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Review

Dexterous movement complexity and cerebellar activation: A meta-analysis

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ABSTRACT

The importance of the cerebellum in coordinates of movement has been established by lesion studies. However, there is no clear understanding of whether there is consistent activation in cerebellum across various motor task complexities or how different parts of the cerebellum contribute to finger coordinates in dexterous manipulation. This article reviews imaging studies with data from healthy subjects. A mini meta-analysis using label-based and activation likelihood estimation (ALE) methods reveals that ipsilateral anterior and vermis regions of the cerebellum were consistently activated across various dexterous movement complexities and were associated with finger and hand movement.

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1. Introduction

Recent evidence has revealed that the cerebellum plays a critical role in nonmotor functions such as temporal processing (e.g., Onoda et al., 2006, 2003), planning and problem solving (for a review, see Unterrainer and Owen, 2006), attention (e.g., Townsend et al., 2001; Barrett et al., 2003), and semantic comprehension (Dien et al., 2003). However, how the cerebellum gets involved in the classical motor task, especially with the increase of task complexity remains unclear.

Extensive studies have attempted to address this question by mapping brain activation patterns with simultaneous repetitive finger movement (for a review, see Pollok et al., 2006). However, different study methods and analysis strategies reveal different aspects of brain activation patterns rendering no confirmative result. The general consensus of previous studies is that complex movements produce activation of the primary motor and sensory areas, as well as the motor association areas and the cerebellum. However, most of these studies were limited to either an independent single sequencing task or merely single finger movement. There are very few studies integrating the magnitude and the pattern of cerebellar activation at differential levels of motor task complexity, that is the specific contrast between the different features of a hand movement, including the increased number of movement components such as from palm tapping (PT), pronation/supination (PS), to fist-edge-palm (FEP) or sequential length (the detailed operational definition was stated separately in the following section). Therefore, in this review, we included a number of imaging studies that covered the neural substrates of different finger/hand movement tasks first to conduct a quantitative meta-analysis. The purpose of this study is to examine whether there is consistent activation of cerebellum despite different levels of complexity in motor tasks. It also examines the activation pattern in different regions of cerebellum associated with motor function across various finger and hand movement tasks by using a label-based review.

2. Materials and methods

2.1. Literature selection

A search of major databases (e.g., Medline, PsycINFO, PubMed) with keywords such as complexity, and motor tasks was performed between Jan 1988 and July 2008 because the first imaging study of brain function mapping (Petersen et al., 1988) was published in 1988. We used a broad definition of “finger movement task” that describes all tasks in which subjects have to perform the motor task in a repetitive or ordered sequence using fingers or hands, i.e., unimanual or bimanual

finger tapping or palm tapping. The inclusion criteria for this review are listed as follows:

1. Studies that used fMRI, SPECT, PET imaging techniques were included, whereas studies using other techniques such as ERP, TMS were excluded.
2. Studies that used finger/hand motor tasks were included, whereas studies that covered cognitive function tasks such as problem solving were excluded.
3. Studies in which more than two types of movement were measured other than the resting state were included, whereas studies in which only one type of finger movement was measured were excluded.
4. Studies in which motor tasks were actually executed were included, whereas studies which only employed or reported imagined finger/hand motor tasks were excluded.

On the other hand, we excluded papers that did not scan whole brain including the cerebellum to eliminate the bias of no-report-because-of-no-scan, and the papers without detailed report of coordinates for the cerebellum in the imaging data in order to get precise activation pattern in different regions of cerebellum. As a result, there were nineteen neuroimaging studies of finger movement task complexity that reported cerebellum activation, including fifteen studies adopted functional magnetic resonance imaging (fMRI), three used positron emission tomography (PET), and the remaining one employed a combined approach of fMRI and transcranial magnetic stimulation (TMS) technique. Studies in Table 1 starred with ‘*’ matched the inclusion criteria and could provide data for effect size calculation. But they did not provide the coordinates in imaging data so they were not included in the following ALE meta-analysis and label-based review but were still listed in Table 1.

