

Frontal Behavioural Inventory-Manual

Background and construction

The Frontal Behavioral Inventory (FBI) was developed and standardized with the purpose of being able to differentiate Frontal Lobe Dementia (FLD) what has become now the behavioural variety of Frontotemporal Dementia (bvFTD) from other dementias, such as Alzheimer's Disease (AD) and Vascular Dementia (VAD) and to quantify the severity of the behavior disorder of FTD (Kertesz et al., 1997 Kertesz et al., 2000, Kertesz et al 2003).

At the time of the development of the FBI other behavioural inventories aimed at FTD had too few items or insufficient scoring systems. There are other scales, similar to the FBI, that have been designed with questions posed to the primary caregiver to identify the behavior and personality changes of FTD patients. Gustafson and Nilsson (1982) attempted to separate FLD and Pick's Disease (PiD) from Alzheimer's disease (AD) by quantitating the items typical of FLD and those of AD and comparing their relative weight,. A retrospective questionnaire was used to correlate diagnostic features with autopsy findings in AD and FLD to verify the diagnostic features by autopsy (Barber et al., 1995). FTD patients were distinguished by disinhibition, lack of insight, lack of empathy, social inappropriateness and eventual mutism. Recent studies were aimed at investigating behavior in FLD and AD using the Neuropsychiatric Inventory (Binetti et al., 1998; Cummings et al., 1994; Levy et al., 1996; Rozzini et al., 1997).

General behavioural rating scales such as the Comprehensive Psychiatric Rating Scale (CPRS) appeared to not capture the behavioral disorder of FTD (Gregory, 1999).

The Neuropsychiatric Interview (NPI) (Levy et al., 1996) and the BEHAVE-AD (Mendez et al., 1998) had somewhat better success in correctly classifying FTD patients approximately 69-77% of the time, but they aim at a general dementia population with too few items for FTD. Some scales were developed especially for the FTD population, for example, the Frontotemporal Behavioral Scale (FBS) (Lebert et al., 1998). While correct classification appears successful for both the FBI (Kertesz et al., 2000) and the FBS (Lebert et al., 1998), the scoring system of these scales is different. The FBS has 4 items (each consisting of 5 sub-items) that are scored as either present or absent (a score of 1 versus 0). As such, a cut-off of 3 points successfully distinguishes FTD from other degenerative dementias. In contrast, the FBI has 24 items that are scored on a range from 0 to 3, capturing severity of various symptoms and not just presence or absence of symptoms.

We constructed the FBI with items incorporating the Lund/Manchester consensus in addition to the symptoms observed in our FTD clinic and in published observations on FTD (Table 1.) The core diagnostic features in the Lund Manchester criteria (1994), modified later by the Neary et al. criteria (1998), were indifference, remoteness, inertia, asponaneity, loss of insight, social awareness, personal hygiene, mental rigidity and inflexibility, disinhibition, perseverative behaviour, utilization behaviour, and reduction of speech. We modified these items, to eliminate some duplication and less easily definable features such as “social awareness”. We also expanded on the disinhibition item, because it encompassed many other behaviours we found typical. The items underwent further slight modifications since its original publication in 1997, but the latest version from 2003 correlates well with the the first version, therefore subsequent

standardizations are compatible with the same total score (Table 2). In this scale, 12 items assess deficit (negative) behaviors (apathy, asponaneity, indifference, inflexibility, personal neglect, disorganization, inattention, loss of insight, logopenia, verbal apraxia, loss of comprehension and alien hand), and 12 items assess disinhibition (positive) behaviors (perseverations/obsessions, irritability, excessive jocularity, social inappropriateness, impulsivity, restlessness, aggression, hyperorality, hypersexuality, utilization behavior, and incontinence). Some of the negative items are aimed at language and motor behaviours.

Objectives of the inventory

1. To complement the spontaneous history offered by the patient and the caregiver. Although history taking is the core of diagnostic effort, directed questions are used at a variable extent. A formal behavioural inventory serves to standardize such questioning. It aids the clinician to cover the spectrum of behaviours more completely.

2. To allow for a standard scoring system to compare patients and determine the severity of their illness.

3. To provide sensitive and specific diagnostic cut scores for bvFTD and analyze the behaviours that are most discriminatory between clinical entities. There are patterns of dissociation and clustering of behaviours that can be explored with the inventory.

