

ORIGINAL ARTICLE

Disturbed cognitive functions after nasal provocation in patients with seasonal allergic rhinitis

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Clinical & Experimental Allergy

Summary

Background Allergic rhinitis (AR) reduces quality of life as a result of impaired psychological well-being and perceived impaired cognitive functioning. Few studies have measured cognitive functions objectively and it remains uncertain whether AR leads to an objective reduction in cognitive functions.

Objective The present study investigated whether AR is associated with a decrement in several aspects of cognitive functioning. Furthermore, the study investigated whether AR patients invest more 'mental effort' in order to achieve the same cognitive performances as healthy controls.

Methods Twenty five patients with seasonal allergic rhinitis (SAR) and 26 healthy controls, matched for age, education and sex, were tested on a battery of time-demanding and strenuous objective cognitive tests and subjective questionnaires, both before and after nasal provocation (NP). The cognitive functions assessed were sustained attention, short- and long-term memory and speed of information processing. Mental effort was assessed using visual rating scales.

Results Sustained but not short cognitive performance was impaired in patients after NP. Patients showed an increased effort on short cognitive tests.

Conclusion SAR patients suffer from cognitive performance decrements that can be compensated by additional mental effort for short tasks only.

Keywords allergic rhinitis, cognitive functions, psychological well-being

Submitted 24 July 2008; revised 7 November 2008; accepted 5 December 2008

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Introduction

Allergic rhinitis (AR) is one of the most common chronic diseases. Its prevalence is 15% to 20% in industrial nations, with an even higher prevalence of up to 42% among children [1]. Sneezing, itching, watery rhinorrhoea and nasal obstruction are classic symptoms. AR is traditionally classified as seasonal allergic rhinitis (SAR) and perennial allergic rhinitis. More recently, the AR and its impact on asthma document proposed the intermittent (ITR) and persistent forms (PER) [2]. In this study, we will use the classical term SAR, also called hayfever, which involves an allergy to tree, grass and weed pollens and mould spores [3].

AR is a common co-morbid condition with asthma, sinusitis, nasal polyposis, respiratory infections and otitis media [4]. Allergic conditions not only affect the patient's health but can also have a detrimental impact on a patient's quality of life (QoL) [5–8]. QoL assessments show that AR patients experience a reduction in cognitive functioning. Our group [9] showed that patients with AR report significant reductions in psychological well-being and cognitive functioning. The latter was, however, not supported with objective performance tests. Other symptoms reported in patients with AR are mood changes and fatigue [10], irritability and stress [9, 11]. Objective measurements of cognitive functions in patients with AR are rarely reported and are mostly inconclusive. Using

experimental performance studies, Marshall *et al.* (2000) [12] found a reduced ability to concentrate and memorize, and Vuurman *et al.* (1993) showed that children with AR have impaired learning abilities.

The fact that AR patients subjectively experience a decrement in cognitive functioning, while no objective decrement could be found, might be explained by the hypothesis that AR patients invest more 'mental effort' in order to maintain a constant level of performance [9, 13, 14]. Effort is limited and cannot be maintained for long periods of time, however. This would explain why the performance of AR patients does not differ from that of healthy participants in relatively short performance tests but that patients' performance does decrease more rapidly or is more pronounced in longer and more effort-demanding situations or performance tests, such as a sustained attention test.

The aim of the present study was therefore to determine whether AR patients invest more effort to maintain performance when they are symptomatic as compared with when they are not symptomatic. To explore this hypothesis, AR patients and healthy controls were asked to perform tests of reaction time (RT), verbal learning and sustained attention, and rate their effort to perform each of them. AR patients performed the tests once when they were symptom free (baseline) and once when they were symptomatic after nasal provocation (NP). After provocation, patients' performance on the relative short tests was not expected to change, but they were expected to report increased effort to execute them. On the longer lasting sustained attention task, however, patients were expected to show a performance decrement after NP in spite of increased effort, because they would no longer be able to compensate their degraded performance by increasing their effort. A group of healthy controls was also tested twice to control for the effects of repeated testing, such as learning or motivational changes. No or little difference in performance between AR patients and controls was expected during baseline when patients are not symptomatic.

