
doi: 10.1093/ageing/afq044
Published electronically 19 May 2010
Published by Oxford University Press
on behalf of the British Geriatrics Society 2010.

Associations between drug burden index and physical function in older people in residential aged care facilities

SIR—The functional decline seen in older people results in a need for increased support from carers, health care services and residential aged care facilities (RACFs) [1]. Impaired physical function in older people predicts nursing home placement and death [2]. While advances in medical management have aided in managing many diseases, certain classes of medications have adverse effects on physical function in older adults [3–5]. Expert consensus panels have compiled criteria for drugs that are potentially inappropriate for older people [5–8]. Anticholinergic and sedative drugs occur frequently in these criteria; however, the effects of cumulative exposure are not addressed.

Studies of community-dwelling older people have found associations between increasing anticholinergic [4, 9] and sedative [9] exposure and poor physical function measures. Research conducted in RACFs has shown associations between polypharmacy, adverse drug reactions and inappropriate drug use but not functional decline [10–12].

The drug burden index (DBI) is a measure of an individual’s total exposure to anticholinergic and sedative drugs, using the principles of dose–response and maximal effect. Increasing DBI is associated with impairments in measures of physical and cognitive function in community-dwelling older people, cross-sectionally in American [3] and Australian [13] populations and longitudinally in the USA [14]. This relationship has not been examined in older people living in RACFs who are frequently excluded from epidemiological studies [11]. We hypothesised that increasing...
DBI is associated with poorer physical performance measures in a population of older people living in RACFs.

Methods

Participants

Data were obtained from a randomised controlled trial designed to determine fall rates in RACFs in the Northern Sydney Central Coast Health (NSCCH) area, Australia. Individuals were eligible if they were ambulant, aged >70 years and likely to survive for 12 months as informed by facility staff. Exclusion criteria were skin cancer and taking vitamin D or calcium supplements. The project was approved by the NSCCH Human Research Ethics Committee, registered on the Australian New Zealand Clinical Trials Registry (ACTR number: ACTRN12607000089437) and funded by a National Health and Medical Research Council grant.

Medication exposure

Medication history including name, dose and frequency was noted from signed nursing administration records at baseline, 6 and 12 months. For participants who self-medicated, details were obtained from medication packaging or prescription, and confirmed with nursing records.

Drugs were classified as anticholinergic or sedative according to the Australian registered prescribing information reference, Monthly Index of Medical Specialties (MIMS) [15]. The burdens of each drug with anticholinergic or sedative properties were calculated using the following equation:

$$DBI = \sum$$

where $D$ is the 24-h dose taken and $\delta$ is the 24-h dose to achieve 50% of the maximum effect ($\text{DR}_{50}$) [3]. The $\text{DR}_{50}$ is usually unknown and therefore estimated using the minimum registered dose taken from MIMS [15].

The DBI was calculated for each individual as the sum of the burdens of these medications. Cumulative exposure over time (AUCDB) was calculated using the principals of trapozoidal area under the curve [14]. ‘Exposed’ individuals were defined as those who were exposed to any drug with anticholinergic or sedative actions.

Outcomes

Objective measures of physical function were performed at baseline, 6 and 12 months. Grip strength, reaction time, walking speed and balance were obtained according to standard methods [16–19].

Covariates

Factors likely to influence the relationship between DBI and physical functioning were included in the analyses. Socio-demographics and medical history were obtained from RACF records. The co-morbidity score was a modified version of the Functional Comorbidity Index, allowing for the limited information available [20]. Cognitive impairment was defined as a Mini-Mental Status Examination score of <24 [21] and depression as a Geriatric Depression Scale score >5 [22].

Statistical analyses

Mean functional outcome values for exposed versus non-exposed individuals after adjusting for covariates were examined. Univariate analyses examined the association between DBI and functional outcomes. Multiple linear regression analyses, adjusted for covariates, including age, gender, cognitive impairment, depression and co-morbidity score, were used to investigate associations between DBI and grip strength, walking speed and reaction time. Balance (measured categorically) was analysed using logistic ordinal regression. These methods were used to investigate AUCDB and physical function after 12 months with the addition of baseline physical function as a covariate. Analyses were performed using SAS 9.1 (SAS Institute, Cary, NC, USA).

