Allergy 2004: 59: 415–420
Printed in UK. All rights reserved

ALLERGY

Original article

Improvements in simulated real-world relevant performance for patients with seasonal allergic rhinitis: impact of desloratadine

Background: Seasonal allergic rhinitis (SAR) diminishes task performance and decreases quality of life. Antihistamines are frequently used to treat the symptoms of SAR. First generation antihistamines often have their own detrimental effects upon human functioning while second generation antihistamines appear to have fewer or no undesirable side-effects.
Objective: This study evaluated the impact of desloratadine on simulated real-world performance demands in individuals suffering from SAR.
Methods: This was a randomized, double-blind, cross-over study where asymptomatic participants were treated with placebo and symptomatic participants were treated with desloratadine or placebo. They then participated in a real-world equivalent task performance simulation that assessed information processing capacity at multiple levels of task difficulty ranging from easy to difficult decision-making tasks.
Results: Desloratadine either completely restored performance to the level of the asymptomatic placebo control or improved performance in six of the nine performance categories, where it had been diminished by the presence of SAR.
Conclusions: These findings suggest that treatment with desloratadine has considerable beneficial effects on work place performance when individuals suffer from SAR.

U. Satish, S. Streufert, M. Dewan, S. Vande Voort

Department of Psychiatry and Behavioral Science, SUNY Upstate Medical University, Syracuse, NY, USA

Key words: allergic rhinitis; decision making; desloratadine; performance; productivity; simulations.

Dr Usha Satish
Department of Psychiatry and Behavioral Science
SUNY Upstate Medical University
750 E Adams Street
Syracuse
NY 13210
USA

Accepted for publication 6 August 2003

Allergic rhinitis (AR), which can be seasonal (SAR) and/or perennial (PAR), is one of the most common chronic respiratory conditions. Generally, AR is an immunologic response to pollen, fungus spores, and other air-borne substances in the absence of viral infection (1) that generates symptoms including sneezing, rhinorrhea, nasal congestion, and nasal pruritus (2). Twenty to 40 million individuals in the United States are affected by AR (3–5), representing approximately 15% of the US population (4, 5) and 12–15 million workers (3, 4). The total direct cost of AR has been estimated to be at least between 1.15 billion and 3.4 billion dollars (5), including 37 million dollars in lost workdays (4). The associated indirect costs may also be quite large as many individuals continue to work with decreased work efficiency and performance (1, 3, 6) while affected by AR (7). In addition, the presence of AR may diminish quality of life (8).

Many patients with SAR have reported central nervous system (CNS) complaints such as slowed or diminished capacity to think, remember, or pay attention during the allergy season (7). These subjective reports have been objectively investigated by several studies, which have confirmed the impact of SAR on cognitive functioning. Marshall and Colon (9) reported a marked decline in verbal working memory, decision-making speed, psychomotor speed, and reaction time in participants experiencing SAR in contrast to asymptomatic individuals. Vuurman et al. (10) found that untreated SAR impaired learning in children and young adults. Several studies have begun to clarify the impact of SAR on cognition and learning (11, 12). Nonetheless, further work is necessary on SAR to understand how such deficits may impact work place performance and quality of life issues.

The recommended first-line treatment for SAR is antihistamines (2). However, first generation antihistamines like diphenhydramine are known to have CNS effects resulting in sedation (13) and in decrements of cognitive functioning (14), leading to impairment of driving performance (15), decreased learning ability (10), and increased risk of injury (16). In contrast, second generation antihistamines, like loratadine and cetirizine, are generally large lipophobic molecules that poorly cross the blood–brain barrier and thus have significantly fewer CNS effects (17, 18). As a consequence, these medications generate better performance and quality of life profiles than first generation antihistamines (17). Yet, even the newer generation drugs can differ in their adverse effect profiles. For example, cetirizine has been shown to cause sedation and psychomotor impairment, although to a lesser degree than first generation antihistamines (19, 20).

