

See “Psychological profiles of irritable bowel syndrome patients with different phenotypes” on page 459-468.

## SUPPLEMENTARY TEXT

### 1. Description of the Additional Items

Sixty additional items are used in the Minnesota Multiphasic Personality Inventory 2 (MMPI-2): 15 content, 14 supplementary, and 31 Harris-Lingoes scales:

- The 15 content scales are Anxiety (ANX), Fears (FRS), Obsessiveness (OBS), Depression (DEP), Health concerns (HEA), Bizarre mentation (BIZ), Anger (ANG), Cynicism (CYN), Antisocial practices (ASP), Type A behavior (TPA), Low-self-esteem (LSE), Social discomfort (SOD), Family problems (FAM), Work interference (WRK), and Negative treatment indicators (TRT).
- The 14 supplementary scales are ego strength (Es), MacAndrew alcoholism revised scale (Mac-R), addiction potential scale (APS), addiction acknowledgment scale (AAS), anxiety scale (A), repression scale (R), over-controlled hostility (O-H), dominance scale (Do), social responsibility scale (Re), college maladjustment (Mt), post-traumatic stress disorder scale (PK), post-traumatic stress disorder scale (PS), masculine gender role (GM), feminine gender role (GF).
- The 31 Harris-Lingoes scales were derived for the MMPI-2, and are used for scales Depression (D), Hysteria (Hy), Psychopathic deviate (Pd), Paranoia (Pa), Schizophrenia (Sc), Hypomania (Ma) and Social introversion (Si). These scales are Subjective Depression (D1), Psychomotor retardation (D2), Physical malfunctioning (D3), Mental dullness (D4), Brooding (D5), Denial of social anxiety (Hy1), Need for affection (Hy2), Lassitude malaise (Hy3), Somatic complaints (Hy4), Inhibition of aggression (Hy5), Familial discord (Pd1), Authority problems (Pd2), Social imperturbability (Pd3), Social alienation (Pd4), Self-alienation (Pd5), Persecutory ideas (Pa1), Poignancy (Pa2), Naiveté (Pa3), Social alienation (Sc1), Emotional alienation (Sc2), Lack of ego mastery, cognitive (Sc3), Lack of ego mastery, conative (Sc4), Lack of ego mastery, defective inhibition (Sc5), Bizarre sensory experiences (Sc6), Amorality (Ma1), Psychomotor acceleration (Ma2), Imperturbability (Ma3), Ego inflation (Ma4), Shyness/Self-consciousness (Si1), Social avoidance (Si2), and Alienation-self and others (Si3).

### 2. Differences in T Scores on the Psychological Characteristics of IBS Patients

The results of the content, supplementary and Harris-Lingoes scales for irritable bowel syndrome (IBS) and non-IBS patients are shown in the Supplementary Table 1.

IBS patients have significantly higher scales for 10 of the 15 content scales: Anxiety (ANX,  $P < 0.001$ ), Obsessiveness (OBS,  $P = 0.001$ ), Depression (DEP,  $P < 0.001$ ), Health concern (HEA,  $P < 0.001$ ), Bizarre mentation (BIZ,  $P = 0.006$ ), Anger (ANG,  $P < 0.001$ ), Cynicism (CYN,  $P = 0.004$ ), Family problems (FAM,  $P < 0.001$ ), Work interference (WRK,  $P < 0.001$ ) and Negative treatment indicators (TRT,  $P < 0.001$ ). Only the Fears scale (FRS,  $P = 0.071$ ) was not different from other functional gastrointestinal disorders (FGIDs) patients.

Among supplementary scales, IBS patients have significantly lower values for 3 items: Ego strength (Es,  $P < 0.001$ ), Dominance scale (Do,  $P = 0.002$ ) and Masculine gender role (GM,  $P = 0.001$ ), and significantly higher values for 5 items: Anxiety scale (A,  $P < 0.001$ ), College maladjustment (Mt,  $P < 0.001$ ), Marital distress score (MDS,  $P < 0.001$ ), and the 2 Post-traumatic stress disorder scales (PS;  $P < 0.001$  and PK,  $P < 0.001$ ).