Results

At baseline, there were 602 participants, with mean age (±SD) of 85.7±6.4 years (range 70–107), and 70.9% were female. The mean number of medications taken was 6.0±3.0. Of the 589 (97.8%) individuals taking medications, 35.7% were exposed to anticholinergic drugs and 42.0% to sedative drugs. The average DBI (0.60±0.66) and other baseline characteristics are shown in Table 1. The most common drug classes for anticholinergic medications were antidepressants (excluding selective serotonin reuptake inhibitors, SSRIs) (17.4%), followed by antipsychotics (9.6%), antihistamines (3.8%) and antispasmodics (3.5%), whilst for sedatives, they were anxiolytics (18.1%), SSRIs (14.5%), opioids (6.0%) and anti-diarrhoeals (1.7%).

At baseline, there was no statistically significant difference in adjusted means of functional measures for participants who were exposed to DBI drugs versus those non-exposed. Longitudinal analysis of adjusted means for exposed versus non-exposed only found a significant difference in the mean balance of exposed (3.3±0.1) compared with non-exposed subjects (3.6±0.2) ($P=0.02$).

Cross-sectionally, univariate analysis found that increasing DBI was only associated with a significant slowing of walking speed ($-0.03$ m s$^{-1}$, $P=0.03$); however, upon multivariate analysis, this lost significance ($-0.01$ m s$^{-1}$, $P=0.30$). There were no statistically significant dose relation response associations between increasing AUCDB and impairments of grip strength, walking speed or reaction time after 12 months. Sedative exposure was significantly associated with poor balance [odds ratio (OR) 1.57, 95% confidence interval (CI) 1.08–2.27].
Amongst Australian residents of RACFs, the mean DBI of 0.60±0.60 (SD) is more than twice that seen in community-dwelling older people in the USA [3, 9] and Australia [13]. Increasing DBI in Australian RACF residents was not independently associated with impairments in measures of physical function cross-sectionally. Higher AUCDB was only associated with an impairment in balance. This differs from the strong associations seen with increasing AUCDB and poorer physical function in the American study [14]. In our study, we observed DBI associations that were not statistically significant and possibly too small to be clinically relevant. Walking speed decreased by 0.01 ms$^{-1}$ for every one-point increase in DBI score, below the 0.04 ms$^{-1}$ considered the value of clinically important changes [23].

The use of the AUCDB as a predictor of poor physical function found a relationship between sedative exposure balance with adjusted OR that suggests having exposure of one unit AUCDB comprised of sedative medications equates to a 1.57 (95% CI 1.08, 2.27) times chance of having a decrease of one balance category compared with those not exposed to any sedative drugs. The lack of significant effect of anticholinergic exposure in this population may be due to the decline in cholinergic receptors present in very old populations with high rates of cognitive impairment, independent of external exposure to anticholinergic medications [24].

The weaker association between DBI and functional impairment compared with that seen in community-dwelling older people [3, 9, 13] may be attributed to the severe, long-standing functional impairment seen in most participants, regardless of drug therapy. RACFs are designed for individuals that require assisted living and, therefore, are more likely to have multiple co-morbidities and decreased functional status. In 2005, Cesari et al. showed older people had a greater risk of falls, hospitalisation, disability and death when walking speed was <1 ms$^{-1}$ [25]. In our cohort, only 14 individuals (2.4%) had a walking speed >1 ms$^{-1}$. An additional possible reason for this weak association is that with physical function so poor medications may not be having a measurable effect. The floor effect can be observed with baseline grip strength (±SD) ranging from 1 to 50 (±8.1) kg, walking speed from 0.11 to 1.41 (±0.21) ms$^{-1}$, balance 1–5 (±1.2) and reaction time from 160 to 1,000 (cutoff point) (±200) ms, suggesting that any meaningful decrease in physical function may be missed due to the sensitivity of the tests [26].