In contrast, loratadine has not been associated with impairment at clinically recommended doses in tests of somnolence, cognition, or psychomotor performance (17, 21). Thus, second generation antihistamines with no significant adverse side-effects may not only alleviate the symptoms of SAR but also improve work performance, learning capabilities, and overall quality of life issues.

A successor to loratadine is its biologically active primary metabolite desloratadine (22, 23). Desloratadine is taken at a single daily dose of 5 mg. It has a rapid onset of action and sustained efficacy to relieve both the nasal and non-nasal symptoms associated with SAR (23). Desloratadine has shown no clinically significant effects on wakefulness or psychomotor performance (23); however, data on the impact of desloratadine on human functioning are, as yet, limited.

In addition, prior studies do not address challenging task settings encountered in the work place, such as managerial and executive job, where the employee must deal with volatility, uncertainty, complexity, ambiguity and potential delayed feedback (24). The present study is designed to address these concerns by investigating the impact of desloratadine on simulated real-world performance demands in individuals suffering from SAR. The strategic management simulation (SMS) which is used in this research was specifically designed as a vehicle to assess information processing capacity at multiple levels of task difficulty, including complex decision-making tasks (25). The SMS has been widely validated (26, 27) as a predictor of effectiveness in complex task settings.

Methods

This investigation was designed as a randomized, double-blind, cross-over study of the effects of desloratadine *vs* placebo on real-world performance in individuals suffering from SAR. This study was commenced before the new classification system (WHO) of allergic rhinitis was published (28) and the patients were not classified as having 'intermittent' and 'persistent' rhinitis.

Participants

Forty-eight adults (25 males and 23 females) aged 18–48, who had suffered from SAR for at least two consecutive years, were recruited with the assistance of physicians specializing in allergy and immunology. Forty-four subjects (91.7%) completed the study. Overall, 52% of the subjects were male; 96% were Caucasian. The median age at entry was 37 years. To qualify for research participation, individuals had to be between 18 and 60 years of age, were skin test positive (prick or intradermal) to a seasonal allergen, which included seasonal molds, prevalent during the study period, have a negative urine screen test for drugs with abuse potential, be free of clinically significant disease (other than SAR) and free of drug treatment that could impact performance. The Michigan alcohol screening test (MAST) was administered. None of the participants abused alcohol or consumed alcohol in more than minimal amounts. All patients either tested negative for asthma or had symptoms under control by use of a B agonist. Pregnant and nursing women were excluded from the sample. Approval by the Institutional Review Board of SUNY Upstate Medical University was obtained. Informed consent, including the agreement to forego treatment of SAR with antihistamines or other drugs for several days during the allergy season, was obtained. Four individuals were excluded from the sample. Two participants relocated, one used drugs that were not allowed, and one was excused because of child-care problems. Forty-four participants completed the study.

Absence/presence of SAR

Participants took part in the research on the following occasions: once outside of the allergy season while asymptomatic (late fall and winter) and twice during the allergy season while symptomatic. On each occasion, participants responded to a symptom checklist to determine the degree to which SAR was present. Eight symptoms were evaluated: 1) rhinorrhea, characterized by nasal discharge, runny nose or postnasal drip, 2) nasal stuffiness/congestion, 3) nasal itching, 4) sneezing, 5) itching/burning eyes, 6) tearing/watering eyes, 7) redness of eyes, and 8) itching of ears or palate. The following four-point scale was used to score each of the eight symptoms listed above: 0 = no evident symptoms, 1 = mild (symptoms clearly present but minimal awareness, easily tolerated), 2 = moderate (definite awareness of signs and symptoms that are bothersome but tolerable) and 3 = severe (signs or symptoms hard to tolerate). A total score ranging from 0 to 24 was generated to determine the degree to which participants experienced the symptoms of SAR. Inclusion in the study outside of the allergy season required that a participant's total score did not to exceed a value of 4; during the allergy season (in the absence of antihistamine treatment) the obtained score had to be at least 8. All participants matched the stated requirements.