Among the 31 Harris-Lingoes scales, 18 were higher in IBS patients: Subjective depression (D1,  $P < 0.001$ ), Physical malfunctioning (D3,  $P < 0.001$ ) Mental dullness (D4,  $P < 0.001$ ), Brooding (D5,  $P = 0.001$ ), Lassitude malaise (Hy3,  $P < 0.001$ ), Somatic complaints (Hy4,  $P < 0.001$ ), Social alienation (Pd4,  $P = 0.001$ ), Self-alienation (Pd5,  $P < 0.001$ ), Persecutory ideas (Pa1,  $P = 0.001$ ), Poignancy (Pa2,  $P < 0.001$ ), Social alienation (Sc1,  $P < 0.001$ ), Emotional alienation (Sc2,  $P < 0.001$ ), Lack of ego mastery, cognitive (Sc3,  $P < 0.001$ ), Lack of ego mastery, conative (Sc4,  $P < 0.001$ ), Lack of ego mastery, defective inhibition (Sc5,  $P < 0.001$ ), Bizarre sensory experiences (Sc6,  $P < 0.001$ ), Ego inflation (Ma4,  $P = 0.003$ ), Alienation-self and others (Si3,  $P < 0.001$ ).

### 3. Frequency of Abnormal Values

We report in Supplementary Table 2 the frequency of subjects that in IBS and non-IBS groups have scored in the abnormal range ( $T > 70$ ). Globally, IBS patients have a higher frequency of 2 abnormal validity scales and 5 clinical scales. The results of the content, supplementary and Harris-Lingoes scales are shown in the Supplementary Table 3 and described in the fourth paragraph of the supplementary text.

Concerning validity scales, IBS patients report a significant higher abnormal scale for Infrequency scale (F,  $P < 0.001$ ) and for Infrequency scale back (Fb,  $P < 0.001$ ), and among clinical scales, IBS patients have a significantly higher frequency of abnormal score for 5 items: Hypochondriasis (Hs,  $P < 0.001$ ), Depression (D,  $P < 0.001$ ), Hysteria (Hy,  $P < 0.001$ ), Paranoia (Pa,  $P < 0.001$ ), and Schizophrenia (Sc,  $P < 0.001$ ).

The logistic regression shows that IBS group is associated to a significant increased frequency of abnormal value for Infrequency scale (F;  $P = 0.004$ ; odds ratio [OR], 1.861; 95% confidence interval [CI], 1.219–2.839) and Hypochondriasis (Hs;  $P < 0.001$ ; OR, 2.908; 95% CI, 2.059–4.107).

### 4. Frequency of Abnormal Values of the Additional Items

The Supplementary Table 3 summarizes the results of this analysis. Among content scales, IBS patients have a significantly higher frequency of abnormal scales for Anxiety (ANX,  $P < 0.001$ ), Depression (DEP,  $P < 0.001$ ), Health concern (HEA,  $P < 0.001$ ), Bizarre mentation (BIZ,  $P = 0.007$ ), Cynicism (CYN,  $P = 0.005$ ), and Work interference (WRK,  $P < 0.001$ ).

IBS patients also report a significantly higher frequency of abnormal scales for 5 supplementary scales: Addiction acknowledgment scale (APS,  $P = 0.004$ ), Anxiety scale (A,  $P < 0.001$ ), College maladjustment (Mt,  $P = 0.007$ ), and the 2 Post-traumatic stress disorder scales (PK,  $P = 0.001$  and PS,  $P < 0.001$ ).

Among the Harris-Lingoes scales, IBS patients report a higher frequency of abnormal scales for Subjective depression (D1,  $P < 0.001$ ), Physical malfunctioning (D3,  $P < 0.001$ ), Mental dullness (D4,  $P < 0.001$ ), Brooding (D5,  $P = 0.007$ ), Lassitude malaise (Hy3,  $P < 0.001$ ), Somatic complaints (Hy4,  $P < 0.001$ ), Social alienation (Pd4,  $P = 0.001$ ), Self-alienation (Sc2,  $P = 0.001$ ), Persecutory ideas (Pa1,  $P < 0.001$ ), Poignancy (Pa2,  $P < 0.001$ ), Social alienation (Pd4,  $P = 0.007$ ), Emotional alienation (Sc2,  $P = 0.001$ ), Lack of ego mastery, cognitive (Sc3,  $P = 0.001$ ), Lack of ego mastery, conative (Sc4,  $P < 0.001$ ), Lack of ego mastery, defective inhibition (Sc5,  $P < 0.001$ ), Bizarre sensory experiences (Sc6,  $P < 0.001$ ), and Alienation-self and others (Si3,  $P = 0.006$ ).

