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"Frontal lobe syndrome"? Subtypes of acquired personality disturbances in patients with focal brain damage

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Abstract

Conceptualizations of the nature of acquired personality disturbances after brain damage, especially to prefrontal cortex, have progressed from clinical observations of a large, disparate set of disturbances to theories concerning neuroanatomically-based subgroups with prefrontal damage. However, hypothesized subtypes have not yet been studied systematically. Based on our previous investigations of acquired personality disturbances, we hypothesized five subtypes of acquired personality disturbances: Executive Disturbances, Disturbed Social Behavior, Emotional Dysregulation, Hypo-emotionality/De-Energization, and Distress, as well as an undisturbed group. Subtypes were investigated in 194 adults with chronic, stable, focal lesions located in various aspects of prefrontal lobes and elsewhere in the brain, using two different cluster analysis techniques applied to ratings on the Iowa Scales of Personality Change. One technique was a hypothesis-driven approach; the other was a set of strictly empirical analyses to assess the robustness of clusters found in the first analysis. The hypothesis-driven analysis largely supported the hypothesized set of subtypes. However, in contrast to the hypothesis, it suggested that disturbed social behavior and emotional dysregulation are not two distinct subtypes, but two aspects of one multifaceted type of disturbance. Additionally, the so-labeled "executive disturbances" group also showed disturbances in other domains. Results from the second (empirical) set of cluster analyses were consistent with findings from the hypothesis-driven cluster analysis. Overall, findings across the two cluster analyses indicated four subtypes of acquired personality disturbances: (1) executive disturbances in association with generalized disturbance,

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(2) dysregulation of emotions and behavior, (3) hypo-emotionality and de-energization, and (4) distress/anxiety. These findings show strong correspondence with subtypes suggested by prominent models of prefrontal systems based on neuroanatomically-defined circuits. Clarification of distinctive subtypes of acquired personality disturbances is a step toward enhancing our ability to tailor rehabilitative interventions for patients with prefrontal brain injuries.

Keywords

Prefrontal cortex; prefrontal systems; focal lesion; personality assessment

1. Introduction

Personality changes after frontal lobe injury were described in the French literature as far back as 1835 by de Nobele (Blumer and Benson, 1975) and in the English popular press in 1840 by Edgar Allen Poe (Altschuler, 2004). A few decades later in North America, an especially compelling demonstration of dramatic personality changes following injury to the frontal lobes was presented by the famous case of Phineas Gage (Harlow, 1868): Gage was a polite, responsible and industrious young man until an accidental explosion drove a tamping iron through his prefrontal cortex, resulting in profound disturbances including poor judgment, lack of planning, disinhibition, socially inappropriate behavior, emotional dysregulation, and insensitivity (H. Damasio, Grabowski, Frank, Galaburda, & A. R. Damasio, 1994). At the end of the 19th century, Phelps (1898, cited in Lishman, 1968) reported an association between disturbances of “higher psychic phenomena and psychiatric disturbance” following damage to frontal lobes based on his investigation of location of brain damage and development of psychiatric disturbance in a series of 225 patients with gunshot wounds. Rylander (1939) catalogued a wide array of personality changes in a series of 32 patients undergoing partial resection of frontal lobes for tumor or abscess; he noted a striking resemblance to the disturbances found in previous studies and concluded that these disturbances were frequent and specific sequela of frontal lobe lesions.

In the early 20th century, several German investigations of personality disturbances in returning soldiers with acquired brain injuries and frontal damage documented apathy, poor planning, irritability, tactlessness, facetiousness, euphoria and moral defects, as well as problems with attention and planning (reviewed by Lishman, 1968). These frequent findings contributed to a conceptualization of generalized personality and emotional disturbances exemplified by Lishman’s conclusion: “We have learned to recognize a ‘frontal lobe syndrome’ which does not depend on cognitive disturbance at its core” (p. 374). Logue (1968) exhaustively catalogued neurological, cognitive, emotional and personality changes in a series of 79 patients surviving anterior cerebral aneurysm ruptures. Principal components analysis yielded four components: The first, most prominent component involved cognitive, executive and memory deficits. The second was bipolar, reflecting decreased tendency to worry, reduced irritability, elevated mood and increased sociability — or changes in the opposite direction. The third reflected disinhibition, “affective flattening” vs. “affective release” (i.e., exaggerated emotional expressiveness), and being more sociable, outspoken, and irritable. The fourth reflected left-sided neurological damage and aphasic

symptoms. Logue noted the pattern of findings to be consistent with those seen in the series of Rylander (1939). Contemporaneously, Storey (1970) reported careful investigation of personality changes and association with lesion sites in 261 patients with subarachnoid hemorrhage. He noted that 41% had personality disturbances involving emotion, cognition and behavior, which he referred as "frontal lobe syndrome" although the nature of observed disturbances was quite varied. Personality changes have been reported following anterior communicating artery aneurysms, and the similarity of such personality changes to the so-called frontal syndrome has been noted (DeLuca & Diamond, 1995; Steinman & Bigler, 1986). Such personality and cognitive disturbances continued to be referred to as "frontal lobe syndrome" by numerous other investigators into the present century (e.g., Lyketsos, Rosenblatt, & Rabins, 2004).

In a departure from the prevailing focus on a general frontal lobe syndrome, some earlier investigators differentiated among the behavioral disturbances. Kleist (1939) noted differences in the consequences of damage to the lateral convexity, with cognitive changes more common, and those involving orbital cortex, with emotional disturbances predominating. Walch (1956), studying a series of 356 patients with frontal brain injuries, and shortly thereafter Kretschmer (1956) and then Luria (1969), each described two major types of personality changes: one including disinhibition, impulsivity and euphoria associated with orbital damage; the other including apathy and restricted interests associated with damage elsewhere. In 1975, Blumer and Benson reviewed 140 years of literature on personality changes after frontal lobe injury and concluded that there are two types of changes: "pseudopsychopathic," associated with orbital prefrontal damage, and "pseudodepressed," associated with damage to the prefrontal convexity.

The development of prominent personality disturbances following frontal lobe damage was a widely recognized phenomenon by this point, but Stuss and Benson (1984) emphasized that such disturbances were a morass of behavioral abnormalities, with the term "frontal lobe syndrome" referring to "an amorphous, varied group of deficits, resulting from diverse etiologies, different locations, and variable extents of abnormalities." They suggested that, although most patients have some mixture of problems, the complex set of behavioral disturbances with frontal damage would be better understood with further attention to distinct functional systems involving different prefrontal regions. They posited that these prefrontal systems could be inferred from the patterns of neuroanatomical connections and from clinical-anatomical correlations, including at least the two behaviorally-separable subtypes described by Blumer and Benson (1975). Thoughtful neuroanatomical and functional analysis led Cummings (1993, 1995) to propose three subtypes of behavioral disorders associated with lesions in three segregated prefrontal circuits: disinhibition with lesions to an orbitofrontal circuit, executive function deficits with lesions to the dorsolateral circuit, and apathy with damage to the anterior cingulate circuit.

Emphasizing behavioral changes as the primary deficits from prefrontal dysfunction, Stuss and colleagues argued that the term "frontal lobe syndrome," referring to a broad heterogeneous complex of disturbances, was a less appropriate term than "frontal personality disturbance" (Stuss, Gow, & Hetherington, 1992). Personality could be properly appreciated as "stable and predictable response patterns of a person interacting with his or her

environment," including mood, affect, drive, and cognitive functions such as such as flexibility, freedom from interference, self-reflectiveness and judgment. It was noted that relatively few quantitative studies had been published, and there were few good methodologies for quantifying the types of behavioral changes seen after frontal lobe injuries (Stuss et al., 1992).