Methods

Participants

Twenty-five Dutch-speaking patients with SAR and 26 healthy volunteers, matched for age, sex and educational level, participated in the study. The patients with SAR were recruited from a database of the Department of Otorhinolaryngology, Head and Neck Surgery of the Academic Hospital Maastricht and from a general practitioners practice in Maastricht. The healthy controls were recruited by means of advertisement in a local newspaper. Inclusion criteria were age between 18 and 45 years; a positive medical history of SAR; anti-allergic treatment

during the previous season; positive radioallergosorbent tests for serum-specific IgE or positive skin prick test for tree- and/or grass- and/or weed pollen in the SAR group; and in all cases an informed written consent. The main exclusion criteria were the presence of any form of rhinitis in the control group; the presence of forms of rhinitis other than SAR in the patient group; the presence or a history of psychiatric disorders in both groups; the use of interfering medications [any nasal decongestants, (nasal corticosteroids,) anticholinergics, sympathomimetics, theophylline preparations, sedatives, antidepressants and all other types of psychotropic drugs], the presence of contraindicated illnesses, e.g. asthma, diseases or traumas of the central nervous system or impaired visual or auditory functions that could disturb communication and/or examination. After written informed consent, participants were included in the study. All participants were paid for their participation. The study was approved by the Medical Ethical Committee of Maastricht University and conducted in accordance with the World Medical Associations Declaration of Helsinki [Edinburgh modification, 2000].

Study design

The study was organized as a parallel-group design consisting of two groups, with repeated measures within groups. The between-subjects factor was Group, which consisted of two levels (patients with SAR and healthy controls), and the within-subjects factor was Day, which consisted of two levels: baseline on Day 1 and NP (SAR-group) and retest (controls) on Day 2.

Procedure

Figure 1 shows the timelines and conditions of the study. Both groups were tested with parallel versions of the same test battery on two occasions (Days 1 and 2) out of the allergy season. Testing occurred at the same time of the day.

In the SAR group, a NP was performed just before the second session. Allergen solution containing pollen of grass, tree or weed (Vivodiagnost[®]; allergen, benzalkoniumchloride 0.0125%, human serum albumin 0.03%, and phosphate buffer 5 mL, ALK (ALK-Abello, Denmark) Pharma) (50 µL) was administered onto the mucosa of the inferior nasal concha on both sides with a calibrated pipette.

Assessments

Long cognitive performance test. Long cognitive performance was measured using a 45-min sustained attention test, based on the Mackworth clock test [15]. Participants sit in front of a computer screen displaying a circular

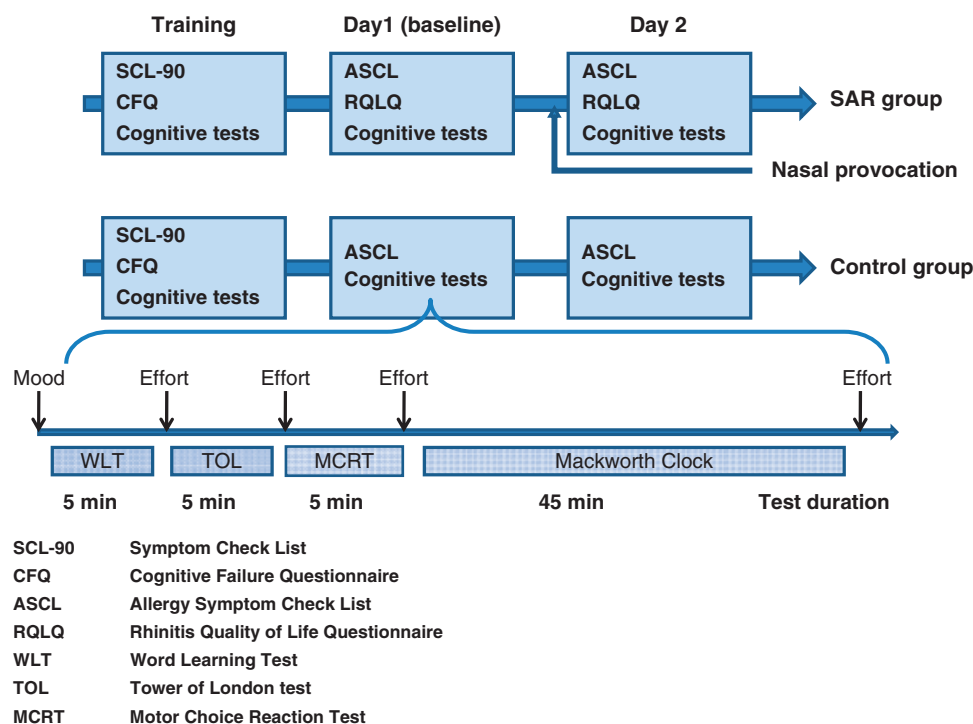


Fig. 1. Timelines and conditions of the study.

