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Personality Disorders in Hypochondriasis: Prevalence and comparison with two anxiety disorders

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Abstract

Objective—Symptoms of hypochondriasis are sometimes attributed to personality psychopathology by health care providers. The goals of this study were to assess the prevalence of personality disorder comorbidity (PD) in hypochondriasis (HYP) and to compare the PD comorbidity profile of patients with HYP to that found among patients with other disorders characterized by intrusive thoughts and fears.

Methods—SCID-I and SCID-II were administered to 179 individuals: 62 with HYP, 46 with Obsessive Compulsive Disorder (OCD), and 71 with Social Anxiety Disorder (SAD). For group contrasts, the samples were "purified" of the comparison comorbid disorders. General linear models were used to test the combined effect of group (HYP, OCD, SAD), age, and gender on the PD outcome variables.

Results—59.7% of HYP subjects had no Axis II comorbidity. The most common PDs in HYP were paranoid (19.4%), avoidant (17.7%), and obsessive compulsive (14.5%). HYP significantly differed from SAD in the likelihood of a cluster C disorder, whereas no significant difference was noted for HYP vs OCD. The proportion of subjects having at least two PDs was not significantly different for HYP vs OCD or for HYP vs SAD.

Conclusion—Although 40% of patients with hypochondriasis have PD comorbidity as assessed by the SCID-II, the amount of PD comorbidity is not significantly different than found among individuals with two comparison anxiety disorders. Therefore, health providers should be aware

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that PD may complicate the clinical profile of HYP but they should avoid assuming that PD psychopathology is the primary source of hypochondriacal distress.

Keywords

Hypochondriasis; Personality Disorders; Obsessive Compulsive Disorder; Social Anxiety Disorder; DSM-5

INTRODUCTION

Hypochondriasis (HYP) is a chronic, disabling disorder characterized by the fear or belief that one is ill based on somatic symptoms that are either medically unexplained or cause excessive distress[1]. Despite the prevalence of hypochondriasis and its adverse impact on both personal and public health, very little is known about the extent to which Axis II disorders accompany hypochondriasis. This is surprising given that these patients are often viewed by the medical community as help-rejecting complainers who in a dependent fashion prefer to don the sick role and who in a paranoid style fail to trust that the doctor has done a complete evaluation or told him/her the truth [2]. Some clinical investigators [3, 4] have suggested that hypochondriasis in sharing many of the features of a personality disorder (PD) might be better classified on Axis II rather than on Axis I.

Research on PD co-morbidity among patients with HYP has been limited by small sample sizes or by the reliance on self-report questionnaires to establish an Axis II diagnosis [5–8]. Two studies[5, 7] used a 5-item self-report screening questionnaire from the PDQ-R[9] to assess the presence of DSM-III-R and DSM-IV PD "caseness" and one study[6] used the 99-item PDQ-4+ as a screen to assess PD prevalence and pattern. These studies have reported high rates of HYP PD comorbidity ranging from 63%[5] to 74%[6] - rates over three times greater than a medical clinic comparison sample; the authors however warn that "the high prevalence...might be inflated." The PDQ – both in its shorter "caseness" version and in its longer versions - while helpful as a screening instrument, was not meant to be used as a diagnostic instrument. Indeed, when compared to "gold standard" structured diagnostic instruments such as the SCID-II[10], some studies have found either close correspondence in personality rates [11] or elevated rates, suggesting that self-report screening questionnaires such as the PDQ over-estimate the presence of personality pathology by 50— 60% [12-16]. To our knowledge, the only prior HYP study using a DSM-based structured interview to assess PD was conducted among consecutive psychiatric outpatients in Greece[8]. Compared to the comparison group of 1273 psychiatric patients who did not have a somatoform disorder, the 23 psychiatric outpatients with hypochondriasis were more likely to have at least one PD (73.9% vs 52.2%, p<.05), more likely to meet criteria for histrionic PD (21.7% vs 7.2%, p<.05) and obsessive compulsive PD (21.7% vs 7.0%, p<.05), and more likely to have at least one cluster C PD (39.1% vs 14.5%, p<.01).