To address this, the *Iowa Rating Scales of Personality Change* (Barrash & Anderson, 1993) was designed to assess a broad array of 30 personality disturbances that may develop with a wide range of brain conditions. In patients with focal cortical lesions, a set of 14 personality disturbances including problems with social behavior, emotional regulation, flexibility, executive control and drive were found to be associated with ventromedial prefrontal lesions, compared to cortical lesions elsewhere (Barrash, Tranel, & Anderson, 2000). Following revision of the Iowa Scales to enhance psychometric properties, the revised version, the Iowa Scales of Personality Change (ISPC; Barrash, Anderson, Hathaway-Nepple, Jones, & Tranel, 1997), was applied to a new sample of patients with focal brain lesions, and found to be sensitive and specific, identifying a similar set of acquired personality disturbances following prefrontal damage, compared to lesions elsewhere (Barrash et al., 2011). The pattern of covariance among the scales was examined with principal components analysis in 124 patients with focal lesions. Five dimensions of acquired personality disturbance emerged: executive disturbances, irascibility (which we now refer to as emotional dysregulation), disturbed social behavior, hypo-emotionality/diminished motivation, and distress. The first four were associated with prefrontal lesions, while the fifth was a nonspecific consequence of lesions throughout the brain. Results were equivocal as to whether the dimensions of emotional dysregulation and disturbed social behavior are distinct types of acquired disturbance, or are two phenomenologically different aspects of the same underlying disturbance.

Another set of rating scales developed to quantify personality changes in individuals with brain damage, the *Frontal Systems Behavior Scale* (Grace & Malloy, 2000) assesses the frequency of current problems in three domains: apathy, disinhibition, and executive dysfunction. Elevations of these scales are associated with frontal lobe dysfunction (Grace, Stout, & Malloy, 1999). Factor analysis of 324 clinically diverse patients with largely non-focal disease showed that items tended to load on the scales they were assigned to, supporting the three-scale structure of the instrument, as designed (Stout, Ready, Grace, Malloy, & Paulsen, 2003). It was also noted that significant intercorrelations between factors were found, and some items loaded on more than one scale, suggesting that particular behavioral disturbances, such as *lacks initiative*, are not necessarily specific to dysfunction in only one domain.

Another instrument adapted from earlier rating scales developed to assess personality changes after TBI (Tyerman & Humphrey, 1984; Brooks & McKinley, 1983) was used to assess 30 personality characteristics in 35 patients approximately nine months post-stroke (Stone, Townend, Kwan, et al., Haga, Dennis, & Sharpe, 2004). Results indicated changes in more than half of the 30 scales, with greatest change for impatience, poor frustration tolerance, emotional lability and dissatisfaction. The pattern of disturbances was similar to that found by Barrash and colleagues (2000; 2011), but limited anatomical information (viz.,

59% had left hemisphere lesions) precluded analysis of the relationship with prefrontal damage.

To summarize the relevant literature spanning almost two centuries, observations of individual patients and then series of patients suggest that the very broad array of personality disturbances seen with prefrontal damage may reflect different types of disturbance. The advent of quantitative assessment of personality disturbances has shed further light on dissociable dimensions of disturbance, although most patients have some mixture of the subtypes of disturbance (Stuss & Benson, 1984), consistent with factor analyses demonstrating a limited number of higher-order dimensions, with significant overlap between the dimensions of disturbance (Barrash et al., 2011; Stout et al., 2003). While the association between damage to the prefrontal region and development of personality disturbances is well-established, it is not clear whether brain damage *not* involving prefrontal cortex is associated with acquired personality disturbances. For example, a syndrome of personality changes in patients with temporal lobe dysfunction from epilepsy was described many years ago (Bear & Fedio, 1977), although evidence for temporal lobe-related personality disturbances has been inconsistent (Devinsky & Najjar, 1998).

The literature has evolved from recognition of a wide range of behavioral disturbances following frontal lobe damage to observing two major subtypes to suggesting three distinct subtypes. However, there has not been a systematic investigation of the nature of (presumed) subtypes of personality. While previous studies demonstrate the presence of higher-order factors, identifying the dimensions of disturbance does not address the question of subtypes. The goal of the present study was to identify and describe frequently occurring subtypes — an extension of our earlier principal components analysis (Barrash et al., 2011) by moving from examining the pattern of overall covariance of personality characteristics *at the group level* (dimensions) to a behavioral investigation of the patterns with which specific disturbances covary *in individual patients*.

In the present study, we performed cluster analysis on a large sample of patients with stable, focal brain lesions located throughout the brain who were assessed on a wide range of personality disturbances. Patients were selected for focal lesions to enable us to eventually propose more precise anatomical validation, and focal lesions provide a brain-based template to eventually examine non-focal neurological diseases. We include patients with lesions outside of the prefrontal region to allow for examination of the frequency with which they may develop disturbances, and whether the nature of such disturbances are distinct from or similar to those seen in prefrontal patients. Based on review of the literature and findings from our earlier principal components analysis, we hypothesized that there are five subtypes of acquired personality disturbances: (1) Executive Disturbances, (2) Disturbed Social Behavior, (3) Emotional Dysregulation, (4) Hypo-emotionality/De-energization, and (5) Distress; as well as a sixth residual group without disturbance. It is noted that findings in the present study were not foreordained by the results of the group-level analysis in the previous study: at the outset of this study it was unknown whether analyses at the individual level (cluster analysis) would demonstrate five subtypes as hypothesized, or would indicate fewer, more or different behaviorally-defined subtypes. In that regard, we note that results from our earlier principal components analysis (2011) were equivocal regarding the nature

of the relationship between the Emotional Dysregulation and Disturbed Social Behavior dimensions, with data suggesting they may be two aspects of a single subtype.

Two parallel cluster analyses were performed. The first employed a hypothesis-driven clustering approach selected to determine whether the five hypothesized subtypes (and a residual normal group) do in fact occur at meaningful rates in a large sample. Given some degree of circularity to the hypothesis-driven approach, we also applied a second method of cluster analysis featuring an atheoretical process by which the clustering algorithm determined the nature and size of each group to emerge. The results of this strictly empirical analysis provided an indication of the robustness of subtypes emerging from the hypothesis-driven approach.

2. Materials and methods

2.1. Participants

Participants were 194 adults (99 male, 95 female) with focal brain lesions selected from the Patient Registry of the Division of Behavioral Neurology and Cognitive Neuroscience at the University of Iowa. 124 of these were also participants in the earlier principal components analysis of personality ratings (Barrash et al., 2011). Criteria for selection were a stable lesion of at least four months duration, lesion onset at age 18 or older, and no history of significant alcohol or substance abuse, psychiatric disorder, or other neurologic disorder unrelated to the lesion. Eligibility required the availability of valid ratings by an individual who knew the participant well and had regular opportunities to interact with and observe the participant in a variety of situations both before and after the lesion onset.

2.2. Procedure

Participants provided informed consent for involvement in research and for obtaining personality ratings. Comprehensive neuropsychological assessment was completed with standard procedures of the Benton Neuropsychology Laboratory (Tranel, 2009). The ISPC was completed by the informant in a separate room while the participant was engaged in neuropsychological testing. In accordance with federal and institutional guidelines, all procedures were approved by the University of Iowa Institutional Review Board, and are in accordance with the Declaration of Helsinki.

