Eur Arch Psychiatry Clin Neurosci (2006) 256:504–511 DOI 10.1007/s00406-006-0671-5

ORIGINAL PAPER

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Contributions of age and alcohol consumption to cerebellar integrity, gait and cognition in non-demented very old individuals

Received: 23 January 2006 / Accepted: 24 April 2006 / Published online: 17 August 2006

Abstract Gait disturbance and cognitive changes are common with ageing. The cerebellum contributes to motor coordination and participates in various aspects of cognition. However, no research has investigated the possible cerebellar contribution to gait and cognition in non-demented very old individuals. The current study aimed to determine the associations between indices of cerebellar size (vermal area and total volume) and measures of motor and cognitive integrity, as well as the role of variables known to impact on cerebellar size (alcohol consumption and chronological age) in a sample of 111 community dwellers (mean age: 85 years; range: 81–97 years). A marginally significant association was present between age and total vermal area. Significant correlations between current daily alcohol intake and some vermal areas were observed. These associations were more pronounced in men, particularly after controlling for cerebrum size. Multiple linear regression models revealed limited unique contributions of cerebellar predictors to neurological and cognitive measures. In summary, the results indicate that the cerebellum may be susceptible to alcohol-related shrinkage in non-demented very old individuals, more so in men, even at low dose. It also appears that the observed changes in cerebellum size in this population contribute little to neurological and cognitive changes.

Key words ageing · cerebellum · cognition · gait · MRI

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Introduction

Cognitive deficits, gait abnormalities and neurological disorders rise with age [30]. They compromise the independence and quality of life of older persons and place high demands on public health resources. The dramatic ageing of the population in industrialised countries is paralleled by an increasing number of individuals affected by these disorders. One major cause of disability and reduced quality of life over the age of 75 years is gait disturbance [9]. Gait ataxia, a component of gait disturbance, was found to be the most common neurodegenerative diagnosis in a large Australian epidemiological study on normal ageing [41]. Decline in memory and other cognitive changes with ageing are also associated with reduced independence and quality of life [43].

How cerebellar changes contribute to gait disturbance and cognitive changes in ageing has received little attention. This is despite the known role of the

cerebellum in the regulation of posture and the modulation of the pattern of walking movements and the planning and coordination of skilled volitional movements. Damage to the cerebellum gives rise to motor disturbances, such as limb incoordination, dysarthria, postural disturbances, movement tremor and gait ataxia. One dramatic example is the susceptibility of the vermis to alcohol with a clear causal relation established between alcohol use and vermal cell loss [21, 35, 36] with resultant gait ataxia; this relation being also reported in moderate drinkers [23].

In cognition, the contribution of the cerebellum to associative learning (e.g., eyeblink conditioning) is well established (e.g., [45]). In addition, studies on congenital and acquired cerebellar pathology consistently report reduced performance on tasks of executive functions [2, 16] as well as slowed information processing, visuospatial difficulties and poor memory retrieval [3, 8, 11]. Neuroimaging studies in normal controls have shown correlations between cerebellar activity and word generativity [34], working memory [15, 33], and, more weakly, with memory retention and possibly IQ [32]. The relation between cerebrum size and age is well documented [14, 20], but the relationship between age and cerebellar size has not been clearly established. Some studies reported a significant decrease in cerebellar size with age [10, 37] while others did not [4, 38].

Most studies, however, investigated young samples with limited cognitive testing and the contributions of variables such as age and gender were, in many instances, not specifically explored. The presence of additional extra-cerebellar lesions in some patient groups also limits the generalisation of some findings. Despite these limitations, studies on pathological and normal populations provide supporting evidence for a role of the cerebellum in cognition in addition to motor planning and motor control. To date, no study has investigated systematically the relations between cerebellum, gait and cognitive status within the very old population.

Thus, the aim of this study was to investigate the role and contributions of the cerebellum to gait impairment and cognitive change in non-demented, very old individuals. The specific hypotheses were that: (i) cerebellar size would show little age-related change; (ii) greater levels of alcohol consumption would be associated with smaller cerebellar sizes, more pronounced in the vermis; (iii) indices of cerebellar size, particularly in the vermis would be associated with aspects of neurological functioning thought to be dependent on cerebellar modulation; and (iv) indices of cerebellar size would be predictive of performance on tasks which place demands on higher-order cognition (e.g., executive function, working memory).