Participants rated symptom severity (both nasal and non-nasal) both prior to as well as during simulation participation.

Treatment

Research participants took two doses (morning and evening) of medication on the day prior to their research participation and another dose on the following morning prior to participation in the SMS simulation. Outside of the allergy season (baseline condition), all three doses were placebo. During allergy season, participants were randomized in a double-blind fashion to be either treated with placebo first or with desloratadine first. Those who received desloratadine (5 mg) on their first allergy season participation were crossed over to placebo for their second participation, and vice versa. For the desloratadine treatment condition, both morning doses (day prior to, and day of simulation participation) were 5 mg desloratadine. The evening dose was placebo. When assigned to placebo treatment, all three doses were matching placebo. All study medications were provided in identical unbranded tablets packaged in blister packs. Participants recorded the time when each medication was taken. After the first SMS simulation participation during the allergy season, a wash-out period of at least 1-week was instituted to prevent any carryover effects of the study medication from the previous treatment period.

Strategic management simulations

Strategic management simulations are used to assess and train decision makers world-wide. Based on complexity theory, this methodology permits the measurement of complex human behavior (required for effectiveness in many work place settings). Participants

are exposed to real-world equivalent simulation scenarios that are designed and proven to match real-world day-to-day challenges (26, 29, 30). Based on the decisions made by participants, measurement profiles are generated which reflect the underlying decision-making capacities of the individual. The profile provides feedback on simple (e.g. activity levels), intermediate (e.g. initiative) and complex (e.g. strategy) functional requirements of everyday life. Several parallel scenarios are available which allow retesting individuals without potential bias due to experience and learning effects.

Procedure

Upon arrival at the laboratory in the morning, participants took the third dose of medication, read a manual and viewed a videotape with additional verbal and pictorial information. This introductory time period lasted 90 min. Each participant was then placed in a room with maps and other relevant props. The room contained a video screen and a computer printer that would provide information throughout the 4 h of simulation. An experimenter who functioned as the participant's 'assistant' operated the computer. Decisions were communicated orally to the participant's 'assistant' who coded and entered the participant's future plans, past relevant decisions, and decision responsiveness to previously received information. Computer generated information (120 items during the simulation) was presented to the participant on video and in printed hard-copy format. After completing the simulations, participants were debriefed and paid $127 per simulation participation.

Assessment of functioning

Computer generated measures focus on 'how' the participant processes information. Measures vary from simple counts (e.g. number of decisions made) via formula-based calculations of intermediate performance characteristics (e.g. use and application of initiative) to calculations of highly complex competencies (e.g. strategic sequencing of multiple broad approaches that focus on interrelated problem areas). The primary measurement categories are briefly described in Table 1.

Table 1. Strategic management simulation performance measures of decision making

1. Activity: *Basic Activity Level* reflects the number of actions taken during simulation participation. Moderately high to high scores reflect an adequate amount of decisions and actions
2. Speed: *Speed of Response* measures the elapsed time between receipt of information and action taken in response to that information. High scores indicate that the participant took enough time to consider important aspects of the situation at hand, but did not take excessive amounts of time
3. Responsiveness: *Task Orientation* measures the participant's focus on actions that are relevant to current situation demands. A high score shows the participant handled issues of current concern and those relevant to incoming information
4. Initiative: *Applied Initiative* reflects 'opportunistic creativity'; i.e. actions that were not suggested by events, yet set the stage for potential subsequent actions. High scores indicate that more initiative was taken
5. Information: *Information Orientation* measures activity to obtain task-relevant information. High scores indicate that more information was sought
6. Emergency: *Emergency Responsiveness* counts the number of actions that respond to the emergency event. A high score indicates that the emergency was handled
7. Breadth: *Breadth of Approach* measures the degree to which multiple approaches are used in solving problems. A high score suggests more effective use of alternate (multiple) options
8. Planning: *Planning Distance* measures whether plans are made with the intent to generate future actions. The time between planning and implementation is measured. High scores were given for plans which can be translated into outcomes in a realistic time scale
9. Strategy: *Strategic Complexity* reflects the application of multiple interactive strategic activities across time toward multiple interrelated goals. High scores indicate excellent strategic competence