The preceding studies are noteworthy in suggesting that patients with hypochondriasis carry a heavy burden of personality pathology - more than non-hypochondriacal patients in a primary care clinic and more than other non-somatoform psychiatric outpatients. Because most of these studies were limited by use of a screening self-report measure and because the one semi-structured interview-based study was limited by a small sample size of HYP and biased by recruitment from a psychiatric sample, the true prevalence of PD in hypochondriasis remains unknown.

While this paper focuses on personality disorders in hypochondriasis, it is worth noting that a different but valuable approach to examine personality pathology would be to examine personality dimensions or traits. This has not yet been done in patients with well-defined

hypochondriasis. In other samples however, it has been shown that there is a strong relationship between negative temperament or neuroticism and hypochondriasis [17–19]. Negative temperament is also a strong predictor of somatic distress[20] and may represent a risk factor for the development of hypochondriasis[21, 22]. A study is needed to examine whether neuroticism (or other personality dimensions such as harm avoidance or compulsivity) is significantly elevated in patients with hypochondriasis to a greater extent than in patients with other psychiatric disorders.

The primary aim of this study was to determine the prevalence of PD comorbidity using a clinician administered structured interview (SCID-II) among research volunteers with HYP who were recruited from the general community (rather than from a psychiatric outpatient clinic). The second aim of this study was to determine whether patients with hypochondriasis have more personality pathology than patients with non-somatoform disorders that share similar psychiatric features. Because hypochondriasis has been referred to as a "health anxiety disorder" [23, 24] or as "illness anxiety disorder" (proposed for DSM-5)[25], we examined the personality profile of patients with hypochondriasis and compared the results to patients with two anxiety disorders – Obsessive Compulsive Disorder (OCD) and Social Anxiety Disorder (SAD). OCD was chosen because similar to hypochondriasis it is characterized by intrusive obsessions and repetitive behaviours[26, 27]. SAD was chosen because similar to hypochondriasis it is characterized by marked circumscribed fear (illness fears for HYP and social situations for SAD)[28].

METHODS

Study Design

A total of 179 subjects who volunteered to participate in research treatment studies for HYP, OCD, and/or SAD were included in this analysis. All subjects completed the Structured Clinical Interview for DSM-III-R PDs (SCID-II, 9/1/1989 version)[10]. Subjects met DSM-III-R (as well as DSM IV) diagnostic criteria for HYP, OCD, or SAD as a primary disorder using a SCID-I interview. The HYP patients (n=62) had participated in one of 3 serotoninreuptake inhibitor (SSRI) treatment studies[29–31]; patients had to be medically healthy or medically stable for at least one year prior to enrolment in the study. The OCD group (n=46) participated in a treatment study which enrolled patients who had not responded to oral clomipramine[32]. The SAD patients (n=71) (86% of whom had the generalized SAD subtype) participated in a treatment study of moclobemide [33]. Participants in each of these studies signed a consent form approved by the NYS Psychiatric Institute IRB. The three diagnostic groups did not differ significantly in the percentage with a comorbid concurrent mood disorder (major depression or dysthymia): 50% (31/62) for the HYP group; 30% for the SAD (21/71) group; and 47.8% (22/46) for the OCD group. A comorbid PD diagnosis that was deemed severe enough to interfere with treatment compliance was an exclusion criteriion for the HYP and OCD studies; however, no subjects screened for the study were excluded for this reason. The SAD study had no PD exclusion criteria. Other exclusion criteria shared by all three studies included active suicidal ideation, recent substance abuse, psychosis, and pregnancy. Subjects were drawn from the general community in response to media advertisements or, for a small subset of the subjects with HYP, by a direct referral from family medicine physicians. Study related evaluations took place in either community based research clinics (in Brooklyn and Staten Island boroughs of New York City) or hospital based research clinics (at the NYS Psychiatric Institute for HYP, SAD, and OCD or at St. Joseph's Medical Center in Stamford, CT for HYP).