2.2. Operational definition of task complexity

In this review, task complexity was considered to be the combination of any two of the following components, namely frequency (the times of movement per second), sequential length, number of movements, movement phase, or finger task nature. For example, where frequency and task nature remained invariable, sequential length or the number of movements could be varied so that the contrast between any two movement lengths was a level of complexity. The effect sizes were calculated to address the magnitudes in various levels of task complexity in terms of activation likelihood estimation (ALE) and label-based review.

2.3. Activation likelihood estimation

Activation likelihood estimation (ALE) analysis (Turkeltaub et al., 2002) is a quantitative method to estimate consistent activation across different imaging studies. In order to get

Table 1 – Summary of the motor task complexity studies

Tasks	Study	Facility	Subject number	Performing hand	Specific contrast	Cerebellum activations	Effect size ^{a,b}
Hand movement	Chan et al. (2006)	1.5 T MRI	10	R	PS vs. PT	n.s.	2.3–2.42
	Umetsu et al. (2002)			R	FEP vs. PT	R anterior hemisphere and vermis	2.47–3.36
				R	FEP vs. knock fist	Ipsi-anterior hemisphere	
				L	FEP vs. knock fist	Ipsi-anterior hemisphere and vermis	
				L	FP vs. knock fist	n.s.	
	Tracy et al. (2001)	1.5 T MRI	10	L	FP vs. knock fist	n.s.	2.64–3.32
		1.5 T MRI	9	UNI/BI	BI vs. UNI	R anterior and L posterior and vermis	
	Debaere et al. (2004)	1.5 T MRI	12	BI	Frequency	Anterior vermis	1.65–2.98
	Heuninckx et al. (2005)	3 T MRI	12 vs. 12	R	Phase	hemisphere	
					Interaction	Posterior vermis	
Complexity old vs. young					L/R hemisphere: V and vermis: VIIIA IX		
Finger tapping	Lewis et al. (2004)	3 T MRI	10	R	Synchronization vs. continuation phase	L anterior hemisphere and R posterior hemisphere	1.87–3.13
	Aoki et al., (2005)	PET	10	R	Frequency, parametric	n.s.	2.8–5.58
Finger/Thumb opposition	Lutz et al., (2000)	1.5 T MRI	10	R	Double vs. single tapping	R anterior hemisphere	
		PET	13	R	Random vs. regular	R cerebellar nuclei and vermis	
	Catalan et al., (1998)	PET	13	R	Complex vs. simple	Vermis	2.45
	Solodkin et al. (2001)*	1.5 T MRI	6 L hand; 7 R hand	R twice/L twice	Repetitive vs. sequential	Ipsi/contra hemisphere	1.23–2.18
	Sadato et al. (1996)	PET	10	R	Sequence level	R superior hemisphere	3.75–6.33
					Complex vs. rest	Vermis	
					Right	Ipsilateral anterior	
	Jancke et al. (1999)	1.5 T MRI	10	R/BI	In phase	Bilateral anterior	
UNI (RH or. LH)				Out of phase	Bilateral anterior and posterior		
Finger key press	Kuhtz-Buschbeck et al. (2003)*	1.5 T MRI	6	BI	RH3 Hz vs.1 Hz	R anterior hemisphere	0.16–1.83
		1.5 T MRI/TMS	12	R/L	LH 3 Hz vs. 1 Hz	L and R anterior hemisphere	
	Haaland et al. (2004)	MRI	14	R/L	BH 3 Hz vs. 1 Hz	R anterior and L posterior	4.9
	Haslinger et al. (2002)	1.5 T MRI	8	R	Opposition vs. rest	Ipsi hemisphere	
	Dhamala et al. (2003)	1.5 T MRI	13	R	Finger compress vs. Rest		2.83–4.89
	Bengtsson et al. (2005)	1.5 T MRI	7	Both conjunction	Transition vs. repetitive	L/R anterior hemisphere	
	Riecker et al. (2003)	1.5 T MRI	8	R	Complexity	R dentate nucleus (in CRB)	
					Sequence complexity	Vermis	
					Sequence vs. isochronous	L/R hemisphere and vermis	
					Frequency main effect and linear effect	R hemisphere	

Note. All of the subjects above were mental and physically healthy adults. R: right; L: left; UNI: unimanual; BI: bimanual; RH: right unimanual, LH: left unimanual; RL: ring and little finger; IM: index and middle finger; FEP: fist-edge-palm; PS: pronation/supination; PT: palm tapping.