4. To record the change of severity with time and analyze the items that change with a variable rate.

5. To measure treatment effect or to detect behaviours that respond to treatment.

Description of the FBI

The FBI is a 24 item, quantifiable questionnaire directed to the caregiver. The inventory requires a reliable observer, unlike some depression or other behavioural inventories directly administered with the patients, as bvFTD patients rarely if ever have sufficient insight into their behaviour. It is intended for a face to face interview style administration, although we had satisfactory experience with nonstandard administrations on the telephone, or the caregiver filling out and scoring the inventory alone in the waiting room or at home to be mailed in. Administration is about 20-30 minutes, depending on the extent and severity of symptoms and the caregiver's verbal capacity. At times caregivers unload a large number of symptoms and disturbing behaviours in a cathartic fashion. Skilled interviewers can usually keep the answers within a reasonable time frame. The questions in the updated version (2003) are bidirectionally scripted, (see examples in item description) to avoid influencing the caregiver towards a yes or no answer.

Item description and interpretation.

1. Apathy: *Has s/he lost interest in friends or activities or is s/he interested seeing people or doing things?*

Apathy is a common symptom in depression, Alzheimer's disease, brain tumors, and other brain disorders affecting the frontal lobes. However, it is a major and early symptom in bvFTD, even though it is often mistaken for depression or "burn-out".

Apathy overlaps with asponeneity, indifference, and social disengagement. It can be differentiated from the apathy of depression by the absence of despair, sadness, crying, or suicidal ideation. Neglecting finances, friends, relatives, chores, duties, and personal

grooming are common symptoms. Abulia is a more severe degree of lack of responsiveness and apathy.

2. Aspontaneity: *Does s/he start things on his/her own, or does s/he have to be asked?*

Lack of spontaneity is lack of initiation of activity, speech, and nonverbal responses, overlapping with apathy, inattention, and indifference. The caregiver complains that the patient has to be told to do everything, even those chores that h/she is quite capable to do. This amotivational state may be an early stage of apathy.

3. Indifference / Emotional Flatness: *Does s/he respond to occasions of joy or sadness as much as ever, or has s/he lost emotional responsiveness?*

Indifference means no reaction to significant events, lack of emotional responsiveness, uncaring attitude or comments, leaving company abruptly, lack of empathy, or social disengagement. It is most obvious when detachment or emotional flatness occurs towards family members. A failure to mourn or commiserate, help in distress, enjoy a new grandchild, or congratulate someone's happy event, are common examples. Indifference overlaps with apathy, aspontaneity, and inattention. These patients also have blunted expression of all emotions.

4. Inflexibility: *Can s/he change his/her mind with reason or does s/he appear stubborn or rigid in thinking lately?*

Mental rigidity, or inflexibility, is an inability to shift thinking or actions. It is often complained of as stubbornness, insistence on routines, and compulsion to be there in time or do things at the same time (clockwatching). Concreteness is also a symptom of rigid thinking, inability to generalize, to draw abstract conclusions, to understand humor and metaphors.

5. Disorganization: *Can s/he plan and organize complex activity or is s/he easily distractible, indecisive, or unable to complete a job?*

Disorganization, lack of planning and sequencing may be one of the earliest behavioural manifestations of the frontal dysexecutive phenomenon. Disorganization is related to inattentiveness, distractibility, impersistence, apathy, and asponaneity. Complex tasks are affected first, requiring problem solving, planning, flexibility, and decision making.

6. Inattention: *Does s/he pay attention to what is going on or does s/he seem to lose track or not follow at all?*

Inattention, or lack of focused and sustained attention to tasks or to people, in its extreme form, leads to disorganization and apathy. It also involves, to some, extent, the inattentiveness to the need of others and social incompetence. Distractibility if the patient can not focus on the problem at hand, and impersistence, if the attention is not sustained.

7. Personal Neglect: *Does s/he take as much care of his/her personal hygiene and appearance as usual, or does s/he neglect to wash or change his/her underwear?*

Personal neglect is related to apathy, inattention, and social disinhibition. It can be a source of constant irritation to the family.