Methods

Participants were part of the 6-year follow-up of the Sydney Older Persons Study (SOPS). SOPS is a longitudinal study following a random sample of 630 community dwellers living in the inner west of Sydney, Australia, aged 75 years and over at the time of enrolment. The methodology and sample selection have been described previously [42]. Of the 299 participants available, those capable of giving informed consent to magnetic resonance imaging (MRI) and high level cognitive testing were invited to participate in the current study, which was approved by the Central Sydney Area Ethics Committee. Some participants were excluded due to poor health and frailty or because of technical criteria associated with MRI procedures (e.g., cardiac pacemaker or claustrophobia). Among the 122 individuals who participated, MRI data were unavailable for 11 (mostly due to movement artefacts). Analyses are reported for the 111 individuals (60 men and 51 women) with a complete data set. No participant met published clinical criteria of dementia. Demographic characteristics of the sample are presented in Table 1. There was no sex difference with respect to age, education, MMSE score but daily alcohol consumption (measured in grams/day) was significantly lower in women than men.

The 188 SOPS individuals who did not participate were significantly older (87.0 ± 3.9 vs. 85.5 ± 3.1 years; $t(297) = 3.477$, $p = 0.001$), had a lower MMSE score (21.7 ± 7.5 vs. 26.7 ± 2.6 points; $t(268) = -3.4$, $p < 0.001$), but a similar level education level (10.0 ± 1.8 vs. 10.2 ± 2.0 years; $t(297) = -1.133$, $p = 0.258$) and lower daily alcohol consumption (3.1 ± 7.1 vs. 7.5 ± 9.7 g; $t(297) = -4.531$, $p < 0.001$) compared to the study participants. All participants were in the "low risk" category of daily alcohol consumption (i.e., up to four drinks/day for men or two drinks/day for women) excepted for one woman who was in the "risky" category (i.e., 3–4 drinks/day) according to the guidelines of the National Health and Medical Research Council of Australia [29].

Briefly, participants underwent a medical and neurological examination, a cognitive assessment, an interview regarding medical history, medication use, alcohol consumption, activity levels and psychological wellbeing and MRI. Aspects of motor functioning known to become compromised with ageing were recorded, the measures being categorised as either requiring cerebellar or extrapyramidal involvement (although some may reflect dual involvement). The cerebellar measures comprised: (a) Bilateral ataxic gait; (b) Heel-to-toe walk; (c) Alternating movement; (d) Cerebellar coordination; (e) Sway path; and (f) Bilateral finger tapping. The extrapyramidal measures included: (a) Composite extrapyramidal (EP) score; (b) Maximum anterior–posterior (AP) reach; (c) Timed walk; (d) Reduced arm swing; and (e) Bradykinetic gait. The neurological measures are described in Table 2.

Table 1 Demographic characteristics for the 51 women and 60 men composing the study sample: mean (SD)

	Women	Men	*t*	*p* Value
Age (years)	85.72 (3.41)	85.29 (2.89)	<1	NS
MMSE score (0–30)	26.85 (2.51)	26.67 (2.66)	<1	NS
Education (years)	10.12 (2.88)	10.2 (1.9)	<1	NS
Daily alcohol intake (g/day)	4.42 (7.28)	10.2 (10.88)	3.33	0.001