A strength of this study was data reliability. There were no cases of missing medication data. Clinical evaluation was

### Table 1. Characteristics of the 602 FREEDOM Study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline (n=602)</th>
<th>Included in longitudinal analysis (n=526)</th>
<th>Excluded from longitudinal analysis (n=76)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years±SD)</td>
<td>85.7±6.4</td>
<td>85.6±6.5</td>
<td>86.8±6.3</td>
</tr>
<tr>
<td>Sex (female %)</td>
<td>70.9</td>
<td>72.1</td>
<td>63.2</td>
</tr>
<tr>
<td>Individuals with cognitive impairment (%)</td>
<td>40.9</td>
<td>39.4</td>
<td>51.3</td>
</tr>
<tr>
<td>Individuals with depression (%)</td>
<td>29.1</td>
<td>27.8</td>
<td>38.2</td>
</tr>
<tr>
<td>Mean co-morbidity score (±SD)</td>
<td>0.95±0.91</td>
<td>0.94±0.91</td>
<td>0.99±0.90</td>
</tr>
<tr>
<td>Exposure to medication (%)</td>
<td>97.5</td>
<td>97.9</td>
<td>97.4</td>
</tr>
<tr>
<td>Mean number of medications (±SD)</td>
<td>6.0±3.0</td>
<td>6.0±3.0</td>
<td>6.2±2.9</td>
</tr>
<tr>
<td>Exposure to anticholinergic medications (%)</td>
<td>35.2</td>
<td>35.0</td>
<td>36.8</td>
</tr>
<tr>
<td>Exposure to sedative medications (%)</td>
<td>42.0</td>
<td>41.8</td>
<td>43.4</td>
</tr>
<tr>
<td>Exposure to both (%)</td>
<td>16.6</td>
<td>16.0</td>
<td>21.1</td>
</tr>
<tr>
<td>Exposure to either (%)</td>
<td>60.6</td>
<td>59.2</td>
<td>60.8</td>
</tr>
<tr>
<td>Mean drug burden of anticholinergic drugs (±SD)</td>
<td>0.27±0.42</td>
<td>0.27±0.43</td>
<td>0.26±0.36</td>
</tr>
<tr>
<td>Mean drug burden of sedative drugs (±SD)</td>
<td>0.33±0.47</td>
<td>0.33±0.18</td>
<td>0.32±0.43</td>
</tr>
<tr>
<td>Mean DBI (±SD)</td>
<td>0.60±0.66</td>
<td>0.60±0.66</td>
<td>0.57±0.60</td>
</tr>
<tr>
<td>Mean AUCDB (±SD) (n=526)</td>
<td>0.63±0.70</td>
<td>0.63±0.70</td>
<td>—</td>
</tr>
<tr>
<td>Mean grip strength (kg±SD)</td>
<td>19.9±8.1</td>
<td>20.1±8.1</td>
<td>19.3±8.5</td>
</tr>
<tr>
<td>1 year n=493</td>
<td>21.0±7.7</td>
<td>21.0±7.7</td>
<td>—</td>
</tr>
<tr>
<td>Mean reaction time (ms$^{-1}$±SD)</td>
<td>394±201</td>
<td>396±201</td>
<td>370±198</td>
</tr>
<tr>
<td>Baseline n=322</td>
<td>381±228</td>
<td>381±228</td>
<td>—</td>
</tr>
<tr>
<td>1 year n=269</td>
<td>0.56±0.21</td>
<td>0.56±0.21</td>
<td>0.54±0.18</td>
</tr>
<tr>
<td>Mean walking speed (m s$^{-1}$±SD)</td>
<td>0.57±0.21</td>
<td>0.57±0.21</td>
<td>—</td>
</tr>
<tr>
<td>Baseline n=594</td>
<td>3.79±1.2</td>
<td>3.79±1.2</td>
<td>3.79±1.1</td>
</tr>
<tr>
<td>1 year n=448</td>
<td>3.3±1.3</td>
<td>3.3±1.3</td>
<td>—</td>
</tr>
<tr>
<td>Mean balance (scale 1–5±SD)</td>
<td>3.79±1.2</td>
<td>3.79±1.2</td>
<td>3.79±1.1</td>
</tr>
<tr>
<td>Baseline n=597</td>
<td>3.3±1.3</td>
<td>3.3±1.3</td>
<td>—</td>
</tr>
</tbody>
</table>

$^a$Co-morbidity score includes stroke, arthritis, osteoporosis, Parkinson’s disease and diabetes.

