WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 9, 87-98. Research Article ISSN 2277–7105

# EFFECTS OF MILD UPPER RESPIRATORY TRACT ILLNESSES AND INCREASED NORADRENALINE ON THE COVERT ORIENTATION OF ATTENTION

**Andrew P. Smith***

Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, 70 Park Place, Cardiff CF10 3AT, UK.

Article Received on
14 March 2025,

Revised on 03 April 2025,
Accepted on 23 April 2025

DOI: 10.20959/wjpr20259-36498

***Corresponding Author**
**Andrew P. Smith**
Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, 70 Park Place, Cardiff CF10 3AT, UK.

## ABSTRACT

**Background:** The aetiology and pathogenesis of mild upper respiratory tract illnesses (MURTIS) have been frequently described. These illnesses lead to malaise, manifesting as fatigue, impaired performance, and reduced well-being. A specific aspect of this, the covert orientation of attention, was examined in the present study. **Methods:** Eighty-one participants completed the study (duration 10 weeks), 17 developed MURTIS, and the others were re-tested as healthy controls. Of the I7 volunteers with MURTIS, eight were given Idazoxan, nine were given a placebo, and of the 64 control participants without a MURTI, 26 were given Idazoxan, and 38 were given a placebo. **Results**: The results confirmed that having a MURTI was associated with slower reaction times, but neither having a MURTI nor drug conditions interacted with task conditions. **Conclusion:** Individuals with a MURTI responded more slowly in the Posner cueing task. However, there were no interactions with cueing conditions. Similarly, the noradrenergic drug Idazoxan did not have selective effects in the covert orientation task.

**KEYWORDS:** Mild upper respiratory tract illnesses (MURTIS); Reaction time; Posner cueing task; Covert orientation of attention.

## INTRODUCTION

The aetiology and pathogenesis of mild upper respiratory tract illnesses (MURTIS) are well documented.[1-3] MURTIS are frequent, widespread, and a significant cause of absence from education and work. In addition, epidemiological studies have shown that MURTIS may reduce work efficiency, productivity and academic attainment.[4-7] MURTIS are caused by viruses such as rhinoviruses and coronaviruses. These viral infections of the nasal cells lead to various symptoms, such as a runny nose, nasal congestion, and a sore throat. Other symptoms, such as fever and myalgia, may occur, but these are more common in influenza than the common cold. Another general symptom, malaise, reflects the increased fatigue and reduced well-being caused by MURTIS.

Research has demonstrated that MURTIS reduce well-being and can impair mental functioning. Initial evidence for such effects came from case histories and anecdotal reports.[8,9] Studies of experimentally induced infections and illnesses have confirmed that these produce behavioural changes. Several reviews discuss research on both effects of experimentally induced MURTIS and naturally occurring illnesses.[10-15] The research on experimentally induced MURTIS showed that MURTIS have selective effects on mental functioning, with only some aspects of performance being impaired.[16-27] MURTIS impaired psychomotor function (e.g., hand-eye coordination; speed of psychomotor response) but had little effect on either detection tasks or those involving higher functions.

Studies of naturally occurring MURTIS have confirmed that such illnesses reduce alertness and lead to psychomotor slowing.[28-39] Studies using simulations of real-life activities such as driving.[40, 41] have also demonstrated MURTI-induced impairments, confirming results from earlier research. Factors such as stress, fatigue and alcohol had a larger effect on those with a MURTI, and stimulants, such as caffeine, removed many of the impairments induced by the MURTI.[42-47] These results suggested that changes in central noradrenaline may underlie the effects of MURTIS on the brain and behaviour, and this was confirmed in a study using Idazoxan.[48] This drug increases the turnover of central noradrenaline. Other possible mechanisms include sensory afferent stimulation, which can be increased by sucking peppermint.

Evidence from animal studies and human clinical studies suggests that brain catecholamines are involved in attention. Clark et al.[49] demonstrated the role of noradrenaline in regulating the brain capacity available for processing information. Furthermore, this research has also

shown the role of noradrenaline in the orientation and the switching of attention.[50] The suggestion that central noradrenaline may be involved in covert orientation was tested in healthy participants by Clark et al.[50] who used a cued reaction time paradigm originally devised by Posner et al.[51] This task measured the directional engagement, disengagement and movement of attention (independent of eye movements). Participants had to press a single key as quickly as possible whenever a target stimulus was presented. A visual arrow (cue) was presented before the onset of the target stimulus. The arrow could be either valid (pointing in the right direction of the target), invalid (pointing in the wrong direction of the target) or neutral (pointing in both directions, indicating that the target would appear either on the left or right of the screen).

