A Comparison of Brain Activation Patterns During Covert and Overt Paced Auditory Serial Addition Test Tasks

Cristina Forn,^{1*} Noelia Ventura-Campos,¹ Antonio Belenguer,²
Vicente Belloch,³ Maria Antònia Parcet,¹ and César Ávila¹

¹*Departament de Psicologia Bàsica, Clínica i Psicobiologia, Universitat Jaume I, Castelló, Spain*

²*Sección de Neurología, Hospital General Castelló, Spain*

³*Servicio de Radiología, Exploraciones Radiológicas Especiales SA, Valencia, Spain*

Abstract: The Paced Auditory Serial Addition test (PASAT) is a sensitive task for evaluating cognitive impairment in patients with diffuse brain disorders, such as multiple sclerosis patients. Brain areas involved in this task have been investigated in diverse fMRI studies using different methodologies to control the subjects' responses during scanning. Here, we examined the possible differences between overt and covert responses during the PASAT task in 13 volunteers. Results showed similar activations in parietal and frontal brain areas during both versions of the task. The contrast between the two conditions (overt and covert) indicated that differences in these two methodologies were minimal. Unlike the covert condition, the overt version of the task obtained significant activations in the left superior and inferior frontal gyrus, bilateral occipital cortex, caudate nucleus and cerebellum. As expected, no significant overactivations were observed in the covert when compared with the overt condition. Discussion focuses on the lower cost of using verbal responses to monitor performance during the PASAT task, which might be generalisable to other frontal lobe tasks requiring discrete responses. *Hum Brain Mapp* 29:644–650, 2008. © 2007 Wiley-Liss, Inc.

Key words: fMRI; cortical activation; overt and covert responses; PASAT task; working memory

INTRODUCTION

The Paced Auditory Serial Additions task (PASAT) is described as a neuropsychological test that measures speed of information processing, sustained and divided attention and working memory functions [Tombaugh, 2006]. The

clinical application of the PASAT consists of presenting 61 random digits sequentially at different rates from an audiotape. The subjects are instructed to add consecutive pairs of numbers (i.e., the first and the second, the second and the third, then the third and the fourth and so on). The result of each sum has to be vocalised before the next digit is presented. Because of its special sensitivity to evaluate cognitive deficits in multiple sclerosis (MS) patients, a modified version of the PASAT has recently been incorporated into diverse MS test batteries, such as the Multiple Sclerosis Functional Composite (MSFC) [Kalkers et al., 2000].

Some recent fMRI studies have focused on brain areas activated during the PASAT test [Audoin et al., 2003, 2005; Forn et al., 2006; Lazeron et al., 2003; Mainiero et al., 2004; Staffen et al., 2002]. One important methodological issue

*Correspondence to: Cristina Forn, Departament de Psicologia Bàsica, Clínica i Psicobiologia, Campus Riu Sec, Fac. Ciències Humanes i Socials, Universitat Jaume I, E-12071 Castelló, Spain. E-mail: forn@psb.uji.es

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during these studies is how to control the subject's performance when conducted inside the scanner. In some studies, subjects were instructed to respond aloud during the scan [Audoin et al., 2003, 2005]. This alternative allows direct monitoring of PASAT performance and facilitates the study of the relationship with brain activity patterns. However, some authors have suggested that spoken responses may result in motion- and magnetic susceptibility-related artefacts that arise from jaw and mouth movements [Barch et al., 1999; Birn et al., 1999]. For this reason, most of the research groups using the PASAT task have used a version requiring covert responses in an attempt to prevent possible secondary effects because of the subject's movement [Forn et al., 2006; Lazeron et al., 2003; Mainero et al., 2004; Staffen et al., 2002]. In these studies, PASAT performance is not monitored while subjects are performing the task inside the scanner, so it is difficult to know whether subjects are performing tasks according to instructions or even whether they are doing the tasks at all [Barch et al., 1999]. For this reason, in one of these studies [Mainero et al., 2004], a further methodological strategy was used to overcome the problem of the lack of control over performance; participants were instructed to raise their finger whenever the sum during the PASAT task matches an a priori criterion (i.e., when the sum was equal to 10). This approach, however, is not devoid of problems, as it increases the difficulty of the task, thus converting PASAT performance into a dual task situation. Even the methodological differences between covert and overt responses, when similar criteria were used to select patients (correct performance of the task), results were highly consistent between them [Audoin et al., 2005; Forn et al., 2006].

