Challenging Behaviour, Epilepsy and Intellectual Disability:  
a secondary analysis of findings from a randomized controlled trial

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The present research is part of a larger study into challenging behaviour supported by an NIHR HTA grant ref 10/104/13.

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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Challenging Behaviour, Epilepsy and Intellectual Disability:
a secondary analysis of findings from a randomized controlled trial

Background As both epilepsy and challenging behaviour are highly prevalent in adults with intellectual disability (ID) it is important to explore any potential relationships between the two to inform patient care. The aim of the present study was to investigate the relationship between epilepsy factors and challenging behaviour in adults with ID.

Method The sample was drawn from a clinical trial cohort (n=246), with all participants displaying challenging behaviour across the range of ID. We described sociodemographic and clinical status (seizure types, seizure frequency and drug burden) in 70 participants with epilepsy (EP). We investigated differences in and predictors of challenging behaviour and mental ill-health, measured by the Aberrant Behaviour Checklist-Community and the Mini Psychiatric Assessment Schedule for Adults with Developmental Disabilities respectively, between participants with and without epilepsy (NEP).

Results More male participants were identified with epilepsy (EP = 76% and NEP = 61%, p = 0.026) and the EP group had lower adaptive behaviour scores than their NEP counterparts (Mean (SD) EP = 44.4 (24.1), NEP = 51.7 (25.0), p = 0.04). EP participants showed significantly less lethargy as measured by the Aberrant Behaviour Checklist-Community than NEP participants (Mean (SD) EP = 11.9 (7.4) and NEP = 15.1 (9.9); t-test p=0.02). Younger age and poorer adaptive functioning were associated with challenging behaviour (beta=-.520, p<0.001 and beta=-0.30, p<0.001 respectively).
**Conclusions** These findings indicate that epilepsy does not appear to be associated with challenging behaviour in adults with ID. Therefore, whilst management of epilepsy is very important in a clinical context, it is essential that professionals should further elucidate reasons for the presentation of such behaviours in order to provide timely and targeted interventions.

Keywords: Challenging Behaviour; Epilepsy; Seizure
1. Background

Epilepsy is the most common serious neurological disorder with a worldwide prevalence of 0.5-1% (Duncan, Sander, Sisodiya, & Walker, 2006) and it disproportionately affects people with intellectual disabilities (ID); a meta-analysis of 48 studies reported a pooled prevalence of 22.2% (95% CI 19.6–25.1) (Robertson, Hatton, Emerson, & Baines, 2015). Even higher rates of the condition are present in people with severe ID (Robertson, et al., 2015). Further, people with both epilepsy and ID commonly have physical, psychiatric and behavioural co-morbidities (Kwok & Cheung, 2007). Arguments contributing to a possible association between epilepsy and challenging behaviour are in the main due to the multiple clinical manifestations of the condition including behavioural change which may present as increased irritability during pre-ictal auras or prodromes, ictal or postictal aggression/violence and postictal confusion (Marsh & Rao, 2002). In addition, there is the potential for Anti-Epileptic Drug (AED) treatment to affect behaviour, for example Levetiracetam may be associated with challenging behaviour in people with ID (Hurtado, Koepp, Sander & Thompson, 2006).

Challenging behaviour has been defined by Emerson (1995) as "culturally abnormal behaviour of such intensity, frequency or duration that the physical safety of the person or others is likely to be placed in serious jeopardy, or behaviour which is likely to seriously limit the use of, or result in the person being denied access to, ordinary community facilities". In line with this, challenging behaviour often has serious consequences for the individual such as exclusion or the implementation of restrictive or aversive practices (Banks et al., 2007).