### 5. Psychological Characteristics of IBS Subtypes Patients

The results of the content, supplementary and Harris-Lingoes scales among IBS patients are shown in the Supplementary Table 4.

The analysis showed significant differences for one content scale, Cynicism (CYN,  $P = 0.009$ ), 6 supplementary scales, Ego strength (Es,  $P = 0.002$ ), Dominance (Do,  $P = 0.003$ ), College maladjustment (Mt,  $P < 0.001$ ), Post-traumatic stress disorder (PK,  $P = 0.005$  and PS,  $P = 0.009$ ), Masculine gender role (GM,  $P = 0.009$ ) and 18 Harris-Lingoes scales: 4 subscales of depression (D1,  $P < 0.001$ ; D3,  $P < 0.001$ ; D4,  $P < 0.001$ ; and D5,  $P = 0.001$ ), 2 subscales of Hysteria (Hy3 and Hy4,  $P < 0.001$  for each item), 2 subscales of Psychopathic deviate (Pd4 and Pd5,  $P < 0.001$  for each), 2 subscales of Paranoia (Pa1,  $P = 0.001$  and Pa2,  $P < 0.001$ ), all 6 subscales of Schizophrenia ( $P < 0.001$  for all items), 1 subscale of Hypomania (Ma4,  $P = 0.001$ ) and 1 subscale of social introversion (Si3,  $P < 0.001$ ).

As shown in the Supplementary Table 4, abnormal scales ( $T > 70$ ) are found in 3 supplementary scales: College Maladjustment (Mt,  $P = 0.002$ ), and the 2 Post-Traumatic Stress Disorder scales PK ( $P = 0.001$ ) and PS ( $P = 0.002$ ), and 2 of the 31 Harris-Lingoes scales: Physical malfunctioning (D3,  $P < 0.001$ ) and Lack of ego mastery, cognitive (Sc3,  $P = 0.003$ ).

### 6. Frequency of Abnormal Values in the Different IBS Subtypes

Supplementary Table 5 shows the frequency of subjects in each IBS subgroup with validity and clinical scales in the abnormal range ( $T > 70$ ). Supplementary Table 6 shows the frequency of abnormal content, supplementary, and Harris-Lingoes MMPI scales according to the IBS phenotypes.

Differences in the frequency of abnormal scales are found in only 2 clinical scales (Supplementary Table 5): Paranoia (Pa,  $P < 0.006$ ), and Schizophrenia (Sc,  $P = 0.001$ ).

## 7. Discussion of the Content, Supplementary and Harris-Lingoes Scales

Classically, patients suffering from IBS who ask for medical help because of their intestinal symptoms, present emotional problems such as depression and anxiety and have a neurotic personality.<sup>1,2</sup> Our findings agree with previous studies conducted among patients inferring that IBS patients tend to have more neurotic and depressed personalities than normal subjects.<sup>2,3</sup>

By comparison to other FGIDs patients, the elevated depression and hysteria scales indicate a personality background characterized by severe emotional disturbance involving low self-esteem, lack of self-confidence, and somatic over-concern. The elevated paranoia scale indicates that IBS patients tend to be more suspicious, oversensitive, and even more negative in their attitudes towards people.

In IBS patients, the increase of hysteria,<sup>3-5</sup> Masculinity-Femininity,<sup>6</sup> and paranoia<sup>3,5</sup> scales were previously described, but these increases were noted by comparison to healthy controls. Our results indicate that the increase of these 3 scales is mainly associated with IBS in FGIDs patients. Other scales found significant after univariate analysis were also described in IBS patients: Hypochondriasis,<sup>4,5,7</sup> Depression,<sup>1,3-5,7,8</sup> Psychasthenia,<sup>9</sup> Schizophrenia,<sup>10,11</sup> and Hypomania.<sup>7</sup> Nevertheless, only Hypochondriasis remains significant after multivariate analysis in the present study. The high level of hypochondriasis associated with the high frequency of abnormal score for this item tends to use hypochondriasis as an important psychological factor in IBS patients. This factor was previously characterized as a risk factor for post-infectious IBS,<sup>12,13</sup> and associated with severe symptoms.<sup>14</sup>

The analysis of content, supplementary, and Harris-Lingoes scales shows that by comparison to non-IBS patients, Anxiety, and Health concern only remain significantly higher in IBS patients after multivariate analysis.