Studies starred with '*' did not provide the coordinates in imaging data. Therefore, they were not included in the following ALE meta-analysis and label-based review.

^a Cohen's $d = 2 * t / \text{sqrt}(df)$, formula from Rosnow and Rosenthal, 1996. This effect size calculation is used here to estimate the range of effect size in these imaging studies.

^b The effect size of paper with * was calculated according to the formula Cohen's $d = (M1 - M2) / \text{pooled std}$ (Cohen, 1988).

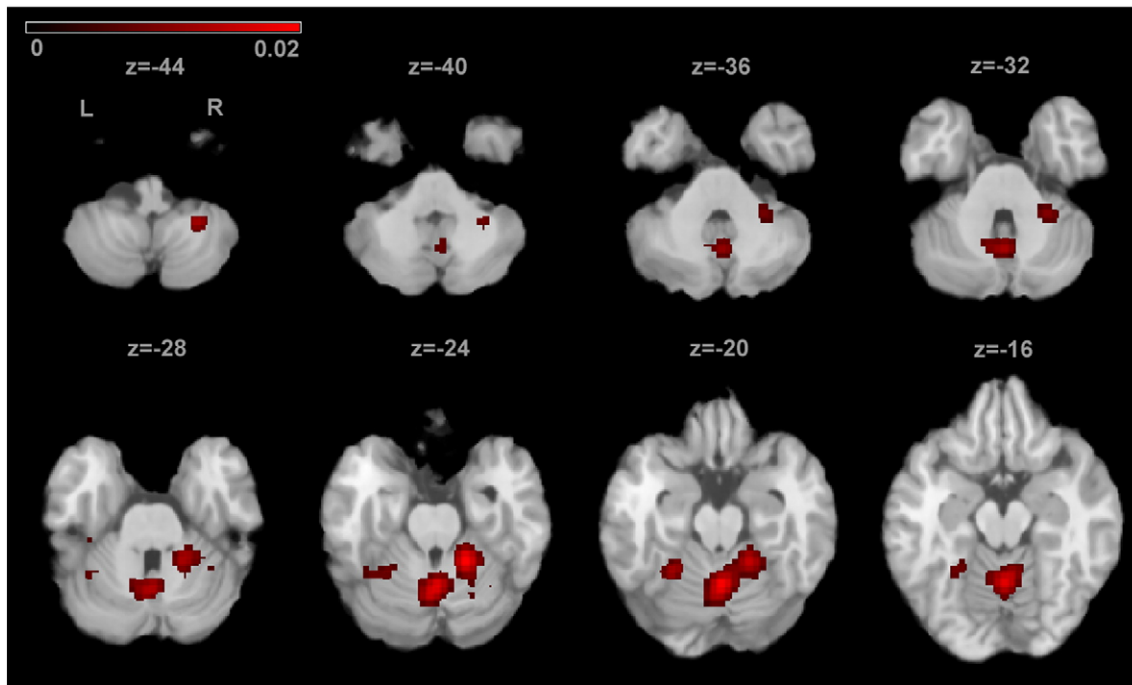


Fig. 1 – Activation likelihood estimation results in cerebellum of hand or finger movement task complexity overlaid onto a Talairach template (Kochunov et al., 2002). The cluster was threshold with a false discovery rate at $p < 0.01$ and a cluster extent of 100 voxels. The z score represent z coordinate in Talairach space. The color scale represents activation likelihood estimation score.

enough coordinates, we pooled all the coordinates in movement tasks into the ALE procedure. In each study, we only selected one contrast with the movement of right hand into the ALE meta-analysis in order to keep the weight of each study the same. As a results, totally forty one foci from seventeen experiment from seventeen studies were included in the present ALE analysis.

The ALE analysis was conducted using Ginger ALE software (Laird et al., 2005). The ALE maps of the forty one foci were created using a full-width half-maximum (FWHM) of 10 mm. Statistical significance was determined using a permutation test of randomly generated foci. No assumptions were made concerning the distribution or spatial separation of these random foci. Five thousand permutations were computed using the same FWHM value and the same number of foci was used in computing the ALE values. The test was corrected for multiple comparisons using the false discovery rate (FDR) method of $p < 0.01$ (Genovese et al., 2002; Laird et al., 2005).