Statistics

The research effort used a within subjects design (three points of data collection for each individual) and multiple measures of performance. While the measures were based on orthogonal factors generated by multiple prior factor analyses, the possibility of limited intercorrelations among measures cannot be excluded. To assure legitimacy of data interpretation, an overall multivariate analysis of variance (MANOVA) is required. Only where MANOVA results for a factor are significant, will subsequent measure by measure comparisons across treatment conditions generate legitimate significance for purposes of data interpretation. Based on MANOVA results, ANOVA comparisons employed significance level calculations employing two-tailed tests.

Results

An overall MANOVA across all dependent variables was employed. The MANOVA comparing the three treatment conditions across all dependent variables generated a value of 45.21 (1/26 d.f.) with a significance level of $P < 0.001$, legitimizing subsequent ANOVA comparison. ANOVA comparisons focused on differences between desloratadine treatment and placebo treatment when SAR was present. In addition, comparisons between symptomatic desloratadine treatment and baseline functioning (asymptomatic placebo treatment) were made. Obtained means and standard deviations (Table 2) as well as ANOVA-based F values (at 1 and 42 d.f.) and significance levels (Table 3) for each of the dependent (within) variables are reported.

A comparison of placebo performance outside of the allergy season *vs* during the allergy season (while symptomatic) indicated that performance on six measures (Task Orientation, Applied Initiative, Information Orientation, Basic Activity Level, Breadth of Approach, and Strategic Complexity) decreased significantly when research participants suffered from allergic rhinitis. Comparison of the data with prior SMS simulation research on treatment with alcohol (ethanol) generated an average decrement similar to the effect of alcohol treatment which attained a blood alcohol level (BAL) of 0.05 (31, 32).

During the allergy season, the same performance categories showed lower (impaired) performance levels during placebo treatment than during desloratadine treatment. Furthermore, in the categories of Task Orientation, Applied Initiative, and Information Orientation, desloratadine treatment of previously symptomatic individuals was not significantly different from performance levels that were measured at baseline (when participants

Table 2. Performance comparison of participants treated with desloratadine (symptomatic for SAR) and placebo (symptomatic for SAR) and under asymptomatic (baseline) conditions

	Symptomatic for SAR		Asymptomatic for SAR
Simulation category	Desloratadine	Placebo	Placebo (baseline)
Basic Activity	48.41 (15.56)	41.60 (16.46)	60.48 (12.66)
Speed of Response	6.41 (2.47)	5.86 (2.67)	6.56 (2.82)
Task Orientation	60.91 (28.9)	54.53 (29.1)	67.00 (27.4)
Applied Initiative	4.23 (3.56)	2.13 (1.10)	4.19 (2.00)
Information Orientation	8.66 (1.19)	7.19 (1.36)	8.56 (1.18)
Emergency Responsiveness	7.50 (2.31)	3.05 (2.27)	7.93 (2.13)
Breadth of Approach	7.89 (1.68)	7.16 (1.49)	8.45 (1.56)
Planning Distance	6.45 (2.86)	6.16 (3.41)	5.61 (3.40)
Strategic Complexity	8.05 (2.20)	5.93 (2.64)	8.89 (3.12)

Values are given as mean (SD).