8. Loss of Insight: *Is s/he aware of any problems or changes in behaviour, or language, or is s/he unaware of them or deny them when discussed?*

Although the patient may be superficially aware of the diagnosis and declare to anyone who asks, "I have Pick's disease" or memory problems, invariably they would not be aware of the inappropriateness or the disastrous consequences of their actions, and they would often argue with the caregiver; "there is nothing wrong with that" or, "I am all right".

9. Logopenia: *Is s/he as talkative as before or has the amount of speech significantly decreased?*

Logopenia is decreased speech output and word finding difficulty, but preserved syntax and phonology. It is common in the behavioral variety of FTD, eventually leading to mutism. Frontal amotivation and lack of initiation probably plays an important role, and it is similar to the transcortical motor aphasia, where initiation is impaired with preserved repetition. Logopenia is also a common phase in primary progressive aphasia, which often converges with bvFTD.

10. Aphasia and Verbal Apraxia: *Does s/he make language or pronunciation errors or has s/he developed stuttering or grammatical errors recently?*

This type of language disturbance is more likely encountered in the context of Progressive Nonfluent Aphasia, and in addition to logopenia, it has articulatory and grammatical errors. It also converges with bvFTD.

11. Comprehension (Semantic) deficit: *Does s/he ask what words mean, has trouble comprehending words, and/or objects, or does s/he know the meaning of words?*

The patients with semantic loss also have word finding difficulty, but they also lose the meaning of words and have difficulty understanding complex situations or conversations. They are often garrulous, even interruptive, pursuing their own agenda. At times the semantic difficulties extends to visually presenting non-verbal material such as face or object recognition, while less semantically loaded material such as numbers and colors are preserved.

12. Alien Hand and/or Apraxia: *Has s/he developed clumsiness, stiff hand, inability to use utensils or appliances, or does a hand interfere with the other, or behaves as if it did not belong, or can s/he use both hands as before?*

Alien hand and apraxia are difficult concepts for lay caregivers and that is the reason for the long question. Although unilateral rigidity or levitating hand may be observed on examination, these features, common in corticobasal degeneration (CBD) may be seen in bvFTD and may not be detected, unless asked for.

13. Perseveration, Obsessions (Stereotypy): *Does s/he repeat or perseverate actions or remarks? Are there any obsessive routines or behaviours, or has s/he always been a creature of habit?*

This is one of the most characteristic of symptoms, but often examples are needed to elicit the actual behaviours. Obsessiveness is probably the most comprehensible to lay people and sometimes using the expression “compulsions to do the same thing over and over again” helps to describe what is technically known as stereotypic behaviour or “stereotypy”. Perseverations are explained by the scripted questions, but Stereotypy is not a lay term. Care should be taken not to mistake this symptom for a preexisting obsessive-compulsive personality or disease, and it is important at this point to ask for such a trait in the past and also how much change there is in the behaviour. At times the caregiver will respond, “Yes, s/he was always a ‘neat freak’” or something to that effect, and then it is a judgment call on how to score the change, or to discount the previous trait.

14. Hoarding: *Has s/he started to hoard objects or money excessively or has her/his saving habits remained unchanged?*

Closely related to the previous item, this was introduced separately in the new version, because of its distinctiveness. It should not be difficult to distinguish from the common personality trait of a ‘pack rat’ as frequently expressed by lay people, because of its bizarre and excessive nature, and above all the change from a previous behavioural trait. These patients hoard not only old clothes, pilfer sugar packets and serviettes from restaurants, but they collect cans, boxes, and sticks on the road, even in garbage.

15. Inappropriateness: *Has s/he kept social rules or has s/he said or done things outside what are acceptable? Has s/he been rude, or childish?*

This is one of the cardinal symptoms of frontally originating disinhibition. It has a multitude of manifestations, but rudeness and childishness are the main ones, and are incorporated in the question. Loss of social intelligence can be as devastating as any other loss of cognition. Caregivers will be acutely aware which social rules have been transgressed, as this is often how the patient gets into trouble with others or the law and causes a minor to major crisis. It ranges from butting into a line to pilfering and even shoplifting. Of course social rules are variable in different cultures, but the caregivers are usually sensitive to the appropriateness of the behaviour.

16. Excessive jocularity: *Has s/he been making jokes excessively or offensively or at the wrong time, or has s/he always had a jocular manner or a quirk sense of humor?*

A flood of jokes, often inappropriately sexual or scatological in content, is well known to be a major sign of disinhibition, characteristic of frontal lobe disease; although there are normal individuals known for their talent of storytelling and witty interjections. However, the change and inappropriateness of this behaviour is not difficult to score. If

humorousness was a preexisting personality character it should not be scored under excessive jocularity.