Whole-brain maps of the ALE values were embedded in the MRICroN software and overlaid onto an anatomical Consortium for Brain Mapping template to Talairach space (Kochunov et al., 2002).

2.4. Label-based reviews

In addition, a label-based meta-analysis was conducted to examine thoroughly the activation patterns in cerebellum for finger and hand movement. For the label-based review, there are two different tabular reviews: author-label review that used author assigned anatomical labels (as-published) and an atlas-label review that utilized labels that derived from the Talairach Daemon (Laird et al., 2005). In the current study, anatomical labels for regions of cerebellum in selected publication might be so brief as just labeling ‘cerebellum’ rather than detailed report of different regions of cerebellum. Therefore, we employed atlas-label review method that

Table 2 – Two clusters of activation in cerebellum using ALE analysis

Cluster	Volume (mm ³)	Maximum ALE value	Talairach coordinates			Label
			x	y	z	
1	11704	0.022	18	-46	-24	Right anterior lobe
		0.021365	2	-60	-20	Right anterior lobe.culmen.
		0.014589	26	-48	-46	Right posterior lobe.cerebellar tonsil.
		0.014246	2	-62	-32	Right posterior lobe.uvula of vermis.
		0.011158	26	-42	-32	Right posterior lobe.cerebellar tonsil.
2	1232	0.013869	-24	-52	-20	Left anterior lobe.culmen.
		0.008981	-34	-54	-26	Left anterior lobe.culmen.

anatomical labels of the regions of activations were collected via the Talairach Daemon using the search for nearest gray matter based on the coordinate data in publications.

3. Results

3.1. Activation likelihood estimation

The ALE meta-analysis of hand or finger movement tasks revealed two clusters of activation in cerebellum (Fig. 1 and Table 2). The first cluster peaked at right (ipsilateral) anterior hemisphere, and extend to right posterior hemisphere and vermis. Extremely high ALE values were observed in the right anterior hemisphere ($x=18, y=-46, z=-24$). The second cluster was mainly at left (contralateral) hemisphere ($x=-24, y=-52, z=-20$).

3.2. Label-based review

Selected contrasts from the finger and hand movement functional imaging literature comparing the complex movement condition and the simple movement condition yielded a total of 63 foci. These foci would be pooled into the atlas-based label. In the atlas-label review of the cerebellum activation in dexterous movement, the coordinates were assigned an anatomical label via the Talairach Daemon and plotted in bar graph format (Fig. 2).

Activations were reported most frequently in the ipsilateral anterior hemisphere of cerebellum (33% for hand movement,

43% for finger tapping, 75% for finger/thumb opposition, 28.6% for finger key press) and vermis (35% for hand movement, 14% for finger tapping, 25% for finger/thumb opposition, 50% for finger key press). Ipsilateral posterior hemisphere of cerebellum was reported activated in finger tapping (14%), finger key press (14%) and hand movement (4%) but not finger/thumb opposition (0%). Contralateral anterior hemisphere in cerebellum was only reported in hand movement (12%) and finger key press (7%). As a supplementary analysis in addition to region function, we calculated the effect size of some studies in Table 1 for the activation volume in specific each contrast.

4. Discussion

4.1. Activation likelihood estimation

The current ALE meta-analysis indicated that the ipsilateral anterior hemisphere and contralateral anterior hemisphere were the two main regions responsible for the dexterous movement complexity.

4.2. Label-based reviews

Several movement paradigms have been used to investigate movement complexity and the activation of the cerebellum. In this review, we focused first on the hand movement task, including fist-edge-palm (FEP), pronation/supination (PS), palm tapping (PT) (e.g., Chan et al., 2006; Umetsu et al., 2002), cyclical flexion–extension of the wrist (Debaere et al., 2004)