Table 3. Comparison of participants treated with desloratadine (symptomatic for SAR) with symptomatic and asymptomatic (baseline) conditions*

Simulation category	Overall	Desloratadine *vs* placebo	Desloratadine *vs* baseline†
Basic Activity	32.40 (0.001)	14.57 (0.001)	32.40 (0.001)
Speed of Response	0.80 (NS)	1.07 (NS)	0.10 (NS)
Task Orientation	7.56 (0.002)	4.27 (.045)	3.02 (NS)
Applied Initiative	20.17 (0.001)	14.05 (0.001)	0.01 (NS)
Information Orientation	3.99 (0.026)	6.98 (0.012)	0.07 (NS)
Emergency Responsiveness	1.79 (NS)	1.25 (NS)	0.85 (NS)
Breadth of Approach	13.46 (0.001)	10.54 (0.002)	4.87 (0.033)
Planning Distance	0.77 (NS)	0.155 (NS)	1.66 (NS)
Strategic Complexity	13.93 (0.001)	19.40 (0.001)	4.55 (0.039)

* Significance levels (*F*-ratios at 1/41 d.f.).
† NS indicates that no significant difference was obtained for a particular variable comparison.

were asymptomatic for SAR outside of the allergy season). Other performance categories (Basic Activity Level, Breadth of Approach, and Strategic Complexity) did show improvement when symptomatic participants were treated with desloratadine, but the improvement did not extend to the level of functioning exhibited by the baseline asymptomatic participants (a decrement similar to alcohol treatment at a BAL of 0.03).

The remaining three measurement categories (Speed of Response, Emergency Responsiveness, and Planning Distance) showed no overall significant differences, indicating that the presence of SAR had no impact upon these performance measures.

Participants ratings of rhinitis symptoms indicated greater symptomatology during the allergy season compared with baseline ratings obtained outside of the allergy season ($P < 0.001$). In addition, the rated symptom severity, both for nasal and non-nasal symptoms of rhinitis, was significantly greater when participants were treated with placebo than when they were treated with desloratadine.

Discussion

This study was commenced before the new classification system (WHO) of allergic rhinitis was published (28) and the patients were not classified as having 'intermittent' and 'persistent' rhinitis (33). SAR is one of the most common chronic respiratory conditions and contributes to decrements in both quality of life (33) and workplace performance (1, 3, 6). SAR has been shown to effect an individual's cognitive function ranging from slowed speed of cognitive processing to difficulty with working memory and learning (9–11). However, many of the previous cognitive and performance studies on antihistamines measured the performance of asymptomatic individuals and, in addition, did not address the challenging task settings encountered in the work place. This research was designed to incorporate these variables by investigating the effect of desloratadine treatment on symptomatic participants in a simulation of real-world workplace performance demands.

The data obtained in this research showed that desloratadine treatment of participants symptomatic for SAR generated enhanced performance (compared with absence, i.e. placebo treatment) in six of the nine performance categories tested by the SMS simulation. The performance level in three of these categories (Task Orientation, Applied Initiative, and Information Orientation) was no different from performance levels measured with placebo treatment of asymptomatic individuals. Interestingly, these three performance indicators reflect intermediate levels of task difficulty. 'Task Orientation' performance can be 'cued' by external information, but involves a general focus on multiple currently relevant aspects of the task at hand, while 'Applied Initiative' indicates opportunistic creativity, and 'Information Orientation' measures activity designed to obtain task-relevant information. Thus, for tasks of moderate difficulty desloratadine treatment of SAR-affected individuals are able to return their performance in a simulated work environment to normal baseline levels.

In contrast, three other simulation categories (Basic Activity Level, Breadth of Approach, and Strategic Complexity) reflect performance categories where it is more difficult to excel. For these performance categories, desloratadine treatment improved effectiveness compared with placebo treatment in *symptomatic* individuals, but it was unable to eliminate all of the decrements imposed by SAR when compared with the *asymptomatic* placebo-treated participants. Among this group of measures, 'Strategic Complexity' presents the most difficult challenge: to score well, participants had to use multiple interrelated strategic action sequences toward multiple interrelated goals. In other words, it appears that highly difficult challenges were most likely to be negatively impacted by SAR. Nonetheless, it is encouraging that performance on all three of these most difficult performance challenges were improved by desloratadine treatment,

although treatment did not attain the level reached by asymptomatic individuals.