Despite these similar results between studies, the importance of this methodological issue seems clear when we consider that previous studies comparing overt and covert verbal conditions with language tasks have produced conflicting results, and the exact nature of the similarities and differences between them has yet to be ascertained. Either way, in studies conducted to compare these two responses, significant activations have been observed during overt response in the cortical and subcortical portions of the speech motor system network [Palmer et al., 2001; Rosen et al., 2000; Shuster and Lemieux, 2005].

The present study was designed to allow direct comparison of the activation patterns of a group of healthy volunteers when performing the PASAT task under covert (silent) and overt (aloud) conditions. We expected to determine the cost of using overt verbal responses in procedures like the PASAT test.

METHODS

Participants

Fourteen volunteers (eight men), with a mean age of 21.9 (SD = 1.6), participated in this study. Before the scan,

the PASAT task was explained and practised. All participants were undergraduate students, Spanish speakers and right-handed. The general exclusion criterion was a score below 75% in the practice session (two females were excluded for this reason). Informed consent was obtained from all the subjects, and each was paid for his or her participation.

fMRI PASAT Task

Participants completed two different 6-min versions of the PASAT task, which involved six 1-min blocks [Forn et al., 2006]. Three of these six PASAT blocks belonged to the control and the other three were part of the activation task. The series of numbers (ranging from one to nine) conforming these blocks were delivered using a computer running Cool Edit Pro v1.2 software (Syntrillium Software Corporation, Phoenix, AZ). Auditory stimuli were presented through fMRI compatible headphones VisuaStim (Resonance Technologies). Sound volume was adjusted so that each participant could hear the stimuli properly. Foam cushioning and tape were used to immobilise the head within the coil to minimise motion degradation. Moreover, subjects were asked to minimise head movement even while speaking.

During the control task, participants were instructed to repeat each number of the series presented. The activation task also consisted of an auditory input made up of a series of single numbers delivered every 3 s and subjects had to sum the last two numbers heard (PASAT). Each participant was asked to perform this task twice under two different conditions. One required participants to respond overtly by verbalising the results, whereas during the other condition responses were covert. In the overt condition, subjects' performance was recorded by an investigator present inside the scanner room. The order of these conditions and the version of the PASAT task were counterbalanced across the subjects.

Data Acquisition

Participants were examined using a 1.5-T Siemens Avanto (Erlange, Germany) using single-shot gradient-echo EPI sequence (TE = 50; TR = 3,000; NEX = 1; FOV = 24 cm; matrix = 64×64 ; 29 slices with a thickness of 5 mm; and a 0.5-mm interslice gap). The 29 slices were acquired in the axial plane parallel to the AC-PC line from bottom to top, thus covering the entire brain. A morphological volumetric sagittal 3D T_1 -weighted fast-field echo sequence (TR/TE = 11/4.2; NEX = 1; FOV = 24×24 cm²; matrix = $256 \times 225 \times 176$; and voxel size = $1 \times 1 \times 1$ mm³) was also acquired to superimpose statistical maps.

Statistical Analysis

MRI images were processed using SPM2 software (Wellcome Department of Cognitive Neurology, London). After

realignment and coregistration using 12-parameter affine transformations, images were spatially normalised (Montreal Neurology Institute, MNI coordinates) and smoothed with a Gaussian kernel (10-mm FWHM). Statistical analysis of the group was performed using the random-effects procedure [Friston et al., 1999]. The data for each participant were modelled using a boxcar design convolved with the haemodynamic response function and time derivative. Motion correction parameters from realignment were included as regressors of noninterest at this first level analysis. Single-subject contrast images were then used in a second level analysis which included within-group one sample *t*-test ($P < 0.0001$ uncorrected) for each task with an extend threshold of 20. Differential activation contrasts were obtained using a one-way ANOVA within-subjects ($P < 0.001$ uncorrected, for multiple comparisons), applying an inclusive mask by an activation map constructed by a concatenation of the two individual activation maps (verbal and mental), and with an extend threshold of 20. MNI coordinates were transformed into Talairach's coordinates using a nonlinear transformation [Talairach and Tournoux, 1988]. Activation clusters were assigned as Brodmann areas (BAs).

Translational movement parameters never exceeded 1 voxel and detected rotations were less than 1° in any direction, subject, or session.