The prevalence of challenging behaviour is high among the ID population with current estimates suggesting a rate of 18% based on an administrative database (Bowring, Totsika, Hastings, Toogood, & Griffith, 2017). For people with multiple disabilities and profound ID this rises to 45% for destructive or aggressive behaviour and 82% for stereotypical or self-injurious behaviour (Poppes, Van der Putten, & Vlaskamp, 2010).
Many publications, summarized in three systematic reviews, have explored the relationship between epilepsy and challenging behaviour in ID (Blickwedel, Ali, & Hassiotis, 2017; De Winter, Jansen, & Evenhuis, 2011; van Ool et al., 2016). While no overall relationship was found, the evidence is not definitive (Blickwedel, et al., 2017) as some studies suggest that there may be specific groups of people with epilepsy and ID where there is an association between challenging behaviour such as attention seeking behaviour, mood swings, being uncooperative, disturbing others at night and lack of empathy behaviour (Deb, Thomas, & Bright, 2001; McGrother et al., 2006). Further, studies also have found associations with aggression and irritability (Cassidy & Chung, 2001; Creaby, Warner, Jamil, & Jawad, 1993). Finally, a small number of studies reported that epilepsy factors may be linked to challenging behaviour in those experiencing tonic clonic seizures (Deb & Joyce, 1999) or higher irritability and incidents of excessive anger in inpatients with generalised epileptiform activity than in matched controls (Deb & Hunter, 1991).

Other mental health problems appear to be prevalent in adults with ID and epilepsy. One study (Espie et al., 2003) reported significantly higher levels of psychiatric disorder, in particular affective/neurotic disorders, in individuals with epilepsy, but concluded that presence of epilepsy itself is likely only a predictor for a minority of people with ID. The authors identified epilepsy related factors such as greater seizure severity and frequency, as well as lower tendency for loss of consciousness during seizures as potentially associated. A more recent prospective case-control study (Turky, Felce, Jones, & Kerr, 2011) reported that adults with epilepsy and ID were significantly more likely to develop psychiatric disorders, particularly depression and unspecified disorder, including dementia over a one year period than those without epilepsy.

2. Aims

We undertook the present study in order to examine the complex relationship between
epilepsy and challenging behaviour in a clinical sample of people with ID and confirmed behavior that challenges and to explore any relevant associations with demographic and clinical variables.

The research questions were as follows:

(1) What are the characteristics of adults with ID and reported epilepsy in a clinical sample of adults with challenging behaviour?

(2) Are there differences in challenging behaviour and mental health status between adults with ID with and without epilepsy?

(3) What are the factors associated with epilepsy in a clinical sample of adults with ID and challenging behaviour?

2. Methods and Procedures

3.1. Participants

The study was conducted as part of a clinical trial of training in Positive Behaviour Support (Hassiotis et al., 2018). The main study is reported elsewhere but briefly 246 participants were recruited from 23 community Intellectual Disabilities services in England which were randomized to receive the intervention (staff training in Positive Behaviour Support) or treatment as usual. Participants were included in the trial if they were eligible to receive services from intellectual disability services, were aged 18 or over and scored at least 15 on the Aberrant Behaviour Checklist-Community (ABC-C; (Aman, Singh, Stewart, & Field, 1985)). 64% of these participants were male with 17% classified as having a mild, 31% a moderate and 52% a severe level of intellectual disability. Full participant characteristics are outlined in the main study paper (Hassiotis et al., 2018). Ethical approval for the clinical trial was obtained by by the National Research Ethics Service Committee London–Harrow (reference 12/LO/1378) and the study described here was approved as a substantial
amendment to this. Consent was obtained using easy-read materials and where a participant lacked capacity to consent, an appropriate consultee was identified.

We utilized the baseline data collected on all participants as part of the main study and a researcher (JB) gathered additional information for all those participants with a reported diagnosis of epilepsy. Participants in the present study were excluded if they either were currently being investigated for epilepsy or did not meet the International League Against Epilepsy (ILAE) criteria for epilepsy (Fisher et al., 2005), i.e. they have not had 2+ unprovoked seizures more than 24 hours apart, they had an age-dependent epilepsy syndrome and are now past the applicable age, they have been seizure-free for 10+ years off AEDs or they have non-epileptic seizure disorders.