2.3. Measure

The ***Iowa Scales of Personality Change*** (ISPC; Barrash et al., 1997, 2017) provides standardized assessment of 30 characteristics that might change as a result of a neurological condition, with characteristics concerning emotional functioning, social and interpersonal behavior, decision-making and goal-directed behavior, behavioral control, and insight. Four of the 30 are control scales yielding ratings of characteristics that are not expected to become disturbed as a consequence of brain damage, and ratings indicating marked change on these scales (in conjunction with the pattern of ratings on clinical scales) contribute to identification of invalid ratings (Barrash, 2017). Information is obtained from a spouse or family member who has had regular, substantial contact with the patient before and after they developed their neuropathological condition. Each characteristic is introduced by a

brief behaviorally-focused definition. Raters make two ratings for each characteristic: "Before," describing a patient's typical functioning over their adult life, and "Now," describing their functioning over the past year (or, if the postmorbid period is not that long, then functioning over the months since emerging from the acute epoch). Characteristics are rated along 7-point scales, with higher ratings reflecting increasing disturbance: 1 indicates very good functioning; 3 is the hypothetically "average" level of the characteristic; 5, indicates the characteristic is present to a problematic degree; and 7 indicates severe disturbance. Points along the scale are accompanied by rating guidelines with multiple behavioral examples to enhance reliability (Schwarz, 1999). The ISPC is a revised version of the Iowa Rating Scales of Personality Change (Barrash & Anderson, 1993), for which psychometric analyses found generally very high interrater agreement weighted by the magnitude of rating discrepancy across all scales, ranging from .80 to .96 (Barrash, 2017).

In this paper, to avoid ambiguity, italicization was used when referring to an ISPC scale; capitalization was used when referring to the five hypothesized subtypes; and plain font was used when referring to the characteristic itself or to post hoc description of a cluster emerging from the cluster analyses.

2.4. Cluster analysis

Cluster analysis (CA) using SPSS™ version 23 was performed on ratings of the current, post-morbid level of personality functioning. Ratings of the current level of disturbance were used rather than change scores for a number of reasons. The focus of this investigation was the nature of *disturbance* after brain damage, not change per se. Furthermore, studies of a wide range of neurological populations with the ISPC have consistently shown normal premorbid functioning across personality characteristics (Barrash, 2017), including the present study (see Results section 3.1), so that ratings indicating postmorbid disturbance essentially indicate acquired disturbance. Additionally, as a composite measure, change scores are inherently less reliable than their component variables (Kessler, 1977). Two distinctive approaches to CA (Aldenderfer & Blashfield, 1984) were employed, as described below.

2.4.1. Hypothesis-driven approach: K-means CA—To test the primary study hypothesis regarding five specific subtypes of personality disturbance, the K-means procedure (Burns & Burns, 2009) allowed specification of the core features ("seeds") of each hypothesized subtype, and these seeds formed the basis for clustering. The number of patients joining a cluster demonstrated the extent to which actual patients had patterns of disturbance that fit the hypothesized subtype. The mean profiles of the resultant clusters provided empirically-derived information about the most salient disturbances of the subtypes.

Prior to analysis, seeds were determined by consensus among investigators of prefrontal behavioral disturbances (authors J.B., D.S., S.W.A., R.D.J., D.T.). Each investigator independently selected a limited number of characteristics that they judged to best characterize each hypothesized subtype. Each characteristic selected by at least three of the investigators was included as a seed. The seeds selected by this process were assigned

ratings of 7 for the following characteristics (except for seeds for which low levels of the characteristic were expected; they were assigned ratings of 1): Executive Disturbances: *Poor Judgment*, *Lack of Planning, Lack of Persistence, Perseveration*, *Impulsivity.* Disturbed Social Behavior: *Insensitivity*, *Socially Inappropriateness*, *Inappropriate Affect, Lack of Insight.* Emotional Dysregulation: *Irritability*, *Lability*, *Impatience*, *Inflexibility, Blunted Affect* (low ratings). Hypo-emotional/De-energized: *Apathy*, *Blunted Affect*, *Lability* (low), *Lack of Initiative*, *Type A Behavior* (low), *Impatience* (low), *Social Withdrawal*. Distressed: *Anxiety*, *Depression*, *Dependency*, *Blunted Affect* (low). Additionally, a sixth cluster of patients without disturbance was defined by seeds with ratings of 3 ("average") for each of the 21 scales with special relevance (i.e., scales that were employed as seeds in the cluster analysis based on the procedure described above). The remaining 9 ISPC scales not selected by investigators with high consistency were not included in the cluster analysis, enhancing the ratio of variables to cases.

2.4.2. Comparison of subsample distributions—The hypothesized subtypes were derived in part from the 124 participants in the 2011 study, and they make up a majority of participants (63.9% of the full sample) in this investigation. The 70 participants that were not in the 2011 study constitute an independent subsample. To examine the extent to which findings in the new subsample were comparable to those in the 2011 sample, we reported their distribution into five a priori groups. Whether the distributions differed was tested with chi-square.

2.4.3. Empirically-based approach: Ward's method CA—Ward's method (Burns & Burns, 2009) was employed to minimize the influence of a priori expectations on the results of the second CA. This is an iterative approach to subdividing the sample. In the first round of the analysis, the full sample is subdivided into two groups by a clustering algorithm that maximizes the overall between-group separation of mean personality profiles. In each successive step, the procedure is repeated de novo to produce a "solution" with n + 1 clusters. There is no automatic end point for this process. In this study, the plan was to continue with iterative steps repeated until results become uninterpretable or with negligible incremental information. This determination required a judgment based on review of empirical results. Ideally, the analysis with Ward's method would have yielded a solution with a limited number of discrete, conceptually-coherent clusters, and subsequent iterations would clearly show that there were no further clusters produced identifying additional subtypes of personality disturbances. That was not the case. Rather, a larger number of clusters was produced that included multiple clusters similar in terms of the nature of disturbances but differing in severity — an unintended consequence of the mathematical clustering algorithm. Accordingly, a post hoc decision was made to collapse clusters that were similar in terms of their most salient disturbances but differing primarily in terms of severity. The specifics of this step are presented in the results section, along with the actual results and the mean profiles of the combined groups.

2.4.4. Interpretation—Clusters were described according to the pattern of highest mean disturbances among the cluster members. By convention, mean ratings of 6.0 or higher were considered to indicate severe disturbance, 5.0–5.9 were considered to indicate moderate

disturbance, and mean ratings of 4.1–4.9 were considered to indicate very mild to mild disturbance. Cluster labels were based on disturbances with the highest mean ratings among cluster members.

Circularity in the hypothesis-driven analysis (i.e., basing development of clusters on expected subtypes, yielding subtypes as expected), was addressed with two analyses: (1) the comparison of the distributions into subtypes of two subsamples, one of which was independent of the derivation of hypotheses; (2) a second cluster analysis based strictly on empirical grounds, without influence from expectations. Accordingly, the number of meaningful clusters found in the latter analysis, the profile of disturbances characteristic of them, and their correspondence with hypothesized subtypes provided a methodologically-independent assessment of the robustness of results from the K-means CA. The congruence of findings was evaluated by comparing the mean ratings of corresponding clusters from the two procedures. Discussion of results was explicitly descriptive in acknowledgement of the exploratory nature of these analyses and lack of a clear statistical test for meaningful null hypotheses such as “there are no clusters” or a given number of clusters (Aldenderfer & Blashfield, 1984).

3. Results

Participants had a mean age of 53.3 (SD = 13.9); education, 13.8 years (2.4); interval since event, 5.1 years (6.1) with a range of 4 months to 30 years; Verbal Intelligence Quotient/Verbal Comprehension Index, 100.8 (14.2); Performance Intelligence Quotient/Perceptual Organizational Index/Perceptual Reasoning Index, 102.7 (13.8); Auditory Verbal Learning Test delayed recall, 7.9 words (4.1); Trails B time, 94.2″ (59.2); Beck Depression Inventory/Beck Depression Inventory-2, 8.9 (7.6). Etiology was nonhemorrhagic stroke for 35.6% of the sample; hemorrhagic stroke, 20.6%; epilepsy surgery, 14.9%; benign tumor resection, 17.0%; other, 11.9%.

3.1. Normalcy of premorbid behavior

The mean Before rating for each of the 30 ISPC scales was examined. On the ISPC, ratings of 3 on the 7-point scales were explicitly defined as the amount of the characteristic that a rater considers typical for persons the same age and sex of the ratee. The highest mean Before rating was 3.53 for Obsessiveness and the next highest rating was 3.32 for Frugality (a control scale), and neither of these scales played a role in any of the subtypes. All other scales had mean Before ratings less than 3.3, and 25 of the 30 scales were at or below 3.0.