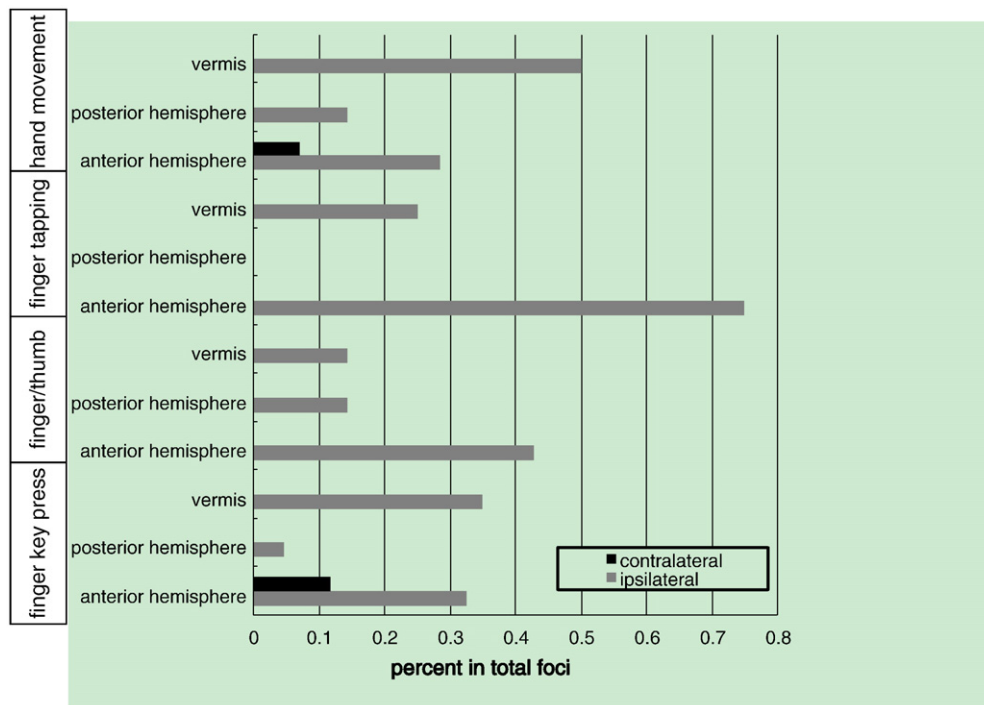


Fig. 2 – Atlas-label review of hand movement, finger tapping, finger/thumb opposition and finger key press tasks. Regions in cerebellum were labeled as anterior hemisphere, posterior hemisphere and vermis based on the coordinates provided in publications by using Talairach Daemon. ‘percent in total foci’ was the percentage of studies reporting activation in that area in the task indicated on the y-axis.

and hand/foot extension (Heuninckx et al. 2005). The consensus of these studies indicates that the vermis might play a role in the hand movement functioning. In addition, Tracy et al. (2001) also showed that when these hand motor tasks are performed bimanually, both the anterior and posterior parts of the cerebellum were activated.

However, many of the empirical studies that we selected used a finger movement task, including finger tapping (Lewis et al., 2004; Aoki et al., 2005; Lutz et al., 2000), finger/thumb opposition (Catalan et al., 1998; Solodkin et al., 2001; Sadato et al., 1996; Habas et al., 2004; Jancke et al., 1999; Kuhtz-Buschbeck et al., 2003), or finger key press (Haaland et al., 2004; Haslinger et al., 2002; Dhamala et al. 2003; Bengtsson et al. 2005; Riecker et al. 2003). Generally speaking, in these studies that used a finger tapping task, complexity was defined as the specific contrast between tasks that involved one and two fingers or between tapping phases that demanded a different response, such as regular tapping versus irregular tapping. Ipsilateral anterior cerebellum was mainly activated with task complexity (Aoki et al., 2005; Lutz et al., 2000; Lewis et al., 2004).

It is easier to vary the task complexity when using finger/thumb opposition and different researchers have investigated varied movement frequency (Jancke et al., 1999), different length of sequencing (Sadato et al., 1996), and ordered or repeated sequencing (Solodkin et al., 2001). When comparing ordered sequencing of finger/thumb opposition to repeated index/thumb opposition that activates the ipsilateral cerebellum or contralateral cerebellum by using the nondominant hand, it was found on a voxel grid that the former is activated more often, regardless of whether the dominant or nondominant hand was used (Solodkin et al., 2001). Imaging studies in which the length of sequencing and number of finger movements varied indicated that the rCBF increased with the level of complexity and that the cerebellar vermis was also activated (Sadato et al., 1996; Catalan et al., 1998). Above all, the ipsilateral anterior hemisphere and the vermis were the mostly activated regions in the cerebellum associated with the brain functioning in the finger/thumb opposition movement.