3.2. Measures

All demographic and questionnaire data were collected by proxies, that is, from a family carer or paid carer who knew the person well. The demographic information included age, gender, ethnicity and additional health conditions and medication. All outcome measures were collected in interviews during the baseline assessment for the main study (between 2013 and 2015; Hassiotis et al., 2018). Information about epilepsy characteristics were collected in additional interviews at a later time point (between 2014 and 2015).

Primary Outcome Measures

Challenging behaviour was assessed with the Aberrant Behaviour Checklist-Community (ABC-C) (Aman, et al., 1985), an instrument commonly used to record behaviour in people with ID which has sufficiently demonstrated both reliability and validity. The scale comprises of 58 items assessing five subscales of challenging behaviour with higher scores indicating more severe challenging behaviour.

Participant mental health and autism spectrum disorder (ASD) status was assessed with the short version of the Psychopathology Assessment Scale for Adults with Developmental
Disabilities (Mini PASADD) (Prosser et al., 1998) administered by trained researchers. The Mini PASADD comprises 86 psychiatric symptoms with threshold scores for eight diagnostic domains and a screen for ASD.

**Other Outcome Measures**

Adaptive Behaviour and was measured with the Short Form Adaptive Behaviour Scale (SABS) (Hatton et al., 2001).

For the participants with a reported diagnosis of epilepsy the researcher used a purpose designed questionnaire to carry out a structured interview. Information was gained on age of onset, seizure frequency, seizure type(s) and epilepsy management. Seizure type was established by seeking detailed description of the seizure(s) from the carer, using prompts based on the 'Questionnaire for Clinical Seizure Diagnosis' (Reutens, Howell, Geber, & Berkovic, 1992) as required. These accounts were then used to classify seizure type according to ILAE criteria (Angeles, 1981) and all classifications were checked by an experienced epilepsy specialist (MW).

**3.3. Statistical analysis**

Differences between the EP and NEP groups were compared with univariate analyses using the Chi-square test for non-continuous variables or independent samples t-test for continuous variables. Multiple tests were carried out without adjustments and a p value of <0.05 was used as the level of significance. A multiple linear regression was performed to test the predictors of the primary outcome, total ABC-C score. Following the rule of thumb that at least ten participants are required for each predictor variable included in a regression analysis (Tabachnick and Fidell, 2007), we restricted the multiple regression to include seven predictors. We explored the effect of: epilepsy status, age, gender, ABS score, presence of a mental illness and autism status (categorised using the mini PAS-ADD). As low levels of clustering were observed in the primary trial, we did not account for clustering in this
analysis (Hassiotis, et al., 2018). For the multiple regression analysis, all assumptions were checked, including normality, homoscedascity and independence of errors. The normality assumptions of the residuals were investigated using residuals plots. All statistical test and confidence intervals are two sided. All analyses were performed using Stata version 14.

4. Results

4.1 Demographic and clinical and characteristics

Data from 240 participants were utilized for this study. Seventy were identified as having epilepsy (figure 1). Four participants were excluded as they were being investigated for epilepsy or had a diagnosis of non-epileptic attack disorder; one participant was excluded as no longer met ILAE criteria, being seizure free and not receiving AED treatment for over 10 years; and another participant had to be excluded as did not meet the ABC-C trial inclusion threshold.

Figure 1

EP participants had a mean age of 40.2 years (standard deviation (SD) 14.2) whilst the mean age in the NEP group was 38.0 (SD 14.7). There was a significantly larger proportion of males in the EP group (76% and 61% respectively, \( \chi^2 \) p=0.026). The majority of participants were white and similar proportions in both groups had a recorded mobility or sensory problem. The mean SABS score for the EP group was 44.4 (SD 24.1) compared with 51.7 (SD 25.0) for the NEP participants which was statistically significant (mean difference = -7.30; 95% CI (-14.22, -0.37) p=0.04). Details are shown in table 1.