17. Poor Judgment and Impulsivity: *Has s/he been using good judgment in decisions, spending or driving, or has s/he acted impulsively, irresponsibly, neglectfully, or in poor judgment?*

These are related symptoms, and can have serious consequences such as car accidents, financial losses, serious occupational errors or loss of business and jobs. Impulsive buying and spending money on mail orders, contests, internet, telephone, door to door sales and lottery are common among FTD patients, who suspend judgment for improbable gains

18. Restlessness / Roaming: *Has s/he been roaming, pacing, walking, driving excessively or is the activity level normal?*

Roaming refers to compulsive walking, the streets, the malls or roaming long distances with the car, but in this category is the restless pacing in the house. Patients are often go for miles and yet rarely get lost early in their illness. It has a highly specific diagnostic value, if it can be identified, this is why it is a separate question.

19. Irritability: *Has s/he been irritable, short-tempered, or is s/he reacting to stress or frustration as s/he always had?*

Although many patients become docile and apathetic, some become irritable when crossed or told not to do or say certain things. Argumentativeness is covered under inflexibility, but it may be associated or take the form of irritability. It is distinct enough from aggression, a separate item below, but irritability may progress to aggression.

20. Aggression: *Has s/he shown aggression, or shouted at anyone, or hurt anyone physically or is there no change in this respect?*

This can be an early sign in FTD in contrast to AD when it occurs in the more advanced cases. It tends to occur when an obsessive routine is interrupted, or the patient is restrained or told not to do something forcefully. Fortunately it is not a common feature, although many patients show some irritability with the same situations.

21. Hyperorality/food fads: *Has s/he been eating excessively anything in sight, or developing food fads, a sweet tooth, eating bananas or cookies excessively, or even putting objects in his/her mouth, or has s/he always had a large appetite? Has s/he lost table manners or have his eating habits not changed?*

Actually these are two or three even four behaviours that can be independent or coexisting. Gluttony or eating in excess anything that is available is often associated with loss of table manners, eating off of others' plates or stuffing their cheeks. Ask about table manners separately as a supplementary question. The other two aspects of hyperorality may have different mechanisms, but they are often associated with gluttony. These are food fads, the excessive eating of bananas or spicy food, chips or sweets, at the exclusion of others, and at the end stages the hyperorality of placing inedibles, even feces in the mouth (Coprophagia)

22. Hypersexuality: *Has sexual behaviour been unusual or excessive? This could include remarks or undressing, or is there no change in this respect?*

Hypersexuality in this population is often reflected in a sexually disinhibited talk and behaviour such as immodesty, disrobing, or less often masturbation and demand for

intercourse, often without consideration of the partner's wishes or mood. The sex act may be more frequently attempted, but performance may be indifferent or emotionless.

23. Utilization Behaviour: *Does s/he seem to need to touch, feel, examine, or pick-up objects within reach and sight, or can s/he keep his/her hands to him/herself?*

This behaviour in the extreme is easily observable in the office, but in early stages it has to be asked for. Unfortunately it often extends to public places and can cause trouble in shops or with displays. It may even lead to pilfering although that is usually scored under socially inappropriate behaviour. Frequent urination in any container, locking or opening doors, and rattling utensils or papers, are examples of perseverative, utilization behaviour, usually a late phenomenon.

24. Incontinence: *Has s/he wet or soiled his or herself, or does s/he have problems that can be explained by urinary infection or childbirth/prostate?*

This is usually a late phenomenon, although at times it appears early in relatively high functioning individuals. The symptom originates from damage to the mesial frontal lobes and not from bladder disease, but this is often investigated and nothing is found. The examiner should ask about such investigation and if the results were negative. Only then can the symptom be attributed to frontal disease.

