

“Outer-Directed Irritability”: A Distinct Mood Syndrome in Explosive Youth With a Disruptive Behavior Disorder?

Stephen J. Donovan, M.D.; Edward V. Nunes, M.D.;
Jonathan W. Stewart, M.D.; Don Ross, Ph.D.; Frederic M. Quitkin, M.D.;
Peter S. Jensen, M.D.; and Donald F. Klein, M.D.

Objective: To examine whether “outer-directed irritability,” a mood construct from the adult literature, characterizes a subgroup of disruptive behavior disordered children and adolescents previously shown to improve on divalproex, a mood stabilizer.

Method: A sample (N = 20) of disruptive youth (aged 10–18 years) entering a divalproex treatment study of temper and irritable mood swings was compared to normal controls (N = 18) on measures of aggression/irritability directed against others (externalizing symptoms) and on aggression/irritability against self, anxiety, and depression (internalizing symptoms). All patients met DSM-IV criteria for a disruptive behavior disorder (oppositional defiant disorder or conduct disorder) in addition to research criteria.

Results: “Outer-directed irritability” most clearly distinguished patients from controls (effect size 4.1) and did not correlate with other mood measures. Patients and controls showed no to minimal differences on internalizing symptoms.

Conclusion: Disruptive behavior disordered children and adolescents characterized by outer-directed irritability exist, can be identified, and should be further investigated, especially since they are potentially treatable.

(*J Clin Psychiatry* 2003;64:698–701)

Received June 26, 2002; accepted Oct. 24, 2002. From the Department of Therapeutics, New York State Psychiatric Institute, New York, N.Y.

Supported by National Institute on Drug Abuse (NIDA) grants 1-K02-DA00451-01A1 (Dr. Donovan), RO1-DA12234-01A1 (Dr. Donovan), and 2-K02-DA00288-06 (Dr. Nunes) and an unrestricted grant from Abbott Pharmaceuticals (Dr. Donovan). Abbott Pharmaceuticals provided funds for recruitment, assessment, and data entry for controls, as well as medication and matching placebo for the double-blind study the patients were entering.

Dr. Donovan has received grant/research support and honoraria from Abbot. Dr. Stewart has received grant/research support from Bristol-Myers; has received honoraria from Organon, Pfizer, Lilly, and GlaxoSmithKline; and has served on the speakers/advisory board for Organon. Dr. Jensen has received honoraria from Alza, McNeil, Janssen, and Shire Richwood and is a major share stockholder in Johnson & Johnson.

Corresponding author and reprints: Stephen J. Donovan, M.D., New York State Psychiatric Institute/Columbia University, 1051 Riverside Dr. #51, New York, NY 10032.

Emotional disturbance is common in children and adolescents with a disruptive behavior disorder. Mixed dysphoric states of anxiety, depression, and irritability, as well as overt self-destructive acts are well described in oppositional and conduct disordered youth.^{1–3} In an open-label study,⁴ we identified children and adolescents in the community with disruptive behavior (temper outbursts) and emotional disturbance (irritable mood) responsive to the anticonvulsant/mood stabilizer divalproex. Surprisingly, they appeared to have neither self-destructive tendencies nor high rates of anxiety or depression. Clinically, they seemed to be “pure externalizers,” in that they were only irritable and their temper and irritability were directed only at the environment (“external” or “outer-directed”), not at the self (“internal” or “inner-directed”). If externalizing symptoms alone characterize disruptive youth who are responsive to a mood stabilizer, our view of emotional disturbance in disruptive youth may require revision.

We therefore designed a double-blind, placebo-controlled, crossover study to: (a) replicate the efficacy of divalproex in irritable disruptive youth and (b) explore the “pure externalizer” hypothesis. The efficacy results, reported elsewhere,⁵ revealed that patients meeting the same criteria as in the open-label study had a high medication and poor placebo response in both phases.