MMSE = Mini-mental state examination

Table 2 Description of the neurological measures

Measure	Purpose/description	Measure/comment
Cerebellar measures		
Ataxic gait	Evidence of bilateral ataxic gait on neurological examination	Absent or present
Heel-to-toe walk	Ability to complete 10 steps heel-to-toe walk	4 point-scale (1 = no putting foot out of line; 2 = sways or puts foot out of line once; 3 = marked sway or puts foot out of line > 1; 4 = unable to complete 10 steps)
Alternating movement	Evidence of incoordination in either upper limb	Absent or present
Cerebellar coordination	Global degree of cerebellar incoordination	3-point scale (1 = normal; 2 = mild; 3 = moderate to severe); average score for all limbs
Sway path	Path of involuntary sway whilst standing on firm ground	Path (mm^2)
Finger tapping[a]	Number of taps during a 5-s period	Average number of taps for left and right index finger
Extrapyramidal measures		
Composite EP score	Combination of 10 separate variables each measured on a 4-point scale	0–10 (from 0 = no EP abnormality to 10 = maximal EP abnormality). See [42] for details
Bradykinetic gait	Evidence of bradykinetic gait on neurological examination	Absent or present
Maximum AP reach[a]	Extent of truncal reach in the AP axis whilst keeping both feet on the ground	Sum of anterior and posterior reach (mm)
Timed walk	Time to complete a 5-m walk	Time adjusted for lower limb arthritis (seconds)
Arm swing	Reduced arm swing in either arm	Absent or present

[a] Indicates cerebellar and EP contribution
AP = anterior–posterior, EP = extrapyramidal

Measures of the five major cognitive domains were administered with an emphasis on tasks tapping into attention and executive functioning given the evidence of cerebellar contribution to these cognitive processes. The measures administered were the Digit span [44], the California computerized assessment package (CalCAP) simple and choice reaction time tasks [28], the Logical memory subtest of the Wechsler Memory Scale-Revised [44], the Judgment of line orientation [7], the Boston naming test [22], the New tower of London [17], the Oral trails making test-part B [24], the Controlled oral word association task (phonemic fluency) [6] and Semantic fluency [40].

Image acquisition was performed on a 1.5-Tesla General Electric Signa scanner. For the purpose of this study, two sequences were acquired: a T1 SE sequence in the sagittal plane (TR/TE 500/16 ms) with slices 5 mm thick, a 22-cm field of view and a 256 × 192 matrix; and a T1 weighted three-dimensional spoiled gradient echo sequence in the coronal plane (TR/TE 12/3.5 ms) with slices 1.5 mm thick, a 22 cm field of view and a 256 × 192 matrix.

Cerebellar measurements were obtained with the ANALYZE PC AVW 3.0 software package [1] using semi-automated and manual procedures. Three regions of the vermis were manually traced on the most medial slice in the sagittal plane, using the T1 SE sequence. The first region, termed V1, included the lobules I–V. The second region, termed V2, included the lobules VI–VII and the third region, termed V3, included the lobule VIII–X. V1 was delineated from V2 by the primary fissure, and V2 was delineated from V3 by the prepyramidal fissure (Fig. 1).

Consistency of area and volume measurements was assessed with intraclass coefficients (ICC) using one-way random effects model. ICC were 0.92 for V1, 0.95 for V2, and 0.96 for V3 (all ps < 0.001). The total cerebellar volumes (TCV) were obtained following a two-step procedure. First, we measured total intracranial and whole brain volumes on the coronal T1 weighted images. In a second step, cerebellar volumes were extracted by manually erasing the cerebrum on each slice. Cerebellar peduncles were also erased on all slices where there was a visible distinction between the white matter of the peduncles and the cerebellar grey matter. ICC for TCV was .99 (p < 0.001). Cerebrum size was obtained by subtracting TCV from whole brain volume.

We investigated the associations of sociodemographic variables (age and daily alcohol consumption) with the cerebellar measures using partial correlations, controlling for total intracranial volume or cerebral volume. Given the different recommended alcohol consumption levels for men and women [29], analyses were conducted for the full sample, as well as for men and women separately. In these analyses, significance level was set at the p value of 0.01 to reduce the likelihood of Type 1 error. Given the a priori hypotheses, we report one-tailed tests of significance.

