Validity and Utility of Subtyping Anorexia Nervosa

Christine Peat, MA[1]
James E. Mitchell, MD[2]*
Hans W. Hoek, MD, PhD[3]
Stephen A. Wonderlich, PhD[2]

ABSTRACT

Objective: The purpose of this article is to review the available literature that addresses the predictive validity and utility of subtyping patients with anorexia nervosa (AN) into binge/purge and restrictor subtypes.

Method: Literature was reviewed including studies that compared individuals with subtype diagnoses on clinical and outcome variables as well as more recent research examining the frequency of diagnostic crossover.

Results: Several studies found that in general the binge/purge subtype patients have more psychopathology, tend to be older, and tend to have a worse outcome. More recent studies which have examined diagnostic crossover suggest that the rate of crossover from the restrictor subtype to the binge/purge subtype is substantial. Crossover from the binge/purge to the restrictor subtype appears to occur less commonly. There is also literature documenting crossover from AN to bulimia nervosa (BN) and a small literature looking at crossover from BN to AN.

Discussion: The results of this article suggest that although there is generally progression from restrictor AN to binge/purge AN to BN in a sizeable number of patients, other crossover patterns can be seen as well and the amount of crossover is quite large. This suggests a lack of predictive validity for subtypes.

Keywords: crossover; diagnosis; subgroups

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Introduction

There has been a growing interest in questions concerning the diagnoses of psychiatric disorders because of the recent initiation of planning for the development of the Diagnostic and Statistical Manual (DSM)-V. As part of this process, certain questions have been identified as important when considering possible modifications to the criteria for eating disorders. One such question concerns the subtyping of anorexia nervosa (AN) into the restrictor versus binge/purge subtypes currently employed in DSM-IV. Several questions can be posed regarding the utility of this subtyping approach, including: (1) Do clinicians use the subtyping scheme appropriately? (2) Do the data support the predictive validity of the subtyping? (3) Are genetic, taxometric, and pharmacotherapy response data consistent with subtyping? and (4) Does the subtyping scheme provide clinically useful information for treatment planning?

All four of these questions are relevant in deciding whether or not the AN subtyping scheme should be maintained as is, eliminated or amended in the next version of the DSM. The purpose of this article is to consider each of these questions by examining the relevant literature as well as by considering the clinical implications of these questions in which empirical data do not exist.

Method

To examine the validity and clinical utility of AN subtyping, we conducted a comprehensive literature review. We searched major computer databases (e.g., MedLine, PsychInfo) and also reviewed reference lists from published literature. Search terms included AN, AN binge eat, AN binge purge, and AN purge.

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Correspondence to: James E. Mitchell, MD, Neuropsychiatric Research Institute, 120 So. 8th St., Fargo, North Dakota 58103. E-mail: mitchell@medicine.nodak.edu
[1] Department of Psychology, University of North Dakota, Grand Forks, North Dakota
[2] Neuropsychiatric Research Institute and the Department of Clinical Neuroscience, University of North Dakota School of Medicine and Health Sciences, Fargo, North Dakota
[3] Parnassia Psychiatric Institute, The Hague, The Netherlands
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TABLE 1. Clinical correlates of AN subtype diagnoses

References	Sample *N*	Results/conclusions
Halmi et al.[1]	42	Purging predicts negative outcome[a]
Casper et al.[3]	105	ANBP have more anxiety, depression, are older, and are more extroverted than ANR[b]
Garfinkel et al.[2]	141	ANBP are more impulsive, report more alcohol misuse, drug use, and suicide attempts[b]
Laessle et al.[4]	41	ANR have comorbidity[b]
Garner et al.[5]	390	ANB and ANP have more psychopathology than ANR[b]
Deter and Herzog, 1994[6]	84	Purging predicts negative outcome[a]
Favaro and Santonastaso[7]	164	Multiple purging methods are associated with impulsivity, self-injurious behavior[b]
Pryor et al.[8]	171	ANBP report more stealing and suicide attempts[b]
Herzog et al.[9]	75	Patients with ANBP are more likely to recover than ANR[a]
Herzog et al.[10]	69	Restrictors have an earlier recovery[a]
Godart et al.[11]	166	Anxiety and depression are equal in ANBP and ANR[a]

[a] Prospective.
[b] Cross sectional.