The task was susceptible to the benefit obtained in simple response time to a visual target when valid pre-cueing resulted in the covert orientation of attention to the location where the target was to occur. It also reliably measured the cost in response time when invalid pre-cueing resulted in covert orientation to the wrong location and necessitated covert switching to the correct location. Both cost and benefit were measured by response time obtained when cueing gave no information about the impending location of the target (neutral cueing).

The Clark et al.[49] study administered Droperidol and Clonidine intravenously to suppress central dopamine and noradrenaline transmission. Both drugs produced reductions in the cost of invalid cueing without a change in the benefit of valid cueing, which suggested that both noradrenaline and dopamine were involved in facilitating the disengagement of attention. This finding indicated that central catecholamine activity plays a role in determining the ease with which attention can be disengaged or shifted. Specifically, clonidine (an alpha agonist known to suppress central noradrenergic activity) had no effect on the speed of response in general or the benefit of valid cueing. However, clonidine did significantly diminish the cost of invalid cueing. This effect indicated that the reduction of central noradrenaline activity affected either the disengagement or switching of attention but did not affect the engagement of directed attention itself.

The present study investigated whether having a cold impaired the covert orientation of attention in humans. Previous results from studies by Smith.[52] showed that those with a cold were slower at performing reaction time and serial choice psychomotor tasks. This effect may reflect impaired covert orientation. Furthermore, if colds impair covert attentional capacity, it is essential to assess the role of Idazoxan (an alpha 2-adrenoceptor antagonist) in possibly

reversing this effect. This is plausible as evidence suggests that Idazoxan improves performance on attention as measured by the place repetition effect.[53] The effect of sensory afferent stimulation was also examined by having participants suck a peppermint.

## METHOD

### *Ethical approval and informed consent*

The study was carried out with the approval of the South-Western Local Ethics Committee. All included participants were required to sign a consent form outlining the experiment, explaining that they were free to withdraw at any time and confirming the confidentiality of all information.

### *Participants*

Ninety-six male students were recruited from the volunteers of the Health Psychology Research Unit, University of Bristol. Only male volunteers were recruited because of the drug used in this study. Eighty-one participants completed the study (duration 10 weeks), 17 developed MURTIS, and the others were re-tested as healthy controls. Of the I7 volunteers with MURTIS, eight were given Idazoxan, nine were given a placebo, and of the 64 control participants without a MURTI, 26 were given Idazoxan, and 38 were given a placebo.

### *Schedule of testing*

All volunteers were familiarised with the testing procedure and practised the tasks. Baseline sessions were conducted in the morning between 9 am and 12.00. During the evenings before test sessions, volunteers were required to limit their alcohol consumption to a maximum of four units. Before baseline testing, participants had to have been healthy for at least a week. Volunteers were instructed to return to ·the laboratory as soon as they began to have increased upper respiratory tract symptoms. All volunteers were tested when their illness had been present for at least 24 hours and no longer than 96 hours. They were asked not to take medication, including over-the-counter cold remedies, for 12 hours before testing. Those who remained free from illness were recalled as healthy controls at the end of the 10-week testing period.

When the volunteers returned for their second visit, they carried out a pre-drug session. One hour after the start of the session, volunteers were given a capsule containing either 40 mg of idazoxan or a lactose placebo. This was administered double-blind. Further post-drug testing

was subsequently carried out with sessions starting 30, 145 and 240 minutes after administration of the capsule.

***Objective signs and symptoms of MURTIS***

The weight of nasal secretion over an hour and sublingual temperature were recorded. Volunteers also completed a symptom checklist, which assessed the presence and severity of common upper respiratory symptoms (e.g. sneezing, runny nose, blocked nose, sore throat, cough, etc.). These were rated on a 5-point scale from 0 = not present to 4 = very severe. Volunteers were instructed to return to the laboratory as soon as they began to have increased nasal symptoms. All the volunteers with MURTIS were tested when their illness had lasted for at least 24 hours but less than 96 hours.