RESULTS

None of the participants manifested any problems or difficulties during performance of the PASAT task scanning sessions. All subjects recruited for the study showed normal performance during the overt PASAT task, with more than 75% of correct responses. The order of administration (the covert version first vs. the overt version first of the PASAT) did not yield significant performance differences in the performance of the overt version of the PASAT ($P > 0.10$). The mean PASAT score for those participants who performed the overt version first was 87.37% (SD = 8.45), whereas the mean PASAT score for those who performed the overt version second was 90.42% (SD = 8.45).

Activation Patterns

Preliminary analysis did not show significant differences in brain activation as a function of order of administration. Thus, this variable was removed from further analyses. PASAT performance resulted in a similar cortical activation pattern regardless of the experimental condition (overt vs. covert). Specifically, during both conditions activations were observed in the prefrontal superior and middle frontal gyrus (BA 6 and 9), inferior frontal gyrus (BA 46 and 47) and superior and inferior parietal (BA 7 and 40) regions, greater activation being observed in the left hemisphere (Table I and Fig. 1). Comparisons between conditions were conducted using a paired *t*-test. This did not

yield any overactivation during the covert condition as compared with the overt condition. However, under the overt condition, enhanced activity was observed in prefrontal regions of the brain, although restricted to the left hemisphere, these regions being the superior and inferior frontal gyrus (BA 6, 44 and 46). Moreover, bilateral occipital cortices (BA 18 and 19) were also activated in this condition. Finally, requiring overt verbal responses resulted in the recruitment of some subcortical brain areas including the cerebellum, the caudate and the substantia nigra. These results are shown in Table II and Figure 2.

DISCUSSION

The results of the present study confirmed that the performance of the auditory PASAT task activated parietal and frontal brain areas that are considered to be the neural substrates of working memory processes. When experimental conditions involving the overt or covert responses were compared, some differences in the brain activation pattern were found. More specifically, the covert condition did not yield any overactivation when it was compared with the overt condition, whereas the overt condition activated the left superior and inferior frontal gyrus (BA 6, 44 and 46), bilateral occipital cortex (BA 18 and 19) and subcortical areas, like the caudate and cerebellum, to a greater extent than the covert condition. This means that discrete overt responses during the PASAT may be recorded without yielding important motion artefacts and with only a few brain overactivations being produced.

As mentioned earlier and also in agreement with previous studies [Audoin et al., 2003, 2005; Forn et al., 2006; Mainero et al., 2004; Staffen et al., 2004], the PASAT task mainly activates brain areas related to working memory. Current models of verbal working memory define two main components, the central executive and the phonological loop, which is further subdivided into the phonological store and the articulatory loop. The activity of the central executive, which exerts attentional control over working memory processes, has been related to a series of brain networks located in prefrontal areas, especially in BA 9 and 10, although some other studies also include BA 6 and 46 as possible substrates of this system [Cabeza and Nyberg, 2000; D'Esposito et al., 2000; Wager and Smith, 2003]. In this regard, during both PASAT conditions (overt vs. covert), there have been reports of a significant increase in activity in some frontal areas, including the middle frontal gyrus (BA 6, 9 and 46) and the superior and medial frontal gyrus (BA 6). Despite the fact that BA 6 (which bridges the prefrontal and primary motor cortex) has been traditionally regarded as involved in motor functions, neuroimaging studies have demonstrated that this area is also activated during various cognitive operations like mental arithmetic operations [Dehaene et al., 1996] and attentional processes [Coull et al., 1996; Hopfinger et al., 2000]. Moreover, activation in the dorsolateral prefrontal cortex, which

♦ Comparison of Covert and Overt PASAT Tasks ♦

TABLE I. Location of brain regions showing significant activation in 14 volunteers participants during overt and covert PASAT task ($P < 0.0001$, uncorrected)