The contributions of cerebellar measures to neurological functioning and cognitive performance were examined with multiple linear regression analyses. A multivariate model was established for each neurological and cognitive measure (i.e., the dependent variable), with the indices of cerebellar size as predictors, as well as other covariates. We first conducted a series of univariate analyses in order to establish the contribution of each predictor and each covariate to the dependent variable, independent from each other predictor. In a second step, the significant predictors and covariates arising from the univariate analyses were entered simultaneously in

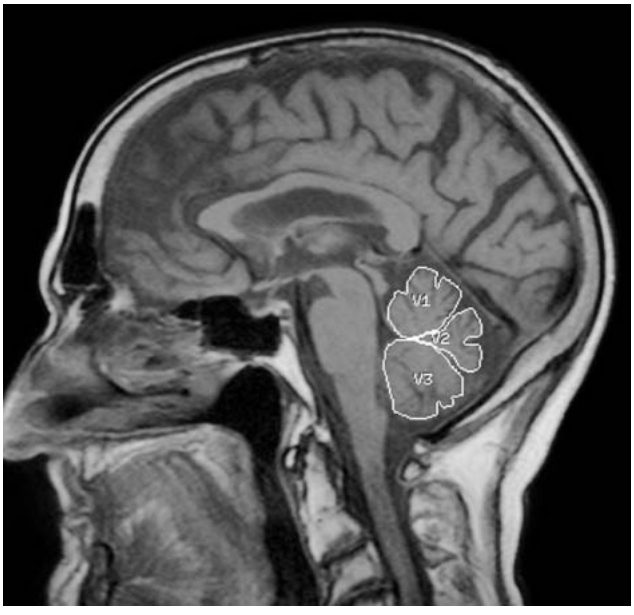

Fig. 1 Midsagittal section showing the manual segmentation of three areas of the vermis, labelled V1 (lobules I–V), V2 (lobules VI–VII) and V3 (lobules (VIII–X). The primary fissure separates V1 and V2 and the prepyramidal fissure separates V2 from V3

Table 3 Cerebellar and cerebral measurements of 111 very old non-demented individuals

	Mean	SD	Range
Area measurements (mm^2)			
V1	455.7	74.40	308–812
V2	302.4	84.97	167–645
V3	408.9	104.63	155–673
Total Vermis (V1–V3)	1167.1	189.67	717–1789
Volume measurements (cm^3)			
Cerebellar volume	124.3	12.3	94.7–167.5
Cerebral volume	967.7	95.9	758.8–1256.3
Total intracranial volume	1381.2	156.9	1006.7–1766.4

V1 = Vermal area 1. V2 = Vermal area 2. V3 = Vermal area 3. See text for V1–V3 definitions

a multivariate model to establish their respective unique contribution to the dependent variable. In these regression analyses, cerebral size and chronological age were used as covariates. Cerebral size was included to ensure that any significant associations were due specifically to variation in the size of the cerebellum rather than a general brain effect. Age was included to control for changes in motor and cognitive functioning associated with ageing. In addition, for the cognitive measures, sex and years of education were also included as covariates as these variables are known to modulate cognitive test performance.

Results

Descriptive cerebellar and cerebral measurements are presented in Table 3. Cerebellar volume measures are similar to those reported in previous studies [10, 37].

One-tailed partial correlations (controlling for total intracranial volume) revealed no significant associations between age and cerebellar measures at the p value of .01 in this group. A marginal correlation was present between the total vermal area measurement and chronological age ($r = -0.18$; $p = 0.03$) (Table 4). Closer examination revealed that this association was due to V3 contribution exclusively ($r = -0.17$; $p = 0.04$).

Controlling for total intracranial volume, correlational analyses on the full sample revealed statistically significant correlations between daily alcohol consumption and V2, V3 and Total vermis, with smaller vermal areas being associated with higher daily alcohol consumption (Table 4). This pattern of associations was strengthened after controlling for cerebrum size, with an additional association with V1 and a marginally significant association with total cerebellum volume (-0.22, $p = 0.02$). These associations indicated a specific effect of alcohol effect on the cerebellum in addition to a general brain effect.

The pattern of associations between alcohol and cerebellar measures was markedly different in women and men. In women, although pointing in the expected direction of smaller cerebellar measures with higher alcohol intake, no correlation reached the p value of .01. A marginally significant correlation was present between alcohol and V2 (-0.25, $p = 0.04$). Further, this pattern of associations did not change after controlling for total intracranial or cerebral volumes. This finding was in sharp contrast with the results found in men. In this group, only marginally significant associations with alcohol were present in V1, V3 and Total Vermis (ps = 0.04, 0.03 and 0.02, respectively) after controlling for total intracranial volume. All the correlations, however, became more pronounced when controlling for cerebrum size (Table 4). This pattern of associations suggested a greater sensitivity of the cerebellum to alcohol in men, comparatively to the rest of the brain whereas women did not appear to show this differential sensitivity.