The “pure externalizer” hypothesis proposes that some explosive youth never deliberately harm themselves and that irritable mood need not be a mixed anxious, depressive state. Overt aggression is a clear construct. The Overt Aggression Scale (OAS) and its modification (the Modified Overt Aggression Scale [MOAS]) distinguish self from environmentally directed, overt, aggressive acts.^{6,7}

Irritability is a less obvious but crucial construct. Previous work by Snaith in adults provided an approach to the problem.^{8,9} Noting that “irritability” is widely used but rarely defined, Snaith first proposed that it comprises 2 moods, both distinct from anxiety and depression; both characterized by impatience, intolerance, and poor anger control; and both differing from each other in the direction of the hostility. “Outer-directed irritability” focuses

on frustrations in the environment, “inner-directed irritability” on self-annoyance. Snaith et al. developed the Irritability, Depression, and Anxiety (IDA) scale to validate these distinctions in adults.⁹ While the independent status of inner-directed irritability remained unclear at the end of their studies, Snaith et al. concluded that outer-directed irritability was indeed a mood construct distinct from anxiety and depression.¹⁰

Since “outer-directed irritability” seemed to characterize our patients, we included modified forms of the Snaith IDA and the MOAS in our double-blind, placebo-controlled study. Inclusion would allow us to compare patients’ baseline scores to controls’ scores. We expected patients’ scores to exceed those of controls on all external measures (i.e., MOAS: aggression against other people, aggression against property, verbal aggression against others and IDA: outer-directed irritability subscale) but not on internal measures (i.e., MOAS: aggression against the self and IDA: inner-directed irritability, depression, anxiety). We further hypothesized that outer-directed irritability scores would not correlate with other mood states, suggesting it is a distinct mood construct in youth, as it had previously been shown to be in adults.¹⁰

METHOD

Controls were 18 children and adolescents (aged 11–18 years, 62% male) recruited via parent employees in 2 hospitals (N = 12) and a youth program (N = 6) in the New York Metropolitan area. Since we expected patient deviance in externalizing behaviors, we sought controls with no behavior disorders. Since we expected no patient deviance on internalizing disorders, we sought controls with no internalizing disorders. To find controls meeting both these specifications, we required they have no history of contact (or recommendation for contact) with the mental health system.

Patients were 20 consecutive subjects entering a double-blind, placebo-controlled, crossover study of divalproex for disruptive youth with explosive temper and irritable mood.⁵ We obtained these patients by asking a community based network of school guidance counselors, adolescent medicine social workers, and substance abuse counselors we knew through previous clinical consultations to refer any child or adolescent with significant temper outbursts and irritable mood whose family was interested in research.

For diagnosis, prior to group assignment, a child and adolescent psychiatrist (S.D.) conducted a complete psychiatric evaluation and administered the Structured Clinical Interview for DSM-IV¹¹ with supplemental questions on attention-deficit/hyperactivity disorder and oppositional defiant disorder from the Diagnostic Interview Schedule for Children.¹² In addition, subjects had to meet research criteria. These required temper outbursts involv-

ing 4 or more episodes of rage, property destruction, or fighting per month plus irritable mood swings consisting of daily and distinct shifts from normal to irritable (i.e., impatient/intolerant) mood.⁵ Current major depression and lifetime bipolar I/II disorder were excluded. Twenty-six potential patients came to the initial appointment. Six were excluded for various reasons (current major depression, N = 1; needed more than outpatient treatment, N = 2; already taking divalproex, N = 1; unwilling to commit to weekly meetings, N = 2). Twenty patients enrolled, and 17 completed at least Phase I. The sample of patients was 80% male and ranged in age from 10 to 18 years. All met DSM-IV criteria for a disruptive behavior disorder (oppositional defiant disorder or conduct disorder) in addition to the research criteria. Current DSM-IV diagnoses in enrolled patients were attention-deficit/hyperactivity disorder (N = 4) and marijuana abuse (N = 6). Onset of symptoms was almost always in prepuberty (N = 16), with most parents reporting the youngster had an explosive temper in most or all settings.

Patients and controls were compared at baseline on 2 measures. The MOAS⁷ assessed frequency and severity of temper outbursts during the previous week. It includes externalizing acts (beating people up, smashing things, and making serious verbal threats) and internalizing acts (cutting one’s wrists or taking an overdose). A score of 12 on a subcategory of the MOAS implies a serious level of pathology in that area (e.g., serious physical injury, destroying several objects, using fighting words repeatedly).