***The Posner Task***

This task was given as part of a more extended battery of tasks.[48] This study's cueing task required participants to press a single key with the right index finger as quickly as possible whenever a target stimulus was presented. Target stimuli were presented at eye level and 9.9 cm laterally to the left or right of a central fixation point on a computer screen. A visual cue was presented on top of the fixation point for one second before the onset of a target stimulus. There were I00 trials in each session. On 34% of target trials in any test session, this cue consisted of an arrow pointing in both directions to indicate that the target was equally likely to occur on the left or right. This was the neutral cue. On the other 66% of target trials, the cue consisted of an arrow pointing to the left or right, indicating with an 80% probability the side on which the target would occur. An arrow cue which wrongly predicts the target side is an invalid one. The cue remained present during the target presentation, and the participant's response terminated both stimuli. Reactions must occur within 100 and 500 msec following target onset to be accepted. Immediately following the response, the participant was given performance feedback for 500 milliseconds below the stimulus display. In order to minimise anticipatory responding, I0 % of all trials completed in any test session were catch trials in which no target was presented following the cue. To prevent overt orientation following the presentation of cues, participants were required to fixate on the central cue until the completion of the response.

**RESULTS**

Separate analyses were conducted for speed and accuracy scores. Initial analyses included trial type (correct, incorrect, and neutral cues). If this factor interacted with the MURTI or

drug condition, separate analyses were carried out on the individual cue types. Baseline measures were used as covariates in the analyses of the effects of having a MURTI.

***Effects of having a MURTI***

As this was a choice reaction time task, it was predicted that having a MURTI would be associated with slower performance.

a) Speed

Response times were slower when the participants had a MURTI, and ·this effect was significant ($p<0.05$, 1-tail). There was no evidence of a significant MURTI x trial-type interaction. The effect of having a MURTI is shown in Figure 1.

b) Accuracy

There was no main effect of having a MURTI on accuracy.

***Idazoxan analyses***

In the present analysis, the pre-drug scores were used as covariates to control for the unwanted differences between drug conditions at this time. Analyses examining the three post-drug measures showed no effects of the drug, no drug x MURTI interactions, nor interactions between these factors and the cue type. This was found for both speed and accuracy.

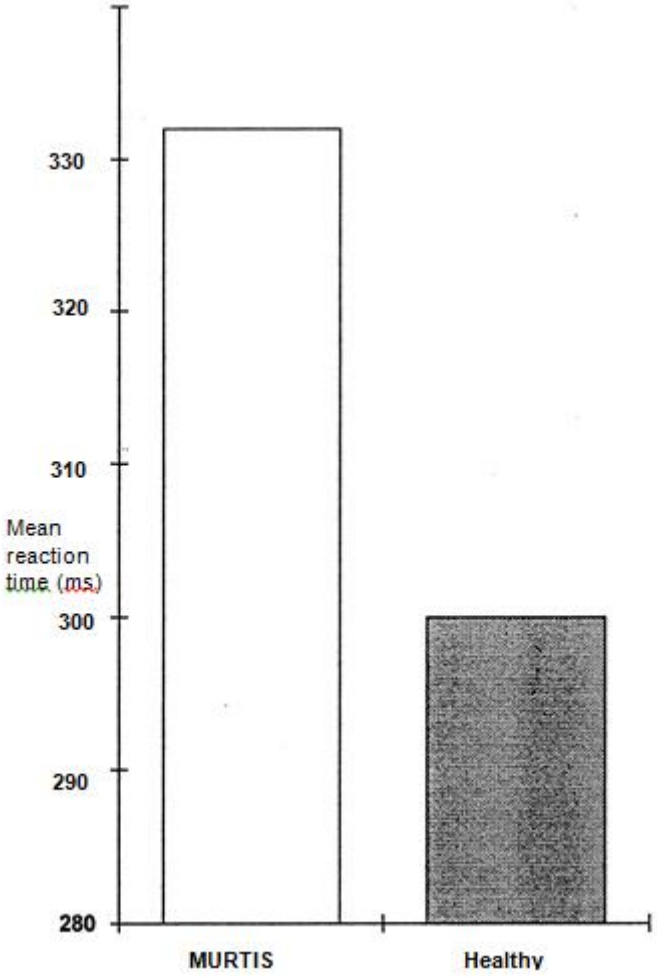


**Figure 1: Overall mean reaction time in the Posner cueing task.**

## DISCUSSION

The results of the present study confirm that having a MURTI is associated with slower reaction times in a choice reaction time task. However, this effect was apparent in all trial types, suggesting that it was either at the input or response stage of the reaction time process. Similarly, the noradrenergic drug Idazoxan did not modify the covert orientation of attention. Other tasks impaired by MURTIS showed improvements when the person was given Idazoxan, suggesting that changes in the turnover of central noradrenaline underlie some of the behavioural effects of MURTIS but not others. Other possible mechanisms, such as sensory afferent stimulation changes, must be investigated.