Administration

Basic interviewing skills and some knowledge of bv FTD is necessary for the administration of the FBI. The more one has encountered these behaviours, the more reliable the score will be. To avoid duplication and for

objectivity the inventory should be given by someone other than the clinician taking the history, but this is not essential. On each score sheet the following brief instructions appear:

Explain to the caregiver that you are looking for a change in behavior and personality. If this is a repeat test specify that you are looking for a change from before the onset, not from the last time of doing the inventory. Ask the caregiver these questions in the absence of the patient. Stick to the script, but elaborate if necessary. If the caregiver does not seem to understand the question, or talks about something else, redirect by repeating the question, or using one word (known to the caregiver). For example, “No, I was wondering about apathy” or, “Is s/he inappropriate?” At the end of each question, ask about the extent frequency and the severity of the behavioural change, and then ask the caregiver to score it according to the following: 0 = none, 1 = mild / occasional, 2 = moderate, 3 = severe / most of the time. If necessary, repeat the scoring instructions after each answer.

In addition to recording a yes-no response and a scoring of the severity, the caregiver should be encouraged to provide examples of the abnormal behaviour, and these should be recorded on the form or on separate sheets attached to the inventory. Not all behaviours listed in the item description or the questions need to be present to obtain a high score. The scoring should be done preferably by the caregiver, but guidance is often necessary. At times the caregiver is unable or unwilling to assign a score, or provides a score that is obviously discrepant from the description given; repeat the instructions for the scoring briefly and if necessary, assist the caregiver to come to an accurate estimate

of the extent and severity of the behaviour. Often the score is a consensus between the caregiver and the interviewer. An assessment of the caregiver's objectivity and intelligence is a necessary part of accurate scoring. Nonstandard administrations should be followed up by a brief questioning of some of the answers.

Common pitfalls of administration include:

1. leading the informant too much;
2. not listening to the answers carefully and missing cues;
4. not interpreting the answers correctly, not asking for elaboration;
5. failure to ask the question again if the answer was vague, failure to ask for examples;
6. failure to elaborate or to provide examples if the informant does not understand the question;
7. failure to redirect. Some informants get off topic easily and require redirection;
8. Letting the informant ramble (this is inefficient). On the other hand, as long as the narrative is relevant to the illness it may uncover symptoms that are relevant to other items where they should be noted, and later revisited;
9. interrupting the informant unnecessarily;
10. commenting, other than in a sympathetic or encouraging manner;
11. failure to ask for an estimate of severity and frequency;
12. not reexamining the score if it is discrepant from the narrative.

Standardization and interpretation

In the initial publication of the FBI we compared 12 bvFTD with 16 AD and 11 patients with depressive dementia (DD) (Kertesz et al., 1997) The total scores clearly differentiated between these control groups and FTD. A group of 9 normal controls had a floor effect of 0 scores and were not considered appropriate for the comparison. Using a cut off score of 27 for FTD, only one false positive was shown in the DD group with a high endorsement of all the negative items. A more specific cut off score of 30 excluded all nonFTD cases in subsequent standardization, but may leave out early and mild cases of bvFTD. The maximum score of 72 is rarely, if ever, reached, but scores above 40 indicate severe disease, between 30 and 30 moderate, and between 25 and 30 mild, disease. High disinhibition (positive behavioural) scores are more diagnostic of FTD, negative scores can overlap with depressive illness or AD. The FBI had high face and content validity when compared to the Lund- Manchester checklist. Indifference, loss of insight, perseveration, and social inappropriateness were the items with the highest mean scores in this pilot study.

The objective of the second standardization study was to determine the interrater reliability and item consistency of the FBI, to study the prevalence of personality and behavioral changes in five clinical groups, to classify patients based on the behavioral profiles obtained from the FBI, to determine the discriminate power of the FBI items, and to determine the diagnostic sensitivity and specificity of the FBI. In this study we prospectively administered the FBI to caregivers of AD, bvFTD (FLD), PPA, Vascular dementia (VaD) and DD (Kertesz et al., 2000).

The FBI has high interrater reliability (Cohen's kappa of .90) and high item consistency (Cronbach's alpha of .89) (Kertesz et al., 2000). The discriminant function

analyses between FLD and NON-FLD, FLD and VaD, FLD and AD groups showed that *indifference* (41%), *alien hand* (25%), *inappropriateness* (18%), *perseveration* (7%) and *impulsivity* (7%) were responsible for the overall separation between the FLD group and the NON-FLD groups. *Indifference* accounted for 65%, *perseveration*, 48%, *alien hand*, 36%, and *concreteness*, 19% of the separation between the FLD and VaD group. Other items that come into the discriminant analysis are *inflexibility* (38%) for the FLD vs. AD comparison, and *personal neglect* (36%) and *hypersexuality* (18%) for the FLD vs. PPA group.