$^b$Deceased=63, moved out of area=13.
completed as a team using objective and clinically validated methods to reduce researcher-induced variation.

A potential limitation of the study is the generalisability of the findings. The exclusion criteria limit this being a true representation of RACFs [27]. Every attempt was made to control for potential confounders; however, there may be residual confounding, particularly from indications for the medications and assessment of co-morbidities. The use of minimum registered dose as an estimate for DR50 may be an overestimate in this frail older population with sarcopenia and impaired clearance [28].

Anticholinergic and sedative drug use was prevalent in this population; however, an association between increasing DBI and impaired physical function in this cohort from RACFs was not shown. This differs from associations seen in community-dwelling older people in Australia and the USA. Further studies are required to ascertain if reducing DBI over time is beneficial in decreasing the functional decline seen in older people or if it can be used as a tool for predicting falls, cognitive decline or other adverse effects.

Key points

- Exposure to anticholinergic and sedative medications is high in residents of aged care facilities.
- No strong associations are found between drug exposure and poor physical function.
- Only longitudinal sedative exposure is associated with impairments in balance.

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Conflicts of interest

None.

References

Effects of footwear on gait and balance in people recovering from stroke

SIR—Stroke often results in impaired mobility and is associated with an increased falls risk [1]. The consequences of falling are serious and include fractures, hospitalisation, nursing home admission and death [2, 3]. Poor footwear has been implicated in up to 50% of falls in the elderly [4, 5]. Poorly fitting slippers are frequently associated with a fall and fracture [6]. Footwear choice may be important for individuals with gait or balance impairment after stroke, but there is little evidence to support this hypothesis. A small pilot study comparing four people after stroke with healthy controls found no group differences for gait measures in footwear and barefoot conditions [7] while in another, stroke patients with spastic hemiparesis walked faster (30.3%) with a longer stride (18.9%) in shoes than barefoot [8]. It is important for clinicians to understand the effects of footwear on mobility after stroke to provide evidence-based education and advice. Therefore, we aimed to examine whether gait or balance were influenced by choice of footwear (closed-fitting shoes, slippers or barefoot) in people recovering from stroke.

Methods

Thirty stroke patients undergoing gait rehabilitation were recruited from the Kingston Centre and the Stroke Clinic at Monash Medical Centre, Southern Health, Melbourne, Australia. They were included if they were able to ambulate without assistance or a gait aid and were medically stable. Exclusion criteria were a significant gait-related disability from other causes, severe dysphasia and severe cognitive impairment. Participants were required to bring their own footwear. The Southern Health Human Research Ethics Committee gave approval for this study and informed consent was obtained from all individuals.

Descriptive data on age, stroke features, disability (Modified Rankin Score) [9] and past medical history were collected using a structured interview and record review. Details of mobility (functional walking category) [10], falls and footwear preference were obtained. Shoes were defined as footwear usually worn for walking or exercising that were low-heeled, closed and could be slipped on or fastened. Slippers were defined as slip-on footwear not requiring fastening. Detailed footwear data were collected using a validated Footwear Assessment Form [11].

Gait and balance

Spatial and temporal gait variables were measured using the 8.3-m GAITRite® system which has established reliability and validity in older people [12, 13]. Participants were asked to ‘walk down the mat at a comfortable pace’. The following gait variables were recorded on each of three walks: speed (centimetre/second), its components step length (centimetre) and cadence (steps per minute), base of support (centimetre), double support time (second), stance percentage and step length differential (centimetre).

The Functional Reach Test (FRT) was used to measure dynamic balance. This is a simple and reliable clinical test sensitive to stroke impairment [14, 15]. Functional reach is ‘the maximal distance one can reach forward beyond arm’s length, while maintaining a fixed base of support in the standing position’ [16]. Please see Appendix 1 in the Supplementary data available in Age and Ageing online for further details on testing.

Data analysis

Random effects regression using generalised linear models (GLM) was used to estimate the within-participant effect of footwear on gait variables and FRT. All regressions were performed using closed-fitting shoes as the reference condition. Analyses were conducted using Stata version 8 (Statacorp, TX, USA). Please see Appendix 2 in the Supplementary data.