arrangement of 60 dots simulating the second marks on a clock. Each dot briefly lights up in a sequential clockwise rotation at a rate of one per second. Occasionally, the rotation proceeds with a 'double jump' by skipping one of the dots in the normal sequence. Participants are instructed to monitor these rare events and respond to them with a fast button press. There are 10 double jumps per 15 min. The dependent variables are the total number of correct detections of the double jump and the mean RT to detect them.

Short cognitive performance tests. The Word-Learning Task [16] assesses verbal memory. In the first part (immediate recall), 15 words are visually presented on a computer screen and directly after the presentation participants are asked to recall as many words as possible. This procedure is repeated three times. The main outcome variable is the number of words recalled and reflects the capacity of working memory. Working memory is the form of memory that is used to store information with a limited capacity for a brief period of time. Approximately 25 min after the initial presentation, participants are asked again to recall the words presented previously (delayed recall). The number of words actively remembered after this interval is a measure of the retrieval of the learned words from long-term memory. Finally, the participants are shown a series of 30 words on the computer. Fifteen of these words are identical to the ones presented previously and the rest are new (delayed recognition). Participants use a button press to indicate which words are new and

which are familiar by pressing corresponding buttons. The secondary outcome variables are the number of words recalled after 25 min and the number of words recognized correctly.

The computerized version of the Tower of London test [17, 18] assesses several executive functions, such as planning, working memory and cognitive flexibility. On a computer screen, two pictures of an array of coloured balls on sticks are shown. Each picture contains three balls. One rod has a capacity of three balls, another holds two balls and the third holds one ball. Participants are asked to indicate the minimal number of steps necessary to rearrange the balls in the one picture to match the arrangement presented in the other picture and then press the appropriate response button (2, 3, 4 and 5 steps). Each ball must be moved separately. The dependent variables are the total number and mean RT (in milliseconds) of correct responses.

The Motor Choice Reaction Task (MCRT) [19] assesses RT as a function of task difficulty. Participants operate a button box with one central red and five white buttons. They are asked to hold the central red button until one of the white buttons lights up. As soon as this happens, the participant has to release the red button and press the illuminated button as fast as possible. Three task conditions with increasing difficulty are used: simple RT (part 1), in which only one (the upper) button illuminates; choice-RT (part 2), in which one of a defined set of three buttons randomly illuminates; and conflict-RT (part 3), which is the same as the choice-RT condition but the

subjects' task is to press the button located to the right side of the illuminated button. The main outcome variable is the RT, defined as the time between presentation of imperative stimulus and the release of the centre button in each test condition.

Subjective rating scales and questionnaires. The Allergy Symptom Check List (ASCL) rates the severity of nasal symptoms (itching, secretion, sneezing and congestion) on an ordinal scale ranging from 0 to 3 (0 = no, 1 = light, 2 = moderate and 3 = severe symptoms). The individual symptom scores are summed to give an overall symptom score. Controls as well as SAR patients scoring 4 or more were excluded [9].

The Rhinitis Quality of Life Questionnaire (RQLQ) was used as a disease-specific questionnaire [7]. The RQLQ assessed the extent of subjective disturbances by scoring the presence of various rhinitis symptoms and their emotional and practical effects. Twenty-eight symptoms, divided into seven subgroups (nasal symptoms, ocular symptoms, general symptoms, sleeping disorders, practical problems, limitations of activity and emotional disorders), were evaluated. Scores ranged from 0 (non-existent) to 6 (maximum). The overall RQLQ was calculated from the mean values of the 28 symptoms.