High anxiety level is frequently reported in IBS patients<sup>1,5,8,15,16</sup> whatever the used test (State and Trait anxiety, Hospital Anxiety, and Depression Scale). In the MMPI-2 test, high anxiety is associated with tension, worry, fears of losing one's mind, lack of confidence, and somatic indications of anxiety such as heart pounding, shortness of breath, and disturbed sleep.<sup>17</sup> High Health concern scale is frequently associated with gastrointestinal symptoms, neurological symptoms, sensory problems, dermatological problems, pain, and respiratory problems.<sup>17</sup>

Health concern was also found high in patients with chronic headache,<sup>18,19</sup> in patients with inflammatory bowel diseases<sup>20</sup> and IBS patients, in those that report severe symptoms,<sup>21</sup> poor quality of life,<sup>22</sup> and food-related symptoms.<sup>23</sup>

Three scales (Ego strength, Dominance scale, Masculine gender role) were lower in IBS patients. However, these changes were not confirmed after multivariate analysis. It was shown previously that Masculine gender scale correlated with psychological well-being,<sup>24</sup> and that Masculine gender scale and Feminine gender scale are more related to personality traits of interpersonal potency and sensitivity, respectively than to masculinity and femininity.<sup>25</sup> In previous studies, psychosocial adaptation to cancer was related to a patient's ego strength, Ego strength scale correlating positively with a patient's use of effective coping strategies.<sup>26</sup> Similarly, weakened ego strength was closely associated with several forms of psychological distress, especially depressive symptoms in patients with multiple sclerosis.<sup>27</sup>

On the 31 Harris-Limoges scales, 17 were significantly higher in IBS patients, but only one scale, Shyness/Self-consciousness, remain significantly lower after multivariate analysis. This Social Introversion subscale was found as a risk factor for anorexia nervosa/purging type.<sup>28</sup> It was shown that the combined Shyness/Self-Consciousness (Si1) and Social Avoidance (Si2) subscales correlated highly with Social Discomfort and are apparent measures of the social introversion construct.

Concerning abnormal values, IBS was associated with 3 Harris-Limoges scales: an increase of abnormal Poignancy, a Paranoia subscale, an increase of abnormal Lack of ego mastery, conative, a Schizophrenia subscale. Poignancy is the depressive component of the Paranoia scale. The items connote excessive emotional sensitivity or vulnerability. Similarly, high value for Lack of ego mastery, conative is in favor of depression, difficulty coping, inertia, regression into fantasy, and pessimism.

It should be noted that the mean T scores of our IBS patients on the Hypochondriasis, Depression, and Hysteria scales were significantly higher from a statistical point of view than those of other FGID's controls. However, their mean T scores were not above 70 and, therefore, not clinically significant. A group of IBS patients can have psychological conditions on the average that are not psychiatrically significant, yet display similar colonic motor and myoelectric behavior in stress and rest to IBS patients in other studies with psychiatrically significant conditions.<sup>4</sup> Our data support our belief that the psychiatric condition of IBS patients may be an important factor in the clinical expression of IBS,<sup>4</sup> but no significant correlation was found between cholinergic innervation and MMPI scales in a study on 40 Rome I IBS patients.<sup>3</sup>

Another concern is that there is no assessment of IBS or FGID severity, quality of life, or other factors that might affect the MMPI results. IBS patients with more severe pain could score more abnormally on MMPI, and despite IBS patients are a chronic pain population, those with milder symptoms could have more marked psychological abnormalities. Some specific tests were used to assess the IBS severity (e.g., IBS-quality of life,<sup>29-31</sup> IBS-symptom severity score<sup>32</sup>). Change of IBS symptom and severity is well known.<sup>33-36</sup> The MMPI-2 was conceptualized to be a measure of longstanding traits, and to be robust to changes over time. The day to day variation of IBS severity<sup>34,35</sup> have a low influence on the MMPI scales.<sup>37</sup>

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