Results

I. Do clinicians use the subtyping scheme appropriately?

We were unable to find any literature that directly addressed this question. Consideration might be given to a field trial to address this question.

II. Do the data support the predictive validity of the subtypes?

Early reports, as well as some more recent work, suggest that the binge/purge or bulimic subgroup of patients with AN differed in significant ways from patients with the restrictor form of AN (**Table 1**).

Halmi et al.[1] reported that purging behavior in patients with AN predicted a more negative outcome. Two classic articles appeared in 1980. Casper et al. reported data on 105 hospitalized patients from a multicenter treatment study of AN.[2] Forty-seven percent had periodic binge eating and purging and 53% were consistently restrictors. Patients with anorexia nervosa binge purge (ANBP) were found to be more extroverted, reported a stronger appetite, tended to be older, and also more commonly reported kleptomania, as well as greater levels of anxiety, depression, and guilt. The same year Garfinkel et al.[2] reported on 141 patients with AN, 68 of whom had bulimic symptoms and 73 of whom were restrictors. They reported that the ANBP subgroup had a history of weighing more and were more commonly premorbidly obese. The bulimic subgroup more commonly reported a variety of impulsive behaviors including use of alcohol and street drugs, stealing, suicide attempts, and self-injurious behavior. They found a positive family history of obesity among the ANBP subgroup. Both articles argued for a subtyping scheme. Laessle et al.[4] reported that in a sample of 41 patients with AN, the restrictor subgroup had lower rates of comorbidity than the ANBP subgroup. Garner et al.[5] reported results of a study examining 390 patients with AN cross-sectionally and concluded that those who binge ate or purged had more psychopathology than did the restrictor group. Deter and Herzog[6] reported on a sample of 84 patients with AN from Heidelberg who were followed up for 12 years. They found that purging predicted a negative outcome in this prospective study.

Favaro and Santonastaso[7] reported on 164 patients with AN, finding that those who used multiple purging methods had greater levels of impulsivity and were more likely to report self-injurious behavior. Pryor et al.[8] reported on a sample of 171 patients with AN finding that the binge/purge subtype reported more stealing behavior and more suicide attempts. However, in contrast to many of the other reports, Herzog et al.[9] reported on a sample of 75 patients with AN from the Boston area followed prospectively and found that the ANBP group was more likely to recover than the anorexia nervosa restricting (ANR) group. However, in the Heidelberg sample, Herzog et al.[10] reported that, in 69 participants with AN at 12 year follow-up, restriction predicted earlier recovery. More recently Godart et al.[11] reported on a sample of 166 participants with AN and found equal rates of anxiety and depression in the AN restrictor and binge/purge subgroups.

In summary, with a few exceptions, binge/purging cross-sectionally appears to be associated with higher rates of impulsivity, more reports of stealing behavior, suicide attempts and self-injurious behavior and, in all but one of the prospective studies, appears to be associated with a more negative outcome.

Literature on subtyping has increasingly focused on the issue of diagnostic crossover (**Table 2**). However, in considering the literature it is important to keep in mind the descriptions as to what constitutes these subtypes have been inconsistent. Some of this literature has focused on crossover between the binge/purge and restrictor subtypes. Eckert et al.[12] in a report concerning a 10-year follow-up of 76 patients reported that the crossover rate from ANR to ANBP was 64%. Strober et al.[13] reporting on a sample of 95 patients followed up for 10 to

TABLE 2. Studies of Diagnostic Crossover from ANR to ANBP and from ANBP to ANR

References	Sample *N*	Sample Years FU	Results/Discussion
Eckert et al.[12]	76	10	ANR → ANBP 64% (Prospective)
Strober et al.[13]	95	10–15	ANR → ANBP 30% (Prospective)
Eddy et al.[14]	136	8	ANR → ANBP 62% (Prospective)
Fichter and Quadflieg[15]	311	12	ANR → ANBP 35% ANBP → ANR 18% (Prospective)
Eddy et al.[16]	216	7	ANBP → ANR 44% ANR → ANBP 55% (Prospective)
Anderluh et al.[17]	70		ANR → ANBP 38% ANBP → ANT 17% (Retrospective)