Regions of interest	Overt response					Covert response				
	Talairach coordinates			Z score	Clusters	Talairach coordinates			Z score	Clusters
	<i>x</i>	<i>y</i>	<i>z</i>			<i>x</i>	<i>y</i>	<i>z</i>		
Right subgyral/right middle frontal gyrus BA 6	28	−3	55	5.24	434					
Right middle frontal gyrus BA 9	38	40	26	3.93	15					
Left superior/middle frontal gyrus BA 6	−26	4	50	4.91	554					
Left middle/inferior frontal gyrus BA 46/6/9						−40	16	18	5.26	1678
Right middle frontal gyrus BA 46						36	32	21	4.06	14
Right superior frontal gyrus BA 6	4	10	51	4.78						
Left medial frontal gyrus BA 6	−8	3	57	4.23	911					
Left inferior frontal gyrus BA 47/bilateral caudate body	−32	29	2	5.55	3967					
Left insula BA 13						−28	24	8	4.05	16
Left parahippocampal gyrus BA 27	−14	−33	−2	4.88	740					
Right superior/inferior parietal lobule BA 7/40	26	−64	44	5.25	1462	34	−43	41	4.71	512
Left superior/inferior parietal lobule BA 7/40	−26	−58	45	5.32	1882	−28	−54	40	5.67	1401
Right superior/inferior parietal lobule BA 40	34	−51	38	5.02	1462					
Left occipital lobe/cuneus BA 17	−20	−73	15	4.64	121					
Right thalamus/pulvinar	20	−30	13	4.24	57					
Left thalamus/medial dorsal nucleus	0	−13	10	5.75	740					
Right red nucleus/substantia nigra	4	−16	−9	4.46	82					
Left caudate body						−20	5	24	4.33	38
Right cerebellum	18	−73	−20	6.05	4180	28	−61	−22	2.25	104
Left cerebellum						−6	−63	−25	4.60	101

BA, Brodmann areas.

comprises BA 9 and 46, is thought to play an important role in executive functions such as updating, monitoring and manipulating new information [Owen, 1997; Petrides, 2000; Rypma and D'Esposito, 1999]. Additional focuses of activity during the PASAT test were bilaterally located in the parietal cortex, specifically in BA 7 and 40. These areas have been proposed as participants in the storage process

of working memory and could be the anatomical substrates of the phonological store [Cabeza and Nyberg, 2000; Wager and Smith, 2003]. Moreover, bilateral cortical activations in the superior parietal cortex (BA 7) are observed during simple calculation and arithmetic procedures [Rickard et al., 2000], and some authors have also interpreted activations in these areas as reflecting proc-

TABLE II. Location of brain regions showing significant activation in 14 volunteers comparing overt PASAT task versus covert task ($P < 0.001$, uncorrected)

Regions of interest	<i>x</i>	<i>y</i>	<i>z</i>	Z score	Clusters
Left superior frontal gyrus BA 6	−10	19	62	3.45	13
Left inferior frontal gyrus BA 46	−42	31	8	3.40	21
Left inferior frontal gyrus BA 44	−44	16	16	3.52	11
Left parahippocampal gyrus BA 27	−12	−33	2	3.83	84
Right middle occipital gyrus/cuneus BA 18	10	−91	16	4.18	209
Left occipital lobe/lingual gyrus BA 18/left cerebellum	0	−78	−15	4.28	1037
Left occipital lobe/cuneus BA 18/7	−24	−67	18	3.83	285
Right fusiform gyrus BA 19	48	−70	−10	3.26	19
Right occipital lobe/fusiform gyrus BA 19/right cerebellum	28	−76	−10	3.91	470
Right substantia nigra	8	−12	−8	4.22	49
Right caudate body	18	18	16	3.95	103
Left caudate body	−20	13	21	4.05	78

BA, Brodmann areas.

Figure 1.

Activations observed during PASAT overt responses (above) and PASAT covert responses (below). Left side of the images represents the left side of volunteers. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

esses involved in attributing semantic knowledge to numerical quantities [Dehaene et al., 1998].

The main purpose of the present study is to compare both overt and covert responses during the PASAT task. Results have shown that the production of overt responses resulted in higher activity in some prefrontal, occipital and

Figure 2.

Regions exhibiting significantly greater activations during overt PASAT task compared with covert PASAT responses. Left side of the images represents the left side of volunteers. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

subcortical areas. Prefrontal activations were circumscribed to the left superior and inferior frontal gyrus (BA 6, 44 and 46), and could reflect the engagement of speech-related processes. Alternatively, the higher activity of these brain areas that was displayed when overt responses were required in the PASAT task could reflect something other than just speech production. Indeed, higher activity in the prefrontal and occipital cortex could be related to a greater cost in rehearsal and executive processes when responding aloud. In other words, responding aloud might diminish the maintenance of information in working memory and, in such a case, proper PASAT performance could require the recruitment of additional resources. In agreement with this rationale, previous research has shown that concurrent articulatory responses disrupt the rehearsal mechanism of the phonological loop and reduce the span of short-term verbal memory [Baddeley et al., 1984; Murray, 1968]. Furthermore, it has been proposed that the output (verbal response) and the input (auditory) may interfere with each other during PASAT performance [Fos, 2000]. Therefore, activations in prefrontal (especially BA 6) areas can be recruited to compensate the reduced short-term memory span and/or cross-modal interferences introduced by the production of overt responses.