3.2. K-means cluster analysis

By the hypothesis-driven K-means CA, 105 (54.1% of the sample) were placed in one of the five a priori groups, and 89 (45.9%) were placed in the residual group with a normal mean profile. The mean ISPC ratings for each cluster are presented in Table 1. These show that for any particular cluster, the highest mean ratings were largely those that had been the a priori defining characteristics of the hypothesized subtype.

The dysexecutive cluster showed highest ratings of disturbance on the expected scales, but a notable feature of this group was that disturbances were also quite widespread across other

dimensions, although to a slightly milder degree. The disturbed social behavior cluster (10.5% of cases in a cluster with disturbance) was the smallest of all clusters. This group's highest mean ratings came not only on the a priori seed-disturbances, but also on the seed-disturbances selected to identify the emotional dysregulation cluster (i.e., the mean ratings for these scales were higher for patients in the disturbed social behavior cluster than for those in the emotional dysregulation cluster). This group also had high ratings for poor judgment and impulsivity. That is, more than being characterized by disturbed social behavior, specifically, this group was characterized by a pattern of disturbances more broadly reflecting emotional and behavioral dyscontrol (accompanied by milder executive deficits and mild distress). This group showed the highest overall level of disturbance of all clusters. The emotional dysregulation cluster had the most prominent disturbance on the expected scales. This group was notable for being the largest and the most mildly disturbed in general. However, the mean profile indicated that next most elevated disturbance in this group was disturbed social behavior (although this was quite mild in keeping with the mild level of disturbance overall). This group is also notable for being the one group without significant executive disturbances. The hypo-emotional/de-energized cluster was characterized not only by the seed-disturbances, but also by lack of stamina, lack of anxiety and unremarkable social behavior (other than reduced social activity), and very low impulsivity. They had mild executive disturbances, with particular disturbances in lack of planning and indecisiveness. Ratings were low for aspects of emotional dysregulation. The distressed cluster was especially characterized by higher levels of anxiety and indecisiveness as well as mild apathy and executive disturbances.

3.3 Comparison of subsample distributions

Frequency distributions presented in Table 2 show that the distribution of the 70 new participants into five a priori groups was highly similar to distribution of the 124 participants from the 2011 study. In the new subsample, 61.4% clustered into a subtype of acquired disturbance, compared to 50% of the initial 124 participants. The mean difference between the two distributions across the five subtypes was 2.3%. The chi-square test indicated that the two distributions did not differ from each other: χ^2 (5, N = 124) =2.59, p = .76.

3.4. Ward's method cluster analyses

The sequence of cluster subdivisions over successive cluster analyses with Ward's method is presented in Table 3. In the first step, the 2-group solution saw the full sample divided into one cluster with mild generalized disturbance (47.4% of the full sample) and a cluster of relatively undisturbed patients (52.6%).

In the 3-group solution, two patients with severe executive disturbance, emotional dysregulation and disturbed social behavior formed one cluster, another patient with severe distress and dysexecutive behavior formed a cluster of one, and the remaining 191 patients formed a residual cluster with a broadly undisturbed mean profile.

In the 4-group solution, 78 patients split off from the large "undisturbed" cluster while the three patients with very severely disturbed behavior remained as two small clusters.

The 5-group solution was largely unchanged from the 4-group solution, other than one more patient with severe emotional dysregulation, disturbed social behavior and executive disturbances splitting off from the large cluster with mild generalized disturbance.

In the 6-group solution, several notable changes occurred. First, rather than one large cluster with mild undifferentiated disturbance and three clusters comprising four individuals with very severe disturbances, these 81 patients plus another 11 patients that had been assigned to the large undisturbed cluster in previous stages were redistributed into four moderately-sized clusters: the largest of these clusters (33 patients) was characterized by moderate emotional dysregulation and mild distress; the next largest (24 patients) was characterized by moderate executive disturbances, moderate emotional dysregulation, mildly disturbed social behavior and mild distress; the third cluster (15 patients) was similar but with moderate executive disturbances accompanied by moderate disturbances in emotional dysregulation, social behavior, distress and apathy/impaired initiative; the fourth disturbed cluster (20 patients) was characterized by moderate hypo-emotionality, de-energization and executive disturbances. In addition to these four clusters of patients with disturbance, the large undisturbed cluster split into a larger undisturbed cluster (59 patients) characterized by largely average personality ratings, and a somewhat smaller cluster (43 patients) that may be referred to as “hyper-normal.”

In the 7-group solution, while other clusters remained unchanged, the cluster featuring prominent moderate hypo-emotionality, de-energization and executive disturbances split into two, with one of the resultant clusters having an absence of distress (9 patients), and the other one with moderate distress (11 patients).

In the 8-group solution, while other clusters remained unchanged, a cluster with moderately severe emotional dysregulation and mildly disturbed social behavior and distress (8 patients) split off from the cluster characterized by moderate emotional dysregulation, leaving a cluster with mild disturbances in emotional dysregulation, social behavior, executive disturbances and distress (25 patients).

In the 7-group solution, while other clusters remained unchanged, the cluster featuring moderate hypo-emotionality, de-energization and executive disturbances split into two, with one of the resultant clusters having minimal distress (9 patients), and the other one with moderate distress (11 patients).

In the 8-group solution, while other clusters remained unchanged, a cluster with moderately severe emotional dysregulation and mildly disturbed social behavior and distress (8 patients) split off from the cluster characterized by moderate emotional dysregulation, leaving a cluster with mild disturbances in emotional dysregulation, social behavior, executive disturbances and distress (25 patients).

In the 9-group solution, while other clusters remained unchanged, a cluster with moderately severe distress and moderate executive disturbances, emotional dysregulation and disturbed social behavior (9 patients) split off from the cluster that had featured moderate executive disturbances, moderate emotional dysregulation, mildly disturbed social behavior and mild

distress. After the distressed group split off from the executive disturbances cluster the latter cluster no longer included distress (15 patients).

In the 10-group solution, while other clusters remained unchanged, the undisturbed "normal" cluster subdivided into two normal clusters (37 & 22 patients) differing only in the exact profiles of slightly-below-average and slightly-above-average characteristics. There was no clinically-meaningful theme to the two normal profiles.

In the 11-group solution, while other clusters remained unchanged, four patients previously in "undisturbed" clusters split off and formed a small cluster characterized rather narrowly by moderately-severe anxiety and dependency and otherwise unremarkable personality profiles.

In the 12-group solution, the heretofore orderly sequence of cluster subdivision was abruptly replaced by several disintegrative changes. Rather than the emergence of one additional subtype as had been the case in the previous five stages, of the 11 groups identified in the previous stage, eight were altered (additions, subtractions or fractured out of existence). Regarding the cluster characterized by moderate disturbances in executive disturbances, emotional dysregulation and social behavior that had remained unchanged in the previous three stages: (a) approximately half of the 15 patients in this cluster forming two small clusters characterized by salient emotional dysregulation and disturbed social behavior and differing from each other primarily in severity, and (b) the other half of patients were reassigned to four different clusters included those with most salient disturbances in hypo-emotionality/de-energization, or distress, or mild emotional dysregulation/disturbed social behavior. Another set of changes from the 11-group solution involved (c) several patients who had been in undisturbed clusters who were reassigned to a moderate distress and emotional dysregulation cluster, and (d) reshuffling of multiple patients across undisturbed clusters.

Considering the "big picture" of the many (uninformative) changes occurring with the 12-group solution, it was concluded that these sequential analyses had run their course, and interpretation was focused on the 11-group solution. It was evident that a major factor in the fractionation of otherwise qualitatively-identical groups was the general severity of disturbances. Given that pattern of results across the sequential analyses, it was decided that the most informative and parsimonious manner of summarizing results from the empirically-based CA was to combine clusters according to each one's most salient characteristics, recognizing that the aspects in which to-be-collapsed clusters primarily differed were severity. It is acknowledged that this is a post hoc decision and that the combined groups include subsets that — beyond the most salient characteristics — are characterized by more narrow or more generalized disturbance.