The IDA scale⁹ contains 4 subscales and also covers the previous week. These include outer-directed irritability (“People upset me so much I feel like slamming doors and banging around”), inner-directed irritability (“I get angry at myself and call myself names”), anxiety (“I can go out on my own without being anxious”), and depression (“I feel happy”). Item endorsement ranges from “not at all” to “not much” to “somewhat” to “definitely” on a 0 to 3 scale. To quantify extent of endorsement, raw IDA subscale scores were converted to percentage of the possible subscale score. A research psychiatrist read aloud the 2 scales to subjects and their parents simultaneously. Scores reflect the consensus of parent and patient. In the rare case when consensus was not achieved, the psychiatrist made a best estimate as to which report was more credible.

We were concerned that some questions might be ambiguous as to inner versus outer pathology in youth. An independent evaluator unfamiliar with the study hypotheses rated each MOAS and IDA item as external pathology, internal pathology, or ambiguous. He judged 2 anxiety items (“I can sit down and relax” and “I feel tense and wound up”) as ambiguous and these were eliminated from the analysis.

Independent t tests compared means for patients and controls. Within patients, Pearson product moment corre-

Table 1. Comparison of Control Scores (N = 18) and Baseline Patient Scores (N = 20) on the Modified Overt Aggression Scale (MOAS) and the Irritability, Depression, and Anxiety (IDA) Scale

Scale	Patients Mean (SD)	Controls Mean (SD)	t Value
MOAS			
Physical aggression against others	13.6 (21.4)	0	-2.83*
Aggression against self	0	0	N/A
Aggression against property	12.6 (19.0)	0.22 (0.94)	-2.78*
Verbal aggression against others	11.3 (14.3)	0.56 (1.9)	-3.47**
IDA (percentage of possible score)			
Outer-directed irritability	80.3 (15.9)	20.6 (13.4)	-13.59**
Inner-directed irritability	30.3 (21.5)	9.5 (10.4)	-3.78**
Depression	20.2 (10.2)	18.9 (17.0)	-.364
Anxiety	31.1 (25.0)	26.6 (19.0)	-.586

* $p < .01$.

** $p < .001$.

Abbreviation: N/A = not applicable.

lation coefficients were calculated among IDA subscale scores.

The New York State Psychiatric Institute Institutional Review Board approved this study. Parents signed informed consent and children/adolescents gave written assent.

RESULTS

Patients exceeded controls on all MOAS scores except "aggression against the self," where both groups registered no pathology (Table 1). IDA anxiety and depression subscores were "not much" (20%–30% of the total possible score) in both groups. Outer-directed irritability was "definite" in patients and "not much" in controls (80.3% vs. 20.6% of total possible score; effect size 4.1). Inner-directed irritability was "not much" in patients and "not at all" in controls (30.3% vs. 9.5% of the total possible score; effect size 1.3). The results were virtually identical when men were analyzed separately. There were too few female patients to conduct a separate analysis.

Correlations between the IDA outer-directed irritability subscale and, respectively, the inner-directed irritability, depression, and anxiety subscales were not significant in patients ($r = -.25$, $p < .30$; $r = -.12$, $p < .62$; $r = .27$, $p < .24$) or in controls ($r = .23$, $p < .36$; $r = .07$, $p < .79$; $r = -.11$, $p < .66$). For patients and controls combined, total MOAS-IDA correlations were outer-directed irritability: $r = .60$, $p < .000$; inner-directed irritability: $r = .45$, $p < .004$; depression: $r = .075$, NS; anxiety: $r = .117$, NS.

DISCUSSION

This study supports the hypothesis that we can extend to our patients Snaith's adult finding that outer-directed irritability is a meaningful and distinct mood construct and one capable of undergoing clinically relevant pathologic change, including overt aggression. Endorsement

of outer-directed irritability clearly separates our patients from our controls ("definitely" vs. "not much"; effect size 4.1) and exists without abnormal levels of depression, anxiety, or self-directed overt aggression. Outer-directed irritability apparently does not correlate with inner-directed irritability, depression, or anxiety. This lack of correlation suggests that outer-directed irritability is not simply a reflection of general emotional disturbance but is a distinct mood. Clinically, outer-directed irritability behaves like a mood, i.e., a global but temporary state, and patients were recruited for shifts into and out of irritable mood. Like other distinct moods, it has a characteristic set of cognitions, captured in the IDA scale items, revolving around the idea that everything in the environment exists to annoy and frustrate. Future research might explore whether psychotherapy directed at these cognitions could alter the underlying mood.