The remaining three measurement categories (Speed of Response, Emergency Responsiveness, and Planning Distance) showed no differences among the treatment conditions. All of these three measurement categories are, in comparison with the other measures, simpler to perform. Speed of Response and Emergency Responsiveness measure responses to external cues while Planning Distance does not necessarily require that the decisions lead to outcomes that are meaningful. For measures which assess simpler attributes of functioning, in other words, performance levels remain intact even while people are suffering from SAR. Under such conditions, desloratadine treatment had no impact on people whose functioning was not diminished by the presence of their disease.

As suggested above, the research reported in this paper employed a measurement technique that differs uniquely from other technologies that have evaluated the effect of drug treatments upon SAR. It focuses on the measurement of simple, intermediate *and* complex performance attributes that are encountered, for example, in white collar and executive settings where volatility, uncertainty, complexity, ambiguity and delayed feedback are common task demand characteristics. The data obtained in this effort show that desloratadine can improve or restore performance *and* that different levels of task demand challenges are differentially affected by both SAR morbidity and by drug treatment.

In sum, treatment with desloratadine either completely restored or improved performance in six of the nine performance categories where it had been diminished by the presence of SAR. As desloratadine both relieves symptoms and generates improved functioning in a real-world equivalent task environment, its use to treat SAR appears to be of considerable value not only to an affected individual's quality of life, but his or her ability to generate production and efficiency benefits in the work place.

Acknowledgments

Research support from Integrated Therapeutics Group, Inc. is gratefully acknowledged.

References

1. Kaliner M, Eggleston PA, Mathews KP. Rhinitis and asthma. JAMA 1987;**258**:2851–2873.
2. Dykewicz MS, Fineman S, Skoner DP. Diagnosis and management of rhinitis complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. American Academy of Allergy, Asthma, and Immunology. Ann Allergy Asthma Immunol 1998;**81**:478–518.
3. Crystal-Peters J, Crown WH, Goetzel RZ, Schutt DC. The cost of productivity losses associated with allergic rhinitis. Am J Manag Care 2000;**6**:373–378.
4. Malone DC, Lawson KA, Smith DH, Arrighi HM, Battista C. A cost of illness study of allergic rhinitis in the United States. J Allergy Clin Immunol 1997;**99**:22–27.
5. Storms W, Meltzer EO, Nathan RA, Selner JC. The economic impact of allergic rhinitis. J Allergy Clin Immunol 1997;**99**:S820–824.
6. Kessler RC, Almeida DM, Berglund P, Stang P. Pollen and mold exposure impairs the work performance of employees with allergic rhinitis. Ann Allergy Asthma Immunol 2001;**87**: 289–295.
7. Reilly MC, Tanner A, Metzer EO. Work, classroom and activity impairment instruments: Validation studies in allergic rhinitis. Clin Drug Invest 1996;**7**:278–288.
8. Fell WR, Mabry RL, Mabry CS. Quality of life analysis of patients undergoing immunotherapy for allergic rhinitis. Ear Nose Throat J 1997;**76**:528–536.
9. Marshall PS, Colon EA. Effects of allergy season on mood and cognitive function. Ann Allergy 1993;**71**:251–258.
10. Vuurman EF, van Veggel LM, Sanders RL, Muntjewerff ND, Hanlon JF. Effects of semprex-D and diphenhydramine on learning in young adults with seasonal allergic rhinitis. Ann Allergy Asthma Immunol 1996;**76**:247–252.
11. Marshall PS, O'Hara C, Steinberg P. Effects of seasonal allergic rhinitis on selected cognitive abilities. Ann Allergy Asthma Immunol 2000;**84**:403–410.
12. Engle R. Individual difference in memory and their implications for learning. In: Sternberg R, editor. Encyclopedia of intelligence. New York: Macmillan Publishing, 1994:700–703.
13. Goetz DW, Jacobson JM, Apaliski SJ, Repperger DW, Martin ME. Objective antihistamine side effects are mitigated by evening dosing of hydroxyzine. Ann Allergy 1991;**67**:448–454.
14. Wilken JA, Kane RL. Vigilance and cognitive functioning during treatment of seasonal allergic rhinitis (SAR): a comparison of diphenhydramine (DPH) and desloratadine (DL). J Allergy Clin Immunol 2002;**109**:S101.
15. Meltzer EO. Performance effects of antihistamines. J Allergy Clin Immunol 1990;**86**:613–619.
16. Gilmore TM, Alexander BH, Mueller BA, Rivara FP. Occupational injuries and medication use. Am J Int Med 1996;**30**:234–239.
17. Kay GG. The effects of antihistamines on cognition and performance. J Allergy Clin Immunol 2000;**105**:S622–627.
18. Simons FE, Simons KJ. The pharmacology and use of H1-receptor-antagonist drugs. N Engl J Med 1994;**330**: 1663–1670.
19. Gonzalez MA, Estes KS. Pharmacokinetic overview of oral second-generation H1 antihistamines. Int J Clin Pharmacol Ther 1998;**36**:292–300.
20. Philpot EE. Safety of second generation antihistamines. Allergy Asthma Proc 2000;**21**:15–20.
21. Kay GG, Harris AG. Loratadine: a non-sedating antihistamine. Review of its effects on cognition, psychomotor performance, mood and sedation. Clin Exp Allergy 1999;**29**(Suppl. 3): 147–150.