## CONCLUSION

The aetiology and pathogenesis of MURTIS are well-established. These illnesses lead to impaired performance and reduced well-being. A specific aspect of performance, the covert orientation of attention, was examined in the present study. Eighty-one male participants

completed the study (duration 10 weeks), 17 developed MURTIS, and the others were re-tested as healthy controls. Of the I7 volunteers with MURTIS, eight were given Idazoxan, nine were given a placebo, and of the 64 control participants without a MURTI, 26 were given Idazoxan, and 38 were given a placebo. The results confirmed that having a MURTI was associated with slower reaction times, but neither having a MURTI nor drug conditions interacted with task conditions. In summary, individuals with a MURTI responded more slowly in the Posner cueing task. However, there were no interactions with cueing conditions. Similarly, the noradrenergic drug Idazoxan did not have selective effects in the covert orientation task. MURTIS would appear, therefore, to induce psychomotor slowing rather than changing specific aspects of attention.

## REFERENCES


1. Tyrrell DAJ, Fielder M. Cold Wars. Oxford University Press, (2002). ISBN 019263285x
2. Smith, A.P., Matthews, O. 2022. Aromatic ointments for the common cold: What does the science say? *Drugs in Context*, 2022; 11: 2022-5-6. https://doi.org/10.7573/dic.2022-5-6 pp 1-9. ISSN: 1740-4398.
3. Smith A, Kardos P, Pfaar O, Randerath W, Estrada Riolobos G, Braido F, Sadofsky L. The treatment of mild upper respiratory tract infections – a position paper with recommendations for best practice. Drugs Context, 2023; 12: 2023-4-2. https://doiorg/107573/dic2023-4-2
4. Bramley TJ, Lerner D, Sarnes M. Productivity losses related to the common cold. J Occup Environ Med., 2002; 44: 822-829. doi: 101097/00043764-200209000-00004
5. Nichol KL, D'Heilly S, Ehlinger E. Colds and influenza-like illnesses in university students: impact on health, academic and work performance, and health care use. Clin Infect Dis., 2005; 40: 1263-1270. doi: 101086/429237
6. Nichol KL, D'Heilly S, Ehlinger E. Burden of upper respiratory illnesses among college and university students, 2002-2003 and 2003-2004 cohorts. Vaccine, 2006; 24: 6724-6725. doi: 101016/jvaccine201005011
7. Palmer LA, Rousculp MD, Johnston SS, Mahadevia PJ, Nichol KL. Effect of influenza-like illness and other wintertime respiratory illnesses on worker productivity: The child and household influenza-illness and employee function (CHIEF) study. Vaccine, 2010; 28: 5049-5056.
8. Tye J. The Invisible Factor: An Inquiry into the Relationship between Influenza and Accidents London: British Safety Council, 1960.

9. Grant J. Post-influenzal judgement deflection among scientific personnel. Asian Journal of Medicine, 1972; 8: 535-539.
10. Smith AP. Respiratory virus infections and performance. Phil Trans R Soc. London B., 1990; 327: 519 – 528. doi: 101098/rstb1990009
11. Smith AP. Twenty-five years of research on the behavioural malaise associated with influenza and the common cold. Psychoneuroendocrinology, 2013; 38: 744-751. http://dxdoiorg/101016/jpsyneuen201209002
12. Smith AP. Colds, influenza and performance. In: Smith, AP, Jones, DM (Eds), Handbook of human performance, Vol2: Health and performance London: Academic Press, 1992; 197-218.
13. Mahoney T, Ball P. Common respiratory tract infections as psychological entities: A review of the mood and performance effects of being ill. Australian Psychologist, 2002; 37: 86-94. doi: 101080/00050060210001706726.
14. Smith AP. Sleep, colds, and performance. In: Broughton, R, Ogilvie, R (Eds) Sleep, Arousal and Performance: A tribute to Bob Wilkinson Boston: Birkhauser, 1991 233-242.
15. Smith AP. The Psychology of the Common Cold and Influenza: Implications for COVID-19. International Journal of Clinical Virology, 2020; 4: 27-31. DOI: 1029328/journalijcv1001011.
16. Smith AP. Effects of influenza and the common cold on the Stroop color-word test. Percept Mot Skills, 1992; 74: 668-670. doi: 102466/pms1992742668.
17. Smith AP, Tyrrell DAJ, Coyle K, Willman JS. Selective effects of minor illnesses on human performance. Brit J Psychol., 1987; 78: 183-188. doi:101111/j2044-82951987tb02238x.
18. Smith AP, Tyrrell DAJ, Al-Nakib W, Coyle KB, Donovan CB, Higgins PG, Willman JS. Effects of experimentally-induced virus infections and illnesses on psychomotor performance. Neuropsychobiology, 1987; 18: 144–148. doi: 101159/000118408.
19. Smith AP, Tyrrell DAJ, Al-Nakib W, Coyle KB, Donovan CB, Higgins PG, Willman JS. The effects of experimentally-induced respiratory virus infections on performance. Psychol Med., 1988; 18: 65–71. doi: 101017/s0033291700001896.
20. Smith AP, Tyrrell DAJ, Coyle KB, Higgins PG. Effects of interferon-alpha on performance in man: A preliminary report. Psychopharmacology, 1988; 96: 414 – 416. doi: 101007/BF00216072.

