressive Disorders in childhood. I. A longitudinal study of characteristics and recovery. **Arch. Gen. Psychiatry,** 41: 229-237, 1984a.
29. Kovacs, M.; Feinberg, T.L.; Crouse-Novak, M.; Paulauskas, S.L.; Pollock, M. & Finkelstein, R. - Depressive disorders in childhood. II. A longitudinal study of the risk for a subsequent major depression. **Arch. Gen. Psychiatry,** 41: 643-649, 1984b.
30. Kovacs, M. & Gatsonis, C. - Secular trends in age at onset of major depressive disorder in a clinical sample of children. **J. Psychiatr. Res,** 28: 319-329, 1994.
31. Kramer, A. & Feiguine, R. - Clinical effects of amitriptyline in adolescent depression. **J. Am. Acad. Child Psychiatry,** 20: 636-644, 1981.
32. Kroll, L.; Harrington, R.; Jayson, D.; Fraser, J. & Gowers, S. - Pilot study of continuation cognitive-behavioral therapy for major depression in adolescent psychiatric patients. **J. Am. Acad. Child. Adolesc. Psychiatry,** 35: 1156-1161, 1996.
33. Kupfer, D.; Frank, E. & Perel, J. - Five-year outcome for maintenance therapies in recurrent depression. **Arch. Gen. Psychiatry,** 49:769-773, 1992.
34. Kutcher, S.; Boulos, C.; Ward, B. et col. - Response to desipramine treatment in adolescent depression: a fixed dose, placebo-controlled trial. **J. Am. Acad. Child Adolesc. Psychiatry,** 33: 686-694, 1994.
35. Kye, C. & Ryan, N.D. - Pharmacologic treatment of child and adolescent depression. **Child and Adolesc. Psychiatr. Clin North Am,** 4: 261-281, 1995.
36. Kye, C.; Waterman, G.S.; Ryan, N.D. et col. - Randomized control trial of amitriptyline in the acute treatment of adolescent major depression. **Am. J. Child. Adolesc. Psychiatry,** 35: 1139-1144, 1996.
37. Lavori, P.W.; Klerman, G.L.; Keller, MB.; Reich, T.; Rice, J. & Endicott, J. - Age-period-cohort analysis of secular trends in onset of major depressions: findings in siblings of patients with major affective disorder. **J. Psych. Residency,** 21: 23-35, 1987.
38. Mandoki, M.W.; Tapia, M.R.; Tapia, M.A.; Sumner, G.S. & Parker, J.L. - Venlafaxine in the treatment of children and adolescents with major depression. **Psychopharmacol. Bull,** 33 (1): 149-154, 1997.
39. Petti, T. & Law, W. - Imipramine treatment of depressed children: a double-blind pilot study. **J. Clin. Psychopharmacol,** 2: 107-110, 1982.
40. Preskorn, S.H.; Weller, E.B.; Hughes, C.W.; Weller, R.A. & Bolte, K. - Depression in prepubertal children: dexamethasone nonsuppression predicts differential response to imipramine vs. placebo. **Psychopharmacol. Bull,** 23: 128-133, 1987.

41. Prien, R.F.& Kocsis, J.H. - Long-term **treatment of mood disorders.** In: Bloom, F.E. & Kupfer, D.J. (eds.) - **Psychopharmacology: The Fourth Generation of Progress.** New York: Raven Press, 1995, pp. 1067-1079.
42. Puig-Antich, J.; Perel, J.; Lupatkin, W. et col. - Imipramine in prepubertal major depressive disorders. **Arch. Gen. Psychiatry,** 44: 81-89, 1987.
43. Rao, U.; Ryan, N.D. & Birmaher, B. - Unipolar depression in adolescence: clinical outcome in adulthood. **J. Am. Acad. Child Adolesc. Psychiatry,** 34: 566-578, 1995.
44. Ryan N.D.; Williamson D.E.; Iyengar, S. et col. - A secular increase in child and adolescent onset affective disorder. **J Amer Academy Child Adolesc Psychiatry,** 31: 600-605, 1992.
45. Simeon, J.; Dinicola, V.; Ferguson, H. & Copping, W. - Adolescent depression: a placebo-controlled fluoxetine treatment study and follow-up. **Prog Neuropsychopharmacol. Biol. Psychiatry,** 14: 791-795, 1990.
46. Stark, K.D.; Reynolds, W.M. & Kaslow, N.J. - A comparison of the relative efficacy of self control therapy and a behavioral problem-solving therapy for depression in children. **J. Abnorm. Child. Psychol,** 15: 91-113, 1987.
47. Swedo, S.; Allen, A.J.; Glod, C.A. et col. - A controlled trial of light therapy for the treatment of pediatric seasonal affective disorder. **J. Am. Acad. Child. Adolesc. Psychiatry,** 36 (6): 816-821, 1997.
48. Vostanis, P.; Feehan, C.; Grattan, E. & Bickerton, W.A. - A randomized controlled outpatient trial of cognitive-behavioral treatment for children and adolescents with depression: 9-month follow-up. **J. Affect. Disord,** 40: 105-116, 1996.
49. Wood, A.; Harrington, R. & Moore, A. - Controlled trial of a brief cognitive-behavioral intervention in adolescent patients with depressive disorders. **J. Child. Psychol. Psychiatry,** 37: 737-746, 1996.