22. Agrawal DK. Pharmacology and clinical efficacy of desloratadine as an anti-allergic and anti-inflammatory drug. Expert Opin Investig Drugs 2001;**10**:547–560.
23. Geha RS, Meltzer EO. Desloratadine: a new, nonsedating, oral antihistamine. J Allergy Clin Immunol 2001;**107**: 751–762.
24. Streufert S. Complexity: an integration of theories. J Appl Soc Psychol 1997;**27**:2068–2095.
25. Satish U, Streufert S, Barach P. Assessing and improving medical competency: using strategic management simulations. Simul Gaming 2001;**32**: 156–163.
26. Streufert S, Pogash R, Piasecki M. Simulation-based assessment of managerial competence: reliability and validity. Personnel Psychology 1988;**41**: 537–557.
27. Satish U, Streufert S, Marshall R, Smith JS, Powers S, Gorman P et al. Strategic management simulations is a novel way to measure resident competencies. Am J Surg 2001;**181**:557–561.
28. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on Asthma. ARIA workshop report. J Allergy Clin Immunol 2001;**108**(Suppl. 5):S147–S334.
29. Breuer K. Lernen mit computersimulierten komplexen dynamischen Systemen. In: Lechner E, Zielinski J, editors. Wirkunssysteme und Reformansaetze in der Paedagogik. Frankfurt: Lang Verlag, 1988:341–351.
30. Streufert S, Swezey R. (1985) Simulation and related research methods in environmental psychology. In: Singer J, Baum A, eds. Advances in environmental psychology, **Vol. 5**. Hillsdale, NJ: Erlbaum, 99–117.
31. Streufert S, Pogash R, Roache J, Severs W, Gingrich D, Landis R. Alcohol and managerial performance. J Stud Alcohol 1994;**55**:230–238.
32. Streufert S. Alkohol und Entscheidingsfaehigkeit be komplexen Fuehrungsproblemen. In: Fisch, Boos, Beck, Scharpf, Winkler, editors. Fuehrung und Zusammenarbeit bei komplexen Verwaltungsaufgaben. Konstanz, Germany: Universitaetsverlag Konstanz, 1995.
33. Meltzer EO. Quality of life in adults and children with allergic rhinitis. J Allergy Clin Immunol 2001; **108**(Suppl. 1):S45–S53.