15 years found a crossover rate from ANR to ANBP of 30%. In the Boston sample, Eddy et al.[14] reported a crossover rate from ANR to ANBP of 62% and in their 2008 article reported a crossover rate from ANR to ANBP of 55%.[16] Fichter and Quadflieg[15] reported on a 12-year follow-up on 311 patients with AN and found a crossover rate from ANR to ANBP of 35%. Anderluh et al. found a crossover rate from ANR to ANBP of 38%.[17] However, crossover can also occur from ANBP to ANR. Fichter and Quadflieg found a crossover rate from ANBP to ANR of 18% in a sample of 311,[15] and Eddy et al.[14] reported a crossover rate from ANBP to ANR of 44%. Anderluh et al. reported a crossover rates from ANBP to ANR of 17%.[17]

Crossover can also occur from AN to bulimia nervosa (BN; **Table 3**). Milos et al. in a sample of 192 treatment seeking patients found that at 30-month follow-up 20% had crossed over from AN to BN.[18] Fichter et al.[15] at a 12-year follow-up of 97 patients with AN found that 10% had crossed over to BN and Eddy et al. in a sample of 216 found that 10% of the ANR and 54% of the ANBP had crossed over to BN.[16] Anderluh et al. found a crossover rate from ANBP to BN of 29%.[17]

Lastly crossover from BN to AN has also been reported (**Table 4**). Fairburn et al.[19] reported a 5-year follow-up on a community sample of 92 participants. They reported that only 2% of patients with BN received a diagnosis of AN over 5 years. Milos et al.[18] in a treated sample of 192 at 30-month follow-up found a BN to AN crossover rate of 9%. However, Tozzi et al.[20] in a retrospective study of 216 patients recruited as part of a genetic sample found a crossover rate over 7 years of 27% from BN to AN. Anderluh et al. found a crossover rate from BN to AN of 17%.[17]

In sum, this literature suggests that, in well-characterized samples followed for intermediate to long periods of time, there is significant crossover between diagnostic subgroups of AN, from AN to BN and some crossover from BN to AN as well.

TABLE 3. Studies of Diagnostic Crossover from AN to BN

References	Sample *N*	Sample Years FU	Results/Discussion
Milos et al.[18]	192	2.5	AN → BN 20% (Progressive)
Fichter et al.[15]	97	12	AN → BN 10% (Prospective)
Eddy et al.[16]	216	7	ANR → BN 10% ANB/P → BN 54% (Prospective)
Anderluh et al.[17]	79		ANB/P → BN 29% (Retrospective)

TABLE 4. Studies of Diagnostic Crossover from BN to AN

References	Sample *N*	Sample Years FU	Results/Discussion
Fairburn et al.[19]	92	5	BN → AN 2%[a] (Prospective)
Tozzi et al.[20]	216	7	BN → AN 27%[b] (Retrospective)
Milos et al.[18]	192	2.5	BN → AN 9%[a] (Prospective)
Anderluh et al.[17]	79		BN → AN 17% (Retrospective)

[a] Prospective.
[b] Cross sectional.

III. Are genetic, taxometric, and pharmacotherapy response data informative on this question?

One consideration is the examination for susceptibility genes for AN. A genome-wide linkage analysis of 192 families with at least one affected relative pair resulted in only modest evidence for linkage, with the highest nonparametric score of 1.80 at marker D4S2367 on chromosome 4. Subsequently linkage analysis was done in a subset of families in which at least two affected relatives had a diagnosis of ANR. The nonparametric linkage score (NPL) nonparametric linkage score observed was 3.03 at marker D1S3721 on chromosome 1.[21] Subsequently genotyping of nine single nucleotide polymorphisms suggested that genes for the serotonin 1D receptor and the opioid delta receptor or linked genes might be involved in the risk for restrictor AN.[22] This suggests the possibility that genetic differences exist between AN subtypes.