21. Smith AP, Tyrrell DAJ, Al-Nakib W, Barrow GI, Higgins PG, Leekam S, Trickett S. Effects and after-effects of the common cold and influenza on human performance. Neuropsychobiology, 1989; 21: 90 – 93. doi: 101159/00011855.
22. Smith AP, Tyrrell DAJ, Barrow GI, Coyle KB, Higgins PG, Trickett S, Willman JS. The effects of experimentally induced colds on aspects of memory. Percept Mot Skills, 1990; 71: 1207 – 1215. doi: 102466/pms1990713f1207.
23. Smith AP, Tyrrell DAJ, Coyle KB, Higgins PG. Effects and after-effects of interferon-alpha on human performance, mood and physiological function. J Psychopharmacology, 1991; 5: 243 – 250. doi: 101177/026988119100500311.
24. Smith AP, Tyrrell DAJ, Al-Nakib W, Barrow GI, Higgins PG, Wenham R. The effects of zinc gluconate and nedocromil sodium on performance deficits produced by the common cold. J Psychopharmacol., 1991; 5: 251 – 254. doi: 101177/026988119100500312
25. Smith AP, Tyrrell DAJ, Barrow GI, Higgins PG, Willman JS, Bull S, Coyle KB, Trickett S. Mood and experimentally induced respiratory virus infections and illnesses. Psychol Health, 1992; 6: 205-212. doi: 101080/08870449208403184
26. Smith AP, Tyrrell DAJ, Barrow GI, Higgins PG, Bull S, Trickett S, Wilkins AJ. The Common Cold, pattern sensitivity and contrast sensitivity. Psychol Med., 1992; 22: 487-494. doi: 101017/S0033291700030427
27. Drake CL, Roehrs TA, Royer H, Koshorek G, Turner RB, Roth T. Effects of an experimentally induced rhinovirus cold on sleep, performance and daytime alertness. Physiol Behav., 2000; 71: 75-81. doi: 101016/S0031-9384(00)0322-x
28. Smith AP, Thomas M, Brockman P, Kent J, Nicholson KG. Effect of influenza B virus infection on human performance. Brit Med J., 1993; 306: 760-761. doi: 101136/bmj3066880760
29. Heazlett M, Whaley, RF. The common cold: its effect on perceptual ability and reading comprehension among pupils of a seventh-grade class. J School Health, 1976; 46: 145-7. doi: 101111/j1746-15611976tb02000x
30. Bucks RS, Gidron Y, Harris P, Teeling J, Wesnes KA, Perry VH. Selective effects of upper respiratory tract infection on cognition, mood and emotion processing: A prospective study. Brain Behav Immun., 2008; 22: 399-407. doi:101016/jbbi200709005
31. Hall SR, Smith AP. An investigation of the effects and after-effects of naturally-occurring upper respiratory tract illnesses on mood and performance. Physiol Behav., 1996; 59: 569-577. doi: 101016/0031-9384(95)021112-4.