Only subjects who met threshold criteria for an Axis II diagnosis were categorized as having a PD. DSM Criteria were delineated by the SCID-II[28, 34]. SCID interviews were completed by clinically-trained raters in each respective study. For the comparison of

personality disorders across the three groups, the samples were "purified" of the subjects who had the other disorders. In other words, the HYP sample of 62 was decreased to 49 by excluding 13 HYP subjects who had comorbid SAD or OCD, the SAD sample of 71 was decreased to 70 by excluding 1 SAD subject who had comorbid OCD, and the OCD sample of 46 was decreased to 34 by excluding 12 OCD subjects who had comorbid SAD or HYP. Finally, to ensure homogeneity in recruitment method (i.e., response to public advertisements) for the group comparisons, the "purified" HYP sample was additionally reduced to a size of 42 by excluding 7 HYP subjects who came by direct referral from family medicine physicians. In addition to reporting the frequency of individual PDs within a diagnostic category, the groups were contrasted on the frequency of PD diagnoses within one of the three PD clusters. Cluster A consists of paranoid PD, schizoid PD, and schizotypal PD. Cluster B consists of narcissistic PD, histrionic PD, anti-social PD and borderline PD. Cluster C consists of avoidant PD, dependent PD, and obsessive-compulsive PD. Self-defeating and passive-aggressive PDs were not included in the analysis by cluster because these were never formally admitted into the list of recognized disorders in the DSM.

Statistical Analysis

To compare the demographic characteristics of the samples within each of the diagnostic groups, chi-square analysis and ANOVA F-tests were used. Four outcome variables were selected to be of primary interest: the presence of multiple PDs (at least 2) and the presence of, at least one Cluster A, B, and C PD. Because the distribution of PDs may vary by gender and age, gender and age were included as variables that might affect outcome. Logistic regression analysis was used to test the effect of age, group (the Axis I diagnosis of HYP, OCD, SAD) and gender (M, F) and the interaction of gender and group on the dichotomous outcome variables. Due to the exploratory nature of the analysis, the interaction term was considered significant if its p-value was below the level of significance of 10%. In such case, the contrasts for different groups and different genders would be evaluated. If the interaction term was not significant, the interaction term was omitted from the analysis and the main effect of group and gender on the outcome was evaluated. In the case of significant main effect of group (p-value < 5%) or trend significance (p-value < 10%), the contrasts between the HYP group and other groups (OCD and SAD) were computed. All contrasts were considered significant if their p-value was below level of significance 5%. Race was not included as an interaction term because our sample was underpowered for an analysis with so many categories.

RESULTS

Demographics (Table 1)

There were no significant differences among the 3 groups in age (F=0.83, df=2, p=0.438) or gender (X^2 =3.47, df=2, p=0.177). There were significant differences in race (X^2 =27.15, df=4, p<.001). Compared to the HYP group, the OCD group had a significant overrepresentation of Caucasians and absence of Hispanics.

Individual Personality Disorders (Table 1)

40.3% (25/62) of the larger sample of study participants with HYP had at least one personality disorder. Table 1 reports the prevalence of individual PDs for the "purified" groups. The high rate of avoidant PD in the social anxiety disorder sample likely reflects the known overlap in symptomatology between SAD and avoidant PD.

Axis II Comorbidity (Table 2)

Table 2 presents the mean number and standard deviations of PDs along with the proportional distribution of PDs (no axis II disorder, one Axis II disorder and multiple (two or more) Axis II disorders) as well as the proportion of subjects with at least one PD within each personality cluster.

Effects of gender, group and age on outcome variables (Table 3)

Table 3 presents logistic regression results for the four outcome variables (the presence of at least 2 PDs, at least one Cluster A, B, and C PD). The interaction between gender and group was not significant for any of the four models. The main effect of gender and age was also not significant in any of the models after removing the interaction term from the model. The main effect of group was significant for 1 outcome variable: at least one cluster C (p-value=.001). The group effect for at least one Cluster A variable showed a trend (p-value=.079) with a between group significant difference for HYP vs. SAD. For those 2 outcome variables, the pair-wise comparisons (shown in the 'Group Contrasts' part of the table) between HYP and OCD or HYP and SAD were evaluated and the odds ratio were presented in the second part of the table along with their corresponding p-values.

- **a.** Outcome variable: 2 or More PDs. We found no significant interaction effect and also no significant main effect of variables gender, group and age.
- **b.** Outcome variable: At Least 1 Cluster A PD. The group differences were significant on the trend level. The HYP group was about 4x (odds ratio = 3.9) more likely to have at least one cluster A PD than the SAD group (p-value=.041).
- **c.** Outcome variable: At Least 1 Cluster B PD. We found no significant interaction effect and also no significant main effect of variables gender, group and age.
- **d.** Outcome variable: At Least 1 Cluster C PD. The SAD group was approximately 5 (odds ratio = 5.08 = 1/0.197) times more likely to have at least one cluster C PD than the HYP group (p-value=<.001).