The mean ratings of the collapsed groups are presented in Table 4. One group was characterized by moderate executive disturbances as well as broadly comparable levels of emotional dysregulation and disturbed social behavior. The second group was characterized by emotional dysregulation and milder disturbance of social behavior. The third group was characterized by hypo-emotionality and de-energization along with mild to moderate

executive disturbances. The fourth group was characterized by distress, especially anxiety and being easily overwhelmed. The fifth group was a residual group without any substantial disturbance.

3.5. Synthesis of cluster analyses

3.5.1. Executive Disturbances subtype—The first subtype to emerge in both analyses was characterized by disturbances in poor judgment, lack of initiative, lack of planning, indecisiveness and lack of stamina. Additionally, with both CA techniques, there were also moderate disturbances outside of the narrower set of core features of executive disturbance, including inflexibility, perseverative behavior, lack of persistence, impatience, being easily overwhelmed, lability, social inappropriateness, apathy and lack of insight. This pattern of executive disturbances accompanied by significant emotional dysregulation and milder generalized disturbance characterized approximately 25%–30% of the patients with acquired personality disturbance across both cluster analytic approaches.

3.5.2. Emotional Dysregulation and Disturbed Social Behavior subtype—Findings from both cluster analyses suggest that emotional dysregulation and disturbed social behavior are two aspects of one underlying disturbance. Indeed, the hypothesis-driven analysis showed the expected core features for the Disturbed Social Behavior cluster, but the very severe disturbances in social behavior were accompanied by severe emotional dysregulation. This group was small, and the disturbances were the most severe of any seen for any group by either CA approach. In the empirically-based CA, the two sets of disturbances co-occurred with a high level of consistency across sequential analyses. In addition to the narrower set of core expected features for the two subtypes included milder disturbances of being easily overwhelmed and with mild anxiety and diminished stamina. Executive disturbances were not prominent with this subtype, appearing to only become a problem with the most very severely disturbed members. In the empirically-based CA, once the subtypes characterized by prominent dyscontrol of emotion and behavior and differing in severity were combined, this was the most frequently subtype, characterizing a third of the patients with significant acquired disturbances. Of note, insight was disturbed in the cluster of 11 patients with severely disturbed social behavior and emotional dysregulation (hypothesis-driven analysis), but insight was rated as quite normal in the larger groupings of less severely disturbed Em/DSB patients.

3.5.3. Hypo-emotionality and De-energization subtype—The salient but relatively mild disturbances matched a priori expectations, including apathy, blunted affect, lack of initiative and social withdrawal, and an absence of type A behavior. Anxiety and depression were low in the subtype, while both CAs indicated that low stamina, deficient planning, indecisiveness and poor judgment were aspects of this subtype. Patient membership in this group was highly consistent across CA procedures, involving a relatively consistent 15% to 20% of the sample. In the empirically-based analyses, this group split off from all other groups in the 6-group solution and then, in the 7-group solution, subdivided into two variants — one without distress and the other with distress. The same 20 patients remained in HE/DE clustered into these two subsets invariantly through all subsequent rounds of subdivision.

3.5.4. Distressed subtype—In both cluster analyses, a distressed subtype emerged in which anxiety was clearly a more prominent problem than depression and, in addition to dependency and being easily overwhelmed, both approaches showed lack of initiative, indecisiveness, poor planning and lack of stamina to be integral features of this subtype. Of note, the empirically-based analysis did not indicate apathy to be significantly disturbed, nor were there prominent disturbances in emotional dysregulation, socially inappropriate behavior or executive disturbances. This group was relatively small, from 14% to 17% of the disturbed patients across the two CA.

3.5.5. Undisturbed—Collectively, the analyses indicate that approximately half of our sample was characterized by one disturbance or another, and the other half were without significant disturbance. However, mean rating for *Lack of Stamina* and *Obsessiveness* were slightly elevated compared to other scales.

4. Discussion

Cluster analysis does not uncover “real” subtypes of acquired personality disturbance in a precise way. Rather, results reflect the general nature of different subtypes, but the exact composition of groups that emerge from cluster analysis necessarily depends on the specific set of patients in the sample, as well as on the details of the CA procedure employed. For this reason, we used a dual approach to cluster analysis to obtain a more reliable picture of subtypes by examining results that are similar across the two fundamentally different procedures. Results showed obvious similarity in the nature and size of subtypes emerging from the two CA approaches, with hypothesized subtypes occurring with some frequency, and with group characteristics that partially support the existence of the hypothesized subtypes.

One subtype was characterized by prominent executive dysfunction, but this group also had generalized disturbance affecting all areas of personality function to varying degrees. Comparable results across the two analytic approaches indicated that emotional dysregulation and disturbed social behavior, rather than two distinctive subtypes, are two aspects a multifaceted subtype. The subtype characterized by hypo-emotionality/diminished energization emerged with notable consistency across the two analyses and, while certain aspects of executive dysfunction such as lack of planning and indecisiveness were part and parcel of this subtype, this was the group with most circumscribed disturbance. Finally, as hypothesized, a subtype emerging from both analyses was labeled as “distress”; we hasten to add, however, that this does not refer to time-limited situational reactions that would be referred to more aptly by a diagnosis of affective disorder. As explicitly referred to in the behavioral guidelines for raters, these patients have an enduring proneness to worry about and be easily overwhelmed by day-to-day life, to be indecisive, and to become dependent on others around them. That is, rather than simply an acute reaction to the onset of a neurological condition, these individuals have experienced significant personality change that remains evident years after onset.

Results did not indicate discrete, non-overlapping subtypes. While it is easy to describe subtypes that are conceptually distinct, findings from the present study are consistent with

earlier observations that in reality some patients have a mixture of types of disturbance (Barrash et al., 2011; Stout et al., 2003; Stuss & Benson, 1984). Nevertheless, the pattern of findings was consistent earlier observations of two important subtypes of acquired personality disturbances (Blumer & Benson, 1975; Kretschmer, 1956; Luria, 1969; Walch, 1956), one involving disinhibition and poor modulation of emotional responses and another associated with apathy and diminished activity, with later explication of a third subtype characterized by executive deficits (Cummings, 1993).

4.1. Correspondence with functional meuroanatomy

The subtypes found in both cluster analyses show obvious correspondence with what is known about prefrontal circuitry. Early cytoarchitectural and myeloarchitectural investigation of human brain development indicated dual development of two basic prefrontal systems, one evolving from olfactory cortices and involved in affective processing, and the second one evolving from hippocampal cortices and involved in cognitive activity (Sanides, 1964). Anatomical studies have shown circuitry also reflecting these two fundamental prefrontal systems (Stuss, 1992): one system in inferior medial cortices is strongly connected to limbic structures and critically involved in emotional control, and a second system in lateral cortices has largely bidirectional connections with posterior cortices and is primarily responsible for cognitive/executive processes (Alexander, DeLong & Strick, 1986; Pandya & Barnes, 1987; Pandya & Yeterian, 1996). Differential patterns of neuroanatomical and neuropsychological changes between the two systems further support their basic distinctiveness (Phillips, MacPherson & Della Sala, 2002). A third system, a superior medial circuit involved in energization, was also indicated by painstaking mapping by Alexander and colleagues (1986). Superimposed on these fundamental systems in humans is the phylogenetically and ontogenetically later-developing frontopolar cortices which, notably, have rich interconnections within prefrontal cortices but do not have prominent frontal-subcortical connections (Petrides & Pandya, 2007), consistent with a hypothesized role integrating emotional and executive processes within the frontal lobes (Stuss, 2011).