Table 1
4.2 Seizure details

Seizure type

The majority had received a diagnosis of epilepsy in childhood or in their teens, with a small proportion (15.3%) being diagnosed after the age of 20 years (data on n=26). Descriptions of seizures, on which seizure classifications were based, were available for 54 participants. Twenty-eight (51.9%) experienced primary generalized seizures of various types such as tonic clonic, atonic, tonic and absences. The remaining 26 (48.1%) suffered focal seizures with or without impairment of consciousness. It was not possible to classify seizure type for 15 participants (20.29%) as the participants had either been seizure free for years with no one currently working with the person having witnessed a seizure and/or there were no records about the person’s seizure type available on file.

Seizure frequency

There were 42 participants with active epilepsy, which we defined as having experienced a seizure within the past 12 months. Out of those whose seizures were not fully controlled, the majority (n=24; 57.1%) had frequent seizures, defined as occurring at least monthly. Thirteen (31.7%) had to visit emergency services as a result of their epilepsy within the past 12 months; a minority (30.8%, n=4) were admitted overnight. One person had an episode of status epilepticus in the past year. Twenty-seven participants had been seizure free for a mean of 5.8 years (SD 4.6).

Epilepsy management

Out of 67 participants, almost half (n=31; 47%,) were receiving care for epilepsy from more than one professional, most commonly the General Practitioner (n=38; 56.7%) followed by a Neurologist (n=29; 43.2%) and a consultant psychiatrist in intellectual disabilities (n=25; 37.3%). Twelve participants (17.9%) reported involvement of an Epilepsy Nurse and in one case monitoring was carried out by the ID nurse.
Antiepileptic (AED) treatment

Information on AED treatment was available for 65 participants. Mono and polytherapy was received by 33 (50.0%) and 32 (48.5%) participants respectively. One person did not take any AED. Ten participants (15.2%) were prescribed the anti-epileptic Levetiracetam. Twelve (19.7%) had been prescribed ‘rescue medication’, i.e. rectal diazepam or buccal midazolam. It should be noted that two thirds of study participants with and without epilepsy also received psychotropic medication for the treatment of mental disorder.

4.3 Clinical outcomes

The EP group was found to have overall lower levels of behaviour that challenges (mean total ABC-C = 61.8, SD = 28.6) than the NEP group (mean total ABC-C = 67.0, SD = 28.7) though this was not statistically significant. Of the ABC-C subdomains only lethargy was found to be significantly lower in the EP group (mean difference = -3.14; 95% CI (-5.72, -0.56), p = 0.017). There was no significant difference in mental health status between EP and NEP although there was an indication of higher levels of severe mental illness (psychosis and manic depression) in the NEP group. Details are shown in table 2.

Table 2
There was no significant difference in ABC-C scores, psychiatric or autism status between those with focal and primary generalized seizures. Neither was there any significant difference in total ABC-C scores between those receiving AED mono or polytherapy. We explored the effect of epilepsy, age, gender, ethnicity, SABS score, mental health status and autism status on the ABC-C total score. The analysis showed that younger age and poorer level of adaptive behaviour were significantly associated with behavior that challenges (Table 3).

Table 3
5. Discussion

We have described a sample of adults with challenging behaviour and epilepsy who have taken part in a clinical trial. In the present sample, we found a higher prevalence of epilepsy at 29.2%, compared to that expected at 22.2% in the general ID population, though this may be explained by the large proportion of participants with more severe intellectual disability within our sample (Robertson, et al., 2015).

We found two non-epilepsy related factors, age and level of ability as predictors of challenging behaviour which have also been implicated in the onset of challenging behaviour in people with ID without epilepsy (McClintock, Hall, & Oliver, 2003). Although the ABC-C subdomain lethargy was significantly lower in the EP group, it could be a chance finding. However, it is counterintuitive as the domain statements appear to map behaviours that may be considered within an autism spectrum disorder, e.g. preoccupied, stares into space; prefers to be alone; responds negatively to affection. We did not find any difference in mental health status between the EP and NEP groups. Arshad and colleagues (Arshad et al., 2011) examined associations between epilepsy and psychopathology in consecutive adult referrals to a community psychiatric clinic for people with ID. They found that severity of ID was a predictor of epilepsy but prevalence of mental disorders was lower in the group with epilepsy than without. Further, the authors found less use of medication in the EP group, however, in our study use of medication was similar across both EP and NEP participants.