The most plausible explanation for the clear MOAS–outer-directed irritability correlation ($r = .60$) is that outer-directed irritability can cause overt aggression. This explanation is consistent with the mood stabilizer response^{4,5} and the magnitude of outer-directed irritability relative to other moods in patients. In contrast, the meaning of the clinically small ("not much" vs. "not at all") but real (effect size 1.3) difference between groups for inner-directed irritability is unclear, as is the moderate ($r = .45$) MOAS–inner-directed irritability correlation. For adults, contrary to his conclusions regarding the outer-directed irritability items, Snaith thought that the inner-directed irritability items probably reflected overall subjective distress (e.g., from obsessions or depression) rather than a separate construct.⁸ Extending this logic, a reasonable interpretation of our patients' mild inner-directed irritability is that it is a consequence of their overt aggression. In other words, chronic anger at the world could cause mild distress when "outer-directed irritability" temporarily re-vents and the consequences of overt aggression are evident. Consistent with this interpretation is the clinical observation that our patients had attachments to others despite their anger. Nonetheless, this distress appears not to reflect anxiety or depression, since these scores did not differ from controls nor did they correlate with the total MOAS score.

Children and adolescents with irritable mood and aggression are often given a diagnosis of childhood bipolar disorder.¹³ It is, of course, possible that outer-directed irritability predicts later bipolar illness. We can only clarify this after a sufficient number of these youngsters are followed past the age of risk for bipolar disorder. However, 2 facts suggest that labeling these youngsters as bipolar is premature. First, so far, the children and adolescents in the present sample had never manifested bipolar symptoms. Lacking euphoria or depressed-anxious mood, both

cross-sectionally and by history, they had never met criteria for bipolar I or II disorder. Second, we conducted direct interviews modeled on questions from the Family History Research Diagnostic Criteria,¹⁴ with at least 1 biological parent (or grandparent) per child. These respondents had passed the age of risk for bipolar disorder. In this, and in previous samples, these interviews produced no parental histories consistent with bipolar I or II disorder. They did, however, produce histories consistent with outer-directed irritability in the previous generation¹⁵ (i.e., histories of chronic temper dyscontrol directed at others), an observation consistent with other research on transmission of temper dyscontrol across generations.¹⁶

The sampling method successfully found disruptive behavior disordered youth with temper outbursts and irritable mood without a history of bipolar disorder or current major depression. While temper outbursts that disrupt the environment logically entail some outer-directed pathology, they do not imply only outer-directed pathology, the defining feature of our irritable patients ("pure externalizers"). Dysthymia, past major depression, all anxiety symptoms, and all other mixed disturbances of emotion and conduct were not excluded a priori. Descriptive data on emotional disturbance in classic disruptive behavior disorders would predict substantial anxious or dysthymic symptoms in this sample,¹ which in turn would correlate with the severity of externalizing symptoms.³ Instead, aggression against the self, anxiety, and depression fell within the normal range in our patients and did not correlate with aggression toward the environment or outer-directed irritability.

Two important limitations of this report are the small sample size, which constrains power to assert a lack of meaningful difference in internalizing symptoms between patients and normals, and the referral pattern, which produced outpatients from intact families, thereby limiting generalizability to other disruptive youth. In addition to replication with a larger sample, future research should examine broad samples of disruptive youth (e.g., from juvenile justice or special education populations). The goal should be to determine the prevalence of outer-directed irritability, its clinical correlates (i.e., low anxiety and depression scores), its longitudinal course (bipolar vs. no bipolar), its treatment response (mood stabilizers vs. serotonin uptake inhibitors), and its biological markers.

Low serotonin has been associated with aggression, both external¹⁷ and self-directed,¹⁸ and serotonergic medications have been used successfully to treat aggressive individuals with internalizing symptoms.¹⁹ The existence of patients with primarily only outer-directed pathology, who are responsive to a mood stabilizer, suggests an alternate mechanism, perhaps involving neuronal excitability related to GABA or excitatory amino acids. The possibility of differential medication response based on phenomenology should be investigated.