Updating and synthesizing this work, Stuss (2011) posited four functional systems important for control of goal-directed behavior, instantiated in specific prefrontal regions: (1) *Energization*, the process of initiation and sustaining responses, which is impaired with damage to the dorsomedial region (primarily areas 24, 9, and 6). (2) *Executive functions*, comprising two functions: (a) task setting, which is impaired with damage to the dorsolateral region on the left (primarily areas 44–46, 9, and 47/12), resulting in inappropriate or ineffective responses to task demands which are especially evident early in the learning of the task; (b) monitoring of response selection and performance, which is impaired with damage to the dorsolateral region on the right resulting, in neuropsychological studies, in increased errors of all types, including false positives and increased variability of performance. (3) *Emotional/behavioral regulation*, which is impaired with damage to the ventromedial region (areas 32, 25, 24, 11–14), resulting in difficulty integrating emotional, motivational and reward/risk aspects of social behavior, and impaired social/interpersonal functioning. (4) *Metacognition/integration*, higher-order processing that is dependent on polar regions (10s, 10i), damage to which leads to impairment in the integration and

coordination of emotional perspective, motivation, energization, and executive capacities to effectively accomplish complex, novel tasks. Other models posit variations on the brain-behavior relationships, while also emphasizing the contributions of functionally-distinct prefrontal regions to the control of behavior. For example, the model elaborated by Koechlin (2013) also ascribes cognitive control in the selection of task sets to lateral prefrontal cortex, and makes the case that monitoring of motivational incentives for potential actions is mediated by medial prefrontal cortex, and together these systems form an integrated system for determination of human decisions and behavioral responses.

Behaviorally, there is strong correspondence between the results of this study and the functionally-distinct systems elaborated by Stuss (2011). The pattern of disturbances in the Hypo-emotionality/De-energization subtype emerging from cluster analyses corresponds closely to the dysfunction expected as a result of damage to the energization system; and disturbances in the Emotional Dysregulation/Disturbed Social Behavior group corresponds closely to the dysfunction expected to result from damage to the emotional/behavioral regulation system. The Executive Disturbances group is less straightforward. This group was characterized by relatively severe dysexecutive disturbances, but also had prominent disturbances in emotion regulation, social behavior and decision-making and apathy, as well as some degree of distress. Several factors may contribute to the widespread disturbance in this group. This group may well include many larger lesions that extend into other prefrontal regions systems, a possibility that requires further study. Also, primary disturbances in executive abilities, when sufficiently severe, may cause secondary problems in other areas (Tate, 1999). Additionally, the wide range of disturbances in this group corresponds closely to the broad nature of dysfunction expected with damage to a metacognition/integration system with downstream effects on the other systems (Stuss, 2011). Evidence suggests that decision-making in complex activities (i.e., with a mixture of task demands on aspects of executive functioning) may require contributions from differing systems (Floden, Alexander, Kubu, Katz & Stuss, 2008), resulting in poor judgment — which was a defining feature of the executive function group in our sample.

The group characterized by prominent anxiety and vulnerability to stress does not correspond to any system in models of prefrontal functional circuitry. Rather, the pattern of our findings are consistent with conclusions from many previous investigations that prominent distress is a commonly found, nonspecific consequence of brain damage (Barrash et al., 2011; Carson et al., 2000; Fleminger, Oliver, Williams, & Evans, 2003; Juengst et al., 2016; Moldover, Goldberg, & Prout, 2004; Velikonja et al., 2010) — if the assessment of personality changes is sufficiently broad as to assess relevant disturbances (Velikonja et al., 2010). Different prefrontal sectors may make differential contributions to severity of depression (Koenigs & Grafman, 2009).

Stepping back to consider a more molar view of the results, findings indicate that the subtypes are not discrete, non-overlapping sets of disturbances. Rather, they tend to have a core set of disturbances as expected, plus some additional disturbances that flesh out the characteristics of a subtype into a conceptually coherent pattern. For example, the group that we have labeled as “Hypo-emotionality/De-energization” not only has prominent core disturbances as expected (apathy, lack of initiative, social withdrawal, blunted affect, and the

absence of type A behavior), but also conceptually related disturbances: lack of stamina, lack of planning, indecisiveness, lack of persistence and poor judgment — disturbances that were second only to the executive disturbance group in severity. In some patients, the latter disturbances may reflect primary impairment of executive functions. In the context of HE/DE, however, these disturbances may be secondary to the effects of deficient energization of cognitive processes (Stuss et al., 2000). The constellation of disturbances in this group is also consistent with the conclusion arising from a wide range of empirical findings that "…too little emotion has profoundly deleterious effects on decision-making" (Tranel, 2002; see also Damasio, 1994).

4.2. Apathy

Apathy was a salient characteristic of the HE/DE subtype, but it was also a component of the executive disturbances and distressed subtypes. We believe this reflects that apathy may be due to differing underlying functional disturbances related to dysfunction of distinctive neural systems (Barrash et al., 2011; Marin, 1996; Stuss & Benson, 1986; Stuss et al., 2000). Although apathy as a symptom of depression is well-established (American Psychiatric Association, 2013) and it occurs in a majority of people with traumatic brain injuries (Lane-Brown & Tate, 2012), in some brain-damaged individuals apathy might not be a consequence of low mood (Cahn-Weiner, Grace, Ott, Fernandez, & Friedman, 2002), but may be associated with cognitive disengagement, attentional impairment and indecisiveness (Siegert, Walkey, & Turner-Stokes, 2009) or impaired drive and self-activation (Ready, Ott, Grace, & Cahn-Weiner, 2003; Stuss et al., 1992). Even if depression is present, in patients with neuropathological conditions, it may be more accurate and clinically useful to consider apathy as a neuropathological symptom with differential causes and with treatment implications than apathy-as-depressive-symptom (Boyle & Malloy, 2004). In an extensive review, Stuss and colleagues (2000) have described different kinds of apathy related to the three prefrontal circuits supporting behavior: (a) Damage to ventromedial/orbitofrontal cortex results in personality blunting that may reflect apathetic behavior due to the absence of limbic affective input, resulting in a disorder of self-initiated behavior (Bechara, Tranel, H. Damasio & A. R. Damasio, 1996). (b) Damage to the dorsolateral prefrontal system results in "executive apathy," an absence of behavior (or impaired behavior) input would normally trigger executive activities of flexibility, selection, novel responsiveness, etc. leading to a response (Stuss, Picton & Alexander, 1999). (c) Damage to the anterior cingulate results in an especially obvious type of apathy with affective placidity, lack of emotional response and impoverished social interactions and, in its extreme form, abulia. Of course, damage to subcortical circuits also may result in various types of apathy depending on connections (Levy & Dubois, 2006), and the interested reader is referred to Stuss et al., 2000. Given the clinical heterogeneity of the symptom, apathy, it is not surprising that significant apathy should be seen in groups characterized by executive disturbances, hypo-emotionality/de-energization, and distress.