Mood was assessed with the help of a scale developed by [20]. Participants assess 16 items on a 100 mm-visual-analogue scale (VAS). Per item participants stated how they felt at that moment by means of a mark on the VAS. The scores of the 16 items are combined into three factors: Alertness, Contentedness and Calmness.

The Mental Effort Scale [21] assesses the subjective experience of mental effort. The scale consists of a 150 mm VAS, which is marked on nine points with a verbal description of the amount of effort, ranging from 'no effort at all' to 'extremely high effort'. After each test, subjects indicated the amount of effort needed to perform it.

The Symptom Check List (SCL-90) is a 90-item multi-dimensional questionnaire designed to screen for a broad range of possible psychological problems [22]. Each of the 90 items is rated on a five-point scale, yielding nine factors of psychological well-being: somatization, obsessive-compulsive, sensitivity, depression, fright, hostility, phobic anxiety, insufficiency and sleep.

The Cognitive Failure Questionnaire (CFQ) is a questionnaire that assesses the frequency of everyday cognitive mistakes [23]. The list consists of 25 items about concentration and memory, scored on a five-point scale. By adding the scores on all 25 items, a total CFQ score is obtained.

Educational level was indexed on an eight-point scale, ranging from elementary education (1) to university degree (8), determined according to a standardized Dutch classification system [24] that is comparable to the International Standard Classification of Education [25].

Statistical analyses

Statistical analyses were performed using the SPSS statistical program (version 12.0.1 for Windows). To evaluate overall differences between groups and test days, a two-way analysis of variance (ANOVA) was carried out with a between-subjects factor Group (Patients vs. Controls) and a within-subjects factor Day (Days 1 and 2). The effects of NP on performance or effort were expected to be revealed by significant statistical interactions between group and test day, indicating differential changes from Days 1 to 2 in patients and healthy controls. When the interaction between groups and days was significant ($P < 0.05$), data were further analysed using independent *t*-tests to compare the performance between groups on each day separately, and paired *t*-tests were used to evaluate performance changes within each group over test days. All statistical tests were performed at the 0.05 level of significance.

Results

Group characteristics

The data of 25 (12 ♀, 13 ♂) SAR patients with a mean (SD) age of 30.4 (6.8) years and a mean educational level of 4.5, and 26 (16 ♀, 10 ♂) healthy controls with a mean (SD) age of 31.4 (9.0) years and a mean educational level of 5.4 were used in this analysis. There were no significant differences between the groups with respect to sex ($\chi^2 = 0.943$; $P = 0.331$), age ($t_{45.751} = 0.349$; $P = 0.564$) and education ($Z = -0.869$; $P = 0.385$).

Symptom Check List -90 and Cognitive Failure Questionnaire

Table 1 shows the factor scores for the SCL-90 and CFQ. Compared with healthy controls, SAR patients scored worse on measures of psychological well-being as there were significant differences between the groups on the subscales *Somatization* ($t_{31.83} = -3.33$; $P = 0.002$) and *Insufficiency* ($t_{38.86} = -2.196$; $P = 0.034$) (Table 1) of the SCL-90. No difference was found between groups on the CFQ.

Subjective rating of allergic symptoms and mood

The SAR group had higher mean (SD) allergic symptom scores of 3.4 (4.0) and 8.0 (4.1) at baseline (Day 1) and after NP (Day 2) compared with the control group, which showed 1.5 (1.9) and 1.4 (1.3), at baseline (Day 1) and on Day 2, respectively. The analysis showed a significant main effect for Day ($F_{1,49} = 20.392$; $P < 0.001$) and Group ($F_{1,49} = 37.7$; $P < 0.001$) as well as a significant interaction effect between Day and Group ($F_{1,49} = 22.5$; $P < 0.001$). Also, a significant difference between baseline and

provocation was found for the SAR group ($t_{24} = -4.79$; $P < 0.001$), but not for the control group ($t_{25} = 0.366$; $P = 0.718$). Furthermore, a significant difference was found between the groups during baseline ($t_{33.487} = -2.15$; $P = 0.039$) and provocation ($t_{28.697} = -7.72$; $P < 0.001$). Symptom scores and performance were low and non-significant on all tests. The analysis of mood scores showed no differences between the groups.