Taxometric studies of eating disorder participants have also been published. In relation to the restricting subtype of AN, Williamson et al. reported that ANBP appeared to occur on a continuum with normality.[23] Both Gleaves et al. [24] and Williamson et al.[23] found that the ANR subtype was qualitatively different from the ANBP subtype, finding that the ANBP subtype showed evidence of continuity with BN. This paralleled the findings from latent class analysis that placed BN and ANBP in the same class.[25]

Other research suggests that those with ANBP do not respond to certain treatments to which patients with BN respond such as fluoxetine.[26] Two studies, however, have found differential responses between those with ANR and ANBP to other pharmacotherapies, including cyproheptadine and an atypical antipsychotic.[27,28]

IV. Does the subtyping scheme provide useful clinical information for the practitioner that can be used in treatment planning?

Although it seems reasonable that clinicians may make use of subtype information in assessing patients and in treatment planning, we were unable to locate any empirical data directly addressing this issue. Again, this might be a focus for a field trial.

Discussion

There appears to be lack of predictive validity for the AN subtypes. There is often progression from ANR to ANBP and from ANBP to BN, but other crossover patterns occur as well. In general, data are lacking concerning whether clinicians use the subtyping scheme appropriately and whether the subtypes provide useful information for practitioners, although the assumption might be that they do. Data on genetic, taxometric, and pharmacotherapy response again are inconsistent.

It is not clear that the definitions offered in the DSM-IV allow clinicians to reliably distinguish between the restrictor versus binge-purge subtype. One consideration is that the criterion for restricting subtype stipulates that those in this subgroup will not have "regularly engaged" in binge eating or purging behavior. How "regularly engaged" is best defined is unclear and no cut points are offered in DSM-IV TR. Therefore, clinicians are free to interpret this criterion as they wish, and there are no data suggested how this is usually done in practice. By extension, it is also unclear what period of time must elapse before a subtype can be considered to have changed, given that it is clear that patients can change subtype diagnoses over time, as will be discussed further. Deciding on the presence or absence of binge eating and purging is probably particularly problematic when patients engage in such behaviors at a low frequency.

Another point of consideration is a lack of clarity as to what constitutes binge eating in AN. Clinical lore suggests that many patients with AN eat relatively modest amounts of food when they indicate they had an eating binge. An example would be a patient who states she has been binge eating, but when asked what she actually consumed, indicates that she ingested a cookie. This amount, and probably the macronutrient content of this food, indicated to her that the amount she had taken in was "excessive" or "forbidden." However, there are data indicating that eating binges in those with AN can be quite large.[29] Thus there may be considerable variability in size of binge eating episodes in patients with AN, which is in line with what we know from feeding laboratory studies in those with BN and binge eating disorder (BED), where size of binge eating episodes varies dramatically.[30,31]

In relation to predictive validity, the data are to some extent clearer. Most research in this area suggests that an individual's diagnostic subtype designation may change over time and that the most common patterns of crossover are from restrictor type AN to binge-purge type AN and from binge-purge AN to BN. However, sizeable subgroups of patients move between subtypes and diagnoses in other ways and move in to and out of subsyndromal states as well. Therefore, subtype diagnoses determined cross-sectionally do not appear to offer strong predictive validity about course or outcome.

This literature review suggests several possible options:

1. One option is to continue the current system. This would provide continuity with the DSM-IV-TR diagnostic nomenclature. The clear advantage of this would be to minimize change, given prior research findings and that many clinicians are familiar with the current subtyping scheme. Also, subtyping logically seems to have potential clinical utility in that it should be of some use in assessment and treatment planning. Retaining the subtyping scheme may also facilitate differential treatment research. The main argument against this choice is the lack of predictive validity of the diagnostic subtypes and the problem of diagnostic crossover. Another consideration is that if the subtyping scheme is to be retained, more precise guidelines might be included regarding the necessary frequency and duration of binge eating and purging required for that subtype diagnosis. However, we could find no data that empirically addressed this issue and the definitions used in the literature in terms of frequency of behaviors have varied considerably.

2. A second possibility would be to alter the subtyping scheme for AN to emphasize that it indicates whether they are currently binge/purge or restric-

tor. This scheme would retain some of the advantages of the current system but the use of the term "currently" would underscore that diagnostic crossover may well have occurred in the past or may occur later. This would be novel and might be confusing to clinicians.

3. A third approach would be to simply eliminate the subtyping scheme for AN. This would be in keeping with the lack of predictive validity but would make more difficult the communication of subtyping information which may be important in assessment and treatment planning.

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