4.3. Lack of stamina

Lack of stamina was elevated for each subtype of disturbance, and also in the normal group (to a much lesser extent). These findings suggest that, at least in part, diminished stamina is a non-specific consequence of brain damage, consistent with findings from our earlier

principal components analysis (Barrash et al., 2011). What is referred to as “Lack of Stamina” in the ISPC is often referred to as “fatigue” in the literature. The term “central fatigue” has been defined as a feeling of constant exhaustion and difficulty in initiation or sustaining a voluntary activity (Chaudhuri & Behan, 2004), to distinguish this symptom from muscle fatigability (or “peripheral fatigue”). Central fatigue is a common symptom and may be among the most disabling in many neurological disorders, including stroke, TBI, Parkinson’s disease, and multiple sclerosis (DeLuca, 2005; DeLuca, Genova, Hillary, & Wylie, 2008; Dobryakova, DeLuca, Genova, & Wylie, 2013; Van der Werf et al., 1998). In a study of the late consequences of mild stroke at one year, fatigue was the most common symptom (72%), almost 20% higher than the next most complaints, memory dysfunction and stress (Carlsson, Möller, & Blomstrand, 2003). Staub and Bogousslavsky (2001) reported that a major sequela of stroke is “primary poststroke fatigue” (i.e., in the absence of depression or significant cognitive sequelae), defined as “a feeling of early exhaustion developing during mental activity, with weariness, lack of energy and aversion to effort.” Possible causal mechanisms are many, including lesions affecting circuits that connect thalamus, basal ganglia, amygdala, and frontal cortex (Bruno, Crenage, & Fick, 1998; Chaudhuri & Behan, 2000; DeLuca et al., 2008; Dobryakova, DeLuca, Genova, & Wylie, 2013; Glader, Stegmayr, & Asplund, 2002); conditions compromising the availability of neurotransmitters (Bradley & Alarcon, 1999; Bruno et al., 1998; Dobryakova, Genova, DeLuca, & Wylie, 2015) or endocrinological disturbances (Chaudhuri & Behan, 2004). It is important to note that the presence of fatigue is commonly overlooked as it is sometimes the only persisting sequela of stroke, but it may severely limit a patient’s return to their previous level of functioning (Staub & Bogousslavsky, 2001).

4.4 Limitations

A limitation of this study is that the series of sequential, empirically-based cluster analyses involved post hoc decisions. Severity of ratings, per se, was clearly a major factor in the subdivision of otherwise qualitatively-identical groups, resulting in analyses that did not unfold in as orderly and parsimonious a fashion as had been expected. Continuing the sequential analyses with a higher number of clusters was decided on to avoid short-circuiting the analyses and potentially missing revealing results regarding distinctive subtypes. The inflated number of clusters due to multiple clusters with largely identical disturbance but differing levels of severity led to the post hoc decision to combine like-clusters differing primarily in overall severity. We attempted to examine the results of the Ward’s method analyses in thoughtful fashion and to fully report the process; nevertheless, decisions regarding informative treatment of the sequential analyses were post hoc. Accordingly, it is emphasized that the results do not confirm the exact nature of subtypes but rather are presented as a supportive demonstration of hypothesized subtypes. It is noted that no other distinctive type of disturbance was identified in the empirically-based CA in this large sample.

Another limitation of this study is the unknown generalizability of our findings. The sample selected for this study was comprised of patients with focal lesions, and the locations of the lesions were scattered throughout the cerebrum, and both of these factors affect findings. Support for generalizability of findings to other patients with focal brain damage is provided

by the finding that the distribution of the 70 new participants into subtypes was highly similar to that found for the 124 participants from the 2011 subsample. That finding indicates that subtypes emerging from the hypothesis-driven cluster analysis were not merely due to circularity. However, the degree to which subtypes found in this study will characterize populations with non-focal neurological diseases, and what percentages of such patients will be characterized by one subtype or another, remain to be determined. Investigations with different clinical populations in independent centers will be important to address the generalizability of the subtypes identified in the present study.

The major future direction for our line of research will be detailed investigation of neuroanatomical correlates of subtypes of acquired personality disturbances identified in the present study, examining hypothesized associations of specific prefrontal regions. Another important step will be further analysis to develop decision rules to permit reliable classification of individual patients as having a certain subtype. Another important future direction includes examination of clinical correlates of the subtypes, including neuropsychological profiles, psychological-emotional assessment, and functional outcomes in real life.

In summary, the present study provides evidence of four subtypes, supported by findings from two distinctive cluster analysis techniques. These subtypes correspond to types of disturbances theorized from models of functionally-distinct prefrontal systems. We believe that study findings indicate it is time move beyond terminology suggesting a unitary “frontal lobe syndrome,” and to move toward terminology that conveys that damage to different prefrontal circuits may result in differential clinical syndromes. Investigation of the neuroanatomical correlates of subtypes will be important, as further understanding of the associations between subtypes of acquired personality disturbance, underlying prefrontal systems, and clinical correlates may enhance our ability to tailor rehabilitative interventions for specific patients (Juengst et al., 2016; Prigatano, 1999; Stuss et al., 2000), working toward improved evidence-based treatment for this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CA	Cluster analysis
ExD	Executive Disturbances
EmD/DSB	Emotional Dysregulation and Disturbed Social Behavior
HE/DE	Hypo-emotionality and De-energization

ISPC Iowa Scales of Personality Change

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Table 1

Mean Ratings[a] of Personality Disturbances by Groups from K-means Cluster Analysis

	DISTURBED SUBTYPES (n = 105, 54.1% of full sample)					NORMAL
ISPC Scale	ExD (n=26) (24.8%)	DSB (n=11) (10.5%)	EmD (n=35) (33.3%)	HE/A (n=15) (14.3%)	DIST (n=18) (17.1%)	(n=89) (45.9%)
Lack of Planning	**5.9**	4.6	3.6	5.3	5.1	2.5
Lack of Persistence	**5.4**	4.2	3.5	4.3	4.6	2.5
Perseverative Behavior	**5.4**	4.7	3.9	4.7	4.6	2.8
Poor Judgment	**5.6**	5.6	4.1	4.3	4.5	2.6
Impulsivity	**5.2**	5.4	3.8	2.7	3.9	2.5
Indecisiveness	5.7	4.4	4.3	4.8	5.4	3.1
Social Inappropriateness	4.9	**6.2**	4.2	3.6	2.9	2.3
Insensitivity	4.5	**6.5**	4.4	3.8	3.2	2.4
Inappropriate Affect	4.4	**5.2**	3.1	2.9	3.7	2.6
Lack of Insight	4.4	**5.6**	3.1	3.5	3.3	2.3
Aggressive Behavior	3.6	4.6	3.2	2.2	2.7	2.2
Irritability	4.7	5.8	**5.1**	2.6	3.2	2.9
Impatience[c]	4.8	5.5	**5.2**	**2.5**	3.2	2.8
Lability[c]	5.0	6.2	**4.9**	**2.3**	4.4	3.1
Inflexibility	4.9	6.4	**4.9**	3.6	3.4	3.2
Apathy	5.0	4.0	3.8	**4.6**	4.8	2.7
Lack of Initiative	5.8	5.4	3.6	**5.1**	5.1	2.6
Blunted Affect[c]	4.6	2.1	**2.5**	**5.5**	**2.4**	2.8
Social Withdrawal	4.5	2.1	4.0	**4.9**	4.3	2.7
Type A Behavior[b]	3.1	3.4	3.1	**1.9**	1.8	2.9
Anxiety	4.4	4.7	4.4	2.0	**6.1**	3.1
Depression	4.7	4.5	3.9	3.4	**4.9**	2.7
Dependency	4.3	4.1	3.9	3.5	**4.9**	2.6
Easily Overwhelmed	5.5	5.4	4.7	3.8	5.7	3.1

	DISTURBED SUBTYPES (n = 105, 54.1% of full sample)					NORMAL
ISPC Scale	**ExD (n=26) (24.8%)**	**DSB (n=11) (10.5%)**	**EmD (n=35) (33.3%)**	**HE/A (n=15) (14.3%)**	**DIST (n=18) (17.1%)**	**(n=89) (45.9%)**
Lack of Stamina	5.8	5.2	4.2	5.1	5.8	3.6
Suspiciousness	*3.7*	*4.1*	*3.6*	*2.2*	*2.8*	*2.8*
Obsessiveness	*3.9*	*5.0*	*4.0*	*3.2*	*4.4*	*3.7*
Frugality	*3.4*	*2.9*	*3.3*	*3.3*	*4.5*	*3.4*
Vanity	3.1	3.7	2.7	1.8	2.2	2.2
Manipulativeness	3.3	4.5	2.8	2.3	3.0	2.3

Note. ExD = Executive Disturbances. DSB = Disturbed Social Behavior. EmD = Emotional Dysregulation. HE/DE = Hypo-emotionality/De-energization. DIST = Distress.

Bolded ratings indicate the scales that were the seeds for characterizing the cluster.