There is some distinct activation in cerebellum for each finger or hand movement, especially for the finger tapping. Further study could examine the more specific function of various regions in cerebellum. The finger/thumb movements could also be performed either unimanually or bimanually. Specifically, in those studies in which finger/thumb opposition tasks were performed by both hands, complexity manifested in the comparison between the in phase and out of phase movements (e.g., Habas et al., 2004). Simple unimanual finger/thumb opposition performance activated the ipsilateral anterior cerebellum, while bimanual simple finger/thumb opposition performance activated the bilateral anterior cerebellum. However, when a finger/thumb opposition task was performed out of phase bimanually, the bilateral posterior cerebellum was activated. Others (e.g., Jancke et al., 1999; Debaere et al., 2004) found that the anterior hemisphere and vermis were activated under higher demands of movement frequency.

For the finger key pressing task, the mode of cerebellar activation might be different because the movement is self-paced (e.g., Chan et al., 2006; Umetsu et al., 2002; Habas et al.,

2004) or externally paced (e.g. Tracy et al. 2001; Kuhtz-Buschbeck et al. 2003). However, a specific contrast in the activation voxel between more complex sequences and less complex sequences indicated that the ipsilateral anterior hemisphere of the cerebellum, sometimes together with the vermis, was consistently activated. Some specific parts of cerebellum were activated with contrasts between different dexterous movements, that is, complexity would exert its impact on cerebellum activation during finger or hand movements. However, the complexity level in different studies might not be comparable to each other so that it is hard to further infer from the current results how cerebellum functions with different levels of complexity. From the neurological circuits between cerebellum and motor cortex, lateral parts of hemisphere, intermediate parts of hemisphere in cerebellum have separate neurological connections to motor cortex (Raminani, 2006) which might implicate that there would be some mechanisms underlying the influence of complexity on the cerebellum function. Further studies could design more comparable conditions of dexterous movements with contrasts of different complexity levels to examine how the complexity works.

4.3. Interaction between task complexity, learning and aging

Some effects such as learning and aging reveal interaction with task complexity, which might provide more information to understand the functional role of cerebellum than only examining motor complexity in the tasks we defined. Although the motor task in these studies did not meet our inclusion criteria, they also shed some light on our understanding of cerebellum's role in different task complexity. Learning is critical in motor performance for during the early phases; movements are unskilled, highly feed-back dependent and require strong demands on attention. With practice, accuracy and velocity of actions increase, whereas feedback processing becomes less important. Strong activation in distributed cerebellar areas has been reported in the initial stages of motor learning (e.g. Flament et al., 1996). van Mier et al., (1998) showed anterior cerebellum and primary motor cortex activations when switching hand of performance. They found patterns of activation related to unskilled performance in left cerebellum, right premotor and parietal areas; regions related to the level of capacity at which subjects were performing included left premotor cortex, ipsilateral anterior cerebellum, right posterior cerebellum and right dentate nucleus. Moreover, Müller et al. (2002) found that there were activations in the anterior hemisphere of cerebellum at the contrast of novel sequence learning versus index finger tapping while vermis was activated at the contrast of novel sequence learning and regular sequence learning. The learning process itself might have different impact on the cerebellum recruitment with different levels of complexity. Further studies could focus on this point and provide more empirical evidence for it.

In contrast, aging may lead to increased cognitive monitoring of movement (Heuninckx et al. 2005). The study of aging (Heuninckx et al. 2005, Riecker et al. 2006) reveals no more activation of aging in the simple task, but when compared

with more complex task such as hand foot coordinates, old group reveals significant more activation compared with young group mainly in cerebellar vermis and left hemisphere. As a result, aging might be another factor that interacts with complexity which could exert impact on the cerebellum structural recruitment.

5. Conclusions

In this review, we have found consistent activation that highlights the role of task complexity in cerebellum for finger/hand motor tasks by using both ALE meta-analysis and label-based review. In general, the anterior ipsilateral cerebellum is activated when the unimanual motor task is simply finger-tapping or finger/thumb opposition in a simple sequence. The vermis are mostly activated in the hand movement and finger key press. Different regions in cerebellum might be associated with various movement demands.

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