DISCUSSION

This study examined the prevalence of personality disorders among research outpatients with hypochondriasis using a structured diagnostic interview. The results demonstrate that 40.3% of these patients with hypochondriasis met criteria for an Axis II disorder. This is a notable finding as prior research found higher rates of personality comorbidity (63–73%)[5–7]; these higher rates however are likely over-estimates reflecting the known limitations of self-report PD measures[12–16] and the greater overall psychopathology typically accompanying patients drawn from a psychiatric outpatient clinic as compared to a community sample[8]. Our study identified hypochondriacal patients from the general community through the use of advertisements in community newspapers. As suggested by others[35], the study of personality disorders among patients with somatoform disorders is best when conducted directly from the community, as personality pathology may be overrepresented when samples are drawn from psychiatric or medical clinic settings.

In theoretical reviews and clinical reports, somatoform disorders have been associated with comparatively high rates of personality comorbidity [36–38], leading some investigators to recommend reconceptualising these disorders as consequences of early developmental trauma or deficit[36]. In a survey of British psychiatrists, over half of the respondents believed that their somatizing patients suffered from personality disorders[39]. An overview concluded that "somatoform disorders are associated with a higher rate of personality disorder than is found in any other group of syndromes classified as mental illnesses (axis I

disorders)"[36]. While this conclusion may be true among patients with somatization disorder or somatoform pain disorder, the results of our study suggest that this conclusion may not be applicable to community patients with hypochondriasis. At least among research volunteers from the general community all of whom were assessed by the same semi-structured diagnostic interview, the prevalence of PD among patients with hypochondriasis is similar to the prevalence among patients with anxiety disorders that also are characterized by excessive worry or fearful thoughts.

The most frequently seen personality disorder in the hypochondriasis sample was paranoid personality disorder (19.1%), accounting for the higher rate of at least one Cluster A diagnosis in the HYP group compared to the SAD group. This finding is consistent with recent research demonstrating that mistrust and hypochondriacal concerns are significantly correlated in a sample of veterans[18]. Could it be that the high rate of paranoid personality disorder identified in our study reflects the consequence of an increasingly negative medical encounter during which one's symptoms are repeatedly dismissed as being "in your head", evolving over time from a specific distrust of doctors to a generalized paranoid interpersonal style? This question can only be answered by a longitudinal study that examines whether patients with hypochondriasis develop generalized paranoid features over years or whether paranoid personality itself is a risk factor for the emergence of hypochondriasis.

In addition to paranoia, other personality features were found to be common among patients with hypochondriasis in this study: obsessive compulsive, avoidant, borderline, selfdefeating and passive-aggressive. An awareness of how these comorbid features adversely affect the doctor-patient relationship can enhance the physician's skill in providing more effective and compassionate care[40]. For example, because the patient with comorbid paranoid features may be angry and suspicious of being deceived by the doctor, the physician should be especially open, thorough, and honest with the patient, clarifying why medical tests are ordered, showing the results, and discussing the rationale for ordering or not ordering additional medical evaluations/interventions. The hypochondriacal patient with obsessive personality highly values details and control; he or she would appreciate the doctor's use of a check list to review symptoms, a detailed discussion of the differential diagnosis and treatment options, and an office visit that does not "cheat" the patient of time. The patient with avoidant features might be fearful to raise questions with the doctor, so the physician should probe more directly for other unexpressed concerns. The patient with comorbid borderline features, fearing separation or abandonment, might react to the physician's upcoming vacation with angry devaluation or increased hypochondriacal anxiety; the physician can help by reassuring the patient of ongoing care and by providing dates of return and the name of a colleague for coverage. Hypochondriacal patients with self-defeating and passive-aggressive features, labelled sometimes as "hateful patients" [41], often develop new symptoms just when recovery is immanent and can mobilize intense feelings in physicians, making them feel helpless, inadequate, and responsible for their severe suffering; with these patients, it is helpful to empathize with the realistic suffering and pain caused by the somatic symptoms and to state that improvement, although likely, is a slow process. These examples demonstrate the valuable role mental health providers can play in educating their medical colleagues about how understanding personality traits can improve patient care.