Cognitive tests

Table 2 provides an overview of the mean scores on all performance tests for both groups on Days 1 and 2, and summarizes the results from statistical tests.

Table 1. Statistics of the SCL-90 and CFQ

	CONT <i>n</i> = 26 Mean (SD)	SAR <i>n</i> = 25 Mean (SD)	<i>t</i> -value	<i>P</i> -value
SCL-90				
Anxiety	12.0 (2.4)	13.3 (4.6)	-1.30	0.201
Phobic anxiety	7.2 (0.5)	7.6 (1.2)	-1.73	0.092
Depression	21.3 (6.0)	22.3 (7.9)	-0.55	0.585
Somatization	14.8 (2.6)	20.1 (7.8)	-3.33	0.002
Insufficiency	12.2 (2.4)	14.4 (4.7)	-2.20	0.034
Sensitivity	24.4 (8.8)	25.0 (9.5)	-0.25	0.808
Hostility	7.4 (1.7)	8.2 (3.2)	-1.12	0.269
Sleep	4.4 (1.6)	5.0 (2.2)	-1.16	0.251
Obsessive-compulsive	11.0 (2.4)	11.0 (3.1)	-0.05	0.960
CFQ	30.3 (9.4)	29.2 (14.7)	0.32	0.751

SAR, seasonal allergic rhinitis; SCL, Symptom Check List; CFQ, Cognitive Failure Questionnaire.

Sustained attention (Mackworth Clock). Figure 2a shows the mean ($\pm$ SEM) number of correct responses. Although no main effects were found for Day and Group, the SAR group showed a lower number of correct responses after provocation compared with the control group, as shown by a significant interaction ($F_{1,49} = 7.376$; $P = 0.009$). Further analysis of the interaction showed a significant difference between the test days in the SAR group ($t_{24} = 2.556$; $P = 0.017$), but not in the control group ($t_{25} = -1.216$; $P = 0.235$), and a significant difference between the groups during provocation ($t_{49} = 2.209$; $P = 0.035$), but not during baseline ($t_{49} = 0.641$; $P = 0.525$). As shown in Fig. 2a, the SAR group showed a decrease in their performance (total number of correct responses diminished) after NP compared with the healthy controls.

Figure 2b shows similar effects for the mean RT; RT increased in the SAR group after NP, whereas the mean RT slightly decreased in the control group. Again, no main effects for Day and Group were found, but the analysis indicated a significant interaction ($F_{1,49} = 5.756$; $P = 0.020$). Further analysis showed a significant difference between days in the SAR group ($t_{24} = -1.791$; $P = 0.086$), but not in the control group ($t_{25} = 1.599$; $P = 0.122$), and a significant difference between the groups during provocation ($t_{31.539} = -2.104$; $P = 0.046$), but not during baseline ($t_{49} = -0.685$; $P = 0.497$).

Word-Learning Test. No differences in performance were found between groups or days on the Word-Learning Test for both the main (working memory) and the secondary (long-term memory) outcome variables.

Tower of London. Both the SAR group as well as the control group showed a small decrease in processing time

Table 2. Mean scores on all performance tests for both groups on Days 1 and 2

		Scores Day 1 (SEM)		Scores Day 2 (SEM)		Statistics			
						Main effects (ANOVA)		Day2 effects (t-test)	
Test	Dependant variable	CONT	SAR	CONT	SAR	Group	Day	Group×Day	SAR≠CONT
Sustained attention test									
	Reaction time (ms)	633.9 (17.9)	653.0 (21.47)	612.7 (13.4)	687.2 (33.3)	NS	NS	<i>P</i> = 0.020	<i>P</i> = 0.046
	# Correct (<i>n</i>)	26.6 (0.8)	25.7 (1.1)	27.3 (0.5)	24.2 (1.3)	NS	NS	<i>P</i> = 0.009	<i>P</i> = 0.035
Word Learning Test									
	Immediate recall (<i>n</i>)	27.9 (1.2)	26.7 (0.8)	28,8 (1.4)	26,8 (1.1)	NS	NS	NS	NS
	Delayed recall (<i>n</i>)	9.1 (0.7)	7.7 (0.6)	9.6 (0.7)	8.3 (0.6)	NS	NS	NS	NS
	Recognition (ms)	26.6 (0.5)	26.7 (0.5)	27.0 (0.8)	27.0 (0.6)	NS	NS	NS	NS
Tower of London									
	Time on task (s)	9.3 (0.5)	9.3 (0.5)	7.7 (0.4)	7.7 (0.3)	NS	<i>P</i> < 0.001		
	# Correct (<i>n</i>)	33.6 (0.7)	32.9 (0.7)	34. (0.6)	34.4 (0.5)	NS	<i>P</i> = 0.006		
Motor Choice Reaction Time									
	Simple RT (ms)	274 (4.6)	301 (7.6)	267 (5.7)	304 (7.5)	<i>P</i> < 0.001	NS	NS	NS
	Choice RT (ms)	311 (4.4)	322 (5.8)	314 (6.9)	328 (5.6)	<i>P</i> = 0.005	<i>P</i> = 0.031	NS	NS
	Conflict RT (ms)	388 (8.4)	415 (9.9)	371 (7.7)	410 (8.5)	NS	NS	NS	NS