The multiple linear regression models for the neurological measures as outcome variables are presented in Table 5. Only one neurological measure (out of 12) showed a unique multivariate contribution from any cerebellar measures: TCV which, together with Age, explained 11% of the score variance on Finger tapping ($p < 0.001$). In five models, Age was the only significant predictor contributing to the scores (Heel-to-toe walk, EP global score, Flexed posture, Bradykinetic gait and Timed walk). AP reach received significant univariate contributions from several cerebellar measures but these failed to show unique contribution above and beyond that of the cerebrum when considered in the multivariate model

Table 4 Partial correlations (controlling for total intracranial volume or for cerebrum size) between age, daily alcohol consumption and cerebellar measures

	Age	Daily alcohol consumption					
		Full sample		Women		Men	
	TICV	TICV	Cerebrum	TICV	Cerebrum	TICV	Cerebrum
V1	−0.04	−0.20	−0.24*	−0.01	−0.01	−0.22	−0.30*
V2	−0.10	−0.23*	−0.27**	−0.25	−0.25	−0.15	−0.20
V3	−0.17	−0.23*	−0.26**	−0.14	−0.14	−0.23	−0.31**
Total vermis (V1–V3)	−0.18	−0.30***	−0.35***	−0.20	−0.19	−0.27	−0.37**
Cerebellum volume	−0.04	−0.13	−0.22	0.15	0.19	−0.16	−0.33*

*$p < .01$, ** $p < .005$, *** $p < .001$ (one-tailed)
Cerebrum = controlling for cerebrum size. TICV = controlling for total intracranial volume. V1 = Vermal area 1. V2 = Vermal area 2. V3 = Vermal area 3. See text for V1–V3 definitions

Table 5 Multivariate models for the cerebellar, extrapyramidal and cognitive measures

Outcome variable	Predictors	Variance explained (%)	*p*
Cerebellar measures			
Ataxic gait	—	—	—
Heel-to-toe walk	Age	6	0.009
Alternating movement	—	—	—
Cerebellar coordination	—	—	—
Sway test	—	—	—
Finger tapping	Age, TCV	11	0.001
EP measures			
EP global score	Age	10	0.001
Flexed posture	Age	5	0.021
Arm swing	—	—	—
Bradykinetic gait	Age	9	0.001
Maximum AP reach	Cerebrum	12	0.0001
Timed walk	Age	11	0.0001
Cognitive measures			
Simple reaction time	Education	5	0.025
Complex reaction time	Age	8	0.002
Complex reaction efficiency	Age	8	0.002
Digit span forward	Age	8	0.002
Digit span backward	Education, Cerebrum	9	0.008
Judgment of line orientation	Education, Cerebrum	14	0.0001
Logical memory immediate	Age, Education	12	0.001
Logical memory % retention	Age	7	0.005
Boston naming test	Education	7	0.004
Phonemic fluency	V3	4	0.02
Semantic fluency	V3	9	0.001
Similarities	Age, Education, TCV	30	0.0001
Oral trails—part B	—	—	—
New tower of London	Age, Cerebrum	16	0.0001

EP = extrapyramidal. TCV = total cerebellar volume. V3 = cerebellar lobules VIII–X
— denotes absence of significant contributions from the set of predictors

(Table 5). Cerebellar variables, or the covariates, failed to contribute to five neurological scores (Ataxic gait, Alternating movement, Cerebellar coordination, Sway test and Arm swing) despite the fact that these measures were deemed to reflect cerebellar integrity (with the exception of Arm swing).