The disruptive behavior disorders cause patients and society considerable morbidity. If we properly categorize the type of concomitant emotional disturbance, we might use this knowledge to direct treatment, e.g., to decide what medication to try first. The subgroup of disruptive youth described in this report has a mood disturbance that tends to improve with divalproex treatment.^{4,5} Distinguishing characteristics of this emotional disturbance are therefore highly relevant to clinicians. This article proposes that a construct from the adult literature subsumes these characteristics, namely outer-directed irritability.

Drug name: divalproex sodium (Depakote).

REFERENCES

1. Angold A, Costello EJ, Erkanli A. Comorbidity. *J Child Psychol Psychiatry* 1999;40:57–87
2. Simic M, Fombonne E. Depressive conduct disorder: symptom patterns and correlates in referred children and adolescents. *J Affect Disord* 2001; 62:175–185
3. Weiss B, Catron T. Specificity of the comorbidity of aggression and depression in children. *J Abnorm Child Psychol* 1994;22:389–401
4. Donovan SJ, Susser ES, Nunes EV, et al. Divalproex treatment of disruptive adolescents: a report of 10 cases. *J Clin Psychiatry* 1997;58:12–15
5. Donovan SJ, Stewart JWS, Nunes EV, et al. Divalproex treatment for youth with explosive temper and mood lability: a double-blind, placebo-controlled crossover design. *Am J Psychiatry* 2000;157:818–820
6. Yudofsky SC, Silver JM, Jackson W. The Overt Aggression Scale for objective ratings of verbal and physical aggression. *Am J Psychiatry* 1986;143:25–29
7. Malone RP, Luebbert RP, Pena-Ariet M, et al. The Overt Aggression Scale in a study of lithium in a study of aggressive conduct disorder. *Psychopharmacol Bull* 1994;30:215–218
8. Snaith RP, Taylor CM. Rating scales for depression and anxiety: a current perspective. *Br J Psychiatry* 1985;19(suppl 1):17S–20S
9. Snaith RP, Constantopoulos AA, Jardine MY, et al. A clinical scale for the self-assessment of irritability. *Br J Psychiatry* 1978;132:164–171
10. Snaith RP, Taylor CM. Irritability: definition, assessment and associated factors. *Br J Psychiatry* 1985;147:127–136
11. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P). New York, NY: Biometrics Research, New York State Psychiatric Institute; 2001
12. Shaffer D, Fisher P, Dulcan MK, et al. The NIMH Diagnostic Interview Schedule for Children Version 2.3 (DISC-2.3): description, acceptability, prevalence rates, and performance in the MECA Study. Methods for the Epidemiology of Child and Adolescent Mental Disorders Study. *J Am Acad Child Adolesc Psychiatry* 1996;35:865–877
13. Biederman J, Klein RG, Pine DS, et al. Resolved: mania is mistaken for ADHD in prepubertal children. *J Am Acad Child Adolesc Psychiatry* 1998;37:1091–1096; discussion 1096–1099
14. Andreasen NC, Endicott J, Spitzer RL, et al. The family history method using diagnostic criteria: reliability and validity. *Arch Gen Psychiatry* 1977;34:1229–1235
15. Donovan SJ, Stewart JWS. Psychopathology in parents of children and adolescents whose explosive irritability responds to divalproex. In: Proceedings of the 39th Annual Meeting of the New Clinical Drug Evaluation Unit; June 1–4, 1999; Boca Raton, Fla. NIMH Abstract 177
16. Mattes JA, Fink M. A family study of patients with temper outbursts. *J Psychiatr Res* 1987;21:249–255
17. Virkkunen M, Goldman D, Nielsen DA, et al. Low brain serotonin turnover rate (low CSF 5-HIAA) and impulsive violence. *J Psychiatry Neurosci* 1995;20:271–275
18. van Heeringen C. Suicide, serotonin, and the brain. *Crisis* 2001;22:66–70
19. Coccaro EF, Kavoussi RJ. Fluoxetine and impulsive aggressive behavior in personality disordered subjects. *Arch Gen Psychiatry* 1997;54: 1081–1088