SAR, seasonal allergic rhinitis; RT, reaction time.

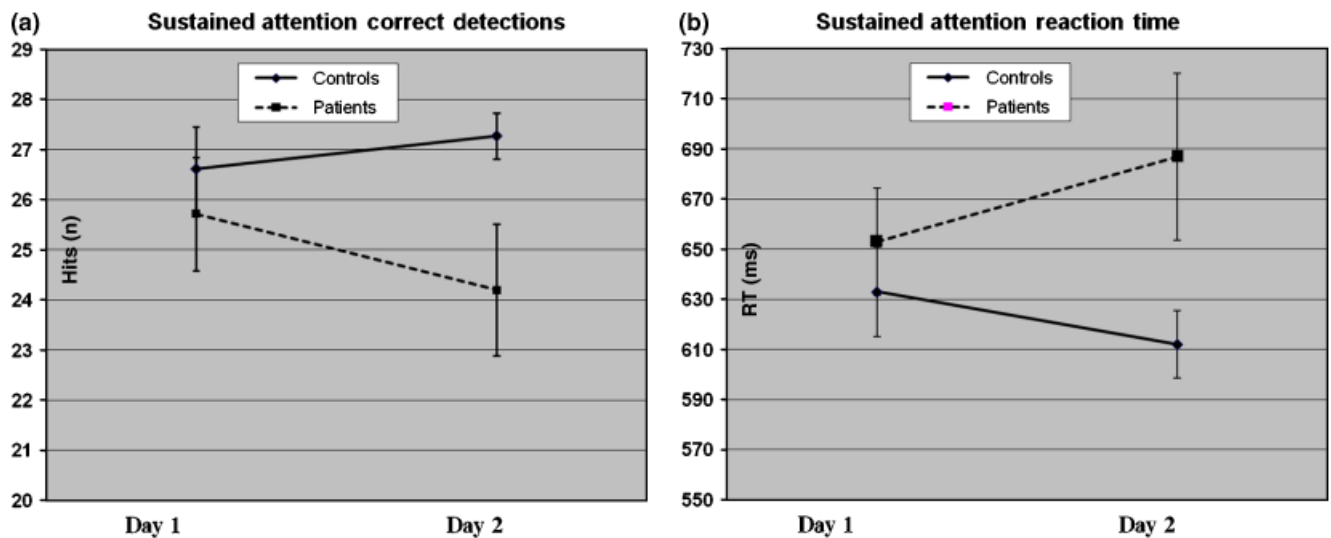


Fig. 2. (a) Sustained attention, total number correct during baseline (B) and provocation (P). (b) Sustained attention, the mean total reaction time during baseline (B) and provocation (P).

on the second test day compared with the baseline. The analyses showed a significant main effect of Day for the mean RT ($F_{1,49} = 40.502$; $P < 0.001$). No significant main effect for group and no significant interaction effects were found for RT. The analyses of the number of correct answers showed a similar pattern: a significant main effect of day ($F_{1,49} = 8.102$; $P = 0.006$), but no significant main effect for group and no significant interaction effect. These improvements in both groups in the mean RT and number of corrects answers might be due to a learning (training) effect.