The analysis of research volunteers with HYP compared to two other anxiety disorders revealed more similarities between HYP and OCD than between HYP and SAD. The HYP and OCD groups shared a high degree of comorbidity with paranoid personality disorder (19.1%, 14.7%, respectively). Both HYP and OCD also had a similar proportionate distribution (none, 1, > 1) of personality disorders (see Table 2). Both groups also had a similar proportion of having at least one cluster A, B and cluster C disorder. These findings

- emerging from a study of personality disorders - suggest that HYP and OCD share important features. Indeed clinical research over the last two decades has identified many areas of overlap between hypochondriasis and obsessive compulsive disorder. On the clinical level, these include repetitive intrusive thoughts, compulsions to check for reassurance, and an intolerance of uncertainty about the meaning of feared stimuli[26, 27, 42]. More recently, case and family data from the OCD Collaborative Genetics Study demonstrates that hypochondriasis is more commonly found in OCD cases and their first degree relatives [43] than in matched controls and their families. These findings, along with the similarities in personality features identified in our study, would suggest that HYP and OCD may share underlying pathophysiologic processes. A DSM-V workgroup has examined whether HYP (as a disorder characterized by intrusive worry and anxiety) would best be moved from the Somatoform section of the DSM manual to the Anxiety Disorder section or grouped into a new section entitled "Obsessive Compulsive Spectrum Disorders"; in fact, the current draft of the DSM-5 manual renames hypochondriasis as "illness anxiety disorder" [23–25, 44–46]. The results of our study do support the growing body of evidence identifying a preferential relationship between HYP and OCD. However, to best be able to draw conclusions about HYP's placement in the DSM manual (a topic beyond the scope of this paper), one would require comparison studies that include patients with somatization disorder as well as those with anxiety and OCS disorders.

Research over the last decade reveals that treatment-seeking patients with personality disorders are accountable for a high financial burden on society[47]. The amount of direct medical costs in particular has been associated with certain personality types – paranoid, borderline, and obsessive-compulsive[48]. Given that these personality types ranked in the top four of all personality types found in our HYP sample, it is likely that treatment interventions among hypochondriacal individuals that address not only illness anxiety but also comorbid personality pathology would result in both improved personal well-being and a reduction in health care costs.

Our study's primary strength is that this is the first U.S. study to describe the range of Axis II comorbidity among patients with hypochondriasis using a structured diagnostic interview that is considered a reliable measure[49]. The sample size is nearly three times as large as the only previously published study of PD in hypochondriasis which used a structured diagnostic instrument[8]. An additional strength of this study was the comparison of HYP patients with a control group of patients carrying two other primary Axis I diagnoses and, for the group contrasts, the "purification" of the samples of individuals carrying the comparison comorbid diagnoses. Given that all patients were volunteer participants in research treatment studies, this study is valuable in its recruitment focus on community volunteers as opposed to patients drawn from a psychiatric or medical clinic. In addition, because the 3 groups were recruited in the same fashion (public advertisements), homogeneity across groups was present by nature of the selection process itself.

This analysis of the relationship between HYP and other anxiety disorders also has limitations. First, confounding variables may have influenced personality comorbidity[50]; larger sample sizes are needed to examine the impact of other variables such as ethnicity or race. Second, because patients with more severe psychiatric disorders may be more likely to have a concomitant personality disorder complicating the course of illness, matching patients based on illness severity would have been useful. Because we did have a scores on severity measure of global psychopathology (SCL-90 Global Symptom Index) on a substantial portion of our patient sample (25 HYP, 34 OCD, 57 SAD) and no significant difference was noted in Global Symptom Index means (1.30 +/-.8 HYP, 0.91 +/-.6 OCD, 1.00 +/-.7 SAD) either across or between groups, we think it unlikely that there was a clinically significant group difference in psychopathology severity; this conclusion however

is tempered by the observation that SCL-90 scores were not available on all patients. Third, our sample size while larger than the only previously reported study that used a clinician administered interview, is still relatively small; larger sample sizes with more closely matched samples are needed to adequately compare personality comorbidity profiles among patients with Axis I disorders. Fourth, the results of this study may not be generalizable to the broader community of individuals who choose not to participate in a research treatment study and they may not be generalizable to a clinical population. Finally, this study relied upon the SCID-II which results in a categorical determination of PDs rather than a dimensional one with continuous data; studies that use other measures to tap different personality dimensions and constructs would also be helpful to clarify the relationship among these disorders.