In the multivariate models with the cognitive measures as outcome variables, the amount of score variance explained ranged between 4% and 14% with the exception of Similarities (30%) (Table 5). Age and Years of education were, alone or together, the only significant predictors in seven out of 14 scores, and associated with another predictor for an additional four scores. Cerebellar measures were found to have little unique contribution to the models with the exception of Phonemic and Semantic fluency tasks (both V3) and Similarities (TCV). Four cognitive measures (Complex reaction time, Complex reaction efficiency score, Digit span forward and New tower of London) received significant univariate contributions from cerebellar predictors but these disappeared when entered simultaneously in the multivariate models, indicating that their contribution to scores was mediated by other predictors in the model, in most cases Age. As was the case for the neurological variables, all contributions to the multivariate models were in the expected directions (i.e., smaller vermal measurements associated with poorer scores). This pattern of results was not altered after taking into account current alcohol consumption. Independent *t*-tests comparing the cognitive performance of drinkers and non-drinkers indicated no significant differences between the two groups.

Discussion

We aimed to investigate the relations between indices of cerebellar size and sociodemographic variables (age and alcohol use), motor functioning and cognitive functioning in a community-based sample of very old individuals. The limited association between total vermal area and chronological age partly confirmed our first hypothesis. This finding is in agreement with previous studies [13, 26, 38]. Unlike Raz and colleagues [37], who reported a significant association between age and the vermis only (lobules VI–VII), we found a marginally significant association with age for the posterior aspect of the cerebellum (lobules VIII–X). A mixed sample of younger volunteers and neurologically intact patients in Raz et al.'s study compared to a much older sample of community dwellers with a relatively limited age range (81–97 years) in the current study probably explain these differences. This finding confirms the greater volume stability of the cerebellum compared to the cerebrum even in very old individuals. When changes occur, they tend to be mild and may be limited to some specific areas of the vermis. This

point probably explains the lack of association of age with TCV, which included the lateral hemispheres. Our sample, arguably included individuals who are healthy survivors and may no longer be representative of the general population of this age group. Although a stronger association between age and cerebellar measurements may exist in the general population of this age, our sample allowed us to investigate the effect of age unpolluted by other contributing variables that are also more common in ageing (e.g., neurodegenerative disorders).

Our second hypothesis was partly confirmed. Controlling for total intracranial volume, higher level of daily alcohol consumption was found to be associated with smaller vermis sizes for V2 (lobules VI–VII) and V3 (lobules VIII–X). Furthermore, these associations increased in magnitude after controlling for total cerebral volume, the association with V1 becoming also significant. Interestingly, the pattern of associations was sex specific. Initial correlations (controlled for intracranial volume) showed that women had a marginal contribution to the significant association for V2 but not V3 and the reverse being true for men. In women, the strength and pattern of associations did not change whether controlling for total intracranial or cerebral volumes. In marked contrast, in men, all the correlations pointing towards smaller cerebellar indices associated with larger daily alcohol consumption became stronger after controlling for total cerebral volume. Thus, our results indicate a greater sensitivity of the vermis to the effect of alcohol unique to men. An additional association with TCV suggests that cerebellar hemispheres are not immune to the effect of alcohol, at least in men. For women in this sample and for this age group, the effect of alcohol appears to be on all brain structures, rather than specific to the cerebellum, as would have been expected. Level of education, reflecting an index of socio-economic status, did not modify this pattern of associations.

These findings are not inconsistent with previous reports of an association between excessive alcohol consumption and reduced vermal size [21, 35, 36] nor with the increased sensitivity of the anterior superior vermis to alcohol-related damage. In addition, they are not inconsistent with reports of an increased sensitivity to the damaging effects of alcohol abuse on the cerebral cortex and white matter in females [19, 27]. In general, women develop an equivalent degree of brain shrinkage at lower levels of alcohol consumption.