Motor Choice Reaction Task. Compared with the control group, the SAR group showed an overall slower simple-RT ($F_{1,49} = 14.293$; $P < 0.001$) and more errors ($F_{1,49} = 5.727$; $P = 0.021$). In the choice-RT condition, a significant main effect of Day ($F_{1,49} = 4.931$; $P = 0.031$) and Group ($F_{1,49} = 8.841$; $P = 0.005$) was found for RT. While patients were overall slower than controls, RTs improved similarly in both groups from Days 1 to 2. No difference in conflict-RT was found.

Subjective rating of mental effort. Figure 3 shows the mean subjective ratings of mental effort for the long cognitive test (sustained attention) and the short cognitive tests combined (Word Learning Task, Tower of London and MCRT). The data were analysed using a repeated measures ANOVA with two within-subjects factors (Day and Test length) and one between-subjects factor (Group). The effect of test length was highly significant ($F_{1,49} = 105.14$; $P < 0.001$). As can be seen in Fig. 3, more mental effort was needed on the long sustained attention test compared with the three short tests. No overall effect of Day was found, but there was a significant interaction of Day $\times$ Group ($F_{1,49} = 3.88$; $P = 0.05$) and Day $\times$ Test length

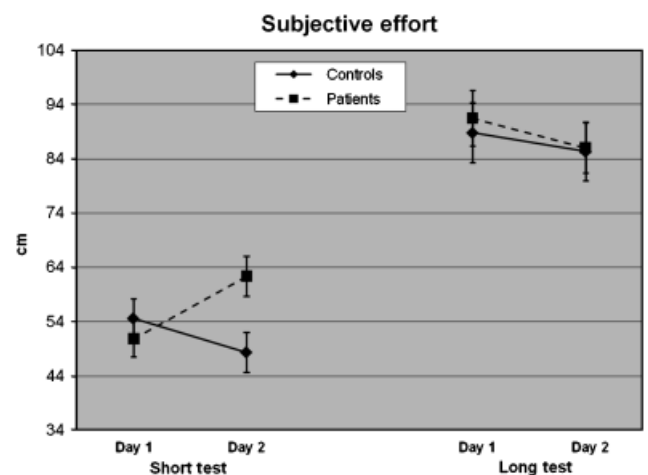


Fig. 3. Mean (SEM) subjective mental effort for the three short cognitive test combined (left) and the long Sustained Attention Test (right).

($F_{1,49} = 5.06$; $P = 0.029$), indicating that changes in effort between days differed between the groups and depended on test length. This is supported by a significant three-way interaction between Day, Group and Test length ($F_{1,49} = 9.82$; $P = 0.003$). Figure 3 shows that a difference in effort is reported between the SAR and the control groups but only in the short tests and only on Day 2.

Discussion

As expected, the NP test was successful in inducing SAR symptoms in the patient group. The magnitude of change on the symptom score list was clinically relevant and comparable to the effects found previously with this procedure [9]. Changes in cognitive function related to

fast effects of SAR could therefore be measured reliably with this procedure. Both groups in this study had a comparable psychological profile: no differences were found on the CFQ, indicating that SAR patients had no chronic cognitive deficiency. The two factors on the SCL-90 that differed between groups at baseline (somatization and insufficiency) indicated that SAR patients were more sensitive to physical discomfort in general.

The main aim of this study was to compare different subjective and objective measures of cognitive functioning and the possible role of increased mental effort in compensating for decreased performance.

As expected, the three short cognitive tests, the Word Learning Test, the Tower of London and the MCRT, showed no difference in performance between the groups. A previous study by Kremer et al. [9] did not find an effect of SAR on verbal memory or speed of information processing.

Possible effects of allergic symptoms on memory functions have been studied previously by Marshall & Colon [12, 27] and Wilken et al. [28]. In contrast to our findings, Marshall & Colon [27] reported that atopic individuals experienced deficits in verbal learning. In their study, however, the participants in the experimental group had a history of depression and were recruited on their belief that experiencing allergic reactions played an important role in the induction of their depressive symptoms. Hence, this small group might represent a distinct, and probably unusual, subgroup of individuals with SAR. In the present study, patients suffering from any psychiatric or mood disorder were excluded. This might explain why no differences in verbal memory were found as depression has been shown to influence memory functions [29, 30]. Marshall & Colon [27] found an effect of AR on psychomotor speed. Again, a possible difference between patient groups could have caused this, as patients with mood disorders or depressive symptoms suffer from slowed motor and cognitive processing speed [30, 31]. Furthermore, Marshall et al. [12] found a subtle slowing of cognitive speed in patients with SAR. However, the evaluation tools used in these studies were short tests. Thus, the difference in findings could be explained by the fact that a different choice RT test was used, which might be more sensitive than the MCRT used in the present study.