Conclusion

About 40% of individuals with hypochondriasis from the general community do have personality disorder comorbidity as assessed by the SCID-II. This comorbid personality psychopathology may affect not only treatment outcome but also treatment preference (e.g., medication vs psychotherapy); future clinical trials should include measures that assess both personality dimensions and personality disorders as potential mediating variables in treatment preference and outcome. This study also shows that patients with HYP are not likely to carry a heavier burden of Axis II comorbidity than individuals with two anxiety disorders also characterized by excessive worry and fear (OCD and SAD). Health care professionals therefore should avoid the automatic assumption that the root cause of hypochondriacal distress is an underlying personality disorder.

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Table 1

Demographics and Diagnoses

	Нуро	chondriasis	Obsessive- Compulsive Disorder	Social Anxiety Disorder
	Full Sample n=62	Purified Sample* n=42	Purified Sample* n=34	Purified Sample* n=70
Age (mean yrs ±SD)	38.0±11.7	36.7±11.51	36.7±10.44	34.5±9.57
Female (%)	59.7	52.4	32.4	38.6
Caucasian (%)	45.2	40.5	94.1	61.4
Hispanic (%)	37.1	42.9	0	20.0
CLUSTER A				
Paranoid (%)	19.4	19.1	14.7	5.7
Schizotypal (%)	0.0	0	2.9	0.0
Schizoid (%)	1.6	2.4	2.9	0.0
CLUSTER B				
Histrionic (%)	1.6	0	2.9	0.0
Narcissistic (%)	4.8	4.8	2.9	4.3
Borderline (%)	8.1	9.5	5.9	2.9
Anti-social (%)	0.0	0.0	2.9	0.0
CLUSTER C				
Avoidant (%)	17.7	11.9	17.7	60.0
Dependent (%)	4.8	2.4	17.7	7.1
Obsessive Compulsive (%)	14.5	14.3	20.6	4.3
OTHER				
Passive Aggressive (%)	6.5	4.8	5.9	0.0
Self-Defeating (%)	9.7	4.8	11.8	5.7
Not otherwise specified (%)	4.8	7.1	0	1.4

^{*}Purified Samples contain the subjects that have the specified diagnosis but not those who also have the comorbid diagnoses of comparison groups..

 Table 2

 Percent subjects with co-morbid Axis II disorders by diagnostic group in purified samples

	Hypochondriasis n=42	Obsessive Compulsive Disorder n=34	Social Anxiety Disorder n=70
Axis II disorders (Mean ± SD)	0.8 ± 1.40	1.1 ± 1.71	0.9 ± 1.11
No Axis II disorders (%)	64.3	52.9	38.6
1 Axis II disorder (%)	14.3	26.5	47.1
2 or more Axis II disorders (%)	21.4	20.6	14.3
At least 1 Cluster A disorder (%)	19.1	17.7	5.7
At least 1 Cluster B disorder (%)	11.9	11.8	7.1
at least 1 Cluster C disorder (%)	23.8	38.2	60.0

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Model-based comparisons of impact of Axis 1 diagnosis, age, and gender on Axis II diagnoses in purified samples

		2 or more PD		At least 1 Cluster A PD	A PD	At least 1 Cluster B PD	3 P.D	At least 1 Cluster C PD	CPD
		Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI) p-value	p-value	Odds Ratio (95% CI)	p-value
Age		1.00 (0.96, 1.04) 0.957	0.957	0.98 (0.93, 1.02) 0.312	0.312	0.96 (0.91, 1.02) 0.145	0.145	1.01 (0.98, 1.05) 0.432	0.432
Gender		0.80 (0.34, 1.91) 0.610	0.610	0.66 (.23, 1.87) 0.436	0.436	0.85 (0.27, 2.74) 0.789	0.789	0.87 (0.43, 1.80) 0.715	0.715
Group			0.590		0.079		0.568		0.001
otombaco, arrono				0.99 (0.30, 3.32) 0.990	0.990			0.49 (0.18, 1.34) 0.164	0.164
Group Contrasts	HYP-SAD			3.83 (1.06,13.89) 0.041	0.041			0.20 (0.08, 0.47) <0.001	<0.001

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