Results of the discriminant analysis between the FTD and the other clinical groups (NON-FTD) show that 100/108 (92.6%) patients were classified correctly. ($X^2=126.0$, $p<.001$) (Table 4). Of the NON-FTD, 5/82 (6.1%) were classified falsely as FTD and 3/26 (11.5%) of the FTD group were classified as not being NON-FTD, on the “leave one out” cross validation. This indicates a diagnostic specificity of 89.5% and sensitivity of 93.9% for FTD. Between groups 3/26 (11.5%) of the FTD were classified as VaD and 3/16 (18.8%) of the VaD’s were classified as FTD’s. FTD’s were classified as DD 11.8% of the time (2/17) and DD’s were classified as FTD 7.7% of the time (2/26). AD and PPA patients correctly classified 100% of the time vs. FTD patients.

Another study compared behavioral and cognitive testing in the clinical diagnosis of frontotemporal dementia (FTD) and AD. A clinically defined cohort of FTD, $n = 52$, is compared to 52 Alzheimer’s disease (AD) patients on a Frontal Behavioral Inventory (FBI) and cognitive tests (MMSE, DRS, WAB, WAIS, WMS, WCS, etc.) (Kertesz et al., 2003). Fourteen patients with FTD had autopsy confirmation and their tests are also compared with the rest of the FTD population. The FTD and AD groups were matched in

sex, duration, and severity of dementia. The total scores on the FBI showed the largest difference. MMSE and DRS total scores did not discriminate between the two groups. Memory subscores were lower in the AD group, and conceptualization and language related scores were worse in the FTD group. Milder and earlier affected patients, who could carry on a large battery of neuropsychological tests, were much better distinguished by the FBI scores on discriminant function analysis. In contrast to 75% by the cognitive tests, 100% of the FTD and AD patients were differentiated by the FBI. In conclusion, although memory scores were lower in AD and language scores were lower in the FTD population, many of the cognitive tests do not distinguish between FTD and AD. On the other hand, a behavioral inventory is a useful adjunct in the diagnosis of FTD. Postmortem validation was carried out in a sizeable subset of the population, showing similar behavioral and cognitive data.

The fourth standardization study aimed to provide construct validation of the FBI scale used to identify the behavioral disturbance in FTD, and to demonstrate that the FBI is both sensitive to change and is longitudinally valid (Marczinski et al. 2004). Currently, there are no published longitudinal data for any of these specialized scales that were developed to assess the behavioral disturbance in FTD. As FTD is a progressive dementia, the FBI scores should remain consistent or rise over time. However, some items may not show changes in the score as immobility or aphasia prevents the manifestations of some behavioral changes. To explore these two aims of this study, the FBI was administered to the primary caregivers of patients with FTD-bv and PPA for three consecutive years. FBI scores rose as the disease progressed in both the FTD-bv and PPA groups over the three years of testing. Initial mean FBI scores of the FTD-bv

group were above the cut off for FTD established for this diagnosis with previous standardization. By the third year, the mean FBI score of PPA patients was also above the established cut-off for FTD. Item analyses for each patient group indicated which items were most sensitive to changes over time. For FTD-bv patients, the indifference and logopenia items increased over the three years of testing. For PPA patients, the apathy, asponaneity, disorganization, inattention, logopenia, judgment, restlessness, inappropriateness, aggression, hyperorality, and personal neglect items increased over time.

The outcome of the study indicates that the FBI is sensitive to changes in behavior and personality in both variants of FTD and is longitudinally valid. The FBI can be used to describe the evolution of symptoms and the course of the illness of Pick Complex patients who present initially with either FTD-bv or who present with PPA and subsequently develop the behavioral disorder.

A recent study of the FBI in nationwide cohort compared the FBI and the NPI. The FBI discriminated FTD from AD in over 70% while the NPI only in 54% of the cases. (Blair et al. 2007)

The current use of the FBI is worldwide. Standardized Italian, French, Portuguese, Spanish, Norwegian, Polish, Hungarian, Turkish, and Japanese versions are in use. It has been used in many research and clinical projects for FTD , Traumatic Brain Injury, and ALS.

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