The increased activity that is observed in some areas of the occipital lobe during the overt condition can be inter-

preted in a similar way. In this regard, a previous study involving an auditory version of the PASAT task suggested that posterior occipital activations might provide a visual mnemotechnic strategy to maintain information [Audoin et al., 2003]. However, it is possible that the recruitment of this cognitive resource was necessary only when the cognitive load of the task was enhanced by requesting the production of overt responses.

Finally, during the overt condition, activations in the caudate nucleus, the substantia nigra and in the cerebellum were also found. All these brain areas have been previously implicated in the initiation, planning and coordination of articulatory movements, and in the modulation and temporal control of speech production [Frim and Ogilvy, 1995; Palmer et al., 2001; Peach and Tonkovich, 2004; Sörös et al., 2006]. It should be mentioned that a previous study [Audoin et al., 2005] requiring overt responses while performing the PASAT task reported similar brain activations in several subcortical areas (e.g., caudate nucleus, thalamus and cerebellum) that are not observed in studies involving the same PASAT task under a covert condition [Forn et al., 2006]. Therefore, it seems reasonable to conclude that the activity of these brain areas is related to the organisation and setting in motion of processes involved in speech production.

In conclusion, the present study has shown that the most important elements of the brain activity pattern elicited during the performance of an auditory version of the PASAT task implicated the frontoparietal anatomical areas, previously proposed as substrates of working memory. Further, the main components of the brain activity pattern underlying PASAT performance have remained unaltered regardless of the response modality (overt vs. covert responses). Indeed, only minor differences were obtained between the two experimental conditions. These differences were observed in prefrontal and occipital areas, which probably reflects a higher cognitive load when producing reporting aloud PASAT responses, as well as in some areas related to speech production (i.e., caudate and cerebellum). The results of the present study are important because the PASAT task has been used in numerous fMRI studies but, to date, no direct analyses have been conducted to compare these two alternative strategies when trying to control subjects' performance. Based on our results, it can be concluded that the auditory PASAT task may be implemented in fMRI studies in both silent and aloud conditions, but additional advantages can be obtained when providing overt responses. First, the subject's performance can be monitored directly, with a minimal effect on the fMRI output. Second, this PASAT form (auditory and requiring loud verbalisation of the results of the successive sums) is closer to the clinical applications of the PASAT task than other methodological alternatives used in previous fMRI studies involving this task [Forn et al., 2006; Mainiero et al., 2004; Staffen et al., 2002].

Present results are important not only for the PASAT test but also for other tasks that depend on the frontal lobe in

which it would be desirable to record verbal responses as a means of controlling performance during the task. One of the most studied, for example, is the Stroop task, in which different methodologies have been employed [see Laird et al., 2005, for a review], including overt verbal responses, covert verbal responses and manual responses. Most fMRI studies used covert or manual responses to avoid motion artefacts. However, the metaanalysis revealed that manual and verbal responses yielded a different pattern of brain activations in key structures such as the anterior cingulate [Laird et al., 2005]. The reason that the PASAT did not show significant activations during the overt responses when compared with the covert responses could be due to the fact that the overt PASAT task demands discrete and brief verbal responses (numbers between 2 and 18). Present results would therefore suggest that the cost of studying brain areas involved in frontal tasks using overt responses in the PASAT task is low, which would help to investigate these processes ecologically, and to probably homogenise the results of different fMRI studies.

Finally, it should be noted that our study presents some limitations. Firstly, the limited number of subjects recruited in the study (14 participants) might limit the generalisation of the results. Secondly, a direct comparison between brain activation patterns observed during the covert and overt PASAT could not account for a putative difference in execution between both conditions. By definition, executing the PASAT under the covert condition does not allow to control for the subjects' performance and this limitation cannot be circumvented. However, we tried to minimise this influence by optimising the conditions under which the comparison between both conditions was made. Thus, we included only subjects who exhibited a good execution of the PASAT task during the training phase conducted before the scanning. Furthermore, we counterbalanced the order of the overt and covert conditions to then discharge a possible test-retest effect. Therefore, although it cannot be totally proven, there is reasonable evidence to presume a similar performance under both conditions, and their corresponding brain activation patterns can be legitimately compared.

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