Importantly, these significant associations were observed despite reported current consumption of alcohol within the National Health and Medical Research Council recommended non-harmful levels [29]. Whilst this finding suggests that even modest alcohol consumption may lead to vermal atrophy, other factors must be considered. Firstly, only data on current, but not lifelong, alcohol consumption were available. It is plausible that the participants currently reporting larger daily alcohol consumption would have been also more likely to have consumed higher levels in the past. Thus, the variations in vermal size may have been associated with previous "risky" or "hazardous" levels of alcohol use. Secondly, the validity of the self-reported levels of alcohol consumption was not confirmed by an independent source and the possibility of under-reported current level of alcohol intake must be borne in mind. Finally, it is possible that the relationships revealed were mediated by nutritional deficiency [4, 18], which was not assessed in this study. Nonetheless, the results highlight the possibility that the ageing cerebellum, in particular the vermis, may be susceptible to alcohol-related shrinkage, especially in men.

Specific guidelines for safe levels of alcohol consumption in older people do not exist, although they are recommended to "consider drinking less" than the non-hazardous levels for young people. The reported association between vermal size and alcohol consumption suggests that more conservative recommendations may be appropriate for older people. However, drinkers and non-drinkers showed no significant differences in cognitive performance. Those consuming larger amounts of alcohol may have exhibited smaller vermal regions but, in this group, such reduction in vermal size was not severe enough to cause functional impairments or cognitive deficits. In addition, there is some evidence to suggest that moderate alcohol intake has health benefits, epidemiological studies reporting significantly lower risks of developing dementia for light to moderate drinkers (1–3 drinks/day) compared to abstinents [31, 39]. Clearly, more research needs to focus on the impact and the possible risks and benefits of moderate drinking in older individuals.

The third and fourth hypotheses received only very limited support. Cerebellar measures failed to contribute to a number of neurological measures, even those thought to reflect cerebellar integrity. Only TCV was found to be predictive of performance of a single neurological measure: Finger tapping. Two previous studies [5, 32] reported a similar relationship between cerebellar size and motor dexterity in groups of healthy young individuals. This supports a contribution of the lateral hemispheres of the cerebellum to motor dexterity. It further highlights the importance of controlling for motor speed and dexterity when patients with cerebellar lesions are cognitively assessed using tasks involving a motor component. Similarly, significant contributions of cerebellar size to cognitive performance were found on three cognitive tasks only (Similarities, Phonemic and Semantic fluency tasks). On most measures, score variance was accounted for by Education and, as with the neurological measures, Age.

How can we explain these findings? The neurological and cognitive measures administered may be

appropriate to identify gross abnormalities in individuals with significant cerebellar lesions but may fail to detect subtle disturbances associated with slight volume change in the cerebellum of relatively healthy older individuals. Furthermore, the multifactorial nature of most cognitive tasks makes it difficult to detect subtle changes in a structure, which supports only one of the many cognitive functions required for a successful performance on the task(s) under investigation. A certain degree of shrinkage may possibly be required before the functional integrity of the cerebellum is compromised, and either motor or cognitive disturbance be detected clinically (i.e., threshold effect). Alternatively, the changes detected in cerebellar size may reflect a loss of white matter in the cerebellum rather than neurodegeneration as has been shown for alcohol abuse [25] and advancing age [12]. The functional consequence of white matter loss may be more subtle and may be reflected in processing time rather than overall performance.

There may be some limitations to the present study. First, volume was only available for the whole cerebellum. Volumetric measurements of the vermal regions might have uncovered associations not detected with surface measurements. Second, the absence of information on nutritional status did not permit us to explore further the reasons underlying the associations between alcohol consumption and vermal size, and the difference between men and women. Finally, the cross-sectional design of the study means that only associations, but not causation, between variables can be established. These limitations notwithstanding, findings from this study provide supporting evidence that the vermal regions of the cerebellum in very old non-demented adults are particularly vulnerable to alcohol-related damage, even when current levels of consumption are well within recommended guidelines. In addition, the effect seems to be gender specific. Our findings also show that alcohol consumption within the current recommended guidelines is not associated with significant cognitive deficits in very old individuals.

Acknowledgments This research was supported in part by grants from the National Health and Medical Research Council of Australia (NHMRC), an Infrastructure Stream C grant from the Department of Health of New South Wales, Australia and by the Ageing and Alzheimer's Research Foundation. We would like to thank Jessica Carroll, Jo Millar and Enid Sawley for data collection. OP is supported by an NHMRC Neil Hamilton Fairley Postdoctoral Fellowship (ID: 222909).

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