32. Matthews G, Warm JS, Dember WN, Mizoguchi H, Smith AP. The common cold impairs visual attention, psychomotor performance and task engagement. Proceedings of the Human Factors and Ergonomics Society 45th Annual Meeting Santa Monica, CA: Human Factors and Ergonomics Society, 2001; 1377-1381.
33. Smith AP. Sleep and the common cold. Journal of Behavioral Health, 2012; 1: 114-117. doi: 105455/jbh20120322073850.
34. Smith AP. Behavioral effects of upper respiratory illnesses: A consideration of possible underlying cognitive mechanisms. Behavioral Sciences, 2012; 2: 38-49. doi: 103390/bs2010038
35. Smith AP. Effects of the common cold on mood, psychomotor performance, the encoding of new information, speed of working memory and semantic processing. Brain Behav Immun., 2012. doi: 101016/jbbi201206012.
36. Smith AP, Brice C, Leach A, Tiley M, Williamson S. Effects of upper respiratory tract illnesses in a working population. Ergonomics, 2004; 47: 363-369. doi: 101080/0014013032000157887.
37. Smith A, Rich N, Sturgess W, Brice C, Collison C, Bailey J, Wilson S, Nutt D. Effects of the common cold on subjective alertness, simple and choice reaction time and eye movements. J Psychophysiol., 1999; 13: 145-151. doi: 101027//0269-8803133145
38. Smith A, Thomas M, Kent J, Nicholson K. Effects of the common cold on mood and performance. Psychoneuroendocrinology, 1998; 23: 733-739. doi: 101016/s0306-4530(98)00042-0.
39. Smith AP, Thomas M, Whitney H. After-effects of common cold on mood and performance. Ergonomics, 2000; 43: 1342-1349. doi: 101080/001401300421789.
40. Smith AP. Effects of the Common Cold on Simulated Driving. In: Bust, PD (Ed), Contemporary Ergonomics, 2006; 621-624.
41. Smith AP, Jamson SL. An investigation of the effects of the common cold on simulated driving performance and detection of collisions. BMJ Open, 2012; 001047. doi: 101136/bmjopen-2012-001047.
42. Smith AP, Thomas M, Brockman P. Noise, respiratory virus infections and performance. Actes Inrets., 1993; 34: 311-314.
43. Smith AP, Thomas M, Perry K, Whitney H. Caffeine and the common cold. J Psychopharmacol., 1997; 11(4): 319-324. doi: 101177/02698819701100406.
44. Smith AP, Whitney H, Thomas M, Brockman P, Perry K. A comparison of the acute effects of a low dose of alcohol on mood and performance of healthy volunteers and

participants with upper respiratory tract illnesses. J Psychopharmacol., 1995; 9: 225-230. doi: 101177/026988119500900310.

45. Smith AP. Effects of upper respiratory tract illness and stress on alertness and reaction time. Psychoneuroendocrinology, 2013; 38: 2003-2009. http://dxdoiorg/101016/jpsyneuen201303012
46. Smith AP. Fatigue, susceptibility to the common cold and its behavioural effects. Medical Research Archives, 2020; 9(4): ISSN 2375-1924. doi: https://doiorg/1018103/mrav9i42390.
47. Smith AP, Nutt DJ. Effects of upper respiratory tract illnesses, ibuprofen and caffeine on reaction time and alertness. Psychopharmacology, 2014; 231: 1963-1974. doi: 101007/s00213-013-3339-7.
48. Smith AP, Sturges W, Rich R, Brice C, Collison C, Bailey J, Wilson S, Nutt DJ. Effects of idazoxan on reaction times, eye movements and mood of healthy volunteers and participants with upper respiratory tract illnesses. J Psychopharmacol., 1999; 13: 148-151. doi: 101177/026988119901300206.
49. Clark CR, Geffen GM, Geffen LB. Role of monoamine pathways in the control of attention: effects of droperidol and methylphenidate in normal adult humans. Psychopharmacology, 1986; 90: 28-34.
50. Clark CR, Geffen GM, Geffen LB. Catecholamines and the covert orientation of attention in humans. Neuropsychologia, 1989; 27(2): 131- 139.
51. Posner MI, Nissen MJ, Odgen WC. Attended and unattended processing modes: the role of set for spatial location. In Modes of Perceiving and Processing Information by Pick, H. L. and Salitman, E (eds.), 1978; 137- 157. Erlbaum, N. J.
52. Smith AP, Whitney H, Thomas M, Brockman P, Perry K. A comparison of the acute effects of a low dose of alcohol on mood and performance of healthy volunteers and participants with upper respiratory tract illness. Journal of Psychopharmacology, 1995; 9(3): 225-230.
53. Smith AP, Wilson SJ, Glue P, Nutt DJ. (1992). The effects and after-effects of the a2-adrenoceptor antagonist idazoxan on mood, memory and attention in normal volunteers. Journal of Psychopharmacology, 1992; 6(3): 376-381.