Our findings indicate that whilst challenging behaviour and epilepsy may coexist, the latter is not a risk factor for severity of challenging behaviour.

Our results contradict those of previous studies (Deb et al., 2001; McGrother et al., 2006) but add to the growing body of evidence that epilepsy is not associated with challenging behavior (Deb & Hunter, 1991; Tyrer et al., 2006; Matthews, Weston, Baxter, Felce, & Kerr, 2008;
Pawar & Akuffo, 2008).

The study benefits from including a standardized definition of epilepsy, and of challenging behaviour based on a well validated measure. All classifications were checked by a clinician with over 20 years of experience of working in epilepsy (MW) in order to be able to classify seizure type accurately based on detailed descriptions obtained from carers by a trained researcher (JB).

However, there are also limitations as this is a post hoc analysis of a nested case control design within a clinical trial. All trial participants were recruited based on having a clinical level of challenging behaviour which whilst it allows us to determine whether the presence of epilepsy affects the severity of the behaviour, it may not provide a definitive answer as to whether epilepsy is a risk factor for the presence of challenging behaviour.

It is also possible that a degree of bias may be present as baseline data were collected prior to the design of the present study. Therefore, carers were not specifically instructed to include behaviour ratings where they were aware that the behaviour may bear a temporal relationship to a seizure occurring, but still experience it as challenging. As a result, some carers may have not rated, e.g. an individual experiencing post-ictal aggression, as episodes of challenging behaviour, whereas others may have included this in their ratings. Finally, while drug treatment was recorded within the scope of this study it was not possible to untangle the effects and interactions of the psychotropics and AEDs some of which are used as mood stabilizers for mental illness and for which indications for prescription may elude family and paid carers.

The findings of the study are highly relevant to clinical practice especially as a number of causative factors such as genetic vulnerability, severity of ID, and the presence of autism have been linked with epilepsy (Kerr et al., 2016). Often, in routine care, the complexity of health issues such as epilepsy in persons with ID, often accompanied by multimorbidity, may
mask other underlying factors for the presentation of challenging behavior. It is accepted that at times, it is difficult to disaggregate the epilepsy related symptoms including those of medication side-effects from the presenting challenging behavior (Ring et al., 2016). However, we urge clinicians to consider all evidence regarding the association (NICE, 2015) and to take a balanced view as to whether further investigations are indeed required before the prompt delivery of interventions for challenging behaviour. Display of challenging behaviour requires skilled multidisciplinary management including support for family caregivers and should be considered a priority in order to mitigate risk for further deterioration in the patient including impact on quality of life.

Future studies may need to adopt the approach suggested by York and Kerr (2014) who argue that focusing closely on the presenting behaviours and possible changes in mental state manifesting in the pre, inter and post ictal period for each patient may prove useful in improving patient care and safety.
7. References


Figure 1. Participant flow in the study
Table 1. Demographic details

<table>
<thead>
<tr>
<th></th>
<th>EP = 70</th>
<th>NEP = 170</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, Mean (SD)</strong></td>
<td>40.2 (14.2)</td>
<td>38.0 (14.7)</td>
<td>0.292¹</td>
</tr>
<tr>
<td><strong>Gender (male), N (%)</strong></td>
<td>53 (75.7)</td>
<td>103 (60.6)</td>
<td>0.026²</td>
</tr>
<tr>
<td><strong>Ethnicity, N (%)</strong></td>
<td></td>
<td></td>
<td>0.847²</td>
</tr>
<tr>
<td>White</td>
<td>52 (74.3)</td>
<td>122 (71.8)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7 (10.0)</td>
<td>18 (10.6)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>7 (10.0)</td>
<td>21 (12.4)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>3 (4.3)</td>
<td>4 (2.4)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.4)</td>
<td>5 (2.9)</td>
<td></td>
</tr>
<tr>
<td><strong>SABS, Mean (SD) n = 239</strong></td>
<td>44.4 (24.1)</td>
<td>51.7 (25.0)</td>
<td>0.04¹</td>
</tr>
</tbody>
</table>