[a]Characteristics are rated along 7-point scales, with higher ratings reflecting increasing disturbance: 1 indicates very good functioning, 3 = is the hypothetically "average" level of the characteristic, 5 indicates that the characteristic is present to the degree that it is considered a problem, and 7 indicates a severe problem.

[b]The absence of disturbance (i.e., rating of 1) for *Impatience*, *Lability* and *Type A behavior* are seeds for the Hypo-emotionality/De-energization subtypes.

[c]The absence of disturbance (i.e., rating of 1) for *Blunted Affect* is a seed for the Emotional Dysregulation and Distressed subtypes.

Table 2

Distributions of subsamples into six K-means clusters

Cluster	2011 subsample (n=124)	New subsample (n=70)
Executive Disturbances	15 (12.1%)	11 (15.7%)
Disturbed Social Behavior	7 (5.6%)	4 (5.7%)
Emotional Dysregulation	21 (16.9%)	14 (20.0%)
Hypo-emotionality/De-energization	9 (7.3%)	6 (8.6%)
Distress	10 (8.1%)	8 (11.4%)
Normal	62 (50%)	27 (38.6%)

Table 3

Sequence of clustering results[a] in successive Ward's cluster analyses

	Clusters[b] (n)				
	EXECUTIVE DISTURBANCES	**EmD/DSB**	**HYPO-EMOTIONALITY/DE-ENERGIZATION**	**ANXIOUS-DISTRESS**	**NORMAL**
2	mGEN (92)			NL (102)	
3		sev EmD,DSB,ExD (2)		sDISTR,ExD (1)	NL (191)
4	mGEN (78) sEmD,DSB,ExD (2)			sDISTR,ExD (1)	NL (113)
5	mGEN (77)	sEmD,DSB,ExD,mod DISTR (1) sEmD,DSB,ExD,mDISTR (2)		sDISTR,mod-sExD (1)	NL (113)
6	Mod ExD,EmD,mDSB,DISTR (24) mod ExD,GEN (15)	mod EmD,mDSB,DISTR (33)	mod HE/DE,ExD (20)		NL (59) Hyper-NL (43)
7	Mod ExD,EmD,mDSB,DISTR (24) mod-sExD,mod GEN (15)	mod EmD,mDSB,DISTR (33)	mod HE/DE,ExD,no DISTR (9) mod HE/DE,DISTR,ExD (11)		NL (59) Hyper-NL (43)
8	Mod ExD,EmD,mDSB,DISTR (24) mod-sExD,mod GEN (15)	mEmD,DSB,DISTR,ExD (25) mod-sEmD,vmDISTR (8)	mod HE/DE,ExD,no DISTR (9) mod HE/DE,DISTR,ExD (11)		NL (59) Hyper-NL (43)
9	mod ExD/EmD/DSB (15) mod-sExD,mod GEN (15)	mEmD,DSB,DISTR,ExD (25) mod-sEmD,vmDISTR (8)	mod HE/DE,ExD,no DISTR (9) mod HE/DE,DISTR,ExD (11)	mod-sDISTR,mod ExD,EmD,DSB (9)	NL (59) Hyper-NL (43)
10	mod ExD/EmD/DSB (15) mod-sExD,mod GEN (15)	mEmD,DSB,DISTR,ExD (25) mod-sEmD,vmDISTR (8)	mod HE/DE, no DISTR (9) mod HE/DE,DISTR,ExD (11)	mod-sDISTR,mod ExD,EmD,DSB (9)	NL-A (37) NL-B (22) Hyper-NL (43)
11	mod ExD/EmD/DSB (15) mod-sExD,mod GEN (15)	6-mEmD,DSB,DISTR,ExD (25) 5-mod-sEmD,vmDISTR (8)	mod HE/DE,ExD (9) mod HE/DE,DISTR,ExD (11)	mod-sAnxiety-dependency (4) mod-sDISTR,mod ExD,EmD,DSB (9)	NL-A (39) NL-B (18) Hyper-NL (41)
12	mod-sExD,mod GEN (15)	mEmD,DSB,ExD (27) mod-sEmD,vmDISTR (8) mod DSB,EmD,mExD,HE/DE (6) sDSB,EmD,ExD (2)	mod HE/DE,ExD(12) mod HE/DE,DISTR,ExD (11)	mod-sAnxiety-dependency (4) mod DISTR,EmD,mGEN (19)	NL (58) very NL (18) Hyper-NL (14)

Note. ExD = executive disturbances; DSB = disturbed social behavior; EmD = emotional dysregulation; HE/DE = hypo-emotionality and de-energization; DISTR = distress; NL = no acquired personality disturbance; GEN = general disturbance (i.e., disturbances within in each dimension, and no dimension stands out as most severely disturbed); vm = very mild; m = mild; mod = moderate; s = severe.

Bold typeface indicates the non-trivial changes from the prior step.

[a] Each successive step summarizes the results for a "solution" with one additional cluster than in the previous step.

[b] The labels assigned to clusters are post hoc, based on highest mean disturbances and severity.

Table 4

Mean personality ratings for clusters from Ward's cluster analysis, collapsed into five groups

	DISTURBED (n=96, 49.5%)				NORMAL (n=98, 50.5%)
Scale	ExD (n=30) (31.3%)	EmD/DSB (n=33) (34.4%)	HE/DE (n=20) (20.1%)	DISTRESS (n=13) (13.5%)	
Lack of Planning	5.7	3.6	5.6	4.8	2.7
Lack of Persistence	5.2	3.5	4.9	4.3	2.6
Perseverative Behavior	5.3	4.2	4.8	4.2	2.9
Poor Judgment	5.8	3.9	4.7	4.6	2.8
Impulsivity	5.0	3.8	3.8	4.1	2.6
Indecisiveness	5.6	4.2	5.0	5.2	3.2
Social Inappropriateness	5.3	4.2	3.3	4.0	2.4
Insensitivity	5.1	4.5	3.5	3.6	2.5
Inappropriate Affect	5.0	3.0	3.0	3.9	2.6
Lack of Insight	5.1	3.0	3.3	3.5	2.4
Aggressive Behavior	4.0	3.2	2.4	2.7	2.3
Irritability	5.1	5.1	2.6	3.9	3.0
Impatience	5.4	5.3	1.8	4.3	2.9
Lability	5.4	5.0	2.8	5.0	3.2
Inflexibility	5.4	4.6	3.4	4.2	3.4
Apathy	5.0	3.9	5.0	3.9	2.9
Lack of Initiative	5.8	3.7	5.2	5.5	2.8
Blunted Affect	3.9	2.4	4.9	1.5	3.0
Social Withdrawal	4.0	4.2	5.2	2.7	2.8
Type A Behavior	3.3	3.3	2.1	1.6	2.9
Anxiety	4.4	4.6	3.8	5.7	3.1
Depression	4.4	4.1	4.0	5.2	2.8
Dependency	4.1	4.0	3.6	5.9	2.7
Easily Overwhelmed	5.3	4.9	4.7	5.7	3.2
Lack of Stamina	5.6	4.6	5.7	5.5	3.6

	DISTURBED (n=96, 49.5%)				NORMAL (n=98, 50.5%)
Scale	ExD (n=30) (31.3%)	EmD/DSB (n=33) (34.4%)	HE/DE (n=20) (20.1%)	DISTRESS (n=13) (13.5%)	
Suspiciousness	3.7	3.6	2.5	2.9	2.9
Obsessiveness	4.0	4.1	3.7	4.4	3.7
Frugality	3.2	3.5	3.7	3.8	3.4
Vanity	3.4	2.7	2.2	2.2	2.1
Manipulativeness	4.0	2.8	2.0	4.0	2.3

Note. ExD = Executive Disturbances (and general disturbance); EmD/DSB= Emotional Dysregulation/Disturbed Social Behavior; HE/DE = Hypo-emotionality/De-energization.