Increasing the effort needed to complete a cognitive test by increasing the total testing time resulted in different performances among the groups in this study. After NP, the SAR group suffered from a decrement in sustained attention as shown by a performance decrement (increased RTs and errors) on the Mackworth Clock task. Wilken et al. [28] also found a decrease in sustained attention in untreated SAR. In this study, they enrolled a large number of subjects and measuring vigilance was designated as the primary end-point of their study using the Kay Continuous Performance Test, which is also a

reliable tool for measuring sustained attention. No effect on sustained attention was found by Marshall [27] because the test used for sustained attention is not a very demanding test, although an effect might have been expected because the individuals suffered from a depressive disorder and depressed individuals have repeatedly shown deficits in attentional processing [32].

In conclusion, no significant effects of SAR on the short cognitive performance tasks were found. More importantly, a significant effect of SAR, after NP, was found on sustained attention.

As stated before, SAR patients could compensate for diminished cognitive performance by increasing the amount of effort while performing a task. This would of course only be possible if task demands are low to moderate and some 'reserve' capacity would be available. This was the case for the short cognitive tests in this study that required significantly less effort to perform compared with the long sustained attention test. Patients reported a significant increase in effort during the short tests after the NP, while their performance remained constant. In contrast, effort invested in the sustained attention test does not increase, and performance deteriorates in the SAR group. Both groups rate effort during this test as extremely high and are most likely close to the maximum they can sustain for this long test. The SAR group could no longer compensate the reduced cognitive performance with increased effort, resulting in slower responses and more errors on the test.

The present study has some limitations. In this study, only patients underwent the allergy challenge. The procedure itself might have caused distress leading up to impaired performance. However, this decrement would have been expected in both short and long tests. Furthermore, the procedure allowed only to evaluate the effects of the early allergic phase and not the delayed phase. It has been shown that the late-phase reaction also affects mood and can cause depressive feelings and lethargy [26, 33]. These mood changes could mediate performance changes and may also have an effect on short cognitive tasks. This should be investigated with a methodology using prolonged provocation in the lab or during natural exposure to allergens. Therefore, it would be interesting to measure cognitive functions in patients with intermittent AR (seasonal) during the allergy season and/or patients with persistent AR (perennial). Our future research will focus on both aspects.

Practically, the results of the present study show that patients suffering from SAR may experience problems with sustained attention, which could cause serious problems in daily life. For example, driving a vehicle or operating dangerous machinery can become a hazardous situation when a person has problems concentrating. Furthermore, impaired vigilance can cause problems with productivity in school, especially considering that final

exams at schools are usually held in spring or summer and therefore exactly in the hayfever season [34]. Vuurman [5] already showed that children suffering from SAR showed decreased learning abilities during the allergy season. This could open a new discussion of whether school exams should be postponed. Not only could AR cause problems at school, it could also influence people's productivity in the working place. Burton *et al.* [10] found that when pollen levels increased, the productivity of AR patients significantly decreased compared with their healthy colleagues. This is of major clinical importance, as a relationship between decreased cognitive functioning and AR could open a new dimension of optimal treatment. Although SAR patients in our study had allergic symptoms only during a short period of time, they already showed impaired cognitive functioning. Hence, when AR symptoms are present for a longer time, like during the allergy season or like in persistent AR, the disturbance in cognitive functioning might be more severe.

To conclude, the results of the present study show that AR induces problems with tasks requiring sustained attention. These results are important as, together with several previous studies, it shows that AR can negatively influence everyday functioning at home, school or work. Therefore, it is important to find the right treatment to keep the cost of AR as low as possible, but most importantly, to improve people's well-being, their productivity and to prevent accidents from happening.

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