¹T-test, ²Chi-square test. EP = epilepsy, NEP = non-epilepsy, SD = standard deviation, N = number, SABS = Short form Adaptive Behaviour Scale
Table 2. Clinical outcomes

<table>
<thead>
<tr>
<th></th>
<th>EP = 70</th>
<th>NEP = 168*</th>
<th>Mean difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABC-C, Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>61.8 (28.6)</td>
<td>67.0 (28.8)</td>
<td>-5.2 (-13.3, 2.8)</td>
<td>0.204</td>
</tr>
<tr>
<td>Irritability</td>
<td>21.1 (11.6)</td>
<td>20.3 (10.1)</td>
<td>0.8 (-2.1, 3.8)</td>
<td>0.588</td>
</tr>
<tr>
<td>Lethargy</td>
<td>11.9 (7.4)</td>
<td>15.1 (9.9)</td>
<td>-3.1 (-5.7, -0.56)</td>
<td><strong>0.017</strong></td>
</tr>
<tr>
<td>Stereotypy</td>
<td>5.3 (4.3)</td>
<td>6.4 (5.3)</td>
<td>-1.05 (-2.5, 0.4)</td>
<td>0.143</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>19.3 (10.0)</td>
<td>20.1 (9.9)</td>
<td>-0.8 (-3.6, 2.0)</td>
<td>0.580</td>
</tr>
<tr>
<td>Inappropriate Speech</td>
<td>4.1 (3.6)</td>
<td>5.1 (3.9)</td>
<td>-1.1 (-2.1, 0.02)</td>
<td>0.055</td>
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<tr>
<td><strong>Mini PASADD, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common mental disorder</td>
<td>30 (42.9)</td>
<td>83 (50)</td>
<td></td>
<td>0.316</td>
</tr>
<tr>
<td>Severe mental illness</td>
<td>8 (11.4)</td>
<td>36 (21.8)</td>
<td></td>
<td>0.062</td>
</tr>
<tr>
<td>Autistic spectrum</td>
<td>13 (18.6)</td>
<td>37 (22.3)</td>
<td></td>
<td>0.523</td>
</tr>
</tbody>
</table>

*ABC-C= Aberrant Behaviour Checklist-Community, PASADD= Psychopathology Assessment Scale for Adults with Developmental Disability. EP = epilepsy, NEP = non-epilepsy, SD = standard deviation, N = number. 1: Mann Whitney U test; 2: χ² test. *The number of participants was slightly reduced due to missing data.
Table 3. Multiple Regression Analysis for total ABC-C score

<table>
<thead>
<tr>
<th></th>
<th>N = 234</th>
<th>B</th>
<th>St. Error</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EP</td>
<td></td>
<td>-4.12</td>
<td>3.86</td>
<td>0.286</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>-0.520</td>
<td>0.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td></td>
<td>3.89</td>
<td>3.68</td>
<td>0.291</td>
</tr>
<tr>
<td>SABS</td>
<td></td>
<td>-0.30</td>
<td>0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Common mental disorder*</td>
<td></td>
<td>1.74</td>
<td>3.66</td>
<td>0.635</td>
</tr>
<tr>
<td>Severe mental disorder*</td>
<td></td>
<td>5.78</td>
<td>4.51</td>
<td>0.201</td>
</tr>
<tr>
<td>ASD *</td>
<td></td>
<td>8.81</td>
<td>4.54</td>
<td>0.054</td>
</tr>
</tbody>
</table>

ABC-C= Aberrant Behaviour Checklist-Community, SAB = Short Form Adaptive Behaviour Scale, ASD= autism spectrum disorder. *: calculated from the mini-PASADD.